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Review Article

Assessment of uremic sarcopenia in dialysis patients: An update

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Abstract

Uremic sarcopenia, which is highly prevalent in dialysis patients, leads to an increased risk of adverse outcomes, such as poor quality of life, falls, fracture, hospitalization, and even mortality. Therefore, early detection of uremic sarcopenia is crucial for administering quick and adequate multidisciplinary therapy to improve clinical outcomes. This review updates the current information about uremic sarcopenia assessment in chronic dialysis patients. We discuss the methods of assessing skeletal muscle mass, strength, and physical performance. We also discuss surrogate markers derived from serum and dialysate creatinine, in addition to emerging screening tools. The prevalence, clinical relevance, and impact of uremic sarcopenia on survival are reviewed and we discuss the limitations and challenges in applying the current working definition of sarcopenia based on the senior population to dialysis patients. The review shows that dialysis patients with skeletal muscle weakness or poor physical performance, either with or without low skeletal muscle mass, should undergo multidisciplinary therapy, included nutritional counseling, lifestyle modification, and exercise intervention, to mitigate the detrimental effects of uremic sarcopenia.

Keywords: *Dialysis, Physical performance, Skeletal muscle mass, Skeletal muscle strength, Uremic sarcopenia*

Introduction

Protein-energy wasting (PEW), a malnutrition status involving a progressive decline of the body's stores of protein and energy fuels, is common in patients with chronic kidney disease (CKD) [1,2]. The prevalence of PEW increases progressively as renal function declines. Up to 75% of end-stage renal disease patients in the United States suffer from PEW [3]. In Taiwan, the estimated prevalence of PEW in dialysis patients ranges from 44% to 58% [1]. The development of PEW leads to a loss of skeletal muscle mass with skeletal muscle weakness or impaired physical performance. This condition is called uremic sarcopenia [4].

Sarcopenia is first described by Irwin Rosenberg in 1989 to define the process of age-related loss of skeletal muscle mass, which leads to poor quality of life and increased risk of adverse outcomes, such as falls, bone fractures, hospitalization, and death [5]. In Asian community-dwelling older adults, the prevalence of sarcopenia ranges from 7% to 12% [6-9]. In CKD patients, renal function deterioration is accompanied by skeletal muscle mass loss [10]. The prevalence of sarcopenia is 6%–14% in non-dialysis CKD [10,11], and this risk is markedly increased in dialysis patients with end-stage renal disease [12-14].

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The pathogenesis of uremic sarcopenia is intricate and multifactorial. Beyond the factors commonly observed in older adults, such as the decline in exercise and protein intake, Vitamin D deficiency, growth hormone resistance, decreased sex hormones, and underlying comorbid conditions, dialysis patients are more susceptible to sarcopenia due to the loss of amino acids and other nutrients during dialysis [15]. In addition, metabolic acidosis, insulin resistance, inflammatory status, and overexpression of angiotensin II and myostatin in dialysis patients activate the ATP-dependent ubiquitin-proteasome system, the main pathway of skeletal muscle protein degradation in CKD [15-19]. Recently, indoxyl sulfate, a poorly dialyzable gut-derived uremic toxin, is also implicated in the pathogenesis of uremic sarcopenia through inducing mitochondrial dysfunction and overexpression of two muscle atrophy-related genes, atrogin-1, and myostatin [20-23].

There is a close link between uremic sarcopenia and mortality in dialysis patients. Compared to those without

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sarcopenia, dialysis patients with sarcopenia have a two-to three-fold increase in the hazard ratio (HR) for mortality [13,24,25]. Therefore, accurate assessment of skeletal muscle mass and function in the clinical setting and timely detection of uremic sarcopenia in these patients is crucial for administering quick and adequate multidisciplinary therapy to improve survival. This review updates the current information about uremic sarcopenia assessment in chronic dialysis patients.

