ESC HEART FAILURE
ESC Heart Failure 2021; **8**: 4593–4606
Published online 13 October 2021 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.13641

ORIGINAL ARTICLE

Body composition analysis in patients with acute heart failure: the Scale Heart Failure trial

Fiorangelo De Ieso[1,2‡], Markus Reinhold Mutke[1,2‡], Noe Karl Brasier[1], Christina Janitha Raichle[1,3], Bettina Keller[1], Celine Sucker[1], Khaled Abdelhamid[1], Tiziano Bloch[1], Pamela Reissenberger[1], Ladina Schönenberg[1], Sandro Kevin Fischer[1], Jonas Saboz[1], Nora Weber[1], Sabine Schädelin[4], Nicole Bruni[4], Patrick R. Wright[4] and Jens Eckstein[1,2*]

[1]*CMIO Office, University Hospital Basel, Basel, Switzerland;* [2]*Department of Internal Medicine, University Hospital Basel, Petersgraben 4, Basel, 4031, Switzerland;* [3]*Department of Gastroenterology, University Hospital Basel, Basel, Switzerland; and* [4]*Clinical Trial Unit, University Hospital Basel, Basel, Switzerland*

Abstract

Aims In this study, we aimed to investigate whether body composition analysis (BCA) derived from bioelectrical impedance vector analysis (BIVA) could be used to monitor the hydration status of patients with acute heart failure (AHF) during intensified diuretic therapy.

Methods and results This observational, single-centre study involved a novel, validated eight-electrode segmental body composition analyser to perform BCA derived from BIVA with an alternating current of 100 μA at frequencies of 5, 7.5, 50, and 75 kHz. The BCA-derived and BIVA-derived parameters were estimated and compared with daily body weight measurements in hospitalized patients with AHF. A total of 867 BCA and BIVA assessments were conducted in 142 patients (56.3% men; age 76.8 ± 10.7 years). Daily changes in total body water (TBW) and extracellular water (ECW) were significantly associated with changes in body weight in 62.2% and 89.1% of all measurements, respectively (range, ±1 kg). Repeated measures correlation coefficients between weight loss and TBW loss resulted with rho 0.43, $P < 0.01$, confidence interval (CI) [0.36, 0.50] and rho 0.71, $P > 0.01$, CI [0.67, 0.75] for ECW loss. Between the first and last assessments, the mean weight loss was −2.5 kg, compared with the −2.6 L mean TBW loss and −1.7 L mean ECW loss. BIVA revealed an increase in mean Resistance R and mean Reactance X_c across all frequencies, with the subsequent reduction in body fluid (including corresponding body weight) between the first and last assessments.

Conclusions Body composition analysis derived from BIVA with a focus on ECW is a promising approach to detect changes in hydration status in patients undergoing intensified diuretic therapy. Defining personalized BIVA reference values using bioelectrical impedance devices is a promising approach to monitor hydration status.

Keywords Acute heart failure; Diuretic therapy; eHealth; Body composition analysis; Bioelectrical impedance vector analysis; Impedance

Received: 5 May 2021; Revised: 29 July 2021; Accepted: 19 September 2021
**Correspondence to: Prof. Jens Eckstein, MD, PhD, Department of Internal Medicine, University Hospital Basel, Petersgraben 4, 4031 Basel, Switzerland. Tel: +41 61 328 7689; Fax: +41 61 265 5353. Email: jens.eckstein@usb.ch*
The work was performed in the Department of Internal Medicine at the University Hospital Basel, Petersgraben 4, 4031 Basel, Switzerland, being also the institutional affiliation of all authors.
‡These authors contributed equally for a shared first authorship.

Introduction

Heart failure (HF) is the leading cause of hospitalization in Europe and the USA, affecting 26 million people and resulting in an economic burden of $108 billion per year worldwide.[1,2] The mortality rate of patients with HF is reportedly 40.2% over a median follow-up of 2.5 years.[3] Rehospitalization rates reach ~30% during the initial 60–90 days following hospital discharge.[4]

The standard treatment for patients with acute HF (AHF) is intensified diuretic drug therapy.[5] Monitoring cardiac congestion and hydration status is vital for the guidance of intensified diuretic therapy and, in turn, for successful treatment and management of HF. Although numerous

clinical scores, imaging tools, and biological tests are available for ascertaining and quantifying cardiac congestion, none have been suitable for use in all stages of patient management, and only few are non-invasive.[6]

According to the European Society of Cardiology guidelines, in clinical practice, hydration status is mainly assessed by daily body weight measurements with subsequent adaptation of diuretic therapy.[5] However, deriving hydration status from body weight is a broad estimation and has been shown to be inaccurate and ineffective as a single monitoring tool to prevent hospitalization due to AHF, as volume redistribution may change despite a stable body weight.[7,8] This can lead to an inadequate use of diuretics or/and a subsequent risk of significant worsening of HF and renal function. Furthermore, volume overload, oedema, or congestion can correlate with diuretic resistance, complicating therapeutic management of HF.[9]

Intensified diuretic therapy is mainly performed using loop diuretics, which increases urinary excretion of sodium chloride to achieve a decrease in water balance and reduces extracellular water (ECW) in the long term.[10]

Body composition is divided into fat-free mass (FFM) and fat mass. FFM consists of body cell mass, bone mineral, and total body water (TBW) [which comprises intracellular water (ICW) and ECW amounting to 44% and 29% of the body weight, respectively, in euvolaemic humans].[11] Application of an alternating current results in a frequency-dependent impedance to the electrical current as a combination of Resistance R (through ICW and ECW as electrical conductors) and Reactance X_c (capacitive character of cell membranes as electrical condensers).[12] Body composition analysis (BCA) derived from bioelectrical impedance vector analysis (BIVA) is based on the detection of this conduction difference. It is a continuously developed and easy-to-use approach to estimate a patient's hydration status in a rapid, cost-effective, safe, and non-invasive manner.[13]

Body composition analysis has been tested in several conditions with altered hydration status.[14] Correlations between BIVA parameters and biomarkers, such as brain natriuretic peptide (BNP),[15] peripheral congestion,[16] mortality risk, and hospital readmission,[17] have been previously demonstrated. Moreover, novel body composition analysers are increasingly available, reaching new levels of accuracy due to thorough validation and improved equations considering age, sex, and anthropometric measurements.[18]

A reliable, non-invasive approach to monitor the hydration status of patients in clinical practice is sorely lacking. This applies to the management of hospitalized patients with AHF and to outpatients with HF at risk for hospital readmission. In this pilot trial, we investigated BCA derived from BIVA to identify whether it adequately determines alterations in the hydration status of hospitalized patients treated with intensified diuretic therapy.

Methods

Participants

We assessed patients who were admitted to the Department of Internal Medicine at University Hospital Basel due to AHF until hospital discharge or until 1 day after completion of intensified diuretic therapy. We included patients with first diagnosis of AHF as well as with acute on chronic HF. The inclusion criteria comprised patients with AHF who underwent intensified diuretic drug therapy, were aged ≥18 years, and were able to give written informed consent. The exclusion criteria comprised patients with implanted cardiac devices, and major amputations or wounds on the limbs. The patient cohort consisted of haemodynamically stable patients without the need of positive inotropic therapy or mechanical circulatory support.

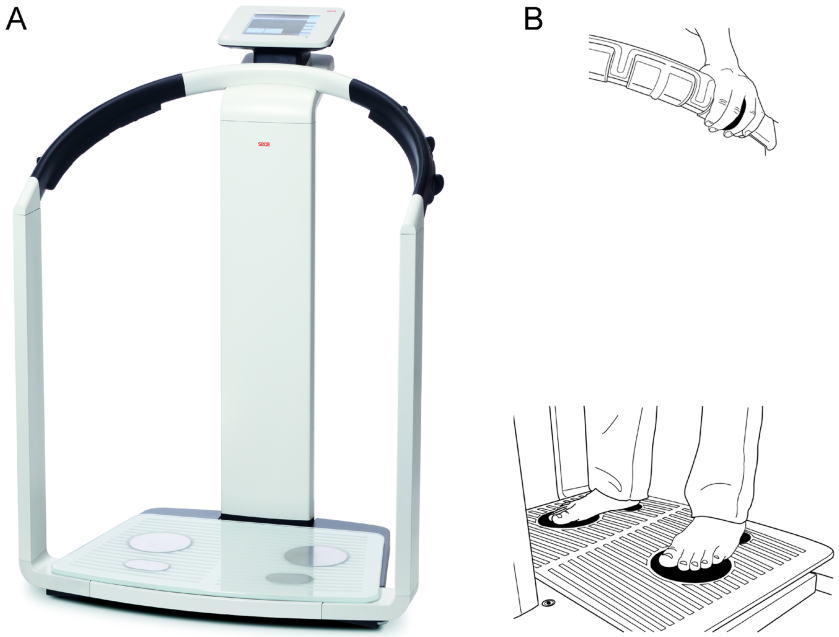
In this prospective, monocentric observational trial, we tested the accuracy of a novel, eight-electrode, segmental, multi-frequency medical whole-body composition analyser (seca® mBCA 515, Hamburg, Germany) (*Figure 1*), previously validated against air displacement plethysmography, whole-body magnetic resonance imaging, densitometry, dual-energy X-ray absorptiometry, and deuterium and sodium bromide dilution.[18] We performed daily BCA of hospitalized patients with AHF during intensified diuretic drug therapy. We investigated the association between the BCA and BIVA parameters, such as TBW, ECW, Resistance R, Reactance X_c, phase angle, body weight, and blood analysis, and routinely assessed echocardiographic parameters and vital signs.

