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Extracellular fluid volume as a key indicator in home-care management of chronic heart failure: The role of nutritional and exercise therapy

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Key Clinical Message

Extracellular fluid volume, rather than body weight, should guide chronic heart failure management in home-care patients. Enhancing muscle mass through pharmacotherapy, nutrition, and exercise is essential to prevent heart failure exacerbation.

KEYWORDS

bioimpedance analysis (BIA), chronic heart failure, exercise, extracellular fluid volume (ECF), nutrition

1 | INTRODUCTION

The number of heart failure (HF) patients in Japan is estimated to be approximately 1.2 million,[1] with projections suggesting that it will reach approximately 1.3 million by 2030.[2] As the incidence of HF increases with age,[1] the number of elderly HF patients in Japan, a superaging society, is growing. This indicates the arrival of a HF pandemic and the consequent strain on the healthcare system, which has begun to be recognized as a societal issue.[3] Therefore, the clinical importance of HF management to prevent readmission is increasingly recognized, highlighting the challenge of providing high-quality care by interdisciplinary teams. In addition to ongoing pharmacotherapy, nutritional management and exercise tailored to cardiac pump function are essential for preventing the exacerbation of chronic HF. Daily blood pressure monitoring and body weight measurements are indispensable.

In particular, body weight is an essential monitoring parameter in HF management. Rapid weight gain, specifically an increase of more than 3 kg within 3 days, is considered a worsening of HF and is significant enough to warrant consideration of diuretic dose adjustment according to the acute and chronic HF treatment guidelines.[4] In-home care relies on weight to evaluate HF when the immediate and simple acquisition of objective indicators is limited. However, recent studies have highlighted the drawbacks of using weight as the sole indicator of fluid status.[5]

The issue with using body weight is that it often does not accurately reflect the patient's fluid status, such as fluid overload or dehydration.[6] Therefore, weight fluctuations do not necessarily indicate direct changes in fluid volume and are particularly susceptible to the effects of edema and nutritional status.[7] Consequently, it is challenging to assess the distribution of fluids within the body of HF patients precisely through weight monitoring alone. Nevertheless, in current HF management, body weight, despite its lack of reliability and accuracy as an indicator of fluid management, is still emphasized. Weight monitoring that neglects body composition may not lead to appropriate decisions regarding cardiac function, body fluid volume, and nutritional status in patients with chronic HF, potentially preventing HF management tailored to an individual's overall condition and circumstances. Therefore, monitoring chronic HF should not rely solely on body weight but rather adopt a comprehensive approach that includes fluid status, nutritional assessment, and functional capacity.[8] Additionally, using biomarkers such as brain natriuretic peptide (BNP) is crucial in managing HF and should be comprehensively used in diagnosis and evaluation.[9]

Therefore, the method focused on in this study is bioimpedance analysis (BIA). BIA is recognized for its superiority over body weight as a more accurate method for quantitatively assessing the fluid status of patients at the bedside.[5] In this study, we attempted to monitor home-based patients with chronic HF by regularly measuring the extracellular fluid volume (ECF volume) and other parameters via BIA and body weight. Studies have reported that using BIA to measure the extracellular fluid volume and total body water volume can be helpful in clinical risk stratification and fluid monitoring in HF patients.[10,11] Additionally, the prognostic significance of chronic HF and its management efficacy have been highlighted by the edema index,[10] calculated from body fluid volume, underscoring the importance of regular monitoring of extracellular and total body water volumes in HF management. In summary, this study has the potential to challenge the disease management paradigm in chronic HF patients, which heavily emphasizes weight monitoring despite its objective shortcomings. This study aims to demonstrate a superior method of disease management via BIA. The bioimpedance devices used for BIA and portable echocardiography equipment enable noninvasive, simple bedside measurements, enabling immediate result verification. Thus, utilizing the measurement results on the spot enhances the utility of our approach to patient care.

1.1 | Aim

This report aimed to continuously monitor the body composition of two home-based patients with chronic HF using BIA and to analyze its correlation with objective indicators, including body weight and BNP levels. We aimed to explore the utility of body composition in addition to body weight as a monitoring indicator for the management of HF.

1.2 | Equipment

A Toray Medical MLT-550N body[12] composition analyzer was used. Compared with the single-frequency bioelectrical impedance method, MLT-550N employs a "multifrequency bioelectrical impedance analysis method," which uses multiple frequencies (2.5 ~ 350 kHz) of current for a more sophisticated analysis of body composition and the distribution of body fluids (intracellular and extracellular fluid volumes). Our preliminary experiments confirmed that the device in question produces measurements with minimal error, comparable to those obtained from the more advanced medical-grade body composition analyzer (Inbody970).[13] Therefore, the data obtained via this device are accurate and reliable.

1.3 | Measurement methods

Measurements were conducted with the consent of the patients. To obtain stable results, the following consistent conditions were maintained:

1. Measurements were taken during hospital stays and regular outpatient visits in the morning, at least 2 h after meals, to avoid impacting the measurement values.
2. The measurement posture was supine. The limbs were extended with slight gaps between the legs, arms, and torso. Four electrode patches were applied to the right wrist and left ankle, with measurements taking approximately 15 s, during which the patients remained still.
3. Three measurements were taken per session to minimize measurement error. After confirming no outliers or abnormal values, the average value was used as the data.

Spearman's correlation coefficient was calculated for each patient for the analysis method, with a significance level set at $p < 0.05$. Statistical analysis was performed via JMP Pro ver.17.

2 | CASE PRESENTATION

We evaluated two male patients in their 70s who began home care after hospital treatment for chronic HF. Both patients lived independently.

2.1 | Patient A (Figure 1, Table 1)

2.1.1 | Clinical course

The patient was urgently transported to the hospital with complaints of dyspnea and chest discomfort and was diagnosed with congestive HF and mild functional mitral regurgitation. Upon admission, the patient's vital signs were as follows: blood pressure (BP) 163/94 mmHg, heart rate (HR) 117 beats per minute (bpm), oxygen saturation (SpO_2) 99% (room air), body temperature (BT) 36.8°C, brain natriuretic peptide (BNP) 2718 pg/dL, and ejection fraction (EF) 20%. The patient weighed 62.8 kg (an increase of approximately 10 kg), with significant edema in both lower limbs.

