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## **Original Article**

## A Study of Factors Affecting Sarcopenia in Outpatients on Dialysis: Comparison with General Outpatients from a Multidimensional Viewpoint



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**Abstract:** [Purpose] This study investigates and compares risk factors for sarcopenia in dialysis patients and among older outpatients attending a cardiology clinic. [Subjects and Methods] A cross-sectional design was utilized, including 24 patients undergoing dialysis treatment and a control group. Participants were stratified into sarcopenia and non-sarcopenia groups for comparative analysis. [Results] Significant differences were identified in lifestyles and musculoskeletal functions based on the basic checklist (p < 0.05). Logistic regression analysis highlighted red blood cell (RBC) count (odds ratio: 1.13, 95% CI: 1.02– 1.15, p < 0.05) as a significant variable within the dialysis group. [Conclusion] These findings underscore the need for targeted interventions to mitigate sarcopenia and frailty, emphasizing the enhancement of daily functional activities and promotion of social participation among dialysis patients to improve quality of life.

**Keywords:** Hemodialysis, General elderly population, Frailty, Sarcopenia

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### I. INTRODUCTION

According to the statistical survey committee of the Japanese Society for Dialysis Therapy, the number of chronic maintenance dialysis patients in Japan reached 349,000 in 2021 and continues to rise<sup>1)</sup>. Nutritional disorders frequently occur in patients undergoing long-term hemodialysis, primarily due to increased catabolism from complications and loss of amino acids and blood proteins during dialysis treatments <sup>2, 3)</sup>. Recently, it has been reported that nutritional disorders contribute to muscle mass loss, a common complication of hemodialysis. Consequently, screening for muscle mass loss has gained importance among hemodialysis patients <sup>4, 5)</sup>.

In 2010, the European Working Group on Sarcopenia in Older People defined sarcopenia as a syndrome characterized by a progressive decline in skeletal muscle mass and strength, leading to an overall deterioration in health <sup>6)</sup>. The prevalence of sarcopenia among hemodialysis patients varies depending on multiple factors, including age, gender, measurements used, diagnostic criteria, and timing of assessments. Among hemodialysis patients in Asia, the frequency of sarcopenia is approximately 40%, according to the diagnostic criteria set by the Asian Working Group for Sarcopenia <sup>7, 8)</sup>.

Sarcopenia among hemodialysis patients is associated with a negative impact on life expectancy <sup>9)</sup>. Sarcopenia is also associated with impaired mobility, decreased ability to perform daily activities, and loss of independence. Sarcopenia can interfere with daily functioning and heighten the risk of falls <sup>10)</sup>. Most hemodialysis patients are elderly; therefore, they often face complications from nutritional disorders, sarcopenia, and frailty, which can

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adversely affect their daily living activities and quality of life. Such multimorbidity can also lead to other health outcomes, such as the onset and progression of cardiovascular diseases, falls, fractures, hospitalizations, and an overall poor prognosis. Therefore, it is crucial to implement continuous measures against sarcopenia and frailty to improve quality of life among hemodialysis patients.

Frailty refers to an increased vulnerability to various health issues stemming from age-related functional changes and diminished physiological reserve <sup>11</sup>). It is estimated that frailty occurs in one out of every two to three dialysis patients, considerably increasing their risk of reduced life expectancy and hospitalization.

Mechanisms underlying sarcopenia differ by disease context. Among people with chronic kidney disease, links to sarcopenia likely involve inflammatory mediators, metabolic and hormonal dysregulation, gut-microbiota dysbiosis, and alterations in non-coding ribonucleic acids (RNAs) <sup>12)</sup>. During heart failure, skeletal myofibers undergo complex, heterogeneous remodeling across disease development and progression, including shifts in myofibrillar protein composition and altered myofibrillar responsiveness to neurohormonal signaling <sup>13)</sup>. Among people with chronic obstructive pulmonary disease, sarcopenia arises from intertwined mechanisms, including metabolic alterations, physical inactivity, mitochondrial dysfunction, oxidative stress, and low-grade systemic inflammation; these collectively drive age-related muscle deterioration <sup>14)</sup>.

