



# Risk assessment and nutritional prognosis of clinical outcome in critically ill patients

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# ABSTRACT

Introduction: Nutrition assessment of critically ill patients is challenging but it should be part of the clinical nutrition routine in the hospital setting. Objective: To assess the nutritional risk and prognosis of patients admitted to the intensive care unit (ICU) of a University Hospital in Natal, Brazil. Methods: Cross-sectional study developed with adult and elderly patients between February 2017 and February 2020. The nutritional risk was detected by the modified Nutrition Risk in Critically Ill score (mNUTRICscore). The nutritional prognosis was assessed using the phase angle (PA), calculated from the resistance and reactance values provided by bioimpedance. Mann-Whitney test was used to verify the association of mNUTRIC-score and PA with the outcome (hospital discharge or death). Spearman's correlation coefficient was used to verify the correlation between mNUTRIC-score and PA. Results: A total of 55 patients were included in this study. The average value of the NUTRIC score and PA was 3.13  $\pm$ 2.35 and 4.19 ± 1.21, respectively. Most patients had low nutritional risk. Among them, 81.8% were discharged and 18.2% died. Both mNUTRIC-score (p≤0.0001) and PA (p=0.04) were associated with the clinical outcome. These two parameters were negatively correlated (r=-0.3804; p=0.0059). Conclusion: Most of the patients had a low nutritional risk determined by the mNUTRIC-score. Those with high nutritional risk had a worse outcome (death). A negative correlation was observed between the mNUTRIC score and the PA, showing that the higher the nutritional risk, the worse prognosis was found in critically ill patients.

Keywords: Intensive Care Units; nutritional status; nutrition assessment; prognosis.

## **INTRODUCTION**

Patients in Intensive Care Units (ICU) are in intensive care due to their critical condition. These patients have catabolic stress, an inflammatory state, organ dysfunction, and functional impairment, with worse outcomes related to factors such as severity, complications, and prolonged hospitalization<sup>1,2</sup>. Malnutrition is common in this population and contributes to a worse clinical prognosis<sup>3</sup>. In this context, nutritional screening and assessment stand out as key processes for appropriate nutritional intervention and monitoring<sup>4</sup>.

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There are several nutritional screening methods available. Among them, the Nutrition Risk in Critically Ill score (NUTRIC-score) was the instrument exclusively developed and validated to assess nutritional risk in critically ill patients<sup>5</sup>. This tool generates a final score based on information about age, severity indicators (APACHE II and SOFA), number of comorbidities, days in hospital before ICU admission, and acute inflammatory profile characterized by increased interleukin-6 (IL-6). Based on their final score, patients can be classified as being at low or high nutritional risk. Those classified as being at high nutritional risk are more likely to benefit from aggressive nutritional therapy<sup>5</sup>. In the modified (mNUTRIC-score) and more recent version, IL-6 was excluded, as this variable is not always available6. Both the NUTRIC-score and mNUTRIC show prognostic accuracy, with no significant difference between them<sup>7</sup>.

Among the nutritional prognostic parameters, the following stand out phase angle (PA), which is a quick-to-obtain, non-invasive measurement, assessed using bioimpedance analysis (BIA). Physiologically, PA is an indicator of cellular health, since it reflects not only body cell mass but also the integrity and function of cell membranes. It is also significantly and positively correlated with lean body mass<sup>8</sup>. Healthy individuals have PA values<sup>9</sup> between 5 and 7. Disease, inflammation, malnutrition, and physical inactivity hurt hydration status and tissue electrical properties, resulting in a decrease in PA<sup>8</sup>. For this reason, reduced PA values predict worse nutritional and functional status, greater risk of complications, worse prognosis, and higher mortality<sup>9,10</sup>.

As malnutrition is a frequent condition in critically ill patients and can influence their prognosis, nutritional screening, and assessment of the early nutritional prognosis of patients admitted to the ICU are imperative for better targeting of nutritional therapy. Due to the often-conflicting results in the literature and the need to know the prevalence of nutritional risk and nutritional prognosis of patients admitted to the ICU of the Onofre Lopes University Hospital (HUOL) of the Federal University of Rio Grande do Norte (UFRN), this study was planned. This study aimed to investigate nutritional risk (using the mNUTRIC-score) and nutritional prognosis (using the PA) in this population, as well as their relationship with the clinical outcome of hospitalization (discharge from the ICU or death).

