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Phase Angle Is Associated With Handgrip Strength in Older Patients With Heart Failure

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Objective To assess the relationships between phase angle and muscle mass, strength, and physical function in patients with heart failure.
Methods This study used a cross-sectional design. The analysis included 51 patients with heart failure. The Short Physical Performance Battery, one-leg standing time, handgrip strength, phase angle, and skeletal muscle index were measured. To identify explanatory variables of phase angle, hierarchical multiple regression analysis was performed.
Results Handgrip strength was found to be an explanatory variable of phase angle independent of age, sex, and body mass index. This model was able to explain 30.4% of the model variance for phase angle.
Conclusion In patients with heart failure, improving muscle strength rather than muscle mass or physical function might be more important for improving phase angle. Handgrip strength is an important outcome for improving prognosis in patients with heart failure.

Keywords Heart failure, Electric impedance, Hand strength, Cardiac rehabilitation

INTRODUCTION

Heart failure is one of the major global health problems. It is estimated that, by 2030, the number of patients with heart failure will reach 1.3 million in Japan and 8 million in the United States [1,2]. Heart failure management involves enormous hospitalization costs and imposes a significant burden on health care systems. Moreover, a recent meta-analysis including more than 1.5 million patients with chronic or stable heart failure estimated a 5-year survival rate of 57% [3]; in addition, heart failure has an enormous cost in terms of poor prognosis. Heart failure is a syndrome that can be viewed as the chronic stage of any underlying disease or condition that leads

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to cardiac impairment, and various factors are associated with its prognosis. In particular, nutritional status is one of the important factors influencing the prognosis of patients with heart failure. Malnutrition increases the risk of developing cardiac cachexia, characterized by unintentional weight loss due to the loss of muscle, fat, and bone mass, which is strongly associated with increased mortality [4]. Therefore, it has been highlighted that an assessment of the general condition of patients with heart failure, including nutritional status and body composition, is important for managing symptoms and predicting prognosis.

Researchers have proposed the use of bioelectrical impedance analysis for the detection of nutritional status and body composition, as it evaluates the electrical properties of tissues as quantified by measurements of bioelectrical impedance. Phase angle is calculated as the ratio of resistance (the opposition to the electrical current stream through intra and extracellular ionic solutions), over reactance (the delay in the flow of current caused by tissue capacitance), and it is highlighted as a relevant indicator of cellular mass, membrane integrity, and hydration status [5]. A low phase angle suggests decreased cellular integrity and is an established predictor of mortality in various clinical situations, including kidney disease, cancer, pulmonary disease, and so on [6]. Heart failure is no exception, and several previous studies have described that the phase angle is independent predictor of mortality in patients with acute or chronic heart failure [7,8]. Therefore, it is important to evaluate phase angle in patients with heart failure in order to develop an effective therapeutic strategy while taking into consideration the patient prognosis.

Various factors are known to affect phase angle, including biological factors, fluid status, nutritional status, and so on. In particular, the loss of skeletal muscle mass and increased noncontractile components in skeletal muscle causes a reduction phase angle. Accordingly, muscle strength weakness and poor physical function have been reported to be associated with low phase angle in healthy adults [9]. Muscle mass reduction, muscle dysfunction, and poor physical function are often observed in patients with heart failure [10-12], and these factors are indicated to be independent predictor of mortality in such patients [12-14]. Resistance training has been recommended to improve muscle mass, muscle strength, and physical function in patients with heart failure [15] and has also been reported to improve phase angle sensitively [16]. These findings might indicate that phase angle is related to muscle mass, strength, and physical function in patients with heart failure. Previous study have indicated a relationship between phase angle and muscle mass, strength (handgrip strength), and/or physical function not only in healthy adults but also in patients with cancer [17], kidney disease [18], and chronic obstructive pulmonary disease [19]. However, this relationship remains unclear in patients with heart failure and thus should be identified to improve phase angle and thus prognosis. Thus, the purpose of this study was to assess the relationship between phase angle and muscle mass, strength, and physical function in patients with heart failure. We hypothesized that skeletal muscle mass reduction, muscle strength weakness, and poor physical function are associated with low phase angle in patients with heart failure.

