

Can bone mass measured via bioelectrical impedance analysis be used to diagnose sarcopenia?

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The simplification of diagnostic criteria is critical to promoting interventions for sarcopenia. This study aimed to evaluate the relationship between sarcopenia and bone mass [measured by bioelectrical impedance analysis (BIA)], as well as to identify new indicators associated with this disease. Basic interviews and measurement of physical function were performed on 474 community-dwelling older adults (aged 77.1 ± 7.6 years), including older adult patients with sarcopenia, in Wakasa Town, Fukui Prefecture. The findings led to 363, 71, and 40 participants being classified as 'normal', 'pre-sarcopenia', and 'having sarcopenia', respectively. An Ordinal Logistic Regression Analysis showed that age, bone mass phase angle (lower limb), Fat-free Mass Index, and leg muscle score were aggravating factors for sarcopenia in both men and women. A receiver operating characteristic analysis of bone mass and sarcopenia status showed that the area under the curve and cut-off value, as well as its sensitivity and specificity, in men were 0.915 [95% confidence interval (CI): 0.853–0.977], 2.2 kg, 81%, and 87%, respectively, and 0.913 (95% CI: 0.858–0.968), 1.6 kg, 91%, and 88%, respectively, in women. This study revealed that the BIA method of measuring bone mass has excellent accuracy in detecting sarcopenia in both males and females.

Key Words: risk factors, sarcopenia, bone mass, cutoff value, bioelectrical impedance analysis

Sarcopenia is a condition in which muscle mass and strength decrease excessive loss of both muscle mass and strength in comparison to a specific body state or condition and are associated with increased adverse outcomes such as falls, functional declines, frailty, and death.⁽¹⁾

To clarify the prevalence, associated factors, and mortality of sarcopenia in Japan, a follow-up study conducted on 1,851 community-dwelling older adults (mean age, 72 years) undergoing health checkups for an average of 5.8 years (up to 9.5 years) has been previously reported.⁽²⁾ According to these follow-up surveys, the prevalence of sarcopenia is about 20% for both men and women aged 75–79 years, about 30% for men over 80 years, and about 50% for women over 80 years. Moreover, once sarcopenia manifests, the risk of death and the need for long-term care nearly doubles.⁽²⁾ As the population of older adults in present Japan increases, it is not uncommon for community-

dwelling older adults to exhibit either a decline in skeletal muscle mass and subsequent decline in muscle strength or a decline in physical function.

While detecting pre-sarcopenia, the precursor to sarcopenia, may aid in the early detection of sarcopenia before its onset, simplifying the diagnostic criteria is critical in the early prevention and treatment of sarcopenia. To date, the phase angle has been reported to be useful as a marker for diagnosing sarcopenia by bioelectrical impedance analysis (BIA).⁽³⁾ Fat-free mass index (FFMI) has also been reported to be a possible substitute marker for skeletal muscle mass index (SMI) in low muscle mass screening in sarcopenia.⁽⁴⁾

Recent findings indicate that using a body composition analyzer with the BIA method is beneficial in screening for sarcopenia as it is less labor intensive and would contribute to sarcopenia prevention and awareness-raising activities. A syndrome known as "osteosarcopenia", in which osteoporosis and sarcopenia coexist, has recently been gaining attention.⁽⁵⁾ Since skeletal muscle mass and bone mass have been reported to be positively correlated,⁽⁶⁾ bone mass measured by the BIA method may serve as an auxiliary marker in diagnosing sarcopenia. In this case, a body composition analyzer that uses the BIA method is a relatively easy technique for the simultaneous assessment of bone mass and SMI in community-dwelling older adults.

The study aimed to evaluate the relationship between sarcopenia and indicators such as bone mass (measured by BIA) and to identify new factors related to sarcopenia. Our secondary aim was to determine the cut-off value of bone mass to detect sarcopenia.

Materials and Methods

Subjects. A total of 1,088 participants were selected from June 2019 to November 2021 in Wakasa Town, Mikatakaminaka District, Fukui Prefecture, who responded to the public call for a health checkup for older adults. Of the 633 individuals who underwent a health check for the first time, 68 individuals who were cardiac pacemaker users and/or had missing body composi-

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tion analyzer data and 91 individuals with osteoporosis were excluded. Finally, a total of 474 (171 males and 303 females, mean age 77.1 ± 7.6 years) participants were included in the analysis.

Ethics approval. This study was conducted with the approval of the University of Fukui Medical Research Ethics Review Committee (Approval No.: 20190014). All researchers involved in this study complied with Ethical Guidelines for Medical and Biological Research Involving Human Subjects (MEXT/MHLW/METI Notification No. 1 of March 23, 2021).

Methods. After obtaining written consent from all older adults who responded to the public call, a basic interview was conducted. Additionally, physical function (walking speed, grip strength, and height) and anthropometric (body weight, muscle mass, bone mass, body fat mass, visceral fat rating, basal metabolic rate, total body water mass, phase angle, and leg muscle score) measurements were taken using a body composition analyzer in the order of explanation of the results. In the basic interview, age, sex, medical history (diabetes, hypertension, heart disease, and dyslipidemia), and lifestyle (smoking status and drinking status) were confirmed. For the measurement of walking speed, the subject was instructed to start walking at normal walking speed, and the time up to when the subject passed 5 m without slowing down was measured. Walking speed was then calculated from there. Grip strength was measured on the left and right sides and the maximum value was used. The standard grip strength values were 28.0 kg for men and 18.0 kg for women. Measurements were performed using body composition analyzers (MC-780A-N and MC-780A; TANITA Co., Ltd., Tokyo, Japan). For taking the measurements using the body composition analyzers, the height and age of the subject are inputted into the device to prepare it. After preparing the device, the subject was instructed to stand barefooted on its electrodes and hold the electrode with his/her bare hands to collect data regarding body composition. The measurement time of the body composition analyzer is about 15 s, which can be measured without burden even for older adults. The body composition analyzer measured muscle mass, fat mass, and body water content from a precise analysis of the internal and external fluids of cells using three multi-frequency measurements (5 kHz, 50 kHz, and 250 kHz) and reactance analysis, which is the electrical information obtained from the cell membrane.

