Original Article

Prevalence and Factors Associated with Sarcopenia in Chronic Kidney Disease Patients Undergoing Dialysis: a Single Center, Cross-sectional Study

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ABSTRACT

Background: Sarcopenia is associated with worse outcomes in stage 5 Chronic Kidney Disease on dialysis (CKD 5D) patients, influenced by various diagnostic criteria and patient characteristics. Nonetheless, the factors contributing to sarcopenia in CKD 5D remain underexplored.
Objective: To investigate the prevalence and factors associated with sarcopenia in the CKD 5D population.
Methods: An observational cross-sectional study was conducted on 132 CKD 5D patients (≥18 years old, dialysis ≥ 3 months) at Hasan Sadikin Hospital from July to August 2024. Descriptive statistics, bivariate analysis, and logistic regression were utilized to determine the prevalence of sarcopenia and its association with the Simplify Creatinine Index (SCI), physical activity, nutritional status, phosphate, and calcium serum levels. Hand Grip Strength (HGS) assessed muscle strength, Bioelectrical Impedance Spectroscopy (BIS) measured muscle mass, the 6-meter walk test evaluated physical performance, and the Asian Working Group for Sarcopenia (AWGS) 2019 criteria were employed for diagnosing sarcopenia.
Results: Sarcopenia prevalence was 15.9%. Bivariate analysis revealed significant correlations with underweight (p=0.014), malnutrition (p=0.041), phosphate serum level (p=0.047), and calcium serum level (p=0.043). Logistic regression indicated that higher serum levels of calcium and phosphate and healthy nutritional status, served as protective factors against sarcopenia, with odds ratios of 0.677 (OR 0.677; CI 95% 0.493-0.93 and OR 0.313; CI 95% 0.130-0.755).
Conclusion: Sarcopenia prevalence was 15.9%. Phosphate and calcium serum levels, underweight, and malnutrition were significantly correlated with sarcopenia. Higher serum phosphate and calcium levels, higher body weight, and good nutrition status were protective factors against sarcopenia in CKD 5D patients.
Keywords: Sarcopenia, CKD 5D, AWGS 2019.

Introduction

Sarcopenia, a condition linked to aging, is defined by a reduction in muscle mass along with a deterioration in muscle function and/or physical performance.[1] In patients with chronic kidney disease (CKD), the prevalence of sarcopenia varies from 4% to 68%, with an average of 37% found in dialysis patients.[2] The Asian Working Group for Sarcopenia (AWGS) in 2019 established criteria for diagnosing sarcopenia. When diagnosing sarcopenia, three factors are evaluated: physical performance, muscle strength, and appendicular skeletal muscle mass (ASM).[3]

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Patients with CKD, particularly those receiving hemodialysis, frequently experience muscle mass loss.[4] The effects of reduced muscle mass extend beyond the physical limitations that are commonly observed in the elderly.[5] Numerous studies have demonstrated a link between CKD patients' loss of muscle mass and protein-energy wasting (PEW). This condition is associated with an elevated risk of fractures, cardiovascular problems, a decline in quality of life, depression, increased hospitalization rates, and mortality risk.[6]

Uremic sarcopenia is the term used to describe sarcopenia in CKD. Chronic inflammation, insulin resistance, low physical activity, oxidative stress, hormonal imbalances, malnutrition, vitamin D deficiency, and negative protein balance brought on by prolonged uremic conditions are some of the factors that lead to the development of uremic sarcopenia.[7,8] Sarcopenia in CKD can occur early in adulthood and can worsen quickly because of a poor protein-energy balance. This is caused by inadequate nutritional intake combined with uremia patients' elevated protein catabolism, which is made worse by the catabolic effects of hemodialysis procedures.[9]

In Indonesia, there have not been many studies on sarcopenia in CKD patients receiving maintenance hemodialysis. The purpose of this study is to ascertain the prevalence of sarcopenia and the risk factors for it in stage 5 CKD on dialysis (CKD 5D) patients at Hasan Sadikin Hospital Bandung.

Methods

Design and participants

This cross-sectional, analytical observational study was conducted in July and August of 2024 at the Hasan Sadikin Hospital Bandung Hemodialysis Unit to evaluate sarcopenia-related factors in patients receiving maintenance hemodialysis. Consecutive sampling was used to collect samples. Age > 18 and having received routine hemodialysis twice a week for at least three months were prerequisites for inclusion. Exclusion criteria were subjects with impaired consciousness, unable to stand, walk and grip hands, subjects with amputated extremities, or refused to participate in the study. The total sample in this study was 132 subjects. This study has received approval from The Hasan Sadikin Hospital Bandung Research Ethics Committee under reference number DP.04.03/D.XIV.6.5/317/2024.