Treatment was initiated with dobutamine (dobutamine hydrochloride; DOB) 150 mg, furosemide (diuretics) 20 mg, and enalapril (angiotensin-converting enzyme inhibitor; ACEI) 2.5 mg, followed by the sequential addition of spironolactone (aldosterone antagonist) 25 mg, dapagliflozin (sodium-glucose cotransporter 2; SGLT2 inhibitor) 10 mg, carvedilol (β-blocker) 2.5 mg, and pimobendan (cardiac agents) 2.5 mg. The DOB was gradually reduced and discontinued on the 13th day of hospitalization, while the pimobendan dosage was increased to 5 mg, and the carvedilol dosage was increased to 12.5 mg. Additionally, 15 mg of azosemide (diuretics) was added on the 25th day of hospitalization.

The patient responded well to pharmacological treatment from the beginning of hospitalization. With disease

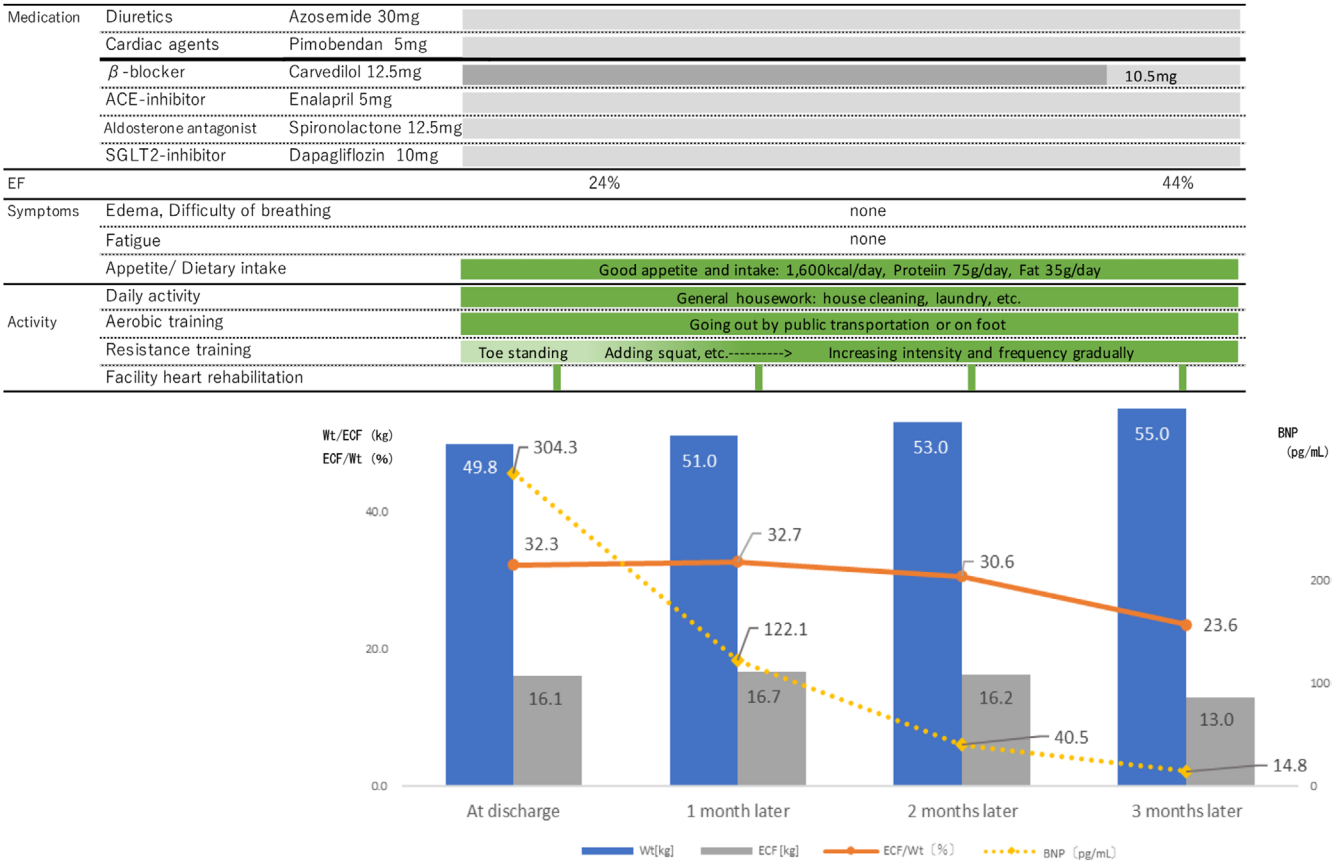

FIGURE 1 Post-discharge progression of chronic heart failure patient A: Stable course. The patient was diagnosed with congestive heart failure and mild functional mitral valve regurgitation and demonstrated a stable clinical course without renal impairment. Postdischarge management included medication adjustments, rehabilitation changes, and dietary adherence, which supported improved clinical outcomes. Spearman correlation coefficient (r) is as follows: BNP and ECF ($r = 0.48$, $p = 0.51$), Wt and BNP ($r = -0.89$, $p = 0.11$).

Time point	BNP (pg/mL)	ECF (kg)	EF (%)	Interpretation
At discharge	304.3	16.1	24	
1 month later	122.1↓↓	16.7 →	-	BNP↓↓, ECF →
2 months later	40.5↓↓	16.2 →	-	BNP↓↓, ECF →
3 months later	14.8↓	13.0↓↓	44↑	BNP↓, ECF↓↓, EF↑

TABLE 1 Changes in BNP, ECF, and EF over 3 months post-discharge in patient A.

Note: **Arrows**: Use arrows to indicate the trend (↑ for increase, ↓ for decrease, → for almost no change: ±1.0). Double arrows (↑↑ or ↓↓) can indicate a more significant change.

