






Cut-Off Values for Sarcopenia and Mortality Risk in Older Dialysis Patients

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ABSTRACT

Objective: Sarcopenia is a common condition in patients undergoing dialysis, yet appropriate diagnostic thresholds tailored to this population remain unclear. In this context, we investigated which measures related to muscular performance and functional status were most predictive of mortality in this population.

Materials and Methods: Hand-grip strength (HGS), skeletal muscle mass index (SMMI), and gait speed (GS) were assessed in relation to 3-year survival. Cox regression analysis was applied, adjusting for age, nutritional status, and serum albumin. Newly determined thresholds were compared with the criteria defined by the European Working Group on Sarcopenia in Older People (EWGSOP2).

Results: This study involved 82 dialysis patients (median age: 66 years; 54.9% female). Mortality-related cut-offs were established as follows: HGS (18.0 kg for male, 11.5 kg for female), SMMI (9.0 kg/m² for male, 6.7 kg/m² for female), and GS (0.53 m/s for male, 0.43 m/s for female). Lower HGS and GS were independently associated with 3-year mortality. The new definitions yielded better prognostic performance than EWGSOP2.

Conclusion: The new cut-off values for HGS and GS are superior predictors of mortality in dialysis patients compared to EWGSOP2 standards.

Keywords: Dialysis, hand-grip strength, mortality, older adults, sarcopenia.

INTRODUCTION

Sarcopenia is a syndrome characterized by a reduction in muscle mass, diminished muscle strength, and impaired muscle function. Muscle mass grows during childhood, reaches its maximum in adulthood, and inherently declines after the sixth decade. While sarcopenia predominantly correlates with the process of aging, it presents various pathological conditions, including chronic kidney disease, cancer, liver disease, and respiratory insufficiency.^{1–4}

Chronic kidney disease (CKD) involves various changes that reflect a catabolic environment, defined by the reduction of muscle mass and closely linked to an increase in protein-energy wasting (PEW). This condition is attributed to factors such as inadequate dietary intake, oxidative stress, nutrient loss during dialysis, hemorrhage, disrupted responses to anabolic hormones, inflammatory processes, and a myriad of metabolic perturbations stemming from uremia.⁴ Moreover, the presence of more than one of these sarcopenia-related conditions may predict poor clinical outcomes in CKD. A study reported that sarcopenia significantly predicted mortality in patients undergoing hemodialysis.⁵ Besides, recent evidence indicates that decreased muscle strength in CKD is the primary negative prognostic factor and is related to higher mortality.^{6,7} Hence, the timely identification and management of sarcopenia could potentially wield significant influence among individuals undergoing dialysis treatment.

Sarcopenia, as defined by the European Working Group on Sarcopenia in Older People² (EWGSOP2), involves a comprehensive assessment of muscle (strength, mass, and performance) across the general population.⁸ However, CKD is a model of accelerated aging. Some studies have stressed that CKD patients may have a different body composition than the general population.^{9,10} Therefore, the eligibility of these sarcopenia criteria for dialysis currently remains uncertain. There are a few studies that offer different threshold values for sarcopenia among individuals with CKD.^{10,11}

To our knowledge, there is no established consensus on the threshold value for detecting sarcopenia among patients undergoing dialysis treatment remains elusive. The EWGSOP2 suggests establishing regional cut-off values for sarcopenia, derived from -2.5 standard deviations (SD) of the normative population, to adopt a more conservative diagnostic strategy under particular circumstances.¹² This study aims to determine and verify cut-off values for HGS (for muscle strength), SMMI (for muscle quantity/quality), and gait speed (m/s, for physical performance) according to -2.5 SD in our subject population to prognosticate all-cause mortality in dialysis patients.