Body mass index (BMI) is an index obtained by dividing body weight by the square of height (m). Appendicular skeletal muscle mass (ASM) is an index of the sum of the muscle mass of limbs. SMI is an index obtained by dividing appendicular skeletal muscle mass by the square of height (m). Bone mass (or bone mineral content) is a statistically estimated index based on the correlation with tissues other than fat (lean mass). It is also highly correlated with figures obtained from dual-energy X-ray absorptiometry (DXA). Percent body fat is an index expressed as the percentage of body fat in body weight. Visceral fat level is an index that statistically judges the risk of visceral fat accumulation by TANITA Inc.'s own analysis that is based on the CT scan data of male and female subjects. Body water percent is an index expressed as the percentage of body water mass in the body weight. Phase Angle is the angle calculated based on impedance and resistance where the magnitude of the phase shift (reactance) created in the myocyte when a weak current passes through the myocyte and impedance derived from the value of resistance, which is the resistive component are used. The average value of the left and right feet was used to determine the phase angle. Leg Muscle Score is the measure of leg muscle mass as a percentage of body weight. FFMI was calculated from weight, percent body fat, and height. The judgment of sarcopenia was based on the AWGS2019 criteria.⁽⁷⁾ The state in which only the SMI was deteriorating was referred to as pre-sarcopenia. SMI and a state of reduced muscle strength and/or physical ability were referred to as sarcopenia.

Statistical analysis. All statistical data were analyzed using the EZR ver. 1.54 (Saitama Medical Center, Jichi Medical University, Saitama, Japan).⁽⁸⁾ Age, height, walking speed, maximum grip strength, body weight, BMI, muscle mass, SMI, ASM, body fat mass, percent body fat, visceral fat rating, Basal Metabolic Rate (BMR), total body water mass, body water percent, bone mass, phase angle of lower limb, leg muscle score are expressed as mean \pm SD. The nominal variables are presented as the number of cases and frequency (%) for each item. A comparison of two groups of nominal variables was performed using the Chi-square test, and that of three groups was performed using Fisher's exact test. The Mann-Whitney *U* test was used for two-group comparisons of continuous variables and the Kruskal-Wallis test was used for three-group comparisons. In addition, to avoid the problem of multiple comparisons, corrections were made using the Bonferroni method.

A multiple logistic regression analysis (Ordinal Logistic Regression Analysis) was performed on (in the order) no sarcopenia, pre-sarcopenia, and sarcopenia as the dependent variables; and age, sex, estimated bone mass, fat mass, phase angle, and leg points as the independent variables to analyze the sarcopenia exacerbation predictors.

The estimated bone mass, phase angle, FFMI, and leg point cutoff values in the presence or absence of sarcopenia were confirmed by receiver operating characteristic (ROC) analysis. In any case, $p < 0.05$ was considered statistically significant.

Results

Background of subjects. Among the 474 older adult patients (171 males and 303 females) included in the study, 363, 71, and 40 participants were classified as 'Normal', 'Pre-sarcopenia', and 'Sarcopenia'. Table 1 shows a two-group comparison of men and women and a three-group comparison of Normal/Pre-sarcopenia/Sarcopenia.

Significant differences were observed between the two groups, namely, men and women regarding smoking, drinking, diabetes, heart disease, height, walking speed, maximum grip strength, weight, BMI, muscle mass, SMI, ASM, FFMI, body fat, percent body fat, visceral fat rating, BMR, total body water mass, body water percent, body water mass, bone mass, phase angle of lower limb, and leg muscle score (Table 1).

Significant differences were observed between the three groups regarding age, height, walking speed, maximum grip strength, weight, BMI, muscle mass, SMI, ALM, fat mass, percent body fat, basal metabolic rate, body water mass, bone mass, phase difference (lower limb), and leg point (Table 1).

Background and sarcopenia exacerbation predictors in men. Significant differences were observed between the three groups regarding age, drinking, height, walking speed, maximum grip strength, weight, BMI, muscle mass, SMI, ASM, fat mass, visceral fat rating, BMR, body water mass, bone mass, phase angle (lower limb), and leg point (Table 1). Sarcopenia exacerbation predictors were found to be age [Odds ratio (OR): 1.12, 95% confidence interval (CI): 1.020–1.250], FFMI (OR: 0.11, 95% CI: 0.044–0.238), bone mass (OR: 0.02, 95% CI: 0.0008–0.565), phase angle of lower limb (OR: 0.17, 95% CI: 0.051–0.530), leg muscle score (OR: 0.83, 95% CI: 0.749–0.913) by multiple logistic regression analysis (Ordinal Logistic Regression Analysis) (Table 2).