Although associations between hemodialysis and sarcopenia are well documented <sup>12)</sup>, evidence on how sarcopenia affects activities of daily living remains limited, and few studies have compared hemodialysis patients with older outpatients attending a cardiology clinic. Accordingly, this study aims to identify factors associated with sarcopenia in hemodialysis patients and to compare these factors—including daily life functions assessed with the Kihon Checklist (KCL)—with those observed in the older outpatients attending a cardiology clinic.

## II. PARTICIPANTS AND METHODS

## 1. Subjects

This study involved patients receiving hemodialysis at [removed for blinding purposes], Japan, who had been undergoing treatment for at least 6 months. Eligible patients (N = 24) were stable and did not have severe comorbidities, such as malignancies or infections. The control group (N = 46) consisted of elderly outpatients attending a cardiology clinic. All participants were clinically stable and had no severe comorbidities (e.g., active malignancy or acute infection).

Both groups were classified according to whether they had sarcopenia or not, using the Asian Working Group for Sarcopenia 2019 diagnostic criteria. Patients with insufficient laboratory data for analysis were excluded from the study.

### 2. Methods

Blood tests were conducted to measure albumin levels, cholesterol levels, and lymphocyte counts. The simplified version of the Nutritional Risk Index for Japanese Hemodialysis Patients (NRI-JH) was then used for blood data and biochemical tests. This index, which includes measurements of albumin, total cholesterol, creatinine, and body mass index (BMI), classifies patients into three risk categories (low, medium, and high) based on their scores. Post-dialysis weight was used for BMI calculations, while pre-dialysis values were applied for biochemical tests <sup>15</sup>).

The Health Check-up Questionnaire basic checklist (hereinafter, this is called "The Kihon checklist (KCL) assessments)", a frailty assessment tool developed by the Japanese Ministry of Health, Labour, and Welfare, was used to screen for daily living function. The KCL assessment questions (KQ) consists of 25 yes/no questions categorized into seven domains as shown in Table 1: Instrumental activities of daily living (IADL;KQ 1-5), physical function (KQ 6-10), nutritional status (KQ 11-12), oral function (KQ 13-15), social activities (KQ 16-17), cognitive function (KQ 18-20), and depressive mood (KQ 21-25). It has been reported to correlate with frailty and sarcopenia, with eight or more applicable items indicating potential concerns (Table 1) 16).

The Simple Frailty Index was also used to assess frailty<sup>17)</sup>. A basic checklist was used to evaluate the daily functioning of elderly participants, comprising simple yes/no questions addressing nutrition and shrinking (FQ-1), physical function (FQ-2), physical activity (FQ-3), forgetfulness (FQ-4), and emotions/exhaustion (FQ-5). Scores of three or more were classified as frail. FQ denotes Frailty Index; these questions can be seen in Table 2.

Table 1. The Health Check-up Questionnaire basic checklist (The Kihon checklist (KCL) assessments)

No			Questions	Answer	
1	KQ-1 KQ-2 KQ-3		Do you go out by bus or train by yourself?	0. YES	1. NO
2			Do you go shopping to buy daily necessities by yourself?	0. YES	1. NO
3			Do you manage your own deposits and savings at the bank?	0. YES	1. NO
4		KQ-4	Do you sometimes visit your friends?	0. YES	1. NO
5		KQ-5	Do you turn to your family or friends for advice?	0. YES	1. NO
6		KQ-6	Do you normally climb stairs without using handrail or wall for support?	0. YES	1. NO
7	tion	KQ-7	0. YES	1. NO	
8	KQ-10  KQ-10		Do you normally walk continuously for 15 minutes?		1. NO
9			Have you experienced a fall in the past year?	1. YES	0. NO
10			Do you have a fear of falling while walking?	1. YES	0. NO
11	tatus	KQ-11 Have you lost 2kg or more in the past 6 months?		1. YES	0. NO
12	Nutritional status	KQ-12 Height: cm, Weight: kg, BMI: kg/m2 If BMI is less than 18.5, this item		1. YES	0. NO
	Nuí		is scored.		
13	KQ-13 Do you have any difficulties eating tough food:		Do you have any difficulties eating tough foods compared to 6 months	1. YES	0. NO
	Oral functions		ago?		
14	rij RQ-14		Have you choked on your tea or soup recently?	1. YES	0. NO
15	KQ-15 Do you often experience having a dry mouth?		Do you often experience having a dry mouth?	1. YES	0. NO

