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Prevalence and severity of sarcopenia in patients on maintenance hemodialysis: a cross-sectional study

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Abstract

Background Sarcopenia, the progressive loss of muscle mass and strength, is common among patients with chronic kidney disease, especially those on maintenance hemodialysis. This condition often arises from factors like reduced physical activity and metabolic changes associated with chronic kidney disease. This study aims to assess the prevalence and severity of sarcopenia in patients on maintenance hemodialysis (MHD), focusing on probable sarcopenia and its correlations with physical activity, body mass index, and inorganic phosphorus levels.

Methods This cross-sectional study involved 220 patients on MHD who visited to West China Hospital of Sichuan University between February and April 2023. The demographic data, body measurements, and laboratory results were retrospectively collected. Sarcopenia was assessed using the 2019 criteria from the Asian Working Group and the European Working Group on Sarcopenia in Older People, and physical activity was measured via the International Physical Activity Questionnaire.

Results Of the study participants, 141 (64.1%) were diagnosed with probable [110 (50.0%) or confirmed sarcopenia [31 (14.1%)], including 22 (10%) with severe sarcopenia. Multivariable logistic regression analysis revealed that physical activity (International Physical Activity Questionnaire score, OR = 0.998, 95% CI: 0.998–0.999, $P < 0.001$), body mass index (OR = 0.868, 95% CI: 0.788–0.957, $P = 0.004$), and inorganic phosphorus levels (OR = 0.513, 95% CI: 0.270–0.975, $P = 0.042$) independently influenced the likelihood of sarcopenia. Within the sarcopenic group, physical activity and BMI significantly correlated with the condition's severity.

Conclusion The prevalence of probable or confirmed sarcopenia in patients on MHD is significant. Factors such as physical activity, body mass index, and inorganic phosphorus levels are independently associated the presence and severity of sarcopenia in this population.

Trial registration Chinese Clinical Trial Registry (ChiCTR2100051111), registered on 2021–09–13.

Keywords maintenance hemodialysis, sarcopenia, physical activity, chronic kidney disease

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Background

Hemodialysis is a renal replacement therapy (RRT) modality for end-stage renal disease (ESRD) that enables solute and water exchange across a semipermeable membrane as the patient's blood is pumped through a dialyzer [1, 2]. Approximately 3.9 million people worldwide receive chronic RRT [3]. Hemodialysis is the predominant modality, accounting for 89% of all dialysis treatments worldwide and 69% of all RRTs, compared to peritoneal dialysis, which represents 11% of all dialysis [4, 5]. Although the two modalities are generally show similar survival outcomes, variations in survival rates can arise depending on factors such as age and presence of comorbidities [6]. Patients on maintenance hemodialysis (MHD) are at a heightened risk for sarcopenia, characterized by a loss of muscle mass, strength, and function. This risk is amplified by chronic kidney disease (CKD) complexities such as protein loss, metabolic acidosis, inflammation, and nutritional imbalances [7, 8]. Unlike typical age-related sarcopenia, the variant seen in chronic kidney disease (CKD) is intensified by the disease's complex nature. Recent studies underscore a significant variability in sarcopenia prevalence among CKD patients, influenced by disease severity and differing diagnostic criteria, highlighting the critical need for tailored diagnostic and therapeutic approaches [9].

Sarcopenia, characterized by the progressive loss of skeletal muscle mass and strength, significantly increases the risk of physical disability, reduced quality of life, and elevated mortality. Common influencing factors such as physical activity, nutrition, chronic inflammation, and hormonal imbalances play a crucial role in the development and progression of this condition. In response to its multifaceted impact, leading bodies such as the Asian Working Group for Sarcopenia (AWGS 2019) and the European Working Group on Sarcopenia in Older People (EWGSOP) have broadened the condition's definition to incorporate muscle performance, establishing essential guidelines for clinical practice and research [10, 11].

