ORIGINAL RESEARCH

Muscle Mass Assessed by Computed Tomography at the Third Lumbar Vertebra Predicts Patient Survival in Chronic Kidney Disease

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Objective: Muscle mass is a key element for the evaluation of nutritional disturbances in patients with chronic kidney disease (CKD). Low muscle mass is associated with increased morbidity and mortality. The assessment of muscle mass by computed tomography at the third lumbar vertebra region (CTMM-L3) is an accurate method not subject to errors from fluctuation in the hydration status. Therefore, we aimed at investigating whether CTMM-L3 was able to predict mortality in nondialyzed CKD 3-5 patients.

Methods: This is a prospective observational cohort study. We evaluated 223 nondialyzed CKD patients (60.3 ± 10.6 years; 64% men; 50% diabetics; glomerular filtration rate 20.7 ± 9.6 mL/min/1.73 m^2). Muscle mass was measured by CTMM-L3 using the Slice-O-Matic software and analyzed according to percentile adjusted by gender. Nutritional parameters, laboratory data, and comorbidities were evaluated, and mortality was followed up for 4 years.

Results: During the study period, 63 patients died, and the main cause of death was cardiovascular disease. Patients who died were older, had lower hemoglobin and albumin, as well as lower muscle markers. CTMM-L3 below the 25th percentile was associated with higher mortality according to the Kaplan-Meier curve ($P = .017$) and in Cox regression analysis (crude hazard ratio, 1.87 [95% confidence interval, 1.11-3.16]), also when adjusting for potential confounders (hazard ratio 1.83 [95% confidence interval 1.02-3.30]).

Conclusion: Low muscle mass measured by computed tomography at the third lumbar vertebra region is an independent predictor of increased mortality in nondialyzed CKD patients.

Introduction

A NUMBER OF metabolic derangements inherent to chronic kidney disease (CKD) lead to increased catabolism resulting in muscle wasting.[1,2] Low muscle mass and low muscle function (i.e., muscle strength and performance) are frequent conditions among patients with CKD, which is of concern due to their association with frailty, functional disability, worse quality of life, and increased mortality.[3–10] Therefore, accurate and precise measurements of muscle mass and muscle function, and the evaluation of their prognostic power, are cornerstones for nutritional evaluations and interventions in patients with CKD.

Findings related to muscle function in CKD are relatively homogeneous, with several studies showing that handgrip strength (HGS) is an independent predictor of clinical

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This is an original paper, and the data collection occurred at the outpatient clinic of the Hypertension and Nephrology Division at Dante Pazzanese Institute of Cardiology in São Paulo, Brazil.

Support: This manuscript was supported by Fundação de Amparo á Pesquisa do Estado de São Paulo[FAPESP] (Process number: 2010/16593-2), and Adib Jatene Foundation.

Financial Disclosure: Baxter Healthcare Corporation employs Bengt Lindholm. None of the other authors have any conflict of interest to declare.

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1051-2276/$36.00
https://doi.org/10.1053/j.jrn.2020.05.007

outcomes.[3,6–10] However, the measurement of muscle mass is under debate, and researchers are still searching for methods less impacted by gross imbalances in hydration status. Many studies have discussed the applicability and reliability of different methodologies for muscle mass evaluation in CKD,[11–14] and dual-energy X-ray absorptiometry (DXA) is recommended by the National Kidney Foundation.[15] However, DXA is also subjected to errors due to the fact that it assumes a constant hydration status of 73% for all patients, which may underestimate the edema that is commonly observed in patients with CKD.[16]

Computed tomography (CT) and magnetic resonance imaging (MRI) are considered gold standards for assessment of body composition, due to their high accuracy and reliability in the evaluation at tissue and organ levels and to not being influenced by hydration status.[14] Body composition assessment in the abdominal area has been traditionally focused on adipose tissue investigation, e.g., visceral and subcutaneous fat, in the general population[17–19] as well as in CKD.[20–23]In healthy adults, a single abdominal image of muscle area by MRI at the third lumbar vertebra (L3) was reported to have the highest correlation with total body skeletal muscle in non-CKD patients.[23] This association was confirmed in oncologic patients by using CT.[24] In addition, in the latter study, its association with mortality has been subsequently demonstrated.[25] Recently, our group has evaluated the agreement of muscle mass by CT at L3 (CTMM-L3) with several surrogate methods of body composition analysis commonly used in the clinical settings in CKD patients.[5] Considering the importance of muscle wasting to screen for risks at earlier stages of CKD, herein we aimed at investigating whether CTMM-L3 was able to predict mortality in nondialyzed CKD 3-5 patients.

