MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.11.518.524

Bioelectric Impedance Analyzer Derived Phase Angle in Indians in the Screening of Malnutrition: The Search for the Right Number

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ABSTRACT

20-60% of patients in Intensive Care Unit are at high nutritional risk in developed countries. Phase angle derived from Bio electrical impedance analyzer(BIA), is an indicator of cellular integrity and nutritional status. There are no Indian studies in intensive care unit that have studied phase angle and its relation to malnutrition screening and diagnosis. This observational study was performed at the Intensive Care Unit of a tertiary care hospital with 85 patients. The NRS-2002(Nutrition Risk Screening-2002), modified NUTRIC(Nutrition Risk in Critically ill), SGA (Subjective Global Assessment) scores were used in the screening for malnutrition in85 consecutive patients. A multi-frequency segmental BIA,(In Body S10®) device was used in the assessment of phase angle and body composition. To determine agreement between NUTRIC, NRS 2002 and SGA with phase angle, Cohen's statistic was calculated. SGA was significantly positively correlated with NRS and NUTRIC score whereas significantly negatively correlated with phase angle and serum albumin ($p<0.05$). ROC was conducted for phase angle, SMI and FFM in correlation to SGA for males and females. Only Phase angle was significantly correlating with malnutrition. In males a cut off of 4.4 and in females a cut-off of 3.25 signified malnutrition. There was a moderate agreement between NUTRIC and SGA and a fair agreement between NRS and SGA. The study results found that a phase angle derived 4.4 in males and 3.25 in females were cut offs that closely correlated to malnutrition in our group of patients. This is quite different to international literature where the cut-offs were 5 and 4.6 for males and females respectively. When current study cut-off for phase angle were used, a moderate agreement was observed between Phase angle and SGA (Cohen's $k= 0.573$, $p<0.001$) which seems to indicates that for the Indian population, a lower cut-off for phase angle would be more appropriate.

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Key Words

Malnutrition, bioelectrical impedance analyser, phase angle, NUTRIC score, SGA score, NRS score

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Received: 10 September 2024
Accepted: 07 November 2024
Published: 11 November 2024

Citation: Sanjith Saseedharan, Chandrima Pramanik, Dhanashree Lapalikar and Elizabeth Mathew, 2024. Bioelectric Impedance Analyzer Derived Phase Angle in Indians in the Screening of Malnutrition: The Search for the Right Number. Res. J. Med. Sci., 18: 518-524, doi: 10.36478/makrjms. 2024.11.518.524

INTRODUCTION

Hospitalized patients may be malnourished to begin with or are "at risk" for malnutrition with one Indian study demonstrating that two-fifth of the patients admitted to the intensive care unit(ICU) were malnourished[1,2]. Critically ill patients are at a higher risk for malnutrition due to prolonged hospital stay, decreased appetite, poor dietary intake, increased rate of catabolism induced by the diseased state, iatrogenic under feeding, gut dysfunction, disordered assimilation etc. This malnutrition may lead to complications like increased nosocomial infections, pressure ulcers, prolonged stay and many more adverse events including a reduction in quality of life[3]. There are currently very few large Indian studies that have extensively looked into malnutrition in the intensive care unit. Presently the nutritional assessment includes the use of modified NUTRIC score, NRS 2002 score and the SGA of which SGA has been recommended by Indian experts[4,5]. But some large hospitals in India have now started using the GLIM(Global Leadership Initiative on Malnutrition) criteria which includes weight loss, body mass index and reduced muscle mass. For the assessment of muscle mass the GLIM recommends the use of Dual Energy X-ray Absorptiometry(DEXA), Bio-electrical Impedance analysis (BIA), Ultrasonography, Computerized tomography (CT) or Magnetic resonance imaging (MRI)[6]. As an alternative, calf or arm circumference and physical examination findings may be used along with calibrated hand-grip strength which is correlated with muscle mass. BIA is a readily available technique that does not involve radiation. This measurement is also cost effective and can be easily employed bedside as compared to CT, DEXA scan or MRI[7-9]. Among the measured values derived from the BIA the phase angle, is regarded as a convenient and a reliable indicator of nutritional status[10-12]. There have been many studies from around the world in this regards and cutoffs have been established accordingly[13-15]. There is a clear lack of studies from Indian population that have studied the phase angle and its relation to nutritional status.

