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Trabajo Original

Valoración nutricional

Body composition changes assessed by bioelectrical impedance and their associations with functional class deterioration in stable heart failure patients

Cambios en la composición corporal por impedancia bioeléctrica y su asociación con el deterioro de la capacidad funcional en pacientes con insuficiencia cardiaca crónica estable

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Abstract

Background: Heart failure (HF) patients develop important changes in body composition, but only a small number of studies have evaluated the associations between these changes and functional class deterioration in a prospective manner.

Objective: The aim of this study was to evaluate whether changes in bioimpedance parameters were associated with NYHA functional class deterioration over six months.

Methods: A total of 275 chronic stable HF patients confirmed by echocardiography were recruited. Body composition measurements were obtained by whole body bioelectrical impedance with multiple frequency equipment (BodyStat QuadScan 4000). We evaluated functional class using the New York Heart Association (NYHA) classification at baseline and after six months.

Results: According to our results, 66 (24%) subjects exhibited functional class deterioration, while 209 improved or exhibited no change. A greater proportion of patients exhibited higher extracellular water (> 5%), and these patients developed hypervolemia, according to location on the resistance/reactance graph. A 5% decrease in resistance/height was associated with functional class deterioration with an OR of 1.42 (95% CI 1.01-2.0, p = 0.04).

Conclusions: Body composition assessment through bioelectrical impedance exhibited a valuable performance as a marker of functional class deterioration in stable HF patients.

Key words:

Bioelectrical impedance analyses. Functional class deterioration. Heart failure.

Resumen

Introducción: los pacientes con insuficiencia cardiaca (IC) desarrollan cambios importantes en la composición corporal; sin embargo, pocos estudios han evaluado prospectivamente la asociación entre estos cambios y el empeoramiento de la clase funcional en pacientes con IC crónica estable.

Objetivo: el objetivo de este estudio fue evaluar si los cambios en los parámetros de la bioimpedancia estaban relacionados con el deterioro de la clase funcional de la clasificación de la New York Heart Association (NYHA) después de 6 meses.

Métodos: se incluyeron 275 sujetos con IC crónica estable confirmada por ecocardiograma. Se les realizaron mediciones de composición corporal por impedancia bioeléctrica de cuerpo completo con un equipo de múltiples frecuencias BodyStat QuadScan 4000 y se determinó la clase funcional por la clasificación de la New York Heart Association (NYHA) después de seis meses.

Resultados: sesenta y seis (24%) sujetos mostraron deterioro de su clase funcional y 209 la mejoraron o no cambiaron. Se encontró mayor proporción de pacientes que cuya clase funcional se deterioró, en los que aumentó > 5% el agua extracelular y que desarrollaron hipervolemia de acuerdo a su localización en la gráfica resistencia/reactancia. La disminución de > 5% de la resistencia/talla se asoció de forma independiente con el deterioro de la clase funcional con un OR = 1.42 (IC 95% 1.01-2.0, p = 0.04).

Conclusiones: la evaluación de la composición corporal a través de bioimpedancia eléctrica en pacientes con IC es un marcador de deterioro funcional.

Palabras clave:

Análisis de impedancia bioeléctrica. Deterioro de la clase funcional. Insuficiencia cardiaca.

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INTRODUCTION

The early diagnosis of deterioration in HF patients can be challenging, and approximately 10 to 20% of initial diagnoses represent false positives (1). Furthermore, rapid diagnosis is useful for the management of these patients (2); therefore, objective measurement instruments are necessary for early diagnosis (3).

The bioelectrical impedance analysis method (BIA) is an attractive tool used for evaluating body composition due to its easy to use, low cost, noninvasiveness, high reproducibility, safety in operation and easy of interpretation, all of which are reasons for its frequent use clinically (4). Additionally, BIA has been demonstrated to be capable of recognizing people at high mortality risk in the short term (5).

