


# The role of bioimpedance analysis in overweight and obese patients with acute heart failure: a pilot study

Ana Venegas-Rodríguez<sup>1</sup> , Ana María Pello<sup>1\*</sup>, Marta López-Castillo<sup>1</sup>, Mikel Taibo Urquía<sup>1</sup>, Jorge Balaguer-Germán<sup>1</sup>, Alicia Munté<sup>2</sup>, Guillermo González-Martín<sup>3</sup>, Sol María Carriazo-Julio<sup>3</sup>, Juan Martínez-Milla<sup>1,4</sup>, Andrea Kallmeyer<sup>1</sup>, Óscar González Lorenzo<sup>1</sup>, Hans Paul Gaebelt Slocker<sup>1</sup>, José Tuñón<sup>1,2</sup>, Emilio González-Parra<sup>2,3</sup> and Álvaro Aceña<sup>1,2</sup>

<sup>1</sup>Department of Cardiology, IIS-Fundación Jiménez Díaz, Avda. Reyes Católicos, 2, Madrid, 28040, Spain; <sup>2</sup>Universidad Autónoma de Madrid, Ciudad Universitaria de Cantoblanco, Madrid, 28049, Spain; <sup>3</sup>Department of Nephrology, IIS-Fundación Jiménez Díaz, Avda. Reyes Católicos, 2, Madrid, 28040, Spain; and <sup>4</sup>Centro Nacional de Investigaciones Cardiovasculares (CNIC), C. de Melchor Fernández Almagro, 3, Madrid, 28029, Spain

## Abstract

**Aims** Residual congestion at the time of hospital discharge is an important readmission risk factor, and its detection with physical examination and usual diagnostic techniques have strong limitations in overweight and obese patients. New tools like bioelectrical impedance analysis (BIA) could help to determine when euvoalaemia is reached. The aim of this study was to investigate the usefulness of BIA in management of heart failure (HF) in overweight and obese patients.

**Methods and results** Our study is a single-centre, single-blind, randomized controlled trial that included 48 overweight and obese patients admitted for acute HF. The study population was randomized into two arms: BIA-guided group and standard care. Serum electrolytes, kidney function, and natriuretic peptides were followed up during their hospital stay and at 90 days after discharge. The primary endpoint was development of severe acute kidney injury (AKI) defined as an increase in serum creatinine by >0.5 mg/dL during hospitalization, and the main secondary endpoint was the reduction of N-terminal pro-brain natriuretic peptide (NT-proBNP) levels during hospitalization and within 90 days after discharge. The BIA-guided group showed a remarkable lower incidence of severe AKI, although no significant differences were found (41.4% vs. 16.7%;  $P = 0.057$ ). The proportion of patients who achieved levels of NT-proBNP < 1000 pg/mL at 90 days was significantly higher in the BIA-guided group than in the standard group (58.8% vs. 25%;  $P = 0.049$ ). No differences were observed in the incidence of adverse outcomes at 90 days.

**Conclusions** Among overweight and obese patients with HF, BIA reduces NT-proBNP levels at 90 days compared with standard care. In addition, there is a trend towards lower incidence of AKI in the BIA-guided group. Although more studies are required, BIA could be a useful tool in decompensated HF management in overweight and obese patients.

**Keywords** Bioimpedance analysis; Obesity; Heart failure; Natriuretic peptides; Acute kidney injury

Received: 18 November 2022; Revised: 9 April 2023; Accepted: 2 May 2023

\*Correspondence to: Ana María Pello, Department of Cardiology, IIS-Fundación Jiménez Díaz, Avda. Reyes Católicos, 2, 28040 Madrid, Spain.

Email: [ampello@quironsalud.es](mailto:ampello@quironsalud.es)

## Introduction

Heart failure (HF) is a global pandemic affecting more than 64 million people worldwide and is increasing in prevalence due to aging of the population, improved treatment of, and the availability of effective evidence-based therapies, prolonging life in patients with HF.<sup>1</sup> One of the major challenges in HF lies in decreasing readmission rates,<sup>2</sup> which are usually driven

by residual pulmonary or systemic congestion. Therefore, decongestion is considered a primary goal of acute therapy,<sup>3</sup> and knowing when euvoalaemic state is reached is essential. Commonly used methods to assess congestion such as clinical and radiographic examinations have high inter-observer variability and may not correlate well with the presence of congestion,<sup>4</sup> particularly in obese patients. Obesity may mask signs of oedema and make difficult the auscultation during

physical examination, and it also diminishes the image quality of echocardiograms and chest radiographs. Furthermore, the use of circulating biomarkers for myocardial stiffness like BNP and N-terminal pro-brain natriuretic peptide (NT-proBNP) is compromised in obese patients as their levels tend to be lower.<sup>5</sup>

This question has become increasingly relevant because the number of overweight and obese adults has increased dramatically in recent years; indeed, obesity is now a global epidemic.<sup>6</sup> People with obesity are at risk for developing HF<sup>7</sup>; consequently, the burden of HF is projected to rise. For this reason, new diagnostic techniques have emerged in response to the need to provide reliability in the diagnosis of HF in obese patients.