Aims and Objectives: To study the relationship between the various scores(i.e. NRS 2002,modified Nutric,SGA)with phase angle in order to find the cut off values for patients with malnutrition in patients admitted to intensive care.

MATERIALS AND METHODS

Study Design: This was a single centre, cross-sectional prospective observational study performed after ethics committee approval(ECR/70/Inst/MH/2013/RR-19).

Setting: This study was conducted at the Medical Intensive Care Unit of a tertiary care hospital in the city of Mumbai ,India from the month of December 2021 to May 2022.Patients were assessed on first day of ICU admission using the NUTRIC score, NRS 2002 score, SGA, serum albumin, body weight and Bioelectrical Impedance analysed (BIA).

Participants: The study population consisted of 85 patients admitted in Intensive Care Unit.

Inclusion Criteria:

- All patients >18 years of age admitted in Intensive Care Unit within 48 hours of transfer from home or other hospital.
- All gender.

Exclusion Criteria:

- Patients with amputated limbs.
- Patients suspected to have documented large sodium shifts(defined as more than or equal to 12 meq /litre in the last 24 hours.
- Patients with burns or skin damage on the areas where the electrodes are applied.
- Patients having a pacemaker or implanted cardiac defibrillator.
- Patients who have underwent haemodialysis in the last 6 hours before measurement.
- Patients having large pleural effusions,(visible on chest x-ray),noticeable edema, ascites and urinary retention.
- Pregnant patients.
- Patient who has received fluid resuscitation defined as >30ml/kg of fluids in the last 6 hours before the measurement.
- Patients having a BMI >34kg/m2 or <16kg/m2.
- Temperature >37.1 degree Celsius.
- Patients with abnormal physical structure.

Variables, Data Sources/Measurement, Quantitative Variables: On the first day of admission the nutritional assessment was done using NUTRIC score, NRS 2002 score and SGA. The albumin levels on admission were noted. All patients were weighed using the weighing scale of the Hillrom Versa Care bed. A multi-frequency Bioelectrical Impedance analyzer (BIA), was used for impedance measurements at 6 different frequencies (1, 5,50,250,500, 100 kHz) with the help of electrodes placed at different segments of the body(right arm, left arm, right leg and left leg). The impedance measurements were carried out on patients in supine position with their arms and legs abducted at an angle of 45 degrees to the body at an ambient temperature. The machine is capable of calculating the composition of the body- total body water with intracellular and extracellular water, body fat volume, fat free mass(FFM),skeletal muscle index(SMI) and phase angle which is measured at a frequency of 50 Hz and derived by the machine from the following equation-

phase angle (°)=(reactance/resistance) × (180 °/π).

Study Size: The study population consisted of 85 patients admitted in Intensive Care Unit.

Statistical Methods: Analyses were performed with the help of SPSS software for Windows (version 25, 2007, IBM Corporation, Armonk, New York, United States). Data were presented as frequency. Correlation of SGA categories with various parameters was observed using Spearman Rho co-relation. To determine the diagnostic agreement between the three screening tools (NUTRIC, NRS 2002 and SGA) with phase angle for malnutrition, Cohen's statistic was calculated. Cohen's Kappa (K) statistics of 0 indicated no agreement between 2 scales whereas 1 indicated complete agreement. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated. Receivers Operating Curve (ROC) was plotted and area under the curve (AUC) was calculated for phase angle, SMI and FFM against SGA categories. Cut-offs were identified using Youden's index. Data presented with 95% CI. P<0.05 was considered to be statistically significant.

RESULTS AND DISCUSSIONS

Descriptive Data: From 85 participants, 44 (51.8%) were males and 41 (48.2%) were females. Based on SGA, 33 (38.8%) were well nourished, 31 (36.5%) were moderately malnourished and 21 (24.7%) were severely malnourished.

Outcome Data: Well-nourished participants were significantly younger in age as compared to malnourished participants (p<0.05). There was no significant difference in weight, BMI, skeletal muscle and fat free mass of 3 groups (p>0.05). Increase in NRS score correlated with increase in SGA score (p<0.05) and increase in SGA score correlated significantly with decrease in phase angle (p<0.05). Patients with lower NRS and NUTRIC score had high albumin value, however there was no significant relationship found between moderately malnourished and severely malnourished participants (p>0.05). Higher percentage of females were in well nourished group as compared to moderately malnourished or severely malnourished group, however, this difference was not significant (p>0.05). (As shown in Table 1). Data presented as Mean±SD a Significant difference between well-nourished and moderately malnourished, b Significantly difference between well-nourished and severely malnourished, c Significant difference between moderately malnourished and severely malnourished.