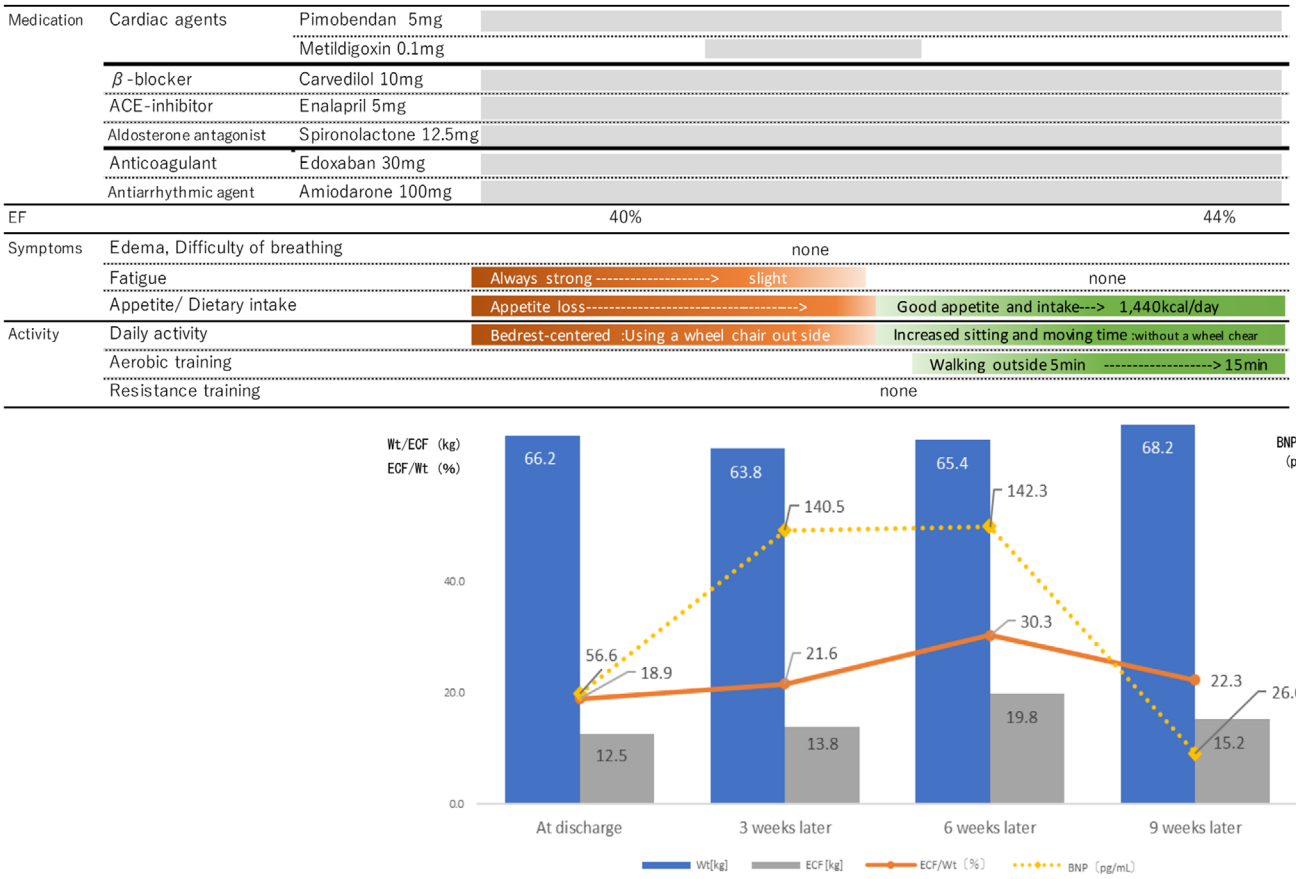

FIGURE 2 Post-discharge progression of chronic heart failure patient B: Unstable course. The patient was diagnosed with chronic heart failure, left ventricular dysfunction, atrial fibrillation, and pulmonary emphysema without renal impairment and had an unstable clinical course and persistent symptoms after discharge. Spearman correlation coefficient (r) is as follows: BNP and ECF ($r=0.25$, $p=0.63$), Wt and BNP ($r=-0.28$, $p=0.58$).

management, which included cardiac rehabilitation and nutritional management (1600 kcal, 70 g protein, 35 g fat, and <6 g salt), the patient's condition progressed, with a blood pressure of 100–110/50–60 mmHg, heart rate of 60 bpm, and weight of 50–51 kg. The dyspnea and edema in both lower limbs disappeared. At discharge (on the 26th day of hospitalization), the patient's EF was 24%, BNP was 304.3 pg/dL, and the inferior vena cava (IVC) diameter was 10 mm. After discharge, the patient's blood pressure stabilized at approximately 110/70 mmHg, and the heart rate remained stable at approximately 70 bpm, with no significant changes from discharge. Additionally, no dyspnea or edema was observed at rest or during daily activities.

2.1.2 | Medication

The discharge prescription was the same as the treatment during hospitalization, including azosemide (diuretics) 15 mg and pimobendan (cardiac agents) 5 mg, as shown in Figure 1. One month after discharge, carvedilol (β-blocker) was reduced from 12.5 to 10 mg, with no other changes in the prescription or dosage. The

TABLE 2 Changes in BNP, ECF, and EF over 9 weeks post-discharge in patient B.

Time Point	BNP (pg/mL)	ECF (kg)	EF (%)	Interpretation
At Discharge	56.6	12.5	40	
3 Weeks Later	140.5↑↑	13.8↑	-	BNP↑↑, ECF↑
6 Weeks Later	142.3↑	19.8↑↑	-	BNP↑, ECF↑↑
9 Weeks Later	26.0↓↓	15.2↓	44↑	BNP↓↓, ECF↓, EF ↑

Note: **Arrows**: Use arrows to indicate the trend (↑ for increase, ↓ for decrease). Double arrows (↑↑ or ↓↓) can indicate a more significant change.

patient maintained good adherence to the medication regimen at home.

2.1.3 | Dietary management

Following nutritional guidance before discharge, the patient consumed 1600 kcal, 75 g protein, 35 g fat, and <6 g salt daily, utilizing commercially processed foods. No supplements were consumed; protein-rich foods such as meat, fish, legumes, and dairy products were included in every meal.

2.1.4 | Exercises

Cardiac rehabilitation sessions, which were previously frequent during hospitalization, were adjusted once per month because of difficulties in commuting. Additionally, the patient engaged in daily home-based resistance exercises, including standing toe raises and squats, for approximately 5 min at a moderate intensity, which allowed conversation. The aerobic exercise included approximately 30 min of walking almost daily. The patients lived alone, managed all household chores, and walked or used public transport.

2.1.5 | Outcomes

Compared with those at the third month after discharge, the patient's weight increased by 5.2 kg (approximately 10.4%), his ECF decreased by 3.1 kg (approximately 19.3%), and his BNP decreased by 289.5 pg/mL (approximately 95.1%). Despite the increase in weight, the significant reductions in ECF and BNP indicated a substantial improvement in HF. There were no subjective symptoms, such as edema or dyspnea. The ratio of ECF to total body fluid followed a trend similar to that of extracellular fluid to body weight, with an increase in lean body mass proportional to body weight. The diameter of the IVC was maintained at 10 mm at 9 weeks after discharge. Three months later, the EF improved from 24% at discharge to 44%.

