ORIGINAL ARTICLE

Association of phase angle with sarcopenia in patients undergoing maintenance hemodialysis: A case–control study

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Background: Sarcopenia, characterized by reduced muscle strength and mass, is commonly observed in patients with kidney disease. This study aimed to investigate the factors that influence sarcopenia in patients undergoing maintenance hemodialysis (HD patients). **Materials and Methods:** A case–control study was conducted from 2022 to 2023, involving a total of 137 HD patients receiving regular dialysis. Relevant data were collected, and based on diagnostic criteria, patients were classified into sarcopenia and nonsarcopenia groups. All patients received polysulfone membrane HD at a flow rate of 500 mL/min. Bioelectrical impedance analysis was used to evaluate phase angle (PhA), muscle volume, and body composition. **Results:** The prevalence of sarcopenia among maintenance HD patients was found to be 40.14%. There was a higher proportion of women (76.36%) with sarcopenia compared to men ($P < 0.001$). Furthermore, a significant difference was observed in PhA ($P < 0.006$) between patients undergoing maintenance HD with and without sarcopenia. PhA was positively associated with body mass index, body cell mass, basal metabolic rate, fat-free mass, soft lean mass, and minerals, whereas age and skeletal muscle index showed an inverse significant correlation. **Conclusion:** Sarcopenia, a condition associated with increased mortality risk, affects a considerable proportion of dialysis patients. It is imperative to urgently identify and develop preventive and therapeutic strategies to counteract the detrimental effects of sarcopenia on the health outcomes of kidney patients.

Key words: Hemodialysis, kidney failure, sarcopenia, skeletal muscles

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INTRODUCTION

Sarcopenia, a condition characterized by a gradual loss of skeletal muscle mass (SMM) and function, primarily affects older adults and was first described by Rosenberg. It is a significant health issue in this population, increasing the risk of disability, falls, and injuries related to falls, hospitalization, loss of independence, and mortality.[1]

Both men and women are highly affected by sarcopenia as they age and the rate of prevalence increases rapidly. The consequences of sarcopenia are becoming more acknowledged, as it has been linked to physical disability in both genders regardless of other factors such as age, ethnicity, obesity, income, or health behavior.[2]

The prevalence of sarcopenia in middle- to old-aged adults has fluctuated significantly, ranging from 7% to over 50%, due to the absence of a universally agreed upon definition and measurement criteria.[3] Sarcopenia, a multifactorial disease,[4] is influenced by various factors. Some of these factors include decreased caloric intake,[5] fibrosis progression, changes in muscle metabolism, chronic inflammation, oxidative stress, and neuromuscular junction degeneration.[6]

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In kidney diseases, the term sarcopenia is commonly used, but referring to reduced muscle strength and reduced the muscle mass.[7]

There is a wide range of studies regarding the prevalence of sarcopenia in hemodialysis (HD) patients. This figure varies from 3.9% to 63.3%.[8]

HD is one of the most common treatments for patients with end-stage renal disease (ESRD). Approximately 84% of patients with ESRD ultimately receive maintenance HD treatment.[9]

Furthermore, studies have shown that patients with ESRD undergoing HD treatment are susceptible to sarcopenia due to chronic inflammatory status, metabolic acidosis, malnutrition, and decreased physical activity.[10] Essentially, sarcopenia has been diagnosed based on whether "muscle strength," "muscle quantity," and "physical performance" satisfy certain criteria. Although muscle mass remains the primary factor of muscle strength, studies have shown that muscle strength is only moderately correlated with muscle cross-sectional area and muscle thickness among living bodies.[11]

There are methods to indicate the muscle mass, for example, bioelectrical impedance analysis (BIA) has recently become quite a popular method for estimating body composition.

To determine body composition, BIA measures the human body's impedance (Z), which is the electrical opposition to the alternating current (AC) of the body composed of resistance (R) and reactance (Xc) represented by the following formula: $Z^2 = R^2 + Xc^2$.[12]

After substituting the obtained impedance values and participant height into the regression equations for each studied population, BIA can estimate lean body mass and body water content, among others.

Phase angle (PhA) is a variable obtained from bioelectrical impedance and is defined as the tangent of the PhA between resistance and reactance.[13] PhA, which is calculated using the arctangent value of the ratio of Xc to R, is independent of conventional regression equations for estimating body composition.[14] When an AC flows through the human body, healthy cell membranes function as capacitors that store electrical energy, consequently causing a delay in its flow. This lag in the current that penetrates cell membranes and tissue interfaces creates the phase difference between the current and voltage, which is expressed as the PhA.[15]

Research has shown that PhA is associated with age, gender, body mass index (BMI), lifestyle factors, and race in healthy individuals. It is also being studied as a potential marker for diagnosing sarcopenia, although its validity for predicting sarcopenia has not yet been evaluated.

