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ORIGINAL ARTICLE

Sarcopenia in chronic kidney disease on conservative therapy: prevalence and association with mortality

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ABSTRACT

Background. In chronic kidney disease (CKD), multiple metabolic and nutritional abnormalities contribute to the impairment of skeletal muscle mass and function thus predisposing patients to the condition of sarcopenia. Herein, we investigated the prevalence and mortality predictive power of sarcopenia, defined by three different methods, in non-dialysis-dependent (NDD) CKD patients.

Methods. We evaluated 287 NDD-CKD patients in stages 3–5 [59.9 ± 10.5 years; 62% men; 49% diabetics; glomerular filtration rate (GFR) 25.0 ± 15.8 mL/min/1.73 m^2]. Sarcopenia was defined as reduced muscle function assessed by handgrip strength (HGS <30th percentile of a population-based reference adjusted for sex and age) plus diminished muscle mass assessed by three different methods: (i) midarm muscle circumference (MAMC) <90% of reference value (A), (ii) muscle wasting by subjective global assessment (B) and (iii) reduced skeletal muscle mass index (<10.76 kg/m^2 men; <6.76 kg/m^2 women) estimated by bioelectrical impedance analysis (BIA) (C). Patients were followed for up to 40 months for all-cause mortality, and there was no loss of follow-up.

Results. The prevalence of sarcopenia was 9.8% (A), 9.4% (B) and 5.9% (C). The kappa agreement between the methods were 0.69 (A versus B), 0.49 (A versus C) and 0.46 (B versus C). During follow-up, 51 patients (18%) died, and the frequency of sarcopenia was significantly higher among non-survivors. In crude Cox analysis, sarcopenia diagnosed by the three methods was associated with a higher hazard for mortality; however, only sarcopenia diagnosed by method C remained as a predictor of mortality after multivariate adjustment.

Conclusions. The prevalence of sarcopenia in CKD patients on conservative therapy varies according to the method applied. Sarcopenia defined as reduced handgrip strength and low skeletal muscle mass index estimated by BIA was an independent predictor of mortality in these patients.

Keywords: chronic kidney disease, handgrip strength, mortality, muscle mass, sarcopenia

INTRODUCTION

Sarcopenia, recently redefined as an age-related syndrome characterized by progressive decline in both muscle mass and

function [1–4], associates with frailty, disability and increased mortality risk. The perceived relevance of this syndrome is reflected by an increasing number of publications related to the term sarcopenia [5–13]. Although originally known as a condition related to aging, various international societies currently recognize the important role of catabolic diseases, such as chronic kidney disease (CKD), in the etiology of sarcopenia [1–4]. In fact, metabolic derangements inherent to CKD lead to increased protein catabolism, resulting in diminished muscle mass and function, independently of age [14, 15]. Therefore, it can be hypothesized that CKD patients are prone to develop sarcopenia.

The criteria and methods to screen for sarcopenia have been recently reviewed and proposed; in the four consensus reports published so far [1–4], decreased muscle mass and function are mandatory conditions for its diagnosis. In this set, while physical performance tests or muscle strength are accepted surrogates of muscle function, markers of muscle mass are still a matter of debate [2]. This is particularly true among CKD patients who are predisposed to hydration disturbances. In general, the appendicular lean mass assessed by dual X-ray absorptiometry (DXA) has been suggested as a preferable method for the evaluation of muscle mass [2, 4, 16]. However, low availability and high costs of DXA limit its use in clinical practice. BIA is an alternative method to assess muscle mass, which gathers characteristics of low-cost and easy operation, being a more suitable method in the clinical setting. Equations to estimate skeletal muscle index by BIA have been proposed by the European Working Group for Sarcopenia in Older People (1) and are widely accepted screening tools for low muscle mass in the elderly population [17–19]. Anthropometric measurements may also be an easy and low-cost option in clinical practice for muscle mass assessment, and several studies have demonstrated the usefulness of MAMC as a surrogate for muscle mass reduction in CKD population [20]. In addition, an MAMC lower than 90% of the standard adequacy has been associated with mortality in CKD patients starting dialysis [21]. Finally, muscle wasting evaluated by subjective global assessment (SGA) has also been pointed out as a valuable marker in the CKD population [22] being associated with worse survival in these patients [23].