Modern BIA methods are based on a similar principle: resistance to the application of an alternating electrical stream is a function of tissue composition. Tissues with long cylindrical cells and that are high in fluid and electrolytes, such as musculoskeletal tissue, exert relatively little resistance to an applied electric stream. In contrast, tissues with globular cells and scarce liquid, such as adipose tissue, exert high resistance to the conductivity of an alternating electrical current of 800 A (2,6).

Body composition data obtained by prediction equations can be used to obtain raw measurements of tissue hydration and integrity based on electrical properties, such as resistance and reactance. Furthermore, bioelectrical impedance vector analysis (BIVA) uses a resistance-reactance (RXc) graph standardized by height (where the resistance "R" is inversely proportional to total body water volume, and the reactance "Xc" is related to body mass) (2) that allows for the rapid establishment of hydration status with greater precision (7). Some authors have referred to a higher correlation of approximately $r = 0.996$ with the gold standard (deuterium dilution) (1). Variations in hydration without changes in tissue structure have been associated with shortening (overhydration) or lengthening (hypohydration) of the impedance vector along the major axis of the tolerance ellipse. The lower pole of the tolerance ellipse has a cut-off of 75% for identifying the presence of edema in adults. Hence, vector analysis can identify subclinical hyperhydration in patients in whom liquids are accumulating before the appearance of edema (8).

Impedance bioelectrical equipment (IBE) has become increasingly available in the clinical setting as a tool for the assessment of volume overload in patients with HF (9). This technology has been used for the subclinical detection and prediction of congestion events, characterized as HF aggravation. Also the evaluation of hydration status BIA was validated in patients with HF (10). Paterna et al. used impedance to evaluate inpatients with refractory HF under treatment with high doses of intravenous furosemide and hypertonic saline solutions (11), demonstrating that the method was useful in these patients.

In previous research, we demonstrated an inverse association between fluid overload estimated by IBE and the NYHA functional class (12). IBE has also been validated as a tool capable of differentiating acute dyspnea due to heart failure in the Emergency Department, and an inverse correlation exists between IBE measurements and concentrations of the natriuretic peptide B (13). However, most existing reports have focused on central fluid overload in hospitalized patients and outpatients with stable chronic heart failure (14). The aim of this longitudinal study was to assess the correlations of changes in bioelectrical impedance measurements with the deterioration of clinical status.

METHODS AND MATERIALS

This study was approved by the Biomedical Research Human Committee of the Instituto Nacional de Ciencias Medicas y Nutrición Salvador Zubirán (INCMNSZ), and all of the patients provided informed consent before the study analysis.

This research was conducted according to the principles of the Declaration of Helsinki.

SUBJECTS

This study included 275 patients with heart failure of NYHA functional class I-III admitted consecutively to the Heart Failure Clinic at the INCMNSZ. Patients who were > 18 years old with HF diagnoses confirmed according the European Society of Cardiology (ESC) criteria through echocardiography (15) and who required hospitalization at baseline were considered as eligible for the study. The exclusion criteria were renal failure, uncontrolled hypothyroidism or hyperthyroidism, liver failure, uncontrolled ischemic heart disease (unstable angina or myocardial infarction, revascularization, angioplasty, coronary artery surgery in the last three months before inclusion), potentially lethal arrhythmias and secondary HF, chemotherapy or suspicious tumor activity or limb amputation.

After the first visit, the patients were included in a study with a prospective cohort design with six months of follow-up. The primary outcome was NYHA functional class deterioration.

BODY COMPOSITION ASSESSMENT

Anthropometry

Weight and height were measured according to an anthropometric standardization manual (16). BMI was calculated by dividing weight (kg) by the square of height (m). Hand strength was measured with a hand dynamometer (Smedley Hand Dynamometer; modified by Stoelting Co., Wood Dale, Illinois, USA), with the patient instructed to apply the most pressure possible with the left hand and then with the right hand. The measurement was repeated twice with each hand, and the higher value was recorded (17).