The study protocol complied with the Declaration of Helsinki, was approved by the local ethics committee (EKNZ BASEC 2017-00845), and was registered with ClinicalTrials.gov (NCT03288701). All patients provided written informed consent. The authors declare that all supporting data are available within the article and supporting information.

Body composition analysis derived from bioelectrical impedance vector analysis

Body composition analysis derived from BIVA was performed with an alternating current of 100 μA at frequencies of 5, 7.5, 50, and 75 kHz. The eight-electrode technique ensured segmental impedance measurement of the whole right and left body (r = right, l = left; RB and LB), each arm (RA and LA) and leg (RL and LL), and the torso (TO). The device consisted of a scale embedded into the floor platform in combination with two electrodes for each foot, and a weight-sensitive, handrail system with six electrodes per side, of which two were connected to each hand. Patients stood upright with an ideal 30° anteflexion of the outstretched arms.

Figure 1 Body composition analyser and electrode positions. (A) Body Composition Analyser seca® mBCA 515, Hamburg, Germany. (B) Electrode positions.



Measurements started automatically after all electrodes perceived sufficient contact lasting 20 s.

The body composition analyser calculated TBW and ECW based on the BIVA parameters Resistance R and Reactance X_c by newly developed equations. Regression analyses showing the impact of weight, height, age, and sex were published earlier by the manufacturer.[18] Application of an alternating current results in a frequency-dependent impedance to the electrical current as a combination of Resistance R (through ICW and ECW as electrical conductors) and Reactance X_c (capacitive character of cell membranes as electrical condensers).

Reference values had been previously developed within a healthy population.[19]

To test the body composition analyser in a real-world setting, patients were not required to comply with a specific fasting protocol or specific dietary intake. They also were not sober and did not have to empty the bladder, and it was not paid attention to the fact if they exercised before or not.

Assessment of anthropometric measurements

Body weight was assessed simultaneously with the BCA, with patients wearing underwear and a hospital shirt (0.5 kg). Weight of the hospital shirt was subtracted from the measured weight. Body height was measured prior to the first assessment, and waist circumference was measured at every assessment.

Data management

Baseline demographic details, medical history, and left ventricular ejection fraction (LVEF) were retrieved from the patient records and entered into a secuTrial® database. Data regarding vital parameters, medication, and blood analysis from the clinical information system were retrieved from the hospital data warehouse. The medication ontology tool to assess medication groups has been described earlier.[20] BCA data were exported as csv-files from the seca® analytics 115 software (Version 1.4.786.6282, Hamburg, Germany) and merged based on a unique patient-identifier, including date and time of the measurement.

Statistical analysis

In this study, we aimed to determine whether loss of water (litres) with regard to TBW and ECW (as assessed using BCA) corresponded to loss in body weight (kilograms), which was a valid approach to gain deeper insights into fluid management and guidance of diuretic therapy.

Assuming that the two water loss measurements differed in $<1\%$ of the participants (defined as a difference of ±1 kg compared with weight loss), we calculated that 153 eligible patients should be recruited to estimate the proportion of clinically relevant differences in water loss, with its 95% confidence interval (CI) entirely $<4\%$ and a power of 80%.

Model and method of analysis

We estimated the water and body weight loss at each assessment using the seca® mBCA 515. The two estimates were compared, and the proportion of clinically relevant difference in estimates (±1 kg) was calculated using a logistic model, including a random intercept for each patient to account for the repeated measures in the patients.

The relationship between the equivalence of water loss measurements for TBW and ECW and the following patient characteristics was examined by including them as additional covariates in the main model: sex, height, whether the patient had pleural effusion, LVEF, N-terminal prohormone of BNP (NT-proBNP), sodium, potassium, creatinine, estimated glomerular filtration rate (eGFR), haemoglobin, and haematocrit. For water loss and the BIVA parameters, the difference between the first and last assessments was presented together with its 95% CI based on a paired *t*-test. To assess the association of water loss with weight loss, systolic and diastolic blood pressure, heart rate, Resistance R, Reactance X_c, and phase angle, each measure was assessed using a mixed model. Water loss (since the last measurement), pleural effusion, sex, height, and age were included as a fixed effect. Participant was included as random factor. If it was not possible to measure the TBW or ECW, we considered this to be a failure of the seca mBCA 515. Missing values were not imputed.

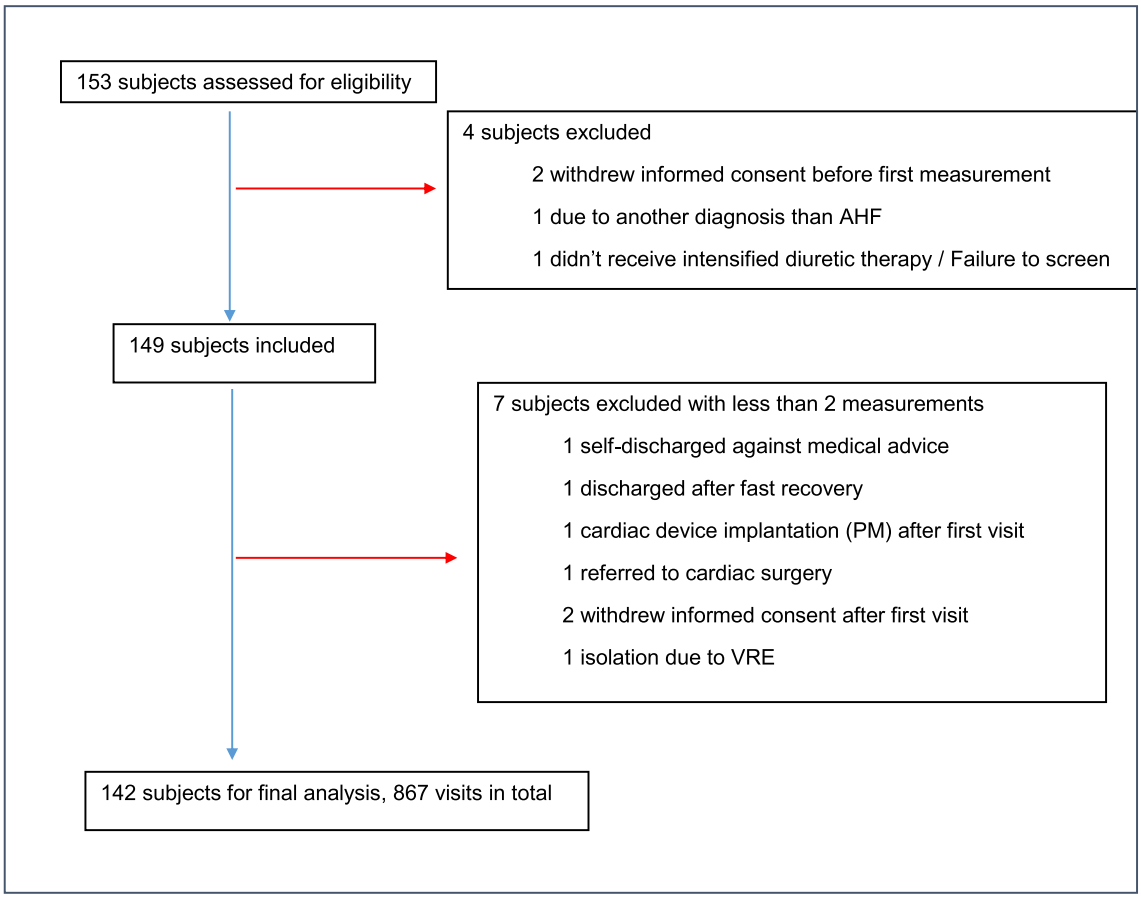
Statistical analysis was performed using R Statistical Software (Version 3.6.2; R Foundation for Statistical Computing, Vienna, Austria).

