Title: Clinical screening and identification of sarcopenic obesity in adults with advanced knee osteoarthritis

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Abstract

Background and Aims: Sarcopenic obesity (defined as low muscle mass and strength with high adiposity) requires attention in adults with advanced knee osteoarthritis (OA) due to implications on treatment outcomes. This study aimed to identify muscle function measures and patient characteristics associated with the presence of low muscle mass that could be used to screen and detect sarcopenic obesity in patients with knee OA in the clinical setting.

Methods: Cross-sectional study of patients with knee OA and a body mass index (BMI) ≥30 kg/m^2. Body composition was measured in n=151 patients (59% female, mean age 65.1±7.9 years) using dual-energy x-ray absorptiometry. Appendicular skeletal muscle mass (ASM) adjusted by BMI and below established sex-specific cut-points was used to differentiate low muscle mass. Muscle function was assessed by four-meter gait speed, six minute walk test, and maximal grip strength (absolute, and relative, adjusted by BMI). Logistic regression was used to assess the relationship between muscle function measures, patient characteristics, and low muscle mass. Receiver operating characteristic curves and area under the curve (AUC) were used to examine the final model and identify potential clinical cut-points.

Results: Sex and relative grip strength were associated with low muscle mass (AUC 0.774, p <0.001). Cut-points for low relative grip strength (<0.65 kg/m^2 in females and <1.1 kg/m^2 in males) were distinguished and used in combination with low muscle mass to screen and identify sarcopenic obesity. Patients with both low relative grip strength and low muscle mass (sarcopenic obesity) had impaired mobility and quality of life.

Conclusion: Relative grip strength shows promise as a clinical screening measure for sarcopenic obesity in patients with knee OA.

Key words: Sarcopenia, obesity, osteoarthritis, screening, grip strength, body composition

Introduction

Sarcopenic obesity is an important health condition requiring increased attention in adults with knee osteoarthritis (OA)[1–3]. It is defined as sarcopenia (a loss of muscle mass and strength related to aging or disease[4]) in the presence of high adiposity[5,6]. Sarcopenic obesity negatively impacts physical function in patients with advanced knee OA[1,3], potentially influencing the decision to proceed to a total knee arthroplasty (TKA)[7] and recovery after this procedure[8]. Importantly, sarcopenia may also be impacting the relationship between obesity and increased TKA surgical risk[9,10]. This clinical population may be particularly at risk for sarcopenia due to accelerated loss of muscle and strength associated with OA pain-related mobility impairments and obesity-related inflammation[2]. Additionally, weight loss is routinely advised in this clinical population prior to TKA eligibility[11], further influencing the risk of muscle loss[12]. However, sarcopenic obesity is not currently identified in OA clinical settings, so implications on patient outcomes remain unclear. Increased screening and recognition of sarcopenic obesity is necessary to clarify the impact on OA treatment outcomes[3,9], and to mitigate disability, morbidity and mortality risk by preventing and minimizing further muscle loss in this population[13,14].

Although there is currently no definitive diagnostic criteria for sarcopenic obesity[15], accepted approaches to identify this condition using body composition are available[13,16,17]. Dual-energy x-ray absorptiometry (DXA) is considered a reference standard for clinical body composition assessment and identification of low muscle mass relevant to sarcopenia[18], and it is suitable for patients with obesity[19]. A prior study from our research group has shown that DXA-measured low muscle mass discerned sarcopenic obesity in a subgroup of patients with knee OA. This subgroup had important impairments in physical function and aspects of quality of life[1], supporting that this condition is relevant to identify in clinical OA settings. However, having all patients with knee OA complete a

DXA scan may not be economically viable or available in publicly funded healthcare settings. Therefore, clinical approaches to first screen and discern patients with likely low muscle mass (and sarcopenic obesity) are needed.

In age-related sarcopenia, accepted clinical screening methods use cut-points for low grip strength or low gait speed[20–23]. Scoring below these cut-points prompts further testing of body composition or early sarcopenia treatment, thus reducing the number of patients requiring body composition assessment. However these screening cut-points for grip strength and gait speed were developed in normal weight, older adults, and may not be transferable to identify sarcopenic obesity, which can occur in younger populations[13]. Further, OA and obesity have independent influences on strength and function, adding additional confounding. Obesity reduces gait parameters of stride length, balance and stance, resulting in slower gait speeds[24]. Similarly, OA-related pain and stiffness can alter gait kinematics and reduce gait speed, with compounded influences in patients with both obesity and OA[24]. Systemic inflammatory-related OA can also affect both knee and hand joints, potentially reducing grip strength. Alternatively, adults with obesity typically have higher grip strength compared to normal body weight peers due to relatively higher muscle mass[25]. This illustrates a challenge in using grip strength and gait speed to discriminate impairments due to disease-related sarcopenia rather than OA or obesity.