Bioelectrical impedance

Whole body impedance and multiple frequencies were measured with the BodyStat QuadScan 400 tetrapolar bioelectrical impedance equipment (BOSYSTAT LTD; Isle of Man, UK). All of the measurements were performed by standardized personnel according to the tetrapolar method reported previously (4) in a comfortable area, with the subject fasting and without a metallic object, no exercise or sauna eight hours before the study and no alcohol consumption within the previous 12 hours. Throughout the examinations, all of the subjects had their arms and legs in abduction; in obese subjects, to avoid contact between the thighs, a towel or a pillow was placed between them.

The impedance values were obtained at frequencies of 5, 50, 100 and 200 kHz. Using a frequency of 50 kHz, we obtained resistance (R50), reactance (Xc50) and phase angle using BodyStat Phase Angle software (version 1.0, 2002). This frequency was selected because it is a standard supported BIVA. Additionally, we obtained the total impedance index, which is a body water distribution indicator, by dividing the 200-kHz frequency by the 5-kHz (Z200/Z5) frequency. The total body water and extracellular water were obtained using prediction equations.

CLINICAL DATA

Medications and the patient's comorbidities were recorded at the time of inclusion. We considered clinical deterioration to have occurred when the patient developed fatigue and worsening of the NYHA functional class over the 6-month follow-up. Moreover, the development of edema was reported when clinically apparent. The clinical evaluations were performed by a cardiologist who was blinded to the body composition evaluation results.

STATISTICAL ANALYSIS

Quantitative variables are expressed as the mean and standard deviation (±), and categorical variables are expressed as relative and absolute frequencies. The Kolmogorov-Smirnov test was used to confirm that all data were normally distributed. To differentiate the baseline between the two groups, one with functional class deterioration and the other without deterioration, Student's t test was performed for independent samples with quantitative continuous variables, and the Chi-square test was performed for categorical variables. After two follow-up measurements, we compared the study groups using the Chi-square test. For this analysis, the percentages changed, and the patients were subsequently classified according to whether or not they exhibited a > 5% change in body composition measurements. Furthermore, logistic regression analysis was performed to determine the changes in body composition that were associated independently with NYHA functional class deterioration. A p-value < 0.05 was considered to be statistically significant. The analysis was performed with the SPSS software, version 17 (SPSS for Windows, Rel 10.0 1999 Chicago, IL, USA, SPSS Inc.).

RESULTS

Six months after tracking the 275 patients included in the study, 66 (24%) exhibited NYHA functional class deterioration.

Table I presents the baseline characteristics and pharmacological treatments of the patients as well as the most frequent comorbidities (dyslipidemia and hypertension). Subjects with impairment exhibited a greater likelihood of having type 2 diabetes mellitus, dyslipidemia, fluid overload according to the RXc graph, and a larger diastolic diameter of the left ventricle, although the differences in the last three variables were not statistically significant. We did not observe statistically significant differences between the groups with respect to pharmacological treatment.

The comparison of the baseline characteristics of body composition between the groups appears in table II and indicates no differences between the two groups in weight loss percentage (0.9 ± 7.8% *vs* 0.2 ± 6%, p = 0.45) in subjects with or without functional deterioration. In contrast, we observed associations between deterioration and parameter changes in body composition as assessed by BIA, with a greater proportion of patients exhibiting decreases of more than 5% in resistance and thus an increase of more than 5% in extracellular body water, greater development of hypervolemia according to the RXc graph and clinical edema, although this outcome was not statistically significant (Table III). Additionally, we observed that the patients did not experience functional class deterioration until increases occurred in the phase angle (5.5% *vs* 1.5%) and in the reactance above the height (8.8% *vs* 1.3%).

In this logistic regression model, the variables were associated in bivariate analysis with functional class deterioration: decrease > 5% in resistance/height was the only statistically significant result.