16	Social activities WO-16		Do you go out at least once a week?	0. YES	1. NO
17	Socactiv	KQ-17	1. YES	0. NO	
18	_	KQ-18	1. YES	0. NO	
	Cognitive function KG-19		e.g."You ask the same question over and over again."		
19	Cognitiv	KQ-19	Do you make a call by looking up phone numbers?	0. YES	1. NO
20		KQ-20	Do you find yourself not knowing today's date?	1. YES	0. NO
21		KQ-21	In the last 2 weeks have you felt a lack of fulfillment in your daily life?	1. YES	0. NO
22		KQ-22 In the last 2 weeks have you felt a lack of joy when doing the things you		1. YES	0. NO
	poo		used to enjoy?		
23	Popusssive mod		In the last 2 weeks have you felt difficulty in doing what you could do	1. YES	0. NO
			easily before?		
24	KQ-24 In the last 2 weeks have you felt helpless?		1. YES	0. NO	
25	KQ-25 In the last 2 weeks have you felt tired without a reason?		1. YES	0. NO	

Abbreviations: KQ, Kihon Checklist (KCL) assessment questions.

Table 2. Frailty screening index

1	FQ-1	1.Have you lost 2kg or more in the past 6 months	Yes=1
2	FQ-2	2.Do you think you walk slower than before?	Yes=1
3	FQ-3	3.Doyou go for a walk for your health at least once a week?	No=1
4	FQ-4	4.Can you recall what happened 5 minutes ago?	No=1
5	FQ-5	5.In the past 2 weeks, have you felt tired without a reason?	Yes=1

Abbreviations: FQ, Frailty Index questions.

Body composition was assessed using the InBody S-10 (Inbody Japan, Tokyo, Japan), which employs bioelectrical impedance analysis. This device applies electrical currents at various frequencies (1 kHz to 1 MHz) through the body. Whole-body impedance was measured using an ipsilateral foot-hand electrical pathway, allowing for analysis of body composition in the right and left arms, legs, and trunk. The Skeletal Muscle Index (SMI) was calculated by summing the skeletal muscle mass (in kg) of the extremities and dividing by the square of height (m²).

Exercise was also measured, with those who engaged in aerobic exercise during dialysis for at least five days per week coded as exercising (vs. not).

To effectively assess sarcopenia, it is essential to measure grip strength, body composition, age, weight, comorbidities, and relevant blood test results. Sarcopenia was diagnosed based on cutoff points established by the Asian Working Group for Sarcopenia: an SMI <7.0 kg/m² in men and <5.7 kg/m² in women. Grip strength was measured using the dominant hand while seated, with the elbow flexed. The highest value from two consecutive measurements was recorded for sarcopenia diagnosis. Grip strength cutoffs were set at 28 kg for men and 18 kg for women. Physical performance was evaluated by measuring usual walking speed, based on the Sarcopenia Clinical Practice Guideline (2017). Walking speed was calculated by dividing the distance traveled by the time taken. A walking speed of less than 1 m/s indicated sarcopenia <sup>18</sup>. Participants were informed of their results and provided with feedback regarding therapeutic effects.

#### Statistical Analysis

Subjects were categorized into dialysis and control groups, before being further divided into four groups based on the presence or absence of sarcopenia. The normality of endpoint values was assessed, followed by post-hoc tests comparing among the four groups of ANOVA tests. Proportional tests were applied to aggregated questionnaire data, and a  $\chi^2$  goodness-of-fit test was conducted for multiple groups. Binomial logistic regression analysis was performed, using the presence or absence of sarcopenia as the dependent variable.