Bioelectrical impedance analysis (BIA) is a non-invasive, inexpensive, and reproducible property-based method to estimate body mass and water composition.<sup>8,9</sup> Its fundamental principle relies on bioimpedance, which is a body's electrical resistance measured using an alternating current.<sup>10</sup> The evaluation of the body composition performed by BIA has been validated in kidney, liver, and heart diseases.<sup>11</sup> Previous studies have demonstrated the utility of BIA as a supplementary tool in the diagnostic algorithm of acute decompensated heart failure (ADHF), providing a useful insight in the detection of peripheral congestion.<sup>11,12</sup> Fluid overload assessed by BIA has been well correlated with plasma concentrations of BNP, so the combined use of both BIA and BNP improves the management of patients visiting the emergency department (ED) because of acute respiratory distress, allows a faster and more accurate diagnosis, and supports physicians' decisions about diuretic therapy.<sup>13</sup> Nevertheless, the role of BIA in overweight and obese patients with HF has not been already assessed.

The aim of this study was to evaluate the usefulness of BIA compared with standard group to detect congestion and as a valid guide in the management of diuretic treatment in overweight and obese patients hospitalized for ADHF. For this objective, we analysed if BIA has impact to reduce acute kidney injury (AKI) rates during hospitalization and NT-proBNP levels measured within 90 days after discharge and then if BIA could reduce short-term adverse events including rehospitalizations for HF, deaths from any cause, or visits to the ED because of congestion symptoms.

## Methods

This study was designed as a single-centre, single-blind, randomized controlled trial conducted at the Fundacion Jimenez Diaz Hospital (Madrid, Spain) from February 2019 to December 2021. It is a pilot study that has the objective of obtaining significant results in order to conduct a major research in the future with the purpose of including broadly the use of BIA in

HF management. This study was approved by an institutional review committee, and all patients provided written informed consent. The research reported in this paper adhered to the Declaration of Helsinki guidelines, and the protocol is registered under the unique identifier NCT05541068.

## Patients

We included 48 patients older than 18 years, who were hospitalized for ADHF (first episode or decompensation), based on Framingham criteria and/or NT-proBNP > 300 pg/mL, and with a body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> at admission. Patients were excluded if they had any of the following: haemodynamic instability, chronic kidney disease with estimated glomerular filtration rate < 15 mL/min/1.73 m<sup>2</sup>, pregnancy, amputated patients, chronic treatment with corticosteroids, severe valvular heart disease with indication for intervention, dementia, or life expectancy of 1 year or less with high probability for non-compliance with the study protocol.

Sample size could not be formally calculated due to the lack of prior research studies that compared outcomes in this kind of population depending on a standard or BIA-guided group. Based on the number of patients with the characteristics mentioned above hospitalized in our centre the previous months, the estimated sample size was initially of 150 patients. However, the insult of the coronavirus disease-2019 (COVID-19) pandemic enforced an interruption of the enrolment of patients in each of the different COVID-19 waves and was probably responsible for a slow recruitment compared with that expected.

## Study protocol

All patients included in the study were measured weight and height at admission, and blood tests with haemogram and serum biochemistry including cardiac biomarkers such as NT-proBNP and troponin I were also ordered.

In the first 24 h after admission, an echocardiogram and a BIA were done in all patients. BIA was always performed by nephrologists from our hospital not involved in the patient's clinical care. The duration of the test was <5 min, and the only requirement before starting the analysis was to enter the patient's weight and height of that day. BIA analysis was performed with the portable Biomass touch i8 (Maltron International, Essex, UK), which provided many parameters about body composition such as body cellular mass, extracellular mass, fat-free mass, intracellular water, extracellular water, total body water ..., and the highlighted 'dry weight', which was the parameter used to guide therapy. During the hospitalization period, blood parameters were measured according to the standard clinical practice in all patients, with

the condition of taking a blood chemistry including NT-proBNP on the day of discharge.

All patients were followed up for 90 days with a new complete blood test including NT-proBNP.

Eligible patients were randomized into two groups (Figure 1):

- Group I (study arm) included 24 patients who received a diuretic treatment guided by BIA. Estimated dry weight by BIA was written down in the patient's medical record by the nephrologist who performed this method, in such manner that physicians involved in the care of this group could see the results of BIA. These patients were discharged when dry weight estimated by BIA ( $\pm 0.5$  kg) was achieved if there was no clinical condition that justified the hospitalization.
- Group II (control arm) included 24 patients who received the standard group. In those patients, BIA parameters were not known by the physician responsible of the patient. These patients were discharged when they achieved the euvoaemic state based in the criteria of their physician.

