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ORIGINAL ARTICLE

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Bioelectrical impedance analysis in the management of heart failure in adult patients with congenital heart disease

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Abstract

Objective: The recognition of fluid retention is critical in treating heart failure (HF). Bioelectrical impedance analysis (BIA) is a well-known noninvasive method; however, data on its role in managing patients with congenital heart disease (CHD) are limited. Here, we aimed to clarify the correlation between BIA and HF severity as well as the prognostic value of BIA in adult patients with CHD.

Design: This prospective single-center study included 170 patients with CHD admitted between 2013 and 2015. We evaluated BIA parameters (intra- and extracellular water, protein, and mineral levels, edema index [EI, extracellular water-to-total body water ratio]), laboratory values, and HF-related admission prevalence.

Results: Patients with New York Heart Association (NYHA) functional classes III-IV had a higher EI than those with NYHA classes I-II (mean ± SD, 0.398 ± 0.011 vs 0.384 ± 0.017, $P < .001$). EI was significantly correlated with brain natriuretic peptide level ($r = 0.51$, $P < .001$). During the mean follow-up period of 7.1 months, Kaplan-Meier analysis showed that a discharge EI > 0.386, the median value in the present study, was significantly associated with a future increased risk of HF-related admission (HR = 4.15, 95% CI = 1.70–11.58, $P < .001$). A body weight reduction during hospitalization was also related to EI reduction.

Conclusions: EI determined using BIA could be a useful marker for HF severity that could predict future HF-related admissions in adult patients with CHD.

KEYWORDS
bioelectrical impedance analysis, congenital heart disease, fluid retention, heart failure

1 | INTRODUCTION

Fluid retention with dyspnea is the most often encountered cause of rehospitalization after acute heart failure (HF). Decompensated HF generally leads to fluid overload caused by elevated ventricular filling pressure or neurohormonal activation. Thus, the ability to recognize and quantify fluid retention is critical for the treatment of HF; however, optimal markers for the presence of fluid retention have yet to be identified. Brain natriuretic peptide (BNP) testing, chest radiography, cardiac ultrasonography, and blood sampling are insufficient for assessing fluid retention.

Bioelectrical impedance analysis (BIA) was recently introduced in many clinical fields, such as cardiology, nephrology, hepatology, nutrition, and rehabilitation.[1-9] BIA is a safe, rapid, and noninvasive assessment method that involves the application of alternating currents to the body to achieve 8-polar tactile-electrode impedance. These impedances are obtained using differences in cell membrane permeability based on variable frequencies.

All authors contributed to the formulation of the concept and critical analysis of this manuscript.

Intracellular water (ICW); extracellular water (ECW); total body water (TBW); and protein, mineral, and fat levels can be determined using BIA. Moreover, BIA can provide the edema index (EI), which represents the ratio of ECW to TBW and can serve as an alternative for assessing body fluid status. The accuracy of this approach was initially concerning but has recently improved. Previous reports demonstrated the value of BIA in treating HF[10-18]; however, data regarding its role in treating patients with congenital heart disease (CHD) are limited. The present study aimed to clarify the correlation between BIA and HF severity as well as the prognostic value of BIA in adult patients with CHD.

2 | METHODS

2.1 | Subjects and measurements

This prospective single-center study included 170 patients aged ≥16 years with CHD who were admitted to Tokyo Women's Medical University for HF treatment, catheterization examination, surgery, transesophageal echocardiography, or other treatments between April 2013 and December 2015. Patients with cardiac pacemakers or who were pregnant were excluded because the electric current generated by BIA may affect their device and/or their health. Patients who could not receive BIA within 2 days after admission were also excluded because treatment provided immediately after admission could have affected the observed results. The mean study period of the present study was 7.1 ± 6.0 months. Informed consent was obtained from all participants who underwent BIA, and the study conformed to the 1975 Declaration of Helsinki ethical guidelines. This study was approved by the institutional ethical committee of Tokyo Women's Medical University.

