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Relationship of Phase Angle with Sarcopenia Components and Comprehensive Geriatric Assessment in Physically Independent Older Adults

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Abstract

Objective: This study aimed to investigate the relationship between phase angle (PhA), sarcopenia components, and comprehensive geriatric assessment in physically independent older adults.

Materials and Methods: This cross-sectional study involved 135 physically independent older adults admitted to a geriatric outpatient clinic. All participants underwent bioelectrical impedance analyses and comprehensive geriatric assessments. The individuals were investigated in two groups regarding PhA: 1st versus 2nd and 3rd terciles. The individuals in the first tercile were considered to have low PhA (for women <4.6° and men <5.4°).

Results: The prevalence of individuals with low PhA was 22% (n=30). PhA was correlated with hand grip strength (HGS) and appendicular skeletal muscle mass (ASMM) overall (r=0.523; p<0.001, r=0.335; p<0.001, respectively). A moderately positive, moderately significant correlation was found between PhA and ASMM in males (r=0.618; p<0.001), with the highest significance of all. In univariate analysis, components of sarcopenia and comprehensive geriatric assessments were not associated with low PhA values overall and in the male group (p>0.05). Only ASMM was significantly associated with low PhA in the univariate and multivariate analyses in the female group (p=0.02 and p=0.03, respectively).

Conclusion: Challenges such as the use of different formulas for calculating ASMM and various cutoff values for different ethnic groups can be barriers to ASMM assessment. PhA might be a simple predictor of ASMM in physically independent older women.

Keywords: Sarcopenia, frailty, older adults, comprehensive geriatric assessment

Introduction

Phase angle (PhA) is a parameter derived from bioelectrical impedance analysis (BIA), a non-invasive method used to assess body composition and cellular health, and it is a new indicator of functional status and muscle quality (1,2). In clinical practice, PhA measurements obtained through BIA are used in diverse settings, including nutritional assessment, muscle health, disease severity and prognosis, hydration status, and overall health and functioning. Recent studies have found a strong link between hand grip strength (HGS), PhA, and nutritional status (3-5). In addition, PhA was found to predict survival in hospitalized patients (3,6).

In both sexes, PhA also decreases progressively after 40 years of age and in the following years (7). The PhA cutoff value for predicting sarcopenia can vary depending on the characteristics of the patient group being studied. Vincenzo et al. (6) conducted a recent meta-analysis and reported that lower PhA with various cutoff values between 4.05 and 5.05 was associated with sarcopenia. In another study, Rosas-Carrasco et al. (8) found that a PhA cutoff value of 4.1 showed a significant association

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between PhA and both frailty and sarcopenia. Similarly, in the case of malnutrition, different PHA cut-off has been found (5,9).

It is important to interpret PhA values in the context of individual patient characteristics, including age, sex, body composition, and underlying health conditions. Additionally, PhA could be used as a component of a comprehensive assessment in conjunction with other clinical data-assessments and biomarkers to guide clinical decision-making. The majority of PhA trials were conducted in frail patients with co-morbidities. We know that it is important to prevent frailty, sarcopenia, and malnutrition before they occur. The PhA could be a quick, easy, and useful screening tool to assess early changes in parameters associated with frailty, sarcopenia, and malnutrition. So, in this study, we aimed to investigate the relationship between bioimpedance PhA, sarcopenia components, and comprehensive geriatric assessment in physically independent older adults.

Materials and Methods

Participants

This study is a part of Scientific Research Projects TGA-2020-21562, and it is a cross-sectional study conducted at the Geriatrics Medicine and Internal Medicine Outpatient Clinics of Ege University Medical Faculty between May 2019 and October 2019. Participants who did not give informed consent, those aged <60 years, with sensory deficits, finger/hand amputations, and active arthritis, as well as hemiplegic/quadriplegic patients, and those with recent (last 3 months) upper extremity surgery and acute infection/symptoms were excluded from the study. Participants were considered physically independent if they were independent in their activities of daily living (ADL) and could walk without assistance. Independence in ADL was defined as a score of 6 on the Katz ADL Scale (10,11). The inclusion and exclusion criteria are explained in detail in Figure 1. The present study was approved by the Ethics Committee of Ege University Medical Research Ethics Committee (approval number: E41277, date: 07.02.2019). All recruited patients provided written informed consent.

