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Sarcopenic Obesity in Chronic Kidney Disease: Challenges in Diagnosis Using Different Diagnostic Criteria

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Highlights of the Study

- Prevalence of sarcopenic obesity varies widely depending on the criteria applied.
- There is low agreement among criteria with low muscle mass versus low muscle strength and those using high total body fat versus central fat, which interfered in the diagnosis of sarcopenic obesity.
- Women were more affected by sarcopenic obesity.
- Low muscle mass or strength and sarcopenic obesity were more prevalent in patients on hemodialysis and obesity among nondialysis-dependent and kidney transplant patients.

Keywords
Body composition · Chronic kidney disease · Muscle mass · Muscle strength · Obesity · Sarcopenia

Abstract
Objectives: Obesity, muscle impairment (low muscle mass or strength), and sarcopenic obesity are present in chronic kidney disease (CKD) and are associated with worse clinical prognosis. However, the various existing definitions for these conditions make the diagnosis variable. The aim of the present study was to evaluate the agreement between diagnostic criteria for sarcopenic obesity and its components in CKD. ***Subject and Methods:*** 267 patients with CKD were included in the study. We assessed body composition by dual-energy X-ray absorptiometry and muscle function by handgrip strength (HGS) and adiposity by body mass index (BMI), waist circumference (WC), fat mass index (FMI), and percentage of FM. Diagnosis of muscle impairment was made by HGS, appendicular lean mass (ALM), and ALM index; obesity by BMI, WC, FMI, and %FM, and sarcopenic obesity was diagnosed by concomitant presence of muscle impairment and obesity. ***Results:*** Prevalence of muscle impairment varied from 11 to 50%, higher when low muscle mass criteria were used. Prevalence of obesity varied from 26 to 62%, higher when WC and %FM criteria were used. Prevalence of sarcopenic obesity varied from 2 to 23%. Women were more affected by sarcopenic obesity. Muscle impairment and sarcopenic obesity were more prevalent among patients on hemodialysis and obesity among nondialysis-dependent and kidney transplant patients. The agreement was poor between muscle mass and strength criteria; substantial be-

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tween FMI, BMI, and %FM and fair between WC and the other measures; for sarcopenic obesity, it varied from poor to almost perfect. ***Conclusion:*** Significant differences were found among the various diagnostic criteria that are used in the diagnosis of sarcopenic obesity. Our results highlight the need for standardization in the diagnosis of sarcopenic obesity.

Introduction

Obesity and muscle loss are common conditions in chronic kidney disease (CKD) [1] and are associated with high mortality [2–4]. The prevalence of obesity in end-stage CKD has increased [5], but the incidence varies by >30% depending on the criteria applied [6]. Obesity is commonly diagnosed by body mass index (BMI) [7], waist circumference (WC) [7], fat mass index (FMI) [8], and FM relative to body weight (%FM) [9, 10]. However, not only quantity but also distribution of body fat is important, as this has a close relationship with negative outcomes and inflammatory status [4].

The prevalence of muscle impairment (low muscle mass or strength) and sarcopenia (low muscle mass in addition to low muscle strength) is higher in CKD patients [1] than in the general population [11]. Diagnostic criteria were recently proposed by the European Working Group on Sarcopenia in Older People [12], but other international entities have proposed their own criteria [13, 14], and there is no consensus. Thus, prevalence of sarcopenia also varies greatly [6].

Sarcopenic obesity, defined as co-occurrence of muscle impairment and obesity [15–17], affects CKD patients and strongly contributes to a worse clinical prognosis than patients with either of the 2 conditions alone [18, 19]. The objective of this study was to evaluate the prevalence of sarcopenic obesity, as well as its components, and to determine the agreement between the different diagnostic criteria when applied to patients with CKD under nondialyses-dependent (NDD) treatment, hemodialysis (HD), peritoneal dialysis (PD), and kidney transplant (KTx).

Subjects and Methods

CKD patients aged ≥18 and ≤60 years were recruited. Inclusion criteria were patients in stages 3b to 5 of CKD in NDD treatment; PD or HD (4-h dialysis session, 3 times per week, through an arteriovenous fistula) for at least 3 months and without peritonitis in the previous 30 days; and patients with KTx at least 6 months prior and with stages 1 to 3a of CKD. Residual renal function was calculated using mean urine creatinine clearance adjusted for 1.73 m^2 obtained through 24-h urine collection performed 1 day to 1 week prior to participation in the study. Kt/V was calculated by weekly clearance of dialyzed urea adjusted by total body water for the week prior to collection. Exclusion criteria were acute infections, cancer diagnosis and other syndromes that might alter body composition, presence of amputated limb or electronic implant, wheelchair user, inpatient, body weight above 140 kg or BMI >40 kg/m^2. The study was approved by the local Ethics Committee (Protocol Number: 2053045). All participants read and signed the informed consent form before the procedures began.