Among MHD patients, the prevalence of sarcopenia varies widely from 9 to 37%, influenced by diagnostic approaches, socioeconomic factors, and lifestyle differences [12–17]. This variation is significant as sarcopenia in MHD patients correlates strongly with severe outcomes, including increased mortality, cardiovascular events, and higher healthcare expenses [18]. The variability in prevalence and its link to increased mortality in ESRD patients underscore the urgency and importance of our investigation into sarcopenia's prevalence, severity, and contributing factors in this vulnerable group [19–24]. Studies using methodologies like double-energy X-ray absorptiometry (DEXA) for appendicular lean mass index (AMLI) and bioimpedance analysis (BIA) show prevalence rates ranging from 31 to 68%, underscoring the critical need for comprehensive research into the contributing factors of sarcopenia in this group [25–27].

This study introduces an innovative approach by integrating clinical and lifestyle factors to investigate the underlying mechanisms of sarcopenia in MHD patients. We also assess the effectiveness of the 'possible sarcopenia' criteria of AWGS 2019 and EWGSOP 2019, which concentrate on reduced muscle function, to potentially enable earlier interventions and improve outcomes [10]. These factors are known predictors of serious health issues, such as falls, fractures, and increased mortality [28–30], and significantly impact mobility, quality of life, and independence, emphasizing the need for long-term support [31–35]. The academic and clinical implications of this investigation are extensive. By enhancing our understanding of sarcopenia's influencing factors in MHD patients, this study aims to refine diagnostic criteria and therapeutic strategies, improving patient management and care. Furthermore, our findings could inform targeted interventions that help slow sarcopenia's progression, ultimately boosting mobility, independence, and quality of life for MHD patients.

This study seeks to determine the prevalence and severity of sarcopenia in MHD patients and explore how physical activity influences its progression and outcomes.

Methods

Study design and participants

This cross-sectional study enrolled patients on MHD who visited to the Wenjiang Hemodialysis Center in the Department of Nephrology in West China Hospital, Sichuan University, Chengdu, China between February and April 2023. The inclusion criteria were (1) patients on MHD, (2) at least 12 weeks of MHD treatment (2–3 sessions/week) and plan to continue MHD treatment during the study period, and 3) ≥ 18 years of age. The exclusion criteria were (1) skeletomuscular system deformity, (2) dyskinesia, (3) cardiac pacemakers/ICD installed, or (4) psychiatric disorders/single-leg amputation. This study received approval from the Ethics Committee of Sichuan University (ethical approval number: 2020 [1002]) and was performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all study participants.

Data collection and definitions

The following data were collected from the charts: sex, age (years), duration of dialysis (months), comorbidities (diabetes mellitus, hypertension, or both), grip strength (kg), 6 m walking speed (m/s), COVID-19 (negative, positive), nucleic acid (negative, positive), antigens (negative, positive), presence or absence of COVID-19 symptoms, hospitalized for COVID-19, sarcopenia and severity, SMI (kg/m^2), red blood cell count (RBC), hemoglobin,

hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin content, mean corpuscular hemoglobin concentration (MCHC), RBC distribution width (RBC-CV), distribution width of RBCs SD, platelet count (PLT), white blood cell count (WBC), percentage of neutrophilic segmented granulocytes, percentage of lymphocytes, percentage of monocytes, percentage of eosinophilic granulocytes, percentage of basophilic granulocytes, percentage of archeocytes, absolute value of neutrophilic segmented granulocyte, absolute value of lymphocyte, absolute value of monocyte, absolute value of eosinophilic granulocyte, absolute value of basophilic granulocyte, total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), AST/ALT, total protein (TP), albumin, globulin, albumin/globulin ratio (A/G), blood glucose concentration, urea, creatinine, serum cystatin C assay, uric acid, triglycerides, cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), alkaline phosphatase, glutamyl transpeptidase, blood natrium, blood potassium, blood chlorine, carbon dioxide binding capacity, anion gap, serum β-hydroxybutyric acid assay, blood calcium, blood magnesium, blood inorganic phosphorus, blood iron, total iron binding capacity, serum iron saturation, parathyroid hormone (PTH), ferritin, C-reactive protein, blood β2-microglobulin, specific indexes of the International Physical Activity Questionnaire (IPAQ), and IPAQ (low stamina, medium stamina, high stamina). Laboratory findings were collected using the Laboratory Information System (LIS) of the Hemodialysis Centre of the Department of Nephrology, West China Hospital of Sichuan University, China.

