Association of Phase Angle and Sarcopenia in Chronic Musculoskeletal Pain Patients: A Retrospective Study

Hironori Tsuji

Okayama Red Cross General Hospital

Tomoko Tetsunaga (✉ kwdtmk1201@yahoo.co.jp)

Okayama University Hospital

Tomonori Tetsunaga

Okayama University Hospital

Haruo Misawa

Okayama University Hospital

Masanori Hamada

Okayama University Hospital

Yoshimi Katayama

Okayama University Hospital

Kentaro Yamane

Okayama Medical Center

Yoshiaki Oda

Okayama University Hospital

Shinichiro Takao

Okayama University

Yuya Kajiki

Okayama University

Yoshitaka Takei

Kurashiki Municipal Hospital

Keiichiro Nishida

Okayama University Hospital

Masuo Senda

Okayama University Hospital

Toshifumi Ozaki

Okayama University

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Association of phase angle and sarcopenia in chronic musculoskeletal pain patients: a retrospective study

Hironori Tsuji, M.D., Ph.D.^a, Tomoko Tetsunaga, M.D., Ph.D.^{b c*}, Tomonori Tetsunaga, M.D., Ph.D.^{b c}, Haruo Misawa, M.D., Ph.D.^b, Masanori Hamada, M.D., Ph.D.^d, Yoshimi Katayama, M.D., Ph.D.^d, Kentaro Yamane, M.D., Ph.D.^e, Yoshiaki Oda, M.D., Ph.D.^b, Shinichiro Takao, M.D.^f, Yuya Kajiki, M.D.^f, Yoshitaka Takei, M.D., Ph.D.^g, Keiichiro Nishida, M.D., Ph.D.^{c f}, Masuo Senda, M.D., Ph.D.^d, Toshifumi Ozaki, M.D., Ph.D.^f

^a Department of Orthopedic Surgery, Okayama Red Cross Hospital, Okayama, Japan, 2-1-1 Aoe, Kitaku, Okayama City, Okayama 700-8607, Japan

^b Department of Orthopedic Surgery, Okayama University Hospital, Okayama, Japan, 2-5-1, Shikata-cho, Kitaku, Okayama City, Okayama 700-8558, Japan

^c Department of Locomotive Pain Center, Okayama University Hospital, Okayama, Japan, 2-5-1, Shikata-cho, Kitaku, Okayama City, Okayama 700-8558, Japan

^d Department of Rehabilitation Medicine, Okayama University Hospital, Okayama, Japan, 2-5-1, Shikata-cho, Kitaku, Okayama City, Okayama 700-8558, Japan

^e Department of Orthopedic Surgery, Okayama Medical Center, Okayama, Japan, 1711-1, Tamasu, Kitaku, Okayama City, Okayama 701-1192, Japan

20 ^f Department of Orthopedic Surgery, Okayama University Graduate School of Medicine,
21 Dentistry, and Pharmaceutical Sciences, Okayama, Japan, 2-5-1 Shikata-cho, Kitaku,
22 Okayama City, Okayama 700-8558, Japan

23 ^g Department of Orthopedic Surgery, Kurashiki Municipal Hospital, Okayama, Japan, 2-39,
24 Kojima-ekimae, Kurashiki City, Okayama 711-0921, Japan

25

26 * Corresponding Author: Tomoko Tetsunaga, M.D., Ph.D.

27 Department of Orthopedic Surgery, Okayama University Hospital, Okayama, Japan, 2-5-1
28 Shikata-cho, Kitaku, Okayama City, Okayama 700-8558, Japan

