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Prevalence of sarcopenic obesity in adults with end-stage knee osteoarthritis

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SUMMARY

Objective: To identify the prevalence of sarcopenic obesity, a phenotype of low muscle mass and high adiposity, in adults with end-stage knee osteoarthritis (OA). Various diagnostic criteria, including assessment of muscle/fat mass, muscle strength and physical function, were used to identify patients with and without sarcopenic obesity, and to compare outcomes of pain, function and quality of life.
Design: Cross-sectional clinical study including adults with a body mass index (BMI) $\geq$30 kg/m^2 and knee OA. Body composition was measured by dual-energy X-ray absorptiometry (DXA). Assessments included gait speed, handgrip strength, six minute walk test, and self-reported pain, physical function, and health-related quality of life using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and EuroQol Foundation (EQ-5D).
Results: 151 adults (59% female) aged 65.1 ± 7.9 years, mean BMI 37.1 ± 5.5 kg/m^2, were included. Prevalence of sarcopenic obesity using diagnostic cut-offs of appendicular skeletal muscle mass (ASM) relevant to height^2, weight and BMI varied from 1.3% (95% confidence interval (CI): 0.2–4.7%) to 14.6% (9.4–21.2%) and 27.2% (20.2–35%), respectively. A combined diagnostic approach including low ASM with either low strength or low function yielded a prevalence of 8.6% (4.7–14.3%). Sarcopenic obesity influenced walking speed, endurance, strength, and patient-reported difficulty with self-care activities, regardless of diagnostic approach.
Conclusion: Prevalence of sarcopenic obesity varied depending on diagnostic criteria. Given the impact of this condition and OA on physical function, we suggest a combined diagnostic approach be used to clarify expected prevalence and enable early clinical identification and management of sarcopenic obesity in patients with knee OA.

Introduction

Obesity [defined using body mass index (BMI)] is associated with knee osteoarthritis (OA) progression and increased surgical infection risk in total knee arthroplasty (TKA)[1,2]. However sarcopenic obesity, a phenotype of low muscle mass and high adiposity[3], may have greater relevance and implications for adverse outcomes in this clinical population. This condition may be present in patients with knee OA but not identified using BMI alone. Sarcopenic obesity is associated with surgical infection[4,5], disability[6], and mortality[7] in other patient populations, but not well-examined in OA[8]. Importantly, OA, obesity and related chronic diseases, like diabetes[9], are pro-inflammatory conditions that can influence muscle catabolism and the development and progression of sarcopenic obesity. Combined with normal muscle senescence beginning in middle age and accelerated during menopause or andropause, individuals with OA are at additional risk of sarcopenic obesity due to the added influence of OA-related pain and disability, resulting in inactivity and further muscle loss. Taken together, these

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data suggest that comprehensive assessments for sarcopenic obesity should be completed in patients with end-stage OA for whom TKA is recommended.

Presently, sarcopenic obesity is not assessed in patients with OA, in part due to a lack of consensus on the definition and diagnosis of this condition, and partially due to insufficient recognition that sarcopenia occurs at any body weight. Few studies have examined sarcopenic obesity in knee OA. Our recently conducted scoping review[8] found only ten studies that examined sarcopenic obesity in knee OA. Prevalence rates between 1.3% and 35.4% were reported[8], however studies were primarily based on Asian population studies using lower BMI cut-offs for obesity and varied identification methods for low muscle mass, limiting comparability. A primary concern with the lack of recognition and screening for sarcopenic obesity in end-stage knee OA is related to clinicians advising weight loss based on patients' BMI[2,10] without realization of the potential harm. Recommending weight loss prior to TKA eligibility could inadvertently exacerbate the sarcopenic obesity condition due to muscle loss that typically occurs during weight loss[11]. In patients with low muscle mass, any additional loss may contribute to reduced wound healing following TKA[12], poorer functional outcomes due to decreased strength to support joint structure and mobility[13], potential alterations to the pharmacokinetics of medications[14], and increased risk of mortality[7].

Greater awareness and screening for sarcopenic obesity in knee OA is essential. As sarcopenia is considered a reportable disease by the World Health Organization (WHO)[15], routine screening should be included in OA clinical care pathways. Several consensus diagnostic criteria have been proposed for sarcopenia in the elderly[16–20] with agreement that identification be based on a combination of low muscle mass with low strength or function. Although there is no current consensus on diagnostic criteria for sarcopenic obesity[21,22], there are several accepted diagnostic approaches using measures of body composition[23]. Regardless, in view of the importance of sarcopenic obesity and the potential prevalence and impact in individuals with OA, screening for this condition should be a priority in clinical settings.

The purpose of this study was to examine the prevalence of sarcopenic obesity in a clinical cohort of adults with end-stage knee OA. Different diagnostic criteria, including assessments of muscle/fat mass, muscle strength and physical function, were used to identify patients with and without sarcopenic obesity, and to compare reported outcomes of pain, function and health-related quality of life.

Methods

Patients

Study patients were community dwelling adults undergoing TKA screening for unilateral or bilateral knee OA at a centralized intake orthopedic clinic in Alberta, Canada from May 2017 to March 2018. Patients were referred to the clinic by their primary care provider. Inclusion criteria were a BMI $\geq$30 kg/m^2 measured in clinic, no history of hip or knee arthroplasty or bariatric surgery, and able to communicate and give written informed consent in English. All eligible patients were approached to enroll in the study in sequence after their clinical visit. Study data were collected prospectively and managed using REDCap[24] electronic data capture tools hosted and supported by the Women and Children's Health Research Institute at the University of Alberta. Ethics approval was provided by the Health Research Ethics Board at the University of Alberta, Edmonton, Alberta.

