

Poor Physical Function as a Marker of Sarcopenia in Adults with Class II/III Obesity

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Abstract

Background: Adults with class II/III obesity [body mass index (in kg/m²) ≥35] may present with a phenotype characterized by low lean mass and excess fat mass, a condition known as sarcopenic obesity (SO). Little is known about the prevalence and relevance of SO in these individuals, primarily due to a lack of relevant diagnostic criteria.

Objective: Here, we explored the definition of SO based on physical function as an outcome of interest in adults with class II/III obesity and applied this definition to compare clinical characteristics between SO and non-SO patients.

Methods: In this cross-sectional analysis, patients' demographic, anthropometric, and biochemical characteristics, as well as comorbidities and physical activity levels, were collected at an obesity specialty clinic prior to any treatment. Body composition was assessed by dual-energy X-ray absorptiometry. Physical function was assessed by self-reported difficulties with activities of daily living (ADLs) from an 11-item questionnaire. Five SO definitions were tested against reported difficulty with ADLs with the use of receiver operating characteristic (ROC) analysis.

Results: A total of 120 subjects (86% women) aged 46 ± 11 y were included. Based on ROC analysis, SO was best defined by an appendicular skeletal mass (ASM)/weight × 100 (%) <19.35% for women and <24.33% for men, resulting in a prevalence of 25% (n = 30, women 22.3%, men 41.2%). SO was significantly associated with older age, higher waist circumference, higher triglycerides, greater use of antihypertensive medications, and lower physical activity.

Conclusions: In this sample of adults with class II/III obesity, difficulties with ADLs were best associated with measures of ASM in relation to total body weight. Patients identified with SO using this criterion presented with poorer clinical outcomes such as factors of elevated cardiometabolic risk. *Curr Dev Nutr* 2018;2:nzx008.

Introduction

Low lean mass, also termed sarcopenia, is a condition primarily studied in the elderly as part of the aging trajectory (1). Lower lean mass is associated with low physical activity, illness, inflammation, certain hormonal and neurologic conditions, and poorer quality of life, among other health consequences (2). Increases in fat mass (FM) are typically seen from middle age up to age 60–70 y, and are associated with a high prevalence of obesity among this age group.

In addition to aging-related changes in body composition, weight loss from obesity treatment may result in reductions in both FM and lean mass. Weight cycling (weight gain after weight loss) is common (3–5) and is associated with increased FM with lean mass remaining lower than



Keywords: activities of daily living, appendicular skeletal mass, class II/III obesity, dual-energy X-ray absorptiometry, lean soft tissue, sarcopenia

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Supplemental Tables 1–3 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at <https://academic.oup.com/cdn/>.

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Abbreviations used: ADL, activity of daily living; ASM, appendicular skeletal mass; CRP, C-reactive protein; DXA, dual-energy X-ray absorptiometry; eGFR, estimated glomerular filtration rate; FFM, fat-free mass; FM, fat mass; LST, lean soft tissue; ROC, receiver operating characteristic; SO, sarcopenic obesity.

baseline (i.e., prior to weight loss) (6). Repeated weight loss attempts, combined with the normal aging trajectory, can put individuals at risk for sarcopenia over time (5).

Sarcopenic obesity (SO) is described as the coexistence of low lean mass with excess FM (7). Several definitions for sarcopenia exist, mostly based on sex-specific cutpoints for low muscle mass derived either from a young reference population or from a study cohort (8). Definitions based on a health outcome of interest are highly relevant and have been increasingly used (9–11). Due to the variety of definitions (for sarcopenia and obesity) and methods to assess body composition, the estimates of the prevalence of SO are highly variable (12). Studies have identified SO in older adults (≥ 65 y of age) and those with certain health conditions (11, 13, 14). In older adults, sarcopenia is associated with difficulties with activities of daily living (ADLs) (15, 16) and functional impairment (17, 18). Excess FM and low lean mass can compound negative effects on cardiovascular and metabolic health (19–23), impacting disability and mortality (24, 25). Although most studies to date have focused on older adults (≥ 60 y of age), recent data suggest younger and middle-aged individuals may also present with SO (26, 27). Nonetheless, the lack of diagnostic criteria for sarcopenia in younger individuals, especially those with class II/III obesity [BMI (in kg/m^2) ≥ 35], has limited our understanding of the prevalence and clinical characteristics of this condition in these individuals. Therefore, the primary purpose of this study was to explore the definition of sarcopenia that best discriminated adults with class II/III obesity based on a clinical outcome of interest (data-driven approach), namely physical function. The second was to apply this definition and compare the clinical characteristics of subjects with and without SO.

