



Applied nutritional investigation

Bioimpedance vector analysis predicts hospital length of stay in acute heart failure



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ABSTRACT

Objective: Congestion in acute heart failure (AHF) affects survival curves and hospital length of stay (LOS). The evaluation of congestion, however, is not totally objective. The aim of this study was to verify the accuracy of bioelectrical impedance vector analysis (BIVA) in predicting the LOS in AHF patients.

Methods: This is a retrospective study. A total of 706 patients (367 male; mean age: 78 ± 10 y) who had been admitted to hospital with an AHF event were enrolled. All underwent anthropometric and clinical evaluation, baseline transthoracic echocardiography, and biochemical and BIVA evaluations.

Results: The comparison among the clinical characteristics of congestion, LOS, and hyperhydration status revealed that the higher the hydration status, the longer the LOS (from 7.36 d [interquartile range: 7.34–7.39 d] in normohydrated patients to 9.04 d [interquartile range: 8.85–9.19 d] in severe hyperhydrated patients; $P < 0.05$). At univariate analysis, brain natriuretic peptide, blood urea nitrogen, New York Heart Association class, hemoglobin, hydration index, and peripheral edema all had a statistically significant influence on LOS. At multivariate analysis, only brain natriuretic peptide ($P < 0.0001$), blood urea nitrogen ($P = 0.011$), and hydration index ($P < 0.0001$) were significantly associated to LOS.

Conclusions: Congestion evaluated by BIVA is an independent predictor of length of total hospital stay in HF patients with acute decompensation. The quick and reliable detection of congestion permits the administration of target therapy for AHF, thus reducing LOS and treatment costs.

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Introduction

Acute heart failure (AHF) is defined as the rapid onset or worsening of symptoms or signs of heart failure (HF) [1]. The role of peripheral and central congestion in AHF or in acute decompensated heart failure (ADHF) is highly significant for outcome purposes [2–4]. Data from the IMPACT-HF (Initiation Management Pre-discharge Assessment of Carvedilol Heart Failure) registry has already highlighted the negative influence of fluid volume overload on clinical outcomes, which can affect mortality and morbidity in these patients [2]. The clinical classification of Nohria et al. [3] revealed the central role of congestion in the clinical expression of acute heart failure and its

influence on outcomes: Survival curves revealed an increased risk of death and/or urgent transplantation in those belonging to profile B (congestion with adequate perfusion: wet/warm) and/or profile C (congestion and hypoperfusion: wet/cold) even after adjusting for confounding factors at multivariate regression analysis [3].

Congestion is also related to the hospital length of stay (LOS) of patients in cardiology departments. Edema at admission is one of the most important determinants of patient LOS, followed by changes in weight and/or days on intravenous diuretic [5]. Nevertheless, the objective identification of peripheral edema is poorly reproducible in clinical practice. Data from the literature [6–12] on AHF patients reveals a change in the presence of lower limb peripheral edema from about 20% to 66%. Bioelectrical impedance vector analysis (BIVA) is a more reliable, faster, and less costly technique able to detect peripheral congestion in AHF better than brain natriuretic peptide (BNP) [13,14].

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Quicker detection of AHF characteristics and prognostic factors would permit treatment to be directly targeted to the features of AHF, thus reducing LOS and treatment costs [15]. Therefore, compared with the identification of peripheral edema, the identification of congestion and the direct application of an adjusted dose of diuretics can restore compensated conditions and predict reduced LOS.

The aim of this research article was to verify the accuracy of BIVA in predicting the length of stay in hospital of AHF patients.

Materials and methods

We retrospectively evaluated 706 patients (367 male, 339 female; age: 78 ± 10 y, mean \pm standard deviation [SD]) admitted to the cardiology departments of the F. Perinei Hospital in Altamura, Bari, Italy and the Civil Hospital of Chioggia in Venice, Italy between January 2014 and December 2016.

The inclusion criteria were 1) age older than 18 y; 2) diagnosis of acute HF according to the European Society of Cardiology guidelines [1]; and 3) absence of congenital heart disease.

The exclusion criteria were 1) acute coronary syndromes; 2) malignant ventricular arrhythmias; 3) acute or subacute pulmonary embolism; and 4) vein disorders or lymphoedema.