Clinical and biochemical data were collected from electronic medical records. Anthropometric measures, handgrip strength (HGS), bioelectrical impedance spectroscopy, and dual-energy X-ray absorptiometry (DXA) were performed consecutively by the same nutritionist after an 8-h fasting, emptying of the urinary bladder, drainage of the peritoneal dialysate, and immediately after the mid-week HD session. Measurements were performed with patients wearing light clothes, without shoes, preferably on the right side of the body (except if a fistula was present).

DXA (Hologic Discovery A®) in total body protocol was used to evaluate appendicular lean mass (ALM), total FM, ALM index (ALMI), and FMI [20]. WC was also measured [21]. A pneumatic dynamometer (MG 4800; Charder®) was used to evaluate HGS [22].

The diagnosis of muscle impairment was performed using 3 measures: ALM, ALMI, or HGS as recommended by the new European Working Group on Sarcopenia in Older People consensus [12]. The diagnosis of obesity was performed using 5 measures: BMI [7], WC [7], FMI [8] as recommended by the International Society for Clinical Densitometry [17]; and using two different cutoff points for %FM [9, 10]. Sarcopenic obesity was determined by the combination of obesity and muscle impairment or by the FMI-adjusted ALMI ($ALMI_{fmi}$) [23]. The methods and cutoff points used for the diagnoses are presented in Table 1.

Data normality was verified by the Shapiro-Wilk test. Prevalence for sarcopenic obesity and its components was estimated. Relative risk (RR) was applied for each condition including diabetes mellitus, sex, ethnicity, muscle mass or obesity status, and CKD treatment group, with each diagnostic criterion adjusted for age. The agreement between the different diagnostic criteria was evaluated with Cohen's kappa coefficient. Pearson's correlation was applied to assess the association. The MINITAB® software was used, and the results were considered statistically significant at the 5% level ($p < 0.05$).

Results

A total of 267 patients with CKD were evaluated (130 men and 137 women). The mean age was 47 ± 10 years, with a mean BMI of 27 ± 5 kg/m^2. According to CKD treatment, 31% ($n = 83$) were on NDD treatment, 30% ($n = 80$) on HD, 9% ($n = 23$) on PD, and 30% ($n = 81$) had undergone KTx. Twenty-seven percent of the patients had diabetes mellitus and 67% systemic arterial hypertension. CKD was secondary to systemic arterial hyperten-

Table 1. Diagnostic criteria and cutoff points applied for muscle impairment, obesity and sarcopenic obesity

Index		Cutoff point		Reference
		men	women	
Diagnosis of muscle impairment				
Dual energy-X-ray absorptiometry (DXA)				
ALM	ALM, kg	<20.0	<15.0	EWGSOP [12]
ALMI	ALMI, kg/m^2	<7.0	<5.5	EWGSOP [12]
HGS				
HGS	HGS, kg	<27.0	<16.0	EWGSOP [12]
Diagnosis of obesity				
Anthropometry				
BMI	BMI, kg/m^2	≥30	≥30	WHO [7]
WC	WC, cm	>102	>88	WHO [7]
DXA				
FMI	FMI, kg/m^2	>9	>13	[8]
%FM1	FM, %	According to ethnicity and age	According to ethnicity and age	[9]
%FM2	FM, %	According to ethnicity and age	According to ethnicity and age	[10]
Diagnosis of sarcopenic obesity (muscle impairment + obesity)				
Diagnosis of muscle mass adjusted for adiposity				
$ALMI_{fmi}$	ALMI, kg/m^2 adjusted for FMI, kg/m^2	According to ethnicity and age	According to ethnicity and age	[23]
Diagnosis of low muscle strength + obesity				
HGS + BMI, HGS + WC, HGS + FMI, HGS + %FM1, HGS + %FM2				
Diagnosis of low muscle mass + obesity				
ALM + BMI, ALM + WC, ALM + FMI, ALM + %FM1, ALM + %FM2				
ALMI + BMI, ALMI + WC, ALMI + FMI, ALMI + %FM1, ALMI + %FM2				

ALM, appendicular lean mass; ALMI, appendicular lean mass index; $ALMI_{fmi}$, appendicular lean mass index adjusted for fat mass index; BMI, body mass index; EWGSOP, European Working Group on Sarcopenia in Older People; FMI, fat mass index; FM, fat mass; HGS, hand grip strength WC, waist circumference; WHO, World Health Organization; DXA, dual-energy-X-ray absorptiometry.