Methods

Subjects

A cross-sectional analysis was conducted on patients from a multidisciplinary obesity specialty clinic in Northern Alberta, Canada (population 1.2 million) (28). Patient history and clinical assessment were completed at the initial visit (i.e., prior to any weight loss treatment). Height (centimeters), weight (kilograms), waist circumference (centimeters), and blood pressure (expressed in mm Hg) were measured using standardized procedures, and BMI calculated as weight over height squared (kg/m^2), and categorized according to WHO criteria (29). Availability of dual-energy X-ray absorptiometry (DXA) scans and further details on data collection have been previously described (8). All subjects were adults (18–69 y of age) with class II/III obesity who completed the initial assessment and had a DXA body composition scan in their medical record (available from consecutive patients seen from January 2009 to June 2012). Exclusion criteria included age (≥ 70 y), and those who had incomplete DXA data. Ethics approval was obtained from the University of Alberta Research Ethics Board.

Body Composition

DXA scans were conducted using Hologic Discovery A/W (Hologic Inc., Bedford, MA) at a local imaging center, based on which FM, lean mass [better termed lean soft tissue (LST)], fat-free mass (FFM; composed of LST and bone) for the whole body, and segmental values [appendicular skeletal mass (ASM); composed of the LST from the

arms and legs] were computed. These measures were adjusted by height in square meters to calculate the FM index and ASM index (30).

Biochemical Analysis and Comorbidities

Biochemical data was collected from medical records and included inflammatory markers, lipid panel, glucose-related measurements, kidney function, albumin, and vitamin D concentrations. Subjects with abnormal biochemical values meeting criteria for either diabetes or prediabetes were combined as a dichotomous variable.

Comorbid conditions were identified based upon review of medical history and prescription medications and clinical and laboratory values collected at the initial assessment. Metabolic syndrome was defined using the National Cholesterol Education Program Adult Treatment Panel III reference values; ≥ 3 out of 5 criteria being met indicated its presence (31).

As was done previously (32–34), a multimorbidity categorical score (0, 1, 2, ≥ 3) was used including 8 comorbidities: diabetes or prediabetes, hypertension, dyslipidemia, metabolic syndrome, mental health, chronic kidney disease, sleep apnea, and osteoarthritis.

Activity Level and Difficulties with Activities of Daily Living

Physical activity levels were categorized as either “met” or “did not meet” Canadian Physical Activity Guidelines for Adults, defined as accumulating ≥ 150 min of moderate-to-vigorous intensity activities in a week, in bouts of ≥ 10 min (35).

An occupational therapy referral screening questionnaire based on the Canadian Model of Occupational Performance (36) was used (see **Supplemental Table 1**). This self-administered questionnaire included 11 items that asked about subjects’ experiences with managing ADLs and the ability to perform a variety of tasks including: transferring in and out of the car, bed, bathtub, or on and off the toilet; bathing; skin care; personal hygiene; household tasks; and leisure activities. Other items asked about home accessibility, falls or balance concerns, the impact of excess skin on completing daily activities, the impact of fatigue on completing daily activities, and whether a client uses or has considered custom footwear or orthotics. Options included “yes” or “no” answers to each item, scored as 1 or 0, respectively. Subjects also had the choice to report, “I have help” for some items, in which case a score of 1 was assigned. A higher overall score represented more items reporting difficulty with ADLs. A composite score for items on the questionnaire was calculated as a continuous variable (range 0–11). Additionally, a dichotomous variable defined as “0–2” or “ ≥ 3 ” items was created to explore the selected definition for SO, as described next.