On admission, blood samples were obtained to analyze the hematocrit (Ht), total protein (TP), albumin (Alb), blood urea nitrogen (BUN), creatinine (Cr), sodium (Na), and BNP levels. Among the patients who received HF treatment, the circulating plasma volume change (CPVC) was calculated using the formula (post-TP − pre-TP)/post-TP.[3] Similarly, the blood volume change (BVC) was calculated using the formula (post-Ht − pre-Ht)/post-Ht.[3]

Standard two-dimensional and Doppler transthoracic echocardiography and tissue Doppler imaging (TDI) were performed in each case by a pediatric cardiologist. Using the M-mode of the parasternal short-axis view, the left ventricular end-diastolic diameter (LVDd) and left ventricular fraction shortening (LVFS) were determined. Using pulsed Doppler imaging with the sample volume at the mitral tip, the early mitral inflow velocity (E) was measured. Using TDI, early diastolic mitral annular velocity (e′) was measured at the septal annulus and E/e′ was calculated. Inferior vena cava (IVC) diameter was measured in the sub-xiphoid view. An IE33 (Philips Electronics Japan, Tokyo, Japan) or Vivid E9 (GE Healthcare Japan, Tokyo, Japan) was used in each case. A chest radiograph was obtained to assess the cardiothoracic ratio (CTR).

2.2 | Bioelectrical impedance analysis

On admission, BIA was performed for each patient using an Inbody 720 (Inbody Japan, Tokyo, Japan). Patients underwent BIA between 2 and 4 hours after having lunch and the oral administration. Eight electrodes were attached to the patient's body (two each on the palms and thumbs and another two each on the front parts of the feet and heels). The patients stood with their feet in contact with the foot electrodes and grabbed the hand electrodes. A low-amplitude current at 4 different frequencies (5, 50, 100, and 200 KHz) was applied through the electrodes. Each analysis lasted 15 s, and the obtained results were recorded electronically. The measured parameters included ICW, ECW, TBW, protein, mineral, and fat. In addition, EI was calculated using the formula EI = ECW/(ICW + ECW). A single BIA was performed in each patient, and the date was blinded to the physicians who determined the HF-related admissions and NYHA classes.

2.3 | Assessments

2.3.1 | Correlation between BIA and HF severity

The patients were classified into two groups based on NYHA classification. To clarify the correlation between BIA and HF severity, the parameters of patients with NYHA classes I-II were compared to those of patients with NYHA classes III-IV. The correlation between EI and other parameters was also assessed.

2.3.2 | Predictors of HF-related admission after discharge

We defined HF-related admission as new-onset decompensated HF or decompensation of chronic HF with symptoms indicating admission. To clarify the risk factors of HF-related admission after discharge, the odds ratio (OR) by each parameter at discharge was determined. NYHA functional class (FC) was classified into four levels. Subsequently, we compared the ratio of HF-related admissions after discharge in patients with a discharge EI over the median value of overall EI in the present study with that of the patients with a discharge EI equal to or less than the median value using Kaplan-Meier analysis.

2.3.3 | Quantitative assessment of fluid retention

The correlation between BW reduction and BIA parameters, CPVC, and BVC was determined in patients who were admitted for HF treatment and received BIA twice during hospitalization.

2.4 | Statistical analysis

The intergroup differences in each continuous parameter were evaluated using Student's *t* test. The correlations between parameters were evaluated using the Pearson correlation coefficient. For

TABLE 1 Patient profiles (N = 170)