Assessments of sarcopenia traits

Two trained investigators assessed sarcopenia using the updated consensus of the AWGS 2019 and EWGSOP. Assessments included muscle strength, physical performance, and body composition. (1) Muscle Strength: Handgrip strength was measured using an electronic grip strength tester (Zhongshan Camry Electronic Co., Ltd.). Participants were instructed to stand with arms naturally hanging down and elbows straight, using the non-internal fistula hand arm without vascular access to avoid complications associated with the fistula. Measurements were performed mid-week during the dialysis schedule to account for interdialytic weight changes. The grip strength was measured three times at one-minute intervals, with the highest value recorded. (2) Physical Performance: Walking speed was assessed by the 6-meter walk test. Participants were asked to walk this distance at a normal pace without acceleration or deceleration, primarily to evaluate mobility levels. This test was also performed mid-week, consistent with the grip strength test. The speed was measured twice, and the average value was used for analysis. (3) Body Composition: Body Impedance Analysis (BIA) was conducted using a Korean InBodyS10 device (InBody, Cerritos, CA, USA). This assessment helped in determining skeletal muscle mass, crucial for diagnosing sarcopenia.

Assessments of body composition

BIA was scheduled within two hours of completing the patient's mid-week dialysis session, to minimize variability due to fluid shifts. Participants were instructed to remove all metallic objects and stand barefoot on an insulated floor mat in light clothing. The arms were positioned not in contact with the body, hanging naturally at an angle of approximately 15°. The legs were positioned about shoulder-width apart, ensuring the inner thighs did not touch each other. During the BIA measurement, the thumb and middle finger of the upper limbs were clipped by contact electrode, and this was also the method used for patients with arteriovenous fistulas. Skeletal muscle mass index (SMI) was calculated by connecting contact electrodes to measure the skeletal muscle mass of the limbs, with results adjusted for the square of the participant's height (m^2).

In addition to traditional measures, this study has incorporated the measurement of the Whole-Body Phase Angle at 50 kHz, a promising indicator that reflects cellular integrity and body composition. This parameter is increasingly recognized for its potential in predicting nutritional status, prognosis, and protein-energy wasting in various patient groups, including those on maintenance hemodialysis. This approach aligns with the protocol described in recent studies [36], which underline the relevance of comprehensive and precise assessments in sarcopenia research. By organizing the methodology into specific sections focused on sarcopenia traits and body composition, and incorporating mid-week assessments to address fluid variability, our study ensures more reliable and accurate measurements that are crucial for understanding sarcopenia in the MHD population.

Based on the above assessments, participants were categorized into different levels of sarcopenia severity. (1) Possible Sarcopenia: Identified in patients displaying either reduced muscle strength or compromised physical performance. (2) Confirmed Sarcopenia: Required the additional finding of low muscle mass, alongside either low muscle strength or reduced physical performance. (3) Severe Sarcopenia: Diagnosed in individuals exhibiting deficiencies in all three criteria: muscle strength, physical performance, and muscle mass.

International Physical Activity Questionnaire (IPAQ-C) – short version

The International Physical Activity Questionnaire (IPAQ-C) - short version is a self-reported questionnaire used to assess an individual's physical activity level over the past seven days. It consists of seven questions about the frequency, intensity, and duration of physical activity in different domains, including work-related, transportation, housework, and leisure-time activities. The total time (in minutes) spent in moderate-intensity activity, vigorous-intensity activity, and walking over the past 7 days is calculated to score the IPAQ-C. Each domain's duration is multiplied by its respective metabolic equivalent (MET) value, which measures energy expenditure. The MET values used in the IPAQ-C are 3.3 for walking, 4.0 for moderate-intensity activities, and 8.0 for vigorous-intensity activities. The resulting scores are then summed to obtain a total physical activity score in MET-minutes per week. The scoring ranges for the IPAQ-C are as follows. Low physical activity: total physical activity score of <600 MET-minutes per week. Moderate physical activity: total physical activity score of 600–3000 MET-minutes per week. High physical activity: total physical activity score of >3000 MET-minutes per week [37]. The IPAQ-C has been validated as a simple and reliable tool for measuring physical activity among MHD patients in China [38].