29 Tel: 81-86-235-7273

30 Fax: 81-86-223-9727

31 E-mail: kwdtmk1201@yahoo.co.jp

Abstract

In chronic musculoskeletal pain patients, early prevention and detection for musculoskeletal dysfunction (i.e., sarcopenia) is an issue of significant clinical interest. Phase angle, which can be measured through bioelectrical impedance analysis, can detect sarcopenia; however, the evidence on chronic musculoskeletal pain patients is limited. This study aimed to assess the relationship between phase angle and sarcopenia in patients with chronic musculoskeletal pain. A total of 190 patients (51 men, 139 women; mean age: 67.2 years) with chronic musculoskeletal pain were included in this retrospective cross-sectional study. Sarcopenia was diagnosed using the Asian Working Group for Sarcopenia Criteria 2019. A total of 51 patients (26.7%) including 10 men (19.6%) and 41 women (29.5%) were diagnosed with sarcopenia. Phase angle, sarcopenia-related factors, age, and BMI differed significantly in patients with and without sarcopenia. On multiple logistic regression analysis, the prevalence of sarcopenia was observed to be significantly correlated with phase angle and BMI. The areas under the curve exhibited high accuracy in discriminating sarcopenia in men and moderate accuracy in both genders and in women. We conclude that phase angle may be a useful tool for detecting sarcopenia in the patients with chronic musculoskeletal pain.

Keywords: sarcopenia, chronic musculoskeletal pain, phase angle, detection, bioimpedance analysis

50 **Introduction**

51 Chronic pain, which affects 20% of the general population, is a global problem that decreases
52 activities of daily living.^{1,2} Meanwhile, 30–50% of older adults suffer with chronic pain, mostly
53 originating in the musculoskeletal system.³ Furthermore, musculoskeletal conditions are the
54 leading cause of disability and also have a large impact on many other aspects of older people's
55 health, such as low physical activity level, poor mobility, frailty, depression, cognitive
56 impairment, and falls.⁴ In chronic musculoskeletal pain patients, physical function and activity
57 are impaired from an early age, and as decreased activity exacerbates and intracts the pain itself,
58 early prevention and detection for musculoskeletal dysfunction is an issue of significant clinical
59 interest.⁵ Sarcopenia, a progressive and generalized musculoskeletal disorder, has attracted
60 attention^{6–8} and is associated with increased adverse outcomes, including falls, fractures,
61 functional decline, and mortality.^{9–13} While chronic musculoskeletal pain and sarcopenia may
62 be correlated and the early detection of sarcopenia may be important in patients with chronic
63 pain, evidence on this correlation is limited.

64 Conversely, phase angle, which can be measured noninvasively through bioelectrical
65 impedance analysis, is reported to reflect the quality of cells, and a lower phase angle suggests
66 decreased cellular integrity.^{14–16} Previous reports have correlated phase angle with nutritional
67 status, muscle strength, and mortality.^{17–19} Moreover, phase angle can be used to detect
68 sarcopenia.^{20–24} However, it is unclear whether phase angle is lower and can detect sarcopenia

in chronic musculoskeletal pain patients. Therefore, this study aimed to assess the relationship between phase angle and sarcopenia in patients with chronic musculoskeletal pain.

Results

Participants' characteristics

The characteristics of the patients are shown in Table 1. The mean age was 67.2 years (standard deviation [SD]: 13.5) and mean Numeric Rating Scale (NRS) score was 5.2 points (SD: 2.5). Sarcopenia was diagnosed in 51 (26.7%), 10 (19.6%), and 40 (29.5%) patients of all, male, and female patients, respectively. The mean phase angle was 4.7 degrees (SD: 1.0). Pain site and other sarcopenia-related factors are also shown on Table 1.

Table 1. Participants characteristics

Variables	All (n = 190)	Men (n = 51)	Women (n = 139)
Age (years)	67.2 ± 13.5	65.3 ± 12.2	67.9 ± 13.9
BMI (kg/m ²)	23.6 ± 4.5	23.7 ± 3.7	23.5 ± 4.8
Sarcopenia	51 (26.7)	10 (19.6)	41 (29.5)
Grip power (kg)	19.6 ± 10.4	29.3 ± 12.0	16.1 ± 6.9
Gait speed (m/s)	1.1 ± 0.4	1.1 ± 0.4	1.3 ± 0.4
SMI (kg/m ²)	6.7 ± 1.3	7.9 ± 1.1	6.1 ± 0.9

Phase angle (°)	4.6 ± 0.9	5.3 ± 0.9	4.4 ± 0.8
NRS (points)	5.2 ± 2.5	4.9 ± 2.8	5.3 ± 2.4
Pain site			
Cranio-cervical	32 (16.8)	11 (21.6)	21 (15.1)
Upper limb	41 (21.5)	15 (29.4)	26 (18.7)
Trunk	111 (58.1)	27 (52.9)	84 (60.4)
Lower limb	98 (51.3)	25 (49.0)	73 (52.5)

Data are expressed as mean ± standard deviation for continuous variables, and as percentages (%) for categorical variables. BMI, body mass index; SMI, skeletal mass index; NRS, numeric rating scale.