Screening for sarcopenia in a vulnerable population such as CKD patients is warranted. However, studies are still scarce in this population, and they are limited to elderly hemodialysis patients [24, 25]. Herein, we aimed to evaluate the prevalence and prognostic power of sarcopenia, assessed by three different criteria, in non-dialysis-dependent (NDD) CKD patients followed up to 40 months.

MATERIALS AND METHODS

Subjects and study design

This study is an ancillary analysis of the Malnutrition, Inflammation and Vascular Calcification (MIVC) cohort [26, 27]. MIVC is composed of 300 consecutive patients with non-dialyzed CKD stages 3–5 recruited at the outpatient clinic of the Hypertension and Nephrology Division at Dante Pazzanese Institute of Cardiology in Sao Paulo, Brazil. The aim of MIVC was to evaluate the association between traditional, novel and uremic risk factors with cardiovascular and general morbimortality in this population. Recruitment took place between March 2010 and March 2013. Exclusion criteria were age of <18 and >80 years, clinical signs of acute infection during the month preceding the inclusion, active cancer or liver disease at the time of evaluation, previous diagnosis of immunological diseases and unwillingness to participate in the study. The presence of CKD was confirmed by glomerular filtration rate (GFR < 60 mL/min/1.73 m^2) based on 24 h of urinary creatinine clearance. A single physician performed a complete chart review and interviewed each patient regarding their clinical history. For the present study, we excluded 13 patients who did not perform BIA, and thus our population is composed of 287 patients [59.9 ± 10.5 years; 62% men; 49% diabetics; GFR 25.0 ± 15.8 mL/min/1.73 m^2]. The patients were followed from the day of inclusion for all-cause death. There was no loss of follow-up during the study. The Ethics Committee at Dante Pazzanese Institute of Cardiology approved the study, and informed consent was obtained from each patient.

Handgrip strength

Muscle strength was assessed in the dominant hand using a dynamometer (Baseline®, NexGen Ergonomics, Inc., Quebec, Canada). Patients were first familiarized with the device and were then examined standing with both arms extended sideways from the body with the dynamometer facing away from the body. Patients were instructed to grip the dynamometer with the maximum strength in response to a voice command, and the highest value of three measurements was considered for the study. Handgrip strength (HGS) values under the 30th percentile (Table 1) from a specific-population reference value adjusted for age and sex were considered as reduced [28].

Anthropometry

Body mass index (BMI) was calculated as weight in kilograms divided by height in squared meters. MAMC was calculated according to the following equation, based on mid-arm circumference (measured at mid-point from the acromion to olecranon) and the triceps skinfold (using caliper Lange®,

Table 1. Handgrip strength values of the 30th percentile of a population-based reference

Age range (years)	Handgrip strength (kg)			
	Male		Female	
	Right	Left	Right	Left
20–29	41.3	39.4	23.8	22.3
30–39	42.2	40.4	25.0	23.5
40–49	37.5	37.1	24.4	22.9
50–59	36.2	35.0	21.1	19.9
60–69	32.9	30.8	19.6	18.2
≥70	27.7	26.6	13.7	13.0

Cambridge Scientific Industries, Inc.).

$$\text{MAMC (cm)} = \text{midarm circumference (cm)} - \pi \times \left[\frac{\text{triceps skinfold } (mm)}{10}\right]$$

Values of MAMC were compared with the 50th percentile of NHANES II [29] and standard adequacy of <90% was considered as reduced muscle mass [30].