Male, *n* (%)	80 (47%)
Age (y)	34 ± 14
Body weight on admission (kg)	53.2 ± 11.5
NYHA functional class, *n* (%)	
I	58 (34%)
II	57 (34%)
III	55 (32%)
IV	0 (0%)
Vital signs	
Heart rate (bpm)	80 ± 16
Systolic blood pressure (mm Hg)	103 ± 15
Diastolic blood pressure (mm Hg)	56 ± 11
SpO_2 (%)	92 ± 8
Comorbidity, *n* (%)	
Hypertension	5 (3%)
AF/AT/VT	69 (41%)
DM	3 (2%)
PLE	6 (3%)
Ventricular morphology	
Biventricular	98 (58%)
ICR (including RVOTR)	45
Unoperated	24
Jatene	11
Senning or Mustard	9
Double switch	5
Others	4
Single ventricular	72 (42%)
Fontan type	54
Glenn or shunt	14
Unoperated	4
Reason for admission	
Heart failure	32 (19%)
Catheterization examination	95 (56%)
Diagnostic	80
Intervention	15
Surgery	6 (4%)
TCPC	4
Rastelli	2
Transesophageal echocardiography	22 (13%)
Other	15 (9%)
Medication, *n* (%)	
β-blocker	81 (47%)
ACEI or ARB	94 (55%)
Pimobendan	16 (9%)

TABLE 1 Continued

Pulmonary vasodilator	29 (17%)
Loop diuretic	100 (59%)
MRA	90 (53%)
Tolvaptan	31 (18%)

Abbreviations: ACEI, angiotensin-converting-enzyme antagonist; AF, atrial fibrillation; ARB, angiotensin receptor antagonist; AT, atrial tachycardia; DM, diabetes mellitus; ICR, intracardiac repair; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; PLE, protein-losing enteropathy; SpO_2, oxygen saturation of the peripheral artery; RVOTR, right ventricular outflow reconstruction; TCPC, total cavopulmonary connection; VT, ventricular tachycardia.
Data are presented as mean ± SD or number (%).

parameters for which a significant correlation was found, multivariate regression analysis was used. The OR of HF-related admission in relation to each parameter was determined using logistic regression analysis. The stepwise method was used to select factors for multivariate analysis. The Kaplan-Meier method was used to analyze the ratio of HF-related admission of patients in the two groups. In addition, the OR of HF-related admission was assessed using the Cox hazard model. Statistical significance was set at $P < .05$ using commercially available statistical software (JMP pro ver. 12; SAS Institute Japan, Tokyo, Japan).

3 | RESULTS

3.1 | Patients' characteristics

The patient profiles are listed in Table 1. The mean patient age was 34 y. Fifty-five patients (32%) were classified as New York Heart Association FC III, 57 (34%) as class II and 58 (34%) as class I. All three patients with NYHA FC IV were excluded because they could not receive BIA within 2 d after admission. Systemic hypertension was found in five patients (3%), atrial fibrillation or atrial tachycardia in 69 (41%), and diabetes in 3 (2%). Fifty-four (32%) patients had Fontan circulation and 6 (3%) had known protein-losing enteropathy (PLE).

3.2 | Correlation between BIA and HF severity

The patients were classified into two groups based on NYHA classification (I-II vs III), and each parameter was compared between groups. A significant difference was found between the EI of patients with NYHA classes I-II and that of patients with NYHA class III; a significant difference was also found in their age and Alb, BUN, Cr, Na, and log BNP levels (Table 2).

A significant positive correlation was found between EI and log BNP, EI and age, EI and BUN level, EI and Cr level, EI and IVC during expiration, and EI and CTR (Table 3). A significant negative correlation was found between EI and Alb level. Moreover, the multivariate analysis showed significant correlations between EI, age, log BNP value, and Alb and BUN levels (Table 4).

TABLE 2 Clinical parameters of Group A (NYHA classes I-II) vs Group B (NYHA class III)

