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Background & aims This study determined the association between phase angle (PhA), by bioelectrical impedance analysis (BIA) and nutritional risk by Nutritional Risk Screening (NRS-2002), Subjective Global Assessment (SGA), hospital length of stay (LOS) and 30 day non-survival in patients at hospital admission compared to healthy controls. Methods PhA was determined by BIA in patients (n = 983, 52.7 ± 21.5 yrs, M 520) and compared to healthy age-, sex- and height-matched controls. Low PhA was set at

Reference


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Low phase angle determined by bioelectrical impedance analysis is associated with malnutrition and nutritional risk at hospital admission

Ursula G. Kyle, Laurence Genton, Claude Pichard

Abstract

Background & aims: This study determined the association between phase angle (PhA), by bioelectrical impedance analysis (BIA), and nutritional risk by Nutritional Risk Screening (NRS-2002), Subjective Global Assessment (SGA), hospital length of stay (LOS) and 30 day non-survival in patients at hospital admission compared to healthy controls.

Methods: PhA was determined by BIA in patients (n=983; 52.7±21.5 yrs) and compared to healthy age-, sex- and height-matched controls. Low PhA was set at <5.0º (men) and <4.6º (women) as previously determined (Kyle, in press).

Results: PhA was lower in patients (men 6.0±1.4º, women 5.0±1.3º) than controls (men 7.1±1.2º, women 6.0±1.2º, un-paired t-test p<0.001). Patients were more likely to have low PhA than controls: NRS-2002: no risk (relative risk (RR) 1.7, 95th confidence interval (CI) 1.2–2.3), moderate risk (RR 4.5, CI 3.4–5.8) and severe risk (RR 7.5, CI 5.9–9.4); similar results were obtained by SGA; LOS ≥21 days (RR 6.9, CI 5.1–9.1) and LOS 5–20 days (RR 5.2, CI 3.9–6.9) and non-survivors (RR 3.1, CI 2.1–3.4) compared to survivors.

Conclusions: There is a significant association between low PhA and nutritional risk, LOS and non-survival. PhA is helpful to identify patients who are at nutritional risk at hospital admission in order to limit the number of in-depth nutritional assessments.

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This storage of the current creates a phase shift that can be regarded as the ratio of resistance and reactance and is expressed geometrically as phase angle (PhA). To avoid problems of disturbances in fluid distribution in subjects with abnormal hydration, several studies suggested the use of raw BIA measurements such as resistance, reactance and PhA. Of all the direct measurements of BIA, PhA has been shown to be predictive for prognosis and mortality in hemodialysis, cancer, human immunodeficiency virus syndrome, liver disease and geriatric. 

The use of PhA is of interest because it is a non-invasive, objective, quick (less than 2 min) method to determine nutritional and morbidity risk in patients. While nutritional screening tools are also non-invasive, they require more time and are subjective. For the purpose of this study, low PhA was defined as \(<5.0^\circ\) in men and \(<4.6^\circ\) in woman, as determined in a previous study.  

The purpose of this study was to determine if there is a significant association between PhA and nutritional risk, determined by subjective. For the purpose of this study, low PhA was defined as \(<5.0^\circ\) in men and \(<4.6^\circ\) in woman, as determined in a previous study. 

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1. Methods

1.1. Patients

All adult patients admitted to the hospital admission center for medical or surgical reasons and subsequently hospitalized were eligible for inclusion. Every 10th patient older than 17 yrs who met entry criteria was included in the study during a 3-month period (n = 983). Two patients refused to participate. Exclusion criteria were visible edema, burns, peritoneal- or hemodialysis, rehydration perfusion and major cardiac-respiratory resuscitation (5.8%, n = 61). Age and gender distribution of patients included in the study did not differ from age of all patients seen in the hospital admission center during the inclusion period. Patients were evaluated in the hospital admission center by the same two trained coworkers of the Nutrition Unit. LOS data was obtained from the computerized patient hospital record after the patients were discharged.

Patients were categorized as Medical, Surgical, Trauma or Cancer patients, based on hospital service to which they were admitted. Patients were also categorized as acute or chronic illness: Acute illness was defined as a recent occurrence with an onset of 1–7 days prior to hospital admission (e.g. broken leg, heart attack, pneumonia, stroke); Chronic illness corresponded to a disease state which included one or more pathologies lasting for more than seven days and necessitating continuous medical treatment (e.g. cancer, AIDS, arthritis, Crohn's disease). Patients with both acute and chronic diseases were assigned to the chronic disease category.