2.2 | Patient B (Figure 2, Table 2)

2.2.1 | Clinical course

During a routine follow-up for COPD, the patient experienced worsening dyspnea and was admitted with a diagnosis of left ventricular dysfunction and atrial fibrillation. Upon admission, the patient's vital signs were as follows: BP 85/54 mmHg, HR 100–131 bpm (AF), SpO_2 98% (room air), BT 36.7°C, BNP 104 pg/dL, EF 25%, and weight 74.0 kg (an increase of approximately 5 kg).

Treatment was initiated with DOB 150 mg, furosemide (diuretics) 10 mg, enalapril (ACEI) 2.5 mg, spironolactone (aldosterone antagonist), carvedilol (β-blocker) 2.5 mg, and edoxaban (anticoagulant) 30 mg, along with bilateral pulmonary vein isolation. Owing to recurrent atrial fibrillation and HF exacerbation from a urinary tract infection, diuretic management is challenging. Amiodarone (antiarrhythmic agent) 100 mg and landiolol hydrochloride (β-blocker) 50 mg were added, with discontinuation and resumption based on the patient's overall condition, and electrical cardioversion was performed. The patient subsequently maintained sinus rhythm, with a stable heart rate of approximately 70 bpm.

On the 16th day of hospitalization, tolvaptan (vasopressin receptor antagonist) 3.75 mg was added, and on the 27th day, pimobendan (cardiac agents) 2.5 mg of was introduced. DOB was gradually reduced beginning on the 30th day and was discontinued on the 34th day. During this period, the carvedilol concentration was progressively increased to 10 mg. While the subjective symptoms of HF, such as edema and dyspnea, disappeared, the patient developed fatigue and loss of appetite, which are considered signs of low cardiac output syndrome (LOS). Therefore, tolvaptan (3.75 mg) was discontinued on the 41st day of hospitalization. The patient's diet during hospitalization was 1400 kcal (65 g protein, 35 g fat, and <6 g salt). Still, their food intake was unstable, necessitating supplemental fluids based on their condition. Additionally, cardiac rehabilitation was conducted.

The patient's condition progressed, with BP 90–100/50–60 mmHg, HR 50–66 bpm (sinus rhythm), and weight 66–67 kg. There was no edema or dyspnea at rest, but the symptoms of loss of appetite and fatigue persisted even after the discontinuation of tolvaptan. There were no other notable symptoms, and the cause could not be identified beyond the LOS, including the possibility of depression. At discharge (45th day of hospitalization), the patient's BNP was 56.6 pg/dL, the EF was 40%, and the IVC diameter was 11 mm. After discharge, the patient's blood pressure remained at 100–110/60 mmHg, and the heart rate was approximately 70 bpm (sinus rhythm).

2.2.2 | Medication

At discharge, the patient continued to receive pimobendan 2.5 mg, metildigoxin 0.1 mg (cardiac agents), and carvedilol 10 mg (β-blocker), among other medications (Figure 2). Between 3 and 6 weeks after discharge, metildigoxin (cardiac agents) 0.1 mg was added, but there were no changes in the prescription or dosage of enalapril (ACEI) or other medications. The patient maintained good adherence to the medication regimen.

2.2.3 | Dietary management

Based on the nutritional guidance provided before discharge, the patient's meals prepared by his wife were aimed at 1440 kcal, 60 g protein, 35 g fat, and less than 6 g salt per day. However, for approximately 5 weeks after discharge, the patient continued to experience a lack of appetite and could consume only 40% of the target nutritional intake. The loss of appetite gradually subsided after 5 weeks postdischarge, and the patient could meet the target nutritional intake. The proportion of protein- and fat-rich foods increased during this period according to the patient's preferences.

2.2.4 | Exercises

From discharge to the fourth week after discharge, the patient primarily led a bedridden lifestyle. After the improvement in appetite in the fifth week after discharge, the patient spent more time sitting and engaging in household activities. Initially, the patient experienced dyspnea after walking approximately 50 m, but by the sixth week, he could walk around his home without any issues. By the ninth week, he could walk for 15 min at a conversational pace. No resistance exercises were performed during this period.

2.2.5 | Outcomes

When comparing the sixth and ninth weeks postdischarge, the patient's weight increased by 2.8 kg (approximately 4.3%), ECF decreased by 4.6 kg (approximately 23.2%), and BNP decreased by 116.3 pg/mL (approximately 81.7%). Despite the increase in weight, the significant reductions in ECF and BNP indicated an improvement in HF. There were no symptoms, such as edema, dyspnea, or fatigue. The ratio of ECF to TBW peaked at the sixth-week post-discharge and then decreased, whereas the fat-free mass increased proportionally to weight gain. The IVC diameter was 16 mm at the ninth week post-discharge. The EF improved from 40% at discharge to 44%.

The difference between patients A and B in terms of disease and treatment lies in the fact that patient A had congestive HF with a reduced EF and recovered smoothly with the early introduction of an SGLT2 inhibitor. In contrast, patient B had left ventricular dysfunction due to atrial fibrillation complicated by a urinary tract infection, which delayed diuretic management. Additionally, patient B underwent bilateral pulmonary vein isolation, electrical cardioversion, and treatment with antiarrhythmic drugs, which distinguishes them from patient A. Despite these differences in disease and recovery processes, both patients responded well to treatment with diuretics, inotropes, β-blockers, and ACE inhibitors. Patient A's EF improved by approximately 80%, and they experienced a weight loss of roughly 12 kg. Patient B achieved sinus rhythm, and their EF improved by 10%. Although there was no statistically significant correlation between BNP and ECF, a positive correlation was suggested. Despite the limited number of EF measurements, EF improvement was observed alongside BNP reduction and ECF decrease (Figures 1 and 2; Tables 1 and 2).

3 | DISCUSSION

3.1 | Inefficiency of weight monitoring in HF management and the potential of ECF for predicting BNP

Although no statistically significant differences were observed because the data were limited to two patients, the measurement of body composition in home-based patients with chronic HF in this study highlighted two key findings:

1. A general correlation among BNP levels, EF, and ECF volume.
2. An inverse correlation among BNP levels, EF, and body weight was detected.