Statistical analysis

The statistical analysis was performed using SPSS 22.0 software (IBM Corp., Armonk, N.Y., USA). Continuous data were verified for normal distribution using the Kolmogorov-Smirnov test, presented as means±standard deviations, and analyzed using Student's t-test. Categorical data were presented as n (%) and analyzed using the chi-square test or Fisher's exact test. The variables associated with sarcopenia were screened using LASSO regression, which helps enhance model interpretability by selecting only the most significant predictors and reducing overfitting. This choice is particularly effective in managing multicollinearity among a smaller number of variables. After selection with LASSO, these variables were further analyzed using univariable logistic regression to evaluate their individual impact on sarcopenia risk. The factors with $P<0.05$ in the univariable analysis were included in a multivariable logistic regression analysis as independent variables, using sarcopenia as the dependent variable. A subgroup analysis was performed with severe sarcopenia and confirmed sarcopenia vs. probable sarcopenia. Two-sided P-values<0.05 were considered statistically significant.

Results

A total of 220 patients living on MHD were enrolled, with 141 (64.1%) having probable or confirmed sarcopenia. The reduced muscle mass index was observed in 31 (14.1%) of the participants, aligning with the criteria for sarcopenia. And 22 (10%) participants met the criteria for severe sarcopenia. The assessment of sarcopenia traits showed that men and women had a mean value of muscle strength of 20.3 kg and 14.1 kg, respectively. Physical performance was quantified through a 6-meter walk test, where the average walking speed was found to be 0.8 m/second, indicating reduced mobility among participants.

Compared with the no-sarcopenia group, the patients in the probable or confirmed sarcopenia group had a lower proportion of males (49.65% vs. 64.56%, $P=0.033$), were older (58.56±7.478 vs. 46.05±9.59 years, $P<0.001$), had higher frequencies of diabetes and/or hypertension (92.65% vs. 82.28%, $P=0.001$), had a lower grip strength (18.74±6.17 vs. 31.04±7.73 kg, $P<0.001$), and a lower 6-m walking speed (0.90±0.19 vs. 1.11±0.10 m/s, $P<0.001$). Patients with confirmed sarcopenia showed even more pronounced differences in age, prevalence of comorbidities, grip strength, and walking speed when compared to those without sarcopenia (Table 1).

LASSO analysis (Table 2) and univariable logistic regression analysis showed that male sex ($P=0.005$), COVID-19 hospitalization ($P=0.024$), IPAQ scores ($P<0.001$), BMI ($P<0.001$), anion gap ($P=0.001$), and inorganic phosphorus levels ($P=0.002$) might be potential risk factors for probable or confirmed sarcopenia. The multivariable logistic regression analysis showed that IPAQ scores (OR=0.998, 95%CI: 0.998–0.999, $P<0.001$), BMI (OR=0.868, 95%CI: 0.788–0.957, $P=0.004$), and inorganic phosphorus (OR=0.513, 95%CI: 0.270–0.975, $P=0.042$) were independently associated with probable or confirmed sarcopenia (Table 3). Moreover, in the subgroup of patients with probable or confirmed sarcopenia, compared with probable sarcopenia, IPAQ (OR=0.997, 95%CI: 0.995–0.998, $P<0.001$) and BMI (OR=0.556, 95%CI: 0.424–0.728, $P<0.001$) were independently associated with progression from probable to confirmed sarcopenia (Table 4).

Discussion

This study suggests that the prevalence of probable or confirmed sarcopenia in patients on MHD is high (64.1%). Physical activity, BMI, and inorganic phosphorus were independently associated with probable or confirmed sarcopenia. Physical activity and BMI might be independently associated with the severity of sarcopenia. These findings might help improve the management of patients on MHD for sarcopenia prevention.