Measurements

Height, weight, waist circumference (WC) (cm), mid-upper arm circumference (MAC) (cm), and calf circumference (CC) (cm) of the participants were measured, and body mass index (BMI) (kg/m^2) was calculated as anthropometric assessment. Participants' height (cm) and weight (kg) were measured using a stadiometer and BIA (Tanita MC-780 body analysis monitor), respectively. The BMI values were assessed using the standard formula: BMI: (kg)/height^2 (m^2). The PhA value (◦) was assessed using a multifrequency tetrapolar instrument (Tanita MC-780

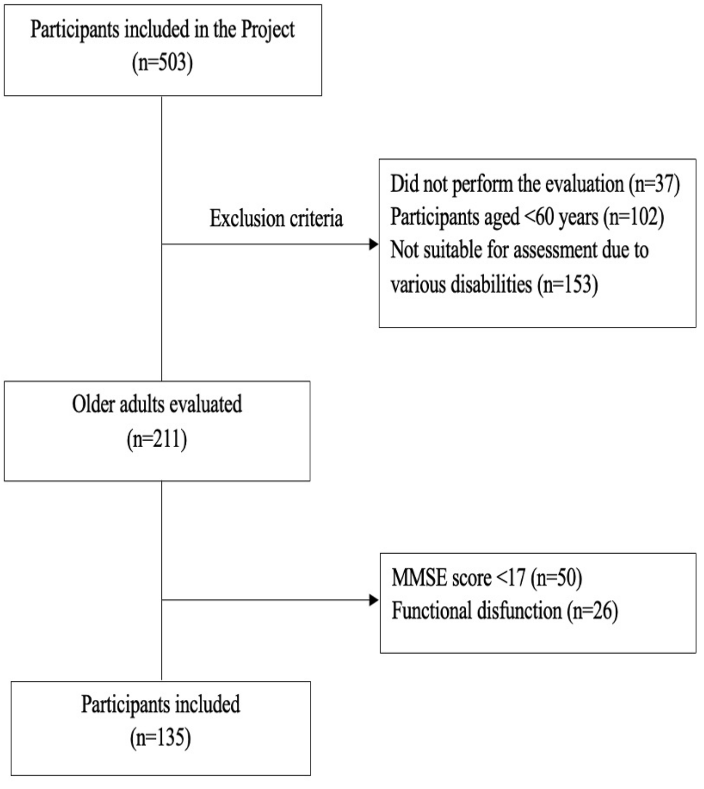

Figure 1. Flowchart of the study

MMSE: Mini-mental state examination

BIA) at 50 kHz based on a previous study (12). The volunteers were instructed to fast overnight (12 hours before the test) and to avoid strenuous physical activity, caffeine, and alcohol consumption the day before. They were asked to remove their shoes and heavy outer clothes before the measurement. The procedures were performed based on the study of Verney et al. (13). Appendicular skeletal muscle mass (ASMM) was estimated in kilograms using the equation of Sergi et al. (14).

Handgrip strength (HGS) was measured using a Jamar Plus+ digital dynamometer (Performance Health Supply, Inc, Cedarburg, WI), and a Takei T.K.K. 5401 digital dynamometer (Takei Scientific Instruments Co. Ltd., Tokyo, Japan). The HGS measurements are described in detail in Savas et al. (15). A four-meter gait speed test was performed to assess physical performance (16). A gait speed (GS) <0.8 m/s was considered to indicate low physical performance.

Sarcopenia Diagnosis

Sarcopenia has been defined in accordance with the criteria of the revised EWGSOP (EWGSOP2) consensus (17) as follows; 1) Low HGS using local thresholds calculated according to Bahat et al. (18) (for males <35 kg, and females <20 kg), 2) Low ASMM calculated according to EWGSOP2 (for males <20 kg, for females <15 kg), 3) Slow gait speed calculated by a four-meter gait speed test (<0.8 m/s). Participants categorized as "probable sarcopenia" if only low muscle strength is present, and "confirmed sarcopenia" if both low muscle mass (MM) and low muscle strength were present.

Comprehensive Geriatric Assessment

The following components of comprehensive geriatric assessment were evaluated: cognitive function using the mini mental state examination (MMSE) (19,20), frailty using the FRAIL scale (21,22), and nutritional status using the mini nutritional assessment-short form (MNA-SF) (23,24).