SO Definition

Although all subjects had obesity (BMI ≥ 35), the variability of percentage of FM was explored to avoid misclassification. As reported previously (and in the hereby shown results), percentage of FM fell within several accepted criteria to define excess FM (8) for all patients. Based upon this previous study (8), 5 previously published DXA-derived definitions of sarcopenia were explored (8, 21, 37–39; see **Table 1**). Because these definitions were not tested in regards to predictive ability, the current study identified sarcopenia based on a clinically meaningful cutpoint (data-driven approach) whereby a value was specified below which individuals would be at increased risk for a health outcome (9–11, 40, 41).

TABLE 1 Bivariate correlations (Pearson's r , $P < 0.05$) for the number of items (0–11) for self-reported difficulty with activities of daily living with continuous body composition variables for the definitions of sarcopenia applied to the study sample¹

Definitions	Reference	Correlations with ADL difficulties, r (P value)		
		All ² ($n = 111$)	Women ($n = 94$)	Men ³ ($n = 17$)
ASM/weight x 100, %	Levine and Crimmins, 2012 (21)	-0.262 (0.005)	-0.232 (0.024)	-0.510 (0.037)
ASM/BMI, kg/m ²	Batsis et al., 2015 (37)	-0.187 (0.049)	-0.158 (0.127)	-0.526 (0.021)
ASM adjusted for height and FM (residuals)	Newman et al., 2003 (38)	0.108 (0.268)	0.195 (0.060)	-0.177 (0.496)
FM:FFM ratio, centile	Johnson Stoklossa et al., 2017 (8)	-0.084 (0.380)	-0.150 (0.148)	0.239 (0.356)
	Siervo et al., 2015 (39)	0.230 (0.015)	0.231 (0.025)	0.453 (0.068)

¹Based on definitions identified/discussed in Johnson Stoklossa et al. (8). ADL, activity of daily living; ASM, appendicular skeletal mass; FMM, fat-free mass; FM, fat mass.

²Self-reported difficulty with ADLs available for $n = 111$.

³Spearman's r reported for men due to small sample size ($n < 30$).

The choice of difficulty with ADLs as the outcome of interest was due to the association with reduced physical function, increased disability, and poor quality of life (15, 24, 40, 42). ADL difficulties are notably a common health consequence of sarcopenia (43). Therefore, our sex-specific cutpoints were developed based on its discriminative and predictive ability, similar to previous studies in health and clinical conditions (18, 24, 26, 41).

Correlation of the continuous body composition variable and the continuous variable for difficulty with ADLs was evaluated for each definition (Table 1), the definition of choice being the one most significantly correlated with difficulty with ADLs. Receiver operating characteristic (ROC) curves were used to determine sex-specific cutpoints of the continuous body composition variable selected to define sarcopenia based upon the 2 categories for difficulty with ADLs (0–2 items compared to ≥ 3 items), with high sensitivity as the priority criteria. The AUC was then explored to identify optimal sex-specific cutpoints for the total difficulties with ADL score (continuous variable). These were used to create a dichotomous variable: SO compared to non-SO based on impaired and non-impaired ADLs, respectively. The body composition variable calculated with the new cohort-derived cutpoints was then compared, using chi-square test and kappa statistics, with the variable calculated using the original study cutpoints from the selected SO definition, to determine the level of agreement between the 2 definitions.

Statistical Analysis

Descriptive statistics were used as appropriate. Normality testing was completed with the Shapiro–Wilk test. Mean values of 2 groups were compared using independent samples t tests (Mann–Whitney U for nonparametric data). Chi-square or Fisher's exact test were used as appropriate. Pearson's or Spearman's correlations were used to test the correlation between 2 continuous variables for normally and non-normally distributed variables, respectively. Cronbach's alpha was used to determine the internal consistency of the items on the questionnaire for difficulty with ADLs. A P value of <0.05 , based on 2-tailed tests, was considered statistically significant. Data analysis was completed with IBM SPSS Statistics v23 (IBM Corp., Armonk, NY).