Table 2. Concordance between the different criteria for muscle impairment and obesity diagnostic

Muscle impairment	HGS		ALM	
ALM	0.06±0.06 (−0.06 to 0.19)			
ALMI	0.06±0.07 (−0.07 to 0.19)		0.80±0.04 (0.72–0.87)	
Obesity	BMI	WC	FMI	%FM1
WC	0.36±0.05 (0.25–0.46)			
FMI	0.74±0.05 (0.65–0.83)	0.35±0.05 (0.25–0.46)		
%FM1	0.29±0.06 (0.18–0.41)	0.37±0.06 (0.26–0.49)	0.45±0.05 (0.35–0.59)	
%FM2	0.35±0.06 (0.23–0.48)	0.28±0.06 (0.17–0.39)	0.62±0.05 (0.52–0.72)	0.64±0.05 (0.55–0.73)

The agreement between the different methods and criteria for muscle impairment and obesity diagnostic was tested by Cohen's kappa coefficient: kappa ± standard error (95% CI). See Table 1 for codes. ALM, appendicular lean mass; ALMI, appendicular lean mass index; BMI, body mass index; WC, waist circumference; FMI, fat mass index; HGS, handgrip strength.

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Table 3. Concordance between the different criteria and methods for sarcopenic obesity diagnostic

	HGS + BMI	HGS + WC	HGS + FMI	HGS+ %FM1	HGS+ %FM2	ALM + BMI	ALM + WC	ALM + FMI	ALM+ %FM1	ALM+ %FM2	ALMI + BMI	ALMI + WC	ALMI + FMI	ALMI+ %FM1	ALMI+ %FM2	$ALMI_{fmi}$
HGS + BMI	1															
HGS + WC	0.48±0.15 (0.20 to 0.77)	1														
HGS + FMI	0.79±0.12 (0.56 to 1.03)	0.57±0.13 (0.33 to 0.82)	1													
HGS+%FM1	0.41±0.16 (0.10 to 0.72)	0.66±0.10 (0.47 to 0.86)	0.60±0.12 (0.35 to 0.84)	1												
HGS+%FM2	0.58±0.16 (0.26 to 0.88)	0.53±0.13 (0.27 to 0.78)	0.79±0.10 (0.59 to 0.99)	0.74±0.09 (0.56 to 0.93)	1											
ALM + BMI	0.11±0.24 (−0.36 to 0.58)	0.05±0.19 (−0.33 to 0.43)	0.08±0.22 (−0.36 to 0.52)	0.03±0.19 (−0.33 to 0.40)	−0.02±0.26 (−0.54 to 0.50)	1										
ALM + WC	−0.01±0.11 (−0.23 to 0.20)	0.13±0.10 (−0.05 to 0.32)	0.03±0.10 (−0.18 to 0.23)	0.08±0.10 (−0.11 to 0.28)	0.01±0.10 (−0.19 to 0.21)	0.20±0.10 (0.02 to 0.39)	1									
ALM + FMI	0.05±0.19 (−0.32 to 0.42)	0.11±0.15 (−0.19 to 0.41)	0.25±0.16 (−0.06 to 0.57)	0.17±0.15 (−0.13 to 0.46)	0.16±0.16 (−0.17 to 0.48)	0.55±0.13 (0.30 to 0.80)	0.55±0.13 (0.30 to 0.80)	1								
ALM+%FM1	−0.01±0.11 (−0.22 to 0.19)	0.08±0.10 (−0.11 to 0.27)	0.08±0.10 (−0.12 to 0.28)	0.23±0.09 (0.04 to 0.41)	0.09±0.10 (−0.11 to 0.28)	0.18±0.10 (−0.01 to 0.37)	0.58±0.06 (0.46 to 0.69)	0.40±0.08 (0.24 to 0.57)	1							
ALM+%FM2	0	0.04±0.12 (−0.19 to 0.27)	0.11±0.12 (−0.14 to 0.35)	0.15±0.11 (−0.07 to 0.37)	0.16±0.12 (−0.07 to 0.39)	0.25±0.11 (0.03 to 0.47)	0.45±0.07 (0.13 to 0.59)	0.57±0.08 (0.41 to 0.73)	1	1						
ALMI + BMI	−0.02±0.30 (−0.61 to 0.57)	−0.03±0.20 (−0.43 to 0.37)	−0.02±0.27 (−0.55 to 0.55)	−0.03±0.22 (−0.45 to 0.39)	−0.03±0.24 (−0.5 to 0.44)	0.56±0.18 (0.21 to 0.91)	0.45±0.20 (0.05 to 0.85)	0.38±0.15 (0.08 to 0.68)	0.09±0.11 (−0.12 to 0.30)	0.13±0.12 (−0.11 to 0.37)	1					
ALMI + WC	−0.04±0.12 (−0.27 to 0.18)	0.09±0.10 (−0.11 to 0.29)	0.01±0.1 (−0.22 to 0.22)	0.04±0.10 (−0.16 to 0.25)	0.02±0.11 (−0.20 to 0.24)	0.07±0.11 (−0.14 to 0.28)	0.07±0.11 (−0.14 to 0.28)	0.21±0.10 (0.02 to 0.40)	0.42±0.07 (0.28 to 0.56)	0.31±0.08 (0.15 to 0.46)	0.14±0.11 (−0.08 to 0.35)	1				
ALMI + FMI	−0.03±0.22 (−0.47 to 0.40)	0.10±0.10 (−0.10 to 0.30)	0.23±0.18 (−0.12 to 0.58)	0.14±0.16 (−0.18 to 0.46)	0.20±0.18 (−0.14 to 0.55)	0.32±0.17 (−0.01 to 0.64)	0.32±0.17 (0.01 to 0.65)	0.80±0.08 (0.64 to 0.96)	0.28±0.09 (0.10 to 0.46)	0.40±0.10 (0.21 to 0.59)	0.51±0.16 (0.20 to 0.83)	0.26±0.10 (0.07 to 0.46)	1			
ALMI+%FM1	−0.04±0.12 (−0.27 to 0.19)	0.04±0.10 (−0.17 to 0.24)	0.04±0.11 (−0.18 to 0.25)	0.16±0.10 (−0.03 to 0.36)	0.12±0.11 (−0.09 to 0.33)	0.07±0.11 (−0.15 to 0.28)	0.41±0.07 (0.27 to 0.55)	0.27±0.09 (0.08 to 0.45)	0.84±0.04 (0.76 to 0.92)	0.66±0.06 (0.55 to 0.78)	0.14±0.11 (−0.08 to 0.35)	0.55±0.07 (0.42 to 0.68)	0.34±0.09 (0.16 to 0.53)	1		
ALMI+%FM2	−0.09±0.11 (−0.34 to 0.16)	0.05±0.12 (−0.19 to 0.28)	0.08±0.13 (−0.18 to 0.34)	0.13±0.12 (−0.10 to 0.36)	0.19±0.12 (−0.05 to 0.43)	0.12±0.13 (−0.13 to 0.36)	0.30±0.08 (0.14 to 0.45)	0.38±0.10 (0.18 to 0.58)	0.65±0.06 (0.53 to 0.77)	0.86±0.04 (0.77 to 0.94)	0.19±0.13 (−0.05 to 0.44)	0.41±0.08 (0.25 to 0.56)	0.48±0.10 (0.29 to 0.66)	0.79±0.05 (0.69 to 0.88)	1	
$ALMI_{fmi}$	0.02±0.11 (−0.20 to 0.25)	0.01±0.10 (−0.20 to 0.22)	0.10±0.11 (−0.11 to 0.32)	0.13±0.10 (−0.07 to 0.33)	0.15±0.10 (−0.05 to 0.36)	0.18±0.11 (−0.03 to 0.40)	0.19±0.10 (−0.00 to 0.40)	0.34±0.09 (0.16 to 0.52)	0.46±0.07 (0.32 to 0.59)	0.53±0.07 (0.40 to 0.67)	0.14±0.11 (−0.08 to 0.35)	0.17±0.08 (0.01 to 0.33)	0.32±0.09 (0.14 to 0.51)	0.49±0.07 (0.36 to 0.63)	0.53±0.07 (0.38 to 0.67)	1