Statistics

Data were analyzed using SPSS version 25.0 for Windows. Data normality was obtained by Kolmogorov-Smirnov test. PhA, ASMM, WC, CC, and HGS by both dynamometers in women, ASMM, MAC, WC, CC, and HGS by both dynamometers in men were normally distributed. Due to the absence of specific cutoff points, the distribution of PhA was divided into terciles, and values below the first tercile were considered low. The individuals were divided into three groups: 1st vs. 2nd and 3rd terciles. The individuals in the first tercile were considered to have low PhA (for women< 4.6° and men< 5.4°). The *t*-test and Mann-Whitney U test were used to analyze quantitative variables when available. Normally distributed quantitative variables, quantitative variables without normal distribution, and categorical variables were expressed by mean±standard deviations, median (interquartile range), and frequency (percentages) respectively. The normally distributed parameters were analyzed using the Pearson correlation coefficient. The correlations were also tested separately for gender groups. While investigating the associations between non-normal distributions, the correlation coefficients and their significance were calculated using the spearman test. A logistic regression model was performed for variables that showed significant relationships with the univariate analysis. Multivariable logistic regression analysis was performed to calculate the adjusted odds ratios (ORs) and 95% confidence interval of individuals with low PhA (first vs. second and third terciles), ASMM, HGS, and GS. Hosmer-Lemeshow goodness-of-fit statistics was used to assess model fit. P<0.05 was considered statistically significant.

Results

Participants Characteristics

A total of 135 physically independent older adults were included in the study after applying extensive exclusion criteria. The median age was 66.5 (min.-max. 60-90) years in women and 70 (min.-max. 60-88) years in men. Females composed 50.4% of the study population. According to the WHO criteria, 30.4% (n=41) of participants were obese (BMI ≥30), 35.6% (n=48) of participants were overweight (30> BMI ≥25). In all, HGS by Jamar and HGS by Takei were 30.9±9 kg, 30.2±7.4 kg, respectively. Forty-six point seven percent (n=63) of all had low ASMM and 18.5% (n=25) had low GS. In females; PhA, HGS by Jamar, HGS by Takei, GS, and ASMM were 5.1±0.7°, 24.5±5.3 kg, 25.2±4.6 kg, 1.1±0.3 m/sn, 15.1±1.9 kg, respectively. In the male group, PhA, HGS by Jamar, HGS by Takei, GS, and ASMM were 5.7° (0.8), 37.5±7.1 kg, 35.3±6.2 kg, 1.1±0.3 m/sn, 20.8±3.2 kg, respectively. Considering the dynamometer used, the rate of probable sarcopenia was the same although the rate of confirmed sarcopenia changed. Forty (70.4%) participants had probable sarcopenia. The rate of confirmed sarcopenia by the Jamar dynamometer was 18.5% (n=25), whereas the rate of confirmed sarcopenia by the Takei dynamometer was 17% (n=23). The prevalence of the individuals with low PhA was 22% (n=30). In terms of comprehensive geriatric assessment, only the MNA score was associated with PhA in men. We have shown the characteristics of the participants according to PhA cutoff points (per tercile) and gender are presented in Table 1.

In the overall group and in men, PhA was weakly correlated with the MNA score (r=0.314; p<0.001, r=0.328; p=0.007, respectively). PhA was correlated with HGS and ASMM in all groups. A positive, moderately significant correlation was found between PhA and ASMM in the older males (r=0.618; p<0.001). In women, PhA was correlated with all components of sarcopenia, although its significance was weak (Table 2). Components of sarcopenia and comprehensive geriatric assessments were not

Table 1. Characteristics of the participants according to phase angle cut-off points (per tercile) and gender