Therefore, if PhA can be used as an indicator for the early identification of sarcopenia, it can be highly significant for improving the quality of life, reducing medical costs, and increasing hope for life in patients with ESRD undergoing HD treatment.

In our knowledge, no study has determined whether muscle quality and quantity are associated with PhA in HD patients. As such, the first aim of this study is to evaluate the association between PhA and muscle parameters and the second aim of this study is to determine the factors affecting the phase angle in patients with ESRD undergoing maintenance HD.

MATERIALS AND METHODS

Patients

In this case–control study, conducted from 2022 to 2023, a total of 137 patients with ESRD undergoing maintenance HD in three hemodialysis facilities in Tehran including Shahid Modarres, Aban, and Shahriar hospitals, were studied.

Patients with amputated limbs, patients with a pervious history of cognitive dysfunction, rheumatologic diseases, malignancies, or those unable to undergo BIA testing were excluded from this study. In addition, critically ill patients with severe edema were also not included in the study.

All patients were treated with polysulfone membrane HD at a flow rate of 500 mL/min. Standard bicarbonate HD was performed every time for 4 h, three sessions a week, with a blood flow rate of 250–300 mL/min. Unfractionated heparin was used for anticoagulation.

Bioelectrical impedance analysis

The patients' PhA, muscle volume, and body composition were assessed through BIA, utilizing the medical professional InBody S10 body water analyzer.

Sarcopenia is diagnosed when the skeletal muscle index (SMI) is below 7 kg/m^2 in men and below 5.70 kg/m^2 in women, indicating a decrease in muscle mass according to the diagnostic criteria established by the 2019 Asian Working Group.

The BIA measurement of dialysis patients was conducted by the same operator 30 min after their midweek HD session. All patients were assessed after fasting for at least 2 h.

All subjects were positioned lying down with their legs apart and arms not touching their torso. Disposable

electrodes were used, with one pair placed on the dorsum of the hand over the third metacarpophalangeal joint and the wrist, and another pair placed over the same side's third metatarsophalangeal and ankle joints. Recorded BIA-derived body components included fat mass (FM), fat-free mass (FFM), body cell mass (BCM), percent body fat (PBF), extracellular water (ECW), total body water (TBW), and PhA values.

ECW/TBW was calculated by dividing the ECW result by the TBW result.

PhA was calculated using the following equation: PhA (°) = Arctangent (reactance/resistance) × (180°/π).[16]

SMI was calculated according to the following formula: SMI (kg/m^2) = SMM (kg)/height.[17] Demographic information such as gender, level of education, duration of HD, nutritional status, and bioimpedance indices including PhA, SMM, BMI, and waist circumference index were collected from the patients' medical records.

After providing information on the aim of the study, all patients gave their informed consent.

Statistical analysis

The results were reported as mean ± standard deviation for quantitative variables. Meanwhile, categorical variables were summarized by absolute frequencies and percentages. To compare categorical variables, either the Chi-square test or Fisher's exact test was utilized in cases where more than 20% of cells had an expected count of <5.

Pearson correlation was used to determine the relationship between the quantitative variable and the PhA and the Student's t-test used for interdependent samples.

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) software version 18.0 for Windows (SPSS Inc., Chicago, IL, USA) was used. $P = 0.05$ or less was considered statistically significant.

RESULTS

Characteristics of participants

The average age was 60.77 ± 15.28 years (23.00–87 year); 46 (33.6%) were women. Of the 137 HD patients, 55 were diagnosed with sarcopenia, with a prevalence of 40.14% [Table 1].

In comparison to men, women were significantly more suffered from sarcopenia in patients undergoing maintenance HD (23.64% men vs. 76.36% women; Fisher's exact test, $P = 0.001$).

Furthermore, the study found that soft lean mass (SLM) ($P < 0.001$), FFM ($P < 0.001$), SMM ($P < 0.001$), TBW ($P < 0.001$), ECW ($P < 0.001$), body FM (BFM) ($P < 0.001$), PBF ($P < 0.001$), ECW/TBW ($P < 0.001$), TBW/FFM ($P < 0.008$), PhA ($P < 0.001$), protein ($P < 0.001$), and minerals ($P < 0.001$) were significantly different between the sarcopenia and nonsarcopenia groups. However, there was no significant difference in BMI ($P = 0.86$) between sarcopenics Vs non-sarcopenic patients. Further information regarding these findings is shown in Table 2.

A significant differences were found between the two genders in case of following parameters: BFM ($P < 0.001$), PBF ($P < 0.001$), FFM ($P < 0.001$), SMI ($P < 0.001$), SMM ($P < 0.001$), TBW ($P < 0.001$), ECW ($P < 0.001$), ICW ($P < 0.001$), PhA ($P < 0.001$), and protein ($P < 0.001$). The details of these findings are presented in Table 3.