Background and sarcopenia exacerbation predictors in women. Significant differences were observed between the three groups regarding age, height, walking speed, maximum grip strength, weight, BMI, muscle mass, SMI, ASM, FFMI, fat mass, percent body fat, BMR, body water mass, bone mass, phase angle (lower limb), and leg point (Table 3). Sarcopenia exacerbation predictors were found to be age (OR: 1.0, 95% CI: 1.010–1.160), FFMI (OR: 0.17, 95% CI: 0.090–0.310), bone

Table 1. Background of the participants

	Comparison of gender differences			Comparison regarding sarcopenia						
	Total n = 474	Male n = 171	Female n = 303	p value	Normal ^a n = 363 (76.6)	Pre-sarcopenia ^b n = 71 (15.0)	Sarcopenia ^c n = 40 (8.4)	a vs b p value	a vs c p value	b vs c p value
Age (years)	77.1 ± 7.6	76.7 ± 7.4	77.2 ± 7.7	0.608	75.8 ± 7.3	78.5 ± 6.6	86.3 ± 4.8	0.0064	<0.0001	<0.0001
Sex (male/female)	171/303	—	—	—	128/235	27/44	16/24	1	1	1
Lifestyle										
Smoking, n (%)	26 (5.5)	24 (14.0)	2 (0.7)	<0.001	21 (5.8)	5 (7.0)	0 (0)	1	0.75	0.47
Drinking alcohol, n (%)	151 (31.9)	111 (64.9)	40 (13.2)	<0.001	124 (34.2)	19 (26.8)	8 (20.0)	0.81	0.23	1
Underlying disease										
Diabetes mellitus, n (%)	55 (11.6)	27 (15.8)	28 (9.2)	0.046	44 (12.1)	6 (8.5)	5 (12.5)	1	1	1
Cardiac disease, n (%)	78 (16.5)	37 (21.6)	41 (13.5)	0.031	55 (15.2)	16 (22.5)	7 (17.5)	0.48	1	1
Dyslipidemia, n (%)	157 (33.1)	48 (28.1)	109 (36.0)	0.098	120 (33.1)	29 (40.8)	8 (20.0)	0.66	0.32	0.11
Hypertension, n (%)	249 (52.5)	99 (57.9)	150 (49.5)	0.096	194 (53.4)	33 (46.5)	22 (55)	0.9	1	1
Pre-sarcopenia, n (%)	71 (15.0)	27 (15.8)	44 (14.5)	0.812	—	—	—	—	—	—
Sarcopenia, n (%)	40 (8.4)	16 (9.4)	24 (7.9)	0.713	—	—	—	—	—	—
Anthropometry and physical function										
Height (cm)	154.0 ± 9.6	163.1 ± 6.7	148.6 ± 6.5	<0.001	154.8 ± 9.4	153.2 ± 8.6	147.6 ± 10.8	0.906	0.00016	0.015
Walking speed (m/s)	1.5 ± 0.4	1.57 ± 0.42	1.45 ± 0.43	0.006	1.5 ± 0.4	1.6 ± 0.4	1.0 ± 0.3	1	<0.0001	<0.0001
Maximum grip strength (kg)	28.5 ± 8.7	36.6 ± 7.5	23.8 ± 5.3	<0.001	29.6 ± 8.9	27.8 ± 6.7	20.1 ± 5.1	0.37	<0.0001	<0.0001
Body composition analyser										
Body weight (kg)	54.2 ± 10.6	62.2 ± 9.8	49.4 ± 7.8	<0.001	56.2 ± 10.3	47.8 ± 7.9	47.3 ± 9.8	<0.0001	<0.0001	1
BMI (kg/m ²)	22.7 ± 3.2	23.3 ± 2.9	22.3 ± 3.2	<0.0005	23.3 ± 3.0	20.5 ± 2.9	21.4 ± 3.2	<0.0001	0.00011	0.342
Muscle mass (kg)	37.1 ± 7.6	45.6 ± 5.5	32.4 ± 3.5	<0.001	38.3 ± 7.7	34.4 ± 5.6	31.3 ± 6.1	<0.001	<0.0001	0.012
SMI (kg/m ²)	6.7 ± 1.0	7.54 ± 0.91	6.22 ± 0.72	<0.001	7.0 ± 0.9	5.8 ± 0.6	5.6 ± 0.8	<0.0001	<0.0001	0.18
ASM (kg)	16.1 ± 4.1	20.1 ± 3.40	13.8 ± 2.3	<0.001	17.0 ± 4.0	13.8 ± 2.7	12.3 ± 2.9	<0.0001	<0.0001	0.005
FFMI (kg/m ²)	16.3 ± 1.7	18.0 ± 1.4	15.4 ± 1.1	<0.001	16.7 ± 1.6	15.3 ± 1.2	15.0 ± 1.7	<0.0001	<0.0001	1
Body fat mass (kg)	14.8 ± 5.8	14.1 ± 5.8	15.2 ± 5.8	0.064	15.6 ± 5.8	11.4 ± 4.7	13.4 ± 6.0	<0.0001	0.11	0.27
Body fat % (%)	27.0 ± 8.2	21.9 ± 6.6	29.9 ± 7.6	<0.001	27.6 ± 8.0	23.7 ± 7.8	28.4 ± 10.0	0.0014	1	0.033
Visceral fat rating (level)	8.5 ± 4.8	12.7 ± 3.5	6.1 ± 2.6	<0.001	8.7 ± 4.5	7.4 ± 3.5	8.5 ± 4.1	0.11	1	0.49
BMR (kcal)	1,092.4 ± 203.5	1,297.1 ± 164.3	974.2 ± 101.5	<0.001	1,130.57 ± 202.9	996.8 ± 140.6	916.5 ± 150.0	<0.0001	<0.0001	0.1
Total body water mass (kg)	28.4 ± 5.4	33.8 ± 4.6	25.4 ± 3.1	<0.001	29.5 ± 5.4	25.5 ± 3.6	23.4 ± 3.8	<0.0001	<0.0001	0.025
Body water % (%)	52.9 ± 5.5	54.8 ± 6.2	51.9 ± 4.7	<0.001	53.0 ± 5.2	53.8 ± 6.1	51.2 ± 6.7	1	0.15	0.13
Bone mass (kg)	2.1 ± 0.4	2.5 ± 0.2	1.8 ± 0.3	<0.001	2.2 ± 0.4	1.9 ± 0.4	1.6 ± 0.4	<0.0001	<0.0001	0.012
Phase angle of lower limb (°)	4.2 ± 0.9	4.5 ± 0.7	4.0 ± 2.0.9	<0.001	4.3 ± 0.9	4.1 ± 0.7	3.2 ± 0.7	0.12	<0.0001	<0.0001
Leg muscle score (point)	86.5 ± 9.3	84.4 ± 7.7	87.7 ± 9.8	<0.001	87.7 ± 9.1	85.7 ± 7.2	77.4 ± 8.1	0.8	<0.0001	<0.0001