	Overall (n=135)				Women (n=68)		
		Low PhA (n=16)	Not low PhA (n=51)	p	Low PhA (n=14)	Not low PhA (n=54)	
Age, y	69 (8)	72.5 (10)	68 (8)	0.01	65.5 (9.8)	67.5 (6)	0.5
Weight, kg	71.7 (13.3)*	75.4 (13.8)*	76.4 (13.9)*	0.8	64.4 (10.2)*	68 (11.5)*	0.3
BMI	27.7 (4.8)*	25.8 (5.3)*	27.6 (4.7)*	0.2	26.5 (3.9)*	28.5 (4.8)*	0.1
CC, cm	37.5 (3.7)*	37.8 (4.1)*	37.3 (3.5)*	0.7	36 (4.1)*	38 (3.7)*	0.09
WC, cm	98 (12.7)*	99.4 (13.2)*	101.5 (13)*	0.6	92.2 (11.5)*	95.8 (11.8)*	0.3
MAC, cm	30.3 (3.6)*	29.5 (3.6)*	30.1 (3.3)*	0.5	28.3 (3.6)*	31.3 (3.5)*	**0.007**
HGS¹, kg	30.9 (9)*	35.7 (6.5)*	38 (7.3)*	0.3	22.3 (3)*	25 (5.7)*	**0.02**
HGS², kg	28.6 (11.2)	33.4 (5.3)*	36 (6.4)*	0.2	22.6 (3.1)*	26 (4.7)*	**0.02**
ASMM, kg	17.3 (5.49)	20.5 (2.4)*	20.8 (3.5)*	0.7	14 (1.7)*	15.4 (1.9)*	**0.02**
GS, m/sn	1.1 (0.3)*	1 (0.2)*	1.1 (0.3)*	0.3	1 (0.2)*	1.1 (0.3)*	0.3
PhA,°	5.4 (1)	4.9 (0.55)	5.9 (0.7)	**0.00**	4.2 (0.2)*	5.4 (0.6)*	**0.00**
MMSE	29 (2)	29 (2)	29 (2)	0.8	29 (2)	29 (2)	0.8
FRAIL	0 (1)	0 (0)	0 (1)	0.3	0 (1)	0 (1)	0.8
MNA	14 (2)	13.5 (2)	14 (1)	**0.04**	13 (2)	14 (2)	0.8

*Normally distributed quantitative variables were expressed by mean (standard deviations) PhA. PhA: Phase angle, Low PhA: Phase angle for women <4.6° and men <5.4°, CC: Calf circumference, WC: Waist circumference, MAC: Mid-upper arm circumference, BMI: Body mass index, HGS¹: Handgrip strength max using Jamar digital, HGS²: Handgrip strength max using Takei max, GS: Gait speed, ASMM: Appendicular skeletal muscle mass, MMSE: Mini-mental state examination, FS: FRAIL scale, MNA: Mini nutritional assessment

Table 2. Correlation analysis between phase angle and components of sarcopenia and comprehensive geriatric assessments

	Overall		Men		Women	
	r	p	r	p	r	p
PhA x HGS¹	0.523	**<0.001**	0.312	**0.01**	0.255	**0.036**
PhA x HGS²	0.528	**<0.001**	0.372	**0.002**	0.281	**0.02**
PhA x ASMM	0.335	**<0.001**	0.618	**<0.001**	0.349	**0.004**
PhA x GS	0.165	0.05	0.133	0.282	0.224	0.066
PhA x CC	0.072	0.406	-0.064	0.605	0.213	0.08
PhA x WC	0.190	**0.027**	0.080	0.521	0.057	0.642
PhA x MAC	0.111	0.199	0.087	0.486	0.226	0.064
PhA x MMSE	-0.023	0.791	0.043	0.73	-0.085	0.492
PhA x FS	-0.117	0.176	0.091	0.463	-0.109	0.378
PhA x MNA	0.314	**<0.001**	0.328	**0.007**	0.163	0.185

Normally distributed and non-normally distributed parameters were analyzed using the Pearson and Spearman tests, respectively.
PhA: Phase angle, ASMM: Appendicular skeletal muscle mass, HGS: Handgrip strength, GS: Gait speed, HGS¹: Handgrip strength max using Jamar digital, HGS²: Handgrip strength max using Takei max, CC: Calf circumference, WC: Waist circumference, MAC: Mid-upper arm circumference, MMSE: Mini mental state examination, FS: FRAIL Scale, MNA: Mini nutritional assessment

associated with low PhA in overall and the male group (p>0.05). Only ASMM was significantly associated with low PhA in univariate and multivariate analysis in females. The results of the regression analyses of sarcopenia components associated with PhA in the female and male group are shown in Table 3.

