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Original article

Prognostic role of phase angle in hospitalized patients with acute decompensated heart failure

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SUMMARY

Background & aims: Patients with acute decompensated heart failure (ADHF) have exacerbation of symptoms and fluid retention, and high risk of re-hospitalizations and mortality. The aim of this study was to evaluate the role of phase angle at hospital admission as a prognostic marker of mortality in patients with ADHF.

Methods: Patients hospitalized for ADHF, with left ventricular ejection fraction (LVEF) <45% and BOSTON criteria ≥8 points were included. The patients were evaluated at hospital admission (first 36 h) and then followed up for assessment of outcomes. Phase angle was measured with tetra polar bioelectrical impedance device. Mortality data was obtained from an average of 24 months after discharge, from the medical records of the hospital and outpatient or telephone contact with patients or family members. The best-discriminatory level of phase angle was selected based on the ROC curve for mortality.

Results: Seventy-one patients were included and the majority was male (63%), with a mean age of 61 ± 12 years, ischemic etiology being the most prevalent (48%) and LVEF average of 26 ± 8%. Mortality was 49% at an average of 24 months after hospital discharge. The average phase angle at hospital admission was 5.6 ± 2°, and lower values were associated with higher mortality. Survivors were compared to died patients in the risk factor variables for mortality. In multivariate analysis adjusting for age, LVEF and urea, phase angle <4.8° was independently associated with increased mortality (HR 2.67; p = 0.015).

Conclusions: Phase angle seems to be a prognostic marker in patients with ADHF independently of other known risk factors.

1. Introduction

The development and progression of heart failure are related to the nutritional status of patients. Changes of anthropometric, biochemical and immunological parameters compatible with nutritional impairment are common in the advanced stages of the disease [1]. Studies evaluating the impact of nutritional status on the prognosis of these patients both in chronic heart failure and in the decompensation of the disease show that malnutrition is an important risk factor for mortality [2,3].

In acute decompensated heart failure (ADHF), patients have exacerbation of symptoms of the disease and fluid retention, an increased risk of re-hospitalizations and mortality [4,5]. The number of hospitalizations after an episode of decompensation reaches around 50% in the 12 months after discharge [6]. Even though the ADHF is a high risk period for patients, there is few data about the nutritional status evaluated during this condition. The few existing

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studies have used body mass index (BMI) as a prognostic indicator, showing mixed results regarding the use of this parameter for predicting mortality in this condition. Furthermore, the studies do not make clear if some adjustment was made to correct the fluid retention, since the weight can significantly interfere with the BMI [7–9].

Malnutrition and cachexia, both prevalent in catabolic chronic diseases and in hospitalized patients such as ADHF, leads to metabolic changes that result in unintentional weight and muscle loss and weakness, resulting in worse prognosis. These body modifications alter body fluid balance and the permeability of cell membranes [10]. Different nutritional status assessments have been made in these patients and more recently the phase angle, a parameter obtained by the ratio of direct measurements of bioelectrical impedance device, has emerged as a good nutritional status indicator [11,12]. The phase angle is calculated by the relation between resistance and reactance measured by electric current flow in the tissues, resulting in an assessment of body cell conditions where higher values are associated with good cell function and lower values indicate apoptosis and reduced components of extracellular matrix [13]. Phase angle relates to prognosis in several clinical conditions, such as in cancer or critical illness [14–16]. There are few studies that explore phase angle in the scenario of heart failure. It has been shown that lower phase angle values are found in patients with heart failure with excess fluid and anemia compared to patients with heart failure without these conditions, indicating that this parameter can reflect the severity of the clinical state [17]. Lower phase angle values (<4.2°) has also been associated with higher mortality in outpatients with heart failure [18]. During hospitalization for ADHF, we previously demonstrated that lower phase angle values are found at hospital admission compared to discharge [19].