# METHODS

### Study design and ethical aspects.

This is a cross-sectional study conducted from February 2017 to February 2020 at the Onofre Lopes University Hospital (HUOL), Natal, Brazil, and approved by the Research Ethics Committee (CAAE: 61106116.5.0000.5292). The non-probabilistic sample included patients over 20 years of age, of both sexes, admitted to the ICU for more than 24 hours. The exclusion criteria adopted were patients with anasarca, amputees, or pacemakers, as these conditions would influence the reliability of the values collected by BIA (resistance and reactance) used to calculate PA. However, no participants met the exclusion criteria.

# **Data Collection and Tabulation**

Data was collected using a pre-prepared instrument by trained nutritionists. Characterization data (date of birth, age, gender, underlying disease, reason for ICU admission), data for calculating the mNUTRIC-score, and the clinical outcome of the patient's hospitalization (ICU discharge or death) were extracted from the medical records of each participant. The mNUTRICscore was calculated and scored as recommended<sup>6</sup>, classifying patients into low or high nutritional risk according to scores  $\leq$ 4 or  $\geq$ 5, respectively. PA was calculated using the formula described in the literature<sup>11</sup>: PA = [arctangent (Xc/R) x  $180/\pi$ ], where Xc represents Reactance, R Resistance, and  $\pi$ =3.14. These parameters were obtained using tetrapolar BIA equipment, called Quantum II® analyzer (RJL Systems, Clinton Township, MI, USA), following the method described by Lukaski et al.<sup>12</sup> Data collection and BIA took place on the first day (first 24 hours) of the patient's stay in the ICU. The data was tabulated in a Microsoft Excel® spreadsheet.

#### **Statistical Analysis**

Statistical analysis was conducted using GraphPad Prism 6.0a (GraphPad Software, Inc., San Diego, CA, USA). The Shapiro-Wilk test was applied to verify the normality of the data distribution. Quantitative variables were described as mean and standard deviation, while qualitative variables were presented as frequency distribution. The Mann-Whitney and Student's t-tests were used to verify the associations between the mNUTRIC-score and PA with the clinical outcome of hospitalization, respectively. Spearman's correlation test was used to check the correlation between the mNUTRIC score and PA. The significance level adopted was 5% (p≤0.05).

### RESULTS

A total of 55 patients took part in this study, and the sample was female. The two main underlying diseases were cancer and cardiovascular disease, accounting for 65.4% of the population. Approximately 80% of the individuals had a low nutritional risk and were discharged from the ICU. The other characteristics of the study population are described in Table 1.

The associations of mNUTRIC-score and PA with the clinical outcome of hospitalization showed that 70% and 89% of patients

who died had high nutritional risk (mNUTRIC-score  $\geq$ 5) and low PA (<5), respectively. Graphically, these associations can be seen in Figure 1.

A negative correlation was observed between the mNUTRICscore and PA (r=-0.3804; p $\leq$ 0.006) (Figure 2). In other words, the higher the metric score, indicating greater nutritional risk, the lower the PA, indicating a worse clinical and nutritional prognosis.

Table 1: Characteristics of the study population.

Features	Total number of patients (n = 55)
Sex, n (%)	
Female	35 (63.6%)
Male	20 (36.4%)
Age (years), average $\pm$ SD <sup>1</sup>	$55\pm16.9$
Baseline disease, n (%)	
Neoplasm	23 (41.8%)
Cardiovascular Disease	13 (23.6%)
Diseases of the gastrointestinal tract	9 (16.4%)
Respiratory Diseases	5 (9.1%)
Neurological Diseases	3 (5.5%)
Kidney Diseases	2 (3.6%)
Others	4 (7.3%)
Profile, n (%)	
Surgical	28 (50.9%)
Clinical	27 (49.1%)
mNUTRIC-score, average $\pm$ SD <sup>1</sup>	$\textbf{3,13} \pm \textbf{2.35}$
mNUTRIC-score, median (IQR) <sup>2</sup>	2,5 (1.0 - 4.0)
mNUTRIC-score, n (%)	
Low risk nutritional	42 (76.4%)
High risk nutritional	13 (23.6%)
Phase angle ( $^{\circ}$ ), average $\pm$ SD $^{1}$	4.19 ± 1.21
Phase angle ( <sup>2</sup> ), median (IQR) <sup>2</sup>	4.15 (3.15 – 5.17)
Outcome	
Discharge from ICU, n (%)	45 (81.8%)
Death, n (%)	10 (18.2%)

<sup>1</sup>SD = Standard Deviation; <sup>2</sup>IQR = Interquartile Range.