Study covariates

Data on baseline characteristics, including age, gender, hemodialysis vintage, history of diabetes mellitus, and hypertension, were extracted from medical records. Nutritional status was evaluated using the Malnutrition Inflammation Score (MIS), while physical activity was assessed through the Indonesian version of the International Physical Activity Questionnaire (IPAQ). Hemodialysis adequacy was assessed based on the Kt/V, while the simplified creatinine index (SCI) was computed based on the Canaud formula.

In this study, sarcopenia was diagnosed based on the Asian Working Group for Sarcopenia (AWGS) 2019 criteria.[3] The evaluations included physical performance, appendicular skeletal muscle mass (ASM), and muscle strength. A Camry EH101 hand dynamometer was employed to measure muscle strength by handgrip strength. The measurement of ASM was conducted using Tanita MC-780 bioelectrical impedance analysis (BIA). The 6-meter walk test was utilized to evaluate physical performance. Sarcopenia was defined as a decline in ASM along with a reduction in muscle strength and/or physical performance.[3]

Statistical analysis

The basic characteristics of the subjects were described by univariate analysis. Normality test was performed using bivariate analysis with chi-square test, Mann-Whitney, and t-test. Serum phosphate, serum calcium, physical activity, SCI, and MIS were all examined in relation to sarcopenia using multivariate analysis and logistic regression. Significance was determined when $p < 0.05$ and for independent variables with $p < 0.25$, logistic regression analysis was continued.

Results

Patient selection

The total subjects at the beginning of the study was 195. There were 16 subjects excluded from the study and 47 subjects who entered the exclusion criteria. The flow diagram of subject-selection process can be seen in Figure 1.

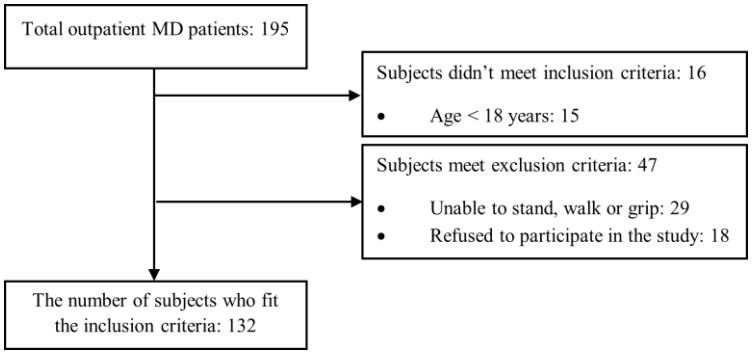

Figure 1. Flow diagram of subject-selection process

In this study, 15.9% of subjects had sarcopenia. Table 1 displays the basic characteristics of the study subjects. The mean age of the subjects was 47.5 years, with age distribution including elderly (13.6%), pre-elderly (47%), and adult (39.4%). Most subjects were male (54.5%), with a median hemodialysis duration of 34 months. Most subjects had a normal body mass index (22.7 kg/m^2). In terms of physical activity, the majority of subjects had a moderate level of activity (45.5%), while low and high activity were 27.3% respectively. Hemodialysis adequacy, measured by Kt/V, had an average of 1.7, with 57.6% of subjects in the poor adequacy category. About 45.5% of subjects showed signs of malnutrition based on MIS, and the majority of female patients had lower ASM and handgrip strength compared to males.

Table 1. Characteristics of the subject

Variables	N=132 n (%)
Age (year), Mean ± SD	47.5 ± 12.6
Age category, n (%)	
Elderly (≥60 year)	18 (13.6)
Pre-elderly (45-59 year)	62 (47)
Adult (18-44 year)	52 (39.4)
Sex, n (%)	
Male	72 (54.5)
Female	60 (45.5)
Dialysis periods (month), Median (IQR)	34.0 (19.0 – 62.5)
Body mass index (kg/m^2), Mean ± SD	22.7 ± 4.3
IPAQ-SF	
Low activity	36 (27.3)
Moderate activity	60 (45.5)
High activity	36 (27.3)
Laboratory	
Albumin serum (g/dL), Median (IQR)	3.9 (3.7 – 4.1)
Creatinine serum (µmol/L), Mean ± SD	13.0 ± 3.4