The study protocol was approved by the Geneva University Hospital Ethics Committee and informed consent was obtained from all subjects.

1.2. Controls

Healthy adults (n = 983), matched for gender, age (±2 yrs) and height (±2 cm), were selected from our database (n = 5635 healthy adults, age 17–98 years) to serve as control group. 

1.3. Measurements

1.3.1. Anthropometric and bioelectrical impedance analysis measurements

All measurements were performed at hospital admission. Body height was measured to the nearest 0.5 cm and body weight to the nearest 0.1 kg on a chair scale or a hoist with attached weighing device for patients who were bed-ridden. The scales were cross-calibrated weekly. The body mass index (BMI) was derived as weight (kg) divided by height (m) squared (kg/m²).

PhA was determined by BIA as previously described. Whole-body resistance and reactance were measured with four surface electrodes placed on the right wrist and ankle. The PhA was calculated as follows:

\[ \text{PhA} = \arctan \left( \frac{\text{reactance}}{\text{resistance}} \right) \]

Normal phase angle was defined as \(\geq5.0^\circ\) for men and \(\geq4.6^\circ\) in women and low PhA was \(<5.0^\circ\) in men and \(<4.6^\circ\) in woman, as determined in a previous study. Briefly, an electrical current of 50 kHz and 0.8 mA was produced by a generator (RJL-101 generator, RJL Systems Inc, Clinton Twp, MI) and applied to the skin by use of adhesive electrodes (3M Red Dot T, 3M Health Care, Borken, Germany) with the subject lying supine. The skin was cleaned with 70% alcohol. RJL-101 generator (RJL Systems Inc, Clinton Twp, MI) was cross-validated at 50 kHz against the Xitron analyzer (Xitron Technologies, Inc, San Diego, CA). Previous studies have established the validity of BIA. FFM was calculated by the following previously validated multiple regression equation:

\[ \text{FFM} = -4.104 + (0.518 \times \text{height}^2/\text{resistance}) + (0.231 \times \text{weight}) + (0.130 \times \text{reactance}) + (4.229 \times \text{sex} (\text{men} = 1, \text{women} = 0)) \]

1.3.2. Nutritional Risk Screening (NRS-2002)

The NRS-2002 is a previously validated nutritional risk assessment score. It consists of a nutritional score and a severity of disease score and an age-adjustment for patients aged >70 yrs (+1). Nutritional score: Weight loss \(<5\%\) in 3 months or food intake below 50–75% in preceding week = 1; Weight loss \(<5\%\) in 2 months or BMI 18.5–20.5 kg/m² and impaired general condition or food intake 25–60% in preceding week = 2; weight loss \(<5\%\) in 1 month or \(>15\%\) in 3 months or BMI \(<18.5\) kg/m² and impaired general condition or food intake \(0–25\%\) in preceding week = 3. Severity of disease score: Hip fracture, chronic patients with acute complications = 1; major abdominal surgery, stroke, severe pneumonia, hematological malignancies = 2; head injury, bone marrow transplantation, intensive care patients with APACHE \(>10 = 3\). NRS score is the total of the nutritional score, severity of disease score and age adjustment. Patients are classified no risk = 0; low risk = 0–1; medium risk = 3–4; and high risk = 5.

1.3.3. Subjective Global Assessment questionnaire (SGA)

SGA is a nutritional assessment score that was performed as previously described. It includes the patient's history (weight loss, changes in dietary intake, gastrointestinal symptoms, and functional capacity), a physical examination (muscle, subcutaneous fat, sacral and ankle edema, ascites), and the clinician's overall judgment of the patient's status (normal, moderately or severely malnourished). Patients are classified well nourished = 1; moderately malnourished = 2; severely malnourished = 3; Controls = 0.

1.3.4. Albumin

Blood samples were routinely drawn at the same time as the samples necessary for diagnosis and treatment, before initiation of IV fluids. Albumin was measured by immunonephelometry. Serum albumin values <35 g/L were considered an indicator of nutritional risk.

1.4. Statistical analysis

The results are expressed as mean ± standard deviation (x ± SD). Normally distributed continuous variables were compared using paired and un-paired t-test and ANOVA. Non-normally distributed variables were compared by Mann–Whitney U-test or Kruskal–Wallis test. Chi-square tests were used to compare the differences in prevalence of nutritional risk. Relative risk (RR), with
95% confidence intervals (CIs) was calculated by Fisher Exact Test for a $2 \times 2$ contingency table (http://statpages.org/ctab2x2.html). Relative Risk (RR) = $(a/r1)/(c/r2)$; confidence intervals for the estimated parameters are computed by a general method (based on "constant chi-square boundaries").