Correlation of SGA with Other Variables: SGA was significantly positively correlated with NRS score, NUTRIC score (p<0.05). On the other hand, SGA was significantly negatively correlated with phase angle and serum albumin (p<0.05). (As shown in Table 2). Increase in NRS, NUTRIC and SGA scores significantly correlate with decrease in phase angle (p value<0.001) (as shown in Table 3). ROC was conducted for phase angle, SMI and FFM to identify a cut-off for identifying malnutrition as identified by SGA separately males and females. Only Phase angle was significantly affecting malnutrition based on current study results (p<0.05). In males a cut off of 4.4 and in females a cut-off of 3.25 was identified with help of Youden's Index. (Fig. 1 and Fig. 2).

Males:

- **Phase Angle:** AUC =0.883, 95% CI =0.770-0.995, p=0.001
- **SMI:** AUC =0.518, 95% CI = 0.343-0.694, p=0.854
- **FFM:** AUC =0.556, 95% CI=0.367-0.745, p=0.571
- **Cut off**: 4.4.

Females:

- **Phase Angle:** AUC=0.619, 95% CI = 0.437-0.802, p=0.001
- **SMI:** AUC = 0.595, 95% CI = 0.415-0.776, p=0.297
- **FFM:** AUC = 0.556, 95% CI=0.386-0.745, p=0.473
- **Cut-off:** 3.25

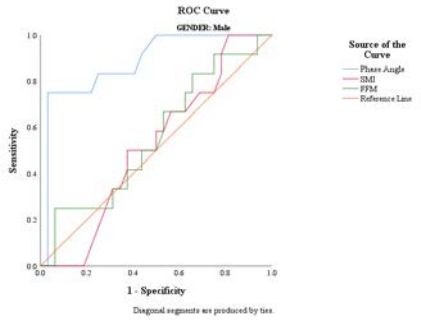

Fig. 1: ROC for Identifying Malnutrition Cut-Offs in Males

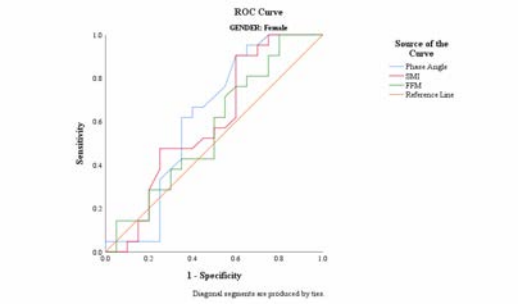

Fig. 2: ROC for Identifying Malnutrition Cut-Offs in Females

Identification of Malnutrition: NRS detected malnutrition in least number of patients whereas

Table 1: NRS, NUTRIC Score, BIA and Anthropometry when Classified According to SGA Categories

	SGA classification			
	Well nourished (n=33)	Moderately malnourished (n=31)	Severely Malnourished (n=21)	P-value
	Mean±SD	Mean±SD	Mean±SD	
Age (years)	55.5±18.4	71.7±12.5[a]	73±11.4[b]	0.001
Height (cm)	160±8.6	161.3±9.3	160±8.7	---
Weight (kg)	66.4±17.1	64.7±12.6	62.3±17.4	0.647
BMI (kg/m2)	26±6.7	24.9±4.1	24.3±6.8	0.562
NRS score	0.8±0.8	1.3±1.1[a]	2.6±0.7[b c]	0.001
NUTRIC score	2.2±1.9	4.3±2.2[a]	5.5±.4[b]	0.001
Phase angle	4.5±1.2	3.7±1.3[a]	2.9±0.7[b c]	0.001
Skeletal Mass Index	6.5±1.2	7.1±6	6±1.9	0.066
Fat free mass	42.1±8.4	43±10.9	41.1±9.8	0.795
Serum albumin	3.4±0.2	3.0±0.5[a]	3.0±0.5[b]	0.001
	Freq (%)	Freq (%)	Freq (%)	
Gender				
Males	12 (36.4%)	19 (61.3%)	13 (61.9%)	0.077
Females	21 (63.6%)	12 (38.7%)	8 (38.1%)	