MATERIALS AND METHODS

The present research was a retrospective observational conducted among individuals with CKD (≥ 60 years old) undergoing dialysis for ≥ 6 months at a university hospital. The Erciyes University's Ethics Committee granted ethical approval for the study (approval number: 2024/244). The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and its later amendments. The required sample was determined as 73 patients, based on an alpha level of % and statistical power of 80%, with an

KEY MESSAGES

- This study establishes new cut-off values for sarcopenia components to predict mortality in older dialysis patients.
- The findings show that lower HGS and GS are more accurate predictors of mortality than the criteria set by the EWGSOP2.
- These new values highlight the importance of assessing sarcopenia to improve mortality predictions and guide treatment strategies in dialysis patients.

anticipated effect size of 0.28. Exclusion criteria included malignancy, less than six months survival expectation, parathyroidectomy, history of surgery, trauma, and severe infection in the three months before enrolling, systemic steroid therapy, and patients who could not undergo BIA due to cardiovascular stent, pacemaker, joint prosthesis, severe peripheral angiopathy, or visible edema.

Anthropometric Assessments

Patients' body weight was assessed with light clothing and barefoot. The height of each subject was assessed with a stadiometer. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Calf circumference was measured at the widest point on the lower leg while the participant remained seated, utilizing a tape measure. Mid-arm circumference (MAC) was assessed at the midpoint between the acromion process and the olecranon. Triceps skinfold thickness (TSFT) was assessed using a caliper, and mid-arm muscle circumference (MAMC) was computed as $MAC - (3.14 \times TSFT)$. Muscle strength was measured when standing with both arms extended sideways using a Jamar hand-held dynamometer. Body composition was evaluated in a standing position utilizing the BIA device (Body Stat Quad Scan 1500, UK). Fat-free mass index (FFMI) was determined using fat-free mass obtained from BIA, divided by height squared (m^2). Total skeletal muscle mass (SMM, kg) was calculated through the equation proposed by Janssen et al.,¹³ derived from BIA, based on the impedance (ohms) values obtained. SMM (kg) was adjusted by height² and expressed as skeletal muscle mass index (SMMI, kg/m^2). Gait speed, an indicator of physical performance, was recorded while patients walked at their usual pace over a 4-meter course, measured in seconds.

Geriatric Assessment

Patients' ability to perform daily living activities (ADL) and instrumental daily activities (IADL) were evaluated using the Katz Index and Lawton Scale, respectively.^{14,15} The ADL score ≤ 12

and IADL ≤ 16 points were defined as dependent. Depressive symptoms were evaluated using the Geriatric Depression Scale (GDS), which ranges from 0 (no depression) to 30 (severe depression), with a score greater than 14 indicating the presence of depression.¹⁶ Malnutrition was assessed according to the criteria recommended by the Global Leadership Initiative on Malnutrition (GLIM).¹⁷ The GLIM approach involves a two-step process: initial screening to identify malnutrition risk utilizing any validated screening tool, followed by the diagnosis of malnutrition. First, malnutrition risk was evaluated using the Mini Nutritional Assessment–Short Form (MNA - SF), which is reliable and valid for the geriatric population.¹⁸ It consists of items related to participant dietary intake over the past three months, anthropometric measurement (body weight, BMI, and calf circumference), and clinical characteristics (mental stress, acute disease, and neuropsychiatric disorders). Per the Mini Nutritional Assessment (MNA), a range of 12–14 signifies adequate nutritional status, 8–11 reflects the risk of malnutrition, and scores below 7 suggest nutritional deficiency.¹⁸ Patients in the two latter categories were accepted as ‘at malnutrition risk’ for the first step of GLIM criteria. Secondly, patients at risk of malnutrition are classified as malnourished if they meet at least one criterion from each of the phenotypic and etiologic categories based on GLIM criteria. The phenotypic components include unintentional weight loss ($>5\%$ during the preceding half-year), reduced BMI ($<20 \text{ kg/m}^2$ for individuals younger than 70 or $<22 \text{ kg/m}^2$ for those older than 70), and decreased muscle mass defined by an FFMI of less than 17 kg/m^2 in males and less than 15 kg/m^2 in females.¹⁹ The etiological criteria encompassed constraints related to dietary intake or absorption (significant or moderate decline in dietary intake over the previous three months or individuals with chronic gastrointestinal disorders adversely affecting food assimilation or absorption) and the existence of inflammation (plasma C-reactive protein (CRP) concentrations exceeding 5 mg/L). All patients’ weight loss and reduced food intake or assimilation amount were obtained from their medical records.