Results

Subject Characteristics

Of 167 cases reviewed, 120 had available DXA data. Subject demographics and anthropometrics are presented in Table 2. The sample was

predominately female, middle-aged, married or common law, educated, and working outside the home. In terms of body composition, women had lower LST and higher FM than did men, with similar findings between derivatives of these variables. Results for biochemical analysis (serum, fasting) are presented in Supplemental Table 2. Five subjects (4.3%) had renal impairment [estimated glomerular filtration rate (eGFR) $<60 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$]. All subjects presented with ≥ 1 comorbidity in addition to obesity (see Supplemental Table 3 for subjects' clinical characteristics). The most prevalent comorbidities were dyslipidemia, followed by metabolic syndrome and hypertension. Multimorbidity was highly prevalent with 80.8% of patients having ≥ 3 comorbid conditions in addition to class II/III obesity. No differences were observed by sex ($P = 0.695$) or BMI category ($P = 0.427$) between those meeting or not meeting physical activity guidelines.

Of the 111 respondents ($n = 9$ with missing data), 11% reported no difficulties with ADLs with no sex differences noted. Subjects across all ages and BMI categories reported difficulties with ADLs, and $>50\%$ reported difficulty with ≥ 3 items. Prevalence of comorbidities was not different comparing subjects reporting difficulty with 0–2 items compared to those reporting ≥ 3 items.

SO Definition

From the 5 sarcopenia definitions explored (Table 1), 2 were significantly correlated with items of difficulty with ADLs: ASM/weight x 100 (%) (21, 22) ($r = -0.262$, $P = 0.005$) and FM:FFM ratio (39) ($r = 0.230$, $P = 0.015$). For both definitions, lower lean mass was associated with a higher number of items of difficulty with ADLs. Nonetheless, only ASM/weight x 100 (%) was significantly correlated for both sexes [women ($r = -0.232$, $P = 0.024$); men ($r_s = -0.510$, $P = 0.037$)]. Therefore, this variable was selected to define sarcopenia in our cohort.

ASM/weight x 100 (%) for the entire cohort ($n = 120$) was $21.7\% \pm 2.6\%$; median and range: 21.5% (16.2–29.2%). Cohort-derived sex-specific cutpoints were then determined; for women the value was 19.4% (sensitivity 86%, specificity 29%) and it was 24.3% (90% sensitivity, 86% specificity) for men. Differences were not driven solely by men, as the best agreement was achieved with the sex-specific cutpoint applied to the entire data-set (data not shown). Applying these cutpoints, the prevalence of SO in the entire sample was 25% (22.3% women; 41.2% men). Mean values for ASM/weight x 100 (%) were $19.3\% \pm 1.8\%$ for subjects with SO and $22.5\% \pm 2.3\%$ for the group with non-SO ($P < 0.0001$).

TABLE 2 Demographic, anthropometric, and body composition characteristics of adults with class II/III obesity ($n = 120$)¹