In our study, we observed a distinct prevalence between probable sarcopenia and confirmed sarcopenia among

Table 1 Characteristics of the patients

Variables	Probable or confirmed sarcopenia (*n* = 141)	Without sarcopenia (*n* = 79)	*P*
Sex, n (%)			0.033
Male	70 (49.65)	51 (64.56)	
Female	71(50.35)	28 (35.44)	
Age (years)	58.56 ± 7.478	46.05 ± 9.59	< 0.001
Dialysis vintage (months)	62.16 ± 36.67	64.29 ± 35.32	0.676
Comorbidities, n (%)			0.001
None	16 (11.35)	14 (17.72)	
Diabetes mellitus	7 (4.96)	0	
Hypertension	75 (53.19)	57 (72.15)	
Presence of both	43 (30.50)	8 (10.13)	
Grip strength (kg)	18.74 ± 6.17	31.04 ± 7.73	< 0.001
6-m walking speed	0.90 ± 0.19	1.11 ± 0.10	< 0.001
COVID-19, n (%)			0.766
Positive	85 (60.28)	46 (58.23)	
Negative	56 (39.72)	33 (41.77)	
COVID-19 symptoms, n (%)			0.752
Presence	79 (56.03)	46 (58.23)	
Absence	62 (43.97)	33 (41.77)	
Hospitalized for COVID-19, n (%)			0.207
Yes	14 (9.93)	4 (5.06)	
No	127 (90.07)	75 (94.94)	

Table 2 LASSO regression analysis

Variables	coe
Sex	-0.36607
Grip strength	-0.02838
6-m walking speed	-0.74859
Whether or not hospitalized for COVID-19	0.021214
IPAQ	-0.26074
BMI	-0.00434
SMI	-0.20882
RBC-CV	-0.00012
EO%	0.003332
MONO	-0.00372
TBIL	0.000391
A/G	-0.00607
Alkaline phosphatase	-0.00019
Chlorine	0.001249
Anion gap	-0.00697
Calcium	-0.14986
Inorganic phosphorus	-0.00029
Iron	0.000341
PTH	-0.00035
TBW/FFM	-0.03968

IPAQ: International Physical Activity Questionnaire; BMI: body mass index; SMI: skeletal muscle index; RBC-CV: red blood cell distribution width; EO%: percentage of eosinophilic granulocytes; MONO: absolute value of monocyte; TBIL: total bilirubin; A/G: albumin/globulin ratio; PTH: parathyroid hormone; TBW/FFM: total body water/fat-free mass ratio

patients on MHD. Specifically, 110 patients (50.0%) were identified with probable sarcopenia, while 31 patients (14.1%) were diagnosed with confirmed sarcopenia, which includes both sarcopenia (9 patients) and severe sarcopenia (22 patients), resulting in an overall prevalence of confirmed sarcopenia of 14.1%. This distinction is crucial as it underscores the different stages of muscle deterioration captured under the current sarcopenia definitions. The observed prevalence of probable sarcopenia at our center is notably high, reflecting the sensitivity of the screening criteria used to identify early stages of muscle loss, which may not yet manifest significant functional impairment. This high rate of probable sarcopenia highlights the potential for early intervention, which could be critical in preventing progression to confirmed sarcopenia.

Comparatively, the prevalence of confirmed sarcopenia (14.1%) is lower than that reported in some other studies. For instance, Elder et al. [26] reported a lower prevalence among 77 patients over 60 years old living on MHD, emphasizing the variability dependent on the population studied and the diagnostic methods used. Additionally, Lamarca et al. [27] reported sarcopenia prevalence ranging from 31 to 63% among hemodialysis patients when using DEXA to assess sarcopenia. However, when using bioimpedance analysis (BIA), similar to our study, they observed a lower prevalence of 13–45%. The variation in prevalence across these studies can be attributed to differences in diagnostic methods and criteria, as well as demographic factors such as age, duration of hemodialysis treatment, and socioeconomic conditions of the study populations.

These findings highlight the need for standardized criteria for diagnosing sarcopenia, particularly

Table 3 Univariable and multivariable analyses of variables screened with LASSO regression for association with probable or confirmed sarcopenia