Statistical significance was set at $p \leq 0.05$ for all tests.

2. Results

Of the patients evaluated at hospital admission, 57% were medical, 25% surgical, 12% trauma and 5% cancer patients (Table 1).

Weight, BMI, fat-free mass and PhA were significantly lower and % body fat mass significantly higher in male and female patients than controls (Table 2). Weight, BMI, fat-free mass and PhA were significantly lower in female than male patients and controls (Table 2).

Patients with low PhA had significantly lower fat-free mass and significantly higher % body fat than patients with normal PhA (Table 3). Patients with low PhA also had lower albumin level than patients with normal PhA (Table 3). PhA decreased with age in patients and controls, as previously reported.28

Patients with no, moderate and severe nutritional risk had lower PhA than controls and PhA was lower with each increasing nutritional risk category (Fig. 1).

Patients classified as at moderate nutritional risk by NRS-2002 were 4.5 and patients at severe nutritional risk were 7.5 times more likely to have low PhA than controls (Table 4). A similar relative risk for low PhA was also associated with SGA (Table 4). Patients with chronic illness were 5.6 times more likely and patients with acute illness were 1.6 times more likely to have low PhA compared to healthy controls. Medical, surgical and cancer, but not trauma, patients were more likely to have low PhA than controls. Low PhA was associated with LOS, with patients being hospitalized $\leq$5 days having 3 times, patients hospitalized 5–20 days 5 times and patients hospitalized $\geq$21 days having 7 times the risk of having low PhA. Non-survivors were 3 times more likely to have low PhA (Table 4). A proportion of patients with moderately and low PhA (Table 4). A proportion of patients with moderately and severely low PhA (Table 4). A proportion of patients with moderately and severely low PhA (Table 4).

3. Discussion

Our study found that patients at moderate and severe nutritional risk by NRS-2002 and SGA were more likely to have low PhA compared to healthy controls. Non-survivors were also more likely to have low PhA compared to healthy controls. The clinical significance of these results is important, in view of the fact that patients were evaluated by BIA on admission to the emergency room, and thus low PhA was preexisting to hospital stay and not the result of hospital acquired malnutrition. In addition, all patients, except trauma patients, were also more likely to have low PhA compared to controls. LOS and non-survival were also associated with low PhA. Patients and controls that were classified as low PhA had lower FFM and higher % BF than patients and controls with normal PhA. Thus nutritional risk as well as clinical diagnosis and outcome were associated with low PhA.

Low PhA was defined as $<5.0^\circ$ in men and $<4.6^\circ$ in women, as determined in a previous study.28 PhA was lower in patients than controls, and in men than in women. The cut-off values in our study of 5.0 and 4.6$^\circ$ in men and women, respectively, fall below the 5th percentile of reference values for a German population published by Bösy-Westphal et al.22 These authors noted that because an age-dependent decline in reactance values in addition to quantitative changes (a decline in body mass) was observed after adjustment for height and body circumference, the electrical properties of tissue, i.e. PhA, may be altered with age, body composition and disease.

PhA was evaluated against nutritional screening tools, i.e. NRS-2002 and SGA. The SGA has been shown to identify patients with risk of nutritional complications and who would potentially benefit from nutritional therapy.27 Increased nutritional risk and alteration in body composition are common in ill subjects and their influence on mortality has been shown in various studies.28 Several studies25,39,40 have demonstrated the association between PhA and markers of nutritional risk. In previous studies,41 serum albumin was significantly associated with PhA (0.872) in liver transplant patients. Norman et al.42 found that standardized PhA is an independent predictor for nutrition, functional status and survival. Furthermore, PhA has been shown to be a sensitive tool to evaluate the effectiveness of nutritional intervention.29 PhA became similar to controls in anorexia nervosa patients after 15 weeks of nutritional therapy even though BMI was still below normal values.43

PhA has been shown to decrease with increased nutritional risk.23,44,45 Low PhA (i.e. reduced reactance and maintained resistance) indicates comparable hydration and a loss of cell mass in
malnutrition. Marra et al. found differences in PhA between different types of underweight that were not due to organic diseases. They found that low body weight in anorexia nervosa caused a decrease in PhA which the authors thought to due to an increase in extracellular water and/or decrease in body cell mass. On the other hand, constitutionally lean subjects who had similar BMI to anorexia patients had PhA similar to controls and lean ballet dancer had higher PhA which suggests higher skeletal mass and BCM. Thus, PhA appears to be able to distinguish between different forms of low body weight.