Binary univariate logistic regressions were used to assess associations between the candidate independent variables and outcomes. Variables showing significant associations were then reduced via a stepwise selection procedure, and the final model was determined with additional consideration of clinical plausibility.

To mitigate overfitting due to the small sample size, we restricted the multivariable model to 3–4 a priori clinically selected predictors in accordance with events-per-variable considerations and fitted bias-reduced logistic regression models. We report odds ratios with 95% confidence intervals (CIs).

Statistical analyses were conducted using SPSS version 20 for Windows (IBM), with a significant level set at 0.05.

#### Ethics approval and consent to participate

This study was approved by the Ethics Review Committee of the Faculty of Fukuoka Medical Technology, Teikyo University (approval n. The protocol adhered to the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of Teikyo University (Teirin 24-12). Data were anonymized to protect participant identification. The study has been approved, and confirmation that it conforms to recognized ethical standards is required such as the Declaration of Helsinki.

#### III. RESULTS

Table 3 shows the patient characteristics. The hemodialysis group comprised 24 patients (12 in the sarcopenia group, 12 in the non-sarcopenia group), with a mean age of  $74.3 \pm 8.2$  years and a mean length of dialysis of  $8.3 \pm 6.6$  years. The control group included 46 patients (14 in the sarcopenia group, 32 in the non-sarcopenia group), with a mean age of  $76.1 \pm 9.9$  years. Age distributions were comparable between the hemodialysis and control groups. Sarcopenia prevalence was higher in males across both the hemodialysis group (18 males, 6 females) and the control group (32 males, 14 females). Notably, the prevalence of sarcopenia was significantly higher in males than in females in both groups.

Red blood cell (RBC) counts were lower in the hemodialysis group compared with the control group. The Skeletal Muscle Index (SMI), a key criterion for diagnosing sarcopenia, was also lower in the

hemodialysis group compared with the control group. Blood tests revealed that blood urea nitrogen and creatinine levels were abnormally elevated in the hemodialysis group, while cholesterol, BMI, albumin, RBC, and hemoglobin levels were lower (Table 3).

Table 4 shows Total Scores of KCL assessment and the Simple Frailty Index were no significant differences in the hemodialysis group.

Significant differences in Total Scores of simple Frailty Index and KCL assessment were observed only in the control group.

IADL were a problematic area for the hemodialysis group (p < 0.05), while the problematic areas of the control group included physical function, oral function, and depressive mood (Table 4).

Logistic regression analysis of sarcopenia was conducted using a stepwise method (conditional), with the presence or absence of sarcopenia as the dependent variable and items showing significant differences as independent variables (Table 5). Among the hemodialysis group, there were statistically significant associations between sarcopenia and RBC (odds ratio: 1.12,95% confidence interval: 1.02-1.15,p<0.05). Among the control group, SMI (odds ratio: 0.14,95% confidence interval: 0.02-0.92,p<0.05) and walking speed (odds ratio: 0.01,95% confidence interval: 0.04-0.14,p<0.05) were significantly associated with sarcopenia.

Table 3. Patient characteristics and comparisons between groups.