## DISCUSSION

In this study, we found that most participants had a low nutritional risk and were discharged from the ICU. We observed a significant association between high nutritional risk and unfavorable nutritional prognosis with a worse clinical outcome (death). We also observed a correlation between the mNUTRIC score and PA, indicating that high nutritional risk indicates a worse clinical and nutritional prognosis.

The most frequent underlying diseases in the study population were neoplasms and cardiovascular diseases, while the clinical and surgical profiles were equally similar among the participants. Although these underlying diseases are present in other studies that have applied the NUTRIC-score<sup>5,13</sup>, they are not always the most prevalent diseases. Similarly, the profile of the patients can change between studies. In the study by Marchett et al.<sup>14</sup> for example, clinical patients were predominant (72.5%) compared to surgical patients (26%) and trauma patients (1.5%). This heterogeneity in underlying diseases and patient profiles may be seasonal, related to the epidemiological profile of the city or even the profile of the hospital.

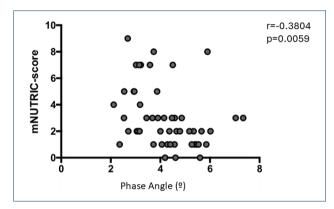


Figure 2: Correlation between mNUTRIC-score and phase angle in critically ill patients.

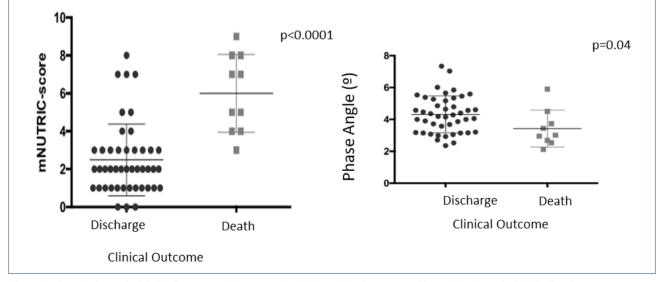


Figure 1: Associations of mNUTRIC-score and phase angle with the clinical outcome of hospitalization of critically ill patients.

In this study, most patients (76.4%) had a low nutritional risk according to the metric score. These results were like other studies with critically ill patients that used the same instrument. For example, Marchetti et al.<sup>14</sup> and Özbilgin et al.<sup>15</sup> found a prevalence of low nutritional risk (mNUTRIC-score  $\leq 4$ ) in 63.5% and 77.6% of patients admitted to the ICU (n=200) and the Postoperative Acute Care Unit (n=152), respectively. However, almost half (48.6%) of the critically ill patients in the study by Mendes et al.<sup>13</sup> were at high nutritional risk. Even higher frequencies of critically ill patients at high nutritional risk were observed in the studies by Aragão et al.<sup>16</sup> and Rahman et al.<sup>6</sup>. The higher average obtained in these studies was due to higher scores in the APACHE and SOFA severity indicators.

It is important to note that malnutrition is common in intensive care, as this type of care involves critically ill patients, who suffer from catabolic stress, hypermetabolism, energy and nutritional deficits, systemic inflammation, and impaired organ function<sup>17</sup>. For this reason, some authors consider critically ill patients to be at high nutritional risk<sup>6</sup>. However, the recognition that not all ICU patients will respond in the same way to nutritional interventions was the crucial concept for the development of the NUTRIC score. For this reason, it points out the critical patients who would benefit (those with high nutritional risk) or not (those with low nutritional risk) from more aggressive nutritional therapy, to achieve better outcomes<sup>5,17</sup>. Thus, the low nutritional risk found in the majority of participants in this study (76.4%) does not eliminate the occurrence of nutritional risk itself but indicates that they would not benefit from more aggressive nutritional therapy.

