ORIGINAL ARTICLE

Journal of Cachexia, Sarcopenia and Muscle 2023; **14**: 279–287
Published online 16 November 2022 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/jcsm.13128

Impact of sarcopenia and phase angle on mortality of the very elderly

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Abstract

Background Sarcopenia is a major component of geriatric syndrome and associated with poor clinical outcomes and mortality. However, diagnosing sarcopenia in the very elderly is difficult, and data on its epidemiology and devastating effects in this group are scarce. Phase angle (PA) is measured using bioimpedance spectroscopy and known to reflect cellular integrity and health. This study aimed to clarify the impact of sarcopenia and PA on mortality risk in very elderly people living in long-term care facilities.

Methods This prospective cohort study enrolled elderly residents living in nine long-term care facilities. We collected the participants' data, such as body mass index (BMI), comorbidities and laboratory data, from September to October 2017 and mortality data until October 2019. Nutritional status was evaluated using the Mini Nutritional Assessment (MNA) score, and multifrequency bioimpedance spectroscopy was used to assess body composition including PA. Appendicular skeletal muscle mass was calculated using the body composition monitor-derived equation of Taiwan's researchers. Sarcopenia was diagnosed using the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) definition (sarcopenia vs. normal group). We divided the participants into two groups according to the median PA value of 3.65° (high vs. low group) and performed multivariate regression analyses to verify the association with mortality risk according to sarcopenia diagnosis or PA group.

Results A total of 279 elderly participants were enrolled; of them, 238 (85.3%) were diagnosed with sarcopenia according to EWGSOP2 guidelines. The median patient age was 83 years, 211 (75.6%) were female and the median BMI was 20.4 kg/m^2. The sarcopenia group was older than the normal group (84 vs. 81 years; $P = 0.002$), had a lower mean BMI (19.8 vs. 26.6 kg/m^2, $P < 0.001$) and had a lower MNA score (9 vs. 12 points, $P < 0.001$). Sarcopenia was associated with a higher mortality risk after the adjustment for age, sex and diabetes mellitus (hazard ratio [HR], 3.744; 95% confidence interval [CI], 1.155–12.134; $P = 0.028$). A low PA was associated with sarcopenia, older age, female sex, low MNA score and overhydration volume; it was also a significant predictor of mortality after the adjustment for age, sex, diabetes mellitus and MNA score (HR, 0.593; 95% CI, 0.420–0.837; $P = 0.003$).

Conclusions Sarcopenia is prevalent among the very elderly patients in long-term care facilities. Sarcopenia and low PA are significantly associated with higher mortality risk.

Keywords bioimpedance; geriatric; mortality; phase angle; sarcopenia

Received: 10 June 2022; Revised: 12 October 2022; Accepted: 25 October 2022
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Introduction

South Korea is a representative country that is rapidly moving from an aged to a super-aged society. The proportion of the elderly population aged 65 years and over was 16.6% in 2021 and is expected to reach 25.5% by 2030 and 40.1% by 2050.[1] Many developed countries are currently facing similar circumstances.[2] Fully understanding and managing the characteristics of elderly patients has become an unavoidable task in these countries.

Sarcopenia is a major component of geriatric syndrome. Since the European Working Group on Sarcopenia in Older People (EWGSOP) published consensus guidelines for diagnosing sarcopenia in 2010,[3] many researchers have investigated the prevalence, diagnostic methods, biomarkers and clinical outcomes associated with sarcopenia. According to one meta-analysis, the prevalence of sarcopenia in people aged 60 years is 10–27%,[4,5] but data on the very elderly are scarce. One Chinese study included 101 elderly men aged 80 years and older, including 75 healthy volunteers, and reported that the prevalence of sarcopenia was 53.2%.[6] Sarcopenia is associated with a higher mortality risk in geriatric patients. Sipers et al. reported that the 2-year mortality risk in the sarcopenia group was 4.3-fold higher among acutely hospitalized elderly patients,[7] whereas Gümüşsoy et al. reported that the mortality risk in patients with both malnutrition and sarcopenia was 19.9 times higher than that in the normal group.[8]

There are various methods for measuring muscle mass to diagnose sarcopenia, such as dual-energy X-ray absorptiometry, magnetic resonance imaging, computed tomography, bioelectrical impedance analysis (BIA) and bioimpedance spectroscopy (BIS). However, there are some hurdles to their practical use in the clinical field, such as cost, accessibility and radiation. Among the methods listed above, BIA and BIS are the easiest for measuring muscle mass. Some BIA/BIS machines are portable, test subjects are not exposed to radiation and the cost is relatively low. Therefore, BIA/BIS can be a useful method for detecting sarcopenia in the very elderly and even in bedridden patients.