Patient characteristics

Socio-demographic and health information about each participant was collected, including age, sex, ethnicity, and comorbid conditions. Smoking status was categorized as current, previous, or never smoked. Height and weight were measured in clinic with footwear and light clothing using wall-mounted measuring tape and electronic scales (Alimed Model CNS1101KG, and Seca Model 813), and measured again at body composition appointment, without footwear and wearing only a hospital gown, using an electronic scale (Seca Model 766). BMI was calculated and categorized according to WHO criteria[25]. Waist and hip circumference were measured to nearest 0.1 cm over light clothing using a non-elastic tape measure. Waist circumference was measured at the top of the iliac crest, and hip circumference was measured at the largest diameter of the gluteal muscle. The average from three consecutive measures was recorded. In addition to collecting age as a continuous variable (in years), it was also dichotomized to enable comparisons between middle-aged (ages 40–64.9 years) and older adults (ages $\geq$65 years).

Body composition

Body composition was assessed using dual-energy X-ray absorptiometry (DXA) (GE Healthcare Lunar iDXA, analyzed with enCORE software version 16) on a separate date and location. Total body and regional lean soft tissue (LST), fat mass (FM) and bone mineral concentration (BMC) were collected. Percent fat mass (%FM) was calculated by total FM divided by the sum of total BMC, FM and LST, multiplied by 100. Fat mass index (FMI) was calculated as FM divided by height in meters^2. Appendicular skeletal muscle mass (ASM), considered an accepted proxy for skeletal muscle mass, was calculated as LST of arms plus legs. Obesity was identified by BMI $\geq$30 kg/m^2 at intake, and confirmed by the additional criteria for obesity of a waist circumference >88 cm in females and >102 cm in males[13], and %FM $\geq$35% in females and $\geq$25% in males[26].

Performance-based physical function

Normal ambulatory walking speed (in seconds) was timed over a four meter course, with untimed one meter allowances on either side as acceleration and deceleration zones. The faster of two attempts was recorded, and gait speed calculated. Patients used assisted walking devices (cane or walker) if normally used for ambulation. Maximal isometric handgrip strength was assessed in the dominant hand using a Jamar handgrip dynamometer. Grip position was adjusted to position 2 or 3 depending on patients' hand size. Patients were seated with elbow flexed to 90°, and no contact with chair arm or backrest, if present. The highest of three attempts was recorded to nearest 0.5 kg. Functional physical performance was assessed in clinic using the six-minute walk test (6MWT), a valid and reliable measure in patients with knee OA[27].

Patient-reported quality of life, pain and function

Health-related quality of life was assessed using an electronic version of the EuroQol Foundation EQ-5D-5L[28]. The EQ-5D questionnaire has patients rate their perceived quality of life from 1 'no problems' to 5 'extreme problems' across five dimensions of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Results were dichotomized into no problems (score of 1), and problems (scores of 2–5). Index scores that can be used for healthcare economic evaluations were calculated based on a Canadian value set[29]. Patients also rated their perceived overall health on the visual analog scale (VAS) from 0 (worst health) to 100 (best

health). The disease-specific Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[30] has patients rate, on a 5-point Likert scale, their pain (0–20; 5 items each scored 0–4), stiffness (0–8; 2 items each scored 0–4) and function (0–68; 17 items each scored 0–4), for a total of 0–96, normalized to 0–100 scale by multiplying total score by 100/96.

Sarcopenic obesity diagnosis and prevalence

Sarcopenic obesity was identified using four diagnostic approaches. Three used accepted criteria from international consensus groups[19,20] for identifying low muscle mass alone using ASM assessed by DXA, adjusted by body size, and compared to established sex-specific cut-offs[13,26,31]. The fourth diagnostic approach used a combination of low muscle mass with the presence of either low strength or low function[16]. Prevalence of sarcopenic obesity was reported as the frequency and proportion of the cohort meeting each identification criteria:

Low muscle mass, alone, assessed by adjusted ASM:

ASM/height^2 = ASM (in kg) divided by height (in meters^2), also called ASM index (ASMI). Cut-offs <5.45 kg/m^2 in females and <7.26 kg/m^2 in males identified low ASM/height^2 [31]

ASM by weight = ASM (in kg) divided by weight (in kg) × 100. Cut-offs <19.43% in females and <25.72% in males% identified low ASM by weight[13];

ASM by BMI = ASM (in kg) divided by BMI (in kg/m^2). Cut-offs <0.512 kg/m^2 in females and <0.789 kg/m^2 in males identified low ASM by BMI[26].

Combined diagnostic approach: a) low muscle mass with low strength, or b) low muscle mass with low function = low muscle mass (low ASM identified by any of the body-size adjusted criteria, as above) with either low muscular strength (maximal isometric handgrip strength <20 kg in females and <30 kg in males), or low physical function (gait speed below <0.8 m/s), recommended by the consensus European Working Group on Sarcopenia in Older Persons (EWGSOP and EWGSOP2)[16,20].

Statistical analysis

A priori sample size (n = 143) was calculated[32,33] to provide a 95% confidence interval (CI) of the prevalence with a precision of 5%, based on a reported sarcopenic obesity prevalence of 10.4% (identified using ASM by weight and obesity identified by waist circumference) in a North American population study of adults age ≥60 years[13]. Analyses were conducted using IBM SPSS Statistics v24 (IBM Corp., Armonk, NY). There were no missing data on the patients included in the analyses. Normality of data distribution was tested with the Shapiro–Wilk test. Univariate analysis was completed and results reported as mean (standard deviation), median (interquartile range), or frequency (proportion). 95% CIs for proportions were calculated using Clopper–Pearson exact. Between-group comparisons were conducted using Student's independent t-test, Mann–Whitney U test, Chi-square or Fisher's exact test, as appropriate, based on the distribution, variable type and number in each group. All testing analyses were two-tailed, and P values of <0.05 were considered statistically significant.