MATERIALS AND METHODS

Study design

This is a cross-sectional study. The intent and purpose of this study was explained to all patients in writing at the start of rehabilitation, and written informed consent was obtained before enrollment. The study was conducted in accordance with the Declaration of Helsinki and the Strengthening the Reporting of Observational Studies in Epidemiology statement. This study was approved by the Institutional Review Board of Kure Kyosai Hospital (Approval No. 2021-30).

Setting

Participant enrollment was conducted from January 2020 to July 2021. Physical therapists performed all data measurements and collection.

Participants

Study participants included elderly patients (≥65 years) who were admitted to the hospital with heart failure and were able to walk without assistance before hospitalization. Heart failure was defined based on the Framingham criteria [20]. We excluded patients who developed complications during hospitalization, underwent pacemaker operation, or had severe dementia (defined as a

Hasegawa Dementia Scale-Revised [HDS-R] score of ≤9). All participants received cardiac rehabilitation treatment including aerobic exercise and resistance training using walking and bicycle ergometer. Exercise intensity was determined based on the target heart rate and exertion level. The target heart rate was set at 40%–50% of heart rate reserve, and target exertion level was set at 12–13/20 on the Borg rate of perceived exertion scale. The sample size was calculated using G*Power version 3.1.9 (Heinrich Heine Universität, Düsseldorf, Germany). Fifty-five cases were calculated by setting the alpha value at 0.05, the statistical power at 0.8, and the effect size f^2 at ≥0.15 [21]. We included the same patients in the analysis in this study as in our previous study [22]. However, that study investigated the relationship between handgrip strength, muscle mass, and extracellular water (ECW)/intracellular water (ICW) ratio, which is an index of muscle quality in patients with heart failure. In addition, there were differences in the purpose of this study, which focuses on phase angles, and the those of previous study. We believe that to develop an effective therapeutic strategy that takes into consideration patients prognosis, it is also necessary to investigate whether muscle strength or muscle mass is associated with phase angle in patients with heart failure.

Variables

Basic patient information and clinical characteristics

Basic patient information included age, sex, body mass index (BMI), HDS-R score, Life-Space Assessment (LSA) score [23], and degree of physical frailty based on the Japanese version of the Cardiovascular Health Study (J-CHS) criteria [24]. LSA measured life-space mobility in five areas, based on the spaces that patients have used in the past 4 weeks. Each life-space level is allocated a subscore based on the average weekly frequency and independence of life-space mobility. The composite score ranges from 0 to 120, with higher scores representing greater mobility [23]. The J-CHS criteria categorized patients as nonfrail, prefrail, and frail based on the following five domains: weight loss, slowness, weakness, exhaustion, and low activity. Patients with three or more score components were categorized as frail, patients with one or two score components were categorized as prefrail, and patients without score components were categorized as nonfrail [24]. HDS-R, LSA, and J-CHS were measured at the start of rehabilitation.

Patient clinical characteristics included New York Heart Association (NYHA) classification, medical history (presence or absence of heart failure, hypertension, and diabetes mellitus), blood biochemistry data (hemoglobin, brain natriuretic peptide [BNP], Geriatric Nutritional Risk Index, and estimated glomerular filtration rate), and left ventricular ejection as echocardiographic data. All of these variables were measured at the time of hospital admission.

Physical functions

The assessments of physical functions included the Short Physical Performance Battery (SPPB), one-leg standing time, and handgrip strength. These were assessed before discharge. The SPPB is an established standardized and reproducible measure of physical function in older patients and provides a comprehensive evaluation of physical function based on three components: static standing balance, 4-m walk time, and time to complete five repeated chair stands. Each component is scored from 0 to 4 points, with higher scores indicating better physical function [25]. One-leg standing time evaluates standing balance. Using a stopwatch, we measured the duration of time patients could stand on one leg with their eyes open and hands on their waist. Measurements were taken two times for both limbs, and the maximum value was adopted as the representative value. Handgrip strength has been regarded as an indicator of overall body strength. We assessed handgrip strength using a grip strength meter (TKK-5101; Takei Scientific Instruments, Tokyo, Japan) with the patients in the standing position and upper limb abducted to approximately 20°. Measurements were obtained two times for both sides, and the maximum value was adopted as the representative value.