At admission, all patients underwent anthropometric and clinical evaluation, baseline transthoracic echocardiography examination in accordance with international guidelines [16], and biochemical evaluation (blood cell count, kidney function evaluation, serum electrolyte concentrations, BNP, troponins).

The Cockcroft-Gault equation was used to estimate creatinine clearance: $eCrCl$ (mL/min) = $[(140 - \text{age}) \times (\text{weight})] / (72 \times \text{serum creatinine}) \times 0.85$ (if female) [16].

The study protocol was approved by the institutional ethics committee and was in agreement with the declaration of Helsinki. Informed consent to scientifically share their clinical data was given by all patients.

Baseline transthoracic echocardiography examination

All patients underwent transthoracic echocardiography examination at hospital admission. A standard echocardiographic machine (Epiq 7, Philips, Medical Systems, Andover, MA) equipped with a 2.5 to 3.5 MHz phased-array sector scan probe was used.

Left ventricular ejection fraction (LVEF), measured by modified biplane Simpson's method, and 2-dimensional cardiac chamber dimensions were calculated according to the standard international American Society of Echocardiography (ASE) and European Association of Cardiovascular Imaging (EACVI) guidelines [17,18]. The patients were divided into three groups: those with normal LVEF (LVEF \geq 50%, i.e. HF with preserved EF), those with reduced LVEF (LVEF < 40%, i.e. HF with reduced EF), and those with an LVEF between 40% and 49%, (i.e. HF with midrange EF) [1].

Peripheral congestion assessment

Digital manipulation was used to clinically assess the peripheral congestion. Thumb pressure was applied to the ankles, below and above the knees, and on perimalleolar zones (swollen tissue over a bony area for 5 s. Edema was confirmed if the indentation in the tissue remained after thumb removal).

Bioelectrical impedance vector analysis evaluation

BIVA was assessed on the right side of the body [13,19]. The patient was in a semiorthopneic or a supine position. A tetrapolar impedance plethysmograph that emitted 50 kHz alternating sinusoidal current (CardioEFG, Akern RJI Systems, Florence, Italy) was used.

To reduce bias, the plethysmograph was calibrated each day by applying a standard resistor supplied by the manufacturer ($R = 380$ ohms, $X_c = 47$ ohms, 1% error).

After applying the electrode according to standard positions [13,19], an alternating current was applied between hand and foot electrodes, and the drop in voltage was detected by the proximal electrodes. The analysis of the alternating current through the body provided the measurements of resistance (R , in Ohm) and reactance (X_c , in Ohm). These values were divided by the subject's height. In addition, we considered phase angle (degrees) (i.e., $\arctan [R/X_c] \times [180/\pi]$) and used dedicated software (Bodygram 1.4, Akern RJI Systems, Florence, Italy) to estimate body hydration as well as the percentage of fat-free mass (hydration index; HI) [20,21].

According to HI values, patients were classified as follows: severely dehydrated (HI < 60%); moderately dehydrated (HI 60–71%); mildly dehydrated (HI 71.1–72.7%); normal hydration (HI 72.8–74.2%); mild hyperhydration (HI 74.3–81%); moderate hyperhydration (HI 81.1–87%); severe hyperhydration (HI 87.1–100%) [22–24].

BNP

BNP was measured by means of microparticle enzyme immunoassay (Architect, Abbott Park, IL). The assay range was from 10 to 5000 pg/mL. The intra- and interassay variability coefficient ranged from 0.9% to 5.6% and 1.7% to 6.7%, respectively.

Statistical analysis

Categorical variables are expressed as counts (percentages), and continuous variables are expressed as values \pm standard deviation (SD). Because the distribution LOS was positively skewed, the values are expressed as median (interquartile range [IQR]). Multiple between-group comparisons of the mean value of each parameter were performed using Kruskal-Wallis test [25]. A multivariate linear regression model was used to ascertain independent predictors of LOS, variables being logarithmically transformed to meet the assumptions of normality [26]. We conducted correlation analyses to reduce collinearity and the number of variables used in multivariate analyses. First we retained the variable perceived as more biologically important from among two or more strongly intercorrelated variables ($r > 0.60$) because they may be considered as estimates of a single underlying factor. Then we included only the variables with a significant univariate difference ($P < 0.1$) in multivariate analyses. All tests are two-tailed; a value of $P < 0.05$ was considered significant. Analyses were performed using SPSS Software for Mac Version 20.0 (IBM Corp., Armonk, NY).