Materials and Methods

Subjects and Study Design

The present study was an ancillary analysis of the Malnutrition, Inflammation and Vascular Calcification (MIVC) cohort.[26,27] The MIVC study enrolled 300 consecutive nondialyzed patients with stages 3–5 CKD recruited at the outpatient clinic of the Hypertension and Nephrology Division at Dante Pazzanese Institute of Cardiology in Sao Paulo, Brazil. The aim of the MIVC study is to evaluate the associations between traditional, novel, and uraemic risk factors and both general and cardiovascular morbidity and mortality in this population. Patients were recruited between March 2010 and March 2013, and the exclusion criteria were age <18 and >80 years, clinical signs of acute infection during the month preceding inclusion, active cancer or liver disease at the time of evaluation, previous diagnosis of immunological diseases, and unwillingness to participate in the study. Sixty-seven patients who did not have CT measures were excluded. Additionally, patients who died within 6 months from baseline (n = 10) were also excluded to avoid bias related to the increased mortality rate of older adults starting dialysis.[28,29] Thus, this study analyzed data from 223 patients.

The diagnosis of CKD was confirmed by glomerular filtration rate (GFR <60 mL/min/1.73 m^2). A single physician performed a complete chart review and interviewed patients to determine their clinical history. Patients were followed up from the day of inclusion up to 4 years for all-cause death, and none of them were lost to follow-up. The Local Ethics Committee approved the study, and informed consent was obtained from all patients.

Anthropometry

Body mass index (BMI) was calculated as weight in kilograms divided by height in squared meters. The following equation was used in order to calculate the mid-arm muscle circumference (MAMC), based on mid-arm circumference (measured at mid-point from the acromion to the olecranon) and the triceps skinfold (using caliper Lange®, Cambridge Scientific Industries Inc., Cambridge, MD, USA).

$$\text{MAMC(cm)} = \text{mid-arm circumference(cm)} - \pi \times [\text{triceps skinfold (mm)} \div 10]$$

MAMC was expressed as a percentage in relation to the 50th percentile of MAMC in the reference population of NHANESII[19] to derive a standardized value.[30]

Subjective Global Assessment

The 7-point subjective global assessment (SGA) was employed based on two major categories: physical examination and clinical history. The physical examination evaluates presence of muscle wasting in different sites, i.e., temples, clavicle, shoulders, spike, pollicis interosseous muscle, knee or quadriceps, loss of body fat, and presence of edema, and ascites related to nutritional condition. The clinical history includes 5 components: dietary intake change, gastrointestinal symptoms, weight change, functional impairment, and comorbidities. Each component is scored from 1 to 7 with the highest value meaning better condition. Patients were classified according to the overall score as follows: 1 to 2 (severely malnourished), 3 to 5 (moderately to mildly malnourished), and 6 to 7 (well nourished). In the present study, patients with SGA scores lower than 6 were considered as malnourished.[31]

Handgrip Strength

Muscle strength was evaluated 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. They were then instructed to apply maximum strength in the dynamometer grip in response to a voice command. For study purposes, the highest value of three measurements was considered.

Skeletal Muscle Mass Index

The following skeletal muscle mass (SMM) equation developed by Baumgartner *et al.*[32] was used in the present study, since we have previously demonstrated that this equation showed a best agreement, sensibility, specificity, and area under the curve when compared to other methods, using muscle mass by CT as the reference method.[5]

$$\begin{aligned}\text{SMM(kg)} = {} & 0.2487 * \text{weight} + 0.0483 * \text{height} - 0.1584 \\ & * \text{hip circumference} + 0.0732 * \text{HGS} + 2.5843 \\ & * \text{sex} + 5.8828\end{aligned}$$

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<5.5 kg/m^2 for women and <7.26 kg/m^2 for men.[32]

Bioelectrical Impedance Analysis

Bioelectrical impedance analysis (BIA) was assessed by a tetrapolardevice (Biodynamics®BIA 450 Bioimpedance Analyzer–Seattle, WA, USA). All measurements were made with patients in the supine position, arms separated from the trunk and lying in parallel, legs separated so the thighs did not touch it other. Two electrodes were positioned on the foot and ankle and another two in the hand and wrist of the nondominant side of the body. Introducing an electrical current of 800 A at 50 kHz into the subject, the resistance and reactance were measured. To calculate total body water, fat-free mass, body cell mass, and phase angle, the Fluid & Nutrition software (version 3.0; RJL Systems, Clinton Township, Michigan, USA) was used.