Correlations among phase angle and measured variable

Table 2 shows the correlation among phase angle and other variables. Phase angle was significantly correlated with age ($r = -0.54$, $p < 0.001$), BMI ($r = 0.21$, $p = 0.003$), grip power ($r = 0.61$, $p < 0.001$), gait speed ($r = 0.42$, $p < 0.001$), skeletal muscle index (SMI) ($r = 0.71$, $p < 0.001$), and NRS ($r = -0.19$, $p = 0.007$).

Table 2. Correlation among phase angle and measured parameters

Variables	Phase angle	
	<i>r</i>	<i>p</i>
Age	-0.54	< 0.001
BMI	0.21	0.003
Grip power	0.61	< 0.001
Gait speed	0.42	< 0.001
SMI	0.71	< 0.001
NRS	-0.19	0.01

BMI, body mass index; SMI, skeletal mass index; NRS, numeric rating scale

Comparison between patients with and without sarcopenia

Table 3 shows the characteristics of patients with and without sarcopenia. All sarcopenia-related factors, phase angle, age, and body mass index (BMI) differed significantly in patients with and without sarcopenia. Multiple logistic regression analysis revealed a significant correlation between the prevalence of sarcopenia and phase angle (odds ratio [OR] = 0.09, $p < 0.001$) and BMI (OR = 0.80, $p < 0.001$) (Table 4).

Table 3. Participants characteristics with and without sarcopenia

Variables	With sarcopenia	Without sarcopenia	<i>P</i> -value
	(n = 51)	(n = 139)	
Age (years)	74.3 ± 11.3	64.6 ± 13.4	< 0.001
Gender (men/women)	10 / 41	41 / 98	0.199
BMI (kg/m ²)	21.2 ± 3.3	24.4 ± 4.6	< 0.001
Grip power (kg)	12.4 ± 5.4	22.3 ± 10.5	< 0.001
Gait speed (m/s)	0.9 ± 0.4	1.2 ± 0.4	< 0.001
SMI (kg/m ²)	5.3 ± 0.5	7.1 ± 1.1	< 0.001
Phase angle (°)	3.9 ± 0.6	4.9 ± 0.8	< 0.001
NRS (points)	5.7 ± 2.3	5.0 ± 2.6	0.076

Data are expressed as mean ± standard deviation for continuous variables. BMI, body mass index; SMI, skeletal mass index; NRS, numeric rating scale.

Table 4. Multiple logistic regression analysis examining factors associated with the sarcopenia

Variables	Odds Ratio	95% CI		<i>P</i> -value
		Lower	Upper	
Phase angle	0.09	0.03	0.23	0.000

BMI	0.80	0.71	0.91	0.000
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110 CI, confidence interval; BMI, body mass index.

111

112

113 **The discrimination capacity of phase angle for sarcopenia**

114 The discrimination value of phase angle for sarcopenia was assessed by the receiver operating

115 characteristic (ROC) curves (Figure 1). The areas under the curve (AUC) for both genders, for

116 men, and for women were 0.851, 0.911, and 0.837, respectively. The cut-off value as calculated

117 by Youden index for both genders, for men, and for women were 4.2, 5.1, and 4.2, respectively

118 (Table 5).

Fig. 1. The receiver operating characteristic curves of phase angle for discriminating sarcopenia in terms of gender: (A) both genders, (B) men, and (C) women.

Table 5. AUCs and cut-off values of phase angle discriminating sarcopenia.

AUC	Cut-off value	Sensitivity, %	Specificity, %
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All	0.85 (0.79 - 0.91)	4.2	78.4	79.1
Men	0.90 (0.81 – 1.00)	5.1	100	68.3
Women	0.84 (0.77 – 0.91)	4.2	82.9	71.4

AUC, area under the curve. Values within parentheses show 95% confidence intervals. The sensitivity and specificity of the cut-off values are shown.