Discussion

The aim of this study was to investigate the relationship between PhA, sarcopenia components, and comprehensive geriatric assessment in physically independent older adults. Correlation analysis revealed that PhA was correlated with all components of sarcopenia, except GS, in both sexes. The results of logistic regression analysis showed no significant relationship between low PhA and sarcopenia components in men, whereas low PhA was associated with ASMM in older women. In the comprehensive geriatric assessment, only the MNA score was correlated with and associated with PhA in the men's group. However, because no other associated factors were found, multivariate analysis could not be performed to assess the association between PhA and MNA score in men. In this study, PhA was positively correlated with HGS and ASMM in

Table 3. Logistic regression analysis of phase angle and components of sarcopenia according to gender

Variables	Low PhA					
	Univariate			Multivariate		
	OR	CI (95%)	p	OR	CI (95%)	p
Women						
HGS[1]	0.897	0.79-1.02	0.096	1.151	0.888-1.493	0.289
HGS[2]	0.823	0.697-0.972	**0.022**	0.751	0.553-1.021	0.067
ASMM	0.656	0.459-0.939	**0.021**	0.636	0.422-0.959	**0.031**
GS	0.305	0.028-3.382	0.333	0.124	0.004-3.934	0.237
Men						
HGS[1]	0.951	0.72-1.036	0.250	-	-	-
HGS[2]	0.932	0.844-1.030	0.166	-	-	-
ASMM	0.967	0.802-1.166	0.723	-	-	-
GS	0.326	0.036-2.957	0.319	-	-	-

PhA: Phase angle, ASMM: Appendicular skeletal muscle mass, HGS: Handgrip strength, GS: Gait speed, HGS[1]: Handgrip strength max using Jamar digital, HGS[2]: Handgrip strength max using Takei, CI: Confidence interval, OR: Odds ratio

all groups. The highest positive significant moderate correlation between PhA and ASMM was observed in males, whereas the highest significant positive correlation between PhA and HGS was observed overall. In contrast to our study, most studies did not separate men and women before the correlation analysis. A study conducted by Kilic et al. (25) on 263 older adults reported a positive correlation between PhA and MM. Similar to our study, Unterberger et al. (26) and Duarte Martins et al. (27) also demonstrated that HGS had a weak positive correlation with PhA overall. Unfortunately, the correlation between PhA and ASSM was not assessed in these two studies. In addition, the correlation results vary depending on the calculation formula and MM parameter used in the studies. Yamanaka et al. (28) determined MM estimated by their clinical formulas, which were not publicly available. They found that PhA was positively and moderately correlated with HGS, skeletal muscle mass (SMM), and GS (28). Do Nascimento et al. (29) have determined muscle mass index (MMI) adjusted by body surface and MM estimated by Sergi et al. (14) equation. They found that PhA had a weak positive correlation with SMMI in patients with Parkinson disease. Araújo et al. (30) have used MMI adjusted by height and MM estimated by Janssen et al. (31) formula, and they found a similar positive weak correlation between PhA and ASMMI (30). On the contrary, Pessoa et al. (16) used a similar adjustment and formula for calculating MMI and MM as Araujo et al (30) they found that PhA was not correlated with MM, MMI, and HGS. The main difference between these two studies is that Pesso et al. (16) only studied women, whereas Araujo et al. (30) studied both sexes. Most meta-analyses have shown a significant relationship between PhA and the different components of sarcopenia (6). In our study, sarcopenia components, such as HGS and ASMM, were found to be associated with low PhA in physically independent older women in the regression analysis. Studies on healthy older adults have yielded diverse outcomes. Most studies have focused on the association between PhA and the presence of sarcopenia, with statistically significant lower PhA values found in the presence of sarcopenia (25,32). In a cross-sectional study involving patients with cancer, the mean age was 60 years, and a 1-degree increase in PhA increased the predicted value of HGS evaluated using a Jamar hydraulic hand dynamometer by 8% (33). Unterberger et al. (26) and Duarte Martins et al. (27) evaluated the physical performance data of older adults, not separating men and women and found that PhA predicted HGS in multiple regression analysis. A recent study found that PhA predicted appendicular ASMMI, adjusted by height, ASMM estimated by Janssen et al. (31) formula in linear regression analysis (30). On the contrary, Pessoa et al. (16) have used similar adjustments and formulas for calculating MMI and MM, and they found that there were no associations between low PhA and any components of sarcopenia in older women in the multivariate logistic regression analysis. Unlike our study and similar studies, Pessoa et al. (16) included only older women. Additionally, we used the first tercile value to identify patients with low PhA, as the aim of the study was not only to detect sarcopenia. Most studies have performed receiver operating characteristic analysis to identify the cutoff values of PhA to identify sarcopenia, and they found lower PhA cutoff values than in our study (6). This may be one reason for the discrepancy between our results and those reported in the literature.