Results

Patient characteristics

A total of 208 adults consented to participate in the study, 16 withdrew or were excluded after consenting (8 due to personal time limitations, and 8 due to prior arthroplasty, bariatric surgery, or BMI < 30 kg/m^2 at intake), and 41 declined to attend DXA body composition assessment appointment (described in supplementary table). Therefore, 151 patients were included in all analyses (see Table I). Age differences were present between DXA completers (n = 151) and non-DXA completers (n = 41), with completers being older (65.1 ± 7.9 vs 61.4 ± 8.0 years, P = 0.008) with a higher proportion retired (45%, vs 29%).

Table I presents cohort characteristics and outcomes, by sex. Patients were predominantly Caucasian (95%, n = 143), with 5% either Indigenous (n = 5), Black (n = 1), Filipino (n = 1), or South Asian (n = 1). Mean age was 65.1 ± 7.9 years (range 40.2–88.3 years). Expected differences in height, weight and body composition were present between sexes. Mean number of comorbidities was 1.6 ± 1.2, with higher rates of hypertension in females. When comparing physical performance outcomes between age categories, middle-aged adults had faster mean gait speed (0.14 m/s, 95% CI 0.06–0.24), higher mean grip strength (4.8 kg, 95% CI 1.6–8.0), and greater mean 6MWT distance (42.1 m/s, 95% CI 4.6–79.6) compared to older adults.

Body composition

All patients had a BMI ≥30 kg/m^2 at study intake, as per inclusion criteria. At the DXA appointment where weight and height were measured without clothing or footwear, six patients' BMI was <30.0 kg/m^2 (28.7–29.8 kg/m^2). These patients were included in the analysis as they met initial BMI criteria, along with waist circumference and %FM criteria for obesity. Waist circumference in the entire sample was above established cut-offs for obesity, ranging from 98.8 to 158.0 cm in females, and 107.7 to 162.6 cm in males. %FM was above sex-specific criteria for obesity in entire cohort, ranging from 40.6 to 61.0% in females, and 26.7 to 50.5% in males. Analyses showed substantial variability in body composition between individuals within the same BMI category [Fig. 1(a) and (b)], and linearity in the relationship between FM (or FMI) and BMI.

Prevalence of sarcopenic obesity

Prevalence of sarcopenic obesity in the overall cohort varied depending on diagnostic criteria (Table II). A higher prevalence was observed in males when sarcopenic obesity was identified with low muscle alone, but not with the combined diagnostic approach. Alternatively, the combined diagnostic approach yielded a higher prevalence of sarcopenic obesity in older adults compared to their younger counterparts, which was not observed with low muscle alone.

Fig. 2(a) illustrates the overlap between the three diagnostic definitions for low muscle mass alone. There was some concordance between criteria, with ASM/BMI identifying 100% of those with low ASM/height^2, and 82% of those with low ASM/weight. There were n = 27 patients uniquely identified as having low muscle mass by separate criteria (n = 23 only with ASM/BMI, and n = 4 only with ASM/weight). Fig. 2(b) illustrates the overlap between individuals identified with low muscle mass, low physical function, or low muscular strength when using the combined diagnostic approach.

Outcomes by sarcopenic obesity diagnosis

Table III presents differences in physical function and patient-reported outcomes by groups identified as having or not having sarcopenic obesity. The prevalence identified with ASM/height^2 alone was too low (1%) for meaningful comparisons, so only comparisons using ASM/weight and ASM/BMI are presented

Table I
Patient characteristics, by sex

		Female, $n = 89$	Male, $n = 62$
Demographics			
Age (years), mean (SD)		64.9 (8.5)	65.5 (7.1)
Age category			
40–64 years (middle-aged adults), *n* (%)		42 (47)	32 (52)
≥65 years (older adults), *n* (%)		47 (53)	30 (48)
Ethnicity, Caucasian, *n* (%)		84 (94)	59 (95)
Current smoker, *n* (%)		7 (8)	9 (14)
Number of comorbid conditions, mean (SD)		1.7 (1.2)	1.6 (1.3)
Types of comorbid conditions			
Type II diabetes, *n* (%)		14 (16)	14 (22)
Dyslipidemia, *n* (%)		28 (31)	20 (32)
Cardiovascular disease, *n* (%)		5 (6)	5 (8)
Hypertension, *n* (%)		55 (62)	27 (43)
Sleep apnea, *n* (%)		25 (28)	21 (34)
Cancer, *n* (%)		11 (12)	11 (18)
Use mobility aid‡		26 (29)	9 (14)
Anthropometrics and body composition			
Height* (cm), mean (SD)		161.6 (6.6)	176.0 (7.5)
Weight* (kg), median (IQR)		97.8 (21.6)	108.6 (24.3)
BMI* (kg/m^2), median (IQR)		37.0 (7.8)	34.3 (7.5)
Waist circumference (cm), median (IQR)		116.3 (13.1)	121.6 (17.5)
Hip circumference (cm), median (IQR)		128.3 (15.3)	119.9 (12.9)
Waist:hip ratio, mean (SD)		0.92 (0.06)	1.02 (0.05)
FM (kg), median (IQR)		49.5 (13.8)	41.7 (14.3)
FM (%), mean (SD)		50.3 (4.3)	39.5 (5.4)
FMI (kg/m^2), median (IQR)		19.0 (4.9)	13.0 (5.6)
LST (kg), median (IQR)		44.8 (6.2)	63.1 (9.6)
ASM (kg), median (IQR)		21.3 (4.4)	30.1 (5.8)
ASM by height^2 (ASMI) (kg/m^2), median (IQR)		8.19 (1.62)	9.85 (1.74)
ASM by weight × 100 (%), mean (SD)		22.1 (2.1)	27.1 (2.3)
ASM by BMI (kg/m^2), mean (SD)		0.574 (0.076)	0.83 (0.114)
Physical function			
Usual gait speed (m/s), mean (SD)		1.06 (0.31)	1.12 (0.24)
Gait speed < 0.8 m/s, *n* (%)		18 (20)	7 (11)
Grip strength (kg), median (IQR)		27.0 (10)	42.0 (14)
Grip strength < sex specific cut-offs†, *n* (%)		9 (10)	10 (16)
6MWT (m), median (IQR)		340.2 (155.0)	390.5 (117.1)
Patient-reported outcomes			
WOMAC pain, 0–20, mean (SD)		10.0 (3.4)	8.8 (3.5)
WOMAC stiffness, 0–8, mean (SD)		4.3 (1.6)	4.0 (1.6)
WOMAC function, 0–68, mean (SD)		34.7 (11.8)	31.0 (11.4)
WOMAC total, normalized 0–100, mean (SD)		51.1 (16.2)	45.7 (16.3)
EQ-5D dimensions:			
Mobility, *n* (%)	No problems	4 (4)	3 (5)
	Problems	85 (96)	59 (95)
Self-care, *n* (%)	No problems	68 (76)	38 (61)
	Problems	21 (24)	24 (39)
Usual activities, *n* (%)	No problems	9 (10)	8 (13)
	Problems	80 (90)	54 (87)
Pain/discomfort, *n* (%)	No problems	3 (3)	2 (3)
	Problems	86 (97)	60 (97)
Anxiety/depression, *n* (%)	No problems	39 (44)	32 (52)
	Problems	50 (56)	30 (48)
EQ-5D VAS, 0–100, median (IQR)		71 (30)	70 (26)
EQ-5D Index, −0.148 to 0.949, median (IQR)		0.706 (0.315)	0.664 (0.251)