Mean ± SD; Number of cases (% or unit). BMI, body mass index; ASM, appendicular skeletal mass; SMI, skeletal muscle mass index; BMR, basal metabolic rate; FFMI, fat-free mass index. Continuous variables: Mann-Whitney U test, Kruskal-Wallis test (multiple comparisons of two groups at a time with Bonferroni adjustment). Nominal variables: χ^2 test (including Yates continuity correction), Fisher's exact test (multiple comparisons of two groups at a time with Bonferroni adjustment).

Table 2. Background and sarcopenia exacerbation predictors in men

	Univariate analysis										Multiple logistic regression analysis (Ordinal Logistic Regression Analysis)		
	Total n = 171	Normal ^a n = 128 (74.8)	Pre-sarcopenia ^b n = 27 (15.7)	Sarcopenia ^c n = 16 (9.3)	a vs b p value	a vs c p value	b vs c p value	p value	Odds ratio	95% CI lower-upper	p value		
Age (years)	76.7 ± 7.4	75.0 ± 7.0	80.3 ± 6.4	84.8 ± 3.3	<0.001	<0.001	0.051	<0.001	1.12	1.020–1.250	0.025		
Lifestyle													
Smoking, n (%)	24 (14.0)	19 (14.8)	5 (18.5)	0 (0.0)	1	0.39	0.42	0.185	—	—	—		
Drinking alcohol, n (%)	111 (64.9)	90 (70.3)	14 (51.9)	7 (43.8)	0.22	0.14	1	0.034	—	—	—		
Underlying disease													
Diabetes mellitus, n (%)	27 (15.8)	19 (14.8)	4 (14.8)	4 (25.0)	1	0.87	1	0.557	—	—	—		
Cardiac disease, n (%)	37 (21.6)	25 (19.5)	8 (29.6)	4 (25.0)	0.9	1	1	0.439	—	—	—		
Dyslipidemia, n (%)	48 (28.1)	35 (27.3)	9 (33.3)	4 (25.0)	1	1	1	0.841	—	—	—		
Hypertension, n (%)	99 (57.9)	75 (58.6)	16 (59.3)	8 (50.0)	1	1	1	0.837	—	—	—		
Anthropometry and physical function													
Height (cm)	163.1 ± 6.7	164.3 ± 6.2	160.7 ± 6.1	157.2 ± 7.0	0.04	<0.001	0.396	<0.001	—	—	—		
Walking speed (m/s)	1.57 ± 0.42	1.63 ± 0.39	1.62 ± 0.42	1.12 ± 0.42	1	<0.001	0.005	<0.001	—	—	—		
Maximum grip strength (kg)	36.6 ± 7.5	38.6 ± 6.9	34.7 ± 4.0	24.1 ± 3.0	0.005	<0.001	<0.001	<0.001	—	—	—		
Body composition analyser													
Body weight (kg)	62.2 ± 9.8	65.3 ± 8.32	53.9 ± 7.4	51.3 ± 9.0	<0.001	<0.001	1	<0.001	—	—	—		
BMI (kg/m ²)	23.3 ± 2.9	24.1 ± 2.5	20.8 ± 2.6	20.6 ± 2.4	<0.001	<0.001	1	<0.001	—	—	—		
Muscle mass (kg)	45.6 ± 5.5	47.7 ± 4.2	40.6 ± 3.1	37.3 ± 4.4	<0.001	<0.001	0.074	<0.001	—	—	—		
SMI (kg/m ²)	7.54 ± 0.91	7.93 ± 0.65	6.53 ± 0.38	6.15 ± 0.55	<0.001	<0.001	0.071	<0.001	—	—	—		
ASM (kg)	20.1 ± 3.40	21.5 ± 2.6	16.9 ± 1.6	15.2 ± 2.1	<0.001	<0.001	0.055	<0.001	—	—	—		
FFMI (kg/m ²)	18.0 ± 1.4	18.6 ± 1.0	16.5 ± 0.9	15.9 ± 1.3	<0.001	<0.001	0.37	<0.001	0.044–0.238	<0.001	<0.001		
Body fat mass (kg)	14.1 ± 5.8	15.0 ± 5.5	11.0 ± 5.7	11.9 ± 5.9	0.003	0.252	1	0.002	—	—	—		
Body fat % (%)	21.9 ± 6.6	22.4 ± 5.8	19.6 ± 8.0	22.0 ± 8.8	0.27	1	1	0.242	—	—	—		
Visceral fat rating (level)	12.7 ± 3.5	13.4 ± 3.2	10.4 ± 3.2	11.2 ± 4.1	<0.001	0.208	1	<0.001	—	—	—		
BMR (kcal)	1,297.1 ± 164.3	1,364.8 ± 131.6	1,146.4 ± 103.9	1,108.6 ± 129.4	<0.001	0.002	1	<0.001	—	—	—		
Total body water mass (kg)	33.8 ± 4.6	35.6 ± 3.5	29.3 ± 2.3	26.7 ± 3.3	<0.001	<0.001	0.086	<0.001	—	—	—		
Body water % (%)	54.8 ± 6.2	54.9 ± 5.4	55.3 ± 8.2	53.1 ± 8.4	1	1	1	0.605	—	—	—		
Bone mass (kg)	2.5 ± 0.2	2.6 ± 0.2	2.2 ± 0.1	2.0 ± 0.2	<0.001	<0.001	0.07	<0.001	0.02	0.0008–0.565	0.024		
Phase angle of lower limb (°)	4.5 ± 0.7	4.7 ± 0.7	4.3 ± 0.6	3.4 ± 0.7	0.046	<0.001	0.001	<0.001	0.17	0.051–0.530	0.003		
Leg muscle score (point)	84.4 ± 7.7	85.5 ± 7.1	83.1 ± 7.9	77.4 ± 8.1	0.567	<0.001	0.039	<0.001	0.83	0.749–0.913	<0.001		