Results

Table 1 summarizes the main characteristics of the study population. The median value of hospital LOS was 7.48 d (IQR: 7.36–8.12 d).

Table 2 outlines the number of patients with clinically detected peripheral edema and the mean and median values of serum concentration of BNP. Furthermore, the BIVA mean measurements related to the entire population have been included, as well as the different classes of hydration index and the patients included in each category of hydration status. Interestingly, more than half of the patients were hyperhydrated (55%).

The comparison among clinical characteristics of congestion, LOS, and hyperhydration status revealed that the higher the hydration status, the longer the LOS (from 7.36 d [IQR: 7.34–7.39 d] in normohydrated patients to 9.04 d [IQR: 8.85–9.19 d] in severe hyperhydrated patients; $P < 0.05$; Fig. 1). A similar situation was found for BNP values and creatinine clearance: The severe hydration status was associated with a decrease in renal function and an increase in BNP plasma values (Table 3).

Therefore we tried to understand the main determinants of LOS. Table 4 shows the univariate and multivariate regression analysis adopted to evaluate those factors able to predict LOS in patients admitted to cardiology departments for acute heart failure. The univariate regression model found that BNP at admission, blood urea nitrogen (BUN), New York Heart Association class, hemoglobin, hydration index, and peripheral edema were all statistically significant variables influencing the length of stay. All the other variables were not significantly related at univariate analysis (Supplementary Table 1). The multivariate regression model outlined important findings. Hydration index was able to predict hospital LOS at multivariate regression analysis. Peripheral edema was not able to predict hospital LOS. This highlights the limited role of peripheral edema compared with hydration index in predicting hospital LOS (Table 4). Therefore hydration status and biochemical evaluations are the main predictors for total hospital stay of HF patients admitted for acute decompensation.

Discussion

The present study found that the major determinants of length of stay of patients admitted to cardiology departments for acute heart failure (de novo or acute decompensation of chronic heart

Table 1
Study population

Characteristics	ADH (n = 706)
Age, y (mean ± SD)	78 ± 10
Male (%)	52
BMI, kg/m ² (mean ± SD)	28 ± 5
Medical history, %	
Coronary artery disease	38
Diabetes	24
Atrial fibrillation	51
AICD	11
De novo HF	34
NYHA class (mean ± SD)	3.2 ± 0.8
LVEF (mean ± SD)	44 ± 14
Preserved LVEF, %	42
Midrange LVEF, %	22
Reduced LVEF, %	36
Laboratory values (mean ± SD)	
Hemoglobin, g/dL	12 ± 2
Hemoglobin <12 g/dL, %	35
Albumin, g/dL	3.2 ± 0.5
Sodium, mEq/L	139 ± 4
Potassium, mEq/L	4.0 ± 0.6
Urea nitrogen, mg/dL	75 ± 42
Creatinine, mg/dL	1.6 ± 1.1
Creatinine >1.5 mg/dL, %	32
eCrCl, mL/min per 1.73 m ²	46 ± 23
eCrCl, <60 mL/min per 1.73 m ² , %	50
eCrCl, <30 mL/min per 1.73 m ² , %	27
Troponin, ng/mL	0.50 ± 2.7
Troponin >0.15 ng/mL, %	28
Therapies, %	
Furosemide	97
Beta-blocker	48
ACE inhibitor	36
ARB	12
Digitalis	27
Calcium antagonists	0
IV inotropes	11
Ultrafiltration/dialysis	4

ACE, angiotensin-converting enzyme; AICD, automatic implanted cardioverter/defibrillator; ARB, angiotensin receptor blocker; BMI, body mass index; eCrCl, estimate creatinine clearance; HF, heart failure; IV, intravenous; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD, standard deviation.