Sarcopenia was defined in two distinct ways: first, as reduced muscle strength, mass, and performance according to the EWGSOP2 recommendations, and second, based on our newly established thresholds.⁸ The HGS for muscle strength, SMMI for muscle quantity/quality, and gait speed (m/s) for physical performance were evaluated. According to the EWGSOP2 criteria, SMMI below 5.5 kg/m^2 in females and 7 kg/m^2 in males is defined as low muscle mass. HGS values less than 27 kg for males or 16 kg for females were classified as indicating reduced muscle strength. A gait speed score $\leq 0.8 \text{ m/s}$ indicated low muscle performance.⁸ All muscle evaluations for defining low muscle quantity/quality

were performed on weekly dialysis sessions. The physical performance evaluations were carried out preceding the dialysis session, and anthropometric measurements were carried out after the dialysis session.

The new cut-off values for sarcopenia were created by observing our patients. Cut-off points of HGS, SMMI, and gait speed were described as below the 25th percentile and 2.5 standard deviations (SD) for the referenced population.

Blood Analysis

Before dialysis, a 20-cc venous blood sample was taken from each participant after 12 hours of fasting. The blood sample was centrifuged, and serum and plasma were obtained and stored in a -80°C refrigerator until analysis. Hemoglobin, fasting blood glucose, prealbumin, albumin, total protein, lipids, 25-OH vitamin D, and homocysteine concentrations were analyzed. C-reactive proteins were evaluated to assess inflammation.

Statistical Analysis

Statistical analyses were conducted with R 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria) software. Normally distributed variables were expressed as Mean \pm SD, whereas variables without normal distribution were summarized as median with interquartile range [IQR (25th–75th percentile)]. Categorical variables were reported as numbers (%). Comparisons between groups were performed with the independent sample t-test for parametric data and the Mann-Whitney U test for non-parametric data. The difference between categorical variables was analyzed using the Pearson Chi-Squared test.

To define sarcopenia, cut-off values for low HGS, low SMMI, and low gait speed were defined as below the 25th percentile and 2.5 SD below the mean values for our study sample (HD and PD patients) using T-score calculation.²⁰ We derived our cut-off values predicting mortality which were HGS (female: 11.5 kg, male: 18.0 kg), SMMI (female: 6.7 kg/m^2 , male: 9.0 kg/m^2), and gait speed (female: 0.43 m/s , male: 0.53 m/s). To substantiate the newly derived cut-off values, the univariate Cox proportional hazard model was realized to evaluate the hazard ratio (HR) for mortality after adjusting for defined confounders and considering age, malnutrition, and albumin level. The HR and 95% confidence intervals (CIs) were presented by running a risk survival analysis. The kappa test was applied on the derived cut-off and EWGSOP2 criteria to examine the agreement in the diagnosis of sarcopenia. The following interpretations of the Kappa (k) value were established: poor agreement: 0.00–0.20, fair: 0.21–0.40, moderate: 0.41–0.60, good: 0.61–0.80, and very good: 0.81–1.00.²¹ A p-value below 0.05 was regarded as statistically significant.

Table 1. Demographic and clinical characteristics of the patients and comparison between survivor and non-survivor patients