The agreement between the different methods and criteria for sarcopenic obesity diagnostic was tested by Cohen's kappa coefficient: kappa±standard error (95% CI). See Table 1 for codes. ALM, appendicular lean mass; ALMI, appendicular lean mass index; $ALMI_{fmi}$, appendicular lean mass index adjusted for fat mat index; BMI, body mass index; WC, waist circumference; FM, fat mass; FMI, fat mass index; HGS, handgrip strength; CI, confidence interval.

sion in 35% of patients and diabetes mellitus in 16%. For the NDD group, the mean glomerular filtration rate was 19 ± 9 mL/min/1.73 m^2 and for the KTx group, 70 ± 18 mL/min/1.73 m^2. The transplant time was an average of 92 ± 61 months. For the HD group, the total weekly KT/V was 2 ± 1 with a mean HD time of 74 ± 62 months. For the PD group, the total weekly KT/V was 3 ± 1 with a mean time of 86 months.

The prevalence of muscle impairment, obesity, and sarcopenic obesity in total, male and female sample is presented in online suppl. Figures S1 and S2, respectively (see www.karger.com/doi/10.1159/000517597). The prevalence of muscle impairment varied from 11 to 50%: lower when detected by HGS criteria and similar between ALM and ALMI. Based on the 3 measures, women were twice as affected as men. The prevalence of obesity ranged from 26 to 62%, higher when detected by WC and lower when detected by BMI and FMI. The prevalence was higher among men, except for WC.

The prevalence of sarcopenic obesity varied from 2 to 23%, being higher when detected by the ALM + WC, ALM + %FM1, ALMI + WC, ALMI + %FM1, and $ALMI_{fmi}$ criteria; and lower when applying HGS for muscle impairment or BMI for obesity criteria. Sarcopenic obesity was more often diagnosed among women (except when diagnosed by $ALMI_{fmi}$).

The agreement between diagnostic criteria for muscle impairment and obesity is presented in Table 2. An almost perfect agreement was found between ALM and ALMI; the agreement between HGS and the other tools was poor. For diagnosis of obesity, the highest agreement was observed between BMI and FMI, FMI and %FM2, and %FM2 with %FM1. Weak agreement was found among the other diagnostic tools for obesity, mainly with WC criteria.