In patient A, a reduction in ECF volume and BNP levels was observed 1 month postdischarge, accompanied by an improvement in the EF, indicating an improvement in HF. A similar phenomenon was observed in patient B at 6 weeks post-discharge when their condition stabilized. Additionally, in patient B, who did not achieve stable HF status by the third week postdischarge, an increase in both BNP and ECF volume was noted, suggesting a positive correlation between the two variables despite the lack of statistical significance (patient A: $r=0.48$, $p=0.51$; patient B: $r=0.25$, $p=0.63$). Patient A's weight consistently increased during this period, whereas patient B's weight fluctuated. This finding indicates that the variable correlated with BNP trends was not body weight, which is emphasized in clinical practice, but ECF.

In this study, Spearman's correlation analysis was conducted, and given the patients' differing conditions, the analysis was performed individually for each patient. The lack of statistical significance is likely due to the limited analyzable data. Nonetheless, a clear positive correlation trend between BNP and ECF was observed. The accumulation of a larger dataset is expected to elucidate further the correlations between BNP, EF, and ECF.

Several factors have been identified as contributing to the inefficiency of weight monitoring in patients with chronic HF:

1. Weight fluctuations can be influenced by factors other than fluid retention, particularly changes in muscle mass.
2. Weight monitoring cannot accurately visualize changes in muscle mass.

For patients with chronic HF, weight gain associated with increased muscle mass is desirable. Both Patients A and B experienced weight gain of more than 2 kg without any worsening symptoms of HF, such as lower limb edema or dyspnea. Despite this, the current HF management that relies on body weight could misinterpret weight gain owing to increased muscle mass as a worsening of HF.

In traditional HF management, body weight is an essential indicator for adjusting medications, including diuretics.[4] However, this study reaffirms that body weight is not always a reliable indicator for home-based chronic HF patients.[5] While HF treatment guidelines recommend contacting a physician or adjusting diuretics in response to rapid weight gain, the clinical effectiveness of this approach is limited. Recent findings indicate that weight monitoring is not necessarily a highly reliable indicator for the early detection of HF progression.[14] The cases in this study where HF improved despite weight gain contradict the guidelines and are not commonly reported.

An example of weight not correlating with clinical status is observed in chronic HF patients with cachexia who, after consuming high-calorie, high-protein nutritional supplements, experienced significant weight gain due to increased adipose tissue without worsening HF symptoms and showed improved quality of life.[15] This aligns with our study, indicating that weight gain is not necessarily a helpful indicator in chronic HF management.

Based on these observations, our study proposes including body composition analysis, rather than body weight alone, as an evaluation metric in chronic HF management. This introduces a novel perspective, suggesting a shift from the traditional weight-centric approach to a more comprehensive management strategy.

Furthermore, a novel finding of this study is that ECF can predict BNP. Previous research has reported the usefulness of ECF volume as an indicator of fluid retention in chronic HF patients.[16] Patients with a high ECF/TBW (extracellular water to total body water) ratio are at a greater risk of fluid overload, contributing to elevated BNP levels. An increase in ECF volume is associated with an increase in BNP, indicating its utility in predicting HF.[7] This finding suggests that extracellular fluid and BNP are correlated, supporting the findings of this study that ECF volume can predict BNP levels.

BNP is a hormone secreted when the ventricles are excessively stretched, and volume overload from increased ECF volume promotes BNP secretion.[17] Conversely, BNP decreases with decreasing ECF volume due to HF treatment. This mechanism logically supports this study's finding that BNP changes follow ECF volume changes, making the prediction of BNP based on ECF volume reasonable. Moreover, NT-proBNP is a biomarker considered more sensitive and capable of detecting HF earlier than BNP.[17] Future research should explore the relationships between ECF and other biomarkers, such as NT-proBNP, to further validate these findings.

Although BNP and proBNP are valuable biomarkers for diagnosing HF, their measurement requires the collection of blood samples by a physician. Therefore, measuring ECF volume can be considered convenient and beneficial, particularly in home care settings where nurses need immediate and objective indicators. This study indicated that changes in ECFs greater than 1 kg could influence BNP levels. A practical application would be to perform an immediate ultrasound examination via a portable echocardiogram[18] when a rapid increase

of >1 kg in ECF volume is detected. This can facilitate the measurement of the EF and IVC diameters. Suppose signs of HF exacerbation, such as a decrease in EF or an IVC diameter exceeding 20 mm, are observed.[4,18] In that case, prompt consultation with the primary physician is recommended to facilitate early intervention. Even when echocardiographic findings do not indicate worsening HF, an increase in ECF volume can still be considered a sign of potential exacerbation.

It has been hypothesized that there is a lag between the increase in ECF volume or body weight and the manifestation of HF symptoms. The use of body composition monitors for tracking such changes helps manage pre-exacerbation conditions of HF and facilitates earlier and more appropriate care before the typical symptoms of HF exacerbation become apparent, potentially helping to prevent hospital readmissions. Given the analysis results regarding weight changes, ECF volume, and BNP levels, measuring ECF volume appears to be a more useful objective indicator than measuring body weight in home-based patients with chronic HF. This finding underscores the potential of adopting ECF volume monitoring as a routine practice in enhancing the efficacy of home care and preventive strategies in chronic HF patients.

3.2 | Mechanisms behind weight gain and a decrease in ECF volume in patients with HF

A notable feature of the two patients studied was improved HF symptoms and increased body weight, whereas the ECF volume decreased. This contradicts the current interpretation of HF treatment, in which weight gain is commonly associated with an increase in ECF volume and is considered an indicator of worsening HF.[4] The following factors might have reduced the ECF volume in these patients:

1. Improving the EF due to pharmacotherapy
2. Adequate nutritional intake, particularly protein consumption, and the resulting increase in muscle cells and metabolism.

3.3 | Medication effects

Both patients received standard HF treatment, which notably included diuretics and inotropes, and these treatments can be interpreted as having reduced venous pressure. Specifically, inotropes improve myocardial contractility, enhance cardiac function and cardiac output,[19] decrease venous pressure, and alleviate edema. Additionally, diuretics promote the excretion of sodium and water,[20] resulting in reduced circulating blood volume and venous pressure, directly contributing to the reduction in ECF volume. For patient A, who had a significant decline in EF, using an SGLT2 inhibitor was notable. SGLT2 inhibitors induce osmotic diuresis, reducing the circulating blood volume and decreasing the preload and afterload on the heart.[20] Moreover, these inhibitors are thought to increase myocardial efficiency through cardioprotective effects.[21] These combined effects likely contributed to the reduction in ECF volume.[22,23]

Although ACE inhibitors, beta-blockers, and spironolactone do not directly reduce ECF volume, their role in blood pressure management and the suppression of myocardial remodeling likely indirectly improves cardiac function and prevents HF exacerbation,[24,25] leading to a decrease in ECF volume.