	Total (n=82)	Survivor (n=52)	Non-survivor (n=30)	p
Age (years)	66.0 (60.0–85.0)	65.5 (60.0–85.0)	67.0 (60.0–80.0)	0.347
Gender, n (%)				0.256
Female	45 (54.9)	31 (59.6)	14 (46.7)	
Male	37 (45.1)	21 (40.4)	16 (53.3)	
BMI (kg/m ²)	26.6±4.6	27.2±4.2	25.5±5.1	0.107
Polypharmacy, n (%)	62	39 (75.0)	23 (76.7)	0.866
Dialysis vintage (month)	39.0 (6.0–300.0)	45.0 (8.0–300.0)	36.0 (6.0–264.0)	0.237
Geriatric assessment				
ADL dependent, n (%)	8 (9.8)	3 (5.8)	5 (16.7)	0.109
IADL dependent, n (%)	40 (48.8)	25 (48.1)	15 (50.0)	0.867
GDS	15.4±7.1	14.2±6.9	17.5±7.1	0.046
MNA-SF	12.0 (4.0–14.0)	13.0 (7.0–14.0)	12.0 (4.0–14.0)	0.025
GLIM				
Malnutrition, n (%)	38 (46.3)	19 (36.5)	19 (63.3)	0.019
Phenotypic criteria, n (%)				
Nonvolitional weight loss	25 (30.5)	11 (21.2)	14 (46.7)	
Low BMI	14 (17.1)	7 (13.5)	7 (23.3)	
Reduced muscle mass	22 (26.8)	10 (19.2)	12 (40.0)	
Etiologic criteria, n (%)				
Reduced food intake or assimilation	25 (30.5)	11 (21.2)	14 (46.7)	
Inflammation	32 (39.0)	17 (32.7)	15 (50.0)	
Anthropometric measurement				
FFMI (kg/m ²)				
Female	16.57±2.49	17.0±2.78	16.0±2.02	0.239
Male	18.21±3.77	19.3±3.47	15.8±3.35	0.003
SMMI (kg/m ²)				
Female	7.56±1.16	7.78±1.08	7.26±1.22	0.183
Male	10.04±1.91	10.3±2.07	9.6±1.44	0.195
Calf circumference (cm)				
Female	33.1±4.69	32.5±4.24	33.9±5.23	0.376
Male	32.4±3.88	33.8±2.86	29.2±4.05	0.001
MAMC (cm)				
Female	22.74±3.32	22.7±3.12	22.8±3.68	0.882
Male	22.76±3.02	23.1±2.48	22.0±3.96	0.246
HGS (kg)				
Female	22.74±3.32	17.3±4.81	13.5±3.85	0.014
Male	24.0±8.15	25.4±7.91	20.9±8.10	0.041
Gait speed (m/s)				
Female	0.59±0.17	0.64±0.16	0.54±0.18	0.077
Male	0.66±0.18	0.69±0.17	0.59±0.17	0.054

Table 1 (cont). Demographic and clinical characteristics of the patients and comparison between survivor and non-survivor patients

	Total (n=82)	Survivor (n=52)	Non-survivor (n=30)	p
Laboratory parameters				
Fasting glucose (mg/dL)	129.0 (62.0–336.0)	138.5 (65.0–336.0)	122.5 (62.0–256.0)	0.240
Triglycerides (mg/dl)	161.0 (35.0–444.0)	176.0 (57.0–444.0)	150.5 (35.0–288.0)	0.157
Total cholesterol (mg/dl)	166.3±50.8	173.2±52.8	154.3±45.4	0.105
HDL-cholesterol (mg/dl)	39.0 (20.0–201.0)	38.5 (20.0–201.0)	41.0 (24.0–78.0)	0.353
Albumin (g/dl)	3.80 (1.96–4.89)	3.96 (1.96–4.89)	3.37 (2.29–4.54)	0.003
Total protein (g/dL)	6.6±0.7	6.8±0.7	6.4±0.8	0.042
Prealbumin (mg/dL)	24.5±9.9	26.4±8.9	21.0±10.7	0.017
Homocysteine (mg/dL)	12.0 (6.0–67.0)	11.5 (6.0–67.0)	12.0 (6.0–34.4)	0.750
25-OH vitamin D (ng/ml)	14.7 (4.3–63.9)	15.2 (4.6–39.0)	12.4 (4.3–63.9)	0.859
Parathormone (pg/mL)	240.5 (12.7–810.0)	253.7 (18.4–810.0)	183.9 (12.8–626.0)	0.470
Hemoglobin (g/dL)	11.3±1.74	11.6±2.0	10.9±1.2	0.055
CRP	3.6 (0.7–19.0)	7.1 (0.7–168.0)	34.4 (8.4–233.8)	0.002