Mean ± SD, Number of cases (% or unit). BMI, body mass index; ASM, appendicular skeletal mass; SMI, skeletal muscle mass index; BMR, basal metabolic rate; FFMI, fat-free mass index; CI, confidence interval. Continuous variables: Kruskal–Wallis test (multiple comparisons of two groups at a time with Bonferroni adjustment). Nominal variables: Fisher's exact test (multiple comparisons of two groups at a time with Bonferroni adjustment).

Table 3. Background and sarcopenia exacerbation predictors in women

	Univariate analysis					Multiple logistic regression analysis (Ordinal Logistic Regression Analysis)					
	Total n = 303	Normal ^a n = 235 (77.5)	Pre-sarcopenia ^b n = 44 (14.5)	Sarcopenia ^c n = 24 (7.9)	a vs b p value	a vs c p value	b vs c p value	p value	Odds ratio	95% CI lower-upper	p value
Age (years)	77.2 ± 7.7	76.2 ± 7.4	77.4 ± 6.5	87.1 ± 5.2	0.86	<0.001	<0.001	<0.001	1	1.010–1.160	0.021
Lifestyle											
Smoking, n (%)	2 (0.7)	2 (0.9)	0 (0.0)	0 (0.0)	1	1	1	1	—	—	—
Drinking alcohol, n (%)	40 (13.2)	34 (14.5)	5 (11.4)	1 (4.2)	1	0.65	1	0.423	—	—	—
Underlying disease											
Diabetes mellitus, n (%)	28 (9.2)	25 (10.6)	2 (4.5)	1 (4.2)	0.82	1	1	0.42	—	—	—
Cardiac disease, n (%)	41 (13.5)	30 (12.8)	8 (18.2)	3 (12.5)	1	1	1	0.594	—	—	—
Dyslipidemia, n (%)	109 (36.0)	85 (36.2)	20 (45.5)	4 (16.7)	0.927	0.211	0.059	0.058	—	—	—
Hypertension, n (%)	150 (49.5)	119 (50.6)	17 (38.6)	14 (58.3)	0.56	1	0.41	0.239	—	—	—
Anthropometry and physical function											
Height (cm)	148.6 ± 6.5	149.5 ± 6.1	148.5 ± 6.3	141.2 ± 7.6	1	<0.001	<0.001	<0.001	—	—	—
Walking speed (m/s)	1.45 ± 0.43	1.49 ± 0.42	1.58 ± 0.37	0.85 ± 0.18	0.94	<0.001	<0.001	<0.001	—	—	—
Maximum grip strength (kg)	23.8 ± 5.3	24.6 ± 5.2	23.5 ± 3.6	17.4 ± 4.4	0.089	<0.001	<0.001	<0.001	—	—	—
Body composition analyser											
Body weight (kg)	49.4 ± 7.8	51.1 ± 7.5	44.0 ± 5.4	43.2 ± 7.1	<0.001	<0.001	1	<0.001	—	—	—
BMI (kg/m ²)	22.3 ± 3.2	22.7 ± 3.0	20.2 ± 3.0	21.8 ± 3.5	<0.001	0.18	0.13	<0.001	—	—	—
Muscle mass (kg)	32.4 ± 3.5	33.2 ± 3.1	30.6 ± 2.6	27.3 ± 2.8	<0.001	<0.001	<0.001	<0.001	—	—	—
SMI (kg/m ²)	6.22 ± 0.72	6.49 ± 0.58	5.43 ± 0.24	5.18 ± 0.61	<0.001	<0.001	0.2	<0.001	—	—	—
ASM (kg)	13.8 ± 2.3	14.8 ± 1.9	11.5 ± 1.5	10.3 ± 1.8	<0.001	<0.001	0.23	<0.001	—	—	—
FFMI (kg/m ²)	15.4 ± 1.1	15.7 ± 0.93	14.6 ± 0.7	14.4 ± 1.7	<0.001	<0.001	1	<0.001	0.17	0.090–0.310	<0.001
Body fat mass (kg)	15.2 ± 5.8	15.9 ± 5.9	11.7 ± 4.0	14.5 ± 6.0	<0.001	0.62	0.21	<0.001	—	—	—
Body fat % (%)	29.9 ± 7.6	30.3 ± 7.5	26.1 ± 6.6	32.5 ± 8.4	<0.001	0.819	0.01	0.001	—	—	—
Visceral fat rating (level)	6.1 ± 2.6	6.1 ± 2.7	5.5 ± 1.8	6.7 ± 2.9	0.61	1	0.32	0.277	—	—	—
BMR (kcal)	974.2 ± 101.5	1,005.9 ± 97.0	922.7 ± 76.1	855.6 ± 101.5	0.011	0.121	0.915	0.003	—	—	—
Total body water mass (kg)	25.4 ± 3.1	26.3 ± 2.7	23.1 ± 1.9	21.3 ± 2.3	<0.001	<0.001	0.006	<0.001	—	—	—
Body water % (%)	51.9 ± 4.7	51.9 ± 4.7	52.9 ± 4.2	50.0 ± 5.2	0.474	0.339	0.095	0.08	—	—	—
Bone mass (kg)	1.8 ± 0.3	1.9 ± 0.2	1.6 ± 0.2	1.3 ± 0.2	<0.001	<0.001	<0.001	<0.001	0.1	0.018–0.534	0.007
Phase angle of lower limb (°)	4.0 ± 2.0.9	4.1 ± 0.9	3.9 ± 0.6	3.0 ± 0.6	0.7	<0.001	<0.001	<0.001	0.48	0.239–0.963	0.041
Leg muscle score (point)	87.7 ± 9.8	88.8 ± 9.9	87.2 ± 6.3	77.4 ± 8.3	1	<0.001	<0.001	<0.001	0.89	0.842–0.945	<0.001