The observed decrease in ECF volume owing to medication aligns logically with the pharmacological goals of HF management. However, the simultaneous increase in body weight observed in both patients cannot be explained solely by the effects of medication. This weight gain likely resulted from increased muscle mass following appropriate exercise, improving heart pump function, and effective medicines and nutritional intake.

3.4 | Nutritional impact: The effects of enhanced protein intake

Both patients exhibited weight gain attributed to adequate nutritional intake, and the data collected suggested that the increase in body composition was primarily in muscle mass rather than in extracellular fluid or fat. Ethical considerations regarding patient burden and its impact on patient's lives precluded this study's collection of detailed dietary records. Despite these data acquisition and analysis limitations, patient A's targeted protein intake at discharge was set at 75 grams, significantly exceeding the 60 grams recommended for his age group.[26] In contrast, Patient B, who did not engage in resistance exercise, maintained an adequate intake of protein-rich foods such as meat and fish, even with a reduced appetite. The common factor between the two cases was the proactive consumption of protein. Adequate protein intake prevents muscle mass loss and promotes muscle recovery irrespective of age, sex, or exercise.[27] Both individuals are free from renal dysfunction, so maintaining such dietary habits likely minimizes muscle loss and facilitates muscle mass recovery.

3.5 | Exercise benefits: Increases in muscle cell numbers and enhanced metabolism

Patients A and B, both of whom showed signs of recovery from HF (after discharge for 6 weeks), engaged in aerobic exercise, which was consistent across their treatment protocols. Patient A engaged in moderate-intensity aerobic and resistance exercises daily, as recommended for cardiac rehabilitation.[28] On the other hand, although patient B did not engage in resistance training, he could perform moderate-intensity aerobic exercises centered around walking after the initial 6 weeks post-discharge, eventually adopting these exercises daily. The physiological significance of exercise in patients with HF includes improved cardiac function,[29] enhanced muscle strength,[30] better blood circulation,[31] reduced inflammation,[29] and improved autonomic function.[30] In our study, the primary benefit of exercise was the increase in muscle strength.[30] Strengthening the skeletal muscles improved the efficiency of oxygen utilization in the muscles, impacting their capacity for daily activities. In conjunction with pharmacotherapy, the increased oxygen supply to the myocardium may have contributed to increased cardiac output and improved cardiac efficiency.[29]

The weight gain observed in these two patients can be attributed to division and the consequent increase in muscle satellite cells during exercise.[32] Moreover, adequate nutritional intake and energy expenditure, particularly protein consumption, further activate muscle satellite cells and promote muscle protein synthesis,[33,34] which causes myofibril hypertrophy and weight gain. An increase in lean-free mass and a decrease in the ratio of ECF to total body water were observed in both individuals. Notably, a lower ratio of ECF to total body water indicates a change in water balance and a state of muscle tonicity, indicating muscle quality.[35] These findings support the interpretation that weight gain is due primarily to increased muscle cells and skeletal muscle protein mass caused by hypertrophy.[34]

An increase in muscle mass is believed to suppress the increase in ECF volume within the homeostasis range. An increase in exercise and muscle mass enhances energy consumption, that is, metabolism, which not only results in a transcellular shift from extracellular to intracellular fluid[16] but also consumes ECFs. Specifically, increased metabolism will likely facilitate energy production, active cellular membrane transport, and intracellular synthesis. During these catabolic and anabolic reactions, the oxygen and nutrients stored in the extracellular fluid are transported and utilized, inhibiting the increase in ECF volume.[16,36] Typically, older adults experience a decrease in metabolism and muscle mass, leading to a reduction in the intracellular fluid volume and an increase in the ECF volume.[16] However, the opposite reaction occurred due to increased muscle mass and metabolism in Cases A and B, unlike in the general elderly population.

Particularly for patient A, who consistently engaged in aerobic and resistance exercises, these activities may have improved insulin sensitivity and activated glucose transporters and enzymes involved in glucose metabolism, thereby increasing nutrient uptake from skeletal muscles.[37] Additionally, resistance training improves mitochondrial function, which is essential for energy production,[38] increasing energy efficiency.

Thus, in patient A, increased nutrient uptake and metabolic efficiency in the skeletal muscles likely facilitated the efficient removal of metabolic products from the extracellular fluid. Neither patient A nor B engaged in the respiratory muscle training recommended for cardiac rehabilitation.[28] If both patients had undergone respiratory muscle training and patient B had performed resistance exercises, further improvements in BNP levels and reductions in ECF volume may have occurred.

These factors underpin the mechanisms by which weight gain occurs alongside a reduction in ECF volume, improving HF symptoms in these two patients with chronic HF.

3.6 | Effectiveness of nutritional and exercise therapy

The observed changes in the study subjects included weight gain associated with increased muscle mass, a reduction in ECF, and improvement in BNP levels. For the management of HF in patients at home, it is essential not only to continue pharmacotherapy but also to combine it with appropriate nutritional intake and exercise therapy tailored to cardiac pump function and living conditions. These sustained interventions are believed to have increased muscle mass and facilitated the improvement of HF.

This study indicated that proactive protein intake is beneficial. For more effective protein digestion and absorption, oral nutritional supplements containing whey peptides and branched-chain amino acids,[39] as well as meal supplements based on essential amino acids,[40] can potentially increase fat mass and physical capability in patients with chronic HF and offer beneficial treatments for elderly individuals with poor physical function. Home-based food substitution methods improve nutritional status and enhance cardiopulmonary function and exercise endurance in elderly patients with chronic HF.[41] Although

the patients did not use supplements, it is crucial to use nutritional support products to intake protein according to the patients' conditions efficiently.

Additionally, exercise is of paramount importance. Cardiac rehabilitation, including a combination of aerobic exercises, resistance training, and respiratory muscle exercises, is highly recommended by evidence-based research.[28] However, neither of our patients consistently performed resistance or respiratory muscle exercises; everyday activities included increased daily activities and aerobic training. Therefore, exercise therapy focused primarily on aerobic activities can improve HF. Thus, for patients with chronic HF who find it challenging to maintain all recommended exercises, such as cardiac rehabilitation, it may be advisable to prioritize daily activities and aerobic training according to symptoms and living conditions, gradually increasing the variety and intensity of activities.