Phase angle (PA) is an emerging index that represents cellular integrity. BIA/BIS machines apply weak alternative currents across the limbs and trunk, and the PA value is derived from the measured resistance (*R*) and reactance (*Xc*) impedance values[9] as follows: $[\mathrm{PA}\ (^\circ) = arctangent(Xc/R) \times (180/\pi)]$. Several previous studies reported that PA is associated with clinical and prognostic indices such as muscle quality, nutritional status and functional status.[10–13]

This study aimed to determine the real-world prevalence and clinical characteristics of sarcopenia in a very elderly population living in long-term care facilities. Second, the clinical features according to the PA level were delineated. Finally, we aimed to clarify the clinical impact of sarcopenia and PA on mortality in the elderly population.

Methods

Study design, participants and endpoints

This prospective observational study enrolled elderly individuals living in one of nine long-term care facilities linked to the Myongji Hospital of Hanyang University College of Medicine in Goyang-si, Gyeonggi-do, South Korea. We initially screened 343 residents, but one institution decided not to conduct the study (n = 17), and 16 candidates were eliminated due to death (n = 2), nursing home discharge (n = 10), admission to another hospital (n = 2) or patient refusal (n = 2). Among the remaining 310 participants, 31 were excluded from the study because they could not be examined using BIS analysis or blood tests due to factors such as being an amputee, having extremely dry skin or having weak blood vessels from which blood could not be drawn. Ultimately, 279 patients were included in the study (*Figure S1*).

Informed consent was obtained from all patients between September and October 2017, and the study was conducted in October 2017. The outcomes data collection continued until October 2019. The participants were divided into two groups based on the median PA value: (1) sarcopenia versus normal (no sarcopenia group) and (2) low-PA ($<$3.65°) versus high-PA ($\geq$3.65°).

The primary endpoint of the study was all-cause mortality.

Baseline characteristics of the study population

Data on age, sex, height, weight, body mass index (BMI), systolic and diastolic blood pressure, pulse rate and comorbidities such as hypertension, diabetes mellitus (DM) and dementia were collected. We also calculated the modified Charlson Comorbidity Index and collected the most recent Korean Mini-Mental State Examination (K-MMSE) score data within the previous year as well as each participant's ability to eat and ambulate independently.

Sarcopenia definition

Sarcopenia was diagnosed by the revised EWGSOP2 definition in 2019.[14] Appendicular skeletal muscle mass (ASM) per height in metres squared (ASM/m^2) was used to define sarcopenia, with values of $<$7.0 kg/m^2 for men and $<$5.5 kg/m^2 for women as the cutoffs.

Bioelectrical impedance spectroscopy for muscle mass measurement

The body composition of each participant was measured using a multifrequency body composition monitor (BCM;

Fresenius Medical Care, Bad Homburg, Germany). One examiner measured the BCM of all participants according to the manufacturer's guidelines. A more detailed measurement protocol is described in Data *S1*. The excessive water volume (overhydration [OH]), lean tissue index (LTI), fat tissue index (FTI), total body water (TBW), extracellular water (ECW), intracellular water (ICW) and PA levels were evaluated. The BCM does not directly report the muscle mass. Therefore, we estimated ASM using the equation described by Lin et al.[15]

Muscle strength, nutritional status and laboratory data

We investigated several anthropometric parameters, including mid-arm circumference (MAC), calf circumference (CC) and skinfold thickness (SFT) of the abdomen and triceps. The same examiner measured the anthropometric data of all participants according to the published anthropometry procedures manual published in January 2004 by the National Health and Nutrition Examination Survey.[16] Furthermore, muscle strength was evaluated by hand grip strength (HGS) of the dominant arm using a Camry digital hand dynamometer (EH101; Zhongshan Camry Electronics Co., Ltd., Guangdong, China), and the cutoffs for low muscle strength were defined as $<$27 kg for men and $<$16 kg for women according to the EWGSOP2 guidelines. The Mini Nutritional Assessment (MNA) score was used as an index of nutritional status. Several laboratory markers, such as serum creatinine, total cholesterol and albumin levels, were tested, but only 137 of 279 participants agreed to undergo a blood test.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows Version 26 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean with standard deviation for normally distributed data or as median with interquartile range (IQR) for skewed data. The Kolmogorov–Smirnov test was used to analyse the normality of the data distributions. Categorical variables are expressed as number (percentage). The differences between the two groups were analysed using Student's *t*-test or the Mann–Whitney *U* test for continuous variables and the chi-squared test for categorical variables. Pearson's correlation analysis was performed to determine the relationship between variables and sarcopenia or PA.

Logistic and linear regression analyses were performed to verify independent predictors of sarcopenia or PA. Receiver operating characteristic (ROC) curve analysis was performed to determine the proper classification thresholds of PA to predict mortality and sarcopenia. The area under the ROC curve (AUC) to delineate the discriminatory ability of PA on mortality and sarcopenia was calculated. To determine the cutoff value of PA for predicting mortality and sarcopenia, we applied Youden's J statistics using Microsoft® Excel® (Microsoft Corp., Redmond, WA, USA). Cumulative survival curves were generated using the Kaplan–Meier method to determine the impact of sarcopenia or PA on mortality, whereas inter-group survival was compared using a log-rank test. Finally, the independent prognostic value of sarcopenia or low PA in relation to mortality was determined using multivariate Cox proportional hazards regression analysis, which included only variables that were significant in the univariate analysis except for sex and DM. Statistical significance was set at $P < 0.05$.