Mean ± SD, Number of cases (% or unit). BMI, body mass index; ASM, appendicular skeletal mass; SMI, skeletal muscle mass index; BMR, basal metabolic rate; FFMI, fat-free mass index; CI, confidence interval. Continuous variables: Kruskal–Wallis test (multiple comparisons of two groups at a time with Bonferroni adjustment). Nominal variables: Fisher's exact test (multiple comparisons of two groups at a time with Bonferroni adjustment).

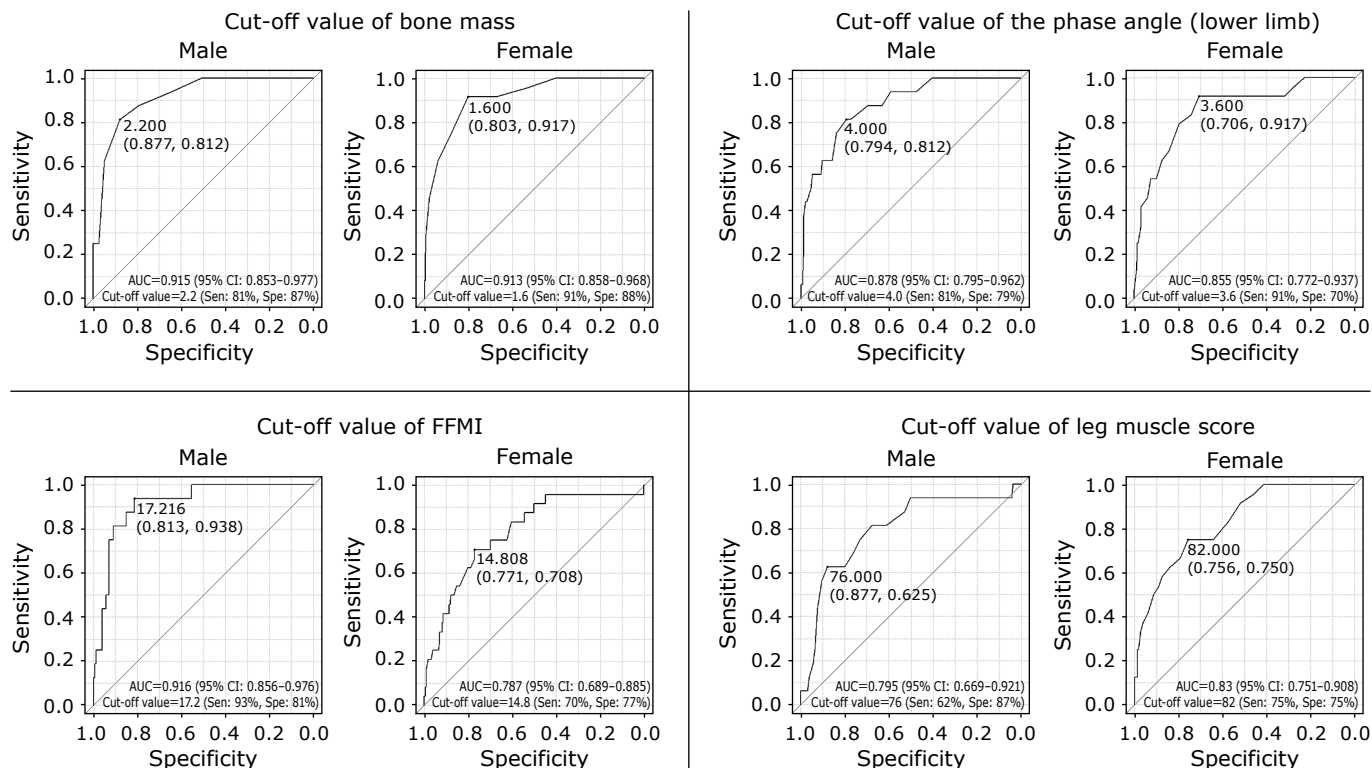


Fig. 1. Estimated bone mass, phase angle, fat-free mass index (FFMI), and leg point cut-off values in the presence and absence of sarcopenia: receiver operating characteristic curve analysis. AUC, area under curve; Sen, Sensitivity; Spe, Specificity.

mass (OR: 0.10, 95% CI: 0.0018–0.534), phase angle of lower limb (OR: 0.48, 95% CI: 0.239–0.963), leg muscle score (OR: 0.89, 95% CI: 0.842–0.945) by multiple logistic regression analysis (Ordinal Logistic Regression Analysis) (Table 3).