Subjective global assessment

The 7-point SGA was employed to evaluate the nutritional status [31]. Briefly, the SGA is based on two major categories: clinical history and physical examination. Clinical history includes five components (weight change, dietary intake change, gastrointestinal symptoms, functional impairment and comorbidities), and physical examination considers aspects such as reduction in muscle and fat, presence of edema and ascites (both related to nutritional condition). Each of these components is scored from 1 to 7 with the highest value meaning better condition. Then, an overall subjective score is attributed to the patient as 1 to 2 (severely malnourished), 3 to 5 (moderately to mildly malnourished) and 6 to 7 (well nourished). For the purpose of this study, alteration in the physical examination in any of the following sites temples, clavicle, shoulders, spike, pollicis interosseous muscle, knee or quadriceps was considered as muscle wasting.

Bioelectrical impedance analysis

BIA was assessed by a tetrapolar device (Biodynamics® BIA 450 Bioimpedance Analyzer, Seattle, WA, USA). The measurements were made with the patient in the supine position, with the arms lying parallel and separated from the trunk and with the legs separated so that the thighs were not touching. Two electrodes were placed on the hand and wrist and another two were positioned on the foot and ankle of the non-dominant side of the body. An electrical current of 800 A at 50 kHz was introduced into the subject, and resistance and reactance were measured. The Fluid & Nutrition software, version 3.0, was used to calculate the total body water, fat-free mass, fat mass, body cell mass and phase angle.

The following skeletal muscle mass equation developed by Janssen *et al.* and recommended by the EWSOP was used in the present study [32].

$$\text{SMM} = \left[\left(\frac{(\text{height})^2}{\text{resistance}} \times 0.401\right) + (\text{sex} \times 3.825) + (\text{age} \times (-0.071))\right] + 5.102$$

SMM = skeletal muscle mass; height in centimeters; resistance in ohms; sex: women = 0, men = 1; age in years.

Then, the absolute muscle mass (kg) was normalized for squared height and defined as skeletal muscle mass index (SMMI). The cutoff to establish reduced muscle mass was SMMI of <6.76 kg/m² for women and <10.76 kg/m² for men [2, 33].

Sarcopenia diagnosis

The diagnosis of sarcopenia was based on the presence of derangements in both muscle function and muscle mass. For the purpose of the study, we considered one muscle function indicator (reduced HGS) associated with one of three indicators of muscle mass (MAMC, SGA or BIA). Therefore, reduced HGS in association with an MAMC of <90% of the standard adequacy (Method A), presence of muscle wasting by SGA (Method B) or reduced SMMI by BIA (Method C) were considered as diagnosis of sarcopenia.

Laboratorial parameters

Morning blood samples were taken after an overnight fast. Plasma and serum were stored at −70°C, if not analyzed immediately. Serum high-sensitivity C-reactive protein was measured by immune-turbidimetry (Vitros 5600, Ortho Clinical Diagnostics, Raritan, NJ, USA). Albumin and hemoglobin were analyzed using certified methods at the Department of Laboratory Medicine at Dante Pazzanese Institute of Cardiology. The protein nitrogen appearance (PNA) for the estimation of protein intake was calculated according to the equation developed by Sargent and Gotch [34]. The GFR was measured by creatinine clearance from 24-h urinary sample.

Comorbidities

History of comorbidities were calculated by the Charlson comorbidity index [35], which assigns one point for history of myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease (transient ischemic attack or cerebrovascular accident with minor or no residua), dementia, chronic pulmonary disease, connective tissue disorder, peptic ulcer disease, mild liver disease and diabetes without end-organ damage; two points are assigned for hemiplegia, moderate-to-severe renal disease, diabetes with end-organ damage, tumor without metastases, leukemia, lymphoma and myeloma; three points are assigned for moderate or severe liver disease; and six points are assigned for metastatic solid tumor or acquired immune deficiency syndrome (AIDS). For every decade over 40 years of age, one point is added to the score. For the purposes of the present study, all patients received two for the presence of renal disease; and there were no patients with connective tissue disorders, AIDS and/or malignant neoplasm.