	Dialysis	patients	Control group			
	Sarcopenia (+) (n=12)	Sarcopenia (-) (n=12)	Sarcopenia (+) (n=14)	Sarcopenia (-) (n=32)	ANOVA p- value	Post-hoc test
Age	79.3±8.8	69.3±7.6	81.8±7.3	70.3±12.7	< 0.05	f
Sex (n (%) male)	8 (66.7)	10 (83.3)	11 (78.6)	21 (65.6)	< 0.05	b,c,e,f
Height (cm)	159.7±5.8	168.8±8.2	149.2±6.6	155.5±28.1	< 0.05	a,b,d,e,f
Weight (kg)	54.8±8.9	67±11.7	46.8±9.1	61.5±13.5	< 0.05	a,d,f
Body Mass Index (BMI) (kg/m²)	21.3±3.4	23.3±2.4	20.9±3.1	23.9±5.3	< 0.05	c,f
Dialysis history (year)	9.4±7.8	7.1±5.4				-
Exercise (yes) †,	6 (50.0)	10 (83.0)	8 (57.0)	24 (75.0)	< 0.05	a, f
Blood tests						
Total protein (g/dl)	6.6±0.2	6.5±0.5	7.1±0.4	6.9±1.3		-
Albumin (g/dl)	3.6±0.3	3.5±0.4	4±0.4	$3.9\pm0.7$		-
Blood-sugar level (mg/dl)	129.1±19.5	128.5±61.3	99.6±10.4	103.8±25.8		-
Total cholesterol (mg/dl)	158.2±46.6	145.4±37.5	205±34.7	194.3±37.9	< 0.05	b,c,d,e
High Density Lipoprotein (mg/dl)	51.2±18.1	51.1±15.2	71.5±16.6	60.2±15.6	< 0.05	b,d,
Low Density Lipoprotein (mg/dl)	87.3±29.5	75.5±26.2	112.1±38.1	116±27.2	< 0.05	c,e
Triglyceride (mg/dl)	101.3±48.8	97.5±33.8	101.6±54	104.6±38.5		-
Blood Urea Nitrogen (mg/dl)	46.1±10.7	48.7±14.6	16.9±4.2	16.1±5.6	< 0.05	b,c,d,e
Creatinine (mg/dl)	8.2±1.3	$10.3\pm2.7$	$0.8\pm0.4$	0.9±0.3	< 0.05	a,b,c,d,e
UA (mg/dl)	6.1±1.5	6.7±1.1	5.3±1.3	5.4±1.5		

Table 3(continued). Patient characteristics and comparisons between groups.

	Hemodialys	sis patients	Control			
	Sarcopenia (+) (n=12)	Sarcopenia (-) (n=12)	Sarcopenia (+) (n=14)	Sarcopenia (-) (n=32)	ANOVA p-value	Post hoc test
AIB NRI	1.1±1.9	1.3±1.8	0.3±1	0.1±0.7	< 0.05	e
Cre-NRI (mg/dl)	2.4±1.9	$1.9\pm2$	2.2 <u>+</u> 2	3.1±1.7		-
NRI-JH	4.7±3.3	$3.4\pm3.2$	$4.3\pm3.2$	$3.9\pm2.1$		-
Red Blood Cell (RBC) count (/μL)	351.8±22.5	378.1±17.4	411.4±75.8	429.9±78.1	< 0.05	a,b,c,e
Hemoglobin (g/dl)	$10.77\pm2$	11.1±0.6	12.5±1.6	$13.3\pm2.5$	< 0.05	a,b,c,e,f
Complications						
Cardiovascular disease (n (%))	10 (83.3)	11 (91.7)	3 (21.4)	9 (28.1)		-
Diabetes (n (%))	7 (58.3)	7 (58.3)	2 (14.3)	3 (9.4)		-
Cerebrovascular disease (n (%))	1 (8.3)	0 (0.0)	1 (7.1)	1 (3.1)		-
Chronic Obstructive Pulmonary	0 (0.0)	0 (0.0)	3 (21.4)	1 (3.1)		-
Hypertension (n (%))	10 (83.3)	10 (83.3)	8 (57.1)	24 (75)		-
Dyslipidemia (n (%))	0 (0.0)	0 (0.0)	9 (64.3)	10 (31.3)		-

Note.

Data means standard deviation unless otherwise stated.

a = Hemodialysis, Sarcopenia (+) vs. Hemodialysis, Sarcopenia (-); b = Hemodialysis, Sarcopenia (+) vs. Control, Sarcopenia (+); c = Hemodialysis, Sarcopenia (+) vs. Control, Sarcopenia (-); d = Hemodialysis, Sarcopenia (-) vs. Control, Sarcopenia (-); f = Control, Sarcopenia (+) vs. Control, Sarcopenia (-); NRI = Nutritional Risk Index; JH = Japanese hemodialysis patients. n.s. = not statistically significant (p≥.05). †, Participants classified as "Exercise (yes)" were those who engaged in nearly 40 minutes of daily physical activity, corresponding to approximately 10 MET-hours per week. Cardiovascular disease was defined as arrhythmias, peripheral arterial and aortic disease, coronary artery disease, or heart failure. Only non-severe cases that did not limit activities of daily living were included.