Ethics

This study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from study participants or their legal representatives. The institutional review board (approval number: 2017-01-023-022) of Myongji Hospital reviewed and approved the study protocol.

Results

Participants' characteristics

A total of 279 elderly participants from eight long-term care facilities were analysed. The median participant age was 83 years (IQR, 78–88 years), and female sex was predominant (75.6% [*n* = 211]). The median BMI of all subjects was 20.4 kg/m^2; according to the World Health Organization Asian BMI classification, the underweight group comprised 30.8% (*n* = 86), whereas the overweight/obese group comprised 23.3% (*n* = 65). The most common comorbidities were dementia (84.2%), hypertension (66.7%) and DM (26.2%). The median K-MMSE score was 12 (IQR, 8–15), and the percentage of participants who could eat or walk by themselves was 81.0% and 22.9%, respectively (*Table 1*). In terms of nutritional status, the median MNA score was 9 (IQR, 7–11), the malnutrition group (MNA score 0–7) comprised 26.2% and the patients who were at risk of malnutrition (MNA score 8–11) comprised 59.1% (*Table 2*).

Among the 279 participants, 238 (85.3%) were diagnosed with sarcopenia according to the EWGSOP2 guidelines. The sarcopenia group was older than the normal group (median age: 84 vs. 81 years; $P = 0.002$) and had a lower mean BMI (19.8 vs. 26.6 kg/m^2; $P < 0.001$). However, the proportion of women did not differ between the two groups. Hypertension, DM, osteoporosis and fracture events were less fre-

Table 1 Baseline characteristics of the study population with or without sarcopenia based on European Working Group on Sarcopenia in Older People 2 criteria

	Total (n = 279)	Sarcopenia (n = 238)	Normal (n = 41)	P
Age (years)	83 (78–88)	84 (78–89)	81 (74–85)	0.002
Age, *n* (%)				0.031
<70 years	15 (5.4)	11 (4.6)	4 (9.8)	
70–79 years	74 (26.5)	58 (24.4)	16 (39.0)	
≥80 years	190 (68.1)	169 (71.0)	21 (51.2)	
Female, *n* (%)	211 (75.6)	178 (74.8)	33 (80.5)	0.555
Height (cm)	153 (147–159)	153 (147–160)	153 (148–158)	0.954
Weight (kg)	47.2 (41.0–55.0)	45.3 (40.0–52.0)	62.6 (56.9–67.4)	<0.001
BMI (kg/m^2)	20.4 (18.0–22.8)	19.8 (17.6–21.6)	26.6 (25.0–28.2)	<0.001
BMI groups, *n* (%)				<0.001
<18.5 (underweight)	86 (30.8)	86 (36.1)	0 (0.0)	
18.5–22.9 (normal)	128 (45.9)	123 (51.7)	5 (12.2)	
23–24.9 (overweight)	24 (8.6)	19 (8.0)	5 (12.2)	
≥25 (obese)	41 (14.7)	10 (4.2)	31 (75.6)	
Systolic blood pressure (mmHg)	123 ± 17	122 ± 17	127 ± 16	0.065
Comorbidities				
Hypertension, *n* (%)	186 (66.7)	152 (63.9)	34 (82.9)	0.019
Diabetes mellitus, *n* (%)	73 (26.2)	53 (22.3)	20 (48.8)	0.001
Osteoarthritis, *n* (%)	25 (9.0)	18 (7.6)	7 (17.1)	0.070
Osteoporosis, *n* (%)	25 (9.0)	16 (6.7)	9 (22.0)	0.005
Stroke, *n* (%)	36 (12.9)	29 (12.2)	7 (17.1)	0.447
Coronary artery disease, *n* (%)	13 (4.7)	12 (5.0)	1 (2.4)	0.700
Heart failure, *n* (%)	16 (5.7)	12 (5.0)	4 (9.8)	0.267
Dementia, *n* (%)	235 (84.2)	202 (84.9)	33 (80.5)	0.488
Parkinson disease, *n* (%)	31 (11.1)	26 (10.9)	5 (12.2)	0.789
Chronic kidney disease, *n* (%)	2 (0.7)	2 (0.0)	0 (0.0)	0.999
Fracture, *n* (%)	31 (11.1)	22 (9.2)	9 (22.0)	0.028
Depression, *n* (%)	13 (4.7)	12 (5.0)	1 (2.4)	0.700
Modified CCI				0.015
Score 0–1, *n* (%)	29 (10.4)	26 (10.9)	3 (7.3)	
Score 2, *n* (%)	157 (56.3)	141 (59.2)	16 (39.0)	
Score 3–6, *n* (%)	93 (33.3)	71 (29.8)	22 (53.7)	
K-MMSE	12 (8–15)	11 (7–15)	15 (12–19)	<0.001
How to eat, *n* (%)				
Eat by themselves	226 (81.0)	186 (78.2)	40 (97.6)	0.010
Needs help	47 (16.8)	46 (19.3)	1 (2.4)	
Tube feeding	6 (2.2)	6 (2.5)	0 (0.0)	
How to walk, *n* (%)				
Self-ambulation	64 (22.9)	56 (23.6)	8 (19.5)	<0.001
Needs assistance	105 (37.6)	78 (32.9)	27 (65.9)	
Cannot self-ambulate	79 (28.3)	73 (30.8)	6 (14.6)	
Bedridden	30 (10.8)	30 (12.7)	0 (0.0)	