Bioelectrical impedance analysis

We assessed body composition via multiple-frequency bioelectrical impedance analysis (S10; InBody, Seoul, Korea) using six different frequencies (1, 5, 50, 250, 500, and 1,000 kHz). Patients remained supine on the bed with their arms and legs abducted, and reusable contact electrodes were placed on the first and third finger of both hands and the medial and lateral side of both ankles. We calculated the phase angle from the relationship between the resistance and reactance vectors based on bioelectrical impedance measurements. We used a resistance and reactance of 50 kHz to calculate the phase angle, and the phase angle in the whole body was used for analysis. It has been demonstrated higher test-retest reliability and accuracy for evaluation of the phase angle [26]. Additionally, we calculated the skeletal muscle index (SMI) by dividing the limb skeletal muscle mass (kg) by the square of the height (m^2). Phase angle and SMI were measured before discharge.

Statistical analysis

The normality of the data distribution was assessed using the Shapiro–Wilk test. The association between phase angle and basic information, clinical characteristics, physical function, and SMI was evaluated by Pearson correlation coefficient or Spearman correlation coefficient. To identify explanatory variables of phase angle, we performed hierarchical multiple regression analysis. The dependent value included phase angle in the whole body, whereas the independent value included basic information, clinical characteristics, physical function, and SMI. Age, sex, and BMI are known to be the major determinants of phase angle [27]. To assess the relationship between phase angle and muscle mass, strength, and physical function, these factors should be controlled as confounders beforehand. Therefore, age, sex, and BMI were first input forcibly as confounding factors in block 1. Thereafter, other independent variables were input using a stepwise method in block 2. We extracted the factors associated with phase angle in the whole body independently from the confounding factors (age, sex, and BMI). To account for multicollinearity, the threshold of the correlation coefficient between independent factors was set to 0.8 to exclude those highly correlated with the dependent variable. We performed all statistical analysis using IBM SPSS Statistics version 28 (IBM Corp., Armonk, NY, USA) with the significance level set at 5%.

RESULTS

A total of 68 patients with heart failure were initially included in this study. Among these, nine patients with pacemakers inserted, six patients who developed complications during hospitalization, and two patients with severe dementia were excluded from the analysis. Finally, 51 patients were included in the analysis. Table 1 shows the characteristics of the patients included in the analysis.

Table 2 shows the results of the correlation analysis between phase angle and basic information, clinical characteristics, physical function, and SMI. Phase angle showed significant positive correlation with age, BMI, LSA, hemoglobin, Geriatric Nutritional Risk Index, one-leg standing time, handgrip strength, and SMI. In addition, phase angle was negatively correlated with sex (male, 1; female, 2).

We did not find a strong correlation in the correlation

Table 1. Patients' characteristics

Characteristic	Heart failure (n=51)
Age (yr)	85±7
Sex, male/female	26/25
Body mass index (kg/m^2)	21.55±4.13
HDS-R score	22±6
LSA score	42±25
Frail, nonfrail/prefrail/frail	2/22/27
NYHA class, 1/2/3/4	0/5/23/23
Medical history	
Heart failure	38
Hypertension	5
Diabetes mellitus	25
Hemoglobin (g/dL)	11.27±2.28
BNP (pg/mL)	928.77±1,066.71
Geriatric Nutritional Risk Index	144.19±28.41
Estimated glomerular filtration rate (mL/min/1.73 m^2)	41.27±19.64
Left ventricular ejection fraction (%)	50.95±18.29
SPPB score	7.83±2.87
Static standing balance	2.88±1.13
4-m walk	2.88±1.02
Five repeated chair stands	2.06±1.46
One-leg standing time (s)	4.81±5.62
Handgrip strength (kg)	18.26±7.89
Phase angle (°)	4.21±0.88
Skeletal muscle index (kg/m^2)	5.54±1.17

Values are presented as mean±standard deviation or number only.
HDS-R, Hasegawa Dementia Scale-Revised; LSA, Life-Space Assessment; NYHA, New York Heart Association; BNP, brain natriuretic peptide; SPPB, Short Physical Performance Battery.