ASM = appendicular skeletal mass, FM = fat mass, FMI = fat mass index, LST = lean soft tissue, 6MWT = six minute walk test, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

* At initial assessment.

† <20 kg in females, <30 kg in males.

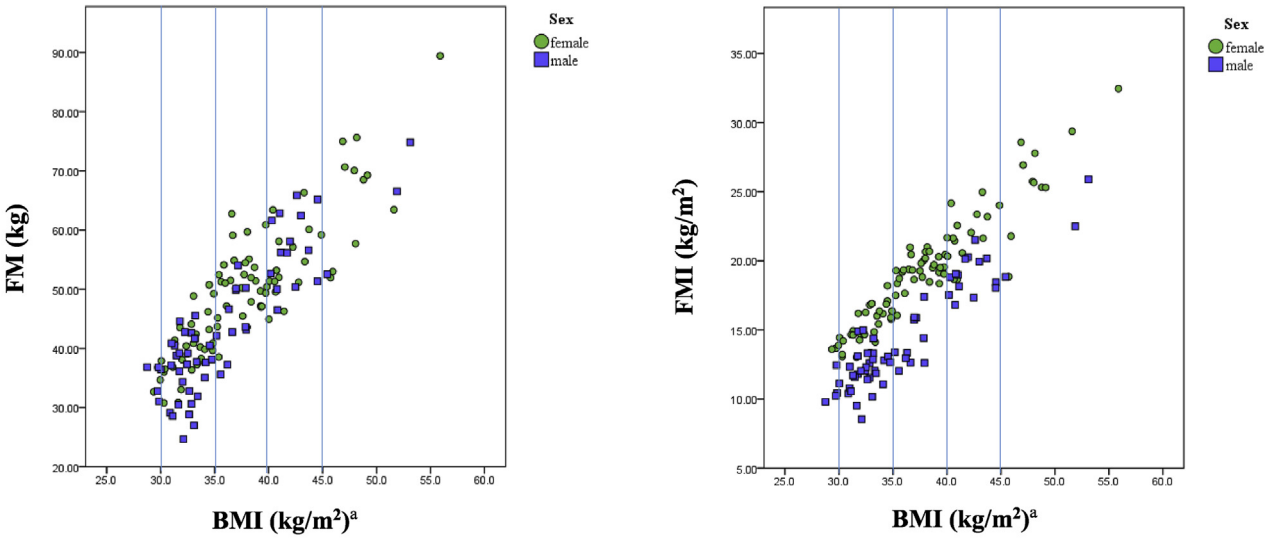
‡ Mobility aids include cane ($n = 26$), walker ($n = 8$) or wheelchair ($n = 1$).

independently. The proportion of patients with type II diabetes was higher in all groups identified with sarcopenic obesity (difference of 10.2%, 14.7% and 30.2%) compared to the group without sarcopenic obesity when categorized using ASM/weight, ASM/BMI, and the combined approach, respectively. The proportion using mobility aids was higher in the sarcopenic obesity group only when categorized by the combined approach (difference of 33.5% compared to group without sarcopenic obesity). There were differences in all physical function outcomes and in patient-reported EQ-5D self-care problems between those having and not having sarcopenic obesity, across all diagnostic methods. Age only differed between groups when using the combined diagnostic approach, with the sarcopenic obesity group being older (mean difference of 5.5 years, 95% CI 1.0–9.9). BMI was only different when using low muscle mass alone, with the sarcopenic obesity groups having a higher BMI (mean difference of 4.0 kg/m^2, 95% CI 1.3–6.8 with ASM/weight, and 2.5 kg/m^2, 95% CI 0.5–4.5 with ASM/BMI).

Discussion

In this cohort of patients with knee OA, we found compelling evidence that sarcopenic obesity is present and influenced physical

a.