Computed Tomography

Muscle mass was assessed at baseline by CT at the third lumbar vertebra (CTMM-L3). The CT from the thoracic and abdominal scan imaging was assessed by a 64-slice CT scanner (Toshiba CT scanner Aquilion 64, Toshiba Medical Systems, Japan). Assessments were performed without contrast with the participants in the supine position with both arms stretched above the head. The CT data were transferred to a remote workstation (Vitrea 2, version 4.0.0.0, Vital Images, Plymouth, Minnesota, USA) for post-processing and subsequent evaluation. The muscle mass (psoas, transversus abdominus, rectus abdominus, external and internal obliques, erector spinae, and quadratus lumborum) was evaluated through the images located at the level of the third lumbar vertebra (L3), which was shown to be highly correlated to the total skeletal muscle mass.[23] In addition, the assessment of muscle mass by CT in the level of L3 was recently recognized by the revised consensus of sarcopenia from European Working Group on Sarcopenia in Older People[33] to provide precise and opportunistic measurements when CT images from trunk are available for diagnostic reasons, as in the case of the current study, in which CT was performed to assess coronary artery calcification of CKD patients.

The Slice-O-Matic software, version 5.0 (Tomovision, Montreal, Canada) was used to calculate the corresponding muscle areas according to the attenuation values from –29 to +150 Hounsfield units(23). The same trained researcher read all the CT images.

Laboratorial Parameters

Blood samples were taken in the morning after an overnight fast. Plasma and serum were stored at -70°C, if not analyzed immediately. Albumin and hemoglobin were analyzed using certified methods at the Department of Laboratory Medicine at Dante Pazzanese Institute of Cardiology. Serum high-sensitivity C-reactive protein was measured by immune-turbidimetry (Vitros 5600, Ortho Clinical Diagnostics, Raritan, NJ, USA). Protein intake was estimated using the protein nitrogen appearance according to Sargent and Gotch equation and normalized by ideal body weight.[34] The GFR was estimated by CKD-EPI equation using serum creatinine.[35]

Comorbidities

The Charlson comorbidity index was used to calculate history of comorbidities,[36] assigning 1 point for history of congestive heart failure, myocardial infarction, cerebrovascular disease (transient ischemic attack or cerebrovascular accident with minor or no residua), peripheral vascular disease, dementia, connective tissue disorder, chronic pulmonary disease, peptic ulcer disease, mild liver disease, and diabetes without end-organ damage; 2 points assigned for moderate to severe renal disease, hemiplegia, diabetes with end-organ damage, leukemia, tumor without metastases, lymphoma, and myeloma; 3 points assigned for moderate or severe liver disease; and 6 points assigned for metastatic solid tumor or AIDS. For every decade over 40 years of age, 1 point is added to the score. For the purposes of the present study, all patients received a score of 2 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 as mean ± standard deviation, median (interquartile range), or proportions (%) as appropriate. Variable distributions were tested by Shapiro-Wilk test. Student *t*-test or Chi-square test was employed for the comparisons between patient groups. Spearman's rank correlation (rho) was used to test correlations between CTMM-L3 and selected variables. The independent associations of CTMM-L3 were evaluated by linear regression analysis, and for this purpose, non-normally distributed variables were log transformed. 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 (95% confidence intervals). Statistical significance was set at the level of $P < .05$, and the analyses were performed by using the SPSS software, version 22 (SPSS Inc., Chicago, IL, USA).