Cut-off of bone mass in the presence or absence of sarcopenia. A ROC analysis of bone mass and status of sarcopenia showed that in males, the area under the curve (AUC) was 0.915 (95% CI: 0.853–0.977), and the cut-off value was 2.2 kg with a sensitivity of 81% and specificity of 87%; and in females, AUC was 0.913 (95% CI: 0.858–0.968), the cut-off value 1.6 kg with a sensitivity of 91% and specificity of 88% (Fig. 1).

Phase angle cut-off in the presence or absence of sarcopenia. An ROC analysis of phase angle and status of sarcopenia showed that in males, the AUC was 0.878 (95% CI: 0.795–0.962), and the cut-off value was 4.0 with a sensitivity of 81% and specificity of 79%; and in females, AUC was 0.855 (95% CI: 0.772–0.937), the cut-off value 3.6 with a sensitivity of 91% and specificity of 70% (Fig. 1).

FFMI cut-off in the presence or absence of sarcopenia. A ROC analysis of FFMI and status of sarcopenia showed that in males, the AUC was 0.916 (95% CI: 0.856–0.976), and the cut-off value was 17.2 with a sensitivity of 93% and specificity of 81%; and in females, AUC was 0.787 (95% CI: 0.689–0.885), the cut-off value 14.8 with a sensitivity of 70% and specificity of 77% (Fig. 1).

Leg muscle score cut-off in the presence or absence of sarcopenia. A ROC analysis of leg muscle score and status of sarcopenia showed that in males, the AUC was 0.795 (95% CI: 0.669–0.921), and the cut-off value was 76 with a sensitivity of 62% and specificity of 87%; and in females, AUC was 0.83 (95% CI: 0.751–0.908), the cut-off value 82 with a sensitivity of 75% and specificity of 75% (Fig. 1).

Discussion

This study reveals that the Bone Mass index measured using BIA can be an independent and useful indicator of sarcopenia. In addition, this study showed that age, bone mass, phase angle (lower limb), FFMI, and leg muscle score are factors that aggravate sarcopenia in both men and women. In addition, an ROC analysis revealed that bone mass showed good accuracy in the prediction of sarcopenia in both sexes, while at the same time showing the best cut-off value.

Age, phase angle, and FFMI have also been previously reported to be associated with sarcopenia.^(1,3,4) The study also found that the Sarcopenia group was relatively older than the healthy (Normal) group, as well as that the phase angle and FFMI were lower in the Sarcopenia group than in the healthy (Normal) group. These results, including those of multivariate analyses, are consistent with previous studies. One of the main features of sarcopenia is age-related loss of muscle mass. In addition, the decrease in skeletal muscle mass in older adults is also associated with functional impairment and physical disability.⁽¹¹⁾ Early detection and intervention are critical in preventing muscle mass loss in old age. As for the characteristics of muscle mass due to aging in Japan, age-related changes in muscle mass differ depending on the body part, with the largest rate of decrease in the lower limbs, followed by the whole body, upper limbs, and trunk.⁽¹²⁾ Therefore, to capture sarcopenia, it is necessary to capture the changes in lower limb muscle mass at an early stage. The leg muscle score compares the ratio of leg muscle mass to body weight with the ideal value and displays the current ratio as a score. This score has been previously reported as a useful indicator for preventing sarcopenia.⁽¹³⁾ Although it is supported even by the results of this study and existing literature, reports of studies on its association with sarcopenia are few, with some

even showing a strong negative correlation, and therefore further examination is also needed.

Studies using DXA suggest a negative association of bone mineral density with sarcopenia.⁽¹⁴⁾ It has also been reported that the dynamic balance between “muscle–bone–lipid” may be associated with the pathogenesis of bone loss.⁽¹⁴⁾ Our study reveals that the progression from a healthy condition to pre-sarcopenia in older adults results in a lower limb fat index (LFI), which is a novel fat index.⁽¹⁵⁾ Conversely, LFI became higher in the process of progression from pre-sarcopenia to sarcopenia, revealing that sarcopenia progression is associated with fat.⁽¹⁵⁾ This suggests that fat infiltration into muscles may capture the mechanism that causes muscle inflammation.⁽¹⁵⁾ Additionally, this study discovered that the use of body composition analyzers employing the BIA method showed a significant difference in bone mass between the healthy (Normal), Pre-sarcopenia, and Sarcopenia groups in the overall examination and that each group can be separated. In the multivariate analysis, bone mass was shown to be a good indicator as a factor of aggravation for identifying sarcopenia in both men and women. Bone and skeletal muscle are integrated organs, and muscles have been demonstrated to provide a mechanical load to bones, thereby acting as the primary regulator of bone metabolism.⁽¹⁶⁾ Additionally, myokines, which are muscle-secreted endocrine factors, may affect bone homeostasis.⁽¹⁷⁾ There is a possibility that myokines may have had some role in the skeletal muscle mass loss associated with pre-sarcopenia. The additional decline in physical function and muscle strength associated with sarcopenia could also be associated with the effect of mechanical load provided by the muscular system.