DISCUSSION

In the current study, we detected an association of worsening functional class with a decrease in resistance, coinciding with the increase in extracellular body water and/or hypervolemia development on the RXc graph because less resistance indicates a decrease in the opposition to alternating current through intra- and extracellular ionic solutions. These results are similar to those showed by Hui-Liu, who demonstrated that patients with volume overload are related to worse NYHA functional class (10). Furthermore, despite these changes in fluids, there were no important variations in weight, nor were the differences statistically significant between groups with or without functional class deterioration, consistent with the outcomes reported by Cotter et al., who compared two groups of patients initially diagnosed with chronic HF: one of these groups consisted of patients whose clinical status changed from chronic to acute, whereas the other group did not experience this change. The authors found that the weight gain was not different between groups until it was approximately 2 kg. These results suggested that volume overload occurs in the form of pulmonary congestion caused by fluid reassignment and

Table I. Baseline characteristics of heart failure patients according to NYHA functional class deterioration

Variables	NYHA deterioration n = 66	Non-NYHA deterioration n = 209	p-value
Age (years)	59.6 ± 16	61.4 ± 17	0.45
Male (%)	54.5	53.1	0.84
Ischemic etiology (%)	57.1	50.3	0.41
Dyslipidemia (%)	81.8	71.9	0.14
Hypertension (%)	70.8	70.2	0.9
Diabetes mellitus (%)	56.1	40.4	*0.02*
Hypothyroidism (%)	19.7	19.2	0.9
Nephropathy (%)	19.7	22.1	0.7
NYHA functional class:			
I	68.3	52.6	0.05
II	27.0	34.4	
III	4.8	12.9	
Edema (%)	48.5	46.6	0.8
Hypervolemia on RXc graph (%)	44.4	34.2	0.14
EFLV (%)	42.7 ± 16	45.2 ± 16.5	0.33
DDLV (mm)	52.3 ± 8.6	49.9 ± 8.8	0.07
SDLV (mm)	37.2 ± 9.7	36.2 ± 10.9	0.6
IVS (mm)	11.4 ± 3.0	11.6 ± 2.8	0.7
PWLV (mm)	10.6 ± 2.2	10.7 ± 2.3	0.7
LAD (mm)	43.7 ± 6.0	44.3 ± 7.3	0.6
SPLA (mm Hg)	58.8 ± 14.5	58.5 ± 17.8	0.9
Beta blockers (%)	87.9	84.1	0.45
ACEI (%)	30.8	34	0.63
BAMR (%)	68.2	67.1	0.88
Thiazide diuretics (%)	40.9	46.4	0.44
Loop diuretics (%)	34.8	30.9	0.55
Oral nitrates (%)	28.8	35.3	0.33
AMR (%)	68.2	65.5	0.69

EFLV: Ejection fraction of the left ventricle; DDLV: Diastolic diameter of the left ventricle; SDLV: Systolic diameter of the left ventricle; IVS: Interventricular septum; PWLV: Posterior wall of the left ventricle; LAD: Left atrial diameter; SPLA: Systolic pressure of the lung artery; ACEI: Angiotensin-converting enzyme inhibitors; BAMR: Blockers of antagonists of mineralocorticoid receptor; AMR: Antagonist of mineralocorticoid receptors. Data are expressed as medians ± standard deviations or as percentages.

not properly by accumulation (18). Therefore, edema detection in these patients might not indicate liquid excess but liquid redistribution.

These findings are important if we consider that American and European guidelines recommended daily weight monitoring because changes in body fluids over a short period of time can be detected by weight gain of more than 2 kg in three days, which is associated with functional class deterioration or HF. However, worsening can occur without weight changes, and an excessive use of diuretics can cause vascular volume depletion and dehydration (19,20). Another limitation of weight change assessment is that it does not detect changes in different body compartments, such as musculoskeletal depletion accompanied by volume overload, hypoalbuminemia or intravenous fluids, without variations in weight (21). Additionally, weight loss could be caused by water decreases after treatment with diuretics and not necessarily by the depletion of lean or fat mass.