The randomization was performed sequentially in such a way that odd-numbered patients were included in the BIA-guided group and that even-numbered patients were included in the standard group.

## Outcomes

Given the pilot nature of the study, we looked for a feasible, clinically meaningful, in-hospital outcome. Develop-

ment of AKI during hospitalization, defined as an increase in serum creatinine by  $>0.5$  mg/dL [Acute Kidney Injury Network (AKIN) classification stage III], was the primary outcome.<sup>14</sup> Patients were followed for at least 3 months after discharge.

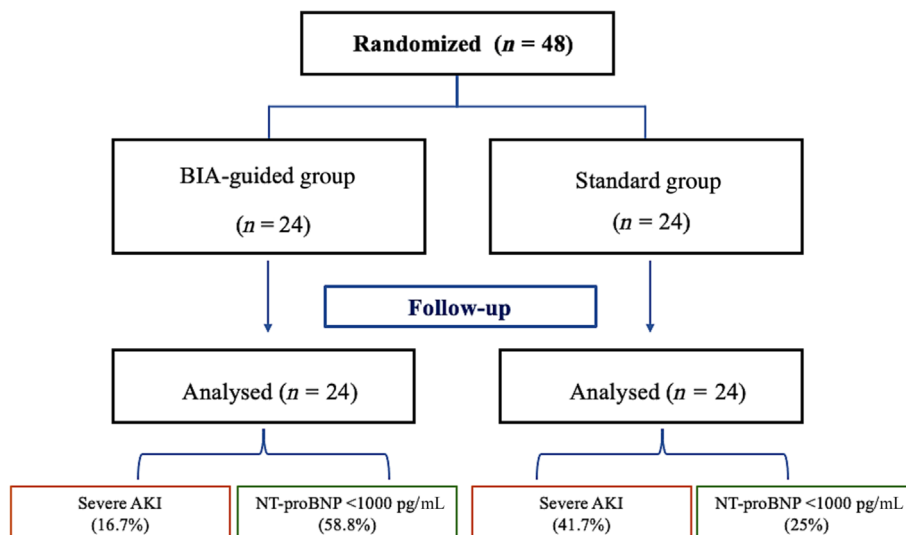
The first secondary outcome was the percentage of patients who achieved levels of NT-proBNP  $< 1000$  pg/mL within 90 days after discharge. The cut-off of 1000 pg/mL was selected based on previous studies, suggesting an inflection point in the risk curve at this concentration.<sup>15–17</sup>

Additional secondary outcomes included length of stay in hospital, NT-proBNP reduction  $> 30\%$  during hospitalization, and the combined endpoint of all-cause death, rehospitalization for HF, or visit to the ED because of congestion symptoms measured at 90 days after discharge. Patients were contacted by telephone or returned for hospital or outpatient visits.

## Statistical analysis

Discrete variables were summarized as counts and percentages. Continuous variables were described using median and interquartile range and were tested for normality using the Kolmogorov–Smirnov or Shapiro–Wilk test. Baseline characteristics were compared among standard group vs. BIA-guided group with the  $\chi^2$  test or Fisher's test for discrete variables and with Student's *t*-test and non-parametric Mann–Whitney's test for normally and non-normally distributed quantitative variables, respectively. Primary and secondary outcomes were also compared between both treatment groups using a  $\chi^2$  test for independence. Results of these analyses were considered exploratory to study future differ-

**Figure 1** CONSORT flow diagram. AKI, acute kidney injury; BIA, bioelectrical impedance analysis; NT-proBNP, N-terminal pro-brain natriuretic peptide.



ences between the groups in terms of time to first adverse outcome or event-free survival. A two-sided *P* value of <0.05 was considered to be statistically significant for all analyses. All statistical analyses were performed using SPSS for Windows Version 19.0 (IBM Corp., Armonk, NY, USA).

## Results

### Baseline characteristics

A total of 48 patients were randomized 1:1 to receive standard clinical treatment (*n* = 24) vs. BIA-guided group (*n* = 24). Baseline characteristics are presented in *Table 1*. The median age of all patients was 75 years (range 62–81.75), 60.4% were men, and median BMI was 31.9 kg/m<sup>2</sup> (range 29.4–34.4). There was a high prevalence of cardiovascular risk factors: 79.2% of patients had hypertension, 66.7% dyslipidaemia, and 37.5% diabetes. Almost half of the patients (43.4%) had been previously admitted to the hospital for HF and 40.8% had left ventricular ejection fraction ≤ 40% evaluated by echocardiogram. The BIA-guided and standard groups were similar in baseline demographic

and clinical characteristics and also in haemogram and serum biochemistry parameters measured at admission. There were also no significant differences in medication before admission between both groups, with the exception of a higher percentage of patients taking angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in the standard group (91.7% vs. 58.3%; *P* = 0.008). The median value of hospital length of stay was 6 days (4–8.75). There were no statistically significant differences between both groups; median leg of stay was 6 (4–10) days in the standard group and 5 (3.25–7) days in the BIA-guided group (*P* = 0.355).