Variables	% or mean \pm SD; median (range)
Demographics	
Sex	
Female	85.8
Age, y	46.9 \pm 11.1; 49.0 (23–69)
Marital status	
Single	23.3
Married/common law	67.5
Divorced/separated/widowed	9.2
Education	
Some high school	2.5
Completed high school	97.5
Completed postsecondary	53.3
Employment	
Full-time	53.3
Part-time	14.2
Unemployed	6.7
On disability	7.5
Homemaker	5.8
Retired	12.5
Smoking	
Never	45.5
Former	47.3
Current	7.3
Age of obesity onset	
Pediatric, ≤ 19 y	46.7
Adult, ≥ 20 y	53.3
Anthropometrics	
Height, cm	166.0 \pm 7.64; 165.0 (148.6–187.1)
Weight, ² kg	120.2 \pm 19.6; 116.2 (88.9–180.7)
BMI, ² kg/m ²	43.5 \pm 5.7; 42.3 (34.9–58.5)
35.0–39.9	33.3
40.0–44.9	32.5
45.0–49.0	19.2
≥ 50.0	15.0
Waist circumference, cm ³	123.3 \pm 13.2; 122.5 (93.5–163.0)
Body composition ⁴	
ASM, kg	F: 24.7 \pm 3.7; 24.2 (17.4–35.4) ² M: 34.2 \pm 5.2; 35.3 (27.0–44.9)
ASMI, kg/m ²	F: 9.2 \pm 1.2; 9.1 (6.7–12.8) M: 10.9 \pm 1.3; 10.9 (8.7–13.6)
ASM/weight x 100, %	F: 21.2 \pm 2.1; 21.0 (16.2–28.3) M: 24.9 \pm 2.8; 24.9 (20.2–29.2)
FM, %	F: 48.0 \pm 4.2; 48.3 (32.3–57.4) M: 41.4 \pm 5.6; 39.7 (31.9–53.2)
FMI, kg/m ²	F: 20.6 \pm 3.8; 20.0 (13.9–30.9) ² M: 18.0 \pm 3.7; 16.9 (13.4–24.9)

¹ASM, appendicular skeletal mass; ASMI, ASM index; FM, fat mass; FMI, fat mass index.

²Variable not normally distributed for women.

³Waist circumference available for 78% ($n = 94$).

⁴All body composition variables were statistically different between sexes.

Correlations for SO definition (as dichotomous variable: SO compared to non-SO) with difficulty with ADLs (0–2 compared to ≥ 3 items) were significant ($P = 0.006$). The ability for these ADL categories to discriminate sarcopenia was moderate for women (AUC = 0.60; 95% CI: 0.49, 0.71) and strong for men (AUC = 0.90; 95% CI: 0.74, 1.00). There was a high level of agreement ($k = 0.915$) between our

cohort-specific definition and Levine and Crimmins' (21) published cutpoints for ASM/weight x 100 (%) derived from a young reference group.

The ADL questionnaire had good internal consistency (11 items, $\alpha = 0.848$). As such, nearly three-quarters of subjects with SO reported difficulty with ≥ 3 items compared to less than half (44%) of non-SO subjects. Values for ASM/weight x 100 (%) were lower for subjects who responded "yes" to 5 separate ADL items: transfers ($P = 0.046$), wiping self ($P = 0.030$), fatigue as a barrier to household tasks ($P = 0.017$) and leisure activities ($P = 0.009$), and access to household rooms ($P = 0.020$). Overall prevalence of difficulty with ADLs by SO status is presented in **Figure 1**, with differences identified for 6 of the 11 items: transfers ($P = 0.023$), falls ($P = 0.030$), dress self ($P = 0.021$), fatigue as a barrier to household ($P = 0.048$) and leisure activities ($P = 0.004$), and excess skin ($P = 0.025$).

Clinical Characteristics of SO

No differences for most demographic variables were observed by sarcopenia status, except for age and sex (prevalence by sex as already reported). Age range was 23–69 and 24–68 y for SO compared to non-SO groups, respectively. Mean age was higher for the SO group (50.7 ± 12.7 compared to 45.7 ± 10.3 y, $P = 0.033$). Prevalence of SO was significantly higher among subjects aged ≥ 65 y (66.7% compared to 22.8%, $P = 0.016$). Smoking status (never compared to former) was not different between groups and no current smokers were identified with SO. Although all waist circumference measurements exceeded recommendations, individuals with SO presented with a higher mean waist circumference compared to their counterparts (130.2 ± 21.1 compared to 121.1 ± 11.7 cm, $P = 0.004$).