Note: One patient refused hand grip strength check. Data are expressed as the mean ± standard deviation or number (%). The Mann–Whitney *U* test was performed for variables that did not satisfy the normality test. These variables are expressed as medians (interquartile ranges). Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; K-MMSE, Korean Mini-Mental State Examination.

quent in the sarcopenia versus normal group (*Table 1*). The median MNA score was lower in the sarcopenia than normal group (9 vs. 12 points; $P < 0.001$), whereas the MAC, CC, HGS and SFT were significantly lower in the sarcopenia than normal group. In the BCM analysis, OH, OH/ECW and ECW/ICW were higher in the sarcopenia group, whereas LTI, FTI, TBW, ECW, ICW and PA levels were lower in the sarcopenia group. Moreover, albumin levels were lower in the sarcopenia than normal group; however, serum creatinine, estimated glomerular filtration rate (eGFR) according to the Chronic Kidney Disease Epidemiology Collaboration equation and total cholesterol levels did not differ between the two groups (*Table 2*).

Related factors for sarcopenia and its clinical implications

To verify the factors correlating with ASM/m^2, we performed Pearson correlation analysis. Age was negatively correlated with ASM/m^2, but MNA score, K-MMSE score, MAC, CC, HGS, SFT, serum creatinine and albumin levels were positively correlated with ASM/m^2. Among the BCM indicators, OH, OH/ECW and ECW/ICW were negatively correlated with ASM/m^2, whereas LTI, FTI, TBW, ECW, ICW, body cell mass index and PA were positively correlated with ASM/m^2. Total cholesterol and eGFR were not correlated with ASM/m^2 levels (*Table S1*). Moreover, multivariate logistic regression

Table 2 Nutritional status, anthropometric indices including body composition monitor measurement and laboratory data based on European Working Group on Sarcopenia in Older People 2 criteria

	Total (n = 279)	Sarcopenia (n = 238)	Normal (n = 41)	P
MNA score	9.0 (7.0–11.0)	9.0 (7.0–10.0)	12.0 (11.0–12.0)	<0.001
MNA group, n (%)				<0.001
Score 0–7 (malnutrition)	73 (26.2)	73 (30.7)	0 (0.0)	
Score 8–11 (at risk of malnutrition)	165 (59.1)	146 (61.3)	19 (46.3)	
Score 12–14 (normal)	41 (14.7)	19 (8.0)	22 (53.7)	
Anthropometric data				
Mid-arm circumference (cm)	25.0 (23.4–27.0)	24.7 (23.0–26.5)	28.0 (28.0–30.1)	<0.001
Calf circumference (cm)	28.1 ± 4.1	27.3 ± 3.8	32.7 ± 2.8	<0.001
Hand grip strength, dominant (kg)	4.9 (1.4–10.5)	4.1 (1.0–9.3)	9.9 (5.3–14.2)	<0.001
Skin fold thickness, abdomen (cm)	20.3 ± 7.2	19.0 ± 6.5	27.3 ± 7.0	<0.001
Skin fold thickness, triceps (cm)	16.0 (12.0–20.0)	16.0 (12.0–20.0)	22.0 (17.0–24.0)	<0.001
Body composition monitor indices				
Overhydration (L)	0.2 (−0.7 to 0.9)	0.2 (−0.6 to 0.9)	−0.3 (−1.9 to 1.0)	0.032
Overhydration/ECW (%)	1.5 (−6.6 to 9.1)	2.2 (0.6–9.2)	−2.4 (−14.3 to 6.8)	0.017
Lean tissue index (kg/m^2)	11.30 ± 3.44	10.69 ± 2.99	14.86 ± 3.74	<0.001
Fat tissue index (kg/m^2)	9.06 ± 4.44	8.63 ± 4.16	11.60 ± 5.15	0.001
Total body water (L)	24.35 ± 5.73	23.18 ± 4.97	31.16 ± 5.11	<0.001
ECW (L)	11.31 ± 2.50	10.84 ± 2.23	14.02 ± 2.21	<0.001
ICW (L)	12.5 (10.3–15.2)	11.9 (10.0–14.0)	16.2 (14.4–19.2)	<0.001
ECW/ICW	0.90 ± 0.17	0.91 ± 0.17	0.84 ± 0.17	0.028
Phase angle (°)	3.65 ± 0.94	3.49 ± 0.89	4.58 ± 0.60	<0.001
Laboratory data				
Creatinine (mg/dL)	0.70 (0.60–0.90)	0.70 (0.60–0.90)	0.70 (0.60–1.10)	0.329
eGFR (mL/min/1.73 m^2)	80.1 (65.5–89.3)	80.4 (68.0–88.6)	80.1 (50.9–90.5)	0.848
Total cholesterol (mg/dL)	159.7 ± 38.0	160.0 ± 36.8	158.7 ± 43.2	0.880
Albumin (g/dL)	3.9 (3.6–4.1)	3.9 (3.5–4.1)	4.1 (4.0–4.2)	0.004