The cut-offs have been shown to be variable in the different studies. Previous ranges of normal PhA in healthy subjects ranged from 4.4 to 10.4 from 4.4 to 10.4. PhA <4.5 has been associated with shorter survival in liver cirrhosis, advanced lung cancer, and amyotrophic lateral sclerosis and increased hospital mortality in

![Fig. 1. PhA in controls and patients by NRS-2002 (top), SGA (middle) and albumin category (bottom). Unpaired t-test between controls and patient nutritional risk categories; and between male or female controls and patients; albumin: between albumin <35 (men n = 275; women n = 274) and >35 g/L (men n = 58; women n = 39), all p < 0.001.

### Table 3
Characteristics of controls (n = 983) and patients (n = 983) with normal and low PhA.

<table>
<thead>
<tr>
<th>Controls (n)</th>
<th>Normal PhA</th>
<th>Low PhA</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>47.8 ± 18.4</td>
<td>78.5 ± 13.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.9 ± 10.2</td>
<td>74.9 ± 10.2</td>
<td>0.912</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.8 ± 2.8</td>
<td>25.9 ± 3.4</td>
<td>0.035</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>58.8 ± 6.3</td>
<td>54.4 ± 7.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>20.8 ± 5.4</td>
<td>27.2 ± 4.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Phase angle (°)</td>
<td>7.3 ± 1.1</td>
<td>4.4 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patients (n)</td>
<td>403</td>
<td>117</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>43.4 ± 16.4⁣</td>
<td>71.7 ± 13.7⁣</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.6 ± 12.5</td>
<td>69.2 ± 13.7⁣</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.4 ± 3.8</td>
<td>24.0 ± 4.1⁣</td>
<td>0.3</td>
</tr>
<tr>
<td>Albumin (g/L)⁣</td>
<td>43.7 ± 5.5</td>
<td>35.9 ± 5.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>56.4 ± 6.8⁣</td>
<td>49.9 ± 7.8⁣</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>22.5 ± 6.5⁣</td>
<td>27.0 ± 7.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Phase angle (°)</td>
<td>6.6 ± 0.9</td>
<td>3.9 ± 0.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*BMI, body mass index; mean ± SD.

a Unpaired t-test between normal and low PhA in controls and patients.
b Unpaired t-test between male or female controls and patients with normal or low PhA p < 0.01.
c Unpaired t-test between male and female controls or patients with normal or low PhA p < 0.01.
d Patients only, normal/low PhA: men n = 242/91, women n = 186/127.

### Table 4
Relative risk for low PhA versus nutritional assessment by SGA, NRS-2002, LOS and non-survival in patients compared to healthy control subjects.

<table>
<thead>
<tr>
<th>Controls</th>
<th>Normal PhA</th>
<th>Low PhA</th>
<th>Relative risk (95% CI) n % (% of)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRS-2002</td>
<td>91.9 (903)</td>
<td>8.1 (80)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>SGA</td>
<td>86.4 (334)</td>
<td>11.6 (44)</td>
<td>1.4 (1.0–2.1) 0.046</td>
</tr>
<tr>
<td>Albumin</td>
<td>69.4 (261)</td>
<td>30.6 (115)</td>
<td>3.8 (2.9–4.9) 0.001</td>
</tr>
<tr>
<td>Acute</td>
<td>87.2 (410)</td>
<td>12.8 (60)</td>
<td>1.6 (1.1–2.2) 0.008</td>
</tr>
<tr>
<td>Chronic</td>
<td>54.6 (280)</td>
<td>45.4 (233)</td>
<td>5.6 (4.4–7.1) 0.001</td>
</tr>
<tr>
<td>LOS</td>
<td>75.7 (527)</td>
<td>24.3 (169)</td>
<td>3.0 (2.3–3.9) 0.001</td>
</tr>
<tr>
<td>5–20 days</td>
<td>56.8 (100)</td>
<td>43.2 (74)</td>
<td>1.5 (1.2–1.9) 0.001</td>
</tr>
<tr>
<td>21 days</td>
<td>43.5 (30)</td>
<td>56.5 (39)</td>
<td>1.9 (1.5–2.3) 0.001</td>
</tr>
</tbody>
</table>

NRS, Nutritional Risk Screening-2002; SGA, Subjective Global Assessment; LOS, length of hospital stay; Normal PhA: ≥5.0 in men and ≥4.6 in women; low PhA <5.0 in men and <4.6 in women.
geriatric patients. These studies suggest that low PhA is associated with low body weight and poor outcome.