In females:

Within BMI category 30.0-34.9 kg/m^2, FM varied from 30.8 kg to 50.7 kg and FMI varied from 13.0 kg/m^2 to 18.2 kg/m^2
Within BMI category 35.0-39.9 kg/m^2, FM varied from 38.5 kg to 62.8 kg and FMI varied from 16.0 kg/m^2 to 21.0 kg/m^2
Within BMI category 40.0-44.9 kg/m^2, FM varied from 44.9 kg to 66.3 kg and FMI varied from 18.6 kg/m^2 to 25.0 kg/m^2

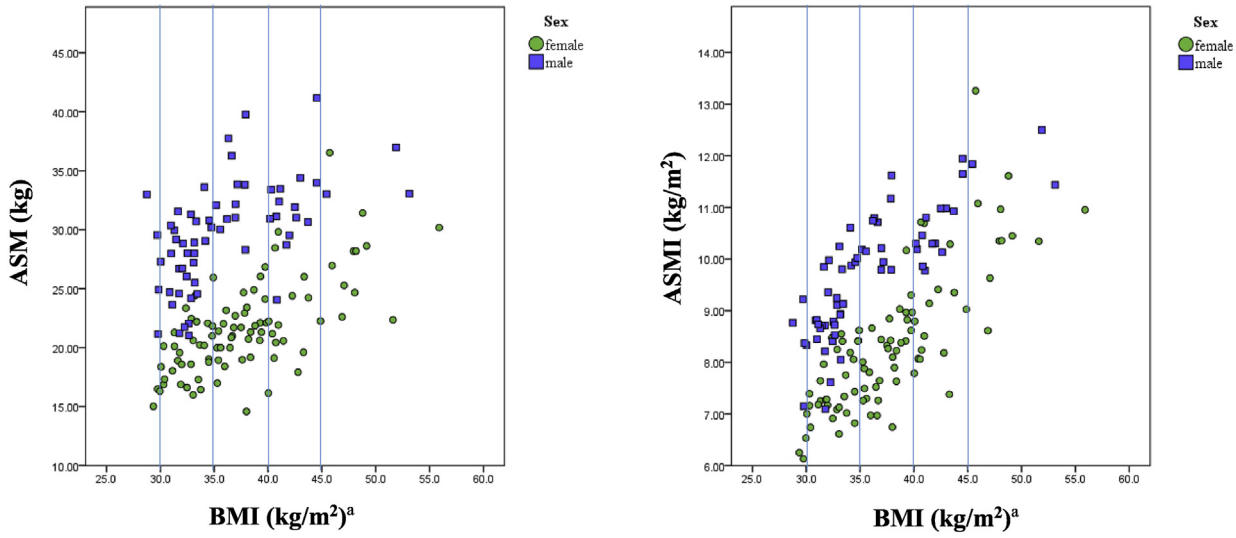
In males:

Within BMI category 30.0-34.9 kg/m^2, FM varied from 24.7 kg to 45.5 kg and FMI varied from 8.5 kg/m^2 to 10.6 kg/m^2
Within BMI category 35.0-39.9 kg/m^2, FM varied from 35.6 kg to 54.0 kg and FMI varied from 12.0 kg/m^2 to 17.4 kg/m^2
Within BMI category 40.0-44.9 kg/m^2, FM varied from 46.5 kg to 65.9 kg and FMI varied from 16.8 kg/m^2 to 21.5 kg/m^2

[a]BMI at DXA

BMI=body mass index (weight/height^2), FM=fat mass, FMI=fat mass index (FM/height^2)

b.



In females:

Within BMI category 30.0-34.9 kg/m^2, ASM varied from 16.0 kg to 26.0 kg and ASMI varied from 6.6 kg/m^2 to 8.6 kg/m^2
Within BMI category 35.0-39.9 kg/m^2, ASM varied from 14.6 kg to 26.8 kg and ASMI varied from 6.7 kg/m^2 to 10.7 kg/m^2
Within BMI category 40.0-44.9 kg/m^2, ASM varied from 16.1 kg to 29.8 kg and ASMI varied from 7.4 kg/m^2 to 10.7 kg/m^2

In males:

Within BMI category 30.0-34.9 kg/m^2, ASM varied from 21.0 kg to 33.6 kg and ASMI varied from 7.1 kg/m^2 to 10.6 kg/m^2
Within BMI category 35.0-39.9 kg/m^2, ASM varied from 28.3 kg to 39.8 kg and ASMI varied from 9.8 kg/m^2 to 11.6 kg/m^2
Within BMI category 40.0-44.9 kg/m^2, ASM varied from 24.0 kg to 41.2 kg and ASMI varied from 9.8 kg/m^2 to 11.9 kg/m^2

[a]BMI at DXA

ASM=appendicular skeletal muscle mass, ASMI=ASM index (ASM/height^2), BMI=body mass index (weight/height^2)

Fig. 1. a. Fat mass variability. **b**. Muscle mass variability.

Table II
Prevalence of sarcopenic obesity by diagnostic criteria

	Sarcopenic obesity identified with low muscle alone						Sarcopenic obesity identified with low muscle† and either low strength‡ or low function§	
	ASM by height²*		ASM by weight*		ASM by BMI*			
	SO	NSO	SO	NSO	SO	NSO	SO	NSO
Total,	2 (1.3)	149 (98.7)	22 (14.6)	129 (85.4)	41 (27.2)	110 (72.8)	13 (8.6)	138 (91.4)
n (%) (CI)	(0.2–4.7)	(95.3–99.8)	(9.4–21.2)	(78.9–90.6)	(20.2–35)	(65–79.8)	(4.7–14.3)	(85.7–95.3)
Female,	0 (0)	89 (100)	6 (6.7)	83 (93.3)	18 (20.2)	71 (79.8)	6 (6.7)	83 (93.3)
n (%) (CI)	(0–4.1)	(95.9–100)	(2.5–14.1)	(85.9–97.5)	(12.4–30.1)	(69.9–87.6)	(2.5–14.1)	(85.9–97.5)
Male,	2 (3.2)	60 (96.8)	16 (25.8)	46 (74.2)	23 (37.1)	39 (62.9)	7 (11.3)	55 (88.7)
n (%) (CI)	(0.4–11.2)	(88.8–99.6)	(15.5–38.5)	(61.5–84.5)	(25.2–50.3)	(49.7–74.8)	(4.7–21.9)	(78.1–95.3)
Age 40–64.9 years,	0 (0)	74 (100)	12 (16.2)	62 (83.8)	17 (23)	57 (77)	2 (2.7)	72 (97.3)
n (%) (CI)	(0–4.9)	(95.1–100)	(8.7–26.6)	(73.4–91.3)	(14–34.2)	(65.8–86)	(0.3–9.4)	(90.6–99.7)
Age ≥ 65 years,	2 (2.6)	75 (97.4)	10 (13)	67 (87)	24 (31.2)	53 (68.8)	11 (14.3)	66 (85.7)
n (%) (CI)	(0.3–9.1)	(90.9–99.7)	(6.4–22.6)	(77.4–93.6)	(21.1–42.7)	(57.3–78.9)	(7.4–24.1)	(75.9–92.6)