Results

In total, 153 patients were enrolled between April 2018 and October 2019; among them, 11 were excluded from the final analysis (*Figure 2*). This resulted in 142 patients being included for the main analysis, each with at least two different measurement time points. The total number of assessments was 867, differing between 2 and 26 (median = 5) per patient.

Among all measurements, there were three missing values for ECW and two for TBW in three patients. Patients were assessed within a median of 1 day following hospital

Figure 2 Flow of participants in the Scale Heart Failure trial. AHF, acute heart failure; PM, pacemaker; VRE, vancomycin-resistant enterococci.



admission due to AHF and then daily until hospital discharge or 1 day following the end of intensified diuretic therapy.

Baseline characteristics

Baseline characteristics for the full analysis set are summarized in (*Table 1*). The mean age was 76.8 years (±10.7 years), and 80 patients (56.3%) were male. Only 49 patients (34.5%) were not obese compared with 52 patients (36.6%) with overweight, 28 patients (19.7%) with Obesity Class I, 10 patients (7%) with Obesity Class II, and 3 patients (2.1%) with Obesity Class III. One hundred nine patients presented with acute on chronic HF, whereas 33 (23.2%) showed a new diagnosed AHF. According to the New York Heart Association (NYHA) functional class, 139 patients were assigned to NYHA Class III (42.3%) and NYHA Class IV (55.6%) at hospital admission. The median value of first occurrence of AHF signs before admission to the hospital was 7 days (lower quartile 3; upper quartile 7), with few patients suffering for up to 4 months of symptoms. The most common trigger of AHF was tachyarrhythmia (n = 33; 23.2%) followed by non-adherence with salt/fluid intake or medications, aggravation of a known chronic valvular heart disease (both n = 19; 13.4%), and infections (n = 18; 12.7%). One patient suffered from volume overload due to kidney failure and required dialysis.

A total of 76 (53.5%) patients presented with global, 46 (32.4%) with left-heart, and 20 (14.1%) with right-heart AHF. Ninety-six (67.6%) patients presented with pleural effusion diagnosed by chest imaging at admission (chest X-ray, chest computer tomography, or sonography).

Based on the LVEF, 46 patients had HF with reduced ejection fraction (LVEF $<$ 40%), 25 had HF with mid-range EF (LVEF 40–49%), and 58 with HF with preserved EF (LVEF $\geq$ 50%). The mean LVEF was 45.3 ± 14.0%. In 12 patients, transthoracic echocardiography was not performed during the hospital stay. The mean NT-proBNP at baseline was 4414 ng/L [2417, 8414], ranging from 161 to 50 315 ng/L.

Diuretic medication at baseline

In total, 109 patients received single diuretic therapy, 31 patients received two diuretics, and two patients received three diuretics at baseline. The most frequently administered diuretic at baseline was IV furosemide (intermittent every 8 h; n = 121; average dose 60 mg/day) followed by torasemide PO (5 mg/day, n = 6; 10 mg/day, n = 17; 15 mg/day, n = 1; 20 mg/day, n = 8; 30 mg/day, n = 2; 100 mg/day, n = 2). Spironolactone PO (25 mg/day, n = 13 and 50 mg/day, n = 2), metolazone (5 mg/day, n = 2), eplerenone (25 mg/day, n = 2), and hydrochlorothiazide (25 mg/day, n = 1) were rarely administered.

Vital and laboratory parameters

During intensified diuretic therapy, no significant association was observed between weight/fluid loss and systolic/diastolic blood pressure or heart rate adjusted for LVEF, sex, and age (Supporting Information, *Table S1*). Moreover, there were no clinically relevant changes in haemoglobin, haematocrit, sodium, potassium, creatinine, and urea (Supporting Information, *Table S2*). Therefore, there was no correlation between BCA parameters and markers of the haemoconcentration (Supporting Information, *Table S3*).

New York Heart Association functional class

New York Heart Association class improved after recompensation like shown in *Table 2* to 0 patients in Class IV and with the majority in Class II (n = 75, 52.8%) and Class I (n = 38 patients, 26.8%) but with 20.4% of the patients remaining in Class III due to coexisting conditions at discharge.

Primary outcome

Body composition analysis: changes in hydration status compared with daily weight measurements

As a primary endpoint, the loss of water in the TBW differed (±1 L, corresponding kg) from the relevant loss in body weight (kg) in 37.8% (CI = [33.0, 42.9]) of all daily measurements across all assessments. The loss in ECW differed in 10.9% (CI = [8.1, 14.7]) of all measurements. Therefore, daily changes in TBW and ECW were significantly associated with changes in body weight in 62.2% and 89.1% of all measurements, respectively [*Figure 3(A)*]. Sex, height, pleural effusion, sodium, potassium, creatinine, eGFR, haemoglobin, haematocrit, urea, and LVEF had no influence on the described difference between body weight and water loss (Supporting Information, *Tables S4* and *S5*).

Between the baseline and the last measurement, the mean weight loss in all patients was −2.5 kg, compared with the mean TBW loss of −2.6 L and mean ECW loss of −1.7 L.

The mean body weight decreased from 78.7 ± 18.4 kg at baseline to 76.2 ± 17.6 kg at the last measurement. The TBW and mean ECW decreased from 37.5 ± 9.1 L to 34.9 ± 8.2 L, and 19.1 ± 3.9 L to 17.4 ± 3.3 L, respectively, between the two time points.

Secondary outcome

Bioelectrical impedance vector analysis: Resistance R, Reactance X_c, and phase angle

Bioelectrical impedance vector analysis demonstrated a frequency-dependent increase in mean Resistance R and

Table 1 Baseline characteristics of the study population

	Overall (n = 142)
Age, years	76.8 (±10.7)
Male, *n* (%)	80 (56.3%)
BMI, kg/m^2	28.3 (±5.8)
Normal weight (BMI 18.5–24.9 kg/m^2)	49 (34.5%)
Overweight (BMI 25.0–29.9 kg/m^2)	52 (36.6%)
Obesity Class I (BMI 30.0–34.9 kg/m^2)	28 (19.7%)
Obesity Class II (BMI 35.0–39.9 kg/m^2)	10 (7.0%)
Obesity Class III (BMI $>$ 40 kg/m^2)	3 (2.1%)
Weight, kg	78.6 (±18.4)
Height, m	1.7 (±0.1)
Waist circumference, m	1.0 (±0.1)
Heart failure type, *n* (%)	
Acute on chronic heart failure	109 (76.8%)
New diagnosed (acute) heart failure	33 (23.2%)
Right-sided	20 (14.1%)
Left-sided	46 (32.4%)
Biventricular	76 (53.5%)
New York Heart Association (NYHA) functional class	
Class I	0 (0%)
Class II	3 (2.1%)
Class III	60 (42.3%)
Class IV	79 (55.6%)
First occurrence of acute heart failure signs before hospitalization in days	
Minimum	0
Lower quartile (25%)	3
Median	7
Upper quartile (75%)	7
Maximum	120
Triggering factors of acute heart failure	
Tachyarrhythmia	33 (23.2%)
Aggravation of chronic valvular heart disease	19 (13.4%)
Non-adherence with salt/fluid intake or medications	19 (13.4%)
Infection	18 (12.7%)
Acute coronary syndrome	13 (9.2%)
Excessive rise in blood pressure	12 (8.5%)
Exacerbation of chronic obstructive pulmonary disease	6 (4.2%)
Unclear	6 (4.2%)
Metabolic/hormonal derangements	4 (2.8%)
Surgery and perioperative complications	3 (2.1%)
Drugs	3 (2.1%)
Hypertensive dilated cardiomyopathy	1 (0.7%)
Volume overload due to kidney failure	1 (0.7%)
Acute mechanical cause	1 (0.7%)
Pulmonary embolism	1 (0.7%)
Bradyarrhythmia	1 (0.7%)
Increased sympathetic drive/stress-related cardiomyopathy	1 (0.7%)
HFrEF: LVEF $<$ 40%	46 (35.7%)
HFmrEF: LVEF 40–49%	25 (19.4%)
HFpEF: LVEF $\geq$ 50%	58 (44.9%)
LVEF mean	45.3 (±14.0)
TTE performed, *n* of 142 patients (%)	130 (91.5%)
Pleural effusion, *n* (%)	96 (67.6%)
Coexisting conditions, *n* (%)	
Atrial fibrillation	83 (58.5%)
New diagnosed atrial fibrillation	15 (10.6%)
Paroxysmal atrial fibrillation	29 (20.4%)
Permanent atrial fibrillation	54 (30.0%)
Myocardial infarction	61 (43.0%)
Aortocoronary bypass	24 (16.9%)
Heart valve replacement	12 (8.5%)
PCI/stent	45 (31.7%)
Hypertension	116 (81.7%)
Diabetes mellitus	57 (40.1%)
Peripheral artery disease	27 (19.0%)
Renal failure	93 (65.5%)
Hypothyroidism	26 (18.3%)