Discussion

Our findings showed that in chronic musculoskeletal pain patients, the phase angle significantly correlated with age, BMI, grip power, gait speed, SMI, and NRS, and was lower in patients with sarcopenia than in those without it. The lower phase angle was significantly correlated with sarcopenia, showing a high accuracy in discriminating sarcopenia in men and moderate accuracy in both genders and in women.

For the treatment of chronic pain, a theory of the Fear-avoidance model, that explains pain chronicity, is important.²⁵⁻²⁷ In this model, pain causes fear, avoidance, and eventually immobilization and disuse syndrome, which exacerbate the pain itself. Therefore, it is very important to perform physical exercise and maintain daily activities for the treatment of chronic musculoskeletal pain.^{28,29} In this study, about 20% of men and 30% of women among patients with chronic musculoskeletal pain exhibited sarcopenia. In these patients, another vicious spiral,

139 that reduces muscle mass may cause fatigue in daily activities, resulting in greater
140 immobilization. Therefore, patients with sarcopenia may be intractable in terms of chronic pain
141 and special attention should be paid to the treatment of sarcopenia patients with chronic
142 musculoskeletal pain.

143 Previous reports have suggested that phase angle was lower in individuals with sarcopenia, and
144 several possible causes were reported to explain it. One of the most commonly reported causes
145 was nutrition, and patients with low phase angle were considered as having malnutrition.²⁰
146 Previous reports that had considered BMI as a nutritional indicator reported that as patients with
147 sarcopenia showed lower phase angle and BMI, and were diagnosed with malnutrition.²⁴ In our
148 study, as multivariate analysis adjusted for age, gender, and degree of pain, low phase angle
149 and BMI were significantly correlated with the prevalence of sarcopenia. Therefore, sarcopenia
150 patients with chronic musculoskeletal pain were diagnosed with malnutrition, which would
151 suggest the need for nutrition therapy. Other reasons which should be considered is that phase
152 angle correlated with functional status or muscle quality.²¹ In our study, phase angle was
153 significantly correlated with physical function and muscle strength, and phase angle of the
154 patients with sarcopenia was lower than of those without it, which was similar to the results of
155 previous reports.

156 As for the treatment of chronic musculoskeletal pain, we think that prevention of sarcopenia is
157 very important, and detecting sarcopenia plays an important role in daily clinical practice.

158 Previous reports suggested that phase angle was useful for detecting sarcopenia.²⁰ In addition,
159 the AUC in ROC curves was 0.73 in kidney transplant recipients,²⁴ and 0.718 for men and 0.721
160 for women in community-dwelling individuals;²¹ and 0.85 in our study, which was similar to
161 the results of previous studies. As for cut-off point of phase angle, previous reports suggested
162 the following: 4.46 for kidney transplant recipients,²⁴ 5.05 for cirrhosis,²³ 4.55 for community-
163 dwelling and hospitalized older adults,²² 4.05 for men and 3.55 for women in community-
164 dwelling individuals²¹ for discriminating sarcopenia. Similarly, our results recommended the
165 following cut-off points: 4.2 for both genders, 5.1 for men, and 4.2 for women with chronic
166 musculoskeletal pain. Therefore, our study demonstrated that phase angle was also useful for
167 detecting sarcopenia in chronic musculoskeletal pain patients.

168 As this study contributed new findings, there were several limitations. First, as this study was
169 conducted on Japanese patients and we used the Asian Working Group for Sarcopenia (AWGS)
170 2019 criteria for sarcopenia diagnosis, the results may differ for those involving other
171 populations and those using other sarcopenia criteria such as those proposed by the European
172 working group for sarcopenia in older people³⁰ or the international working group on
173 sarcopenia.³¹ Second, it was known that psychosocial factors were intricately intertwined in
174 patients with chronic musculoskeletal pain, and such items were not considered in this study.
175 Third, as this study was a retrospective cross-sectional study, it was difficult to evaluate
176 chronological order or change among phase angle, sarcopenia, and chronic musculoskeletal

pain. With these limitations, further prospective studies which include more detailed assessments and countries would be needed to explore the relationships among phase angle, sarcopenia, and chronic musculoskeletal pain.