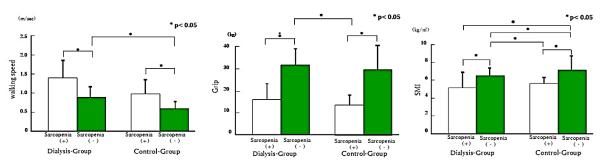


Figure 1. Comparison between dialysis patients and control groups ANOVA and post hoc tests. \*P < 0.05

Figure 1 shows that walking speed was significantly slower, and grip strength was reduced in both groups. SMI was significantly lower in the hemodialysis group.

Table 4. Clinical assessment scores and comparisons between groups.

		Hemodialy					
				Sarcopenia (+)	-	ANOVA	Post hoc
		(n=12)	(n=12)	(n=14)	(n=32)	p-value	test
Frailty Index		$1.7\pm1.1$	$1.2\pm0.8$	$1.9\pm0.7$	$0.9\pm0.7$	< 0.05	f
Frailty Index							
Nutrition/shr	•	1 (8.3)	2 (16.7)	1 (7.1)	2 (6.3)		-
Walking spec	ed	6 (50.0)	7 (58.3)	8 (57.1)	9 (28.1)		-
Seclusion		4 (33.3)	3 (25)	4 (28.6)	7 (21.9)	0.05	-
Forgetfulnes	S	5 (41.7)	0 (0.0)	6 (42.9)	10 (31.3)	< 0.05	a
Emotions		3 (25.0)	0 (0.0)	3 (21.4)	3 (9.4)		-
	sment (n, %)	5 (50 O)	5 (41.5)	1 (20.6)	5 (15.6)	0.05	
IADL	Go out by Bus	7 (58.3)	5 (41.7)	4 (28.6)	5 (15.6)	< 0.05	b, c
	Shopping	7 (58.3)	2 (16.7)	2 (14.3)	1 (3.1)	< 0.05	a, b, c
	Manage your money Visit friends	8 (66.7)	2 (16.7)	0 (0.0)	3 (9.4)	< 0.05	a, b, c
	Friends for advice	11 (91.7)	7 (58.3)	5 (35.7)	3 (9.4)	< 0.05	a, b, d, f
Physical	Climb stairs	7 (58.3) 5 (41.7)	2 (16.7) 3 (25.0)	2 (14.3)	2 (6.3)	< 0.05	c, f
function	Normally stand up	0 (0.0)	1 (8.3)	8 (57.1) 5 (35.7)	5 (15.6) 3 (9.4)	<0.03	-
Tunction	Normally walk	2 (16.7)	2 (16.7)	3 (21.4)	3 (9.4)		-
	Experienced a fall	2 (16.7)	6 (50.0)	3 (21.4)	2 (6.3)	< 0.05	d
	Fear of falling	3 (25.0)	3 (25.0)	7 (50.0)	4 (12.5)	< 0.05	f
Nutritional	Lost Weight	0 (0.0)	1 (8.3)	2 (14.3)	3 (9.4)	<0.05	-
status	BMI	2 (16.7)	0 (0.0)	0 (0.0)	4 (12.5)		
Status	Eating tough foods	0 (0.0)	1 (8.3)	5 (35.7)	3 (9.4)	< 0.05	f
Oral	Choked	4 (33.3)	1 (8.3)	5 (35.7)	2 (6.3)		
function	Dry mouth	3 (25.0)	4 (33.3)	7 (50.0)	5 (15.6)		
Social activities	Go out at least weekly	0 (0.0)	1 (8.3)	3 (21.4)	0 (0.0)		
	Go out less	6 (50.0)	3 (25.0)	6 (42.9)	5 (15.6)	< 0.05	c, f
Cognitive	frequently Memory loss	0 (0.0)	1 (8.3)	4 (28.6)	1 (3.1)	< 0.05	f
function	Make a call	3 (25.0)	1 (8.3)	3 (21.4)	2 (6.3)		
	Not knowing date	6 (50.0)	4 (33.3)	6 (42.9)	4 (12.5)	< 0.05	c, f
Depressive	Lack of fulfilment	3 (25.0)	4 (33.3)	1 (7.1)	2 (6.3)		
mood	Lack of joy	2 (16.7)	3 (25.0)	4 (28.6)	3 (9.4)		
	Helpless	3 (25.0)	3 (25.0)	8 (57.1)	3 (9.4)	< 0.05	f
	Felt tired	3 (25.0)	2 (16.7)	2 (14.3)	3 (9.4)		
KCL assess Total domain	sment Total Score	7.2±4.1	5.6±2.7	7.4±4.8	1.8±4.7	< 0.05	c, f
IADL		2.6±1.4	1.3±1.2	1.2±1.6	0.6±0.9	< 0.05	a, b, c, e
Physical fund	ction	1±0.9	1.1±0.8	1.9±1.4	1±1.3	< 0.05	b, e, f
Nutritional s		0.2±0.4	0.1±0.2	0.1±0.3	0.2±0.4		
Oral function	n	0.8±0.9	0.5±0.6	1±1	$0.4\pm0.7$	< 0.05	f
Social activit	ties	$0.8\pm0.6$	$0.3\pm0.4$	$0.6\pm0.7$	$0.3\pm0.4$		
Cognitive fu	nction	$0.6\pm0.7$	$0.4\pm0.7$	0.5±0.8	$0.3\pm0.5$		
Depressive n	nood	$1.6\pm0.9$	$0.9\pm1.3$	$1.8 \pm 1.8$	$0.6\pm1.2$	< 0.05	f