The agreement among diagnostic tools for sarcopenic obesity is presented in Table 3. Poor agreement was observed among the diagnostic criteria for sarcopenic obesity using HGS with the ones applying ALM or ALMI for muscle impairment; similarly, only a fair agreement was seen among the diagnostic criteria for sarcopenic obesity using WC with the other obesity criteria. Correlation coefficient with BMI was 0.90 for WC, 0.82 for FMI, and 0.50 for %FM. Correlation coefficient with WC was 0.73 for FMI and 0.45 for %FM. Correlation between FMI and %FM was 0.89. For HGS, the correlations coefficients were 0.74 for ALM and 0.60 for ALMI. Correlation between ALM and ALMI was 0.92. Data of RR for muscle impairment, obesity, and sarcopenic obesity are presented in Tables 4 and 5.

The number of patients diagnosed with muscle impairment by the 3 criteria varied greatly: 30 patients had low HGS, 14% (12) of NDD, 14% (11) of HD, 13% (3) of PD, and 5% (4) of KTx; 132 had low ALM, 28% (23) of NDD, 69% (55) of HD, 52% (12) of PD, and 52% (42) of KTX; 136 had low ALMI, 25% (41) of NDD, 65% (52) of HD, 43% (10) of PD and 41% (33) of KTx. The HD group presented the highest prevalence of muscle impairment and the NDD group the lowest. In addition, for ALM and ALMI diagnostic criteria, high BMI and WC were protective for muscle impairment. Although women were more affected than men for the 3 criteria of muscle impairment, female sex was a risk factor only for ALM and ALMI criteria.

Great variation was found for prevalence of obesity among the 5 different diagnostic criteria: 69 patients had high BMI, 42% (35) of NDD, 19% (15) of HD, 9% (2) of PD, and 21% (17) of KTx; 164 had high WC, 63% (52) of NDD, 58% (46) of HD, 52% (12) of PD, and 67% (54) of KTx; 74 had high FMI, 39% (32) of NDD, 19% (15) of HD, 13% (3) of PD, and 30% (24) of KTx; high %FM1 and %FM2 were present in 142 and 97 patients, 58% (48) and 39% (32) of NDD, 45% (36), and 29% (23) of HD, 43% (10) and 35% (8) of PD, 59% (48) and 42% (34) of KTx, respectively. NDD and KTx CKD subgroups had the highest obesity prevalence. Female sex was a risk factor for obesity diagnosed by WC criteria and protective for obesity diagnosed by %FM criteria. For obesity diagnosed by BMI and WC, diabetes mellitus was a risk factor.

Great variation was found for prevalence of sarcopenic obesity also among the different diagnostic criteria: HGS + BMI diagnosed 6 patients (NDD = 4, HD = 2), HGS + WC diagnosed 18 patients (NDD = 7, HD = 6, PD = 2, KTx = 3), HGS + FMI diagnosed 9 patients (NDD = 4, HD = 4, KTx = 1), HGS + %FM1 diagnosed 17 patients (NDD = 6, HD = 7, PD = 1, KTx = 3), HGS + %FM2 diagnosed 12 patients (NDD = 6, HD = 4, KTx = 2); ALMI + BMI diagnosed 9 patients (HD = 7, KTx = 2), ALM + WC diagnosed 62 patients (NDD = 5, HD = 30, PD = 5, KTx = 22), ALM + FMI diagnosed 19 patients (NDD = 1, HD = 10, KTx = 8), ALM + %FM1 diagnosed 62 patients (NDD = 7, HD = 27, PD = 4, KTx = 24), ALM + %FM2 diagnosed 44 patients (NDD = 6, HD = 17, PD = 3, KTx = 18); ALMI + BMI diagnosed 5 patients (HD = 5), ALMI + WC diagnosed 56 patients (NDD = 5, HD = 29, PD = 4, KTx = 18), ALMI + FMI diagnosed 14 patients (NDD = 1, HD = 9, KTx = 4), ALMI + %FM1 diagnosed 46 patients (NDD = 8, HD = 26, PD = 3, KTx = 9), ALMI + %FM2 diagnosed 40 patients (NDD = 7, HD = 16, PD = 3, KTx = 14) and $ALMI_{fmi}$ diagnosed 55 patients (NDD = 14, HD = 22, PD = 1, KTx = 18). Generally, HD and KTx groups had

Table 4. RR and 95% CI of muscle impairment and obesity for sex, total and central obesity, low muscle mass and strength, ethnicity, diabetes mellitus, and CKD treatment