	Group A (n = 115)	Group B (n = 55)	P value
Age (y)	31 ± 13	41 ± 13	<.001
Laboratory data			
Hematocrit (%)	44 ± 7	45 ± 13	.365
Albumin (g/dL)	4.3 ± 0.7	4.0 ± 0.7	.009*
BUN (mg/dL)	15.6 ± 8.2	36.0 ± 25.1	<.001*
Cr (mg/dL)	0.77 ± 0.35	1.20 ± 0.47	<.001*
Sodium (mEq/L)	140 ± 3	138 ± 4	.006*
log BNP (pg/mL)	1.74 ± 0.53	2.33 ± 0.55	<.001*
Echocardiologic parameters			
LVDd (mm)	45 ± 10	45 ± 17	.736
LVFS	0.31 ± 0.09	0.30 ± 0.10	.59
TAPSE (mm)	13.9 ± 5.9	13.5 ± 6.3	.851
E/e′	11.4 ± 6.1	11.7 ± 6.6	.867
IVC during expiration (mm)	17 ± 5	19 ± 6	.159
IVC respiratory change	0.31 ± 0.15	0.33 ± 0.21	.575
CTR (%)	53 ± 7	61 ± 9	<.001
Bioimpedance analysis			
ICW (L)	17.5 ± 4.2	17.2 ± 3.1	.608
ECW (L)	10.9 ± 2.6	11.4 ± 2.5	.206
TBW (L)	28.4 ± 6.8	28.6 ± 5.4	.843
Protein (kg)	7.56 ± 1.82	7.46 ± 1.36	.711
Mineral (kg)	2.70 ± 0.58	2.80 ± 0.50	.307
Fat (kg)	12.2 ± 6.1	13.1 ± 5.32	.339
Edema index	0.384 ± 0.011	0.398 ± 0.017	<.001*

Abbreviations: BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CTR, cardiothoracic ratio; Cr, creatinine; ECW, extracellular water; ICW, intracellular water; LVDd, left ventricular end-diastolic diameter; LVFS, left ventricular fraction shortening; TAPSE, tricuspid annual plane systolic excursion; TBW, total body water.
Data are presented as mean ± SD.
*$P < .05$.

TABLE 3 Correlation between edema index and other parameters

	r	*P* value
Age (y)	0.45	<.001*
Hematocrit (%)	0.01	.869
Albumin (g/dL)	−0.44	<.001*
BUN (mg/dL)	0.52	<.001*
Cr (mg/dL)	0.5	<.001*
Sodium (mEq/L)	−0.22	.006*
logBNP (pg/mL)	0.51	<.001*
LVDd (mm)	0.2	.031*
LVFS	−0.04	.71
TAPSE (mm)	−0.12	.42
E/e′	0	.99
IVC during expiration (mm)	0.27	.003
IVC respiratory change	0.19	.05
CTR (%)	0.52	<.001*
ICW (L)	−0.07	.37
ECW (L)	0.26	<.001*
TBW (L)	0.06	.436
Protein (kg)	−0.07	.404
Mineral (kg)	0.11	.183
Fat (kg)	−0.06	.46

Abbreviations: BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CTR, cardiothoracic ratio; Cr, creatinine; ECW, extracellular water; ICW, intracellular water; LVDd, left ventricular end-diastolic diameter; LVFS, left ventricular fraction shortening; TAPSE, tricuspid annual plane systolic excursion; TBW, total body water.
*$P < .05$.

TABLE 4 Multivariate regression analysis for edema index ($R^2 = 0.47$)

	B	SE	*t*	*P* value
Age (y)	0.00018	7.58E−05	2.27	.025
Albumin (g/dL)	−0.0058	0.001	−4.54	<.001
BUN (mg/dL)	0.00025	5.86E−05	4.36	<.001
logBNP (pg/mL)	6.20E−06	1.87E−06	3.15	<.001

Abbreviations: BNP, brain natriuretic peptide; BUN, blood urea nitrogen.

No significant difference was found between the EI of the patients who underwent the Fontan procedure and those who did not (mean 0.388 ± 0.017 vs 0.387 ± 0.014, $P = .943$).

3.3 | Predictors of HF-related admission after discharge

Thirty-eight (22%) patients were admitted for HF over a mean period of 6 ± 4 mo after their baseline BIA. Fifteen of 32 patients (56%) in the HF admission group and 23 of 148 patients (16%) in the other groups were admitted for HF after discharge. The univariate analysis showed that age; initial HF admission, Ht level, Alb level, Na level, BUN level, log BNP value, and EI were significant predictors of HF-related admissions after discharge (Table 5). In addition, the multivariate analysis showed that EI, NYHA FC, and BUN level were independent predictors associated with HF-related admissions after discharge. Initial HF admission was not a significant predictor in the multivariate model.