Statistical analyses

The variables were expressed in mean ± SD, median (interquartile range) or proportions. Variable distributions were tested by Shapiro Wilk test, and those not normally distributed were standardized by using z-score. Student *t*-test or Chi-square test was employed for the comparisons between sarcopenic and non-sarcopenic patients. Kappa test was used to evaluate the agreement among the methods. Survival analyses were made with the Kaplan–Meier survival curve and the Cox proportional hazard model. The univariate and multivariate Cox-regression analyses are presented as hazard ratio [HR; 95% confidence intervals (CI)]. Statistical significance was set at the level of $P < 0.05$, and the analyses were performed by using the SPSS software version 18 (SPSS, Inc., Chicago, IL, USA).

RESULTS

General characteristics of the patients

The majority of the patients were men (62%), and 53% were over 60 years old. Almost half of the cohort (49%) had diabetes. Mean BMI was indicative of overweight (29.3 ± 5.8 kg/m^2); and 41% of the patients had BMI of ≥30 kg/m^2, 35% a BMI of 25–29.9 kg/m^2, 22% a BMI of 18.5–24.9 kg/m^2 and 2% a BMI of < 18.5 kg/m^2. There were 33% of the patients in stage 3 of CKD, 38% in stage 4 and 29% in stage 5.

Patient characteristics according to the diagnosis of sarcopenia

Figure 1 illustrates the prevalence of sarcopenia by the three methods considered. Demographic, nutritional and laboratory characteristics of the sarcopenic and non-sarcopenic patients according to each method are displayed in Table 2. BMI as well as body cell mass and phase angle were significantly lower among sarcopenic patients when compared with non-sarcopenic ones regardless of the method. GFR, albumin and hemoglobin were all lower among sarcopenic patients identified by Methods A and B. Sarcopenia diagnosed by Method B was the only one that associated with a higher CRP and a lower nPNA. According to the Kappa agreement test, the strongest association was found between Methods A versus B (kappa value of 0.69). The agreement between Methods A and C was 0.49 and between Methods B and C was 0.46.

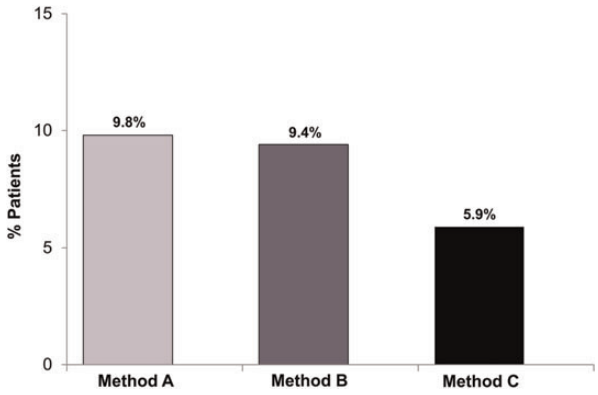

FIGURE 1: Proportion of patients with sarcopenia defined by three different methods in 287 NDD CKD patients. Method A = reduced HGS in association with MAMC of <90%; Method B= reduced HGS in association with muscle wasting by SGA; Method C = reduced HGS in association with reduced SMMI by BIA.

Association of sarcopenia with mortality

During the follow-up, 51 patients (18%) died. Cardiovascular complications accounted for 41% of deaths and included strokes, sudden cardiac death, acute myocardial infarction and aortic artery disease. The remaining causes of death were sepsis, gastrointestinal bleeding, gastrointestinal cancer, respiratory tract infection, respiratory failure, polytrauma, traumatic brain injury and acute pulmonary edema. Table 3 shows the comparison between survivors and non-survivors. The frequency of sarcopenia was significantly higher among non-survivors, independently of the method. In addition, the non-survivors had lower values of phase angle, GFR, albumin, hemoglobin and nPNA. Kaplan–Meier curves showed that sarcopenic patients had lower survival rate, regardless of the diagnostic criterion (Figure 2). In the crude Cox-regression analysis, the three methods were associated with a higher hazard for mortality. However, after the adjustments for potential confounders such as age, sex, BMI, GFR, albumin and Charlson index, only sarcopenia diagnosed by method C remained as an independent predictor of mortality (Table 4).