A comparison of clinical variables (metabolic and functional) by sarcopenia status is presented in **Table 3**. No differences between groups were identified for most biochemical variables, except for albumin and triglycerides. Only 2 subjects had hypoalbuminemia and both had sarcopenia. SO was associated with higher triglyceride concentrations (2.06 ± 1.00 compared to 1.62 ± 0.73 mmol/L, $P = 0.040$), which in turn overall exceeded the normal reference value (< 1.7 mmol/L). Only a trend towards a difference was found between groups comparing abnormal to normal triglyceride concentrations (see **Table 3**).

SO was associated with a greater prevalence of renal impairment (eGFR < 60 mL \cdot min⁻¹ \cdot 1.73 m⁻²), yet overall the majority of the cohort had normal renal function. There were no differences for mean C-reactive protein (CRP) concentrations (SO, 8.07 ± 5.40 compared to 7.58 ± 6.51 mg/L for non-SO, $P = 0.731$). Presence of comorbid conditions was not different between groups. Use of medications for hypertension was higher among SO patients, although no difference was identified for the prevalence of hypertension or blood pressure measures among groups (data not shown).

Individuals with SO were less likely to meet physical activity guidelines (see **Table 3**). For subjects who met the guidelines, 95.8% were in the non-SO group.

Discussion

This is the first study to define SO in an adult cohort with class II/III obesity using a clinically relevant outcome of interest, ADL difficulty.

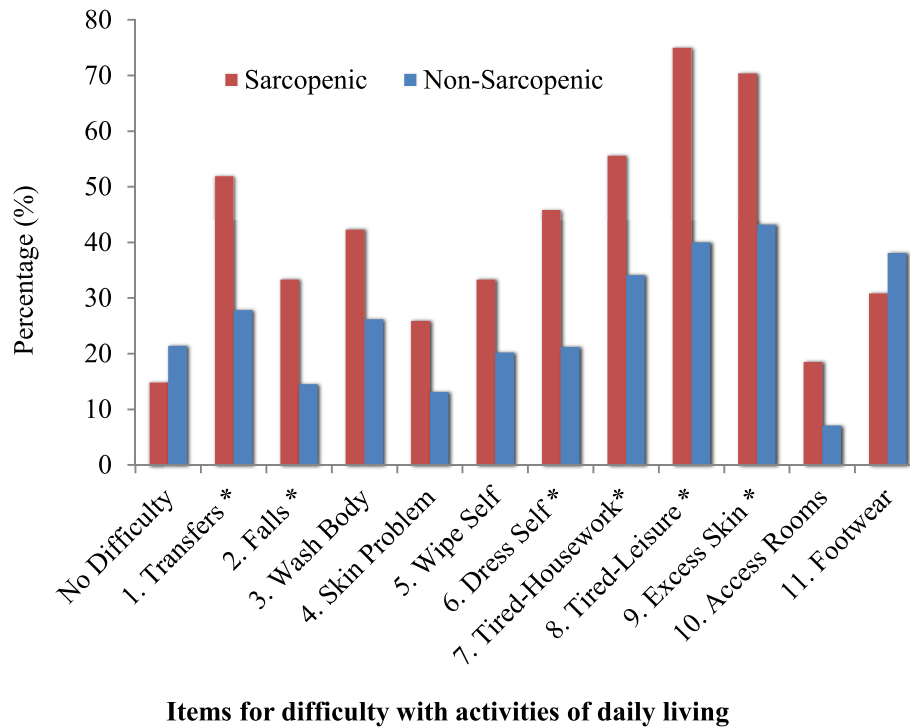


FIGURE 1 Comparison of items for self-reported difficulty with activities of daily living with body composition phenotype groups: sarcopenic obese ($n = 27$, left bar) compared to nonsarcopenic obese ($n = 84$, right bar). The occupational therapy screening questionnaire was completed by each subject at the initial clinic assessment with 11 items that asked about their experiences and ability to perform a variety of activities of daily living tasks. *Results for items that were significantly different between the groups, $P < 0.05$.