During the mean follow-up period of 7.1 mo, the Kaplan-Meier analysis of HF-related admission-free survival showed that a discharge EI > 0.386, the median value of overall EI in the present study, was significantly associated with an increased risk of HF-related admission after discharge (HR = 4.15, 95% CI = 1.70–11.58, $P < .001$, Figure 1).

3.4 | Quantitative assessments of fluid retention

Seventeen (10%) patients were admitted for HF treatment and received BIA twice during hospitalization. The average BW reduction was 3.1 ± 2.4 kg. A significant positive correlation was found between BW reduction and ECW reduction ($r = 0.74$), TBW reduction ($r = 0.58$), and EI reduction ($r = 0.75$). In contrast, no significant correlation was found between BW change and ICW reduction or CPVC or BVC (Figure 2).

4 | DISCUSSION

Here, we reported the following two main findings. First, we found a significant correlation between EI and HF severity in patients with CHD. Subsequently, we established that a high EI is an independent predictor of HF-related admission after discharge.

4.1 | Correlation between BIA and HF severity

The present study clarified the correlation between EI and HF severity in patients with CHD. Decompensated HF generally leads to fluid retention caused by increased ventricular filling pressure and neurohormonal activation.[19-25] In the present study, EI was significantly correlated with NYHA FC or log BNP level. These results suggests that EI reflects fluid retention caused by HF in accordance with the findings of Okamoto et al suggesting that EI is significantly associated with human atrial natriuretic peptide levels, which responds to plasma volume, in 36 patients on chronic hemodialysis.[1] The results of the present study also agree with those of Castillo et al reporting the correlation between NYHA FC and fluid overload estimated by BIA in 243 patients with HF.[26] ECW includes interstitial fluid and that in the blood. In the present study, BW change was strongly correlated with ECW change. Considering that BW change did not correlate with BVC or CPVC, both of which represent blood volume, increased ECW or EI in patients with HF should represent mainly increased interstitial fluid that is the main cause of HF

TABLE 5 Multivariate logistic regression analysis of the factors associated with HF-related admission after discharge

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age (y)	1.059 (1.030-1.093)	<.001*		
NYHA FC	4.781 (2.712-8.990)	<.001*	7.945 (2.737-29.46)	<.001*
Initial HF admission	6.440 (2.931-14.58)	<.001		
Hematocrit (%)	1.044 (1.004-1.086)	.031*		
Albumin per 0.1 (g/dL)	0.869 (0.811-0.924)	<.001*		
BUN (mg/dL)	1.055 (1.028-1.089)	<.001*	1.051 (1.002-1.123)	.017*
Sodium (mEq/L)	0.813 (0.701-0.935)	.034*		
logBNP per 0.1(pg/mL)	1.245 (1.112-1.423)	.001*		
ICW (L)	0.994 (0.858-1.141)	.932		
ECW (L)	1.096 (0.863-1.384)	.442		
TBW (L)	1.011 (0.922-1.103)	.815		
Edema index per 0.01	2.040 (1.290-3.615)	.002*	1.963 (1.109-4.003)	.021*

Abbreviations: BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CI, confidence interval; ECW, extracellular water; FC, functional class; ICW, intracellular water; NYHA, New York Heart Association; OR, odds ratio; TBW, total body water.
*$P < .05$.

symptoms. Therefore, EI may be considered a reliable marker of HF severity. Conversely, the presentation of echocardiographic parameters, such as LVFS, tricuspid annular plane systolic excursion, and E/e′, did not differ significantly between the NYHA classification groups. This is likely due to heterogeneity in the patients' heart diseases.