In the univariate analysis, HGS using Takei was associated with PhA, whereas HGS using Jamar digital was not. Recently, various instruments have been used to measure handgrip strength, and the results have varied. In general, previous studies have found a significant relationship between HGS assessed by the Jamar hydraulic dynamometer and PhA (27,34,35). A recent study using a Saehan hydraulic hand dynamometer to assess

HGS found no association between PhA and HGS (30). In another study investigating the relationship between PhA and muscle performance, there was no correlation between PhA and HGS measured using a Jamar handgrip dynamometer in older adults (36). With aging, MM loss accompanied by increased extracellular fluid levels leads to decreased PhA (2,37). Norman et al. (38) concluded that PhA decreases as fat mass increases in older people. In a study of patients with cancer with a mean age of 60.4±11.4 years, PhA decreased as the percentage of muscle fat infiltration increased, whereas GS and HGS did not change (39). A study of 207 older adults referred for comprehensive geriatric assessment by Basile et al. (40) found similar results. In light of these studies, PhA appeared to have a linear relationship with MM, independent of multiple factors such as age. Given that moderately low SMM is associated with shorter survival rates in older adults, PhA may be an inexpensive early marker for the detection of sarcopenia (27). In the literature, PhA has been found to be associated with various health outcomes, including nutritional, inflammation, and hydration status. The present study found that the MNA score was associated with PhA in men. Ramos da Silva et al. (41) showed that changes in nutritional risk index influenced PhA as a nutritional status marker in women with breast cancer undergoing chemotherapy. A similar relationship between subjective global assessment and PhA was shown in hemodialysis patients (42). In contrast, Unterberger et al. (26) found that PhA was not associated with protein intake in healthy older adults. The latest studies have shown that the combination of PhA and MNA-SF is predictive of sarcopenia, whereas PhA is predictive of malnutrition and oropharyngeal dysphagia (9,43,44). In this study, we found no significant association between PhA and frailty. This may be due to the fact that we included older adults with Katz scores of 6 were included in the study. However, the relationship between frailty and PhA has been demonstrated in many studies. PhA was lower in frail patients than in those with robust in community-dwelling older adults (8,45). A similar relationship between frailty and PhA was also observed in patients with cancer (39). Uemura et al. (32) followed up 4452 community-dwelling older adults for 24 months, and they found that only PhA was an independent predictor of incident disability in both sex groups in Cox regression analysis. It was also found that an increased PhA was positively associated with improved ADL during rehabilitation after osteoporotic fractures (46).

Study Limitations

There are a number of limitations to this study. First, there are no definitive data on patients at risk of sarcopenia due to comorbidities, such as COPD and diabetes. This makes it difficult to reach any concrete conclusions about them. Although multi-frequency BIA measurements were used in this study, only the PhA value at 50 kHz was used for statistical analyses. The differences in measurements between BIA devices from different manufacturers and the fact that these measurements vary depending on whether a single-frequency or other multi-frequency BIA device is used make it difficult to generalize the results. In addition to technology harmonization, cross-calibration of electrical resistances is also required to allow direct comparison of results from different studies and to facilitate the use of commonly accepted reference values. To gain a more complete understanding of the prognostic utility of PhA, analyzing PhA at different frequencies would be interesting in future studies. The cross-sectional study design is another limitation of this study. Due to the relatively small sample size, no clear causal relationship was established. Our study did not include a physical activity questionnaire. This may be a limitation if PhA is also related to physical activity.

Conclusion

Our study showed that PhA in physically independent older women was associated with components of sarcopenia, except GS, suggesting that PhA is reduced in sarcopenic individuals. Challenges such as the use of different formulas for calculating ASMM and various cutoff values for different ethnic groups can be barriers to ASMM assessment. PhA may be a simple predictor of ASMM in physically independent older women. Further studies are needed to determine whether PhA can be used as an additional parameter to detect poor muscle quality and to define sarcopenia.

Ethics

Ethics Committee Approval: The present study was approved by the Ethics Committee of Ege University Medical Research Ethics Committee (approval number: E41277, date: 07.02.2019).

Informed Consent: All recruited patients provided written informed consent.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.Ö.K.K., A.K., S.S., Concept: F.Ö.K.K., A.K., S.S., Design: A.K., S.S., Data Collection or Processing: F.Ö.K.K., A.K., S.Ç., Analysis or Interpretation: F.Ö.K.K., A.K., S.Ç., Literature Search: F.Ö.K.K., A.K., S.Ç., S.S., Writing: F.Ö.K.K., A.K., S.Ç., S.S.

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