Muscle impairment	ALM RR (95% CI)		ALMI RR (95% CI)		HGS RR (95% CI)
Sex					
Female	2.00 (1.57–2.55)		2.34 (1.76–3.11)		1.66 (0.82–3.34)
Obesity[1]					
BMI ≥ 30 kg/m^2	0.32 (0.17–0.60)		0.18 (0.08–0.43)		0.71 (0.28–1.84)
Central obesity[1]					
High waist circumference	0.55 (0.44–0.69)		0.60 (0.46–0.77)		0.88 (0.40–1.95)
Ethnicity					
Nonwhite	0.90 (0.70–1.17)		1.00 (0.76–1.31)		0.33 (0.10–1.04)
Comorbidity					
Diabetes mellitus	0.91 (0.70–1.17)		1.01 (0.77–1.34)		0.85 (0.35–2.02)
CKD treatment group					
HD	Reference		Reference		Reference
PD	0.66 (0.45–0.95)		0.54 (0.35–0.84)		0.88 (0.28–2.77)
Nondialysis	0.49 (0.35–0.68)		0.49 (0.34–0.71)		1.17 (0.54–2.52)
KTx	0.86 (0.68–1.08)		0.71 (0.55–0.94)		0.39 (0.12–1.21)
Obesity	**BMI RR (95% CI)**	**WC RR (95% CI)**	**FMI RR (95% CI)**	**%FM1 RR (95% CI)**	**%FM2 RR (95% CI)**
Sex					
Female	1.35 (0.97–1.89)	1.87 (1.56–2.24)	0.76 (0.51–1.12)	0.77 (0.60–0.98)	0.65 (0.46–0.93)
Low muscle mass[1]					
Low ALMI	0.10 (0.04–0.22)	0.55 (0.45–0.68)	0.36 (0.21–0.61)	0.97 (0.75–1.25)	1.11 (0.78–1.56)
Low muscle strengh[1]					
Low HGS	0.76 (0.39–1.49)	0.91 (0.68–1.21)	1.26 (0.67–2.34)	1.12 (0.79–1.58)	1.27 (0.78–2.05)
Ethnicity					
Nonwhite	1.24 (0.87–1.76)	0.91 (0.75–1.11)	1.09 (0.73–1.64)	0.93 (0.71–1.20)	1.30 (0.93–1.80)
Comorbidity					
Diabetes mellitus	1.53 (1.05–2.22)	1.21 (1.02–1.44)	1.42 (0.95–2.13)	1.15 (0.89–1.48)	0.97 (0.67–1.41)
CKD treatment group					
HD	Reference	Reference	Reference	Reference	Reference
PD	0.33 (0.09–1.22)	0.85 (0.59–1.22)	0.65 (0.22–1.94)	1.07 (0.64–1.80)	1.37 (0.71–2.63)
Nondialysis	0.94 (0.59–1.48)	0.84 (0.65–1.07)	1.16 (0.68–1.96)	1.15 (0.83–1.58)	1.31 (0.85–2.03)
KTx	0.55 (0.31–0.97)	0.98 (0.77–1.24)	0.98 (0.55–1.77)	1.16 (0.84–1.60)	1.41 (0.91–2.19)

RR adjusted for age; BMI, body mass index; CKD, chronic kidney disease; RR, relative risk; 95% CI, 95% confidence interval; ALM, appendicular lean mass; ALMI, appendicular lean mass index; WC, waist circumference; FM, fat mass; FMI, fat mass index; HGS, handgrip strength; HD, hemodialysis; PD, peritoneal dialysis; KTx, kidney transplant. [1] See Table 1 for codes and diagnostic reference.

higher prevalence of sarcopenic obesity. Female sex was a risk factor for sarcopenic obesity by diagnostic criteria that applied WC as obesity measurement.

Discussion

When different diagnostic criteria are used for the evaluation of muscle impairment, obesity, and sarcopenic obesity, their estimated prevalence varies greatly. Significant differences were also found when criteria related to muscle function (HGS) or mass (ALM and ALMI) were applied to diagnose muscle impairment or when central (WC) or whole-body adiposity (BMI, FMI, and %FM) were used to diagnose obesity. The differences are higher when diagnosing sarcopenic obesity. These findings are reinforced in the agreement and RR analyses.

The lack of standard diagnostic criteria for sarcopenic obesity has been a great challenge in the clinical manage-

Table 5. RR and 95% CI of sarcopenic obesity for sex, ethnicity, diabetes mellitus, and CKD treatment