Maintaining ADL functioning is essential for independence and optimal quality of life (44, 45). In our definition (ASM/weight $\times 100$, %), reduced ADLs in an adult cohort with class II/III obesity were predicted by the amount of body weight (load) in proportion to their lean mass (capacity—load bearing) (12). In other words, this concept accounts for the magnitude of body weight in relation to lean mass that would lead to functional impairments. This concept is in accordance with other studies that reported an association between lower relative lean mass and greater difficulty with ADLs and function (18, 21, 46). We propose that the relation between body composition and physical function may provide a useful marker for the clinical diagnosis of SO in adults with class II/III obesity defined as measure of ASM in relation to total body weight. Using this definition, we reported that, although present across the age spectrum, SO was associated with older age, higher waist circumference, higher triglycerides, use of anti-hypertensive medications, and inactivity.

Defining SO is challenging (12). As explored in our previous publication (8), definitions accounting for measures of body mass or FM may better identify these individuals. Here, lower ASM/weight $\times 100$ (%) was correlated with a higher number of items for difficulty with ADLs. Per our previous study (8), Levine and Crimmins' (21) cutpoints identified 23.2% women and 58.5% men with SO in the present cohort. Due to the uniqueness of our cohort (non-elderly adults with class II/III obesity) and the interest to tie the definition to a clinical outcome, cohort- and sex-specific cutpoints were explored using the same body composition variable (ASM/weight $\times 100$, %). The resulting cutpoints (women $<19.35\%$, men $<24.33\%$) were very similar for women and

slightly lower for men, compared to the Levine and Crimmins (21) values, leading to an overall higher prevalence of SO (25% compared to 10% for the former study; sex-specific prevalence not reported).

SO was identified in more men than women (41.2% compared to 22.3%). Sex differences in the prevalence of SO are variable, with some studies reporting a higher prevalence for women (38, 46), others for men (15, 26, 47), or mixed results depending on the definition applied (37, 48). Interestingly, we showed a consistently higher prevalence in men, among 18 definitions (8). Differences in body composition between the sexes may be associated with sex hormones including estrogen and testosterone, influencing both fat and lean tissues (49–52).

There were not as many differences as expected when comparing biochemical variables between sarcopenic and nonsarcopenic obese groups. Although hypoalbuminemia was correlated with SO, our $n = 2$ precludes any meaningful conclusion. Elevated CRP, a biomarker for systemic inflammation and associated with obesity, sarcopenia, metabolic syndrome, and cardiovascular disease, was identified in $\sim 30\%$ of the study cohort, but the prevalence was not different between groups. Our results are in agreement with those of Levine and Crimmins (21), who found no difference in CRP values between both sets of subjects in their obese groups (sarcopenic and nonsarcopenic). Although studies of older adults report an association between SO with metabolic syndrome and insulin resistance (21, 22), we were unable to observe such differences. Unfortunately, fasting insulin was not available for our cohort.

Although the prevalence of metabolic syndrome was similar between groups, a greater prevalence of reporting 2 of the 5 criteria

TABLE 3 Comparison of clinical variables between sarcopenic obese versus nonsarcopenic obese groups ($n = 120$)¹