BNP level has been widely used to manage HF. However, it has some limitations. BNP has a gray zone value and is often influenced by factors independent of HF such as age, obesity, pulmonary embolism, and pulmonary infection. Patients with CHF may paradoxically have high or low BNP levels.[10,27] BNP is a reliable marker for central edema, but it is not correlated with peripheral edema. In contrast, EI can detect peripheral edema and may be superior for detecting the early stages of HF that are not accompanied by central edema.[28,29] In the present study, EI had a higher OR of HF-related admission than BNP level. As stated before, this is probably a result of the heterogeneity in our patients' heart diseases. Diseases that accompany systemic ventricle load, such as ventricular septal defect, mitral valve regurgitation, and aortic stenosis, lead to pulmonary edema (central edema). Conversely, diseases that accompany venous side ventricle load, such as atrial septal defect, tricuspid regurgitation, and pulmonary hypertension, lead to peripheral edema and renal and hepatic dysfunction. Fontan circulation features a high central venous pressure and decreased systemic ventricle load volume. BNP is secreted by the myocardium in response to the loads in the atria and ventricles.

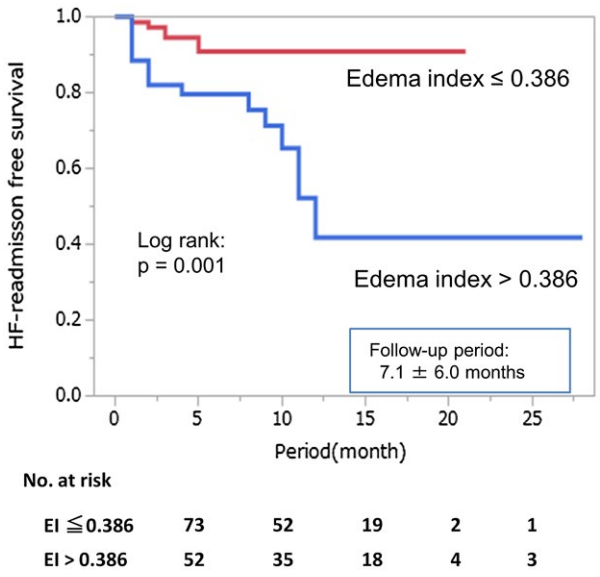

FIGURE 1 Kaplan-Meier analysis of the incidence of heart failure-related admissions by discharge EI ($n = 125$). The red line shows the patients with an EI ≤ 0.386, whereas the blue line shows those with an EI > 0.386. Abbreviations: EI, edema index; AUC, area under the receiver operating characteristic curve

Thus, patients without loads in the heart chambers but with peripheral edema do not have high BNP levels. The former patient group generally exhibits high BNP levels; however, the latter two groups often do not.[30-33]