Data are mean  $\pm$  standard deviation unless otherwise stated. a = Hemodialysis, Sarcopenia (+) vs. Hemodialysis, Sarcopenia (-); b = Hemodialysis, Sarcopenia (+) vs. Control, Sarcopenia (+); c = Hemodialysis, Sarcopenia (+) vs. Control, Sarcopenia (-); d = Hemodialysis, Sarcopenia (-) vs. Control, Sarcopenia (+); e = Hemodialysis, Sarcopenia (-) vs. Control, Sarcopenia (-); f = Control, Sarcopenia (+) vs. Control, Sarcopenia (-); n. s. = not statistically significant ( $p \ge .05$ ).

Table 5. Multiple logistic regression analysis

		β	Wald	Odds Ratio (95% CI)	p value
Hemodialysis patients	Red blood cell (RBC) count	0.12	6.66	1.13(1.02 – 1.15)	< 0.05
Control group	Skeletal muscle index (SMI)	-1.95	4.15	0.14 (0.02 - 0.92)	< 0.05
	Walking speed	-9.80	5.97	0.08 (0.04 - 0.14)	< 0.05

The dependent variable was the presence of sarcopenia. The independent variables were reduced via stepwise selection, and, in the final models. The independent variables in Hemodialysis patients were walking speed, grip strength, Red Blood Cell (RBC) count. The independent variables in Control group were walking speed, grip strength, SMI.

## IV. DISCUSSION

The prevalence of sarcopenia in our outpatient hemodialysis group was found to be 50% (12 out of 24 patients). This prevalence is notably high, aligning with existing literature that reports rates of sarcopenia in dialysis patients ranging from 27.4% to 68.0% <sup>19</sup>). Patients in this study had been on dialysis for an average of more than 8 years and were primarily very elderly. A study by the Tokyo Metropolitan Geriatric Hospital and Gerontology Center indicated that the prevalence of sarcopenia increases with age, from approximately 22% in both men and women aged 75–79 years to 40% in those aged 80 or older <sup>20</sup>).

The elevated prevalence of sarcopenia in the hemodialysis group may be attributed to nutritional disorders, as indicated by low SMI values and low albumin levels. Dialysis patients are particularly susceptible to protein-energy wasting, which is characterized by a decrease in skeletal muscle mass, visceral protein, and fat stores <sup>21)</sup>. Protein-energy wasting can arise from inadequate nutrient intake, increased catabolism due to inflammation, the accumulation of uremic toxins, and nutrient loss during dialysis, ultimately leading to sarcopenia.