Note: Of 279 participants, only 137 consented to the blood test. Abbreviations: ECW, extracellular water; eGFR, estimated glomerular filtration rate; ICW, intracellular water; MNA, Mini Nutritional Assessment.

analysis to determine independent predictors of sarcopenia revealed that PA, female sex, BMI and DM were significant predictors of sarcopenia. However, age and MNA scores were not statistically significant (*Table S2*). In terms of the primary endpoint, we performed univariate and multivariate Cox proportional hazard regression analyses to determine the association between mortality and sarcopenia and conducted the Kaplan–Meier plot analysis. The sarcopenia group showed a higher mortality risk than the normal group (log-rank test, P = 0.005) (*Figure 1*). In the univariate Cox regression analysis, mortality was significantly associated with sarcopenia (hazard ratio [HR], 4.541; 95% confidence interval [CI], 1.429–14.429; P = 0.010). In addition, Model 1, which was adjusted for age, female sex and history of DM, showed that sarcopenia was a significant risk factor for mortality (HR, 3.744; 95% CI, 1.155–12.134; P = 0.028). However, in Model 2, in which the serum albumin level and MNA score were adjusted in addition to Model 1, sarcopenia was not significantly associated with mortality risk (HR, 1.315; 95% CI, 0.263–6.578; P = 0.739) (*Table 3*).

Characteristics of phase angle and mortality risk

We divided the patients into two groups (low-PA vs. high-PA) according to the median PA (3.65°). A comparison of the low-PA and high-PA groups with respect to baseline characteristics is presented in *Tables S3* and *S4*. In contrast to the sarcopenia analysis, there were more women in the low-PA than high-PA group. Comorbidities including hypertension, DM, osteoporosis and fracture events were not statistically different between the two groups (*Table S3*). The MNA score, anthropometric data (MAC, CC, HGS and SFT) and serum albumin levels were higher in the high-PA than low-PA group. OH/ECW, LTI, TBW, ECW and ICW levels were higher and OH and ECW/ICW levels were lower in the high-PA group than in the low-PA group. The FTI did not show any statistical differences (*Table S4*).

The Pearson correlation analysis showed results similar to those of the sarcopenia analysis; that is, age, OH, OH/ECW and ECW/ICW were negatively correlated with PA, but the MNA score, K-MMSE score, MAC, CC, HGS, SFT, serum creatinine and albumin levels, LTI, FTI, TBW, ECW, ICW and body cell mass index were positively correlated with PA (*Table S5*). In addition, we performed univariate and multivariate linear regression analyses to identify the independent predictors associated with PA levels. Increased ASM/m^2 and MNA scores were associated with an increased PA, whereas age, BMI and OH increment were associated with a decreased PA. Sex was not a significant factor in the multivariate linear regression analysis (*Table S6*).

Multivariate Cox regression analysis showed that PA was a statistically significant predictor of survival after adjusting for age, sex and DM (Model 1). Furthermore, we added the MNA