Measurement of skeletal muscle mass

Mid-arm muscle circumference

Mid-arm muscle circumference (MAMC) is a conventional anthropometric measure to evaluate skeletal muscle mass. It is calculated as follows:

MAMC (cm) = Mid-arm circumference (cm) – (3.14 × Triceps skinfold thickness [cm]) (1)

Noori *et al*. showed that the MAMC is well correlated with the lean body mass measured by dual-energy X-ray absorptiometry (DEXA) in hemodialysis (HD) patients; a higher MAMC was associated with a better quality of life and 5-year survival in 792 maintenance HD patients [26]. Similarly, a median follow-up of 1709 HD patients for 2.5 years showed that a lower MAMC is associated with higher overall mortality [27]. A low MAMC is one of the criteria for diagnosing PEW and is defined as a decrease of >10% in relation to the 50th percentile of the reference population [4]. However, well-trained anthropometric operators should perform measurements in order to avoid measurement errors, and preferably, the same operator should monitor series changes to minimize inter-observer variability.

Computed tomography and magnetic resonance imaging

Computed tomography (CT) and magnetic resonance imaging (MRI) are gold standards for measuring regional skeletal muscle mass. In addition, they are useful for quantifying inter-and intramuscular fat infiltration [28-30], which are hallmarks of skeletal muscle wasting in dialysis patients [31]. Increased adipocyte tissue infiltration is a major factor to influences muscle quality, defined as the force generated by each volumetric unit of skeletal muscle tissue [32].

Unfortunately, the widespread use of CT and MRI in the clinical setting is hampered by their high cost and radiation exposure, especially for longitudinal follow-up. DEXA is an alternative low-radiation, high-precision reference standard tool for estimating skeletal muscle mass [33]. Several current consensuses recommend using DEXA for measuring skeletal muscle mass in the assessment of sarcopenia [34-37].

Bioelectrical impedance analysis

Another widely used reliable clinical tool for evaluating the body composition, either total body or appendicular skeletal muscle mass, of dialysis patients is bioelectrical impedance analysis (BIA) [38]. Through the evaluation of electrical characteristics (resistance and reactance), skeletal muscle mass can be estimated by predictive equations.

In dialysis patients, bioelectrical impedance has a good correlation and agreement with DEXA in the assessment of body composition [39-41]. In addition, several studies have confirmed its prognostic significance [42-44]. Moreover, phase angle, the phase difference between voltage and current sinusoidal waveforms, is regarded as an important indicator of cellular integrity and health [45,46]. A low phase angle is associated with increased mortality in both HD and peritoneal dialysis (PD) patients [47-49].

The 2020 National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines recommend BIA's clinical utility for monitoring the nutrition status [50]. Both single-frequency BIA and multi-frequency BIA show adequate accuracy in assessing the body composition compared to DEXA [51]. Although both of them are useful tools for longitudinal follow-up, multi-frequency BIA can provide more precise estimates of intracellular and extracellular fluid [52,53].

To avoid hydration effects in dialysis patients, it is recommended that measurements be performed after an HD session in HD patients and on an empty stomach in PD patients [54]. Since different devices might show significantly different measurements, the same device should be used for a patient [55].

Ultrasound

Another emerging tool for diagnosing sarcopenia is ultrasound, which is easily applicable at the bedside. Studies have shown the validity and reliability of ultrasound in older adults [56,57]. In HD patients, the quadriceps rectus femoris and quadriceps vastus intermedius thickness is significantly correlated with the nutritional status, as assessed by the body mass index, serum albumin, and malnutrition-inflammation score [58]. In addition, the quadriceps rectus femoris thickness is positively correlated with the phase angle and body cell mass assessed by BIA [59]. Beyond the skeletal muscle size, echo intensity can be used as a muscle quality index to predict physical performance in non-dialysis CKD patients [60]. Therefore, ultrasound is a promising assessment tool not only for measuring skeletal muscle mass but also for assessing skeletal muscle quality in dialysis patients. However, further studies are required to confirm these findings.

A comparison of different methods for the assessment of skeletal muscle mass is summarized in Table 1.