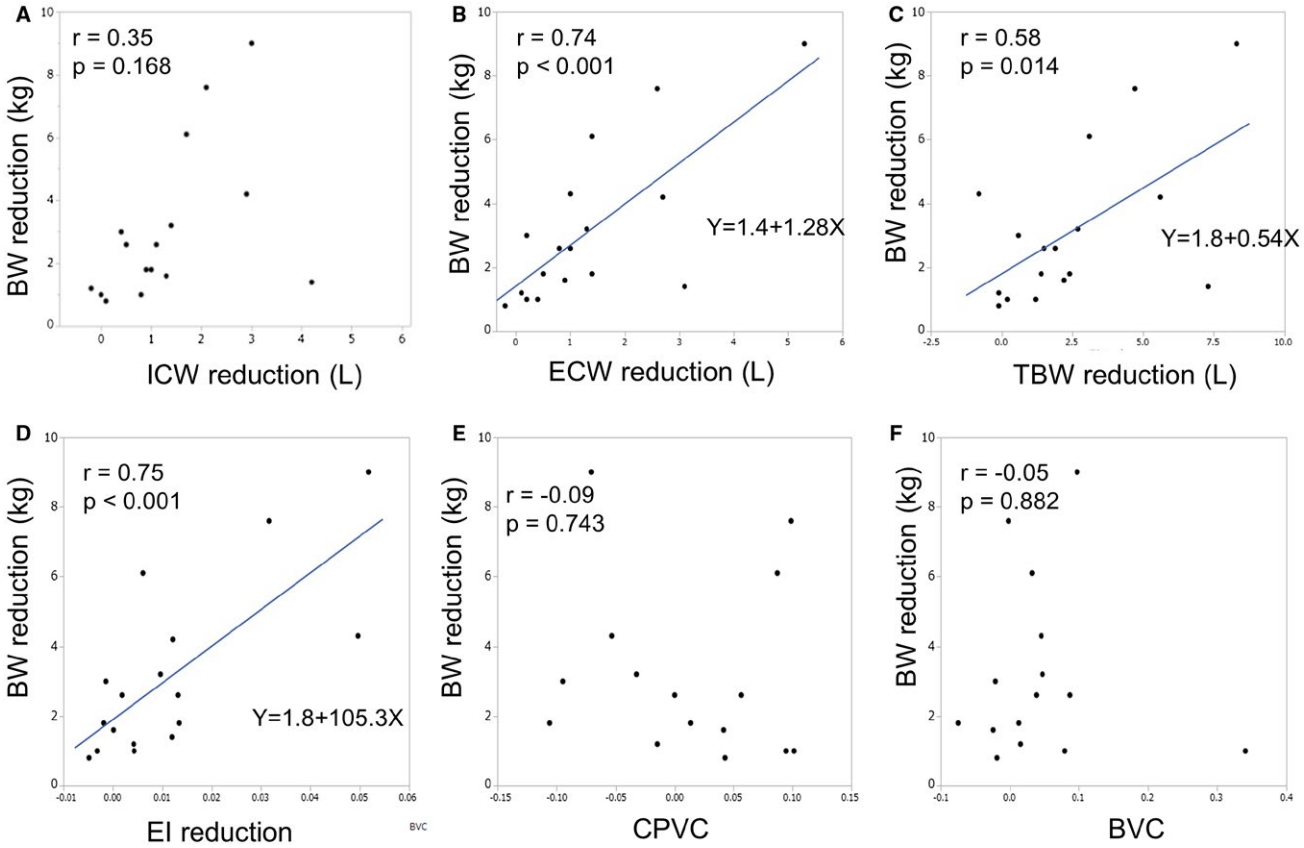

FIGURE 2 Relationship between body weight reduction and other parameters (A, ICW reduction; B, ECW reduction; C, TBW reduction; D, EI reduction; E, CPVC; F, BVC). The solid line is the regression line. BVC, blood volume change = (post-Ht − pre-Ht)/post-Ht; CPVC, circulating plasma volume change = (post-TP − pre-TP)/post-TP. ECW, extracellular water; EI, edema index; HF, heart failure; Ht, hematocrit; ICW, intracellular water; TBW, total body water; TP, total protein

4.2 | Predictors of HF-related admission after discharge

Our findings suggest that EI may be a useful predictor of HF-related admission after discharge in patients with CHD. In the present study, NYHA FC correlated with HF-related admission after discharge. Baseline HF severity is clearly a strong predictor of a next admission for HF. In the multivariate analysis, EI also had a significantly high OR for HF-related admission after discharge. EI may be useful for identifying high-risk patients for HF-related admission among patients with equivalent NYHA FC. The prognostic importance of EI was suggested by Liu et al, who reported that an EI > 0.39 predicted a higher incidence of HF-related admissions and that an increase in EI by 0.001 increased HF-related events by 6% in 112 patients with acute HF.[28,34] Sakaguchi et al reported that the ratio of measured ECW to predicted ECW at discharge was a prognostic marker for cardiac events in 130 patients with acute decompensated HF.[12] However, their subjects were restricted to those with a normal heart structure. The present study clarified the prognostic importance of EI in a complex circulation with CHD.

Liu et al also reported the superiority of EI-guided therapy to avoid HF-related admissions.[28] In treating HF of patients with CHD, the absence of clinical signs of and presence of a normal EI are important to avoiding future HF-related admissions.

4.3 | Quantitative assessments of fluid retention

We found a significant correlation between BW reduction and EI reduction in patients who received HF therapy. The linear regression equation of BW reduction and EI reduction indicates that an EI reduction of 0.01 is equivalent to a BW reduction of 1.1 kg.