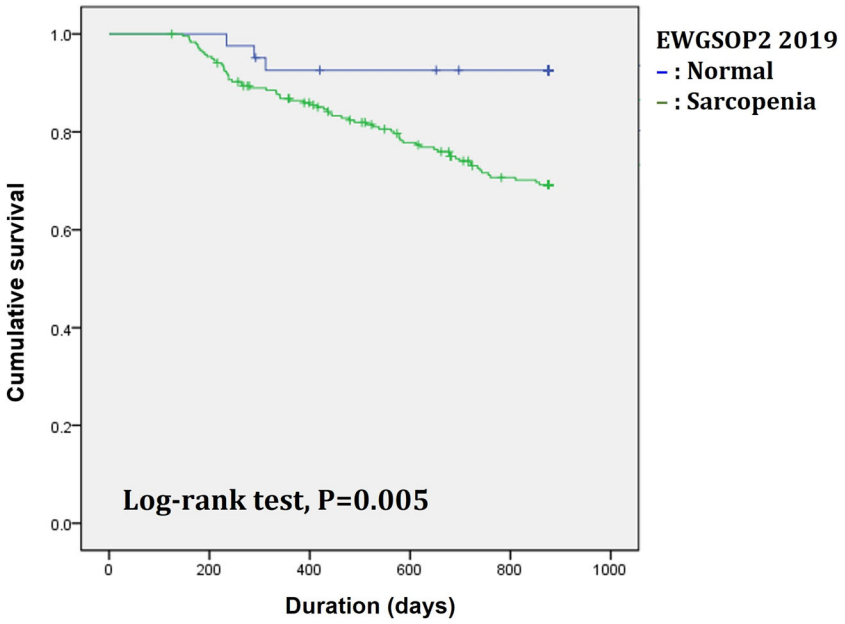

Figure 1 Kaplan–Meier plot for mortality risk according to sarcopenia diagnosis based on the EWGSOP2 guideline. EWGSOP2, European Working Group on Sarcopenia in Older People 2

Table 3 Cox regression analyses for mortality according to sarcopenia

	Univariate analysis			Multivariate analysis					
				Model 1			Model 2		
	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Sarcopenia (vs. no sarcopenia)	4.541	1.429–14.429	0.010	3.744	1.155–12.134	0.028	1.315	0.263–6.578	0.739
Age (per 1 year increase)	1.076	1.040–1.113	<0.001	1.072	1.036–1.109	<0.001	1.083	1.031–1.137	0.002
Female (vs. male)	0.915	0.542–1.546	0.741	0.726	0.427–1.235	0.238	0.693	0.324–1.480	0.343
DM (vs. no DM)	1.095	0.654–1.835	0.729	1.385	0.820–2.339	0.224	1.189	0.536–2.636	0.670
Albumin (per 1 g/dL increase)	0.225	0.124–0.408	<0.001	–	–	–	0.329	0.161–0.673	0.002
MNA score (per 1 point increase)	0.794	0.724–0.870	<0.001	–	–	–	0.871	0.725–1.047	0.141

Abbreviations: CI, confidence interval; DM, diabetes mellitus; HR, hazard ratio; MNA, Mini Nutritional Assessment.

Table 4 Cox regression analyses for mortality according to phase angle

	Univariate analysis			Multivariate analysis					
				Model 1			Model 2		
	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Phase angle (°)	0.488	0.372–0.640	<0.001	0.462	0.340–0.628	<0.001	0.593	0.420–0.837	0.003
Age (per 1 year increase)	1.076	1.040–1.113	<0.001	1.065	1.031–1.101	<0.001	1.071	1.037–1.107	<0.001
Female (vs. male)	0.915	0.542–1.546	0.741	0.439	0.248–0.775	0.005	0.499	0.281–0.885	0.017
DM (vs. no DM)	1.095	0.654–1.835	0.729	1.100	0.653–1.854	0.720	1.082	0.642–1.825	0.767
MNA score (per 1 point increase)	0.794	0.724–0.870	<0.001	–	–	–	0.844	0.747–0.954	0.006

Abbreviations: CI, confidence interval; DM, diabetes mellitus; HR, hazard ratio; MNA, Mini Nutritional Assessment.

score as a variable to adjust for nutritional status in Model 1 (Model 2), and PA was a significant predictor of survival in Model 2 (*Table 4*). The Kaplan–Meier plot using the log-rank test verified that the low-PA group had a higher cumulative mortality risk than the high-PA group (*Figure 2*). Moreover, a ROC curve analysis was performed to determine the cutoff value correlated with survival and non-sarcopenia diagnosis in the very elderly group. The AUC of the PA values for the prediction of survival and non-sarcopenia was 0.687 and 0.863, respectively (*Figure 3*). The cutoff values for mortality and sarcopenia diagnosis were <3.19° and <4.02°, respectively (data not shown).

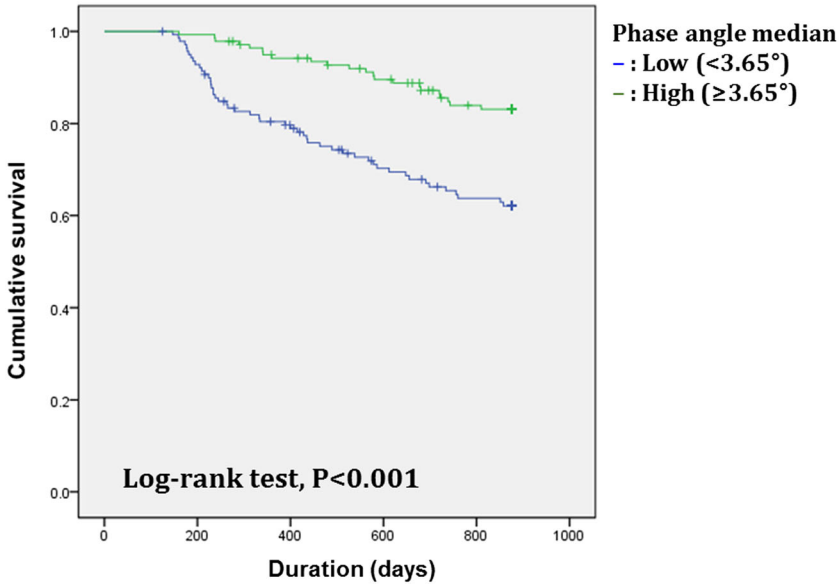

Figure 2 Kaplan–Meier plot for mortality risk of the two groups according to median phase angle value (3.65°)