Measurement of skeletal muscle strength and physical performance

A dialysis patient's skeletal muscle strength and physical performance depend not only on his or her skeletal muscle mass but also on his or her cardiopulmonary function, overall nutritional status, anemia degree, dialysis dose, underlying comorbidities, and nervous system coordination, which can be considered a comprehensive manifestation of multiple organ systems. Compared to healthy individuals, dialysis patients show significant deficits in skeletal muscle strength and physical performance [15,61].

Table 1: Comparison of available clinical tools for skeletal muscle mass measurement

Tools	Accuracy	Cost	Radiation	Fat infiltration assessment	Operator-dependent	Clinical feasibility
MAMC	++	Low	No	No	Yes	High
BIA	+++	Low	No	No	No	High
DEXA	++++	Moderate	low	No	No	High
CT	++++	High	High	Yes	No	Low
MRI	++++	High	No	Yes	No	Low
Ultrasound	++	Low	No	Yes	Yes	High

MAMC: Mid-arm muscle circumference, BIA: Bioelectrical impedance analysis, DEXA: Dual-energy X-ray absorptiometry, CT: Computed tomography, MRI: Magnetic resonance imaging

Skeletal muscle strength

Handgrip strength measurement using a dynamometer is a simple, widely used tool for assessing skeletal muscle strength in dialysis patients, which is inversely correlated with the malnutrition-inflammation score [62]. Studies have consistently reported the correlation between low handgrip strength and increased mortality in dialysis patients [63-66]. A meta-analysis of nine prospective cohort studies by Hwang *et al*. showed that compared to the high-handgrip-strength group, the low-handgrip-strength group had 1.88 times higher risk of all-cause mortality, while a per kilogram unit increase in handgrip strength decreased the HR for mortality by 5% [67]. Vogt *et al*. established the best cut-off to predict mortality in dialysis patients is <22.5 kg in males and <7.0 kg in females [65]. Two studies compared the handgrip strength differences before and after HD sessions and reported a significant decrease in handgrip strength after HD sessions [68,69]. Therefore, handgrip strength assessment of HD patients should be performed before the HD session.

The isokinetic dynamometer is a gold standard for evaluating the skeletal muscle strength of lower extremities in the general population and also in dialysis patients with good accuracy [70,71]. However, the equipment is expensive and not widely available in clinical practice. An alternative is the portable hand-held dynamometer, whose results, which when used by well-trained operators, correlate well with those of isokinetic testing [72,73].

Physical performance

Among various physical performance assessments, the simplest method widely used in clinical practice is the usual gait speed measurement during walking for 4–6 m in a straight path at the usual speed. Gait speed is not only closely correlated with quality of life but also strongly linked to the risk of falls, hospitalization, and mortality in dialysis patients [25,74-76]. Compared to HD patients with a gait speed of ≥0.6 m/s, the adjusted HRs for mortality are 2.17 and 6.93 for HD patients with a gait speed of <0.6 m/s and those unable to walk, respectively [75].

Other common tests for assessing physical performance and evaluating the effects of exercise on dialysis patients include the 6-min walk, repeated sit-to-stand, time-up-and-go, intermittent shuttle walk, stair climb, and short physical performance battery tests. The last comprises three tests: 4 m gait speed, five-time repeated sit-to-stand, and balance assessment in different standing positions. Painter and Marcus provided an excellent review of the evaluation of physical function in CKD patients [77].

Working diagnosis of sarcopenia and related research in dialysis patients

Table 2 summarizes the current consensus for the operating definitions of sarcopenia. The skeletal muscle mass, measured by either DEXA or BIA, is usually divided by height squared or the BMI for adjustment. Diagnosis of sarcopenia is based on the presence of low muscle mass as an essential criterion, accompanied by either low HGS or slow gait speed.

