Title

Association of phasae angle dynamics with sarcopenia and activities of daily living in osteoporotic fracture patients

Running title

PhA changes in osteoporotic fracture outcomes

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Author Contributions

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Abstract

**Background:** This study aimed to determine whether changes in phase angle during rehabilitation are associated with clinical outcomes such as activities of daily living (ADL), skeletal muscle index (SMI), and strength in patients with osteoporotic fractures.

**Methods:** This retrospective observational study included patients with osteoporotic fractures admitted to convalescent rehabilitation wards. Changes in phase angle were defined as the difference between the phase angle values at discharge and on admission. The primary outcome was the Functional Independence Measure Motor (FIM-motor) score at discharge. The secondary outcomes were SMI and handgrip strength at discharge. We used multivariate analysis to adjust for confounding factors and examine the association between changes in the phase angle and outcomes.

**Results:** We analyzed a total of 115 patients (97 women, mean age 81.0 ± 10.0 years), with a median change in phase angle of 0.0° during hospitalization. We observed increased phase angles in 49 patients (43%), with a median increase of 0.2°. Multiple regression analysis showed that changes in phase angle were independently associated with FIM-motor score at discharge ($\beta = 0.238$, $P = 0.027$). Changes in phase angle were not significantly associated with SMI ($\beta = 0.059$, $P = 0.599$) or handgrip strength ($\beta = -0.032$, $P = 0.773$) at discharge.

**Conclusions:** An increased phase angle during rehabilitation was positively associated with
ADL improvement in patients with osteoporotic fractures. These findings may help clinicians make informed decisions regarding patient care and treatment strategies for better outcomes.

**Keywords:** Osteoporotic fractures, Body composition, Prognosis, Convalescent, Rehabilitation
Introduction

The phase angle calculated using bioelectrical impedance analysis (BIA) is of interest as a nutritional indicator and a marker of muscle quality. The phase angle is also an indicator of cellular health and reflects cell membrane integrity and cellular function, with a lower value indicating poor cellular function and malnutrition (1). Cutoff values for phase angle have been reported for diseases including stroke (2), heart failure (3), and cancer (4). As an indicator of muscle quality, the phase angle has demonstrated high accuracy in detecting sarcopenia (5-7) and is correlated with skeletal muscle mass and strength in older hospitalized patients (8). The usefulness of the phase angle in predicting prognosis has also been demonstrated in rehabilitation research. The admission phase angle is an independent predictor of discharge physical function in patients with stroke in acute-care settings (9), and discharge physical function and swallowing function in post-acute rehabilitation (2). In addition, phase angle is independently associated with gait and balance at discharge in patients with hip fractures (10). Therefore, the phase angle may be useful for predicting rehabilitation outcomes.

However, the phase angle lacks sufficient evidence for clinical application. Few reports have described the impact of improving the phase angle on activities of daily living (ADL), skeletal muscle mass, and muscle strength in patients with osteoporotic fractures. Osteoporotic fractures occur frequently in older adults, with an estimated 9 million cases occurring annually
worldwide (11). Furthermore, osteoporotic fractures negatively affect ADL (12,13) and quality of life (14,15). Recently, the phase angle has also been studied in patients with hip fractures and was associated with quality of life (16) and the ability to walk and balance (10). Moreover, changes in phase angle have been studied for further clinical application (17-19). A randomized controlled trial in older women showed that the phase angle could be changed using an exercise intervention with resistance training (18). In addition, the phase angle changes during rehabilitation in cancer survivors, and are significantly and positively correlated with changes in muscle strength (19). Hence, changes in phase angle may be useful for predicting clinical outcomes in different populations. However, evidence of the association between changes in phase angle and outcomes in patients with osteoporotic fractures is scarce. Therefore, we examined whether changes in phase angle during rehabilitation were associated with ADL, muscle mass, and strength in patients with osteoporotic fractures.

Materials and methods

Participants and setting

This was a single-center, cross-sectional study of patients admitted to a private hospital in Japan with a 116-bed convalescent rehabilitation ward. The study population consisted of patients with osteoporotic fractures admitted to the convalescent rehabilitation ward between
August 2017 and July 2022. The presence of osteoporosis was determined from the medical records of all patients with a history of osteoporosis. Osteoporotic fractures were defined as non-traumatic fractures caused by low external forces, such as falls from less than standing height (20). Patients with contraindications to bioelectrical impedance techniques, such as pacemakers, those with artificial joint insertions (defined as previous artificial joint insertion or those with artificial joint insertion after a recent fracture) that could affect the results of bioelectrical impedance techniques, and those with missing data on the survey items were excluded.