In conclusion, this study demonstrated that in chronic musculoskeletal pain patients, phase angle was significantly correlated with prevalence of sarcopenia, and showed high accuracy in discriminating sarcopenia in men and moderate accuracy in both genders and in women. Phase angle may be useful in detecting sarcopenia among patients with chronic musculoskeletal pain.

Methods

Study Participants

This retrospective study was conducted at Okayama University Hospital and Kurashiki Municipal Hospital. The participants included 190 patients (51 men and 139 women) with chronic musculoskeletal pain who visited our pain outpatient clinic between June 2019 and February 2021. The inclusion criteria for this study were the following: (i) age over 40 years, (ii) pain for longer than 3 months, and (iii) complete self-report questionnaires and physical examination. The exclusion criteria were as follows: (i) ongoing litigation, (ii) dementia, (iii) delirium, or (iv) other conditions that made completion of questionnaires and physical examinations difficult. The institutional review board of Okayama University Hospital approved this study (approval number 2104-035) and the need for patient informed consent was

waived due to its retrospective design. This study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

Diagnosis of sarcopenia

Diagnosis of sarcopenia was performed according to the AWGS Criteria 2019.³² Gait speed, grip strength, and muscle mass were used in this study. The criteria for low muscle strength was handgrip strength < 28 kg for men and < 18 kg for women, and the criteria for low physical performance was 6-m walking speed of < 1.0 m/s. The SMI was assessed using Inbody 770 and S10 (InBody Japan, Tokyo, Japan), and low muscle mass was defined by an SMI < 7.0 kg/m² in men and < 5.7 kg/m² in women. Sarcopenia was defined by the presence of low muscle mass and either low muscle strength or low physical performance.

Assessment of phase angle

Phase angle was defined by the following equation using 50-kHz current:

$$\text{Phase angle (degrees)} = \arctangent(\text{reactance (Xc)} / \text{resistance (R)}) \times (180/\pi)$$

This calculation was performed automatically in the device, and we used the data which was obtained during SMI assessment.

215 **Pain intensity assessment**

216 The NRS was used for assessment of pain intensity. NRS scores ranged from 0 to 10, with 0
217 representing no pain and 10 representing the worst imaginable pain.³³ The average pain
218 intensity in the past one week was used in this study.

219

220 **Statistical analyses**

221 Descriptive statistics were presented as mean $\pm$ SD for continuous variables and as numbers
222 and percentages for categorical variables. The Kolmogorov–Smirnov test was used to assess
223 normality for continuous variables. We analyzed correlations of phase angle with each
224 measured variable by using Spearman’s rank correlation coefficient. Then, we performed the
225 Mann–Whitney U test to compare the measured parameters in patients with and without
226 sarcopenia. In a subsequent analysis, we performed multiple logistic regression analysis to
227 evaluate the factors and OR associated with sarcopenia, and the explanatory variables included
228 phase angle, body mass index, age, and gender. Next, to evaluate the discrimination
229 performance of phase angle, AUC was calculated by using a ROC analysis. Then, the sensitivity
230 and specificity were calculated by using the best cut-off point of phase angle for both and each
231 gender with the Youden index for the ROC, respectively. For the statistical analyses, we used
232 EZR software (Saitama Medical Center Jichi Medical University, Tochigi, Japan), which is a

graphical user interface for R (The R Foundation for Statistical Computing). Results were considered significant for $p < 0.05$.

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Authors' contributions

Conceptualization: H. T. and Tomoko T. *Methodology:* H. T. and Tomoko T. *Formal analysis and investigation:* H. T. and Tomonori T. *Writing – original draft preparation:* H. T., Tomoko T. and Tomonori T. *Writing – review and editing:* H. M., K. Y. and Y. O. *Funding acquisition:* Tomoko T. *Resources:* M. S., M. H., Y. Katayama, Tomoko T., S. T., Y. Kajiki, and Y. T. *Supervision:* K. N., M. S. and T. O.

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Conflicts of interest

The authors have no conflicts of interest to report.

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Figures

Figure 1

A, both genders; B, men; C, women