Results

Baseline Characteristics

Clinical and demographical data of the patient population are depicted in Table 1. In summary, there were 143 men (64%), half of the patients had diabetes, and 25% of them were malnourished according to SGA. Mean BMI was indicative of overweight (29.0 ± 5.5 kg/m^2); and 39% of the patients had BMI ≥30 kg/m^2, 38% BMI from 25 to 29.9 kg/m^2, 21% BMI from 18.5 to 24.9 kg/m^2, and 2% BMI <18.5 kg/m^2. The patients were divided according to the sex-specific 25th percentiles of CTMM-L3 distribution (<138 cm^2 for men and <98 cm^2 for women), and comparisons between the groups are also presented in Table 1. Patients within the lowest quartile were older, had lower hemoglobin level, as well as a lower prevalence of DM, and were more often malnourished (SGA<6). Additionally, BMI, muscle mass, and muscle strength were reduced in this group.

Associations of CTMM-L3

As depicted in Table 2, CTMM-L3 correlated negatively with age and positively with most nutritional parameters in both men and women. Correlation of CTMM-L3 with SGA was observed only among men. In the linear regression analysis, age, sex, BMI, GFR, and HGS emerged as independent predictors of CTMM-L3, as shown in Table 3.

Follow-up Analyses

During the 49-month follow-up, 63 patients (28%) died, the majority (43%) due to cardiovascular disease, including acute myocardial infarction (n = 13), stroke (n = 10), or sudden death (n = 2), and aortic artery disease (n = 2). The remaining causes of death were infectious disease (n = 24), hypervolemia (n = 7), gastrointestinal bleeding (n = 2), trauma (n = 2), and cancer (n = 1). Table 4 presents the demographic, nutritional, and laboratory characteristics according to patient's survival. The nonsurvivor group had higher prevalence of diabetes and malnutrition, as well as a higher comorbidity index, and lower HGS, hemoglobin and albumin levels as compared to the survivor group. The proportion of patients with low SMMI and with CTMM-L3< 25th percentile was significantly higher in the nonsurvival group.

Patients with lower CTMM-L3 had lower cumulative survival during follow-up (Log-rank $x^2 = 5.72$; $P = .017$; Figure 1). Cox proportional hazard analyses (Table 5) showed that low CTMM-L3 was associated with a higher mortality hazard in crude analysis, and this association remained after adjustments for potential confounders including age, GFR, diabetes, and C-reactive protein.

Discussion

We report that low muscle mass assessed by CT at the L3 (CTMM-L3) is an independent predictor of mortality in CKD 3-5 patients. To the best of our knowledge, this is

Table 1. Comparison of the Patients in the Lowest Quartile With the Patients in the Higher Quartiles of Muscle Mass Assessed by Computed Tomography at the Third Lumbar Vertebra (CTMM-L3)

Variables	Total Population (n = 223)	CTMM-L3<25th Percentile (n = 58)	CTMM-L3>25th Percentile (n = 165)	*P* value
Age (years)	60.3 ± 10.6	64.3 ± 9.9	58.9 ± 10.6	<.001
Men [n (%)]	143 (64%)	37 (64%)	106 (64%)	.536
Diabetes mellitus [n (%)]	112 (50%)	21 (36%)	91 (55%)	.010
Charlson index	6 ± 2	7 ± 2	6 ± 2	.331
GFR (mL/min)	20.7 ± 9.6	19.8 ± 10.5	21.0 ± 9.3	.44
Hemoglobin (g/dL)	12.3 ± 2.1	11.7 ± 2.2	12.6 ± 2.0	.003
Albumin (g/dL)	3.8 ± 0.6	3.8 ± 0.5	3.9 ± 0.6	.660
C-reactive protein (mg/dL)	0.37 (0.13-0.80)	0.48 (0.13-0.82)	0.35 (0.13-0.80)	.562
BMI (kg/m^2)	29.1 ± 5.6	25.6 ± 4.3	30.2 ± 5.4	<.001
nPNA (g/kg)	0.95 (0.76-1.17)	0.92 (0.74-1.10)	0.95 (0.76-1.19)	.174
SGA≤5 [n (%)]	55 (25%)	22 (38%)	33 (20%)	.006
HGS (kg)	35 (28-44)	31 (25-37)	37 (29-46)	<.001
MAMC (% of standard)	102.1 (91.5-116.1)	88.5 (78.2-101.7)	106.3 (95.6-119.0)	<.001
LBMBIA (kg)	56.4 ± 11.9	49.9 ± 10.4	58.7 ± 11.6	<.001
SMMI (kg/m^2)	8.01 (7.04-8.77)	7.26 (6.50-8.14)	8.23 (7.34-8.98)	<.001
Low SMMI [n (%)]	13 (6%)	9 (16%)	4 (2%)	.035
CTMM-L3 (cm^2)	140.3 ± 34.8	109.9 ± 21.1	150.1 ± 32.4	NA