(*Continues*)

Table 1 (continued)

	Overall (n = 142)
Hyperthyroidism	8 (5.6%)
Pulmonary embolism	13 (9.2%)
Laboratory results	
Median [lower quart., upper quart.], NT-proBNP, ng/L	4414 [2417, 8414]
Mean (±SD), Na, mmol/L	138.2 (±5.3)
K, mmol/L	4.3 (±0.6)
Creatinine, μmol/L	132.3 (±61.4)
eGFR, mL/min/1.73 m^2	49.1 (±22.0)
Urea, mmol/L	12.3 (±8.1)
Haemoglobin, g/L	122.9 (±26.4)
Haematocrit, L/L	0.4 (±0.1)
Vital parameters	
Systolic blood pressure, mmHg	131.5 (±25.0)
Diastolic blood pressure, mmHg	89.3 (±16.6)
Heart rate, b.p.m.	82.0 (±19.5)
Body composition analysis	
Total body water, L	37.5 (±9.1)
Extracellular water, L	19.1 (±3.9)
Resistance R at 75 kHz, Ω	534.5 (±106.0)
Resistance R at 50 kHz, Ω	545.0 (±108.2)
Resistance R at 7.5 kHz, Ω	586.2 (±118.3)
Resistance R at 5 kHz, Ω	590.0 (±119.5)
Reactance X_c at 75 kHz, Ω	34 (±10.6)
Reactance X_c at 50 kHz, Ω	34.7 (±11.2)
Reactance X_c at 7.5 kHz, Ω	21.2 (±8.3)
Reactance X_c at 5 kHz, Ω	17.8 (±7.0)
Phase angle, °	3.6 (±0.8)

BMI, body mass index; eGFR, estimated glomerular filtration rate; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; K, potassium; LVEF, left ventricular ejection fraction; Na, sodium; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; PCI, percutaneous coronary intervention; SD, standard deviation; TTE, transthoracic echocardiography.

Table 2 Change of different parameters between the first and last visits [see also *Figure 3(B)*]

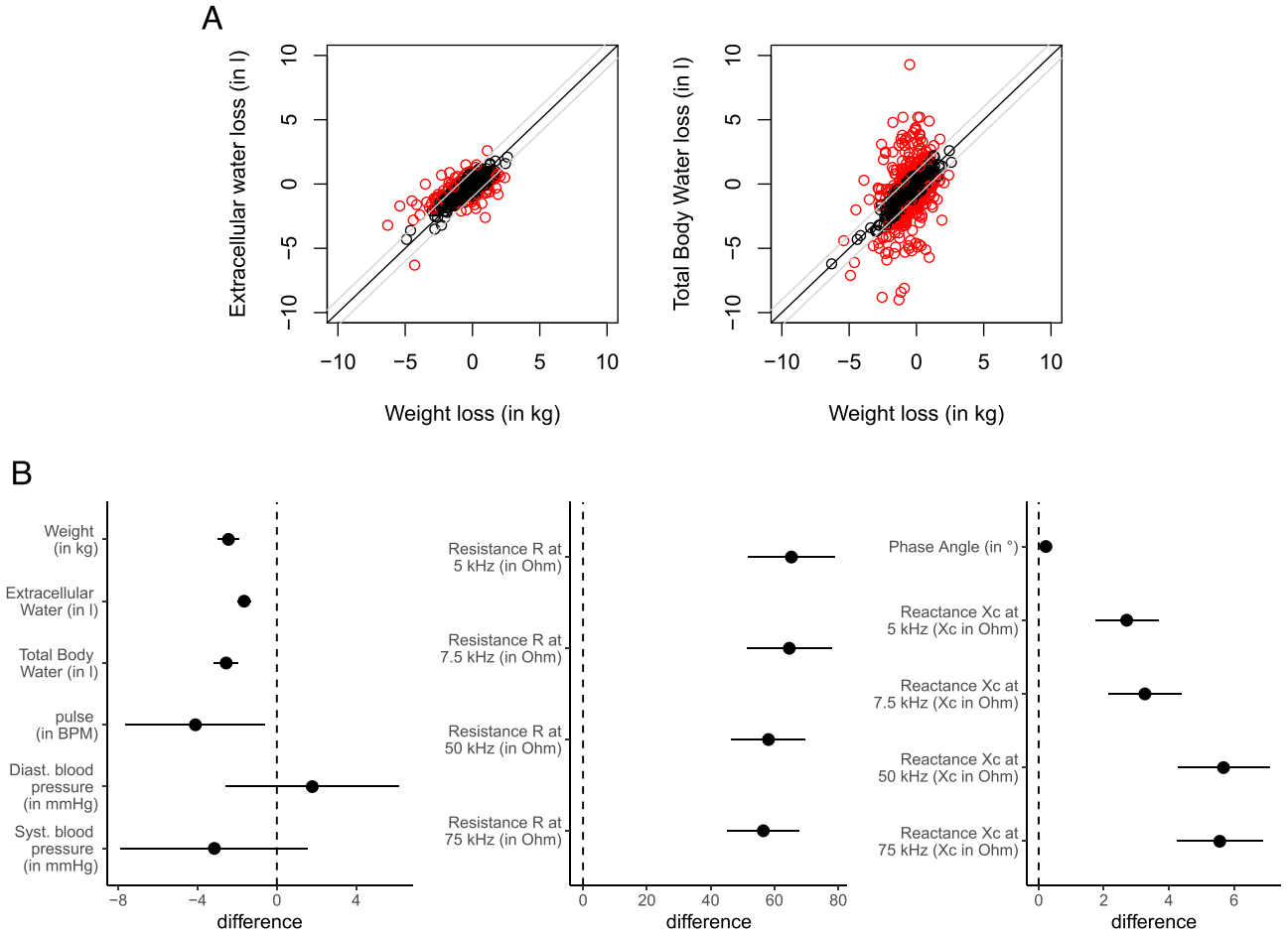
		First visit	Last visit		
NYHA Class	I	0 (0%)	38 (26.8%)		
	II	3 (2.1%)	75 (52.8%)		
	III	60 (42.3%)	29 (20.4%)		
	IV	79 (55.6%)	0 (0%)		
		Mean first visit	Mean last visit	Difference	CI
Weight, kg		78.65	76.21	−2.44	[−2.97, −1.91]
Total body water, L		37.50	34.90	−2.56	[−3.16, −1.95]
Extracellular water, L		19.10	17.43	−1.65	[−1.98, −1.32]
Whole-body Resistance R at 75 kHz, Ω		534.53	591.04	56.51	[45.24, 67.78]
Whole-body Reactance X_c at 75 kHz, Ω		34.03	39.60	5.56	[4.24, 6.89]
Whole-body Resistance R at 50 kHz, Ω		544.98	603.12	58.14	[46.52, 69.76]
Whole-body Reactance X_c at 50 kHz, Ω		34.70	40.38	5.68	[4.27, 7.09]
Whole-body Resistance R at 7.5 kHz, Ω		586.22	650.89	64.66	[51.30, 78.03]
Whole-body Reactance X_c at 7.5 kHz, Ω		21.20	24.46	3.26	[2.14, 4.39]
Whole-body Resistance R at 5 kHz, Ω		590.91	656.24	65.33	[51.72, 78.93]
Whole-body Reactance X_c at 5 kHz, Ω		17.84	20.54	2.70	[1.73, 3.68]
Phase angle, °		3.61	3.83	0.22	[0.15, 0.29]
Systolic blood pressure, mmHg		132.04	128.89	−3.15	[−7.86, 1.56]
Diastolic blood pressure, mmHg		85.48	87.26	1.79	[−2.57, 6.14]
Pulse, b.p.m.		80.79	76.69	−4.11	[−7.63, −0.58]

CI, confidence interval; NYHA, New York Heart Association.

Reactance X_c across all frequencies, with the subsequent reduction in body fluid (including corresponding body weight). There was a higher increase between the first and last measurements in Resistance R at lower frequencies of 5 kHz (+65.33 Ω) and 7.5 kHz (+64.66 Ω), compared with that at 50 kHz (+58.14 Ω) and 75 kHz (+56.51 Ω). Further, measurements at higher frequencies of 50 kHz (+5.68 Ω) and 75 kHz (+5.56 Ω) showed a greater increase in Reactance X_c than

DOI: 10.1002/ehf2.13641

Figure 3 (A) Left: Association between weight loss (in kilograms) and extracellular water loss (in litres). (A) Right: Association between weight loss (in kilograms) and total body water loss (in litres). Red points are measurements that exceed the clinical relevant difference of 1 L (10.9% for extracellular water and 37.8% for total body water). (B) Change of different parameters between the first and last assessments.



that at lower frequencies of 5 kHz (+2.70 Ω) and 7.5 kHz (+3.26 Ω). The mean phase angle increased from 3.61 ± 0.82° to 3.83 ± 0.74° between these two time points [*Figure 3(B)* and *Table 2*].