The results indicated a positive significant association between PhA and FFM ($r = 0.45$, $P < 0.001$), SLM ($r = 0.43$, $P < 0.001$), and minerals ($r = 0.42$, $P < 0.001$). In addition, there is a negative significant association between age and PhA ($r = -0.55$, $P < 0.001$), as shown in Table 4.

Table 1: Baseline demographic and disease characteristics of the participants

Variable	Frequency (%)
Sex	
Male	91 (66.4)
Female	46 (33.6)
Age, mean±SD	60.77±15.28
BMI, mean±SD	24.96±4.91

BMI=Body mass index; SD=Standard deviation

Table 2: The differences between bioelectrical impedance analysis in the sarcopenia and nonsarcopenia groups

	Mean±SD		*t*	Mean difference	*P*
	Sarcopenia	Nonsarcopenia			
BMI	24.87±5.91	25.03±4.14	−0.186	−0.16	0.86
SLM	35.96±6.91	49.59±10.48	−9.17	−13.63	0.001
FFM	38.04±7.31	52.91±11.87	−9.06	−14.86	0.001
SMM	19.95±4.4	28.99±7.21	−9.09	−9.04	0.001
Phase angle	4.17±1.21	4.78±1.32	−2.72	−0.60	0.007
TBW	28.23±5.37	38.69±8.04	−9.11	−10.45	0.001
ECW	11.40±2.13	14.92±3.34	−7.51	−3.51	0.001
Protein	7.27±1.45	10.27±2.4	−9.08	−2.99	0.001
Minerals	2.54±0.55	3.96±2.45	−5.04	−1.41	0.001
BFM	27.63±12.72	21.22±10.01	3.29	6.41	0.001
PBF	40.42±12.47	28.18±11.58	5.87	6.41	0.001
TBW/FFM	74.22±0.48	73.36±2.82	2.69	0.85	0.008
ECW/TBW	0.40±0.01	0.39±0.4	3.26	0.01	0.001

BMI=Body mass index; SD=Standard deviation; SLM=Soft lean mass; FFM=Fat-free mass; SMM=Skeletal Muscle Mass; TBW=Total body water; ECW=Extracellular water; BFM=Body fat mass; PBF=Percent body fat

Binary logistic regression analysis revealed that age (odds ratio [OR] =0.09; 95% confidence interval [CI]: 0.97–1.05; $P < 0.68$), BMI (OR = 0.07; 95% CI: 0.95–31.21; $P < 0.23$), and PhA (OR = 0.47; 95% CI: 0.85–3. 03; $P < 0.14$) were not independent factors influencing sarcopenia.

DISCUSSION

Sarcopenia has recently regained attention as a concept that encompasses both low muscle mass and function. Despite numerous proposed methods and cutoff limits, it remains unclear which ones are more effective in identifying individuals at risk for adverse outcomes associated with sarcopenia, including reduced quality of life, frailty, and increased mortality rates.[18]

In contrast to the Asian Working Group diagnostic criteria for sarcopenia, which includes muscle mass (SMI), muscle strength (handgrip strength), and physical function (gait speed), we only assessed SMI for the diagnosis of sarcopenia in this study. Our findings revealed that a prevalence of sarcopenia is 40.14% with a higher frequency of women. In agreement with our study, As'habi *et al*.[19] showed that the prevalence of dynapenia (the presence of low muscle strength) was 43.0% in patient's peritoneal dialysis. In addition, Leal *et al*.,[20] in Brazil, reveal that the prevalence of low muscle strength was 55.8% in HD patients.

Our results showed that gender plays a significant role in the development of sarcopenia, with women being more likely to develop sarcopenia than men. In contrast, Pereira *et al*. showed that men are more likely to have sarcopenia.[21]

According to our results, age did not play a significant role in suffering from sarcopenia. Bataille *et al*. suggest that older patients are more likely to have sarcopenia.[22] Our results, along with those of As'habi *et al*., suggest that age and dialysis duration were not significant risk factors for sarcopenia.[19] This could be attributed to the fact that the study population had a higher percentage (10.9%) of individuals under 40 years old.