Although the definition of sarcopenia is well established in the older population [34-37], there is no consensus on the working diagnosis of uremic sarcopenia in dialysis patients. Most research on uremic sarcopenia applies the geriatric definition to dialysis patients, which leads to heterogenicity in the prevalence of uremic sarcopenia. For example, in older maintenance HD patients, the prevalence of uremic sarcopenia by applying different criteria widely ranges from 3.9% to 63.3% [79]. In addition, the best indices for adjusting the skeletal muscle mass in dialysis patients are unclear. In HD patients, while adjustment by height squared is commonly adopted, the prevalence of uremic sarcopenia using four different indices for low skeletal muscle mass ranges from 3.9% to 15.9%. There is a risk of underestimating the prevalence of low muscle mass if the skeletal muscle mass is normalized to height squared, especially in overweight and obese patients. Adjustments for body size, such as the BMI and body surface area, might better define uremic sarcopenia in these patients with low muscle mass [80].

Table 3 summarizes some of the recent studies on dialysis patients. Compared to HD patients, two studies showed that PD patients have a lower prevalence of sarcopenia [83,85]. This discrepancy could be largely explained by different characteristics between HD and PD patients. Regarding the difference risk of sarcopenia between diabetes mellitus (DM) and non-DM dialysis patients, Mori *et al*. showed that DM has a 3.11-fold odds ratio to have sarcopenia [12].

Relevance of skeletal muscle mass and strength in dialysis patients: dilemma regarding uremic sarcopenia diagnosis

Although low skeletal muscle mass is well-established to be associated with poor clinical outcomes in dialysis patients, few previous studies evaluated its impacts together with muscle

Table 2: Current consensus for the operational definitions of sarcopenia

Measures	**EWGSOP 2019** [78]	**AWGS 2019** [9]	**FNIH 2014** [37]	**IWGS 2011** [36]
Skeletal muscle mass	ASM:	ASMI (BIA):	ASM:	ASMI (DEXA):
	Male <20 kg	Male <7.0 kg/m^2	Male <19.75 kg	Male <7.23 kg/m^2
	Female <15 kg	Female <5.7 kg/m^2	Female <15.02 kg	Female <5.67 kg/m^2
	ASMI:	ASMI (DEXA):	ASM/BMI:	
	Male <7.0 kg/m^2	Male <7.0 kg/m^2	Male <0.789	
	Female <6.0 kg/m^2	Female <5.4 kg/m^2	Female <0.512	
Muscle strength	HGS:	HGS:	HGS:	
	Male <27 kg	Male <28 kg	Male <26 kg	—
	Female <16 kg	Female <18 kg	Female <16 kg	
			HGS/BMI:	
			Male <1.0	
			Female <0.56	
Usual gait speed (m/s)	≤0.8	<1.0	≤0.8	<1.0
Other physical performances	SPPB ≤8	SPPB ≤9		
	5-time STS >15 s	5-time STS ≥12 s	—	—
	TUG ≥20 s			
	400 m walk test ≥6 min or non-completion			
Screening tools	SARC-F ≥4	Calf circumference:		
		Male <34 cm	—	—
		Female <33 cm		
		SARC-F ≥4		
		SARC-CalF ≥11		
Diagnostic criteria	**Sarcopenia probable:** low muscle strength or poor STS test	**Possible sacropenia:** low muscle strength or poor performance	**Sacropenia:** low muscle mass+low muscle strength	**Sarcopenia:** low muscle mass+slow gait speed
	Sarcopenia: low muscle mass + low muscle strength	**Sarcopenia:** low muscle mass + low muscle strength or poor performance		
	Severe sarcopenia: low muscle mass+low muscle strength + poor performance	**Severe sarcopenia:** low muscle mass + low muscle strength + poor performance		