DISCUSSION

In the present study, we showed that the prevalence of sarcopenia in NDD-CKD patients varied between 5.9 and 9.8% depending on the method used to define muscle mass. The diagnostic criterion based on SMMI by bioelectrical impedance

Table 2. Characteristics of the 287 NDD CKD patients according to the three methods used to diagnose sarcopenia

	Method A (HGS + MAMC)		Method B (HGS + SGA)		Method C (HGS + BIA)	
	Sarc (28)	Non-Sarc (259)	Sarc (27)	Non-Sarc (260)	Sarc (17)	Non-Sarc (270)
Age (years)	59.9 ± 11.8	59.9 ± 10.4	59.0 ± 10.6	60.0 ± 10.5	60.3 ± 11.9	59.8 ± 10.4
Men (%)	82.1	60.2[a]	77.8	60.8	82.4	61.1
Charlson index	7.1 ± 2.3	6.3 ± 2.1[a]	7.3 ± 2.4	6.2 ± 2.0[a]	6.8 ± 2.7	6.3 ± 2.0
Diabetes (%)	53.6	48.3	66.7	46.9	35.3	49.6
BMI (kg/m^2)	23.2 ± 3.2	30.0 ± 5.7[a]	23.6 ± 3.8	29.9 ± 5.7[a]	21.8 ± 3.2	29.8 ± 5.7[a]
Body cell mass (kg)	21.4 ± 5.7	26.3 ± 6.4[a]	21.3 ± 6.0	26.3 ± 6.3[a]	19.4 ± 5.4	26.2 ± 6.3[a]
Phase angle (°)	5.0 ± 1.2	6.2 ± 1.1[a]	4.7 ± 1.0	6.2 ± 1.1[a]	5.4 ± 1.1	6.1 ± 1.1[a]
nPNA (g/kg)	0.91 ± 0.3	1.0 ± 0.3	0.9 ± 0.4	1.0 ± 0.3[a]	0.9 ± 0.3	1.0 ± 0.3
GFR (mL/min)	15.1 ± 7.9	26.0 ± 16.1[a]	14.8 ± 10.0	26.0 ± 15.9[a]	18.1 ± 12.8	25.4 ± 15.9
Albumin (g/dL)	3.4 ± 0.8	3.8 ± 0.5[a]	3.4 ± 0.7	3.8 ± 0.6[a]	3.5 ± 0.5	3.8 ± 0.6
Hb (g/dL)	10.6 ± 2.2	12.3 ± 2.1[a]	10.5 ± 2.1	12.3 ± 2.1[a]	11.5 ± 2.7	12.1 ± 2.1
CRP (mg/dL)	1.4 ± 2.1	0.7 ± 1.3	1.6 ± 2.1	0.7 ± 1.2[a]	1.6 ± 2.4	0.7 ± 1.3
SGA ≤ 5 (%)	78.6	20.8[a]	88.9	20.0[a]	82.4	23.0[a]

Method A, reduced HGS in association with MAMC <90%; Method B, reduced HGS in association with muscle wasting by SGA; Method C, reduced HGS in association with reduced SMMI by BIA; BMI, body mass index; nPNA, protein nitrogen appearance; GFR, glomerular filtration rate; Hb, hemoglobin; CRP, C-reactive protein; SGA, subjective global assessment.
[a]Statistically significant difference (P < 0.05) between patients with and without sarcopenia within each method.

(BIA) analysis was able to predict mortality in this population. To the best of our knowledge, this is the first study that evaluated sarcopenia by assuming muscle mass in combination with muscle function in CKD patients on conservative therapy.

Table 3. Characteristics survivors versus non-survivors during prospective follow-up ($n = 287$)