Patients with HF usually have water displacement into the extravascular space and interstitial space; for example, lung edema develops without body weight changes and can mask the loss of chemical and cellular compounds. Furthermore, depletion of the body protein reserves causes a greater increase in the extracellular water volume, so it is difficult to assess free fat mass (22). Therefore, without assessing the fluid variation, treatment with diuretics cannot be indicated without reincorporating the intravascular space. Bioelectrical impedance can be a very useful and

Table II. Baseline anthropometric composition of heart failure patients according to NYHA functional class deterioration

Variables	NYHA deterioration n = 66	Non-NYHA deterioration n = 209	p-value
Height (cm)	157.7 ± 9.9	157.5 ± 10.2	0.84
Weight (kg)	72.3 ± 24.9	69.2 ± 17.3	0.30
BMI (kg/m^2)	28.6 ± 7.8	27.8 ± 5.9	0.35
Resistance (ohms)	530.2 ± 109.1	536.1 ± 105.1	0.70
Reactance (ohms)	46.0 ± 12.1	47.8 ± 13.1	0.30
R/H (ohms/m)	338.0 ± 80.9	343.0 ± 78.9	0.70
Xc/H (ohms/m)	29.0 ± 7.8	30.7 ± 8.8	0.20
Phase angle (°)	5.0 ± 1.2	5.1 ± 1.2	0.47
Total body water (L)	36.6 ± 9.7	35.8 ± 7.9	0.47
Extracellular water (L)	16.4 ± 3.7	16.1 ± 2.9	0.53

R/H: resistance/height; Xc/H: reactance/height. Values are expressed as medians ± standard deviations.

Table III. Changes from baseline at six months in bioelectrical impedance according to NYHA functional class deterioration

Variables	NYHA deterioration n = 66	Non-NYHA deterioration n = 209	p-value
Increase in ECW > 5%	23.6	13.4	0.06
Resistance/height decrease > 5%	37.7	23.2	*0.02*
Resistance and reactance/height decrease > 5%	24.2	13.9	*0.04*
Hypervolemia development on RXc graph	41.3	28.4	*0.05*
Clinical edema development	13.6	6.7	0.08

ECW: extracellular water. Values are expressed as subject percentages.

Table IV. Logistic regression to determine associations with functional class NYHA deterioration

Variables	Exp (β)	Confidence interval	p-value
Diabetes (yes/no)	2.11	1.1-4.1	*0.03*
DDLV (mm)	1.03	0.99-1.07	*0.07*
Age (years)	0.99	0.97-1.0	*0.24*
Resistance/height decrease > 5% (yes/no)	1.42	1.01-2.0	*0.04*

DDLV: diastolic diameter of the left ventricle.

sensitive method clinically. This usefulness was emphasized by Sergi, who analyzed body water distribution in elderly adults with HF and indicated that extracellular water measurements compared with total body water could more accurately predict the presence of edema (23).

The results of the present research support the need for an integral compartment study conducted in an objective manner. Subjective measurements could not identify these mechanisms; thus, we proposed the evaluation of extracellular water in clinical practice.

Moreover, ESC guidelines for the diagnosis and treatment of patients with HF suggest that initial symptoms and signs are essential for the early detection of disease. However, the guidelines also recognize that these data are difficult to be interpreted, in both elderly and obese patients. Therefore, in this study, we attempted to provide tools to help clinical teams quickly and accurately identify the manifestations of illness to prevent functional class deterioration.

LIMITATIONS

The incidence of articular fibrillation was not considered in these patients, which is remarkable because articular fibrillation is an independent factor in deterioration. Nonetheless, in this case, redistribution (i.e., lung congestion) was attributable to a change in weight, and the absence or appearance of edema could explain clinical deterioration. We recommend longer follow-up periods and a larger sample size to obtain more conclusive results.

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