For example, a decrease in body weight of 1 kg was associated with an increase of +4.83 Ω in Resistance R at 75 kHz, +4.97 Ω at 50 kHz, +5.77 Ω at 7.5 kHz, and +5.88 Ω at 5 kHz. Being male or having pleural effusions was significantly associated with a lower Resistance R and Reactance X_c, whereas height and age showed very small effects on higher Resistance R (Supporting Information, *Figure S1* and *Tables S6–S8*).

Weight loss and corresponding fluid loss had a much lower effect on the increase in segmental Reactance X_c (i.e. weight loss of 1 kg associated with increase of 0.26 Ω at a frequency of 75 kHz in RA). The segmental analysis revealed the weakest effect in the TO segment (Supporting Information, *Tables S9–S16*).

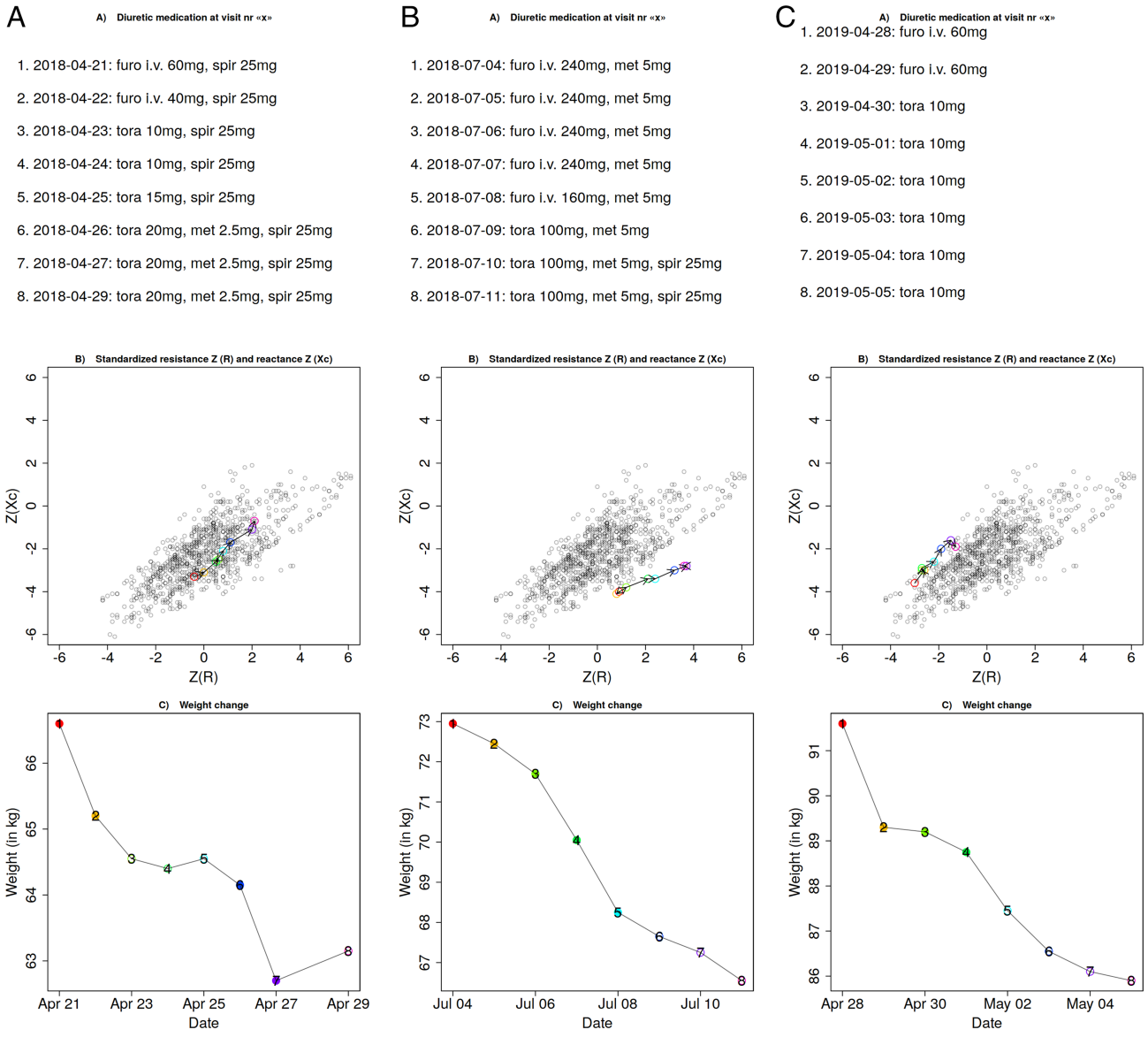
An inverse association in changes between weight loss and the impedance parameters [standardized resistance Z (R) and reactance Z (X_c)] was demonstrated.

Weight/fluid loss resulted in an increase of Z (X_c) and Z (R) during intensified diuretic therapy, with a concomitant increase in the standardized impedance from the left lower area to the right upper area of the BIVA charts [*Figure 4(A)–4(H)*].

Discussion

The BCA derived from BIVA identified significant changes in hydration status at different time points (start, middle, and end) during the intensified diuretic drug therapy. However, the BCA did not reveal a strong correlation between weight loss and measured changes in TBW during the daily measurements in individual patients. Therefore, the primary endpoint

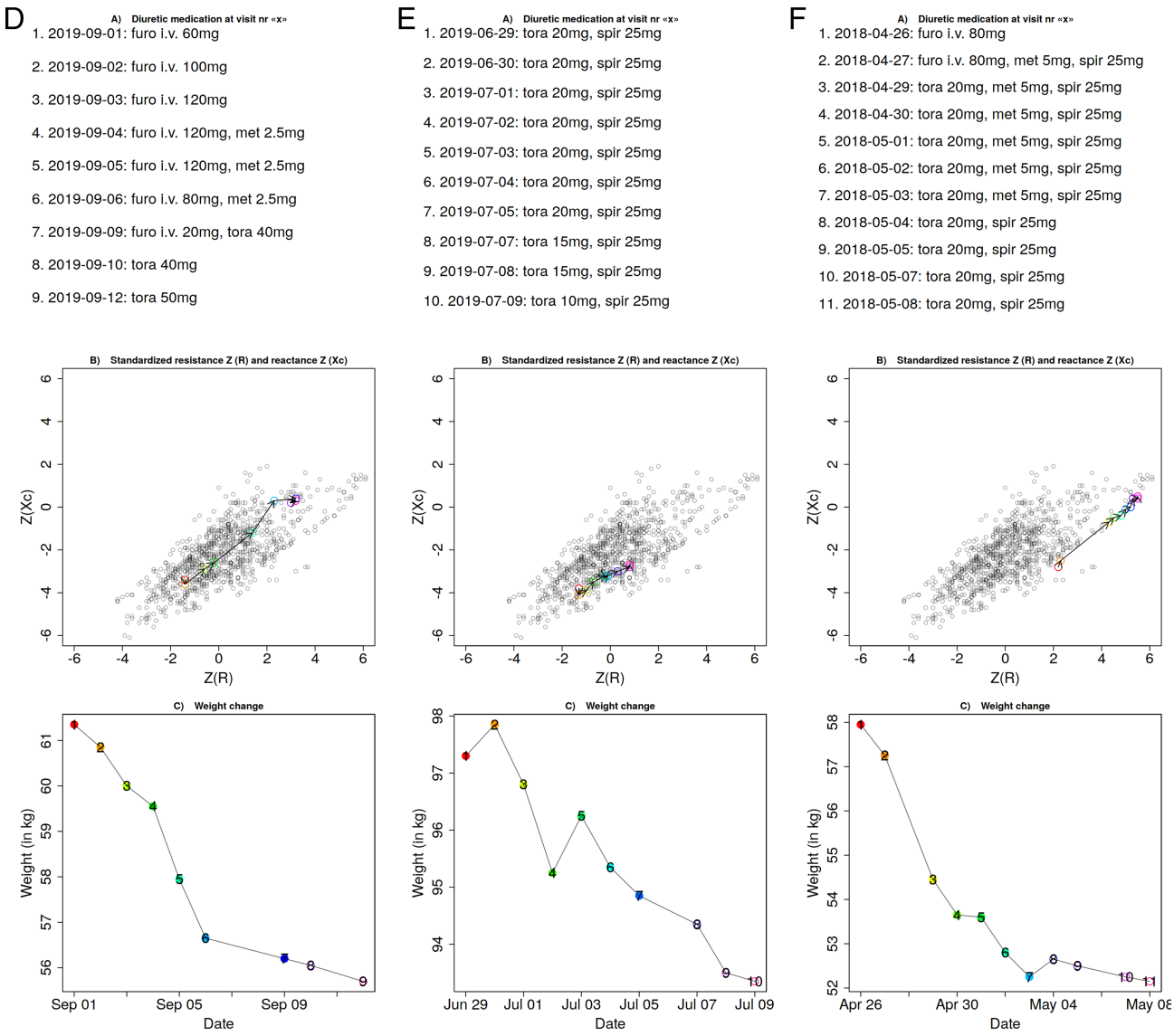
Figure 4 (A–H) Diuretic drugs, weight, and bioelectrical impedance vector analysis [with standardized Resistance Z (R) and Reactance Z (X_c)] during hospitalization in the six patients with the most measurements, ranging from 8 to 26 body composition analysis for each patient. The upper third describes the prescribed diuretic medication during hospitalization, whereas the middle third shows the bioelectrical impedance vector analysis graphs compared with the weight loss in the lower third. furo, furosemide IV; IV, intravenous; met, metolazone PO; PO, per os; Spir, spironolactone PO; tora, torasemide PO.