Table 2
Peripheral congestion, BNP, and BIVA data

Characteristics	Values
Lower extremity edema, %	44
BNP, pg/mL (median [IQR])	830 [479–1810]
BNP, pg/mL (mean ± SD)	1286 ± 1160
BIVA (mean ± SD)	
R/H, Ohm/m	289 ± 73
Xc/H, Ohm/m	24 ± 8.1
Angle phase, degrees	4.7 ± 1.2
Hydration index (%)	77.7 ± 5.8
Severe dehydration (%)	1
Moderate dehydration (%)	1
Mild dehydration (%)	3
Normohydration (%)	40
Mild hyperhydration (%)	30
Moderate hyperhydration (%)	15
Severe hyperhydration (%)	10

BIVA, bioelectrical impedance vector analysis; BNP, brain natriuretic peptide; IQR, interquartile range; R/H, resistance/height ratio; SD, standard deviation. Hydration index mean ranges: severe dehydration: <60%; moderate dehydration: 60–71%; mild dehydration: 71.1–72.7%; normohydration: 72.8–74.2%; mild hyperhydration: 74.3–81%; moderate hyperhydration: 81.1–87%; severe hyperhydration: 87.1–100%.

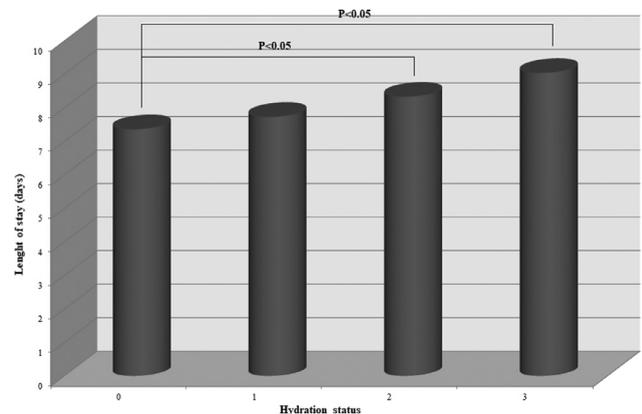


Fig. 1. Relationship between hydration status and length of stay (LOS). Data represented as median. Hydration index mean ranges: 0, normohydration: 72.8–74.2%; 1, mild hyperhydration: 74.3–81%; 2, moderate hyperhydration: 81.1–87%; 3, severe hyperhydration: 87.1–100%.

failure) were hydration index evaluated by means of BIVA and biochemical elements such as BNP and blood urea nitrogen. BIVA is able to better predict LOS than peripheral edema [13].

The LOS is a reliable indicator for short-term mortality and HF readmission rates in AHF patients [27,28]. This promotes an increase in health system costs. Corrao et al. [29] calculated an average per capita cost equal to €11 000 for heart failure patients admitted to Italian cardiology departments; most of this cost is related to hospitalization. Therefore identifying the main determinants for LOS is fundamental in order to predict the hospitalization course of AHF patients and also to plan the financial costs of HF hospitalization.

Several predictors of length of stay in HF patients have been proposed in literature. Palmer et al. [30] reported that the persistent decrease in renal function was associated with the highest mortality rate of AHF patients, whereas the presence of a transient deficiency in renal function could promote increased LOS in these patients. Such results were confirmed by the detailed meta-analysis of Butler et al. [31], who found a constant association between worsening renal failure and LOS, as well as a correlation with primary endpoints such as mortality, readmission risk, and short-term outcomes such as in-hospital mortality and complications. Although our analyses revealed the association between creatinine clearance and LOS, the multivariate regression model did not confirm such results. Indeed, the usefulness of creatinine clearance in practically predicting LOS in AHF was detrimental because it did not reveal the real congestion level of the patient.

The role of BUN is rather different in the risk stratification and prognosis of patients with AHF [32–34]. Studies [32–34] reported an increased mortality rate in patients with a progressive increase in BUN during hospitalization for AHF. The rate of adverse prognostic events seemed independent from congestion signs [33] and worsening in renal function [34]. In particular, evidence has pointed out the better performance of BUN in predicting events in patients hospitalized for heart failure compared with N-terminal pro-BNP measurements [35].

Therefore BUN can theoretically affect LOS-to-BUN levels were related to readmission for HF decompensation [36], and higher BUN levels were recently associated with longer-than-average LOS [37]. In line with these findings, our study outlined the impact of BUN at admission on LOS by identifying BUN as an independent determinant for LOS, even after adjusting for confounding factors.

Although BUN reveals a more pronounced prognostic influence on AHF prognosis and outcomes, natriuretic peptides are more

Table 3
Relationship between hydration status and BNP/kidney function

Variables	Hydration status			
	0	1	2	3
BNP (pg/mL)	1134.02 ± 1083.85	1206.48 ± 1101.38*	1630.59 ± 1363.60* [†]	1698.77 ± 1215.03* [†]
Clearance creatinine (mL/min per 1.73 m²)	49.2 ± 22.35	47.1 ± 22.86*	39.7 ± 20.35* [†]	40.9 ± 24.02* [†]

Numbers are expressed as mean ± standard deviation. BNP, brain natriuretic peptide.