	Survivors (236)	Non-survivors (51)
Age (years)	59.6 ± 10.3	61.3 ± 11.2
Men (%)	62.7	60.8
Charlson Index	6.3 ± 0.1	6.6 ± 2.2
Diabetes (%)	49.2	47.1
BMI (kg/m^2)	29.3 ± 5.8	29.3 ± 6.3
Body cell mass (kg)	26.0 ± 6.3	24.8 ± 7.0
Phase angle (°)	6.1 ± 1.1	5.7 ± 1.3[a]
HGS (kg)	35.9 ± 11.2	30.0 ± 10.1[a]
nPNA (g/kg)	1.0 ± 0.3	0.9 ± 0.3[a]
GFR (mL/min)	26.1 ± 16.1	19.7 ± 13.3[a]
Albumin (g/dL)	3.8 ± 0.6	3.5 ± 0.6[a]
Hb (g/dL)	12.3 ± 2.1	11.4 ± 2.3[a]
CRP (mg/dL)	0.7 ± 1.3	1.1 ± 1.5
Method A (%)	7.6	19.6[a]
Method B (%)	7.6	17.6[a]
Method C (%)	3.4	17.6[a]

Method A, reduced HGS in association with MAMC <90%; Method B, reduced HGS in association with muscle wasting by SGA; Method C, reduced HGS in association with reduced SMMI by BIA; BMI, body mass index; HGS, handgrip strength; nPNA, protein nitrogen appearance; GFR, glomerular filtration rate; Hb, hemoglobin; CRP, C-reactive protein; SGA, subjective global assessment.
[a]Statistically significant difference ($P < 0.05$) between survivors and non-survivors.

Available literature at a community level shows that the prevalence of sarcopenia varies from 5 to 16% at the age of sixty [36, 37] and from 7 to 34% at the age of seventy [5, 17, 18]. These findings are not only attributed to the differences in studied populations and clinical conditions but also to the differences in the methods applied for the screening of sarcopenia. Although the combination of muscle function and muscle mass parameters chosen is an important factor, variations in the later seems to be one of the most relevant aspects. For instance, the prevalence of sarcopenia found by Arango-Lopera *et al.* (37%) [5] by using calf circumference in combination with reduced HGS or reduced gait speed differed substantially from that reported in other studies (8–13%) with age-matched individuals, which used non-anthropometric surrogates of muscle mass [17, 18]. Accordingly, in the present study, the method using BIA (Method C) exhibited lower prevalence of sarcopenia when compared with MAMC or SGA. In addition, the prevalence of sarcopenia by MAMC (9.8%) and BIA (5.9%) evidenced here was similar to that of other studies that used the same methods, such as Gariballa *et al.* by using MAMC in hospitalized patients [38] and Volpato *et al.* by using BIA in institutionalized elderly [18]. In elderly hemodialysis patients, Lamarca *et al.* also found a lower prevalence of sarcopenia when using BIA in comparison with MAMC (respectively 13