Data collection

On admission, patient information including age, sex, fracture site (vertebral, hip, pelvic, and other fractures), surgery, onset of admission, Charlson Comorbidity Index (CCI) (21), and total number of medications was collected from medical records. Information collected on admission included Mini-Mental State Examination (MMSE) score, handgrip strength, Food Intake Level Scale (FILS) score, body mass index (BMI), energy intake, Functional Independence Measure (FIM) score on admission, days to body composition measurement, skeletal muscle index (SMI), and phase angle. The length of hospital stay, rehabilitation duration, rehabilitation time, handgrip strength, FIM score, SMI, and phase angle were
recorded at discharge. Grip strength was defined as the maximum of two measurements taken twice on each side in the standing or sitting position using a grip strength meter (TKK5001; Takei Scientific Instruments Co., Ltd., Tokyo, Japan) (22). Energy intake was calculated from the intake of staple foods and side dishes, each rated by nurses on a five-point scale. If nutritional supplements were used, the dietary supplement intake was checked by a dietician and added to the energy intake. The FIM on admission was assessed within 24 h of admission; whereas, the FIM on discharge was assessed by nurses and care workers on the day before or on the day of discharge. The average daily rehabilitation time was calculated by dividing the total time spent on physiotherapy, occupational therapy, and speech therapy during the hospital stay by the length of stay.

Phase angle

Body composition assessment included the phase angle and SMI were calculated by BIA using a body composition analyzer (In Body S10; In Body, Tokyo, Japan). This device can be used for patients who are unable to maintain a standing or sitting position, or who are bedridden. The patients were asked to refrain from exercise for one hour before measurement and to lie in a resting position. All measured limbs were positioned in a unified back-lying posture. Body composition was measured within 48 h of admission and discharge. Phase angle
was measured from the resistance (R) and reactance (Xc) of the right hemisphere and was calculated using the following formula: \( \text{Phase angle} = \arctan \left( \frac{Xc}{R} \right) \times \left( \frac{180}{\pi} \right) \). In this equation, a 50 kHz resistance and reactance were used. Cutoff values for phase angle have been reported for diseases including stroke (2), heart failure (3), and cancer (4). However, the cutoff values for phase angle in patients with osteoporotic fractures, the subject of this study, have not been reported. Some studies stratified the median phase angle as the cutoff value in participants for whom previous research is lacking (9, 23). Therefore, we also classified the participants into low and normal baseline phase angle groups using median values. The difference between the phase angles at discharge and on admission was calculated and defined as the change in phase angle during hospitalization (phase angle at discharge - phase angle on admission). The SMI was calculated as limb muscle mass divided by height squared (kg/m²).

**Outcome**

The primary outcome was the FIM motor score (FIM-motor) at discharge, which is used to quantify the amount of help patients receive with ADL. The FIM-motor consists of 13 motor items and five cognitive items, each scored on a seven-point scale from 1 to 7, with a total score of 18–126. The FIM is a valid and reliable assessment method (24).

The secondary outcomes were SMI and handgrip strength at discharge.
Sample size calculation

The standard deviation of the FIM-motor score upon admission for patients with fractures in the convalescent rehabilitation ward was 16 (25). If the true difference between the groups was 14 (25), an estimated minimum of 51 patients in each group was needed to reject the null hypothesis with a power of 0.95 and an error of 0.05.

Statistical analysis

Continuous variables are expressed as means (standard deviation [SD]) for parametric data and median (interquartile range [IQR]) for non-parametric data. Nominal variables are expressed as numerical values (%).

We performed univariate analysis on the changes in phase angle from admission to discharge, dividing the patients into two groups: increased phase angle and decreased phase angle. Comparisons between the two groups were analyzed using t-test Mann-Whitney U test, χ2 test, or Fisher's exact test, depending on the variable type. The following tests were used, depending on the type of variable:

Multiple regression analysis was used to determine whether the changes in phase angle were independently associated with FIM-motor score, handgrip strength, and SMI at discharge. We
performed multivariate analysis using three models: all patients, patients with normal phase angle values at admission, and patients with low phase angle values at admission. Propensity scores and baseline values for each outcome were included to optimize the number of variables included in the statistical model and avoid overfitting (26). We applied logistic regression analysis to estimate the propensity score for changes in phase angle, with age, sex, fracture site, surgery, admission onset, MMSE, CCI, handgrip strength, FILS, BMI, SMI, energy intake, total number of medications, and FIM score at admission as explanatory variables.