Table 1 (cont.)	
Ion calcium (mmol/L), Median (IQR)	4.3 (4.0 – 4.5)
Phosphate serum (mg/dL), Mean ± SD	5.1 ± 1.8
SCI (mg/kg/day), Mean ± SD	24.2 ± 3.2
Hypertension, n (%)	
Yes	59 (44.7)
No	73 (55.3)
Diabetes Melitus, n (%)	
Yes	15 (11.4)
No	117 (88.6)
Single Pool (Sp) Kt/V, Mean ± SD	1.7 ± 0.3
Hemodialysis adequacy, n (%)	
Good (≥1,8)	56 (42.4)
Poor (<1,8)	76 (57.6)
MIS, Median (IQR)	5.0 (3.0 – 7.0)
MIS criteria, n (%)	
Malnutrition (> 5)	60 (45.5)
Normal (≤ 5)	72 (54.5)
ASM (kg/m2), Mean ± SD	
Male	8.0 ± 1.4
Female	6.7 ± 1.1
Hand grip strength (kg), Mean ± SD	
Male	26.5 ± 10.3
Female	16.2 ± 5.8

Note, data were presented in mean ± SD; n, frequency; %, percentage; SD, *Standard Deviation*; IQR, *Inter Quartile Range*; SCI, simplified creatinine index; MIS, malnutrition inflammation score; ASM, appendicular skeletal muscle mass; IPAQ-SF, international physical activity questionnaire short form

Furthermore, the factors in Table 2 linked to sarcopenia in CKD 5D patients were subjected to bivariate analysis. Age category and sarcopenia are significantly correlated (p=0.016). The elderly (≥60 years old) had more sarcopenia (33.3%) than other age groups. Subjects with sarcopenia had significantly lower BMI than non-sarcopenia (18.9 vs 23.5 kg/m², p<0.001), suggesting a strong correlation between sarcopenia and low BMI.

Table 2. Bivariate analysis of factors associated with sarcopenia in CKD 5D patients

Variables	**Sarcopenia n=21**	**Non-sarcopenia n=111**	**p**
Age (year), Mean ± SD	51.8 ± 16.2	46.7 ± 11.7	0.182[a]
Age category, n (%)			0.016[c]*
Elderly (≥60 year)	7 (33.3)	11 (9.9)	
Pre-elderly (45-59 year)	8 (38.1)	54 (48.6)	
Adult (18-44 year)	6 (28.6)	46 (41.4)	
Sex, n (%)			0.460[c]
Male	13 (61.9)	59 (53.2)	
Female	8 (38.1)	52 (46.8)	
Dialysis periods(month),median IQR	30.0 (9.0 – 73.5)	34.0 (22.0 – 61.0)	0.325[b]
Body mass index (kg/m²), Mean ± SD	18.9 ± 2.5	23.5 ± 4.1	<0.001[a]*
IPAQ-SF, n (%)			0.137[c]
Low activity	7 (33.3)	29 (26.1)	
Moderate activity	12 (57.1)	48 (43.2)	
High activity	2 (9.5)	34 (30.6)	
Laboratory			

Albumin (g/dL), Median (IQR)	3.9 (3.5 – 4.1)	3.9 (3.7 – 4.1)	0.431[b]
Creatinine (µmol/L), Mean ± SD	12.2 ± 3.9	13.2 ± 3.3	0.245[a]
Ion calcium (mmol/L), Median	4.1 (3.6 – 4.4)	4.3 (4.1 – 4.5)	0.115[b]
Phosphate (mg/dL), Mean ± SD	4.5 ± 2.1	5.2 ± 1.7	0.086[a]
SCI (mg/kg/day), Mean ± SD	23.4 ± 3.6	24.4 ± 3.1	0.204[a]
Hypertension, n (%)			0.507[c]
Yes	8 (38.1)	51 (45.9)	
No	13 (61.9)	60 (54.1)	
Diabetes Melitus, n (%)			0.259[d]
Yes	4 (19)	11 (9.9)	
No	17 (81)	100 (90.1)	
Single Pool (Sp) Kt/V, Mean ± SD	1.8 ± 0.3	1.7 ± 0.3	0.253[a]
Hemodialysis adequacy, n (%)			0.599[c]
Good (≥1,8)	10 (47.6)	46 (41.4)	
Bad (<1,8)	11 (52.4)	65 (58.6)	
MIS, Median (IQR)	6.0 (4.5 – 8.0)	5.0 (3.0 – 6.0)	0.016[b]*
MIS criteria, n (%)			0.009[c]*
Malnutrition (> 5)	15 (71.4)	45 (40.5)	
Normal (≤ 5)	6 (28.6)	66 (59.5)	
ASM (kg/m2), Mean ± SD			
Male	6.4 ± 0.3	8.4 ± 1.3	<0.001[a]*
Female	5.4 ± 0.3	6.9 ± 1.0	<0.001[a]*
Hand grip strength (kg), Mean ± SD			
Male	15.9 ± 4.6	28.8 ± 9.8	<0.001[a]*
Female	12.8 ± 6.3	16.7 ± 5.7	0.083[a]