As outlined above, maintaining appropriate nutritional intake, continued exercise, and other lifestyle improvements is not easy for patients to manage independently at home with minimal involvement from healthcare professionals. Therefore, exercise and nutritional therapy must be tailored to meet each patient's individual needs and supported continuously. This requires not only physician-centered support in outpatient settings but also the practice of team-based care through collaborative efforts with multidisciplinary professionals.

3.7 | Practical application: Proposal for continuous monitoring via BIA

Support for pharmacotherapy, nutrition, and exercise therapy, which contribute to the prevention of worsening conditions and improvement in quality of life (QOL) in home-based patients with chronic HF, should not be limited to outpatient visits. Instead, these interventions are carried out by a multidisciplinary team according to patient needs, including home nursing and rehabilitation visits. Furthermore, I propose shifting from current weight-centric evaluations to incorporating regular body composition assessments via BIA into standard home care practices to analyze the patient's condition and treatment effects more accurately. This approach would enable more reliable and precise management of HF, nutritional status, and the impact of physical activity.

This allows for immediate assessment of HF management, nutritional status, and the impact of physical activity. Based on these measurements, supporters should provide feedback to patients and deliver on-the-spot dietary and exercise guidance, facilitating personalized care to help prevent worsening HF and improve QOL.

4 | CONCLUSION

For patients managing chronic HF at home, the volume of ECF serves as a more reliable and objective indicator than weight fluctuations. It may act as a predictor of BNP levels. Furthermore, increasing muscle mass through pharmacotherapy, nutritional, and exercise therapy is essential for preventing the worsening of HF, and BIA is an effective tool for this assessment. Therefore, I propose the incorporation of BIA into standard protocols for home management of HF. Future research should evaluate the outcomes of incorporating BIA into HF management and explore the correlations with additional biomarkers, including NT-proBNP, in large-scale studies.

AUTHOR CONTRIBUTIONS

Junko Shida: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; visualization; writing – original draft; writing – review and editing. **Ryosuke Watanabe:** Formal analysis; writing – original draft; writing – review and editing. **Itsuro Kazama:** Formal analysis; supervision; visualization; writing – original draft; writing – review and editing. **Masahiro Wanezaki:** Investigation; writing – review and editing. **Hiromi Misawa:** Writing – original draft; writing – review and editing. **Chisaki Uno:** Writing – review and editing. **Yumi Matsuda:** Supervision; writing – review and editing.

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DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

CONSENT

This study was conducted after obtaining approval from the Ethical Review Committee of the university to which the researcher belongs (approval number 2021-367). The purpose, research methods, voluntary participation, confidentiality issues, and plans for publishing the research results were explained to all patients both in writing and orally. All patients' written consents have been signed and collected in accordance with the

guidelines of the ethical review committee and the journal's patient consent policy.