of the trial, assuming that loss in TBW is mainly correlated to weight loss, was considered to be missing, taking into account that the rate of relevant differences in TBW loss during intensified diuretic therapy across all measurements was 37.8%, compared with weight loss.

However, at the group level, the mean weight loss (−2.5 kg) was strongly associated with the mean TBW loss (−2.6 L) between the baseline and the last measurement at the end of the intensified diuretic drug therapy. Therefore, TBW did not qualify as a hydration status parameter during intensified diuretic therapy for monitoring cardiac congestion. ECW proved to be the most accurate parameter for rapid hydration status changes in daily individual measurements during intensified diuretic therapy, with a 10.9% rate of relevant differences in ECW loss across all visits, compared with weight loss. This was probably due to the elimination of mainly ECW as a result of the diuretic therapy, with diuretic adaptation and resistance due to complex effects of loop

Figure 4 Continued



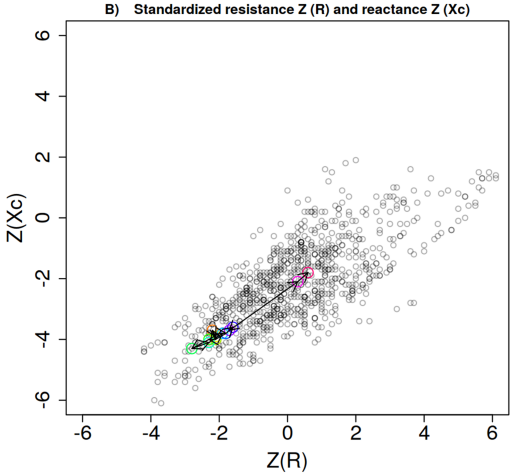
diuretics on ECW, as well as ICW and TBW.[10] Further, between the baseline and the last measurement at the group level, ECW loss appeared to be less correlated (−1.6 L) to weight loss (−2.5 kg). Therefore, daily measurement of ECW is a promising approach for monitoring the effects of diuretic treatment during more intensified diuretic therapy. It has to be taken into account that ECW and TBW are predictive parameters of an equation, with weight as an influencing factor. This mathematically conditions an association between weight change and ECW/TBW change. Therefore, it may be more appropriate to associate the weight independent parameters like Resistance R, Reactance X_c, and phase angle with weight loss. Resistance R, Reactance X_c, and phase angle were adequate BIVA parameters to monitor individual hydration status, showing a significant association with fluid/weight change as previously described by Alves *et al.*[21] In contrast to that trial, the patients in our trial did not fast and were investigated daily, and a multi-frequency, multi-segmental eight-electrode approach was used. Regarding the segmental impedance values, there were no clinically relevant differences in Resistance R or Reactance X_c between the segments, except for the TO segment (Supporting Information, *Tables S9–S16*). Increase in Resistance R was substantially higher than in Reactance X_c, confirming the hypothesis that Resistance R represents the impedance of the current through ICW and ECW and that this increases with fluid/weight loss [*Figure 3(B)* and *Table 2*]. Phase angle was higher at discharge, also reflecting the change in hydration status

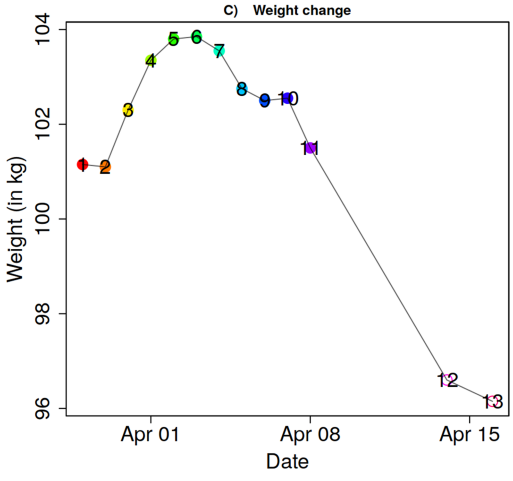
Figure 4 Continued

G

A) Diuretic medication at visit nr «x»

1. 2019-03-29: furo i.v. 120mg
2. 2019-03-30: furo i.v. 120mg
3. 2019-03-31: furo i.v. 120mg
4. 2019-04-01: furo i.v. 200mg
5. 2019-04-02: furo i.v. 330mg, spir 25mg
6. 2019-04-03: furo i.v. 375mg, met 5mg, spir 25mg
7. 2019-04-04: furo i.v. 500mg, met 5mg
8. 2019-04-05: furo i.v. 500mg, met 5mg, spir 25mg
9. 2019-04-06: furo i.v. 500mg, met 5mg
10. 2019-04-07: furo i.v. 500mg, met 5mg
11. 2019-04-08: furo i.v. 500mg, met 5mg
12. 2019-04-14: tora 150mg, met 5mg
13. 2019-04-16: tora 100mg

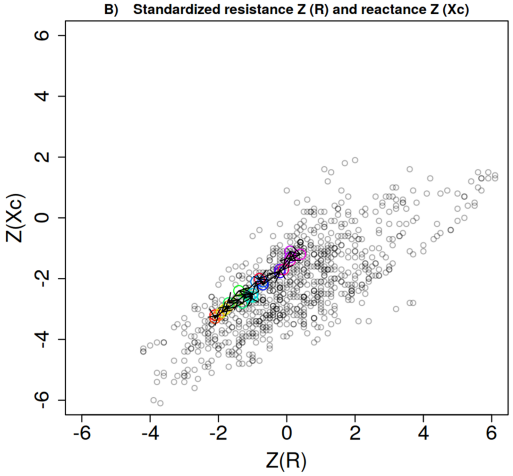


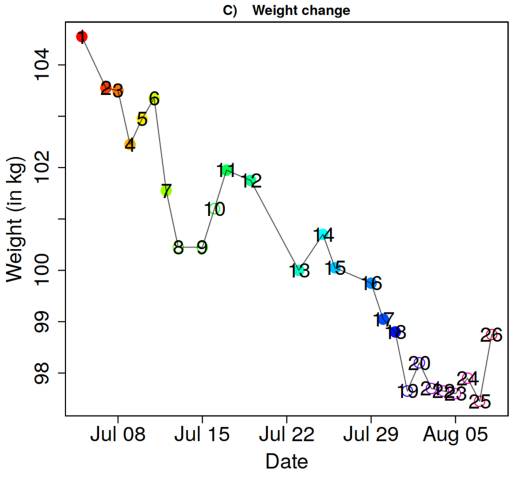


H

A) Diuretic medication at visit nr «x»

1. 2019-07-05: furo i.v. 100mg
2. 2019-07-07: furo i.v. 100mg, spir 25mg
3. 2019-07-08: furo i.v. 100mg, spir 25mg
4. 2019-07-09: furo i.v. 100mg
5. 2019-07-10: furo i.v. 120mg
6. 2019-07-11: furo i.v. 160mg, met 2.5mg
7. 2019-07-12: furo i.v. 240mg, met 2.5mg
8. 2019-07-13: tora 100mg
9. 2019-07-15: tora 100mg
10. 2019-07-16: tora 50mg
11. 2019-07-17: furo i.v. 160mg, tora 50mg
12. 2019-07-19: furo i.v. 160mg
13. 2019-07-23: furo i.v. 240mg
14. 2019-07-25: furo i.v. 320mg, met 2.5mg
15. 2019-07-26: furo i.v. 320mg, met 2.5mg
16. 2019-07-29: furo i.v. 240mg, met 5mg
17. 2019-07-30: furo i.v. 240mg, met 5mg
18. 2019-07-31: furo i.v. 80mg, tora 200mg, met 5mg
19. 2019-08-01: tora 200mg, met 5mg
20. 2019-08-02: tora 200mg, met 5mg
21. 2019-08-03: tora 200mg, met 5mg
22. 2019-08-04: tora 200mg, met 5mg
23. 2019-08-05: tora 100mg





and its potential effects on cell regeneration, as well as a more general prognostic parameter of recovery.