The differences between discharge weight and admission dry weight estimated by BIA in both groups are presented in *Figure 2*. There was a difference of −0.2 kg (−1.5 to +0.4 kg) in the BIA-guided group; however, the difference was of −1.3 kg (−4.9 to +0.02 kg) in the standard group. These results show a tendency towards less weight loss during hospitalization in management of patients guided by BIA, but not statistically significant (*P* = 0.172). An increase in loop diuretics dosage was observed in both groups at discharge, without significant differences between both groups of treatment. The median increase in the dose of furosemide taken orally between discharge and admission was 40 mg (range 5–55 mg) in the BIA-guided group vs. 40 mg (range

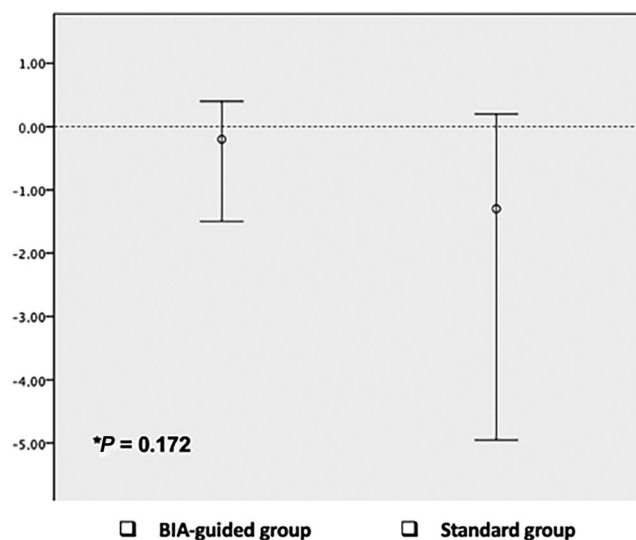
**Table 1** Baseline characteristics of patients

	BIA-guided group ( <i>n</i> = 24)	Standard group ( <i>n</i> = 24)
Median age (years)	69 (59–83)	75 (69.7–81)
Male sex	14 (58.3)	15 (62.5%)
BMI > 30 kg/m <sup>2</sup>	19 (79.2)	15 (62.5%)
Cardiovascular risk factors		
Diabetes	9 (37.5)	9 (37.5)
Hypertension	18 (75)	20 (83.3)
Current or former smoker	11 (45.8)	9 (37.5)
Dyslipidaemia	14 (58.3)	18 (75)
Previous medical condition		
Myocardial infarction	4 (16.7)	6 (25)
Atrial fibrillation	11 (45.8)	15 (62.5)
LVEF at admission	45 (21.3–60)	45 (25–60)
LVEF ≤ 40%	11 (45.8)	9 (37.5)
Peripheral artery disease	2 (8.3)	2 (8.3)
Stroke	3 (12.5)	0
Chronic pulmonary disease (COPD/OSAS)	8 (33.3)	5 (20.8)
CKD (eGFR < 60 mL/min/m <sup>2</sup> )	4 (16.7)	6 (25)
Home medication		
Beta-blockers	10 (41.7)	16 (66.7)
ACEI/ARB	14 (58.3)	22 (91.7)
ARNI	1 (4.2)	2 (8.3)
MRA	7 (29.2)	5 (20.8)
Diuretics	13 (54.2)	16 (66.7)
Antiarrhythmic drugs	4 (16.7)	7 (29.2)
Cardiac biomarkers at admission		
NT-proBNP (pg/mL)	3310 (1640–5030)	3930 (1980–8100)
Troponin I (ng/mL)	0.02 (0–0.03)	0.02 (0.01–0.05)

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BIA, bioelectrical impedance analysis; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-brain natriuretic peptide; OSAS, obstructive sleep apnoea syndrome.

Categorical variables are presented as counts (percentages), and quantitative variables as median (interquartile range).

**Figure 2** Box plot showing the differences in kilograms between discharge weight and admission dry weight estimated by bioelectrical impedance analysis (BIA) in both treatment groups: BIA-guided and standard group.



**Table 2** HF treatment at discharge

	BIA-guided group (n = 24)	Standard group (n = 24)	P value
Beta-blockers, n (%)	19 (79.2)	18 (75)	0.731
ACEI/ARB, n (%)	17 (68)	22 (91.7)	0.064
ARNI, n (%)	5 (20.8)	5 (20.8)	1
MRA, n (%)	18 (75)	18 (75)	1
Diuretics, n (%)	23 (95.8)	24 (100)	0.312
SGLT2 inhibitors, n (%)	6 (25)	11 (45.8)	0.131

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BIA, bioelectrical impedance analysis; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium glucose cotransporter-2.

20–75 mg) in the standard group ( $P = 0.41$ ). There were also no differences in HF medication at discharge between both groups (Table 2).