BIA, bioimpedance analysis; BMI, body mass index; CVD, cardiovascular disease; CTMM-L3, muscle mass measured by computed tomography at L3; GFR, glomerular filtration rate; HGS, handgrip strength; LBM, lean body mass; MAMC, mid-arm muscle circumference; nPNA, normalized protein nitrogen appearance normalized by ideal body weight; SGA, subjective global assessment; SMMI, skeletal muscle mass index.

Table 2. Associations (Spearman's Rank Correlation Coefficients) of Muscle Mass Assessed by Computed Tomography at the Third Lumbar Vertebra (CTMM-L3) With the Main Study Variables

	CTMM-L3			
	Men		Women	
Variables	R	*P*	r	*P*
Age (years)	−0.34	<.001	−0.32	.004
GFR (ml/min/1.73 m^2)	0.06	.41	−0.01	.89
Albumin (mg/dL)	0.06	.489	−0.07	.534
C-reactive protein (mg/dL)	0.02	.812	0.15	.193
BMI (kg/m^2)	0.54	<.001	0.52	<.001
SGA	0.24	.004	0.21	.060
HGS (kg)	0.34	<.001	0.43	<.001
MAMC (cm)	0.62	<.001	0.48	<.001
LBMBIA (kg)	0.55	<.001	0.67	<.001
SMM (kg)	0.58	<.001	0.64	<.001

BIA, bio impedance analysis; BMI, body mass index; GFR, glomerular filtration rate (CKD-EPI equation); HGS, handgrip strength; LBM, lean body mass; MAMC, mid-arm muscle circumference; SGA, subjective global assessment; SMM, skeletal muscle mass.

the first study showing the association of abdominal muscle mass by CT against a hard outcome in CKD. In addition, CTMM-L3 was significantly associated with other surrogates methods of lean body mass (LBM) assessment such as LBM-BIA, SMM by Baumgartner equation, and standard MAMC. Our findings are complementary to those reported from the study by Morrel et al[37] that assessed muscle mass by MRI in 105 adult hemodialysis patients. The authors observed that the psoas and paraspinous muscles, both located at the level of L4-L5, were strongly associated with total LBM assessed by DXA ($r = 0.74$ and $r = 0.58$; $P < .01$, respectively). Moreover, in a logistic regression model of sarcopenia, defined using the same criteria from the current study, that is LBM <25th percentile, C-statistics for the psoas and paraspinous muscle were 0.81 and 0.69, respectively.[37] Altogether, the findings from Morrel et al[37] and from the current study suggest that the assessment of muscle mass located in the level from L3 to L5 provide a good estimate of total LBM and is a good predictor of mortality rate in patients with CKD and end stage renal disease.

Table 3. Linear Regression Analysis Showing the Coefficients of Different Variables for Muscle Mass Assessed by Computed Tomography at the Third Lumbar Vertebra (CTMM-L3)

Variables	Unstandardized Coefficient	95% CI	*P* value
Sex (men)	41.44	33.93; 48.95	<.001
Age (year)	−0.50	−0.77; −0.23	<.001
BMI (kg/m^2)	2.17	1.64; 2.69	<.001
GFR (ml/min/1.73 m^2)	0.18	7.53; 48.5	.008
logCRP (mg/dL)	−0.94	−5.89; 3.97	.706
HGS (kg)	0.55	0.17; 0.92	.004

BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; GFR, glomerular filtration rate (CKD-EPI equation); HGS, handgrip strength.