BMI: Body Mass Index; CRP: C-reactive protein; FFMI: Fat Free Mass Index; GDS: Geriatric Depression Scale; GLIM: Global Leadership Initiative on Malnutrition; HDL: High density lipoprotein; HGS: Handgrip strength; MAMC: Mid-arm muscle circumference; MNA-SF: Mini Nutritional Assessment-Short Form; SMMI: Skeletal Muscle Mass Index.

RESULTS

A total of 82 patients undergoing dialysis participated in the study (survivor: 52 and non-survivor: 30). The median age was 66.0 years (60.0–85.0), and the median duration of dialysis was 39.0 months (6.0–300.0). According to MNA-SF and GLIM criteria, 25 patients (30.5%) and 7 patients (8.5%), respectively, were malnourished. Non-survivor patients were significantly more malnourished according to both MNA-SF and GLIM criteria compared to survivor patients ($p=0.025$ and $p=0.019$, respectively). Additionally, survivors exhibited markedly lower GDS scores compared to non-survivors ($p=0.046$) (Table 1).

The survivor and non-survivor patients had similar anthropometric measurements, excluding HGS. The HGS values in non-survivors were significantly lower compared to survivors (p -values: 0.041 for males and 0.014 for females) (Table 1). Additionally, survivor patients demonstrated notably higher levels of albumin, total protein, prealbumin, and lower CRP values than the non-survivors ($p=0.003$, $p=0.042$, $p=0.017$, and $p=0.002$, respectively). Patients' laboratory findings are shown in Table 1 in detail.

As shown in Table 2, patients were grouped into high and low groups based on the newly established cut-off values for HGS, SMMI, and gait speed to assess their prognostic value. After adjusting for age, malnutrition, and serum albumin levels, Cox regression analysis revealed that patients with lower hand-

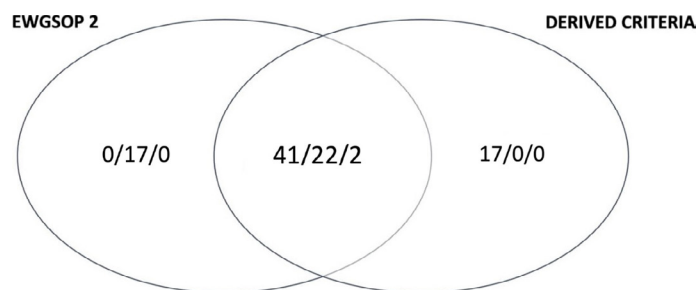


Figure 1. EWGSOP2: European Working Group on Sarcopenia in Older People 2.

grip strength (HGS) and gait speed exhibited a significantly elevated risk of mortality compared to those with higher HGS and gait speed. This was indicated by the adjusted hazard ratios (HR) of 2.41 (95% CI: 1.24–5.30, $p=0.005$) and 1.12 (95% CI: 1.03–1.42, $p<0.001$), respectively.

Furthermore, we classified patients into four groups according to HGS, SMMI, and gait speed cut-off points. The results confirmed that the thresholds determined for HGS and gait speed acted as important prognostic indicators for mortality prediction. Reduced gait speed alone significantly predicted 3-year mortality (HR: 3.02, 95% CI: 1.99–6.51, $p=0.032$). In addition, our framework involving cut-off of HGS, SMMI, and gait speed was a prognostic value for mortality with HR: 3.92, 95% CI: 2.91–7.98, $p=0.002$) (Table 2).