Table 2. Correlation between phase angle and other variables

Variable	R-value	p-value
Age (yr)	0.37	0.031
Sex, male, 1; female, 2	-0.27	0.005
Body mass index (kg/m^2)	0.43	0.001
HDS-R score	-0.08	0.305
LSA score	0.28	0.025
Frail, nonfrail, 0; prefrail, 1; frail, 2	-0.13	0.190
NYHA class	-0.17	0.130
Medical history, absence, 0; presence, 1		
Heart failure	-0.07	0.329
Hypertension	0.13	0.191
Diabetes mellitus	-0.25	0.046
Hemoglobin (g/dL)	0.41	0.002
BNP (pg/mL)	-0.24	0.049
Geriatric Nutritional Risk Index	0.29	0.024
Estimated glomerular filtration rate (mL/min/1.73 m^2)	0.20	0.091
Left ventricular ejection fraction (%)	0.02	0.453
SPPB score		
Static standing balance	0.13	0.191
4-m walk	0.16	0.141
Five repeated chair stands	0.20	0.087
One-leg standing time (s)	0.29	0.024
Handgrip strength (kg)	0.54	<0.001
Skeletal muscle index (kg/m^2)	0.33	0.012

HDS-R, Hasegawa Dementia Scale-Revised; LSA, Life-Space Assessment; NYHA, New York Heart Association; BNP, brain natriuretic peptide; SPPB, Short Physical Performance Battery.

analysis, and the final independent value included all variables: age, sex, BMI, HDS-R score, LSA score, degree of physical frailty, NYHA classification, presence or absence of medical history, blood biochemistry data, left ventricular ejection, three components of SPPB, one-leg standing time, handgrip strength, and SMI. Table 3 shows the results of the hierarchical multiple regression analysis. We found handgrip strength to be an explanatory variable of phase angle independent of age, sex, and BMI. The standardized regression coefficient of handgrip strength was 0.53, and the adjusted coefficient of determination was 0.30. This model was able to explain 30.4% of the model variance (adjusted R^2) for phase angle.

DISCUSSION

The results of this study provide partial support for our hypothesis that handgrip strength is an explanatory variable of phase angle in patients with heart failure. However, contrary to our hypothesis, SMI, one-leg standing time, and SPPB were not included as explanatory variables of phase angle. These results might be affected by the process of muscle weakness and cardiorespiratory capacity in patients with heart failure. Our findings suggest that improving the pure muscle strength of the whole body, rather than muscle mass or physical function, could be more important for improving phase angle in patients with heart failure.

We found that low handgrip strength was associated with a low phase angle in patients with heart failure. Previous studies reported a positive association between phase angle and handgrip strength in older adults [28] and in patients with various diseases states and clinical conditions [17-19]. Our findings showed that this relationship is also applicable to patients with heart failure. Phase angle is created by a correlation between the resistance and reactance in bioelectrical impedance analysis and is affected by body fluid balance between ICW and ECW [9,29]. Prior researchers found that approximately 75% of total body water is present in muscle [29], and muscle function has a great impact on phase angle. A relative expansion of ECW against ICW is considered an increase in noncontractile tissue, and an increase in the ECW/ICW ratio is associated with low muscle strength in older adults [30]. Recently, we reported that handgrip strength is affected by the upper limb ECW/ICW ratio in patients with heart failure [22]. Although BNP is also considered to be a biomarker of congestion and is used in clinical practice to quantify fluid overload [31], it has been shown that BNP cannot be used to accurately assess congestion and that bioelectrical impedance analysis is a more accurate assessment of body fluid balance than BNP. Thus, phase angle, which is affected by the body fluid balance between ECW and ICW, might be affected by muscle strength rather than clinical characteristics.

On the other hand, previous researchers reported that phase angle was associated with muscle mass in healthy older adults [32], but SMI was not an explanatory variable of phase angle in our patients with heart failure. Patients with heart failure often develop muscle atrophy and

Table 3. Hierarchical multiple regression analysis results of the variable that affected phase angle

Variable	Regression coefficient	Standardized regression coefficient	95% confidence interval	p-value	VIF
Block 1					
Constant	3.12	-	-	-	-
Age	-0.01	-0.06	-0.05 to 0.03	0.683	1.26
Sex	0.47	0.27	-0.02 to 0.96	0.057	1.10
BMI	0.07	0.34	0.01 to 0.13	0.024	1.24
Block 2					
Constant	0.38	-	-	-	-
Age	0.02	0.13	-0.02 to 0.06	0.393	1.61
Sex	-0.07	-0.04	-0.69 to 0.55	0.811	2.00
BMI	0.06	0.30	0.01 to 0.12	0.033	1.26
Handgrip strength	0.06	0.53	0.02 to 0.11	0.011	2.68