Variables ²	All ³ (n)	Sarcopenic obese ⁴ (n = 30)	Nonsarcopenic obese ⁴ (n = 90)	P value
Biochemical, %				
Fasting glucose > 6.0 mmol/L	114	30.8	31.8	0.511
HbA1C > 6.5	115	18.5	28.4	0.306
eGFR < 60 mL · min ⁻¹ · 1.73 m ⁻²	116	10.7	2.3	0.055
TChol > 6.2 mmol/L	115	11.1	9.1	0.755
LDL > 3.2 mmol/L	115	29.6	38.6	0.495
HDL: F < 1.3, M < 1.0 mmol/L	115	55.6	63.6	0.450
TG > 1.7 mmol/L	115	59.3	38.6	0.059
CRP > 10.0 mg/L	112	28.0	28.7	0.943
Albumin < 35 g/L	114	100	0.0	0.009
25-OH vitamin D ₃ <80 nmol/L	113	61.5	65.5	0.710
Comorbidities, %				
Abnormal glycemic control	114	34.6	43.2	0.436
On medication	120	13.3	18.9	0.588
Hypertension	115	71.4	69.0	0.805
On medication	120	50.0	28.9	0.035
Dyslipidemia	115	96.4	90.9	0.342
On medication	120	26.7	15.6	0.173
Mental health	120	56.7	55.6	0.915
On medication	120	36.7	27.8	0.358
Metabolic syndrome	117	72.4	69.3	0.819
Osteoarthritis	120	40.0	23.3	0.077
Sleep apnea	120	43.3	34.4	0.382
Multimorbidity score, %	120			
≥3		80.0	81.1	0.885
Activity level, %	120			0.007
Meets guidelines		3.3	25.6	
Difficulty with ADLs, %	111			
Any item		85.2	78.6	0.584
Less vs. more items				0.008
0–2 items		25.9	56.0	
≥3 items		74.1	44.0	

¹ADL, activity of daily living; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HbA1C, glycated hemoglobin; TChol, total cholesterol; TG, triglyceride.

²Variables were compared by category: biochemical (abnormal vs. normal); comorbidities (present vs. absent); multimorbidity score (<3 vs. ≥3); difficulty with ADLs: any item (yes vs. no).

³All: total number of participants with data for each variable from the entire cohort.

⁴Percentages reported as a total within each body composition group.

for metabolic syndrome (high triglycerides and high waist circumference) was reported among the SO group. The hypertriglyceridemic waist phenotype has been used to identify those with increased visceral adiposity, which in turn is associated with increased cardiometabolic risk and mortality (53, 54). In addition to cardiometabolic risk, the difference in serum triglyceride concentrations between subjects with SO and those without may serve as a biomarker for other abnormalities.

Regarding physical activity, 80% of subjects did not meet activity guidelines, which is similar to nationally reported levels (78%) (55). No difference by sex or BMI categories between those who met or did not meet the guidelines was observed, but a greater proportion of individuals with SO did not meet the activity guidelines. It is possible that a proportion of SO patients were unable to perform physical activity, and hence did not meet the guidelines.

Our study has several limitations including the tool to assess ADLs. Although each item addressed a category of ADL difficulty, such as transfers, the question as stated often included >1 option (i.e., car, bed, bathtub, and toilet). It was not possible to evaluate, for example, if patients only had difficulty with transferring in and out of their

car or if they experienced difficulty with transfers for all the examples provided. Additionally, reasons for the difficulties or the level of difficulty experienced cannot be ascertained. Nonetheless, this tool was able to differentiate patients by sarcopenia status, highlighting the potential use of this or similar tools in research and clinical settings. Unfortunately, measures of muscle strength, quality, or function were not available. Further assessment of factors influencing difficulty in participation and performance of ADLs, including physical function, cognition, and strength, is needed (45). Additional limitations of our study include a small sample size of a convenience sample, and the cross-sectional design. Our data-driven approach to define this abnormal body composition type should not be seen as a limitation, as similar approaches have been previously used (18, 24, 26, 41, 56). Nonetheless, the definition hereby used requires external validation in different patient cohorts.

Our study used state-of-the-art body composition data (DXA) contributing to the limited research on subjects with BMI >40 who may be excluded from studies due to equipment weight capacity limits (57). Additionally, this study highlights the impact of SO in younger and middle-aged adults, who, contrary to expectations, may also experience SO and its clinical consequences. Further research is needed to validate

cutpoints for SO in relation to clinical outcomes, such as the items of self-reported difficulty with ADLs, for adults with class II/III obesity. Unfortunately, we were unable to evaluate whether the performance and discriminative capacity of SO are body size dependent—i.e., valid for those with obesity class I. Likewise, our definition of SO does not account for age (although <6% of participants were ≥ 65 y old), which is an important determinant of difficulties with ADLs and would probably lead to lower cutpoints for younger individuals. Notably, age was not different by sarcopenia status.

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