In this study, ROC analysis was also performed for bone mass, phase angle (lower limb), FFMI, and leg muscle score to determine sarcopenia. It showed that each index had a good AUC of 0.7 or higher. Since differences in physical characteristics have been confirmed in the comparison of men and women, ROC analysis was also conducted separately for each sex. Bone mass was observed to be a very good indicator for predicting sarcopenia as it had an AUC of 0.9 or higher for both men and women. It has been suggested that the use of PhA in the diagnosis of sarcopenia requires establishing cut-off values for age groups as well as sex.⁽³⁾ Since there is also an age-related phenomenon in terms of bone mass, further longitudinal studies are needed to assess the effect of cut-off values and changes over time in each age group. The highest AUC for FFMI were 0.916 and 0.787 in males and females, respectively. FFMI allegedly provides anthropometric information, regardless of height.⁽¹⁸⁾ However, since men and women in this study showed significant differences in muscle mass and percent body fat and FFMI is calculated using percent body fat, it is assumed that the system has failed in identifying sarcopenia in women with low muscle mass and high percent body fat.

There are some limitations to this study. First, since this was a cross-sectional study, a causal relationship cannot be inferred. Second, our data is limited to older adults living in a limited geographic area, which may limit generalization. Therefore, to enable the generalization of our findings, we aim to conduct a similar study on older adults living in different geographical regions in the future. Third, bone mass determined by the BIA method is a value statistically estimated based on its correlation with lean mass (tissue other than fat) and may depend on certain assumptions. Therefore, in the future, we aim to conduct studies to make comparisons with the DXA method, which is the gold

standard. Fourth, bone loss in sarcopenia and the characteristics or bio-metabolic mechanisms of other participants are currently unknown and require further investigation in future studies.

Conclusion

This study reveals that age, bone mass, phase angle (lower limb), FFMI, and leg muscle score are factors involved in sarcopenia progression in both men and women. Furthermore, this study demonstrated that the measurement of bone mass by the BIA method has excellent accuracy in detecting sarcopenia in both males and females. The cut-off value of bone mass to predict sarcopenia was 2.2 kg for older adult men and 1.6 kg for older adult women. Our findings may help simplify the diagnosis of sarcopenia.

Author Contributions

OY and HO contributed significantly to the conceptualization of the study; NK, HO, YM, RI, TT, HT, TK, HH, and OY contributed significantly to data acquisition; NK, HO, and OY contributed significantly to data analysis and interpretation; and NK, HO, HH, and OY contributed to manuscript preparation. All authors critically reviewed and revised the manuscript and approved and submitted the final version.

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Conflict of Interest

No potential conflicts of interest were disclosed.

References

- 1 Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet* 2019; **393**: 2636–2646.
- 2 Kitamura A, Seino S, Abe T, et al. Sarcopenia: prevalence, associated factors,

and the risk of mortality and disability in Japanese older adults. *J Cachexia Sarcopenia Muscle* 2021; **12**: 30–38.

- 3 Akamatsu Y, Kusakabe T, Arai H, *et al.* Phase angle from bioelectrical impedance analysis is a useful indicator of muscle quality. *J Cachexia Sarcopenia Muscle* 2022; **13**: 180–189.
- 4 Kawakami R, Tanisawa K, Ito T, *et al.* Fat-free mass index as a surrogate marker of appendicular skeletal muscle mass index for low muscle mass screening in sarcopenia. *J Am Med Dir Assoc* 2022; **23**:1955–1961.
- 5 Paintin J, Cooper C, Dennison E. Osteosarcopenia. *Br J Hosp Med (Lond)* 2018; **79**: 253–258.
- 6 Qin H, Jiao W. Correlation of muscle mass and bone mineral density in the NHANES US general population, 2017–2018. *Medicine (Baltimore)* 2022; **101**: e30735.
- 7 Chen LK, Woo J, Assantachai P, *et al.* Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. *J Am Med Dir Assoc* 2020; **21**: 300–307.e2.
- 8 Kanda Y. Investigation of the freely available easy-to-use software ‘EZR’ for medical statistics. *Bone Marrow Transplant* 2013; **48**: 452–458.
- 9 Rosenberg IH. Summary comments: epidemiologic and methodologic problems in determining nutritional status of older persons. *Am J Clin Nutr* 1989; **50**: 1231–1233.
- 10 Rosenberg IH. Sarcopenia: origins and clinical relevance. *J Nutr* 1997; **127** (5 Suppl): 990S–991S.
- 11 Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. *J Am Geriatr Soc* 2002; **50**: 889–896.
- 12 Tanimoto Y, Watanabe M, Kono R, Hirota C, Takasaki K, Kono K. Aging changes in muscle mass of Japanese. *Nihon Ronen Igakkai Zasshi* 2010; **47**: 52–57. (in Japanese with English Abstract)
- 13 Wada T, Kawasaki Y, Inaji J. Establishing borderline and at-risk regions for estimated skeletal muscle mass of legs determined with a body composition meter. *Ningen Dock Int* 2014; **2**: 14–18.
- 14 Cheng L, Wang S. Correlation between bone mineral density and sarcopenia in US adults: a population-based study. *J Orthop Surg Res* 2023; **18**: 588.
- 15 Mizukami Y, Onishi H, Mifuku Y, *et al.* The role of fat indices as factors leading to sarcopenia in older adults residing in underpopulated areas. *J Clin Biochem Nutr* 2023; **74**: 70–73.
- 16 Goodman CA, Hornberger TA, Robling AG. Bone and skeletal muscle: key players in mechanotransduction and potential overlapping mechanisms. *Bone* 2015; **80**: 24–36.
- 17 Gomasasca M, Banfi G, Lombardi G. Myokines: the endocrine coupling of skeletal muscle and bone. *Adv Clin Chem* 2020; **94**: 155–218.
- 18 Kyle UG, Schutz Y, Dupertuis YM, Pichard C. Body composition interpretation. Contributions of the fat-free mass index and the body fat mass index. *Nutrition* 2003; **19**: 597–604.



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