CKD is associated with a number of metabolic derangements leading to changes in body composition,[1,2] including muscle wasting, which may be present even in overweight or obese patients (obese sarcopenia).[38] Muscle mass is a key prognostic element in CKD owing to its strong association with morbidity and mortality.[39-41] However, evaluation of muscle mass has historically been challenging in CKD due to a number of factors that affect its assessment.[14,42,43] Most of the currently used methods to evaluate muscle mass are subjected to errors due to the technique limitations *per se* or due to factors related to the disease, such as frequent abnormalities in hydration status, particularly in advanced stages of CKD.[14,16] As such, the magnitude of the errors for body composition assessment are greater in patients with CKD than in healthy individuals.[14]

Our results showing an association of CT-derived abdominal muscle mass with mortality is in accordance with those by Fukasawa et al,[44] who showed that lower thigh muscle mass was significantly associated with all-cause and cardiovascular mortality in elderly hemodialysis patients. They suggested that assessment of muscle mass of lower extremities was of particular value to predict clinical outcomes of hemodialysis patients. Although there are no comparative studies to derive definite conclusions on the optimal site for muscle mass assessment by CT in CKD patients, it is plausible to assume that abdominal muscle mass is an equally appropriate site from a prognostic point of view.

The estimation of body muscle mass through a single cross-sectional image area at the third lumbar vertebra (located 5 cm above L4–L5) was first suggested by Shen et al.[23] who found the strongest association with the total body skeletal muscle volume assessed by magnetic resonance imaging. Subsequently, it was validated also in oncologic patients by confirming high correlation with fat-free mass as well as appendicular skeletal muscle assessed by DXA.[24,25] We have recently compared the agreement of several muscle mass surrogates used in the clinical settings in CKD with CTMM-L3 and found that the predictive equation by Baumgartner was the one with the best agreement with the reference.5 In the current study, CTMM-L3 was significantly associated with LBM-BIA, SMM by Baumgartner equation and with MAMC. Other significant association found with CTMM-L3 was age, BMI, and SGA, although SGA significance in the group of females. This finding was in line with the study by Giusto et al.,[45] who in cirrhotic patients found stronger association of MAMC with CTMM-L3 in males, but not in females. In fact, muscle mass distribution is not uniform in the body and can vary according to sex and age in the general population[46,47] as well as in CKD patients.[48] Moreover, as expected, sex, age, BMI, and HGS were the predictors of

Table 4. Characteristics of Survivors and Nonsurvivors During Follow-up (n = 223)

Variables	Survivors (n = 160)	Nonsurvivors (n = 63)	*P* value
Age (years)	59.8 ± 10.7	61.8 ± 10.5	.197
Men [n (%)]	106 (66%)	37 (59%)	.352
Diabetes [n (%)]	73 (46%)	39 (62%)	.037
Charlson index	6 ± 0	7 ± 2	.020
GFR (mL/min)	20.3 ± 10.0	20.9 ± 9.5	.673
Hemoglobin (g/dL)	12.6 ± 1.9	11.7± 2.4	.003
Albumin (g/dL)	3.9 ± 0.5	3.7 ± 0.6	.025
C-reactive protein (mg/dL)	0.34 (0.12-0.80)	0.50 (0.19-0.80)	.147
BMI (kg/m^2)	29.2 ± 5.2	28.6 ± 6.3	.462
nPNA (g/kg)	0.95 (0.77-1.18)	0.93 (0.75-1.17)	.577
SGA≤5 [n (%)]	30 (19%)	25 (40%)	.003
HGS (kg)	37 (30-45)	30 (26-38)	<.001
MAMC (% of standard)	102.4 (92.8-115.4)	101.9 (83.7-116.6)	.407
LBM-BIA (kg)	57.1 ± 11.8	4.7 ± 12.2	.191
SMMI (kg/m^2)	8.09 (7.21-8.81)	7.77 (6.62-8.65)	.078
Low SMMI [n (%)]	6 (4%)	7 (11%)	.035
CTMM-L3 (cm^2)	142.3 ± 33.2	132.8 ± 37.4	.081
CTMM-L3<25th percentile [n (%)]	34 (21)	24 (38)	.017

BIA, bioimpedance analysis; BMI, body mass index; CTMM-L3, muscle mass measured by computed tomography at L3; GFR, glomerular filtration rate (CKD-EPI equation); HGS, handgrip strength; LBM, lean body mass; MAMC, mid-arm muscle circumference; nPNA, normalized protein nitrogen appearance; SGA, subjective global assessment; SMMI, skeletal muscle mass index.