BW is the total weight of fluid, muscle, fat, and bone. During short-term HF treatment, as was mentioned, a BW change was strongly correlated with a fluid change; in contrast, it was not correlated with changes in other components. Measuring EI daily is unrealistic given the medical cost. In contrast, measuring BW is simple and free. Therefore, when treating fluid retention caused by HF, targeting BW is reasonable.

A useful marker for fluid retention has been lacking. Therefore, several methods have been used to predict fluid retention in patients with HF. Serum Alb level, which is generally related to edema, is often influenced by several factors, such as malnutrition, liver dysfunction, nephritic syndrome, and PLE. IVC diameter is often difficult to measure in obese patients. In contrast, EI is a direct marker of fluid retention.

In the present study, ECW change had a higher correlation coefficient with BW change than ICW change. In other words, excess body water in patients with HF consists mainly of ECW, which agrees with the findings of Sakaguchi et al regarding the quantitative assessment of fluid accumulation using ECW.[12] Since the normal range of ECW differs among body sizes and sexes, adjusting HF therapy by referring to EI, which has a universal normal range, may be more useful.

Yamazoe et al established the model formula for BW reduction using EI, sex, IVC diameter, and BW in 60 patients with a normal heart structure.[11] One reason for the difference between their formula and ours is most likely due to differences in the patients' diagnoses. The other reason is that we adapted more parameters using BIA. Sex and IVC diameter are not included in our formula because they did not demonstrate significant correlations with BW reduction. Further studies are needed to confirm the compatibility of the required BW reduction determined in the present study.

The well-known upper limit of EI was 0.39, and Liu et al reported that EI-guided management improved the outcomes in patients with acute HF and did not cause dehydration.[28] This normal range of EI has three limitations. First, decreased renal perfusion in patients with renal dysfunction by excessive water reduction can easily lead to further dysfunction. Second, patients with both hypoalbuminemia and an EI value > 0.39 may have insufficient intravascular volumes since patients with hypoalbuminemia have lower osmotic pressure and intravascular volume. Third, in patients with Fontan circulation, since both pulmonary and systemic outputs depend on preload, decreased preload easily leads to circulatory collapse.[35] In these patients, the target EI may be higher. In the field of preventive medicine, the use of BIA for outpatients and subsequent adjustment of HF may clarify subclinical HF and prevent HF-related admission. The target EI of patients with CHD should be clarified in future studies.

4.4 | Reproducibility of BIA

The accuracy of single-frequency BIA was a concern in the past. However, multiple-frequency BIA was developed and has provided us with accurate data.[11] In fact, many studies have reported the reproducibility of multiple-frequency BIA.[1,2,10-12]

4.5 | Study limitations

The present study has four limitations. First, we did not include a healthy control group. The standard value of the EI for healthy individuals has already been established to be approximately 0.380 (<0.390).[3,11] In the present study, the mean EI level was 0.384 for patients with NYHA I-II and 0.398 for patients with NYHA III-IV. Hence, we predict that patients with CHD are more likely than those without CHD to have edema, which indicates the presence of latent HF in patients with CHD. Second, the reproducibility of BIA in patients with CHD has not been sufficiently reported yet. The subjects of studies that reported the reproducibility of BIA were patients without CHD. Hence, the reproducibility of BIA with respect to CHD should be confirmed in further studies. Third, the echo operators and those who assessed the CTR on radiographs were not blinded to the patients' conditions, which could have introduced bias. Fourth, BIA reportedly lacks sensitivity for detecting cases of localized edema such as pleural or abdominal effusion.[10]

5 | CONCLUSION

EI determined by BIA may be correlated with HF severity and predict future HF-related admissions in patients with CHD.

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CONFLICT OF INTEREST

The authors report no relationships that could be construed as conflicts of interest.

AUTHOR CONTRIBUTIONS

Kei Inai, involved with the conception and design of the study, and interpretation of the data analysis, drafting the original article, and critically revised the original article.

Mikiko Shimizu, involved with the interpretation of the data analysis.

Hisashi Sugiyama, involved with the interpretation of the data analysis.

Toshio Nakanishi, involved with the conception and design of the study.

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