Although a lower heart rate and blood pressure would have been expected after recompensating, values at the first and last measurements do not differ significantly. A possible explanation could be that patients were already treated and stabilized in the emergency room before they were included into the study and the first measurement was performed.

Furthermore, Lyons *et al*. have shown that the use of BIVA to estimate hydration status may be beneficial in determining patient prognosis and treatment outcome when other outcome predictors are not immediately available.[22]

In corroboration with our findings of increase in bioelectrical impedance during diuretic therapy, the IMPEDANCE-HF trial demonstrated a reduction in hospitalization rate using a lung-bioimpedance-guided management to prevent rehospitalization in patients with chronic HF and lung-fluid overload due to AHF. This was achieved by monitoring the lung impedance dynamic from baseline up till a follow-up period of at least 12 months and medical intervention by drug modification with decreasing impedance values.[23]

Upon comparing the heterogeneous patients in this study, we observed that the BIVA parameters were independent; however, they showed the same trend, confirming the hypothesis that volume overload is associated with lower resistance and reactance, independent of physiology. Comparing our findings visualized in *Figure 4(A)–4(H)*, a similar prospective trial set-up is conceivable in the future.

With the emergence of novel wearable devices using BIVA, this study serves as a baseline to further investigate the clinical implementation of BIVA in hospitalized patients and (remote) monitoring of intensified diuretic therapy in patients with AHF using novel personalized digital biomarkers.[24]

Non-invasive wearables, including BIVA sensors such as the wrist-wearable bioelectrical impedance analyser with miniature electrodes for daily BCA by Jung *et al*.,[25] can be connected to automated hospital monitoring infrastructures and even remain with the patient following discharge.[26] This enables collecting continuous health data and closes the monitoring gap during transition between hospital discharge and follow-up management. Smartphone-based biosensors and wearables can reliably detect AHF triggering factors such as atrial fibrillation.[27]

Patient-worn accelerometers provide continuous assessment of physical activity and may more accurately reflect functional status, resulting in higher activity levels with less decongestion due to HF.[28] In patients with AHF, longitudinal monitoring of hydration status derived from wearable BIVA could, therefore, have a major impact on managing patients with HF in the future.

Another approach to further research the role of BCA as a new biomarker for AHF treatment is to test its reproducibility in comparison with other biomarkers associated with HF diagnosis and management such as natriuretic peptide change.

Combining BIVA with further molecular digital biomarkers may result in personalized and holistic management of AHF.[29]

Limitations

One of the major limitations of this trial lies within the observational study design.

Furthermore, the differing number of measurements for each patient at different times of the day as well as the unstandardized measuring conditions to test the usefulness of BCA in clinical practice with real-world conditions may have led to a major variation in the BCA parameters. Patients did not comply with a specific fasting protocol or specific dietary intake. They were not sober, did not have to empty the bladder, and had a different physical activity before the measurements with varying intensities of diuretic therapies resulting a greater error for TBW and ECW and a smaller effect on Resistance R and Reactance X_c according to the ESPEN guidelines.[30]

An additional limitation of the seca mBCA 515 was its earlier validation with euvolaemic healthy persons between 18 and 65 years of age. Our study patients were older (mean age, 76.8 ± 10.7 years) and presented with altered hydration status, which likely contributed to the discrepancy between the BCA and weight measurements. Therefore, further validation studies with older adults with and without cardiac congestion are needed.

Intrapersonal variance as a possible factor was not investigated in this study. Other studies using the same device have shown reproducibility of 0.4% and 0.6% and reliability of 1.2%.[18,31]

The patients had to stand upright for the BCA measurements, even though they were immobile due to AHF or associated comorbidities, and often wore stockings as compression bandage, which prevented direct skin contact of the electrodes. Moreover, dry hands and feet sometimes presented an obstacle by reducing current flow through the skin and impeded the automated start of measurement. Additionally, wounds and amputations in at least one of the limbs also posed restrictive conditions.

Patients with implanted cardiac electronic devices were excluded due to safety aspects, although it has been shown for another bioimpedance analyser that this technique is safe.[32] Validation trials in patients with implanted cardiac devices using the seca® mBCA 515 would be needed to demonstrate safety of electromagnetic interference in these patients. Among all screened patients, 92 were not included due to implanted cardiac devices (61 pacemakers and 31 implantable cardioverter-defibrillator).

Conclusions

Body composition analysis derived from BIVA is a promising approach to detect qualitative and quantitative changes in hydration status of patients undergoing intensified diuretic therapy due to AHF; however, further adaptation of the BCA equations (especially for TBW) is needed for this patient group. Defining personalized BIVA reference values using bioelectrical impedance devices seems to be a promising approach to monitor hydration status. Extensive research investigating bioimpedance-guided diuretic therapy and implementing novel bioimpedance wearables is needed in the context of tele-monitoring efforts and to determine whether BIVA contributes to new personalized digital HF biomarkers and can be used for personalized guidance in diuretic treatment.

Acknowledgements

The authors would like to thank Aura Winterhalder and Ulrike Margarete Schmitt for study coordination and monitoring and the CDWH team of the Research & Analysis services department for their help in retrieving data from the clinical information system.

Conflict of interest

No conflicts of interest to declare.

Funding

The study was supported by grants from the University Hospital Basel (Wissenschaftspool Innere Medizin).

The data warehouse project was financed in part by the direct Grant of the Swiss Personalized Health Network (SPHN) to the ICT-Department of the University Hospital Basel. The medical Body Composition Analyser was a loan from seca®, Hamburg, Germany.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Association between blood pressure and heart rate and body weight (water) loss.
Table S2. Summary laboratory parameters at first and last assessment.
Table S3. *Repeated measures correlation coefficients between creatinine, haematocrit, weight loss and BCA/BIVA parameters.*
Table S4. Total body water (TBW).
Table S5. Extracellular water (ECW).
Table S6. Association between mean Resistance R and weight (=water) loss, height, sex and age.
Table S7. Association between mean Reactance X_c and weight (=water) loss, height, sex and age.
Table S8. Association between mean phase angle and weight (=water) loss, height, sex and age.
Table S9. Association between segmental Resistance R at 75 kHz and weight (=water) loss, height, sex and age.
Table S10. Association between segmental Reactance X_c at 75 kHz and weight (=water) loss, height, sex and age.
Table S11. Association between segmental Resistance R at 50 kHz and weight (=water) loss, height, sex and age.
Table S12. Association between segmental Reactance X_c at 50 kHz and weight (=water) loss, height, sex and age.
Table S13. Association between segmental Resistance R at 7.5 kHz and weight (=water) loss, height, sex and age.
Table S14. Association between segmental Reactance X_c at 7.5 kHz and weight (=water) loss, height, sex and age.
Table S15. Association between segmental Resistance R at 5 kHz and weight (=water) loss, height, sex and age.
Table S16. Association between segmental Reactance X_c at 5 kHz and weight (=water) loss, height, sex and age.
Figure S1. Association between Resistance R, Reactance X_c and weight loss, adjusted for height, presence of pleural effusion, sex and age.

References

1. Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M, Nodari S, Lam CSP, Sato N, Shah AN, Gheorghiade M. The global health and economic burden of hospitalizations for heart failure. Lessons learned from hospitalized heart failure registries. *J Am Coll Cardiol* 2014; **63**: 1123–1133.
2. Cook C, Cole G, Asaria P, Jabbour R, Francis DP. The annual global economic burden of heart failure. *Int J Cardiol* 2014 2014/02/15/; **171**: 368–376.
3. Pocock SJ, Ariti CA, McMurray JJV, Maggioni A, Køber L, Squire IB, Swedberg K, Dobson J, Poppe KK, Whalley GA, Doughty RN, on behalf of the Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC). Predicting survival in heart failure: a risk score based on 39 372 patients from 30 studies. *Eur Heart J* 2013; **34**: 1404–1413.
4. Fonarow GC, Stough WG, Abraham WT, Albert NM, Gheorghiade M, Greenberg BH, O'Connor CM, Sun JL, Yancy CW, Young JB. Characteristics, treatments, and outcomes of patients with preserved systolic function hospitalized for heart failure: a report from the OPTIMIZE-HF registry. *J Am Coll Cardiol* 2007 2007/08/21/; **50**: 768–777.
5. Coats AJS, Pieske B, Linde C, Jankowska EA, Ruschitzka F, Rutten FH, Rosano GMC, Bueno H, Riley JP, Cleland JGF,

Parissis JT, González-Juanatey JR, Ruilope LM, Jessup M, van der Meer P, Nihoyannopoulos P, Anker SD, Harjola V-P, Falk V, Voors AA, Ponikowski P, Group ESD. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016; **37**: 2129–2200.