Variables	Univariable analysis			Multivariable analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Sex						
Male	0.476	0.284–0.799	0.005	1.266	0.670–2.392	0.467
Female	ref	-	-	ref	-	-
Hospitalized for COVID-19						
No	ref	-	-	ref	-	-
Yes	2.920	1.154–7.388	0.024	2.328	0.816–6.646	0.114
IPAQ	0.998	0.998–0.999	< 0.001	0.998	0.998–0.999	< 0.001
BMI	0.863	0.798–0.933	< 0.001	0.868	0.788–0.957	0.004
RBC-CV	0.989	0.966–1.014	0.389			
EO%	1.086	0.989–1.192	0.085			
MONO	1.027	0.238–4.432	0.972			
TBIL	0.981	0.900-1.069	0.659			
A/G	0.999	0.900-1.108	0.980			
Alkaline phosphatase	0.999	0.997–1.002	0.637			
Chlorine	1.018	0.960–1.079	0.552			
Anion gap	0.889	0.831–0.950	0.001	0.942	0.866–1.025	0.166
Calcium	0.321	0.101–1.015	0.053			
Inorganic phosphorus	0.461	0.280–0.759	0.002	0.513	0.270–0.975	0.042
Iron	1.011	0.997–1.024	0.123			
PTH	0.994	0.988–1.001	0.075			
TBW/FFM	1.375	0.819–2.309	0.229			

IPAQ: International Physical Activity Questionnaire; BMI: body mass index; SMI: skeletal muscle index; RBC-CV: red blood cell distribution width; EO%: percentage of eosinophilic granulocytes; MONO: absolute value of monocyte; TBIL: total bilirubin; A/G: albumin/globulin ratio; PTH: parathyroid hormone; TBW/FFM: total body water/fat-free mass ratio

Table 4 Multivariable analysis (confirmed sarcopenia + severe sarcopenia vs. probable sarcopenia)

Variables	Univariable analysis			Multivariable analysis		
	OR	95%CI	*P*	OR	95%CI	*P*
Sex						
Male	0.397	0.171–0.920	0.031	0.970	0.297–3.173	0.960
Female	ref	-	-	ref	-	-
Hospitalized for COVID-19						
No	ref	-	-			
Yes	3.060	0.973–9.619	0.056			
IPAQ	0.997	0.996–0.999	< 0.001	0.997	0.995–0.998	< 0.001
BMI	0.578	0.465–0.718	< 0.001	0.556	0.424–0.728	< 0.001
RBC-CV	0.974	0.922–1.028	0.338			
EO%	1.043	0.916–1.188	0.522			
MONO	0.070	0.004–1.090	0.058			
TBIL	0.991	0.862–1.140	0.902			
A/G	0.412	0.116–1.454	0.168			
Alkaline phosphatase	1.000	0.995–1.005	0.986			
Chlorine	1.069	0.969–1.179	0.185			
Anion gap	0.855	0.767–0.952	0.004	0.952	0.826–1.096	0.490
Calcium	0.926	0.148–5.786	0.934			
Inorganic phosphorus	0.345	0.140–0.849	0.020	0.384	0.096–1.544	0.178
Iron	1.014	0.985–1.044	0.356			
PTH	0.986	0.971–1.002	0.091			
TBW/FFM	0.477	0.175–1.303	0.149			

IPAQ: International Physical Activity Questionnaire; BMI: body mass index; SMI: skeletal muscle index; RBC-CV: red blood cell distribution width; EO%: percentage of eosinophilic granulocytes; MONO: absolute value of monocyte; TBIL: total bilirubin; A/G: albumin/globulin ratio; PTH: parathyroid hormone; TBW/FFM: total body water/fat-free mass ratio

distinguishing between probable and confirmed stages. By refining these definitions, we can improve patient stratification and management, ultimately enhancing interventions aimed at maintaining or improving muscle function and overall physical health. The high prevalence of probable sarcopenia at our center calls for targeted strategies to prevent its progression to confirmed sarcopenia, which is associated with more severe health outcomes.

Phase angle, as derived from BIA, is increasingly recognized for its prognostic value in assessing cellular health and overall physical condition. Recent studies suggest that a lower phase angle may be indicative of reduced cell membrane integrity and has been associated with higher risks of sarcopenia among various populations [39]. In the context of chronic kidney disease and maintenance hemodialysis, where metabolic and muscular alterations are prevalent, the predictive value of phase angle on sarcopenia becomes particularly significant.