ASM = appendicular skeletal muscle mass, CI = 95% confidence interval, NSO = not sarcopenic obesity, SO = sarcopenic obesity.
* Cut-off criteria for females, males, respectively: ASM by height², kg/m² (<5.45, <7.26), ASM by weight, % (<19.43, <25.72), ASM by BMI, kg/m² (<0.512, <0.789).
† Any criteria for low muscle: ASM by height², kg/m² (<5.45, <7.26), or ASM by weight, % (<19.43, <25.72), or ASM by BMI, kg/m² (<0.512, <0.789) in females and males, respectively.
‡ Handgrip strength <20 kg in females, <30 kg in males.
§ Gait speed <0.8 m/s.

function and aspects of quality of life. To the best of our knowledge, this is the first study to compare sarcopenic obesity diagnostic procedures that consider low muscle mass alone and in combination with low strength or function in a clinical OA cohort, and only the second study[34] to examine the influence of this condition on physical function in OA. Research on sarcopenic obesity in knee OA has been limited[8], with few population and clinical studies. Interestingly, sarcopenic obesity occurred across age categories in this cohort, illustrating its relevance across the age spectrum.

Prevalence of sarcopenic obesity

Sarcopenic obesity prevalence varied depending on diagnostic criteria used. Low muscle mass (low ASM) alone yielded a prevalence ranging from 1.3% to 27.2%. This variability is consistent with other studies on sarcopenic obesity in knee OA reporting prevalence from 1.3% using ASM/height², to between 3% and 35.4% using ASM/weight and ASM/BMI[34–38]. ASM adjusted by weight or BMI identified more individuals with sarcopenic obesity compared to ASM/height², suggesting that ASM/height² may not be sensitive to identify low ASM in adults with higher body mass. This is consistent with findings from other studies[39,40]. Further, ASM relative to body weight and BMI have stronger associations with physical function[19,23], so they may be most relevant to identify sarcopenic obesity in adults with obesity and OA. More males were identified with sarcopenic obesity in this cohort, similar to the results of Ji *et al.*[37] who examined prevalence in patients undergoing orthopedic surgery (including TKA). Age-related reductions in testosterone hormones in men (andropause) have been associated with an increased decline in skeletal muscle mass[41]. Sex-related factors may be more important than age in the development of sarcopenic obesity in the OA population[42], but further examination is required.

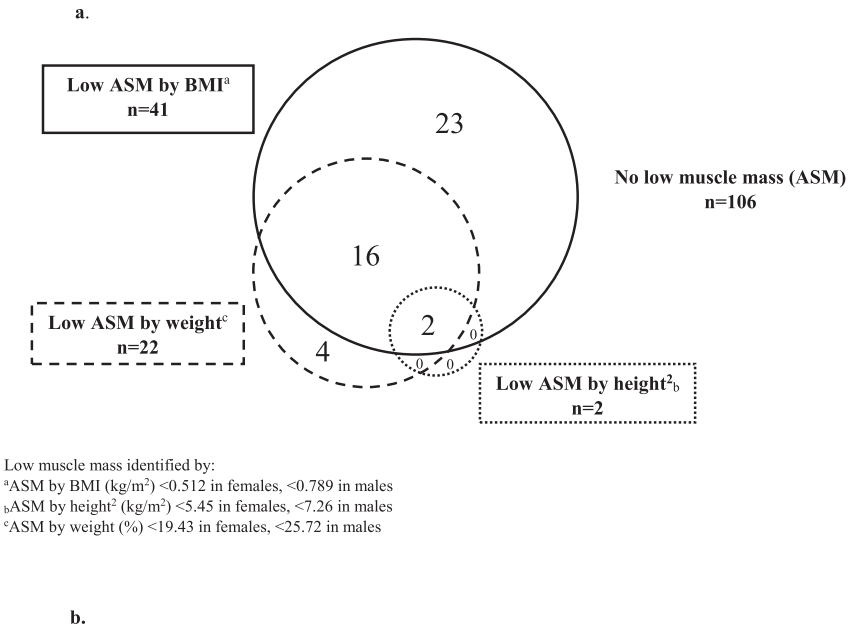
When using the combined diagnostic approach to identify sarcopenic obesity, higher prevalence rates were observed in older adults. This could indicate that the tests and/or cut-offs used to assess low physical function or low muscle strength may preferentially identify limitations in older adults (≥65 years), the population age where the cut-offs were established[43]. In our cohort, middle-aged adults had higher scores on all physical performance tests compared to older adults. Different cut-off levels or types of tests may better discriminate low muscle mass impacting function in middle-aged adults with OA. A consensus definition for sarcopenic obesity is needed[21,22], and may need to include different diagnostic approaches for different populations, ages or disease specific groups[21]. Further, criteria are needed for early identification in clinical settings. There is a benefit of practitioners being able to easily identify the presence or absence of sarcopenic obesity before it impacts physical function and to prevent or mitigate disability (by treating with diet or physical activity, or avoiding recommendations for weight loss that could exacerbate skeletal muscle loss).