In our study, the sarcopenia group exhibited less exercise and reduced social activity. Additionally, RBC, hemoglobin, and hematocrit levels were lower than in the control group. Prior research indicates that anemia diminishes activities of daily living (ADL) and that inpatients with hemoglobin levels below 10 g/dL experienced decreased independence in ADL at discharge, suggesting a clear association between hemoglobin levels and functional outcomes <sup>22</sup>).

Prior research has also found that hemodialysis patients often experience a chronic decline in physical activity due to restrictions, leading to a motor function decrease to approximately 70% of that observed in healthy individuals <sup>23)</sup>.

Hemodialysis is a primary treatment for end-stage kidney disease. Beyond its physiological burden, dialysis can adversely affect patients' social participation and quality of life. It may also cause anxiety and/or depression, which may further contribute to reduced social engagement <sup>24)</sup>.

Engaging in regular exercise was associated with sarcopenia in this study. In the hospital from which participants were recruited, aerobic exercise during dialysis is encouraged, and its effectiveness was evident in the lower incidence of sarcopenia among patients who engaged in regular exercise. Previous studies have reported that aerobic exercise during dialysis can reduce fatigue both during and after sessions <sup>25</sup>.

Binomial logistic regression analysis revealed that anemia (RBC levels) and walking speed were associated with sarcopenia in the hemodialysis group, whereas SMI and walking speed were associated with sarcopenia in the control group. In this study, sarcopenia was diagnosed according to the criteria established by the Asian Working Group for Sarcopenia, which focuses on muscle mass and physical performance. The loss of skeletal muscle mass associated with aging (often due to early declines in type II muscle fibers and morphological changes at neuromuscular junctions) might contribute to reduced physical performance <sup>26, 27)</sup>. However, in the hemodialysis patient population, renal anemia is a significant factor. It results from insufficient erythropoietin production in the kidneys, compounded by factors such

as impaired erythropoiesis and nutritional deficiencies.

Iron deficiency anemia can be a further risk factor impacting sarcopenia, highlighting the role of iron in maintaining skeletal muscle mass and strength <sup>28</sup>. Additionally, chronic increases in cardiac workload and activation of the renin-angiotensin system due to fluid volume fluctuations can trigger inflammatory cytokine production, promoting muscle protein catabolism and type II muscle fiber atrophy <sup>29</sup>. These mechanisms appear to be specific contributors to sarcopenia in hemodialysis patients, distinct from the general age-related factors typically associated with muscle weakness <sup>30</sup>.

This study reaffirms the critical need for exercise guidance to prevent sarcopenia in hemodialysis patients. The endocrine system, including growth hormones, is involved in protein synthesis, and engaging in exercise (both resistance and aerobics) can stimulate insulin-like growth factor 1 secretion, which is beneficial for muscle health. Research suggests that well-designed dietary interventions alone may not be sufficient to synthesize muscle protein effectively, and that exercise is one of the more important factors. Thus, it is imperative to encourage hemodialysis patients to engage in physical activity to enhance muscle strength and prevent frailty and sarcopenia <sup>31)</sup>.

#### Limitations

This study has several limitations. First, the cross-sectional design precludes causal inference. Second, it was conducted at a single center, which may limit generalizability. Third, there is likely residual confounding, particularly because detailed exercise intervention information was unavailable and comprehensive dietary data were lacking. Notably, protein intake among hemodialysis patients often differs between dialysis and non-dialysis days <sup>32)</sup>, underscoring the need to assess outcomes under conditions of stable nutritional status. Fourth, the small sample size limits statistical power. Future studies should increase participant numbers, adopt multicenter designs, and incorporate longitudinal or interventional approaches with standardized measures of exercise and nutrition to better control confounding and strengthen causal interpretation.

In conclusion, nutritional guidance, increased exercise, and fostering social engagement are vital strategies for preventing frailty and sarcopenia among patients with chronic kidney disease. Collaborative efforts within the community are essential for effective intervention.

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Not applicable.

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