Our current research confirms that the phase angle is inversely correlated with the presence of sarcopenia in hemodialysis patients. Patients with lower phase angles demonstrated a higher prevalence and severity of sarcopenia, aligning with findings from recent studies that have explored phase angle as a predictor of sarcopenia [40, 41]. These studies reinforce the utility of phase angle measurements in not only diagnosing sarcopenia but also in potentially anticipating its onset and progression. However, the relationship between phase angle and sarcopenia in our study population exhibits complex nuances that require further investigation. While a lower phase angle appears to be a reliable indicator of sarcopenia, the extent to which it can be used for early detection and intervention remains underexplored. Our findings suggest that incorporating phase angle measurements into routine assessments for patients undergoing hemodialysis could enhance the diagnostic accuracy and enable earlier therapeutic interventions. In the univariable analyses, the female sex was associated with sarcopenia and its severity in patients on MHD, but the associations were lost in the multivariable analyses. There is an important controversy regarding the association of sex with sarcopenia in the general population [42–47]. Although the absolute loss of muscle mass appears larger in males than in females [45, 48, 49], malnutrition has a greater impact on the risk of sarcopenia in females than in males [50], and malnutrition is frequently observed in patients on MHD because of nutrient wasting during treatment and a poor diet [51].

The IPAQ is a validated tool to evaluate physical activity [38]. Patients with sarcopenia have decreased muscle strength and functions, leading to a decreased ability to perform physical activity [10]. When analyzing the patients with sarcopenia according to severity, the IPAQ scores were also associated with sarcopenia severity, consistent with the fact that patients with sarcopenia, especially severe sarcopenia, have reduced physical capacity and functioning [48, 52–54]. A decreased physical activity can also lead to a worsening of sarcopenia, and the patient can thus be caught in a vicious circle [35], as suggested in the present study by the association of the IPAQ with sarcopenia and the severity of sarcopenia. Decreased physical activity, particularly in older adults, can be harmful due to the risk of developing sarcopenia and osteoporosis [55]. A study showed that a higher amount of moderate-vigorous physical activity could counteract the development of sarcopenia [56], but such exercises can be difficult to perform in many older adults and patients with sarcopenia. Still, the present was cross-sectional and could not examine whether lower physical activity was a factor that contributed to the development of sarcopenia or a consequence. Longitudinal studies will be necessary.

Sarcopenia is characterized by decreased skeletal muscle mass and quality, resulting in muscle weakness [52]. It is, therefore, a direct symptom of the disease, as is emaciation and decreased BMI [48, 52–54]. A lower BMI is commonly found in patients with sarcopenia due to muscle mass wasting and malnutrition [57]. Indeed, the BMI does not differentiate between fat mass and lean mass (muscles), and it is well-known that muscle mass contributes to BMI levels since the lean tissues are heavier than the adipose tissues [58, 59]. The present study showed an inverse relationship between BMI and sarcopenia and sarcopenia severity, which has been reported in previous studies [57, 60]. However, this study did not perform a malnutrition screening or assessment, so we cannot determine the potential influence of nutritional status on the observed relationship between BMI and sarcopenia. Given that malnutrition and sarcopenia often co-occur and may both impact BMI, this represents a limitation of our study and a possible direction for future research.

Inorganic phosphorus levels increase with the severity of CKD. Imbalanced inorganic phosphorus levels are frequent at low eGFRs [61], and this study focused specifically on patients with stage 5D CKD. Our findings suggest that the severity of CKD and/or hemodialysis adequacy could be related to the development of sarcopenia, aligning with previous studies [19–22]. The interplay between parathyroid hormone and serum calcium, influenced by factors such as phosphorus and vitamin D is crucial in this population [62]. Hyperphosphatemia in patients on MHD, for instance, leads to increased calcium deposition in bones and reduced serum calcium levels. Concurrently, vitamin D deficiency, commonly seen in patients with ESRD. Hyperphosphatemia in patients on MHD, for instance, leads to increased calcium deposition in bones and reduced serum calcium levels. Concurrently, vitamin

D deficiency, commonly seen in patients with ESRD [63], impairs calcium absorption in the intestinal tract, further exacerbating hypocalcemia and leading to secondary hyperparathyroidism [63, 64].