Note, data were presented in mean ± SD; n, frequency; %, percentage; SD, *Standard Deviation*; IQR, *Inter Quartile Range*; SCI, simplified creatinine index; MIS, malnutrition inflammation score; ASM, appendicular skeletal muscle mass; IPAQ-SF, international physical activity questionnaire short form; CKD 5D, stage 5 Chronic Kidney Disease on dialysis. Analysed with [a]Unpaired t-test, [b]Mann-Whitney, [c]Chi Square, [d]Fisher Exact

Sarcopenia was significantly associated with malnutrition, with 71.4% of subjects with sarcopenia being malnourished compared to 40.5% in the non-sarcopenia group (p=0.009). Subjects with sarcopenia had lower ASM in both males (6.4 vs 8.4 kg/m², p<0.001) and females (5.4 vs 6.9 kg/m², p<0.001). Hand grip strength was also lower in subjects with sarcopenia, especially in males (15.9 vs 28.8 kg, p<0.001). Several other factors, such as gender, dialysis period, physical activity, and laboratory parameters, showed no significant association with sarcopenia. Overall, sarcopenia in CKD 5D patients was more common in older age, lower BMI, malnutrition, and lower muscle mass and hand grip strength.

Multivariate analysis, as listed in Table 3, showed a number of important variables linked to a higher risk of sarcopenia in CKD 5D patients. Elderly patients (≥60 years) had a 27 times greater risk of developing sarcopenia compared to adult patients (18-44 years) (AOR 27.230; 95% CI 2.573-288.144; p=0.006). The pre-elderly group (45-59 years) showed no significant risk for sarcopenia (AOR 2.317; p=0.318).

Table 3. Multivariate analysis of factors associated with sarcopenia in CKD 5D patients

Variable	AOR (95% CI)	p
Age category, n (%)		
Elderly (≥60 year)	27.230 (2.573 – 288.144)	0.006*
Pre-elderly (45-59 year)	2.317 (0.445 – 12.078)	0.318
Adult (18-44 year)	1 (ref)	
BMI category		
Underweight (< 18,5 kg/m²)	5.876 (1.44 – 23.981)	0.014*
Not Underweight (≥18,5 kg/m²)	1 (ref)	
IPAQ-SF, n (%)		
Low activity	2.096 (0.308 – 14.262)	0.449
Moderate activity	3.776 (0.642 – 22.214)	0.142
High activity	1 (ref)	
Laboratory		
Creatinine (g/dL)	0.819 (0.382 – 1.753)	0.606
Ion calcium (µmol/L)	0.375 (0.145 – 0.969)	0.043*
Phosphate (mmol/L)	0.655 (0.432 – 0.994)	0.047*
SCI (mg/kg/day)	1.581 (0.656 – 3.811)	0.307
MIS criteria, n (%)		
Malnutrition (> 5)	3.603 (1.055 – 12.307)	0.041*
Normal (≤ 5)	1 (ref)	

Note, SCI, simplified creatinine index; MIS, malnutrition inflammation score; IPAQ-SF, international physical activity questionnaire short form; CKD 5D, stage 5 Chronic Kidney Disease on dialysis.

Subjects with underweight status (BMI < 18.5 kg/m2) had almost 6 times greater risk of developing sarcopenia compared to patients with normal or higher BMI (AOR 5.876; 95% CI 1.44-23.981; p=0.014). Each one-unit decrease in calcium levels was correlated with a 62.5% increased risk of sarcopenia (AOR 0.375; 95% CI 0.145-0.969; p=0.043), and a one-unit decrease in phosphate levels was correlated with a 34.5% increased risk of sarcopenia (AOR 0.655; 95% CI 0.432-0.994; p=0.047). Subjects with Malnutrition Inflammation Score (MIS) indicating malnutrition (MIS > 5) had a 3.6 times greater risk of developing sarcopenia compared to patients with normal nutritional status (AOR 3.603; 95% CI 1.055-12.307; p=0.041).