Table 2. The prognostic value of cut-off points of HGS, SMMI and gait speed for all-cause mortality in the patients (n=82)

	Model 1		Model 2	
	HR (95%CI)	p	HR (95%CI)	p
Reference				
Low HGS	2.71 (1.30–5.64)	0.008	2.41 (1.24–5.31)	0.005
Reference				
Low SMMI	1.57 (1.26–2.21)	0.144	1.02 (0.92–1.89)	0.102
Reference				
Low gait speed	1.29 (1.14–1.60)	<0.001	1.12 (1.03–1.42)	<0.001
Reference				
Low HGS (<18.0 (males) / <11.5 (females))	1.60 (1.26–2.39)	0.230	1.83(1.35–3.34)	0.301
Low SMMI(<9.0 (males) / <6.7 (females))	1.62 (1.29–2.33)	0.220	1.54 (1.19–2.01)	0.247
Low gait speed (m/s) (≤0.53 (males) / ≤0.43 (females))	3.63 (2.13–7.10)	0.024	3.02 (1.99–6.51)	0.032
Low HGS, low SMMI, and low gait speed	3.81 (2.78–7.79)	0.005	3.92 (2.91–7.98)	0.002

Model 1: Non-adjusted, Model 2: Adjusted for age, malnutrition and serum albumin. CI: Confidence interval; HGS: Handgrip strength; HR: Hazard ration; SMMI: Skeletal Muscle Mass Index. Low HGS: <18.0 kg for male and <11.5 kg for female, Low SMMI: <9.0 kg/m² for male and <6.7 kg/m² for female, Low gait speed: ≤0.53 m/s for male and ≤0.43 m/s for female.

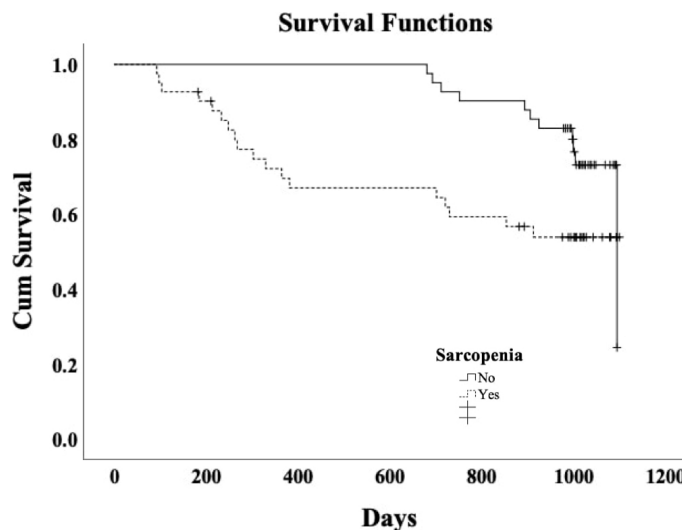
While 39 patients (47.6%) had probable sarcopenia and two patients (2.5%) had sarcopenia according to EWGSOP2 criteria, 22 patients (26.8%) had probable sarcopenia and two patients (2.5%) had sarcopenia according to the newly derived criteria. The total agreement rate between the EWGSOP2 criteria and newly derived cut-off values for sarcopenia was 0.60 ($p<0.001$) (Fig. 1).

Non-sarcopenic patients diagnosed with newly derived cut-off values exhibited statistically significant a prolonged survival period when compared with sarcopenic patients [mean (95% CI)=1034 (995–1073) vs. 774 (651–897) days, $p=0.033$] (Fig. 2).

According to the derived cut-off values and EWGSOP2 criteria, the proportion of patients with decreased HGS was 23.2% versus 50.0%, and the total agreement of HGS cut-off points was 69.5% (Kappa=0.29) versus 57.3% (Kappa=0.146). The agreement rate of prognostic mortality by gait speed was 72.0 (Kappa=0.150), and it was higher than the cut-off values for EWGSOP2 (51.2, Kappa=0.139). The newly established cut-off values of all components (HGS, SMMI, and gait speed) had a higher rate than the EWGSOP2 cut-off points (63.4% vs 57.3%, Kappa=0.146) (Table 3).