EWGSOP: European Working Group on Sarcopenia in Older People, AWGS: Asian Working Group for Sarcopenia, FNIH: Foundation for the National Institutes of Health, IWGS: International Working Group on Sarcopenia, ASM: Appendicular skeletal muscle, ASMI: ASM index, BMI: Body mass index, HGS: Handgrip strength, SPPB: Short Physical Performance Battery, STS: Sit-to-stand test; TUG: Time up and go test, BIA: Bioelectrical impedance analysis, DEXA: Dual-energy X-ray absorptiometry, SARC-F: Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls; SARC-CalF: SARC-F combined with calf circumference

strength and physical performance. Isoyama *et al*. showed in 330 incident dialysis patients that low skeletal muscle mass alone does not increase the risk of mortality, while patients with low skeletal muscle strength are at increased risk of mortality regardless of skeletal muscle mass [13]. Similarly, in our chronic HD patients with normal skeletal muscle mass, those with skeletal muscle weakness or slow gait speed remain at high risk of hospitalization and mortality [84]. Kittiskulnam *et al*. showed that, in HD patients, slow gait speed and weak handgrip strength are independently associated with mortality, but low skeletal muscle mass is not, regardless of normalization to height squared, body weight, BMI, or body surface area [25]. Altogether, compared to skeletal muscle mass, skeletal muscle strength and physical performance are more closely correlated with the risk of mortality in dialysis patients.

Notably, the prevalence of skeletal muscular dysfunction is considerably higher compared to low skeletal muscle mass in dialysis patients [14,83-85]. Therefore, the diagnosis of uremic sarcopenia in dialysis patients by applying geriatric criteria is mainly driven by skeletal muscle mass, which is the prerequisite for diagnosing sarcopenia. This approach might overlook patients with only skeletal muscle weakness. In addition, during the muscle wasting process, the loss of skeletal muscle strength could occur earlier and be more rapid than the loss of skeletal muscle mass [86]. Accordingly, dialysis patients diagnosed as having sarcopenia, with concurrent low skeletal muscle mass and strength, may implicate the late stage of muscle wasting. In this regard, skeletal muscle strength and physical performance measurement should be the initial step in uremic sarcopenia assessment. Dialysis patients with skeletal muscle weakness or poor physical performance should be encouraged to modify their lifestyle, diet, and exercise, even with preserved skeletal muscle mass.

Regardless of the methods and criteria used, periodic and longitudinal monitoring of the body composition,

Table 3: Prevalence rates of uremic sarcopenia among different studies

Author	Population	Age (years)	Definition	Prevalence	Main findings
Kim *et al*., 2014 [81]	95 prevalent HD patients	63.9±10.0	EWGOSP, 2010	33.7%	Sarcopenia is associated with subjective global assessment, inflammatory markers, beta2-microglobulin, depression and cognitive dysfunction.
Isoyama *et al*., 2014 [13]	330 incident dialysis patients	53±13	EWGOSP, 2010	20%	Low muscle strength was more closely associated with aging, protein-energy wasting, physical inactivity, inflammation, and mortality than low muscle mass.
Ren *et al*., 2016 [82]	131 prevalent HD patients	49.4±11.7	EWGOSP, 2010	13.7%	1. The prevalence of sarcopenia increased with age. 2. Dialysis duration, diabetes, serum phosphorus level and malnutrition are the predisposing factors for sarcopenia. 3. The 1-year mortality risk of sarcopenic patients was higher than that of non-sarcopenic patients.
Kittiskulnam *et al*., 2017 [80]	645 prevalent HD patients	56.7±14.5	Low SMI: (A) muscle mass/height^2 (kg/m^2): <7.89 in men and 6.05 in female (B) muscle mass/weight (%): 32.68 in men and 27.85 in female (C) muscle mass/BSA (kg/m^2): 14.31 in men and 11.64 in female (D) muscle mass/BMI (m^2): 0.97 in men and 0.72 in female Low HGS: <30 kg for men and<20 kg for women	(A) 3.9% (B) 11.4% (C) 15.9% (D) 14.0%	1. Skeletal muscle mass normalized to height square may underestimate the prevalence of low muscle mass, particularly among overweight and obese patients. 2. Valid detection of sarcopenia among obese patients receiving HD requires adjustment for body size.
Bataille *et al*., 2017 [14]	111 prevalent HD patients	77.5 (70.8-84.8)	EWGSOP, 2010	31.5%	Regarding the low muscle strength in the large majority of HD patients, the diagnosis of sarcopenia was mainly driven by muscle mass measurement.
As'habi *et al*., 2018 [83]	79 prevalent PD patients	18 to 40 years: 21.5% 41 to 64 years: 52.0% ≥ 65 years: 26.5%	EWGSOP, 2010	11.5%	1. Dynapenia was associated with age, physical activity level, and the presence of diabetes mellitus. 2. Male patients had a significantly higher prevalence of sarcopenia than female patients.
Giglio *et al*., 2018 [24]	170 prevalent HD patients	70±7	EWGSOP, 2010	36.5%	1. Reduced muscle mass was strongly associated with poor nutritional status, while low muscle strength was associated with worse quality of life. 2. Low muscle strength alone and sarcopenia were independently associated with higher hospitalization, and sarcopenia was a predictor of mortality.
Mori *et al*., 2019 [12]	308 prevalent HD patients	54.4±11.0 (non-sarcopenic patients) 63.5±11.0 (sarcopenic patients)	AWGS, 2014	40%	1. Patients with sarcopenia exhibited a higher all-cause mortality rate than those without sarcopenia. 2. Diabetes mellitus was independently associated with sarcopenia and was an independent risk factor of all-cause mortality.
Lin *et al*., 2020 [84]	126 prevalent HD patients	63.2±13.0	EWGOSP, 2010 Taiwanese criteria	13.5% 8.7%	1. Sarcopenia was associated with 3-year mortality. However, in patients without sarcopenia, close associations between increased hospitalization and mortality risk with low handgrip strength and slow gait speed remained unchanged. 2. Muscle quality and serum creatinine were independently associated with composite outcomes of hospitalization or death.