Block 1: ANOVA p=0.004, R^2=0.258, adjusted R^2=0.208.
Block 2: ANOVA p<0.001, R^2=0.363, adjusted R^2=0.304.
VIF, variance inflation factor; BMI, body mass index.

changes in total muscle mass [33]. However, Kinugasa et al. [34] found that 40.3% of patients with heart failure had muscle weakness despite normal muscle mass. In addition, it has been suggested that muscle atrophy develops only secondary to inactivity in patients with heart failure [33]. These studies suggest that muscle weakness in patients with heart failure is not necessarily associated with a reduction in muscle mass. The course of the muscle atrophy process in patients with heart failure is suggested to be associated with the infiltration of fatty tissue in the muscle [35], and our findings might suggest that in patients with heart failure, focusing on muscle quality rather than muscle mass is more important for improving phase angle.

In addition, our results showed that SPPB and one-leg standing time were not explanatory variables of phase angle. Previous studies reported that walking speed, chair stand, and balance ability were associated with phase angle in healthy older adults [29,36,37], and an association has been demonstrated between SPPB and increased risk of hospitalization and mortality in patients with heart failure [12]. These relationships between phase angle and physical function in patients with heart failure might be affected by cardiorespiratory capacity. Most patients with heart failure in this study were classified as NYHA 3 or 4. In addition, another study reported that 4-m walk time and the time to complete five repeated chair stands were associated with exercise tolerance in cardiopulmonary disease [38]. As mentioned above, phase angle is affected by muscle strength, but in patients with heart failure, because physical function is affected by various factors including cardiorespiratory capacity, it is possible that SPPB and one-leg standing time were not directly related to phase angle. Future studies should examine this possibility in detail.

Handgrip strength has been used as a reliable and responsive measure in cardiac rehabilitation, and it has been regarded as an indicator of overall body strength. Phase angle is known to increase sensitively with resistance training, and our findings may indicate the importance of improving whole-body muscle strength for increasing phase angle in patients with heart failure. However, our study has several limitations that warrant mention. First, our results may include some confounding effects. The body weight of patients with heart failure might be affected by fluid retention. Thus, SMI adjusted for confounders, including BMI, may not clearly assess the relationship between phase angle and skeletal muscle mass in patients with heart failure. Additionally, as phase angle has been suggested to be an indicator of cellular health [5], the degree of disability or dependence in the daily activities such as modified Rankin Scale is likely to have an impact on phase angle. However, the effects of the premorbid modified Rankin Scale have not been controlled in present model. In the future, an investigation of the relationship among phase angle, skeletal muscle mass, and handgrip strength in patients with heart failure might be required while controlling for confounding effects of these factors. Second, our findings were obtained by a cross-sectional study. Thus, it is not certain whether increased handgrip strength improves phase angle in patients with heart failure. A future longitudinal study is required to clarify that relationship. Third, bioelectrical impedance analysis was conducted the day before discharge, but the time of measurement and the patient's condition, such as the presence or absence of urine, were not standardized in this study. It has been indicated that the volume of the urine or skin temperature changes impedance data [39,40], and our results may be affected by these factors.

In conclusion, the results of our study show that phase angle is associated with handgrip strength but not with SMI, SPPB, and one-leg standing time in patients with heart failure. We found that phase angle is not related to muscle mass or physical function in patients with heart failure because of the difference in the process of muscle weakness and cardiorespiratory capacity, and improving muscle quality might be more important for improving phase angle than improving muscle mass or physical function in these patients. Our findings indicate that handgrip strength is a simple and important outcome for improving phase angle, and thus prognosis in patients with heart failure.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTION

Conceptualization: Kawakami W, Umehara T. Methodology: Kawakami W, Umehara T. Formal analysis: Umehara T. Funding acquisition: Umehara T. Project administration: Takahashi M, Katayama N. Visualization: Kawakami W, Umehara T. Writing – original draft: Kawakami W, Umehara T, Iwamoto Y. Writing – review and editing: Kawakami W, Umehara T. Approval of the final manuscript: all authors.

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