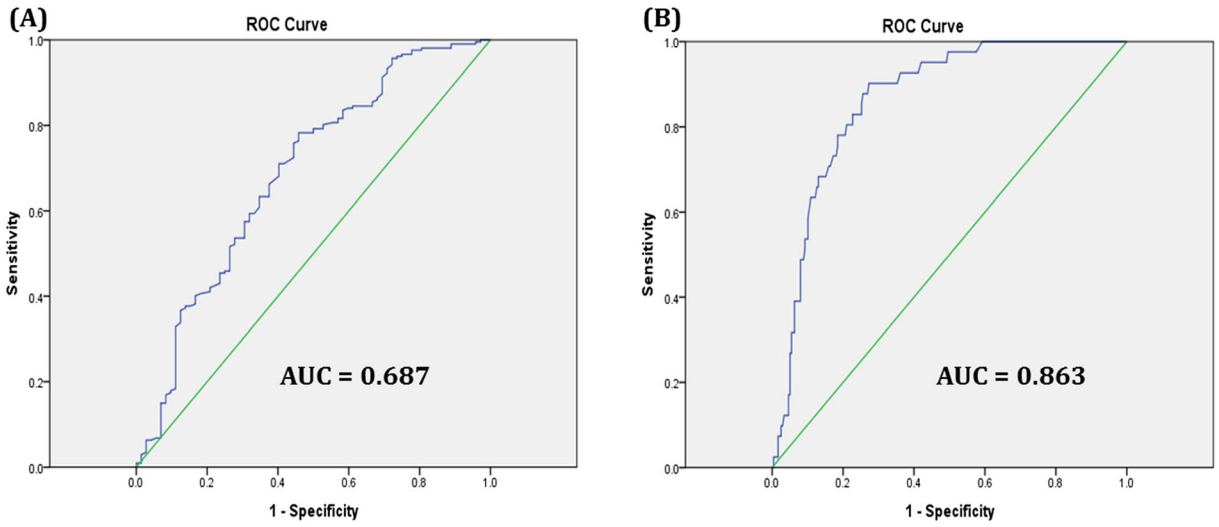

Figure 3 ROC curves of phase angle values for prediction of (A) survival and (B) non-sarcopenia diagnosis according to the European Working Group on Sarcopenia in Older People 2 guideline. AUC, area under the curve; ROC, receiver operating characteristic

Discussion

The current study delineated the very high prevalence of sarcopenia in the elderly living in long-term care facilities using a noninvasive BIS. HGS was weaker and MAC, CC and SFT were thinner in the sarcopenia versus normal group. PA, a marker of functional cell membrane integrity, is associated with muscle mass and power. With regard to mortality, sarcopenia increased the mortality risk by 3.7-fold versus the normal group. An increase in PA value of 1° was found to be associated with a 54% decrease in mortality risk in the elderly.

Decreased skeletal muscle mass was previously considered a natural aging process. However, it has more recently been considered a factor in geriatric syndromes, and its identification and management have been highlighted to prevent grave outcomes. The EWGSOP had a consensus meeting and published guidelines on sarcopenia diagnostic criteria in 2010 (EWGSOP)[3] and revised them in 2019 (EWGSOP2).[14] Moreover, muscle quantity and quality, such as muscle strength and physical performance, have received focus as important components of sarcopenia in EWGSOP2. Dynapenia (low muscle strength) is a key characteristic of

sarcopenia and an influential predictor of poor clinical outcomes. In this study, 266 patients (95.3%) had dynapenia, making it more prevalent than sarcopenia (*n* = 238; 85.3%). The participants in the normal muscle strength group did not die during the follow-up period. Although this study focused on muscle mass, additional research on muscle strength is required.

In addition, many elderly patients in long-term care facilities cannot walk by themselves; therefore, even visiting a hospital is not easy for them. Therefore, diagnosing sarcopenia using a portable BIS and predicting mortality risk through PA are considered useful diagnostic techniques for this patient group in real-world clinical scenarios.

Reports on sarcopenia in the very elderly are insufficient. Sobestiansky et al. studied the prevalence and mortality risk of sarcopenia in men aged 85–89 years living in the community. The authors reported that the sarcopenia prevalence was 20% according to the EWGSOP2 guideline, and the mortality risk increased 1.95-fold in the sarcopenia group.[17] One Japanese study of community-dwelling elderly women (mean age, 78 years) showed that the prevalence of sarcopenia was 39.6%.[18] Şimşek and Uçar recently described sarcopenia and nutritional status in nursing home residents,[19] and the average participant age was similar to that in our study (>80 years old). The authors compared the sarcopenia and non-sarcopenia groups and reported that the proportion of patients in the former was 51.2% (*n* = 88). Based on our current findings, we reported a very high prevalence of sarcopenia (85.3%) among the very elderly living in long-term care facilities.