Contd...

Table 3: Contd...

Author	Population	Age (years)	Definition	Prevalence (%)	Main findings
Abro *et al*., 2020 [85]	155 Prevalent PD patients	63.0±14.9	FNIH EWGSOP, 2011 AWGS, 2014	11.0-15.5	1. The prevalence of sarcopenia in PD was much lower compared to studies in HD patients. 2. There was similar prevalence of sarcopenia using EWGSOP, FNIH, AWGS definitions.

EWGOSP, 2010: low ASMI: <7.23 kg/m^2 in men and<5.67 kg/m^2 in women or low SMI: <10.76 kg/m^2 in men and<6.76 kg/m^2 in women; low HGS: <30 kg for men and<20 kg for women; slow GS: ≤ 0.8 m/s . AWGS, 2014: low ASMI: <7.0 kg/m^2 in men and<5.7 kg/m^2 in women; low HGS: <26 kg for men and<18 kg for women; slow GS: ≤ 0.8 m/s . Taiwan criteria: low SMI: <8.87 kg/m^2 in men; <6.42 kg/m^2 in women (≥ 2 SD below the means of healthy young Taiwanese adults); low HGS: <26 kg for men and<18 kg for women; slow GS: ≤ 0.8 m/s

skeletal muscle strength, and physical performance changes in dialysis patients could provide a more comprehensive assessment of uremic sarcopenia, which may be more closely associated with prognostic significance compared to single measures [87,88].

Surrogate markers of sarcopenia

Creatinine is a breakdown product of creatine phosphate from skeletal muscle tissue and is a well-known serum surrogate for skeletal muscle wasting in dialysis patients. Low serum creatinine levels (pre-HD levels for HD patients), which indicate low skeletal muscle mass, increase the risk of mortality for dialysis patients without residual renal function [89,90]. Creatinine kinetics, which estimates the skeletal muscle mass from pre-HD serum creatinine, 24-h dialysate, and urinary creatinine excretion with a steady status, is significantly correlated with skeletal muscle mass measured by BIA and DEXA in both HD and PD patients [91,92].

Given the complexity of creatinine kinetics, Noori *et al*. and Canaud *et al*. developed formulas for estimating the skeletal muscle mass of HD patients using pre-HD serum creatinine levels and routine clinical parameters [93-95]. The skeletal muscle mass estimated by the two formulas had a good correlation with the skeletal muscle mass measured using multifrequency BIA and near-infrared interactance. Table 4 summarizes the skeletal muscle mass estimation formula using creatinine kinetics, the Noori formula, and the Canaud formula.