## Outcomes

Table 3 summarizes clinical and analytical outcomes of the general population and of each treatment group. There were 14 patients (29.2%) who developed AKI during hospitalization (defined as AKIN stage III). The incidence of AKI was remarkably lower in the group of patients guided by BIA than in the standard group (16.7% vs. 41.7%), being the difference between both groups borderline significant ( $P = 0.057$ ).

Median NT-proBNP levels at discharge and at 90 days of follow-up are described in Table 2. No differences were found between the two treatment groups when analysing the percentage of patients who achieved >30% of NT-proBNP reduc-

tion during hospitalization (86.4% in the BIA-guided group vs. 76.2% in the standard group;  $P = 0.457$ ). Nevertheless, the proportion of patients who reached the target of NT-proBNP value < 1000 pg/mL within 90 days after discharge was significantly higher in the group whose treatment was guided by BIA than in the standard group (58.8% vs. 25%;  $P = 0.049$ ). NT-proBNP levels measured as a continuous variable were also lower at 90 days of follow-up in the BIA-guided group than in the standard group ( $P = 0.047$ ).

The combined secondary endpoint, which was defined including death from any cause, rehospitalization for HF, or visit to the ED because of congestion symptoms measured at 90 days, occurred in only 4 (8.3%) of 48 patients enrolled in the study. There were no significant differences in this combined endpoint between the BIA-guided group (4.2%) and the standard group (12.5%) ( $P = 0.609$ ). The three adverse secondary outcomes in the standard group comprised readmissions for HF ( $n = 2$ ) and a visit to the ED due to congestion symptoms ( $n = 1$ ). Only one subject in the BIA-guided group had a visit to the ED at 90 days after discharge. There were no deaths at 90 days in either group.

## Discussion

The main finding of our study is that the use of BIA to guide diuretic treatment in overweight and obese patients admitted to the hospital because of HF congestion symptoms is related to low natriuretic peptide levels at 90 days after discharge and, also, that there is a tendency for fewer episodes



**Table 3** Outcomes during hospitalization and 90 days of follow-up

	General population (n = 48)	BIA-guided group (n = 24)	Standard group (n = 24)	P value <sup>a</sup>
During hospitalization				
AKI stage AKIN-III, n (%)	14 (29.2)	4 (16.7)	10 (41.7)	0.057
Median NT-proBNP (pg/mL) at discharge	1410 (496–2912.5)	1310 (361.8–2282.5)	1440 (975.8–3982.5)	0.153
At 90 days				
NT-proBNP < 1000 pg/mL, n (%)	20 (42.4)	14 (58.8)	6 (25)	0.049
Median NT-proBNP (pg/mL)	1320 (438.5–3330)	902 (290.5–1910)	2845 (896–5232.5)	0.047
Death from any cause, n (%)	0	0	0	—
HF rehospitalization, n (%)	2 (4.2)	0	2 (8.3)	0.489
Visit to the ED, n (%)	3 (6.4)	1 (4.2)	1 (4.2)	1
Combined endpoint <sup>b</sup> , n (%)	4 (8.5)	1 (4.2)	3 (12.5)	0.609

AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; BIA, bioelectrical impedance analysis; ED, emergency department; NT-proBNP, N-terminal pro-brain natriuretic peptide.

<sup>a</sup>P value of differences among baseline characteristics between the BIA-guided group and the standard group.

<sup>b</sup>Combined endpoint defined as the combination of deaths from any cause, rehospitalizations for HF, and visits to the ED within 90 days after discharge.

of acute renal failure stage III during the hospitalization period.

To the best of our knowledge, the current study is the first to investigate the usefulness and the prognostic importance of BIA in acute HF management in patients with BMI > 25 kg/m<sup>2</sup>.

The evaluation of the body composition performed by BIA has been validated in kidney, liver, and heart diseases.<sup>9</sup> Prior studies have evaluated the additive diagnostic and prognostic value of BIA in HF patients. In patients with HF and preserved ejection fraction, the use of BIA allows the detection of fluid overload and identifies those patients who are at increased risk of cardiovascular events or death.<sup>18</sup> Within the field of emergency medicine, a quantitative evaluation of fluid congestion obtained by BIA in ADHF patients at the time of ED arrival provides a significant additive diagnostic and 30 day prognostic value to BNP, particularly in the BNP 'grey zone'.<sup>19</sup>

Furthermore, BIA has already been compared to traditional diagnostic tests for HF like the inferior vena cava ultrasound, lung ultrasound (LUS), and natriuretic peptides.<sup>20</sup> BIA has been described to be even more accurate than BNP in detecting peripheral congestion in both ADHF and chronic HF patients, and recent studies have reported that the combined use of BNP and BIA has a significant predictive value for 90 days of cardiovascular mortality.<sup>21</sup> Therefore, whereas LUS has already demonstrated its excellent diagnostic value in patients with both acute and chronic HF and represents a useful prognostic tool for predicting adverse outcomes,<sup>22</sup> BIA could also have a place as an additional diagnostic test with the capacity to increase prognostic power in ADHF patients.