Factors such as physical activity, creatinine serum, and SCI did not show a significant correlation with sarcopenia based on multivariate analysis results. Overall, CKD 5D patients were much more likely to develop sarcopenia if they were older, underweight, malnourished, or had low calcium and phosphate levels.

Discussion

Patients with CKD, particularly those receiving hemodialysis, frequently experience a decrease in muscle mass. Numerous diagnostic criteria and patient characteristics significantly influenced the prevalence of sarcopenia. According to several studies, 4-68% of CKD patients have sarcopenia.[3] The prevalence of sarcopenia in this study was 15.9%. Increased protein degradation and decreased protein synthesis are two categories of etiological factors contributing to muscle loss in CKD 5D patients. Lack of protein consumption and calories, insulin resistance, inflammation, metabolic acidosis, oxidative stress, and vitamin D deficiency are all factors linked to increased protein degradation. Reduced regeneration stimuli, aging, hormonal imbalances, and the loss of proteins and amino acids during dialysis are some of the factors that lead to decreased protein synthesis.[3,10,11]

Patients with chronic kidney disease also frequently have problems with muscle regeneration. This is supported by reduced expression of myogenic regulatory factors and cell activation, which are negative regulators of

skeletal muscle mass. Chronic inflammation, oxidative stress, uremic toxin accumulation, elevated ubiquitination, vitamin D deficiency, and malnutrition also contribute to increased catabolism in CKD.[8]

There is a correlation between phosphate and muscle function. High phosphate concentrations in CKD patients were connected to a greater likelihood of cardiovascular complications and mortality. Therefore, lowering serum phosphate levels is the goal of pharmacotherapeutic and dietary interventions.[12,13] However, a study by Block et al. discovered that at lower serum phosphate concentrations (<4.0 mg/dL), the relative risk of death increased significantly.[14] This study's multivariate analysis showed a strong correlation between sarcopenia and low phosphate levels. This is consistent with study by Jauwerissa et al.[15] conducted in Jakarta, Indonesia on 96 maintenance hemodialysis patiens. This study also in line with the findings of research conducted by Umakanthan et al.[16], Ren et al.[17] and Cai et al.[18] The results of these studies indicated that uremic syndrome patients typically experience anorexia or loss of appetite, and high-protein diets contain high levels of phosphate. A decrease in energy and protein intake led to a reduction in serum phosphate levels, which can result in sarcopenia, protein catabolic disorders, and malnutrition. Hypophosphatemia in sarcopenia is explained by the fact that inorganic phosphate is also involved in cell membranes, energy production, and signal transduction in every cell in the body.[16–19]

According to this study, underweight and malnutrition are significantly linked to sarcopenia. Most sarcopenic subjects (71.4%) had a lower BMI than non-sarcopenic subjects and were malnourished (MIS>5). According to the study by Vettoretti et al., the sarcopenia group in CKD 3b-5 patients had a higher MIS (6.6±6.5 vs. 4.5±4.0) and a lower BMI (24.8±3.0 vs. 28.4±5.5Kg/m2).[20] Macedo et al. discovered that aged patients receiving routine hemodialysis who had sarcopenia had 66.7% malnutrition, according to the subjective global assessment (SGA) tool. The study found that older hemo-dialysis patients with sarcopenia and malnutrition had diminished nutritional status, experienced lower quality of life, and they are also at a higher risk of dying.[21]

Conclusion

At Hasan Sadikin Hospital in Bandung, 15.9% of CKD 5D patients had sarcopenia. In this study, low body weight, malnutrition, advanced age, and low serum phosphate and calcium levels were all significantly linked to sarcopenia. However, there was no discernible correlation between sarcopenia and IKD or physical activity level. Higher body weight, better nutritional status, and elevated serum phosphate and calcium levels are protective factors against sarcopenia in CKD 5D patients, according to multivariate analysis. These results imply that sarcopenia in CKD 5D patients can be avoided by improving nutritional status and that early detection of sarcopenia is crucial.

Limitations of the Study

One of the limitations of this research was its cross-sectional design, which constrained the capacity to make causal inferences, and the potential for selection bias due to the specific hospital setting.

Declarations

Ethics approval and consent to participate

This study received approval from the Ethics Committee of the Hasan Sadikin Hospital Bandung under reference number DP.04.03/D.XIV.6.5/317/2024.

Competing interests

There are no conflicts of interest in writing this article.

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Author's Contribution

Idea/concept: FR. Design: FR. Control/supervision: RB, RS, LD. Data collection/processing: FR. Analysis/interpretation: FR, RB, RS, LD. Literature review: -. Writing the article: FR. Critical review: -. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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