DISCUSSION

In this cohort study, we established the cut-off values for HGS (18.0 for males and 11.5 for females), SMMI (9.0 for males and 6.7 for females), and gait speed (0.53 for males and 0.43 for females) to diagnose sarcopenia within the study population, based on the lowest 25th percentile. Based on the newly established cut-off values, 22 patients

**Figure 2.** Kaplan-Meier survival analysis curves for all-cause mortality.

(26.8%) were identified with probable sarcopenia, while two patients (2.5%) met the criteria for sarcopenia. Compared to the EWGSOP2 criteria, the newly established cut-off points for HGS and gait speed demonstrated better prognostic value for predicting overall mortality in the diagnosis of sarcopenia. EWGSOP2 criteria present a diagnosis of sarcopenia derived from healthy individuals.⁸ Depending on the changing physiology and body composition in CKD, the sarcopenia components (muscle strength, mass, and

Table 3. Agreement rate of mortality according to EWGSOP2

	Cut off value			Percentage of below reference			Total agreement rate			Kappa	
	Female	Male	Total	Female	Male	Total	Female	Male	Total	Female	Male
HGS (kg)											
Derived cut off	<11.5	<18.0	19	9	10	69.5	70.3	68.9	0.288	0.361	0.212
EWGSOP 2	<27	<16	41	16	25	57.3	56.8	57.9	0.146	0.119	0.190
SMMI (kg/m ²)											
Derived cut off	<6.7	<9.0	20	9	11	63.4	59.5	66.7	0.152	0.152	0.154
EWGSOP 2	<5.5	<7.0	2	2	0	65.9	62.2	78.9	0.144	0.140	0.153
Gait speed (m/s)											
Derived cut off	≤0.43	≤0.53	611	26	37	72.0	69.3	72.3	0.150	0.144	0.167
EWGSOP 2	≤0.8	≤0.8	80	33	37	51.2	54.1	44.4	0.139	0.169	0.106
In combination (HGS, SMMI and gait speed)											
Derived cut off			24	9	15	63.4	59.5	66.7	0.193	0.131	0.152
EWGSOP 2			41	16	25	57.3	56.8	57.8	0.146	0.119	0.190

EWGSOP: European Working Group on Sarcopenia in Older People; HGS: Handgrip strength; SMMI: Skeletal Muscle Mass Index.

physical function) may differ from the general population.²² There is no universally accepted sarcopenia definition tailored for CKD patients, and body composition differences may influence the applicability of existing criteria. Future studies should aim to validate population-specific thresholds that better predict clinical outcomes in dialysis patients. Previous studies reported that the sarcopenia prevalence, according to different classifications, widely ranged between 11–63% in dialysis patients.^{2,23–25} This may be attributed to the fact that new cut-off values need to be derived for individuals treated with dialysis. To search for appropriate cut-off values in our study sample, we applied the lowest quartiles for each sarcopenia component recommended by several study groups.¹² Our findings showed that gait speed and muscle strength might be more predictive of survival than muscle mass.

The HGS cut-off value derived from our patients had a higher total agreement rate of 69.5 versus 57.3 and was a better prognostic value for predicting mortality than cut-off points of EWGSOP2 criteria. The HGS cut-off value derived from our patients showed a higher total agreement rate of 69.5% compared to 57.3% and proved to be a more effective prognostic indicator for predicting mortality than the cut-off points based on EWGSOP2 criteria. Xu et al.¹⁰ determined the HGS cut-off values as 24.5 for males and 14.0 for females in adult patients on peritoneal dialysis. These points were higher than our cut-off for HGS. We argue that this may be related to a younger sample than our study.

Similar to our study, lower sarcopenia cut-off values than EWGSOP2 criteria were more compatible with mortality.¹⁰ Our results are consistent with Vogt et al.,²⁶ who reported that HGS was an independent all-cause mortality risk factor among patients undergoing hemodialysis or peritoneal dialysis. Muscle mass did not significantly differ when determined by MAMC among survivors and non-survivors.²⁶ Besides, a few studies showed that HGS using various cut-off points to define low muscle strength was an independent mortality risk factor.^{6,27} Since the HGS test is simple, cheap, and unaffected by the hydration situation, its use in dialysis patients may be considered to improve mortality estimates.