Of the 279 participants, 72 died within 2 years. Thus, the 2-year mortality rate was 7.3% (*n* = 3) in the normal group and 29.0% (*n* = 69) in the sarcopenia group (*P* = 0.003). A mortality risk analysis using Cox regression also demonstrated that sarcopenia increased the mortality risk by 3.7-fold after the adjustment for age, sex and DM (Model 1 in *Table 3*). However, sarcopenia was not a statistically significant factor for mortality risk after the adjustment for albumin and MNA levels in Model 2; this is because nutritional status and albumin are very powerful predictors of mortality in addition to sarcopenia (*Figures S2* and *S3*), and they are interconnected and mutually influence each other. In other words, sarcopenia and nutritional status are key factors affecting mortality in the elderly population.

Unexpectedly, osteoporosis and fracture history were more prevalent in the normal elderly group in the present study. Osteoporosis is often associated with sarcopenia because it shares common pathophysiological factors. It is presumed that the opposite result to that of previous research is as follows: Osteoporosis does not cause pain or discomfort to patients until they experience a fracture. The participants of this study were living in long-term care facilities, so they usually did not visit the hospital unless they felt discomfort or suffered from a severe disease. Therefore, they visit a hospital when a fracture occurs and are diagnosed with osteoporosis in most cases. This is the reason why the proportions of fracture history and osteoporosis prevalence were similar, and the proportion of osteoporosis was lower in the sarcopenia versus normal group. Moreover, the subjects at risk for fracture were persons who could ambulate themselves or who needed assistance walking. Patients who are bedridden are less likely to experience a fracture because they always stay in bed. The proportion of patients at risk for fracture was higher in the normal group (85.4%) than in the sarcopenia group (56.5%).

In addition to measuring muscle mass and diagnosing sarcopenia using BIS, we verified that PA was a useful factor for correlating nutritional status and muscle power and a negative predictor of sarcopenia and mortality. Basile et al. reported a relationship between PA, muscle mass and strength. The average muscle mass (8.8 kg/m^2 in Basile et al.'s study; 4.6 kg/m^2 in this study) and HGS (29.5 kg in Basile et al.'s study; 7.0 kg in this study) values were higher than those in this study. Nevertheless, the trends in PA and muscle mass were similar. Multivariate linear regression analysis showed a statistically significant positive relationship between PA and muscle mass/HGS.[20] Moreover, the findings of studies of the association between PA and mortality were summarized in a systematic review.[21] The authors reported that 42 of 48 studies showed a correlation between PA and mortality. The PA cutoff points, which increased the risk of death, varied among diseases and studies: 3.6° to ≤8° in kidney disease, 4.2° to <5.5° in heart disease, 4.1° to <6° in critically ill patients and <4.4° to <5.8° in cancer patients. Our findings revealed that the cutoff PA degree for sarcopenia diagnosis in very elderly nursing home residents was <4.02°, indicating that their results were similar to those of chronic and critically ill patients. Sarcopenia prediction using PA showed a significantly good AUC value (0.863). Therefore, we suggest that a PA value < 4.0° can be a very convenient screening tool for sarcopenia in the very elderly group.

Our study has some limitations. First, the prevalence of sarcopenia might have been underestimated in our study because participants who dropped out after screening were more fragile than the final participants. Second, the Jamar hydraulic hand dynamometer is the gold standard for measuring HGS,[22] but we used a different digital hand dynamometer. However, a study that compared the Camry and Jamar dynamometers in healthy adults aged 40–59 years showed that the Camry could replace the Jamar dynamometer.[23] Third, we could not examine physical performance, such as 6-min walk distance, because many participants were too old to safely undergo the test. And finally, approximately half of the participants (162 of 279) did not agree to the blood test; thus, accuracy might be lacking in this related analysis. Nevertheless, it is considered a valuable study that is difficult to conduct with this group of participants.

Conclusions

Evaluating muscle mass and PA using BIS is a very useful technique for diagnosing sarcopenia among elderly individuals living in long-term care facilities. Sarcopenia was highly prevalent in this group, and a diagnosis of sarcopenia combined with low PA was a strong predictor of increased mortality risk.

Acknowledgements

We would like to express our deepest gratitude to the long-term care facilities' staffs and directors who participated in this study. All authors of this article complied with the guidelines of ethical authorship and publication in the *Journal of Cachexia, Sarcopenia and Muscle*.[24]

Conflicts of interest

All authors declared that they have no conflicts of interest.

Funding

This research was supported by a faculty grant from the Myongji Hospital (1701-03-21).

Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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