Nutritional screening in critically ill patients, despite providing essential information, should not replace nutritional assessment. Conducting nutritional assessment in critically ill patients is a challenge and, as there is no gold standard method, a variety of methods should be considered, depending on their feasibility and usefulness for nutritional diagnosis and intervention<sup>1</sup>.

The average PA observed in the participants in this study was  $4.19 \pm 1.2$ . Silva et al.<sup>10</sup> conducted the same type of assessment on critically ill patients and found mean PA values of  $4.91 \pm 1.36$  in a sample of 95 participants. There are still no reference values for PA in critically ill patients. Some studies suggest cut-off points in specific clinical situations<sup>18-21</sup>. The average PA found in this study was below the range or average expected for a healthy population<sup>9,22</sup>. This is important given that low PA values are associated with increased mortality and longer ICU stays<sup>23</sup>.

Although the calculation of PA does not require body weight, it can vary with hydration status. According to Lukaski et al.<sup>8</sup>, the decline in PA in critically ill patients may be due to a reduction in body cell mass caused by catabolism, inflammation, water retention, disruption of cell membrane integrity, and the passage of water from the intracellular to the extracellular environment. In the study by Denneman et al.<sup>24</sup>, the authors observed an increase in the hydration status of critically ill patients during their ICU stay

and a concomitant reduction in PA. Thus, the authors suggest that in critically ill patients, changes in PA partially reflect changes in hydration status. In this study, the standardization of BIA in the first 24 hours of admission to the ICU helped to minimize the bias related to changes in hydration status during hospitalization.

When it came to clinical outcomes, Cândido and Luquetti<sup>25</sup> found a death rate of 23.2%, while 76.8% of patients were discharged from the ICU. Özbilgin et al.<sup>15</sup> found an even lower mortality rate (9.2%) about the number of survivors (90.8%). In line with these findings, the results of the present study also showed a higher frequency of ICU discharges (81.8%), compared to the frequency of deaths (18.2%), for critically ill patients in intensive care. This can be explained by the lower severity of the patients, by a lower nutritional risk, and by the treatments received during hospitalization.

This study showed a positive association between the mNU-TRIC score and patient outcome, with high statistical significance ( $p\leq0.0001$ ). Özbilgin et al.<sup>15</sup> found a positive correlation between the NUTRIC score and mortality in acute postoperative patients. Other studies have evaluated the correlation between the NUTRIC score and 28-day mortality in ICU patients with sepsis and other complications. In addition, authors have found a positive correlation between the two variables<sup>13,26</sup>. Although the NUTRIC score is a relatively new nutritional screening tool, there is already a range of studies showing its effectiveness in assessing the nutritional risk of critically ill patients, as well as predicting various unfavorable clinical outcomes, such as time on mechanical ventilation (MV), length of ICU stay, increased intestinal permeability and death<sup>5,27-29</sup>.

In this study, in addition to the positive association with the outcome, the mNUTRIC score was negatively correlated with patients' PA. Although this correlation was weak (r = -0.3804), it was significant (p=0.0059). Corroborating our results, Al-Kalaldeh<sup>30</sup> evaluated critically ill patients of various etiologies using the NUTRICscore and PA and found a statistically significant (p≤0.001) negative correlation (r= -0.251) between the variables, showing that patients at high nutritional risk tend to have lower PA values. Because PA is related to cellular integrity and functionality, the amount of lean body mass and hydration, it is an important parameter in assessing sick individuals and can be used in various clinical conditions to monitor the progression of a disease, verify the effectiveness of an intervention or estimate clinical outcomes in patients, including those in serious condition<sup>8,10</sup>. More research on this subject is needed so that the NUTRIC score and PA can support evidencebased nutritional guidelines. In addition, reference values for PA in critically ill patients still need to be established.

In conclusion, most of the critically ill patients studied had a low nutritional risk as determined by the mNUTRIC-score. Patients with a high nutritional risk had a worse outcome (death). There was a negative correlation between the mNUTRIC score and PA, showing that the higher the nutritional risk, the worse the clinical and nutritional prognosis in critically ill patients.

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