Based on our findings, muscle strength, and functional performance seem to serve as more robust indicators of mortality compared to muscle mass among dialysis patients. While low muscle mass was not significantly linked to mortality, loss of muscle strength was related to physical ability and survival. This may suggest that other factors, such as muscle relaxation and atrophy, also play a contributory role in muscle weakness beyond just low muscle mass.^{28,29} Additionally, muscle strength's better reflection of neuromuscular functions and physical performance may have been influential, as these factors are critical for daily activities and survival. Moreover, skeletal muscle mass index (SMMI) may be affected by factors such as fluid retention and hydration status, which could limit its prognostic reliability in dialysis patients. A study presented that 78% of the dialysis patients in the muscle biopsies had

morphological abnormalities. Of these patients, 45% had atrophy in fiber type I provided by slow-switch and in fiber type II provided by fast-switch (40% of all patients).²⁸ There is also evidence of muscle hydration changes in calf muscles during the dialysis process.

Recently, Isoyama et al.⁶ derived cut-off values according to below 2 SD of EWGSOP2 reference for muscle mass. In addition, they found that reduced quantity is not linked to death among individuals on dialysis. Another longitudinal study defined low muscle mass as ≤ 2 SD of the normal range for the young population and low muscle strength based on EWGSOP2 criteria cut-off values in older adults undergoing HD. It was reported that both reduced muscle quantity and strength were associated with all-cause mortality. This finding contradicts our findings for two reasons: first, the study was conducted on an Asian population, which generally has lower lean tissue mass compared to other populations. Second, they used cut-off values derived from a young reference population for sarcopenia definition.⁵ Our findings support the hypothesis that muscle function deteriorates independently of muscle mass loss.

When we defined slow gait speed as below 0.53 m/s for males and below 0.43 m/s for females, slowness seemed to be a better predictive value for mortality than EWGSOP2 criteria (total agreement rate: 72.0 for the derived cut-off value versus 51.2 for EWGSOP2 cut-off value). Indeed, slow gait speed was a more prognostic factor than HGS and SMMI in predicting mortality. A study determined a cut-off of 0.6 m/s for gait speed in hemodialysis patients, and low gait speed was associated with mortality.³⁰ In a study adopting a methodology similar to our study, using the new cut-off values for sarcopenia, both low HGS and low gait speed were good predictors, and low muscle mass was less critical for predicting mortality, thereby corroborating the findings of our study.³¹ HGS and gait speed provide integrated information about muscle strength, size, activation, and neural regulation, with the possible additional balance for gait speed. HGS and gait speed offer comprehensive insights into muscle size, strength, activation, and neural regulation, with gait speed potentially reflecting an additional aspect of balance.

Our study sample was limited to a single center. We plan to confirm these findings with a larger sample through a multi-center prospective study. Concerns about bias may arise because BIA measurements of lean body mass can be influenced by the individual's fluid balance. Therefore, we carried out a BIA assessment for all patients in the post-dialysis period to maintain fluid normalities.

CONCLUSION

Throughout the follow-up examination, the newly derived cut-off values for low muscle strength (reflected by HGS) and low physical performance (reflected by gait speed) showed a stronger correlation with mortality risk compared to low muscle mass (reflected by SMMI). These results need further validation by employing an expanded sample for a diagnosis of sarcopenia in individuals treated with dialysis. The assessment of HGS and gait speed are simple, cheap, and unaffected by hydration situation; their use in patients undergoing dialysis may be regarded as improving mortality estimates. In light of these findings, treatment strategies for dialysis patients should focus not only on preserving or increasing muscle mass but also on enhancing muscle functionality. Improving muscle functionality could represent an important step towards the enhancement of physical functioning and reduction of mortality in older adult dialysis patients.

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Informed Consent: Written informed consent was obtained from patients who participated in this study.

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