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REFERENCES

1. National Cerebral and Cardiovascular Center. Epidemiology of heart failure and ischemic heart disease. https://www.ncvc.go.jp/coronary2/column/20211209_05.html
2. Okura Y, Ramadan MM, Ohno Y, et al. Impending epidemic: future projection of heart failure in Japan to the year 2055. *Circ J*. 2008;72:489-491. doi:10.1253/circj.72.489
3. The Nikkei. Beware of the Heart Failure Pandemic: 10% Increase in Deaths Due to the COVID-19 Pandemic. 2023. https://www.nikkei.com/article/DGXZQOUA30C7G0Q3A530C2000000/
4. The Japanese Circulation Society/The Japanese Heart Failure Society. JCS/JHFS. Guideline Focused Update on Diagnosis and Treatment of Acute and Chronic Heart Failure. 2021. https://www.j-circ.or.jp/cms/wp-content/uploads/2021/03/JCS2021_Tsutsui.pdf
5. Koratala A, Kazory A. Point of care ultrasonography for objective assessment of heart failure: integration of cardiac, vascular, and extravascular determinants of volume status. *Cardiorenal Med*. 2021;11(1):5-17. doi:10.1159/000510732
6. Parrinello G, Greene SJ, Torres D, et al. Water and sodium in heart failure: a spotlight on congestion. *Heart Fail Rev*. 2015;20(1):13-24. doi:10.1007/s10741-014-9438-7
7. Costanzo MR. Methods to assess intra- and extravascular volume status in heart failure patients. In: McCullough PA, Ronco C, eds. *Textbook of Cardiorenal Medicine*. Springer; 2021. doi:10.1007/978-3-030-57460-4_15
8. National Institute for health and care excellence (NICE). Chronic heart failure in adults: diagnosis and management. NICE guideline [NG106]. Guidance. 2018.
9. Chang AM, Cheng AB. Volume assessment in heart failure. In: Peacock W, ed. *Short Stay Management of Acute Heart Failure*. Contemporary Cardiology. Humana Press; 2017. doi:10.1007/978-3-319-44006-4_10
10. Accardi AJ, Matsubara BS, Gaw RL, Daleiden-Burns A, Heywood JT. Clinical utility of fluid volume assessment in heart failure patients using bioimpedance spectroscopy. *Front Cardiovasc Med*. 2021;8:636718. doi:10.3389/fcvm.2021.636718
11. Hanna D, Baig I, Subbiondo R, Iqbal U. The usefulness of bioelectrical impedance as a marker of fluid status in patients with congestive heart failure: a systematic review and meta-analysis. *Cureus*. 2023;15(4):e37377. doi:10.7759/cureus.37377
12. TORAY. Body Composition Analyzer MLT-600N. https://www.toray-medical.com/medical/touseki/pdf/tou_0200.pdf
13. INBODY. InBody970. https://inbody.co.jp/inbody-970/
14. Swedberg K, Cleland J, Dargie H, et al. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005): the task force for the diagnosis and treatment of chronic heart failure of the European Society of Cardiology. *Eur Heart J*. 2005;26(11):1115-1140. doi:10.1093/eurheartj/ehi204
15. Rozentryt P, von Haehling S, Lainscak M, et al. The effects of a high-caloric protein-rich oral nutritional supplement in patients with chronic heart failure and cachexia on quality of life, body composition, and inflammation markers: a randomized, double-blind pilot study. *J Cachexia Sarcopenia Muscle*. 2010;1(1):35-42. doi:10.1007/s13539-010-0008-0
16. Sergi G, Lupoli L, Volpato S, et al. Body fluid distribution in elderly subjects with congestive heart failure. *Ann Clin Lab Sci*. 2004;34(4):416-422.
17. Ruzhanskaya A, Tuglu MM, Poh TW. An Overview of BNP and NT-proBNP Whitepaper Report. Beckman Coulter. https://m.beckmancoulter.com/rs/213-HFT-078/images/Whitepaper_An%20Overview%20of%20BNP%20and%20NT-proBNP.pdf
18. Han BG, Song SH, Yoo JS, Park H, Kim J, Choi E. Association between OH/ECW and echocardiographic parameters in CKD5 patients not undergoing dialysis. *PLoS One*. 2018;13(4):e0195202. doi:10.1371/journal.pone.0195202
19. Kilter H, Böhm M. Cardiac Glycosides. In: Offermanns S, Rosenthal W, eds. *Encyclopedia of Molecular Pharmacology*. Springer; 2008. doi:10.1007/978-3-540-38918-7_36
20. Agyekum RE. Medications used for the renal system. In: Hood P, Khan E, eds. *Understanding Pharmacology in Nursing Practice*. Springer; 2020. doi:10.1007/978-3-030-32004-1_8
21. Blair HA. Dapagliflozin: a review in symptomatic heart failure with reduced ejection fraction. *Am J Cardiovasc Drugs*. 2021;21:701-710. doi:10.1007/s40256-021-00503-8
22. Söderberg M, Hahn RG, Cederholm T. Bioelectric impedance analysis of acute body water changes in congestive heart failure. *Scand J Clin Lab Invest*. 2001;61(2):89-94. doi:10.1080/00365510151097520
23. Elkinton JR, Squires RD. The distribution of body fluids in congestive heart failure I. Theoretic considerations. *Circulation*. 1951;4(5):679-696. doi:10.1161/01.cir.4.5.679
24. Smith W, Ball S. ACE inhibitors in heart failure: an update. *Basic Res Cardiol*. 2000;95(Suppl 1):8-14. doi:10.1007/s003950070003
25. Boxer RS, Dunlap ME. Aldosterone antagonists in the treatment and prevention of heart failure. *Curr Treat Options Cardiovasc Med*. 2005;7:431-436. doi:10.1007/s11936-005-0027-x
26. Ministry of Health, Labour and Welfare. Dietary Reference Intakes for Japanese (2020 Edition). 2020.
27. Tagawa R, Watanabe D, Ito K, et al. Dose–response relationship between protein intake and muscle mass increase: a systematic review and meta-analysis of randomized controlled trials. *Nutr Rev*. 2020;79(1):66-75. doi:10.1093/nutrit/nuaa104
28. Taylor JL, Myers J, Bonikowske AR. Practical guidelines for exercise prescription in patients with chronic heart failure. *Heart Fail Rev*. 2023;28(6):1285-1296. doi:10.1007/s10741-023-10310-9
29. Edwards J, Shanmugam N, Ray R, et al. Exercise mode in heart failure: a systematic review and meta-analysis. *Sports Med Open*. 2023;9:3. doi:10.1186/s40798-022-00549-1
30. Fisher S, Smart NA, Pearson MJ. Resistance training in heart failure patients: a systematic review and meta-analysis. *Heart Fail Rev*. 2022;27:1665-1682. doi:10.1007/s10741-021-10169-8
31. Fuertes-Kenneally L, Manresa-Rocamora A, Blasco-Peris C, et al. Effects and optimal dose of exercise on endothelial function in patients with heart failure: a systematic review and meta-analysis. *Sports Med Open*. 2023;9:8. doi:10.1186/s40798-023-00553-z
32. Masschelein E, D'Hulst G, Zvick J, et al. Exercise promotes satellite cell contribution to myofibers in a load-dependent manner. *Skelet Muscle*. 2020;10(1):21. doi:10.1186/s13395-020-00237-2

33. Beaudry KM, Binet ER, Collao N, et al. Nutritional regulation of muscle stem cells in exercise and disease: the role of protein and amino acid dietary supplementation. *Front Physiol*. 2022;13:915390. doi:10.3389/fphys.2022.915390
34. Nunes EA, Stokes T, McKendry J, et al. Disuse-induced skeletal muscle atrophy in disease and nondisease states in humans: mechanisms, prevention, and recovery strategies. *Am J Physiol Cell Physiol*. 2022;322(6):C1068-C1084. doi:10.1152/ajpcell.00425.2021
35. Ribeiro AS, Avelar A, Schoenfeld BJ, Ritti Dias RM, Altimari LR, Cyrino ES Resistance training promotes increase in intracellular hydration in men and women. *Eur J Sport Sci* 2014;14(6):578-585. doi:10.1080/17461391.2014.880192
36. Hall JE. *Guyton and Hall Textbook of Medical Physiology Thirteen Edition*. Elsevier; 2015.
37. Lorenzo I, Serra-Prat M, Yébenes JC. The role of water homeostasis in muscle function and frailty: a review. *Nutrients*. 2019;11(8):1857. doi:10.3390/nu11081857
38. Kim HJ, Kim YJ, Kim IY, Seong JK. Resistance exercise training-induced skeletal muscle strength provides protective effects on high-fat-diet-induced metabolic stress in mice. *Lab Anim Res*. 2022;38(1):36. doi:10.1186/s42826-022-00145-0
39. Hotta K, Taniguchi R, Nakayama H, Yamaguchi F, Sato Y. The effects of an oral nutritional supplement with whey peptides and branched-chain amino acids for cardiac rehabilitation of patients with chronic heart failure. *Int Heart J*. 2021;62(6):1342-1347. doi:10.1536/ihj.21-102
40. Azhar G, Wei JY, Schutzler SE, et al. Daily consumption of a specially formulated essential amino acid-based dietary supplement improves physical performance in older adults with low physical functioning. *J Gerontol A Biol Sci Med Sci*. 2021;76(7):1184-1191. doi:10.1093/gerona/glab019
41. Zhou C, Wang S, Sun X, et al. Application of food exchange portion method in home-based nutritional intervention for elderly patients with chronic heart failure. *BMC Cardiovasc Disord*. 2023;23(1):80. doi:10.1186/s12872-023-03072-7

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