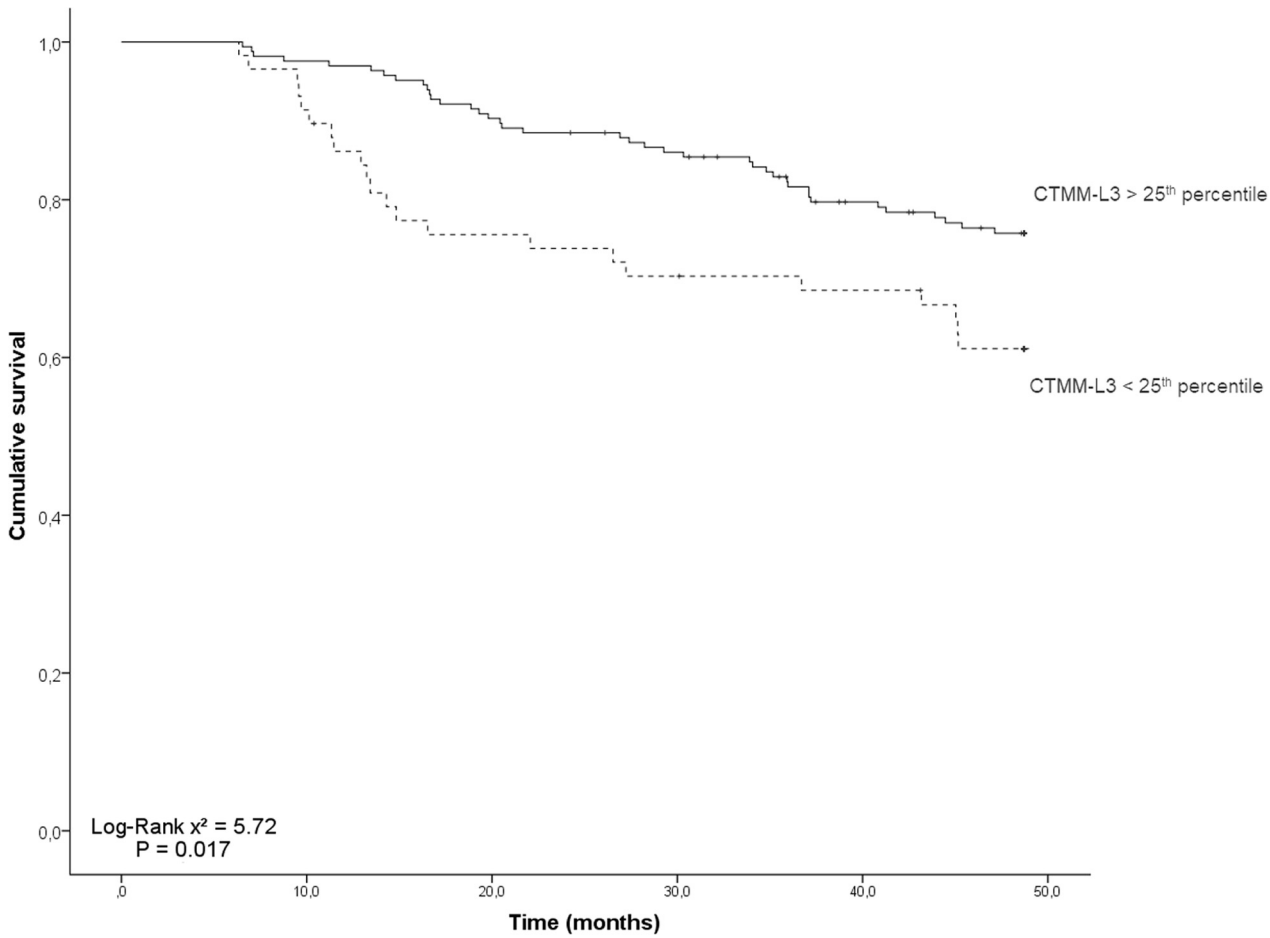

Figure 1. Kaplan-Meier curve for muscle mass assessed by computed tomography at the third lumbar vertebra (CTMM-L3) <25th percentile versus>25th percentile.