In our study, we found that the percentage of patients with NT-proBNP < 1000 pg/mL within 90 days after hospital discharge was significantly higher in the BIA-guided group than in the standard group (59% vs. 25%). The main implication of this finding is that natriuretic peptides are well-known

prognostic biomarkers in HF.<sup>23</sup> Actually, NT-proBNP concentrations above 1000 pg/mL have been reported as a threshold associated with increased risk in HF, and those patients who achieved a fall in NT-proBNP to <1.000 ng/mL have less risk of HF hospitalization and cardiovascular mortality than those who did not.<sup>15–17</sup>

On the other hand, we did not find any differences between both groups in NT-proBNP reduction > 30% during hospitalization. Prior studies have reported the NT-proBNP reduction percentage < 30% during hospitalization as the best cut-off for the identification of patients at risk of events.<sup>24,25</sup> Nevertheless, a strategy of NT-proBNP-guided therapy has not been demonstrated to be more effective than a usual care strategy in improving outcomes.<sup>26</sup> Regarding obese patients, the European practical guidance on the use of natriuretic peptide concentrations proposes the use of lower cut-off concentrations (~50% lower) in these patients and the higher the BMI, the lower the cut-off concentration that provides the highest accuracy.<sup>27</sup>

Focusing on renal function, our data suggest that those patients in which treatment was guided by BIA seem to have a lower risk of AKI during hospitalization. Although this result was not statistically significant ( $P = 0.057$ ), the study population included was certainly small (48 patients), and then we cannot rule out that, by increasing the sample size, patients managed with BIA would show less AKI rates. Prior literature has evaluated the relation between worsening of renal function (WRF) and poorer prognosis in patients with ADHF, finding that WRF alone is not an independent determinant of outcomes in patients with acute HF, whereas it has an additive prognostic value when it occurs in patients with persistent signs of congestion.<sup>28</sup> That has been explained because transient WRF may be due to haemodynamic alterations rather than histological deterioration and, therefore, most of the patients with in-hospital WRF had preserved renal function at 1 year after discharge.<sup>29</sup> However, WRF at 1 year

after hospital discharge for ADHF is a strong predictor of all-cause and cardiovascular death.<sup>30</sup>

Our data show that patients guided by BIA were discharged with lower fluid volume depletion than those in the standard group, which means that patients managed in a standard way were more dehydrated at discharge. Patients' hydration state and dry weight were immediately evaluated by BIA at admission in all patients, and we detected that patients in the standard group had discharge weights further from BIA-estimated dry weight (−1.3 vs. −0.2 kg). A relationship between a more intensive fluid depletion and higher renal failure rates during hospitalization was noticed in our study. In addition, the relation between high diuretics doses and activation of the circulating renin-angiotensin system in patients with symptomatic HF has already been described.<sup>31</sup> For this reason, the use of diuretics should be cautious as they are well known to increase plasma renin activity and it could promote HF progression.

Despite the mentioned favourable results for the BIA-guided group in terms of NT-proBNP levels at 90 days and AKI rates during hospitalization, the low number of adverse outcomes at 90 days, including deaths, rehospitalizations for HF, or visits to the ED due to congestion symptoms, precludes any conclusion regarding the prognostic value of BIA in overweight and obese patients with HF.

Although statistical analysis did not show any significant differences, it can be observed that there is a higher number of absolute adverse events in the standard group. Actually, there were only two readmissions for HF registered in the entire study population and both of them occurred in the standard group. This might indicate that, with a larger sample size, significant differences could have been found. Finally, it is striking that no deaths were noticed in either group. These results are not consistent with what has been described in previous HF registries,<sup>32</sup> in which 1 year all-cause mortality ranged from 15% to 35% in patients with acute HF. This could be explained because of our short follow-up time (90 days) and a small sample size; nevertheless, the median age of our population and the number of comorbidities are similar to the rates described in prior studies,<sup>32</sup> and several trials have described that the highest readmission rates occur during the first 30 days after discharge and that nearly half of HF readmissions occurred before the first ambulatory visit.<sup>33</sup>

Our findings are possibly explained by a lower fluid depletion in patients guided by BIA, which means that these patients were less dehydrated at discharge. However, because of the pilot nature of our study, this hypothesis remains speculative. Definitely, future randomized controlled trials are necessary to clarify whether BIA could provide more accurate evidence of congestion in ADHF patients rather than other more common diagnostic tests and also if the use of BIA could reduce adverse events during follow-up in overweight and obese patients admitted for ADHF.