We used IBM SPSS Statistics for Windows, version 29.0 (IBM Corporation, Armonk, NY, USA) to perform the statistical analyses, with a significance level of 5%.

Ethical approval

The study was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by the corporation's internal ethics committee (approval number 68). Written informed consent was not obtained as this was a cross-sectional study. Therefore, an opt-out method was used, and the participants were allowed to refuse to participate.

Results

In total, 186 patients with osteoporotic fractures were admitted to our hospital during the
study period. Of these, 115 patients were included in the analysis after excluding those with pacemaker implants (n = 9), artificial joint insertions (n = 43), or missing survey item data (n = 19) (Fig. 1).

Table 1 presents the baseline patient characteristics. The mean age of the patients was 81.0 ± 10.0 years, with 18 men and 97 women. The median baseline phase angles were 4.1° and 3.6° in men and women, respectively. When comparing the two groups, patients of both sexes with a low baseline phase angle were older and had lower handgrip strength, BMI, and SMI on admission compared with those with a normal phase angle. These patients also had a higher incidence of sarcopenia. Among women, those with a low baseline phase angle had lower FIM-motor, FIM-cognitive, and MMSE scores on admission compared with those with normal phase angles.

Table 2 shows the results of the univariate analyses of FIM-motor score, handgrip strength, and SMI at discharge for the groups with increased and decreased phase angles during hospitalization according to sex. The median change in the overall phase angle was 0.0°. In the increased and decreased phase angle groups, the changes were 0.2° and -0.2°, respectively. Univariate analysis of the increased and decreased phase angle groups showed no significant differences in FIM-motor score, handgrip strength, or SMI at discharge.

The results of multiple regression analysis of the FIM-motor score, SMI, and handgrip
strength at discharge, adjusted for potential confounders, are shown in Table 3. We performed multivariate analysis using three models according to the baseline phase angle values. Model 1 included all patients, model 2 included patients with low baseline phase angle values, and model 3 included patients with normal baseline phase angle values. We observed no multicollinearity between variables in any model. In model 1, changes in phase angle during hospitalization were independently and positively associated with discharge FIM-motor score ($\beta = 0.238, P = 0.027$). Changes in phase angle during hospitalization were not significantly associated with SMI ($\beta = 0.059, P = 0.599$) or handgrip strength ($\beta = -0.032, P = 0.773$). Model 2 was similar to model 1, with changes in phase angle during hospitalization showing an independent and positive association with FIM-motor score at discharge ($\beta = 0.398, P = 0.006$) and not with SMI ($\beta = 0.100, P = 0.519$) or handgrip strength ($\beta = 0.047, P = 0.763$). In model 3, changes in phase angle during hospitalization were not significantly associated with FIM-motor score ($\beta = 0.189, P = 0.328$), SMI ($\beta = 0.190, P = 0.326$), or handgrip strength ($\beta = 0.006, P = 0.972$) at discharge.

The results of changing the outcome to “change in FIM”, “change in SMI”, and “change in handgrip strength” are shown in the Supplementary Table. The results of the multiple regression analysis adjusted for potential confounders showed that in model 1, changes in phase angle during hospitalization were not significantly associated with changes in FIM-
motor score (β = 0.179, P = 0.114), SMI (β = 0.150, P = 0.169) or handgrip strength (β = -0.027, P = 0.804) at discharge. In model 2, changes in phase angle during hospitalization were not significantly associated with changes in FIM-motor score (β = 0.302, P = 0.05), SMI (β = 0.035, P = 0.822), or handgrip strength (β = 0.043, P = 0.779) at discharge. In model 3, changes in phase angle during hospitalization were not significantly associated with changes in FIM-motor score (β = 0.065, P = 0.730), SMI (β = 0.171, P = 0.358), or handgrip strength (β = -0.243, P = 0.208) at discharge. Therefore, the original data are of high clinical value and this is the conclusion of the present study.