Low muscle strength + obesity	HGS + BMI RR (95% CI)	HGS + WC RR (95% CI)	HGS + FMI RR (95% CI)	HGS+%FM1 RR (95% CI)	HGS+%FM2 RR (95% CI)	
Sex						
Female	1.06 (0.22–5.15)	3.32 (1.13–9.74)	1.25 (0.35–4.47)	1.35 (0.53–3.45)	1.08 (0.36–3.25)	
Ethnicity						
Nonwhite	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.33 (0.04–2.49)	0.37 (0.09–1.58)	0.54 (0.12–2.40)	
Comorbidity						
Diabetes mellitus	1.69 (0.40–7.24)	0.82 (0.29–2.28)	1.81 (0.57–5.78)	1.25 (0.47–3.30)	1.50 (0.51–4.40)	
CKD treatment group						
HD	Reference	Reference	Reference	Reference	Reference	
PD	0.00 (0.00–0.00)	1.01 (0.22–4.59)	0.00 (0.00–0.00)	0.53 (0.07–4.35)	0.00 (0.00–0.00)	
Nondialysis	1.60 (0.33–7.87)	1.29 (0.48–3.47)	0.84 (0.23–2.99)	0.77 (0.29–2.04)	1.31 (0.40–4.25)	
KTx	0.00 (0.00–0.00)	0.59 (0.15–2.36)	0.20 (0.03–1.49)	0.39 (0.09–1.64)	0.43 (0.08–2.38)	
Low muscle mass + obesity	**ALM + BMI RR (95% CI)**	**ALM + WC RR (95% CI)**	**ALM + FMI RR (95% CI)**	**ALM+%FM1 RR (95% CI)**	**ALM+%FM2 RR (95% CI)**	
Sex						
Female	1.74 (0.46–6.63)	5.05 (2.71–9.41)	0.90 (0.39–2.10)	1.06 (0.70–1.62)	0.88 (0.51–1.51)	
Ethnicity						
Nonwhite	0.96 (0.21–4.33)	0.75 (0.45–1.26)	0.96 (0.36–2.54)	0.81 (0.48–1.35)	1.04 (0.58–1.88)	
Comorbidity						
Diabetes mellitus	0.00 (0.00–0.00)	1.08 (0.71–1.63)	0.79 (0.27–2.26)	0.82 (0.48–1.40)	0.63 (0.31–1.28)	
CKD treatment group						
HD	Reference	Reference	Reference	Reference	Reference	
PD	0.00 (0.00–0.00)	0.60 (0.30–1.20)	0.00 (0.00–0.00)	0.56 (0.22–1.41)	0.64 (0.20–1.99)	
Nondialysis	0.00 (0.00–0.00)	0.18 (0.07–0.43)	0.09 (0.01–0.69)	0.25 (0.11–0.55)	0.35 (0.15–0.85)	
Kidney transplant	0.50 (0.11–2.37)	0.84 (0.56–1.28)	0.77 (0.31–1.88)	0.89 (0.55–1.46)	1.13 (0.60–2.10)	
Low muscle mass + obesity	**ALMI + BMI RR (95% CI)**	**ALMI + WC RR (95% CI)**	**ALMI + FMI RR (95% CI)**	**ALMI+%FM1 RR (95% CI)**	**ALMI+%FM2 RR (95% CI)**	**$ALMI_{fmi}$ RR (95% CI)**
Sex						
Female	2.70 (0.30–24.10)	6.82 (3.23–14.40)	1.27 (0.47–3.46)	1.26 (0.80–2.01)	1.06 (0.59–1.89)	0.62 (0.38–1.01)
Ethnicity						
Nonwhite	0.67 (0.11–4.14)	0.86 (0.52–1.42)	1.49 (0.54–4.08)	1.02 (0.62–1.67)	1.21 (0.67–2.19)	1.43 (0.90–2.29)
Comorbidity						
Diabetes mellitus	1.46 (0.21–10.42)	1.12 (0.73–1.72)	1.07 (0.30–3.81)	0.84 (0.47–1.50)	0.56 (0.24–1.29)	0.62 (0.33–1.15)
CKD treatment group						
HD	Reference	Reference	Reference	Reference	Reference	Reference
PD	0.00 (0.00–0.00)	0.48 (0.20–1.13)	0.00 (0.00–0.00)	0.40 (0.13–1.21)	0.63 (0.20–1.98)	0.16 (0.02–1.20)
Nondialysis	0.00 (0.00–0.00)	0.19 (0.08–0.46)	0.10 (0.01–0.79)	0.31 (0.15–0.65)	0.46 (0.20–1.06)	0.62 (0.34–1.13)
Kidney transplant	0.00 (0.00–0.00)	0.73 (0.46–1.15)	0.41 (0.12–1.39)	0.77 (0.44–1.33)	1.01 (0.49–2.05)	0.85 (0.48–1.49)

RR adjusted for age. See Table 1 for codes. CKD, chronic kidney disease; RR, relative risk; 95% CI, 95% confidence interval; ALM, appendicular lean mass; ALMI, appendicular lean mass index; $ALMI_{fmi}$, appendicular lean mass index adjusted for fat mat index; BMI, body mass index; WC, waist circumference; FM, fat mass; FMI, fat mass index; HGS, handgrip strength; HD, hemodialysis; PD, peritoneal dialysis; KTx, kidney transplant.