Sarcopenic obesity and performance-based physical function

Sarcopenic obesity significantly impacted physical function and strength in the study cohort, with slower walking speeds, lower grip strength, and lower walking endurance yielded using all diagnostic approaches. Sarcopenic obesity has been associated with negative impacts on functional mobility, including difficulty walking, slower walking speed, and difficulty climbing stairs in other populations[44], but in OA it may compound the impact of OA-related physical disability. Manoy *et al.*[34] also found sarcopenic obesity negatively influenced grip strength, gait speed and 6MWT distance in patients with knee OA independent from obesity. Low muscle mass likely contributes clinically significant functional limitations over and above those due to both obesity and OA, which should be considered in OA management approaches and recommendations.

Sarcopenic obesity and patient-reported pain, function and quality of life

Interestingly, there were only differences in one EQ-5D dimension, self-care activities, when classified by sarcopenic obesity status. This dimension has patients identify level of difficulty washing or dressing themselves. Sex differences were present prior to differentiating sarcopenic obesity, with more problems reported by males, which may reflect the higher prevalence of low muscle mass in males in our cohort. Visser *et al.*[45] also found that low fat free mass (assessed by bioelectrical impedance analysis) interacted with knee OA to further reduce health-related quality of



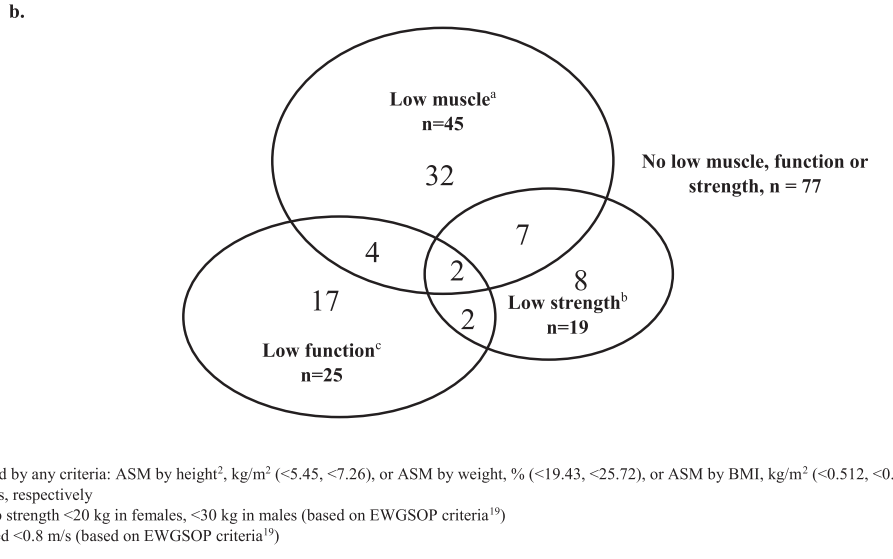


Fig. 2. **a**. Overlap of different diagnostic criteria for sarcopenic obesity identified by low muscle mass alone. **b**. Overlap of identification of low muscle mass, function or strength in study population.

life in men only. Sarcopenic obesity may impart additional or unique influence on self-care in males, independent from obesity and OA. Future studies should include formal assessments of self-reported difficulties with activities of daily living in addition to health-related quality of life, to see if this influence persists across instruments. We found no difference in WOMAC scores between those who had or did not have sarcopenic obesity, in contrast to Manoy *et al.*[34] who reported higher WOMAC scores in patients with knee OA and sarcopenic obesity compared to those with obesity or normal weight. Differences in WOMAC scoring methods (they used a 0–10 scale-based system), in addition to methodological differences between studies likely accounts for the disparate findings.

Sarcopenic obesity and patient characteristics

Mean BMI was higher in the groups with sarcopenic obesity when identified using ASM/weight and ASM/BMI, reflecting greater disproportion in the load:capacity relationship between fat and muscle mass when body mass increases. Diabetes prevalence in the sarcopenic obesity groups were higher when compared to the groups without sarcopenic obesity, highlighting the relationship between diabetes and accelerated muscle loss related to sarcopenia[41]. This higher prevalence of diabetes alongside sarcopenic obesity is important for consideration of surgical risk with TKA, as both are independent risk factors for surgical infection and poorer outcomes, potentially magnified by interaction.

Other considerations

Muscle is a complex organ, and the quantity and quality of muscle tissue and muscle fibers are influenced by inflammatory, metabolic, and endocrine factors[46] including age and obesity[47,48]. Low muscle mass has been considered a primary proxy measurement for metabolic control and physical disability, yet the composition of the muscle may be an underlying factor that is not clearly investigated. Increased storage of fat within and between muscle cells (called myosteatosis) occurs with aging and obesity[49,50], reducing contractile strength per muscle unit and

Table III
Difference in outcomes by sarcopenic obesity status and diagnostic criteria

	Sarcopenic obesity identified by low muscle mass alone		Sarcopenic obesity identified by low muscle mass‡ and either low function§ or low strength‖
	ASM by weight*	ASM by BMI†	
	SO $n = 22$¶ Compared to NSO $n = 129$	SO $n = 41$ Compared to NSO $n = 110$	SO $n = 13$¶ Compared to NSO $n = 138$
Physical function outcomes:			
Gait speed (m/s)	−0.12 (−0.01 to 0.2)*	−0.12 (−0.22 to −0.01)*	−0.24 (−0.4 to −0.08)*††
Grip strength (kg)	1.4 (−3.3 to 6.1)	−2.6 (−6.3 to 1.1)	−9.9 (−15.6 to −4.2)*††
Grip strength, female	1.4 (−3.7 to 6.6)	−4.1 (−7.3 to −1.0)*	−8.0 (−12.9 to −3.1)*††
Grip strength, male	−6.3 (−11.8 to −0.9)*	−6.9 (−11.8 to −2.0)*	−15.4 (−22.2 to −8.5)*††
6MWT (m)	−65.3 (−118.2 to −12.3)*	−50.9 (−92.9 to −8.9)*	−105.1 (−170.9 to −39.4)*††
Patient reported outcomes:			
WOMAC pain 0–20	0.4 (−1.2 to 2.0)	1.2 (−0.05 to 2.4)	0.6 (−1.4 to 2.6)
WOMAC stiffness 0–8	0 (−0.7 to 0.7)	0.1 (−0.5 to 0.7)	0 (−0.9 to 0.9)
WOMAC function 0–68	0.7 (−4.7 to 6.1)	0 (−4.3 to 4.3)	0.8 (−6.0 to 7.6)
WOMAC total 0–100	1.1 (−6.4 to 8.6)	1.4 (−4.5 to 7.3)	1.5 (−7.9 to 10.9)
EQ-5D VAS, 0–100	−0.2 (−8.5 to 8.1)	−4.8 (−11.3 to 1.7)	−17.1 (−27.2 to −7.0)*
EQ-5D index score	0.006 (−0.086 to 0.097)	−0.029 (−0.101 to 0.044)	−0.052 (−0.167 to 0.063)
EQ-5D self-care dimension#	18.3	19.4*	34.7*