The analysis of our findings revealed that individuals with sarcopenia had a lower BMI in comparison to the nonsarcopenia group, although this difference was not statistically significant. In a study conducted by Souza *et al*., it was demonstrated that having a low BMI is also associated with sarcopenia.[23]

Our findings revealed significant differences in PhA between patients with sarcopenia and those without sarcopenia. The study conducted by Dos Reis *et al*.[24] included kidney transplant recipients and compared those in the first tertile of PhA with those in other tertiles. The results showed no significant differences in the prevalence of nonsevere sarcopenia or severe sarcopenia between the two groups. Furthermore, a multivariate logistic regression analysis

Table 3: The differences between gender and skeletal muscle index

	Women	Men	Overall average	*P*
Age	57.96±14.09	62.12±15.73	60.77±15.28	0.114
BMI	25.89±5.67	24.49±4.44	24.96±4.91	0.150
BFM	28.92±11.53	21.2±10.75	23.79±11.57	0.001
PBF	42.4±11.02	28.39±11.89	33.09±13.34	0.001
FFM	37.75±8.25	5.59±11.85	46.94±12.59	0.001
SMI	7.42±1.79	8.82±2.14	8.35±2.13	0.001
SMM	19.85±4.94	28.15±7.26	25.36±7.64	0.001
TBW	27.99±6.08	37.77±8.03	34.49±8.74	0.001
ECW	11.23±2.42	14.65±3.22	13.50±3.38	0.001
ICW	16.76±3.78	23.77±15.28	20.99±5.86	0.001
ECW/TBW	0.4±0.18	0.39±0.042	0.3941±0.036	0.066
Protein	7.24±1.63	9.99±2.41	9.07±2.53	0.001
Phase angle	4.28±1.22	4.66±1.33	4.53±1.31	0.09

[a]Student's *t*-test for independent samples. Data presented as mean±SD. SD=Standard deviation; SLM=Soft lean mass; FFM=Fat-free mass; SMM=Skeletal muscle mass; TBW=Total body water; ECW=Extracellular water; BFM=Body fat mass; PBF=Percent body fat; BMI=Body mass index

Table 4: Univariate analysis of age and skeletal muscle index in association with the phase angle

	Age	BFM	FFM	SLM	SMM	Minerals	Phase angle
Age	1						
BFM	*r*=−0.04 *P*<0.609	1					
FFM	*r*=−0.14 *P*<0.095	*r*=−0.19 *P*<0.021	1				
SLM	*R*=−0.14 *P*<0.09	*r*=−0.18 *P*<0.034	*r*=0.99 *P*<0.001	1			
SMM	*r*=−0.18 *P*<0.03	*r*=−0.16 *P*<0.048	*r*=0.99 *P*<0.001	*r*=0.98 *P*<0.001	1		
Minerals	*r*=−0.08 *P*<0.332	*r*=−0.21 *P*<0.011	*r*=0.71 *P*<0.001	*r*=0.62 *P*<0.001	*r*=0.72 *P*<0.001	1	
Phase angle	*r*=−0.55 *P*<0.001	*r*=0.14 *P*<0.1	*r*=0.45 *P*<0.001	*r*=0.43 *P*<0.001	*r*=0.52 *P*<0.001	*r*=0.42 *P*<0.001	1

SLM=Soft lean mass; FFM=Fat-free mass; SMM=Skeletal muscle mass; BFM=Body fat mass

showed that low PhA was not associated with a higher prevalence of sarcopenia after adjusting for potential confounders. In addition, the result of a systematic review conducted by Di Vincenzo *et al*.[25] showed that the prevalence of sarcopenia is higher in subjects/patients with low PhA and the results of the selected studies strongly suggest that PhA is decreased in sarcopenic subjects/patients.

The findings of our study indicated a significant correlation between BMI, BCM, BMR, FFM, SLM, minerals, age, SMI, and PhA. Previous research has suggested that PhA is associated with nutritional status, muscle strength, and mortality.[26,27] Di Vincenzo *et al*. have proposed that PhA can be utilized for detecting sarcopenia.[25] However, our study did not find any significant relationship in this regard. Tsuji *et al*.'s study on chronic musculoskeletal pain patients demonstrated that the relationship between PhA and sarcopenia is unclear, and whether PhA is effective in detecting sarcopenia remains uncertain.[28]

CONCLUSION

Sarcopenia, a clinical condition associated with a higher risk of mortality, affects a significant proportion of dialysis patients. We found a high prevalence of sarcopenia in patients with chronic HD. In this study, we demonstrated that age, BMI, BCM, FFM, SLM, and SMI were the significant factors related to PhA.

Future longitudinal studies are needed to improve management strategies and reduce health-care burdens on families and society. It is important to address the limitations of this study, such as the relatively low sample size and the fact that it was conducted in limited centers without a control group. In addition, the patients' nutritional status, muscle strength (hand grip strength), and physical function (gait speed) were not evaluated.

To combat the detrimental effects of sarcopenia on vital health outcomes in the kidney patients, there is an urgent need to identify and develop preventive and therapeutic strategies. Despite these limitations, we believe that our observations contribute to the understanding of sarcopenia and can stimulate further research on this topic.

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Conflicts of interest

There are no conflicts of interest.

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