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ment of CKD patients. CKD is a catabolic condition associated with muscle loss and decreased protein synthesis [2, 6]. Muscle strength is influenced not only by muscle mass but also by muscle quality and its neural activation [24]. In addition, low muscle mass seems to be related to poor outcomes only if accompanied by weakness [25], and mortality is more strongly associated to low muscle function than to low muscle mass [25]. Given that the equipment for measuring muscle mass, such as DXA, is seldom available in clinical practice, functional evaluations, such as HGS and gait speed tests that are easily applicable are an alternative. This study showed that women are more at risk for muscle impairment, obesity, and sarcopenic obesity, probably related to a more sedentary lifestyle [26], a traditional risk factor for the development of sarcopenia, obesity, and also sarcopenic obesity [6].

The HD group had the greatest muscle impairment, in agreement with previous studies [1, 6]. HD patients had an increased catabolism and metabolic acidosis, decreased protein synthesis, and a higher inflammatory condition [27]. The prevalence of obesity diagnosed by other measures is even greater, highlighting the limitations of BMI to evaluate body composition in CKD, with high specificity and low sensitivity [5].

In our RR analyses, BMI ≥30 kg/m^2 and high WC were protector factors for muscle impairment by ALM and ALMI. In general population, extremes of BMI are associated with higher mortality risk. However, in CKD only low BMI is associated with increased mortality [18]. In addition, the association of high BMI with higher mortality is further reduced with the progression of CKD and is not observed in stages 4 and 5 [28]. The obesity paradox in CKD could be the result of the protective effect of lean mass even in the presence of greater adiposity. The clinical and survival advantages resulting from the higher lean mass are greater than the disadvantages of increased adiposity [3, 18]. In sarcopenic obesity, due to the reduced protection of lean mass, mortality rates rise with the increase in BMI [18, 19].

The role of obesity in CKD depends also on the CKD stage. In the early stages of CKD, excess fat may lead to progression of the disease. In the final stages of CKD, excess subcutaneous fat appears as a protective factor, especially in the presence of protein-energy wasting syndrome. For KTx, obesity increases the risks of graft rejection and loss [4, 18]. However, in addition to high body fat, body fat distribution is strongly related to morbidity and mortality. Visceral fat is more strongly related to complications of obesity, such as metabolic syndrome than subcutaneous fat [29]. Elevated WC, a diagnostic criterion for obesity [30] with the highest prevalence in the present study, was associated with higher cardiovascular mortality among patients in HD [29]. These data suggest that in end-stage CKD patients, the negative effects of visceral fat override with the inverse association between BMI and mortality. Thus, the different outcomes among patients with obesity defined by several criteria can be explained by the different relationship that the variables applied in obesity definition have with total body fat (BMI, FMI, and %FM) and local body fat (WC). As BMI is not adequate for evaluation of adiposity [5] and DXA is rarely available for routine use, WC appears as an easy and important measure for adiposity.

As stated by a recent review from 2020 [17], the lack of consensus for sarcopenic obesity remains, with definitions that applied only low muscle mass and obesity, others with low muscle strength and obesity (dynapenic obesity), and more rarely sarcopenia in addition to obesity. Our data evaluated the first 2 definitions which are more frequently applied.

Limitations of the present study include the fact that HGS was the only measure applied for functional capacity. As the study sample consisted of young adults, extrapolation of the findings to the elderly, children, and adolescents may not be accurate. Because of the observational design, causality between the different diagnostic criteria cannot be inferred as also relationship with prognosis and mortality; the assumptions were based on the previous data.

The strengths of our study were (i) large sample size; (ii) evaluation of renal patients on NDD, HD, PD, and KTx treatment; (iii) diagnosis of muscle impairment according to the most recent consensus; (iv) obesity diagnoses accounting for both total FM and visceral FM; (v) evaluations carried out by a single professional and in accordance with high-quality standard protocols, with reference method for body composition analysis (DXA) in total sample; and (vi) deep statistical analyzes.

Conclusion

The prevalence of sarcopenic obesity in patients with CKD varied widely depending on the diagnostic criteria used, especially among criteria for low muscle mass versus low muscle strength and for high total body fat versus high visceral fat. The increasing rates of obesity and

sedentarism among nephrology patients and the association of high adiposity and muscle impairment with higher morbidity and mortality and worse clinical prognosis reinforce the need for standard criteria for diagnosis and research. This would enable effective treatment strategies to be instituted in order to improve the clinical outcome. As HGS and WC are easily applied in clinical settings, they can be used for sarcopenic obesity diagnosis (also named as dynapenic obesity); however, studies investigating the relationship of dynapenic obesity with prognosis and mortality are needed before widespread use.

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Statement of Ethics

The study was conducted according to the Declaration of Helsinki and received the approval of the Local Ethics Committee (Protocol Number: 2053045). All participants provided written informed consent prior to the initiation of the study procedures.

Conflict of Interest Statement

The authors declare no conflicts of interest. The funding agencies had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

Author Contributions

N.T. Bellafronte and P.G. Chiarello contributed to the conception of the research; N.T. Bellafronte and A.Q.M. Ono contributed to the acquisition of the data; N.T. Bellafrronte contributed to the design of the research, analysis, and interpretation of data, and drafted the manuscript. All the authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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