3.1. Phase angle as a measure of nutritional risk

The use of raw data from BIA has gained popularity in nutritional risk assessment. PhA is a direct measure of BIA and therefore not influenced by assumptions that can affect body composition measurements. The advantage of the use of pure electrical properties of tissue without equations means that the main assumption of a consistent hydration is not required. It can be directly calculated from resistance and reactance as the arc-tangent (reactance/resistance × 180°/π). Therefore the PhA is, on the one hand, dependent on the capacitance behavior of tissues (reactance) and is associated with cellularity, cell size and integrity of the cell membrane and, on the other hand, on its pure resistive behavior (resistance), which is dependent on lean tissue mass and tissue hydration. BIA vector which is determined by PhA, correlated with muscle function. This supports the idea that PhA is a measure of cell mass, nutritional risk and general health.

A proportion of patients with moderately and severely nutritional risk by NRS–2002 (53%) and SGA (59%) were classified as normal PhA. Thus, not all patients who were classified as at nutritional risk had low PhA. It is possible that the pathophysiology of disease may differ with respect to the effects on cell mass, cell membrane integrity and cellular hydration. Therefore, the prognostic value of PhA may also differ between groups of patients with different clinical conditions. Bosy-Westphal et al. suggested that there might be a close correlation between low PhA and, for instance, liver disease, whereas there might be no differences in PhA between patients with metabolic syndrome and healthy controls. This suggests that low PhA in combination with patient diagnosis, anthropometric or physical condition might improve the diagnostic predictive value of PhA in clinical practice. Future studies should further explore the factors that distinguish patients who are at nutritional risk with normal and low PhA.

Although controls and patients >50 yrs in our study had significantly lower PhA than younger subjects, the older controls did not have a significantly higher incidence of having low PhA. Previous studies have proposed age- and sex-specific percentile cut-offs for PhA, which have been shown to be clinically useful in cancer patients. We did not adjust the PhA cut-offs for age because there was no increase in the prevalence of low PhA in controls >50 yrs, compared to younger controls, and age was similar between controls and patients with normal and low PhA. The higher incidence of low PhA in patients >50 yrs may reflect a decrease in functional ability that occurs with illness and age. Further research should determine the effects of age on PhA in patients and controls >65 yrs.

3.2. Study limitations

Limitations of this study are the heterogeneity of the patient populations. However, they reflected our general hospital population on admission. Our PhA values have been previously shown to be 10.5% lower in men and 7.7% in women compared to studies in the American population. The explanation of the discrepancy between different populations which were all cross-validated for body composition measurements.

A further limitation of this study was that BIA measurements were performed not entirely under standardized conditions because body composition was measured immediately after hospital admission and therefore was unplanned. However, none of the patients had visible edema. Food intake prior to BIA measurement is unknown. All patients were measured by the same analyzer. Multiple instruments were used to measure the controls subjects but which were all cross-validated for body composition measurements.

4. Conclusions

Patients had significantly lower PhA than age-, sex- and height-matched healthy controls. There is a significant association between low PhA and nutritional risk and low PhA and LOS and 30 day non-survival. Thus PhA is helpful to identify patients who are at nutritional risk at hospital admission in order to limit the number of in-depth nutritional assessments.

Conflict of interest/source of funding

There is no conflict of interest or association with pharmaceutical/biotechnology companies or other associations of any of the authors. Nutrition 2000Plus is a private Foundation to promote “Good Nutrition” and fund nutrition research and publish research results, train physicians in nutrition, and organize seminars on topics of nutrition. C. Pichard (senior author) is the President of the Foundation.

Statement of authorship

Each author has participated sufficiently, intellectually and practically, in the work to take public responsibility for the content of this article, including the conception, design and conduction of the study and for the interpretation (authorship). UK conceived and carried out the study, carried out the data analyses and drafted the manuscript. LG participated in the design of the study, contributed to the data analysis and drafting of the manuscript. CP participated in the design of the study, the data analysis, and drafting of the manuscript. All authors read and approved the final manuscript.

Acknowledgments

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