Discussion

This study investigated the association between changes in phase angle during rehabilitation and outcomes including ADL, skeletal muscle mass, and muscle strength at discharge in patients with osteoporotic fractures. Three notable clinical findings were observed: First, changes in phase angle were independently and positively associated with improvements in ADL. This association was stronger in patients with a lower baseline phase angle than in those without. Second, changes in phase angle were not statistically associated with increases in SMI or handgrip strength. Third, 43% of the patients had an increased phase angle during hospitalization, with a median increase of 0.2°. The three results are discussed below.
Changes in phase angle were positively associated with improvements in ADL in patients with osteoporotic fractures. This association was stronger in patients with lower baseline phase angles. Because the phase angle reflects nutritional status and muscle quality (5,6,27-31), it is reasonable to assume that an increased angle is closely associated with improved nutritional status and muscle quality. Furthermore, our findings support those of previous studies showing that improved nutritional status may lead to greater improvement in ADL in patients receiving rehabilitation, especially those with hip fracture (32,33). Improvements in sarcopenia during hospitalization are reportedly independently and positively associated with improvements in ADL (34). However, poor muscle quality is associated with worse ADL (35). In addition, the association between increased phase angle and improved ADL in this study was stronger in patients with a lower phase angle at admission. A low phase angle is associated with poor cellular health and increased morbidity (36), suggesting that it may indicate the overall patient health status. Therefore, patients with a lower baseline phase angle may experience greater improvements in physical function and health status compared with patients with a normal baseline phase angle receiving comprehensive interventions such as early rehabilitation, nutritional status, oral health, and polypharmacy assessment and management. Furthermore, owing to the ceiling effect of the phase angle scores, patients with a lower baseline phase angle may demonstrate more pronounced improvements in phase angle over the study period than
those without. This suggests that phase angle may be an important indicator for early screening and intervention in patients with osteoporotic fractures, especially in those with a low phase angle. These findings suggest that the therapeutic effects of nutrition and exercise are more likely to be reflected in phase angle changes when patients have a good nutritional status and muscle quality at the time of admission.

Changes in phase angle were not significantly associated with increases in skeletal muscle mass or handgrip strength. The possible explanations for this finding include the fact that changes in skeletal muscle mass and handgrip strength were not the primary outcomes of this study and that the study design and adjustment for confounders in the multivariate analysis were designed based on the primary outcome. Thus, although this association was not statistically significant, this does not mean no association was present. Indeed, recent research has shown a positive association between changes in phase angle and increases in muscle mass and strength in post-stroke patients (37). Therefore, further high-quality studies are required to verify this association.

In this study, 43% of patients experienced an increase in phase angle during rehabilitation, with a median increase of 0.2°. Few studies have examined changes in phase angle over time; thus, the present study is novel and clinically significant. The phase angle is more sensitive to changes than skeletal muscle mass (38). A recent systematic review and meta-analysis showed
that resistance training interventions were effective and safe for changing phase angles in older adults (39). Resistance training has been incorporated into the rehabilitation programs for patients with fractures to prevent bone loss, reduce fall risk, and prevent or improve sarcopenia. Additionally, systematic reviews and meta-analyses have shown that nutritional interventions for patients with cancer can change their phase angles (40). These findings suggest that rehabilitation, including resistance training, nutritional management, or their combination, may have a greater potential to improve the phase angle. Therefore, to maximize improvement of patient outcomes, careful observation of the phase angle and its trends, rather than routine and conventional treatment, may help facilitate high-quality treatment, including personalized nutrition and exercise, in a multidisciplinary manner.

This study has several limitations, the first of which is its single-center design, which limits its generalizability. Future multicenter studies are needed to confirm these findings. Second, as a cross-sectional study, it was not possible to obtain detailed information regarding the influences of preoperative ADL, presence or absence of pain, type of rehabilitation provided during hospitalization, and changes in energy intake on the results. Further high-quality prospective studies adjusting for these confounders are warranted.

Conclusion
In conclusion, changes in phase angle during rehabilitation were independently and positively associated with improvements in ADL in patients with osteoporotic fractures. Furthermore, this association was stronger in patients with a low baseline phase angle compared with patients without. Therefore, changes in phase angle are a useful indicator of functional outcomes in patients with osteoporotic fractures and may be used to improve discharge outcomes.