Table 2: Correlation of SGA with Various Parameters

	Spearman Rho Value	P-value
BMI	-0.133	0.302
NRS score	0.685	0.001
NUTRIC score	0.613	0.001
Phase angle	-0.541	0.001
Skeletal Mass Index	-0.120	0.275
Fat free mass	-0.032	0.771
Serum albumin	-0.443	0.001

Table 3: Correlation of Phase Angle with NRS, NUTRIC and SGA Score

	Spearman Rho value	P-value
NRS score	-0.371	<0.001
NUTRIC score	-0.521	<0.001
SGA score	-0.541	0.001

Table 4: Malnutrition Identified with Help of Various Cut-offs and Scores

	Well nourished	Malnourished
SGA	38.8%	61.2%
NUTRIC(5 or more in both males and females)	58.8%	412%
NRS(6 or more in both males and females)	78.8%	21.2%
Phase angle (Previous study cut-off for males<5 degrees, females <4.6 degrees)	23.5%	76.5%
Phase angle (current study cut-off for males <4.4, females <3.25)	48.5%	51.8%

Table 5: Agreement of Various Scores with SGA

	NUTRIC		NRS 2002		Phase angle (Previous study cut-off for males<5 degrees, females <4.6 degrees)		Phase angle (current study cut-off)	
SGA	Low risk	medium/high risk	low risk	medium/high risk	low risk	medium/high risk	low risk	medium/high risk
well nourished	29	4	33	0	14	19	28	5
malnutrition	21	31	34	18	6	46	13	39
	%	95%CI	%	95%CI		%	95%CI	
sensitivity	88.57	73.26-96.80	100	81.47-100	70.77	58.17-81.40	88.64	75.44-96.21
Specificity	58	43.21-49.25	71.81	36.82-61.76	70.00	45.72-88.1	68.29	51.91-81.92
Positive Predictive value	59.62	51.07-34.62	67.62	29.49-40.13	88.46	79.40-93.84	75.00	65.41-82.64
Negative Predictive value	87.88	73.67-100	94.95	-----	42.42	3143-54.52	84.85	70.51-92.92
Accuracy	70.59	59.71- 60	79.98	48.8-70.48	70.59	59.71-793.98	78.82	68.61-86.94
Cohen's Kappa (K)	0.434	0.262-0.291	0.552	0.132-0.390	0.333	0.133-0.533	0.573	0.401-0.745
P Value for kappa	0.001		0.001	0.001			0.001	

phase angle (previous study cut-off) identified highest number of malnourished patients (shown in table 4). (Table 5) presents cross tabulation of classification of malnutrition based on SGA v/s NUTRIC, NRS 2002 and phase angle. 31 cases were identified as malnourished by SGA and NUTRIC score, 18 cases were identified as malnourished by SGA and NRS 2002, 46 cases were classified as malnourished by SGA and phase angle (based on previous study cut-off) whereas 39 cases were identified as malnourished by SGA and phase angle cut-offs as identified in current study. NUTRIC score had phase angle cut-off identified in current study had the best sensitivity to identify malnourishment. Phase angle cut-off identified in the current study had the highest accuracy to identify malnourishment in comparison to SGA. There was a moderate agreement between NUTRIC and SGA (Cohen's K=0.434, p<0.001) and a fair agreement between NRS and SGA (Cohen's k=0.291, p<0.001). When malnourished was analysed using previous study cut-off for phase angle, a fair agreement was observed between SGA and phase angle (Cohen's K=0.333,