Clinical approach of uremic sarcopenia

A proposed algorithm for the evaluation of uremic sarcopenia is shown in Figure 1. We suggest measurement of handgrip strength and physical performance as the initial approach. Patients with preserved handgrip strength and physical performance, who are not at increased risk of adverse outcomes, should be regularly re-evaluated, while those with either low handgrip strength or poor performance should be further evaluated through BIA or DEXA to determine the skeletal muscle mass volume. If BIA and DEXA are not available, it is reasonable to estimate skeletal muscle mass through creatinine kinetics, Noori formula, and simplified creatinine index. Multidisciplinary management should be provided for any patients with low handgrip strength or poor performance, either accompanied by low skeletal muscle mass (sarcopenia) or not (poor muscle quality).

Potential tools for screening uremic sarcopenia: SARC-F and SARC-CalF questionnaires

To our knowledge, no tool has been validated for screening uremic sarcopenia. SARC-F, an easy-to-apply, semi-reported questionnaire, is recommended for initial screening of geriatric sarcopenia by the Asian Working Group for Sarcopenia and the European Working Group on Sarcopenia in Older People (EWGSOP)[9,78]. The SARC-F questionnaire contains five items: Sluggishness, assistance in walking, rise from a chair, climb stairs, and falls. Each item is scored as 0 (no difficulty), 1 (some difficulty), or 2 (many difficulties or inability). The total score ranges from 0 to 10, and SARC-F ≥4 is considered an increased risk of sarcopenia [96]. Table 5 shows details of the SARC-F questionnaire.

However, despite its high specificity for diagnosing sarcopenia, the SARC-F questionnaire yields low sensitivity in the geriatric population. To overcome this issue, the SARC-CalF questionnaire was developed, which includes an additional item, calf circumference measurement. In the SARC-CalF questionnaire, 10 points are added to the original SARC-F score if the calf circumference is ≤34 cm for males and ≤33 cm for females. SARC-CalF ≥11 is considered an increased risk of sarcopenia [97].

In HD patients, Yamamoto *et al*. first reported the use of the SARC-F questionnaire and showed good accuracy in identifying HD patients with physical limitations [98]. However, further studies are required to determine whether the SARC-F or SARC-CalF questionnaire can be a useful tool for initial screening of dialysis patients and what the best cut-off in this population should be.

Management of uremic sarcopenia

In addition to optimal dialysis delivery and treatment of comorbidities that accelerate muscle loss (such as infection, DM, cardiovascular disease, chronic wounds, gastrointestinal disorders, depression, and malignancy), nutritional supplementation and physical exercise are the cornerstones of uremic sarcopenia management [99]. Adequate energy (30–35 kcal/kg/day) and high protein intake (daily protein intake 1.2 g/kg/day) should be achieved to overcome the devastating process of muscle wasting [100]. Aerobic and resistance exercise, which are feasible and safe in dialysis patients, is not only shown to improve functional capacity and

Table 4: Skeletal muscle mass estimation equations from creatinine kinetics, Noori formula and simplified creatinine index

Creatinine kinetics [91]
Excretion (mg/day) = Urine volume (mL/day) × Urine creatinine (mg/mL) + Dialysate volume (mL/day) × Dialysate creatinine (mg/mL)
Metabolic degradation (mg/day) = 0.38 × Serum creatinine (mg/dL) × Post-HD weight (kg)
Production (mg/day) = Excretion+Metabolic degradation
Skeletal muscle mass (kg) = 0.029 × Production +7.38
Noori formula [93]
Skeletal muscle mass (kg) = 0.34×Pre-HD Serum creatinine (mg/dL) + 5.58 × (1 if male; 0 if female) + 0.30 × Post-HD weight (kg) + 0.67 × Height (inches) - 0.23 × URR - 5.75
Canaud formula [94,95]
Simplified creatinine index (mg/kg/day) = 16.21+1.12 × (1 if male; 0 if female) - 0.06×Age (years) - 0.08 × spKt/V + 0.009 × Pre-HD serum creatinine (μmol/L)
Skeletal muscle mass (kg) = Simplified creatinine index × Post-HD weight (kg) × 0.029 + 7.38