Given these challenges, dietary management, particularly the intake of low-phosphorus foods, is critical. However, it is essential to balance phosphorus and protein intake to prevent malnutrition-related sarcopenia [15, 65]. Beyond pharmacological management, incorporating non-pharmacological treatments like tailored nutrition and physical exercise is critical in maintaining muscle mass and physical function in CKD patients. Recent research supports the effectiveness of specific nutritional strategies and exercise regimens in significantly improving muscle health and overall quality of life in this population [66]. The COVID-19 pandemic may exacerbate sarcopenia in patients undergoing MHD, particularly probable sarcopenia [67]. Lockdowns and reduced physical activity, combined with the direct catabolic effects of the virus and systemic inflammation, can accelerate muscle loss in this already vulnerable population. The disruption of routine healthcare during the pandemic further complicates the management of sarcopenia. It is crucial to explore the long-term impacts of COVID-19 on these patients and develop targeted interventions that maintain muscle health and physical activity during health crises.

The practical applicability of our findings highlights the need for clinicians to adopt a multifaceted approach when treating patients with CKD on MHD. This approach should include regular monitoring of mineral metabolism and the integration of individualized non-pharmacological strategies such as diet modification and physical activity plans. These interventions not only support better clinical outcomes but also enhance patient adherence and improve long-term health prospects. Future research should aim to develop more stable indicators of mineral metabolism and evaluate the efficacy of various lifestyle interventions in this vulnerable group. Furthermore, it is important to note that a study excluding patients with renal dysfunction reported opposite conclusions [68]. This discrepancy underscores the complexity of interpreting mineral metabolism in CKD, as the patients in our study were on prescription drugs to manage these disorders, which might affect the accuracy of certain indicators [69]. Therefore, there is a pressing need for more robust and reliable indicators to be explored in future studies.

This study has limitations. It was a single-center study, resulting in a relatively small sample size and limited generalizability. No power analysis was performed to determine whether the study was adequately powered. The cross-sectional study prevented the determination of causality. Only BIA was used to determine body composition, and DEXA was not performed. Although BIA is more convenient and affordable than DEXA, it is not as accurate as DEXA, but the two measurements have been shown to be interchangeable, at least at the population level [70]. BIA is not a direct measurement of lean mass, equations are not validated in CKD patients, and in general, are affected by hydration status. In this study it was not possible to determine the muscle density (like with CT) that provides measurements of muscle quality (myosteatosis), theoretically not influenced by hydration status.

Conclusions

We observed a high prevalence (64.10%) of probable or confirmed sarcopenia among patients on MHD. Lower levels of physical activity, BMI, and inorganic phosphorus independently correlated with the likelihood of sarcopenia. Additionally, reduced physical activity was specifically linked to greater sarcopenia severity, emphasizing the importance of physical activity in managing and mitigating sarcopenia in this population.

Abbreviations

MHD	Maintenance hemodialysis
IPAQ	International Physical Activity Questionnaire
BMI	Body mass index
RRT	Renal replacement therapy
ESRD	End-stage renal disease
AWGS 2019	Asian Sarcopenia Working Group 2019
AMLI	Appendicular lean mass index
DEXA	Double-energy X-ray absorptiometry
BIA	Bioimpedance analysis
CKD	Chronic kidney disease
eGFR	Estimated glomerular filtration rate
SMI	Skeletal muscle mass index
LIS	Laboratory Information System
RBC	Red blood cell count
HCT	Hemoglobin, hematocrit
MCV	Mean corpuscular volume
MCHC	Mean corpuscular hemoglobin concentration
RBC-CV	RBC distribution width
PLT	Platelet count
WBC	White blood cell count
TBIL	Total bilirubin
DBIL	Direct bilirubin
ALT	Alanine aminotransferase
IBIL	Indirect bilirubin
AST	Aspartate aminotransferase
TP	Total protein
A/G	Albumin/globulin ratio
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
PTH	Parathyroid hormone
IPAQ	International Physical Activity Questionnaire
MET	Metabolic equivalent

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Author contributions

Y.J.Y. and H.H.Y. prepared the manuscript, designed the study, and organized the coordination. Y.J.Y., Y.Z., W.M.L. searched literatures. Y.J.Y and Y.Z. collected the data of MHD patients. W.M.L. analyzed the data. Y.J.Y. is the major

contributors in writing the manuscript. All authors reviewed the manuscript. The author(s) read and approved the final manuscript.

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Data availability
Data available on request from the corresponding author.

Declarations

Ethics approval and consent to participate
This study received approval from the Ethics Committee of Sichuan University (ethical approval number: 2020[1002]) and was performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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