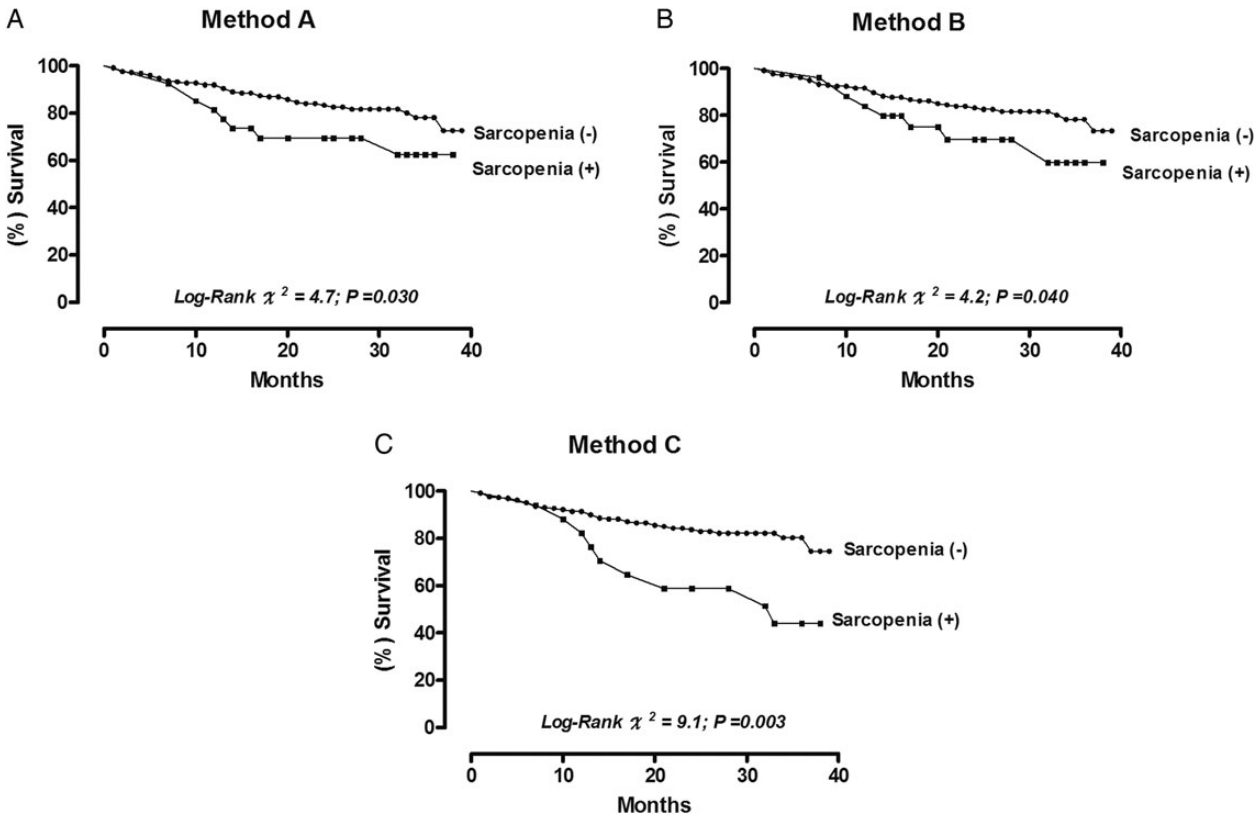

FIGURE 2: Kaplan survival analysis of survival associated with the presence (+) or not (−) of sarcopenia defined by three different methods in NDD CKD patients ($n = 287$). Method A = reduced HGS in association with reduced MAMC <90%; Method B = reduced HGS in association with the presence of muscle wasting evaluated by SGA; Method C = reduced HGS in association with reduced SMMI by BIA.

Table 4. Cox-regression analysis showing the death hazards associated with sarcopenia as diagnosed by different methods in NDD CKD patients ($n = 287$)

	Mortality hazards		P value
	HR	95% CI	
Method A (HGS + MAMC)			
Univariate	2.11	1.06–4.23	0.03
Model 1	2.57	1.15–5.74	0.02
Model 2	1.69	0.72–3.97	0.20
Model 3	1.62	0.69–3.82	0.30
Method B (HGS + SGA)			
Univariate	2.08	1.01–4.28	0.05
Model 1	2.51	1.12–5.63	0.03
Model 2	1.89	0.84–4.31	0.10
Model 3	1.80	0.78–4.17	0.20
Method C (HGS + BIA)			
Univariate	2.89	1.40–5.96	0.004
Model 1	3.58	1.54–8.31	0.003
Model 2	3.11	1.34–7.22	0.008
Model 3	3.02	1.30–7.05	0.010

Method A, reduced HGS in association with MAMC <90%; Method B, reduced HGS in association with muscle wasting by SGA; Method C, reduced HGS in association with reduced SMMI by BIA.
Model 1: adjusted for sex, age and BMI.
Model 2: Model 1 + GFR and albumin.
Model 3: Model 1 + Model 2 + Charlson index.

versus 31%) both in association with reduced HGS [25]. However, when using an unconventional definition for low muscle mass by BIA (<20th percentile of health individuals), the prevalence rose up to 45%, highlighting the importance of cutoffs adopted when interpreting the prevalence of sarcopenia.