p<0.001). When current study cut-off were used, a moderate agreement was observed between Phase angle and SGA (Cohen's K=0.573, p<0.001) (shown in Table 5). This indicates that probably for Indian scenario, a lower cut-off for phase angle is applicable. Bioelectrical impedance has been increasingly used in the ICU for outcome prediction, study fluid status and in the management of nutrition. BIA is an objective, simple, quick (takes 2-5mins), non-invasive, painless technique which gives an estimate of the various compartments of the body including total body water, fat mass, fat free mass, skeletal muscle mass and phase angle without any exposure to radiation[14]. Unlike conventional BIA machines, new generation multifrequency machines measure impedance directly from each segment of the body assuming the entire human body as a five-compartment model and has been found to be 98% as accurate as DEXA Scan[16]. The electrical impedance measured consists of two components-Reactance and Resistance. Total body water and body fat offer resistance to the electrical current whereas cell membranes and tissue interfaces act as capacitors contributing to the reactance component. Reactance, resistance, impedance and phase angle, are often referred to as '"raw'" BIA parameters which are measured and thus not "derived" from controls or from calculations (for eg:fat mass, fat free mass, appendicular skeletal muscle mass etc).Phase angle is defined as the ratio of resistance (sum total of intracellular and extracellular resistance) to reactance and reflects cell membrane integrity and thus body cell mass. Thus, a higher phase angle is consistent with a large body cell mass (BCM) relative to Extra cellular water. A drop in the body cell mass indicates malnutrition. BCM is not affected by hydration status thus theoretically making it more reliable in critically ill patients[17,18]. Normal values of phase angle ranges between 4-6 degrees. Maria C.G. Barbosa- Silva et al in their study found that in healthy individuals, phase angle was larger in males than females (7.48±1.10 degrees in males and 6.53±1.01 degrees in females) and showed positive correlation with BMI and negative correlation with fat percentage of patients. They also found out that phase angle varied with difference in race- 6.82±1.13 degrees in whites, 7.21±1.19 in African Americans, 7.33±1.13 in Hispanics, indicating that phase angle varies with ethnicity[19]. Another study among hospitalized patients by Ursula G Kyle *et al.* found the cut-off of 5 degrees in males and 4.6 degrees in females to have the highest sensitivity for predicting nutritional risk in patients[20]. Yoojin Lee and co-workers from Korea studied the role of BIA in evaluating nutritional status and predicting clinical outcomes in 69 critically ill patients .The results of their study that revealed that the phase angle decreased to 4.1 degrees in moderate malnutrition and to 3.1 degrees in severe malnutrition[21]. In another similar study done by Razzera *et al.* in a group 89 patients admitted to the ICU ,a phase angle less than 5.58 showed an accuracy of 79% in identifying patients at high nutrition risk (NUTRIC score >5)[22]. The current study used NRS, SGA, NUTRIC and phase angle as analysed BIA to identify malnutrition and study the correlation between the values in intensive care patients. Firstly there was a strong positive correlation of SGA with both the NRS 2002 and the NUTRIC score. A consistent inverse relationship between NUTRIC score, NRS 2002 and SGA with the phase angle was seen. Our study identified a cut off of 4.4 (AUC=0.883, 95% CI =0.770-0.995, p=0.001)and in females a cut-off of 3.25 (AUC=0.619, 95% CI=0.437-0.802, p=0.001).These findings are very similar to that of Yoojin lee and co-workers however much lower to that shown by Razzera and co-workers[21,22]. In our study the Skeletal mass index (SMI) and Fat free mass (FFM) did not show any corelation to malnutrition and hence, in our opinion, cannot be used in the diagnosis of malnutrition. There has been a dearth of research to date that has examined the role of BIA in the clinical care of critically ill patients and thus our study adds a lot of value to the existing sparse literature in this subject. However our study has some limitations as it is a single centre study comprising of a small sample size of 85 patients due to which we were unable to classify subjects according to disease status. We also excluded patients with chronic kidney disease, amputated limbs, pacemaker, burns and pregnancy limiting generalizability across the ICU. No recommendations can be made regarding the validity of using BIA in this scenario as the evidence in this regards is weak. Nevertheless the data that is presented can be a good starting point for further studies in India. Due to the proprietary nature of manufacturer-specific BIA regression models to procure body composition data the data used in this study may be valid only with the specific type of device used in this study. Since this is a specific group of patients admitted to the intensive care unit ,the use of the derived data might not be applicable to other group of patients or the general population.

CONCLUSION

The results suggest that the NRS 2002 score, the NUTRIC score, SGA and phase angle derived from Bioelectric impedance analyzer identify patients with impaired nutritional status. Using lower-cut-off than

the standard cut-off for phase angle shows better agreement with SGA in identifying malnutrition in Indian patients demonstrating a potential utility of BIA in critically ill patients.

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