Hydration index mean ranges: normohydration (group 0): 72.8–74.2%; mild hyperhydration (group 1): 74.3–81%; moderate hyperhydration (group 2): 81.1–87%; severe hyperhydration (group 3): 87.1–100%. Comparison performed by means of Kruskal-Wallis test.

**P* < 0.05 versus normohydration (group 0).

[†]*P* < 0.05 versus mild hyperhydration (group 1).

Table 4
Univariate and multivariate regression analysis: the role of clinical, instrumental and biochemical variables on length of stay

Variables	Univariate model		Multivariate model	
	Beta	Significance	Beta	Significance
BNP (pg/mL)	0.250	0.000	0.178	0.000
NYHA class	0.153	0.000	0.064	0.106
BUN (mg/dL)	0.183	0.000	0.102	0.011
Hemoglobin (g/dL)	-0.176	0.000	-0.072	0.077
Hydration index (%)	0.267	0.000	0.183	0.000
Peripheral edema	0.102	0.019	-0.010	0.821

BNP, brain natriuretic peptide; BUN, blood urea nitrogen; NYHA, New York Heart Association.

Dependent variable: length of stay. The tests were carried out on the variables logarithmically transformed.

challenging when considered in such a setting [38–40]. Nevertheless, the evaluation of natriuretic peptides at admission can be fundamental for the evaluation of length of hospitalization of patients suffering from AHF [41,42]. The higher the plasma values of BNP and N-terminal pro-BNP at admission, the longer the duration of hospitalization [43]. Such results were not confirmed by Omar and Gugliin [37]: Their model for the identification of determinants of longer LOS did not reveal BNP measurements as being able to predict hospitalization for more or less than 7 d.

The combination of BNP and hydration index by means of BIVA surely offers more chances for the prediction of the prognosis of AHF patients [13,22]. As previously reported [13,22], hydration status evaluation can affect AHF diagnosis, management, and prognosis because it is a reliable instrument, able to quickly evaluate the congestion status of the patient, guide the pharmacologic treatment, and give reasonable information about the prognosis at early-, medium-, and long-term follow-up [44].

Our study identified another fundamental aspect of hydration status: the prediction of LOS in patients admitted for AHF. Bueno et al. [45] identified a general reduction in LOS for HF patients, although the rate of 30-d readmissions was higher over the previous 16 years despite the advances in pharmacologic and non-pharmacologic treatments of HF. Such results may derive from the incomplete “decongestion” of the AHF patients. Data from the Diuretic Optimization Strategy Evaluation in Acute Decompensated Heart Failure study and Cardiorenal Rescue Study in Acute Decompensated Heart Failure revealed that 48% of patients had persistent peripheral congestion at discharge [46]. The persistence of congestion was related to increased 60-d rates of death, rehospitalization, and unscheduled visits [46]. Therefore BIVA can be a reliable biomarker for hydration status and, consequently, for the correct management of AHF. The results from our study—that is, the prediction of LOS by means of BIVA—is closely related to the inner characteristics of BIVA. The constant monitoring of congestion and

the tailoring of diuretics or fluid integration in accordance with BIVA results can result in fewer days spent in hospital.

Study limitations

The first limitation of this study was the retrospective design. Furthermore, this was a sort of multicenter study because it involved patients admitted to two independent cardiac centers. Nevertheless, all the AHF treatment protocols were in agreement with international guidelines and the researchers were all experts in measuring hydration status. Although the cardiac centers involved in the study are situated in two different Italian regions (Apulia in Southern Italy and Veneto in Northern Italy), this could positively affect the results because it could be considered representative of the general treatment of AHF patients in Italy.

Conclusions

To the best of our knowledge, our research is the first to confirm the determinant role of hydration status in LOS prediction in patients admitted for AHF. The identification of clear signs of congestion at hospital admission and the association of biochemical evaluations (BUN and BNP in particular) can provide a useful means of evaluation of patients with AHF because the more AHF patients are hydrated, the longer their LOS.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.nut.2018.10.028.

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