## Limitations

- The main limitation of our study is that the sample size is small. The estimated sample size was initially going to be larger; however, the insult of the COVID-19 pandemic enforced an interruption of the enrolment of patients in each of the different COVID-19 waves and was probably responsible for a slow recruitment compared with that expected. Consequently, the sample size was smaller than expected and this could be a key factor in the low significance of the results; nevertheless, we would like to emphasize that the findings of the present study should be considered exploratory or hypothesis generating.
- It is important to remark the pilot nature of our study. Our study was designed with the objective to explore a novel intervention in overweight and obese patients admitted for ADHF and with the aim to achieve interesting results in order to conduct a larger multicentre trial about this field in the future with better recruitment strategies and financial support, longer inclusion period, and longer patient's follow-up.
- The sample size was underpowered to detect differences in clinical long-term outcomes such as all-cause death, rehospitalizations due to HF, or visits to the ED. In addition, the incidence of these adverse outcomes was remarkably low in both groups.
- This is a single-centre study that has been developed in only one hospital in Spain, and the follow-up of 3 months is short.
- Our study was designed as a single-blind trial, in which only physicians involved in the care of the patients knew which intervention was received (BIA or standard group). Although we tried to ensure complete independence between physicians involved in the care of Groups I and II, we cannot guarantee that some communications could have taken place between care teams of the two arms, introducing some bias in our results.
- The patients were relatively old and with a higher prevalence of comorbidities in comparison with previous studies. This is typical for patients with obesity and HF. However, these comorbidities, which have not been controlled, could lead to biases.
- Clinical experience with BIA indicates that the estimation of dry weight with this method may show slight variations of approximately  $\pm 1.5$  kg over the hospitalization period. In our study, BIA measurements were performed only once, so we cannot determine if dry weight estimated by BIA would have changed or not.
- Finally, our results in terms of AKI rate during hospitalization and NT-proBNP levels could have been influenced by lower fluid depletion in the BIA-guided group. This could represent a limitation because we accepted dry weight estimated by BIA as the truthful weight, so it could have been involved in a circular reasoning.

## Conclusions

Our results demonstrate that, among overweight and obese patients admitted to the hospital due to HF, the use of BIA reduces NT-proBNP levels at 90 days compared with the standard group. In addition, our study suggests that there is a trend towards lower incidence of AKI during hospitalization in the BIA-guided group. However, larger trials with longer follow-up are needed to validate BIA as a useful tool in the management of overweight and obese patients with acute HF.

## Acknowledgement

This work would not have been developed without the invaluable work of our friend and colleague Juan Martinez Milla

MD PhD, who passed away unexpectedly at the age of 33 years old. He will be deeply missed, but his legacy as a brilliant cardiologist and a formidable person will live on through the impact he made on us all. Rest in peace, dear friend.

## Conflict of interest

The authors declare no conflict of interest.

## Funding

This research received no external funding.