MAMC has been the most traditionally used marker of muscle mass in the clinical settings. Nevertheless, its applicability in the context of sarcopenia has been controversial [2]. Gariballa *et al.* considered the lowest tertile of MAMC (<21.1 cm for men and <19.2 cm for women) in combination with reduced HGS to diagnose sarcopenia in elderly hospitalized patients and found an association with poorer outcomes [38]. In our study, we used MAMC of <90% of the adequacy, as suggested by the International Society for Renal Nutrition and Metabolism for protein-energy wasting diagnosis [30]. We found that reduced MAMC associated with reduced HGS was related to lower survival. However, this association disappeared after adjustment for possible confounders. Indeed, although MAMC is an easy and low-cost method, caution has been recommended for routine use of this anthropometric measure in the diagnosis of sarcopenia due to its vulnerability to errors potentially resulting in low accuracy and reproducibility [2, 16].

Muscle wasting evaluated as part of SGA has been broadly accepted in research as well as in the clinical practice [22]. Further, muscle wasting assessed by SGA has been demonstrated to be a predictor of mortality in CKD patients: Carrero *et al.* studied a large number of incident and prevalent dialysis patients and demonstrated that a worse degree of muscle wasting by SGA was associated with a worse 5-year survival [23]. In the current study, only Method B (reduced HGS in combination with muscle wasting by SGA) was able to differentiate inflammatory state between sarcopenic and non-sarcopenic patients. This finding support data regarding the association between inflammation and decreased food intake, which might contribute to the reduction in muscle mass and function by inducing catabolism [39]. Nevertheless, the method failed to detect risk of mortality after the adjustment for confounders. This may be a consequence of the limitations of SGA in detecting the early stages of muscle wasting. In fact, the assessment of muscle mass remains a challenge in several clinical settings, particularly in CKD population.

In our study, reduced muscle mass index by BIA, an inexpensive, noninvasive and easy to reproduce method, in combination with reduced HGS was the only criterion that remained associated with all-cause death, even after adjustment for confounders. The first operational diagnosis of sarcopenia based on muscle mass was stated by Baumgartner and colleagues in 1998, suggesting the usefulness of the height-adjusted appendicular muscle mass index derived from dual-energy X-ray absorptiometry (DXA) [8]. In order to detect a portable alternative to DXA, skeletal muscle by BIA has emerged as a surrogate of muscle mass. Among several threshold approaches established by using BIA [19], the height-adjusted SMMI is the only one that was developed considering physical disability in elderly [33]. Although limitations of BIA have been pointed out for the estimation of specific body compartment such as body fat in CKD patients [40], the muscle mass index derived by BIA, tested by the first time in this population, showed to be a promising predictor of outcomes.

Finally, the decline of muscle function and muscle mass goes beyond aging in patients with chronic diseases, who are additionally predisposed to a number of risk factors for changes in body composition and functional capacity [14, 41]. As alluded earlier, CKD has particular aspects that lead to impairments on skeletal muscle tissue, either in terms of mass or function. Especially in elderly CKD individuals, conditions that take into account similar domains of sarcopenia, such as the frailty syndrome, may overlap with it, leading to a misdiagnosis of this condition [42, 43]. Thus, it has been suggested that detecting sarcopenia in patients with mild-to-moderate renal impairment, when the skeletal muscle complications may still be reversible, is important for the well-being of CKD patients [14]. Actually, an earlier screening of sarcopenia in CKD population may contribute to prevent the frailty syndrome as well. Therefore, to seek reliable and reproducible methods for sarcopenia diagnosis in CKD patients at the earlier stages of the disease is a relevant research line.

Some limitations of this study should be acknowledged such as the lack of information on frailty and physical performance indicators other than HGS. In addition, sample size was relatively low, and a control group was not included. However, we believe that such factors do not compromise the quality of the study and hopefully our observations can contribute to improve the understanding of uremic sarcopenia and stimulate further insight into this topic.

In conclusion, the prevalence and mortality-predictive role of sarcopenia in CKD patients on conservative therapy varied according to the method applied to define muscle mass. Sarcopenia defined as reduced HGS in combination with reduced SMMI estimated by BIA was more strongly associated with mortality risk than HGS combined with either muscle wasting

(obtained by SGA) or reduced muscle mass defined by anthropometry (MAMC). Further studies testing different diagnostic criteria for sarcopenia in different cohorts of CKD patients are warranted.

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CONFLICT OF INTEREST STATEMENT

None declared.

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