Table 5. Cox Regression Analyses of the Association Between Muscle Mass Assessed by Computed Tomography at the Third Lumbar Vertebra (CTMM-L3) <25th Percentile by Gender and Mortality in 223 CKD Patients

All-Cause Mortality		
Model	Variables	CTMM-L3<25th Percentile
1	Crude model	1.87 (1.11 – 3.16)
2	1 + Age	1.82 (1.05 – 3.15)
3	2 + GFR	1.92 (1.11 – 3.34)
4	3 + DM	2.28 (1.30 – 4.03)
5	4 + CRP	2.15 (1.21 – 3.84)

CTMM-L3, computed tomography muscle mass at L3; DM: diabetes; GFR, glomerular filtration rate (CKD-EPI equation); CRP, C-reactive protein.

CTMM-L3, a finding similar to that observed in previous studies with other markers of muscle mass.[7,9,44]

When evaluating association with mortality, other surrogate measures of muscle mass (LBM BIA, MAMC, and SMM) did not present independent association with mortality (data not shown). In a previous study, we tested MAMC, SGA, and BIA-derived SMMI in regards to the prognostic power in combination with HGS measures in nondialyzed CKD patients, and we have found that the SMMI equation by using BIA predicted mortality in this group of patients.[9] In the current study, the lack of significant difference found between survivals and nonsurvivals for CTMM-L3 (described as a continuous variable) was also observed with the other surrogates of muscle mass assessed in the study, such as standard MAMC, LBM-BIA, and SMMI. However, the proportion of patients with low SMMI and CTMM-L3< 25th percentile was significantly higher in the nonsurvival group. This finding suggests that muscle mass is predictive of worse survival when reduced muscle mass is present as also previously reported in hemodialysis patients.[44]

The limitations of this study are that our results may not be representative of the entire CKD population. Besides, the cutoff point of the lowest quartile by sex was used to define low muscle mass by CT, which is arbitrary since there is no established value for the diagnosis of low muscle mass in CKD patients. Therefore, upcoming investigations are warranted to identify threshold values to evaluate and define low abdominal muscle mass in CKD patients. Nonetheless, it should be noticed that this is the first time that the association of a single slice of abdominal muscle area with mortality was investigated among CKD patients. A gold-standard methodology was used to guarantee high accuracy, and to minimize errors coming from interobserver readings, the same observer performed the reading of all CT images for the entire CKD group. In addition, the assessment of muscle mass by CT in the level of L3 was recently recognized by the revised sarcopenia consensus from European Working Group on Sarcopenia in Older People as a precise method for the assessment of muscle mass,[33] but its performance in CKD patients to predict outcome of mortality have not yet been evaluated to the best of our knowledge. Since muscle mass is indeed the target compartment to evaluate nutritional abnormalities in patients prone to develop chronic catabolic disorders, such as CKD, our study is aligned with the need of investigations focusing on methods free of bias. In the present study, we demonstrated that low CTMM-L3 was able to predict mortality. However, since CT exposes the patient to radiation, its use to assess muscle mass could be opportunistically used for this end when images are available for other diagnostic purposes, such as in the case of the current study. Future studies evaluating the muscle quality, such as the infiltration of fat in muscle in the region of L3 would be of great interest.

Practical Application

The results of this study confirm previous findings of the importance of muscle mass assessment of CKD patients. In addition, they bring awareness of the utility of computed tomography images from the trunk (which include the slice of the third lumbar vertebra) available for other purposes, such as for the assessment of coronary arteries calcium as in the current study, for the assessment of muscle mass. This would allow a more precise assessment of skeletal muscle mass by a gold-standard method without additional radiation exposition for the patient.

Credit Authorship Contribution Statement

André V. Bichels: Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Antonio C. Cordeiro:** Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Carla M. Avesani:** Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Fernanda C. Amparo:** Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Juliana Giglio:** Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Nilian C. Souza:** Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Nivaldo Pinho:** Writing - original draft, Writing - review & editing. **Celso Amodeo:** Writing - original draft, Writing - review & editing. **Juan J. Carrero:** Writing - original draft, Writing - review & editing. **Bengt Lindholm:** Writing - original draft, Writing - review & editing. **Peter Stenvinkel:** Writing - original draft, Writing - review & editing. **Maria A. Kamimura:**

Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing.

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