Values presented are mean differences (CI) in group classified as SO compared to group classified as NSO, unless otherwise indicated.
*$P < 0.05$.
ASM = appendicular skeletal mass, CI = 95% confidence interval, NSO = not sarcopenic obesity, SO = sarcopenic obesity, VAS = visual analog scale.
* ASM by weight <19.43% in females and <25.72% in males.
† ASM by BMI <0.512 kg/m^2 in females and <0.789 kg/m^2 in males.
‡ Identified by any ASM criteria: ASM by height^2, kg/m^2 (<5.45, <7.26), or ASM by weight, % (<19.43, <25.72), or ASM by BMI, kg/m^2 (<0.512, <0.789) in females and males, respectively.
§ Low gait speed <0.8 m/s.
‖ Low grip strength <20 kg in women or <30 kg in men.
¶ Between group comparisons conducted using non-parametric Mann–Whitney *U* test or Fishers exact.
# Difference in proportion (%) of SO group reporting problems compared to NSO group (no between group differences were present in other EQ-5D dimensions).
†† Caution should be taken when interpreting functional outcomes using the combined definition, as cut-points for low grip strength or low gait speed were used in the diagnostic definition.

muscular endurance[21], in turn affecting mobility[51]. Unlike with cancer, where advanced body composition imaging with computerized axial tomography or magnetic resonance imaging is often completed, assessments of muscle mass in OA clinical populations may be limited to imaging methods like DXA which cannot assess myosteatosis[47]. Increased myosteatosis with muscle loss and aging-related adiposity gains, further increased by OA pain-related immobility, could be a mitigating factor between differences in decreased function or strength and decreased muscle mass[49].

Body composition analyses in this study revealed large variations in adiposity and muscularity within BMI categories, adding further evidence of the limitations of BMI as a surrogate marker for individual-level body composition[52]. BMI alone does not adequately identify sarcopenic obesity in patients with OA. This is also a limitation in the research evidence on the impact of obesity (defined only as BMI ≥30 kg/m^2) on TKA surgical infection rates, as differentiation between body compartments of adipose and muscle tissue could elucidate which primarily influences infection risk in this population.

Strengths and limitations

Notable strengths of this study include the use of a DXA for body composition analysis with larger scanning surface and higher weight capacity, preventing exclusion of patients with larger body size. Further, performance-based physical function has not been well examined in patients with sarcopenic obesity and OA, and thus these results are uniquely informative. Limitations include the primarily Caucasian sample and cross-sectional design, with potential for reverse causation. Results on physical function and quality of life should be interpreted with caution. Gait speed and grip strength were used both in the combined diagnostic criteria (as cut-points to define low function or strength) and also as continuous outcome variables, limiting the interpretability of the functional outcomes in this subgroup. Additionally, we were not able to control for confounding due to smaller samples in subgroup analyses. Differences in self-reported pain and impairments of physical function may have been impacted by other treatment interventions patients were receiving, including varied prescription pain medications, cortisone injections, and therapeutic rehabilitation, which were not controlled for. Further we did not collect information on physical activity or diet, which could be relevant for differences in muscle mass, and we did not control for weight change between initial clinic visit and DXA visit. Some patients may have been actively trying to lose weight during this period, but length of time between appointments was minimal (median 16 days). Furthermore, some patients may have had hand OA in addition to knee OA, which could have affected their maximal grip strength. Patients with severe pain or mobility limitations may have been less likely to complete the study, due to required attendance at the DXA appointment at an unfamiliar clinic on a separate day. However, efforts were made to reduce barriers to study completion (e.g., detailed maps, handicap parking stalls, access ramps and elevators, paid parking fees). Lastly, this study included patients referred to the orthopedic clinic by their primary physician, and not all patients may be interested, willing or eligible to undergo TKA. This sample may not be representative of all patients with end-stage knee OA.

Conclusions

Sarcopenic obesity (identified by low muscle mass alone, or low muscle mass with either low strength or low function), was present in patients with end-stage knee OA, and impacted physical function and quality of life relative to self-care activities. While prevalence

varied depending on diagnostic approach, it is apparent that BMI alone is inadequate to screen for this condition. Given the impact of sarcopenic obesity on outcomes in this population, increased clinical awareness and screening is important. A diagnostic method that considers a combination of low muscle mass with low strength or function is suggested to clarify expected prevalence and enable increased identification and management of this condition in patients with knee OA.

Authors' contributions

KG, CMP, LJW and MF contributed to the conception and design of the study. KG prepared the first draft, and KG, CMP, LJW and MF contributed to the manuscript revision and approval of the final version.

Conflict of interest

All authors declare they have no competing interests that would create a conflict of interest in connection with this manuscript. KG, CMP and MF have no disclosures; LJW has received consulting fees from Eli Lily and Scholar Rock.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2019.05.026.

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