HD: Hemodialysis, URR: Urea reduction ratio, spKt/V: Single-pool $Kt/_{Vurea}$

Table 5: SARC-F questionnaire for sarcopenia screening

Item	Question	Scoring
Strength	How much difficulty do you have in lifting and carrying 10 pounds?	None=0 Some=1 A lot or unable=2
Assistance in walking	How much difficulty do you have walking across a room?	None=0 Some=1 A lot, use aids, or unable=2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None=0 Some=1 A lot or unable=2
Climb stairs	How much difficulty do you have climbing a flight of 10 stairs?	None=0 Some=1 A lot or unable=2
Falls	How many times have you fallen in the past year?	None=0 1-3 falls=1 4 or more falls=2

SARC-F: Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls

quality of life but also increase muscle strength and physical performance [101,102].

Some other emerging and promising treatment strategies included vitamin D, androgens, growth hormone, anti-myostatin antibody, and AST-120, as well as novel strategies targeting myogenic satellite cells, epigenome, and pro-inflammatory cytokines [103-105]. However, more trials are warranted before firm conclusions can be drawn.

Conclusion

This review highlighted the importance of uremic sarcopenia assessment in clinical practice, which should be incorporated into the general nutritional assessment for dialysis patients. Given the relevance and clinical effects of skeletal muscle mass and function, dialysis patients with skeletal muscle weakness or poor physical performance, either with or without low skeletal muscle mass, should be identified early for nutritional counseling, lifestyle modification, and exercise intervention to mitigate the detrimental effects of uremic sarcopenia.

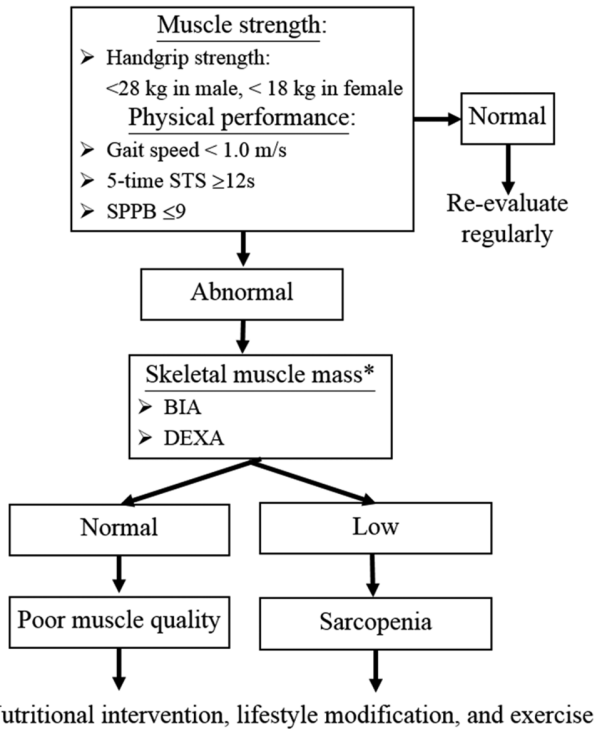

Figure 1: Proposed algorithm for the evaluation of uremic sarcopenia. *Creatinine kinetics, Noori formula and simplified creatinine index may be used for skeletal muscle mass estimation if BIA or DEXA is not available. STS: Sit-to-stand test, SPPB: Short Physical Performance Battery, BIA: Bioelectrical impedance analysis, DEXA: Dual-energy X-ray absorptiometry

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Conflicts of interest

Dr. Bang-Gee Hsu, an editorial board member at *Tzu Chi Med J*, had no role in the peer review process or decision to publish this article. The other author declared no conflict of interest in writing this paper.

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