6. Girerd N, Seronde M-F, Coiro S, Chouihed T, Bilbault P, Braun F, Kenizou D, Maillier B, Nazeyrollas P, Roul G, Fillieux L, Abraham WT, Januzzi J, Sebbag L, Zannad F, Mebazaa A, Rossignol P. Integrative assessment of congestion in heart failure throughout the patient journey. *JACC: Heart Failure* 2018 2018/04/01/; **6**: 273–285.
7. Zhang J, Goode KM, Cuddihy PE, Cleland JGF, Investigators obotT-H. Predicting hospitalization due to worsening heart failure using daily weight measurement: analysis of the Trans-European Network-Home-Care Management System (TEN-HMS) study. *Eur J Heart Fail* 2009; **11**: 420–427.
8. Lewin J, Ledwidge M, O'Loughlin C, McNally C, McDonald K. Clinical deterioration in established heart failure: what is the value of BNP and weight gain in aiding diagnosis? *Eur J Heart Fail* 2005; **7**: 953–957.
9. Ronco C, Bellasi A, Di Lullo L. Cardiorenal syndrome: an overview. *Adv Chronic Kidney Dis* 2018 2018/09/01/; **25**: 382–390.
10. Ellison DH, Felker GM. Diuretic treatment in heart failure. *N Engl J Med* 2017; **377**: 1964–1975.
11. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gómez JM, Heitmann BL, Kent-Smith L, Melchior J-C, Pirlich M, Scharfetter H, Schols AMWJ, Pichard C. Bioelectrical impedance analysis—part I: review of principles and methods. *Clin Nutr* 2004 2004/10/01/; **23**: 1226–1243.
12. Lukaski HC, Bolonchuk WW, Hall CB, Siders WA. Validation of tetrapolar bioelectrical impedance method to assess human body composition. *J Appl Physiol* 1986; **60**: 1327–1332.
13. Kushner RF. Bioelectrical impedance analysis: a review of principles and applications. *J Am Coll Nutr* 1992; **11**: 199–209.
14. Piccoli A. Bioelectric impedance measurement for fluid status assessment. *Contrib Nephrol* 2010; **164**: 143–152.
15. Di Somma S, De Berardinis B, Bongiovanni C, Marino R, Ferri E, Alfei B. Use of BNP and bioimpedance to drive therapy in heart failure patients. *Congest Heart Fail* 2010; **16**: S56–S61.
16. Massari F, Iacoviello M, Scicchitano P, Mastropasqua F, Guida P, Riccioni G, Speziale G, Caldarola P, Ciccone MM, Di Somma S. Accuracy of bioimpedance vector analysis and brain natriuretic peptide in detection of peripheral edema in acute and chronic heart failure. *Heart Lung* 2016 2016/07/01/; **45**: 319–326.
17. Núñez J, Mascarell B, Stubbe H, Ventura S, Bonanad C, Bodí V, Núñez E, Miñana G, Fácila L, Bayés-Genis A, Chorro FJ, Sanchis J. Bioelectrical impedance vector analysis and clinical outcomes in patients with acute heart failure. *J Cardiovasc Med* 2016; **17**: 283–290.
18. Bosy-Westphal A, Schautz B, Later W, Kehayias JJ, Gallagher D, Müller MJ. What makes a BIA equation unique? Validity of eight-electrode multifrequency BIA to estimate body composition in a healthy adult population. *Eur J Clin Nutr*. [Original Article] 2013 01/09/online; **67**: S14.
19. Peine S, Knabe S, Carrero I, Brundert M, Wilhelm J, Ewert A, Denzer U, Jensen B, Lilburn P. Generation of normal ranges for measures of body composition in adults based on bioelectrical impedance analysis using the seca mBCA. *Int J Body Compos Res* 2013; **11**: 67–76.
20. Whetzel PL, Noy NF, Shah NH, Alexander PR, Nyulas C, Tudorache T, Musen MA. BioPortal: enhanced functionality via new web services from the National Center for Biomedical Ontology to access and use ontologies in software applications. *Nucleic Acids Res* 2011; **39**(Web Server issue: W541–W545.
21. Alves FD, Souza GC, Aliti GB, Rabelo-Silva ER, Clausell N, Biolo A. Dynamic changes in bioelectrical impedance vector analysis and phase angle in acute decompensated heart failure. *Nutrition* 2015 2015/01/01/; **31**: 84–89.
22. Lyons KJ, Bischoff MK, Fonarow GC, Horwich TB. Noninvasive bioelectrical impedance for predicting clinical outcomes in outpatients with heart failure. *Crit Pathw Cardiol* 2017; **16**: 32–36.
23. Shochat MK, Shotan A, Blondheim DS, Kazatsker M, Dahan I, Asif A, Rozenman Y, Kleiner I, Weinstein JM, Frimerman A, Vasilenko L, Meisel SR. Non-invasive lung IMPEDANCE-guided preemptive treatment in chronic heart failure patients: a randomized controlled trial (IMPEDANCE-HF trial). *J Card Fail* 2016 2016/09/01/; **22**: 713–722.
24. Kramer F, Butler J, Shah SJ, Jung C, Nodari S, Rosenkranz S, Senni M, Bamber L, Cichos S, Dori C, Karakoyun T, Köhler GJ, Patel K, Piraino P, Viethen T, Chennuru P, Paydar A, Sims J, Clark R, van Lummel R, Müller A, Gwaltney C, Smajlovic S, Düngen HD, Dinh W. Real-life multimarker monitoring in patients with heart failure: continuous remote monitoring of mobility and patient-reported outcomes as digital end points in future heart-failure trials. *Digital Biomarkers* 2020; **4**: 45–59.
25. Jung MH, Namkoong K, Lee Y, Koh YJ, Eom K, Jang H, Jung W, Bae J, Park J. Wrist-wearable bioelectrical impedance analyzer with miniature electrodes for daily obesity management. *Sci Rep* 2021 2021/01/13; **11**: 1238.
26. Brasier N, Geissmann L, Käch M, Mutke M, Hoelz B, De Ieso F, Eckstein J. Device- and analytics-agnostic infrastructure for continuous inpatient monitoring: a technical note. *Digital Biomarkers* 2020; **4**: 62–68.
27. Brasier N, Raichle CJ, Dörr M, Becke A, Nohturfft V, Weber S, Bulacher F, Salomon L, Noah T, Birkemeyer R, Eckstein J. Detection of atrial fibrillation with a smartphone camera: first prospective, international, two-centre, clinical validation study (DETECT AF PRO). *EP Europace* 2019; **21**: 41–47.
28. Redfield MM, Anstrom KJ, Levine JA, Koepp GA, Borlaug BA, Chen HH, LeWinter MM, Joseph SM, Shah SJ, Semigran MJ, Felker GM, Cole RT, Reeves GR, Tedford RJ, Tang WHW, McNulty SE, Velazquez EJ, Shah MR, Braunwald E. Isosorbide mononitrate in heart failure with preserved ejection fraction. *N Engl J Med* 2015; **373**: 2314–2324.
29. Brasier N, Eckstein J. Sweat as a source of next-generation digital biomarkers. *Digital Biomarkers* 2019; **3**: 155–165.
30. Kyle UG, Bosaeus I, de Lorenzo AD, Deurenberg P, Elia M, Manuel Gómez J, Lilienthal Heitmann B, Kent-Smith L, Melchior J-C, Pirlich M, Scharfetter H, M W J Schols A, Pichard C, ESPEN. Bioelectrical impedance analysis—part II: utilization in clinical practice. *Clin Nutr* 2004; **23**: 1430–1453.
31. Bosy-Westphal A, Jensen B, Braun W, Pourhassan M, Gallagher D, Müller MJ. Quantification of whole-body and segmental skeletal muscle mass using phase-sensitive 8-electrode medical bioelectrical impedance devices. *Eur J Clin Nutr*. [Original Article] 2017 03/22/online; **71**: 1061.
32. Chabin X, Taghli-Lamallem O, Mulliez A, Bordachar P, Jean F, Futier E, Massoullié G, Andonache M, Souteyrand G, Ploux S, Boirie Y, Richard R, Citron B, Lusson J-R, Godet T, Pereira B, Motreff P, Clerfond G, Eschalier R. Bioimpedance analysis is safe in patients with implanted cardiac electronic devices. *Clin Nutr* 2019 2019/04/01/; **38**: 806–811.