The evaluation of the phase angle in patients admitted for ADHF can therefore be a promising tool, as a method of easy application and reproducibility, providing a prognostic evaluation, and thus assisting in the development of effective therapeutic strategies. The aim of this study was to evaluate the role of the phase angle value, obtained at hospital admission for ADHF, as a prognostic marker of mortality.

2. Material and methods

2.1. Population

Patients were recruited from a university hospital in Porto Alegre, RS, Brazil. The study included adults (over 18 years of age) hospitalized for ADHF, left ventricular ejection fraction (LVEF) ≤45% and BOSTON screening score ≥8 points. Patients with active malignancy, advanced renal failure (serum creatinine >2.5 ml/dl or dialysis), pacemaker or implantable cardioverter (because of bioimpedance protocol), or inability to answer the questionnaires were excluded.

The study was conducted according to rules and ethical guidelines, respecting the Declaration of Helsinki and approved by the ethics committee of the institution. Consent was applied to all participants prior to the evaluations.

2.2. Assessment

Patients were evaluated at hospital admission. In the first evaluation, data was collected up to 36 h from admission at the emergency room for signs and symptoms of ADHF, demographics, etiology, functional class according criteria of the *New York Heart Association* (NYHA) [20] and hemodynamic classification according to Stevenson quadrants [21] with support of medical and nursing staff. Echocardiography data was obtained from medical records, and the exam performed during hospitalization or in the previous six months were selected. Laboratory emergency routine tests requested by the cardiology staff (urea, creatinine, sodium, potassium, blood count, albumin and C-reactive protein) were used for the description of patients on arrival at the hospital and for adjustment of prognostic factors. B-type natriuretic peptide (BNP) was collected to confirm the heart failure decompensation (chemiluminescence Centaur® XP - Siemens).

The phase angle was then obtained, within 36 h of admission, on fasting condition for at least 4 h to avoid the influence of food intake in the assessment, and the examination was performed with a tetrapolar bioelectric impedance device (Biodynamics 450: Biodynamics Corp. Seattle, Washington, USA), using current of 800 microA and frequency of 50 kHz, with the patient lying down, with legs apart and electrodes glued on his right hand and foot.

Other variables of body composition were also collected and included: arm circumference with non-extensible tape (Sanny®), triceps skinfold with scientific adipometer (Cescorf®) and these two measures were used to estimate the muscle circumference of the arm. Handgrip strength with a dynamometer (Jamar®) was evaluated in the dominant hand, adjusted for the size of the patient's hand, measured in triplicate where the highest values were used.

2.3. Outcome

Mortality data was obtained from an average of 24 months after discharge, from the records of the hospital (when the outcomes were identified on this place) and through telephone or contact with patients or family.

2.4. Statistical analysis

Continuous data were reported as mean and stand deviation or median and interquartile range, categorical variables as absolute numbers and percentages.

As there were no studies classifying the phase angle in ADHF, patients were previously classified in accordance with Colin-Ramirez et al. (2012)[18], that evaluated prognosis in chronic heart failure patients and found association with mortality when phase angle values were lower than 4.2°. However, in the case of a population with greater severity, a new determination of the cutoff point for phase angle analysis and mortality was obtained by the ratio between specificity and sensitivity in the ROC curve. Cox and Kaplan–Meier regressions were performed for associations of phase angle values with the outcome. Student t test or Mann–Whitney U Test and chi-square were used to compare continuous and categorical variables, respectively, which could be associated with mortality among patients who died during follow-up and those who survived. It was also conducted multivariate analysis including phase angle and the variables that could influence in prognosis according to the results of the comparison between the groups with and without death. Pearson's correlation was made between the variables of body composition and phase angle.

3. Results

Seventy-one patients were enrolled at admission for ADHF, where the majority were males (63%), with more than 60 years of age (66%), ischemic being the most prevalent (48%) and 43% with LVEF lower than 25%. All patients were in NYHA functional class from III to IV, with the majority classified as Class IV (67%). Clinical and demographic variables of the study population are shown in Table 1.

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