## References

- Savarese G, Becher PM. Global burden of heart failure: a comprehensive and updated review of epidemiology. *Cardiovasc Res*. 2022; **118**: 3272–3287.
- Goldgrab D, Balakumaran K. Updates in heart failure 30-day readmission prevention. *Heart Fail Rev*. 2019; **24**: 177–187.
- Lala A, McNulty SE. Relief and recurrence of congestion during and after hospitalization for acute heart failure: insights from Diuretic Optimization Strategy Evaluation in Acute Decompensated Heart Failure (DOSE-AHF) and Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARESS-HF). *Circ Heart Fail*. 2015; **8**: 741–748.
- Chakko S, Woska D. Clinical, radiographic, and hemodynamic correlations in chronic congestive heart failure: conflicting results may lead to inappropriate care. *Am J Med*. 1991; **90**: 353–359.
- Sergy G, Bussolotto M. Accuracy of bioelectrical impedance analysis in estimation of extracellular space in healthy subject and in fluid retention states. *Ann Nutr Metab*. 1994; **38**: 158–165.
- Hurt RT, Kulisek C. The obesity epidemic: challenges, health initiatives, and implications for gastroenterologists. *Gastroenterol Hepatol (NY)*. 2010; **6**: 780–792.
- Jamaly S, Carlsson L. Heart failure development in obesity: underlying risk factors and mechanistic pathways. *ESC Heart Fail*. 2021; **8**: 356–367.
- Madamanchi C, Alhosaini H. Obesity and natriuretic peptides, BNP and NT-proBNP: mechanisms and diagnostic implications for heart failure. *Int J Cardiol*. 2014; **176**: 611–617.
- Sergi G, Bussolotto M. Accuracy of bioelectrical impedance analysis in estimation of extracellular space in healthy subjects and in fluid retention states. *Ann Nutr Metab*. 1994; **38**: 158–165.
- Nunez J, Mascarell B. Bioelectrical impedance vector analysis and clinical outcomes in patients with acute heart failure. *J Cardiovasc Med*. 2016; **17**: 283–290.
- Parrinello G, Paterna S. The usefulness of bioelectrical impedance analysis in differentiating dyspnea due to decompensated heart failure. *J Card Fail*. 2008; **14**: 676–686.
- Massari F, Iacoviello M. Accuracy of bioimpedance vector analysis and brain natriuretic peptide in detection of peripheral edema in acute and chronic heart failure. *Heart Lung*. 2016; **45**: 319–326.
- Di Somma S, De Berardinis B. Use of BNP and bioimpedance to drive therapy in heart failure patients. *Congest Heart Fail*. 2010; **16**: S56–S61.
- Mehta RL, Kellum JA. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007; **11**: R31.
- Cleland JG, McMurray JJ. Plasma concentration of amino-terminal pro-brain natriuretic peptide in chronic heart failure: prediction of cardiovascular events and interaction with the effects of rosuvastatin: a report from CORONA. *J Am Coll Cardiol*. 2009; **54**: 1850–1859.
- Masson S, Latini R. Prognostic value of changes in N-terminal pro-brain natriuretic peptide in Val-HeFT (Valsartan Heart Failure Trial). *J Am Coll Cardiol*. 2008; **52**: 997–1003.
- Felker GM, Ahmad T. Rationale and design of the GUIDE-IT study: guiding evidence based therapy using biomarker intensified treatment in heart failure. *JACC Heart Fail*. 2014; **2**: 457–465.
- Koell B, Zotter-Tufaro C. Fluid status and outcome in patients with heart failure and preserved ejection fraction. *Int J Cardiol*. 2017; **1**: 476–481.
- Di Somma S, Lalle I. Additive diagnostic and prognostic value of bioelectrical impedance vector analysis (BIVA) to brain natriuretic peptide ‘grey-zone’ in patients with acute heart failure in the emergency department. *Eur Heart J Acute Cardiovasc Care*. 2014; **3**: 167–175.
- Curbelo J, Rodriguez-Cortes P. Comparison between inferior vena cava ultrasound, lung ultrasound, bioelectric impedance analysis, and natriuretic peptides in chronic heart failure. *Curr Med Res Opin*. 2019; **35**: 705–713.
- Santarelli S, Russo V. Usefulness of combining admission brain natriuretic peptide (BNP) plus hospital discharge bioelectrical impedance vector analysis (BIVA) in predicting 90 days cardiovascular mortality in patients with acute heart failure. *Intern Emerg Med*. 2017; **12**: 445–451.
- Coiro S, Rastogi T. How and when to use lung ultrasound in patients with heart failure? *Rev Cardiovasc Med*. 2022; **23**: 198.
- Zile MR, Claggett BL. Prognostic implications of changes in N-terminal pro-B-type natriuretic peptide in patients with heart failure. *J Am Coll Cardiol*. 2016; **68**: 2425–2436.
- Bayés-Genís A, Lopez L, Zapico E. NT-proBNP reduction percentage during admission for acutely decompensated heart failure predicts long-term cardiovascular mortality. *J Card Fail*. 2005; **11**: S3–S8.



25. Verdiani V, Ognibene A. NT-ProBNP reduction percentage during hospital stay predicts long-term mortality and readmission in heart failure patients. *J Cardiovasc Med (Hagerstown)*. 2008; **9**: 694–699.
26. Felker GM, Anstrom KJ. Effect of natriuretic peptide-guided therapy on hospitalization or cardiovascular mortality in high-risk patients with heart failure and reduced ejection fraction: a randomized clinical trial. *JAMA*. 2017; **22**: 713–720.
27. Mueller C, McDonald K. Heart Failure Association of the European Society of Cardiology practical guidance on the use of natriuretic peptide concentrations. *Eur J Heart Fail*. 2019; **21**: 715–731.
28. Metra M, Davison B. Is worsening renal function an ominous prognostic sign in patients with acute heart failure? The role of congestion and its interaction with renal function. *Circ Heart Fail*. 2012; **5**: 54–62.
29. Blair JE, Pang PS. Changes in renal function during hospitalization and soon after discharge in patients admitted for worsening heart failure in the placebo group of the EVEREST trial. *Eur Heart J*. 2011; **32**: 2563–2572.
30. Ueda T, Kawakami R. Worsening of renal function during 1 year after hospital discharge is a strong and independent predictor of all-cause mortality in acute decompensated heart failure. *J Am Heart Assoc*. 2014; **3**: e001174.
31. Francis GS, Benedict C. Comparison of neuroendocrine activation in patients with left ventricular dysfunction with and without congestive heart failure. A substudy of the Studies of Left Ventricular Dysfunction (SOLVD). *Circulation*. 1990; **82**: 1724–1729 PMID: 2146040.
32. Martínez Santos P, Bover Freire R. Mortalidad hospitalaria y reingresos por insuficiencia cardíaca en España. Un estudio de los episodios índice y los reingresos por causas cardíacas a los 30 días y al año. *Rev Esp Cardiol*. 2019; **72**: 998–1004.
33. Desai AS, Stevenson LW. Rehospitalization for heart failure: predict or prevent? *Circulation*. 2012; **126**: 501–506.