Exploration of screening for sarcopenic obesity in patients with knee OA is novel. While an association between lower physical performance and lower muscle mass has been reported in cohorts with knee OA[3,26], this has not been examined from a screening or diagnostic approach. Therefore, the purpose of this study was to examine the screening and identification of sarcopenic obesity in adults with knee OA and obesity using clinically available measures. We aimed to examine associations between muscle function measures, patient characteristics, and the presence of low muscle mass defined by accepted

cut-points. Associated variables were then evaluated as a clinical screening method to discern groups with and without sarcopenic obesity, and compare outcomes of pain, function and quality of life.

Materials and Methods

This is an a priori planned sequential and connected study that builds on the findings of our prior analysis of data from a cross-sectional cohort of adults with end-stage knee OA and obesity[1]. The study included community dwelling adults with unilateral or bilateral knee OA undergoing screening for total knee arthroplasty (TKA) at an orthopedic centre from May 2017-March 2018. Inclusion criteria were: BMI $\geq$ 30 kg/m^2; no history of hip or knee arthroplasty or bariatric surgery and; able to communicate in English. Informed written consent was obtained from all participants and their rights were protected. A consecutive sampling approach was used to sequentially enrol eligible and consenting patients at their initial clinical visit. Study data were collected prospectively. Ethics approval was provided by an institutional Health Research Ethics Board.

Patient characteristics

Socio-demographic and health information about each patient was collected, including age, sex, ethnicity, and smoking status. Comorbid conditions were identified by asking patients whether a doctor had told them they had type II diabetes, dyslipidemia, cardiovascular disease, hypertension, sleep apnea, cancer, or hand OA. Height and weight were measured at the patients' initial visit in clinic, and measured again at the patients' body composition appointment on a separate date and location. BMI was calculated at each visit. Initial BMI was only used for inclusion criteria, and all analyses were conducted using BMI from the body composition appointment. Waist and hip circumference were measured at initial visit over light clothing using a non-elastic tape measure, recording the average from three consecutive measures.

Body composition

Body composition was assessed using dual-energy x-ray absorptiometry (DXA) (GE Healthcare Lunar iDXA, analyzed with enCORE software version 16). DXA is considered a reference standard for measurement of muscle mass for identification of sarcopenia[18]. Total body and regional lean mass (LM), fat mass (FM) and bone mineral concentration (BMC) were measured. Appendicular skeletal muscle mass (ASM) was calculated as LM of arms plus legs. All patients were identified with obesity based on the inclusion criteria of a BMI ≥30 kg/m^2 at clinic intake, however all patients met alternate obesity definitions of waist circumference >88 cm in females and >102 cm in males[27], and %FM ≥35% in females and ≥25% in males[28].

Low muscle mass

ASM adjusted by body size is accepted by sarcopenia consensus groups[22,29] to identify low muscle mass relative to sarcopenic obesity. ASM/BMI is preferred to identify low muscle mass in adults with obesity due to a stronger relationship with physical function[29,30]. Previous work completed by our research team found ASM/BMI cut-points were more sensitive than ASM/height^2 cut-points for identifying sarcopenic obesity-related impairments in this clinical population with knee OA[1]. Low muscle mass was defined using established sex-specific cut-points of ASM/BMI <0.512 kg/m^2 in females and <0.789 kg/m^2 in males[28].

Muscle function

Objective measures of muscle function (strength and physical performance) were assessed in the clinic, using grip strength, gait speed, and the six-minute walk test (6MWT). Gait speed was measured over four metres, and calculated in metres/second. Patients used assisted walking aids (cane or walker) during the assessment if normally used for ambulation. Maximal isometric grip strength of the

dominant hand was assessed (using a Jamar handgrip dynamometer) in a seated position with elbow flexed to 90 degrees. Grip position was modified to fit hand size, and the highest score of three attempts was recorded. Grip strength adjusted to body size (termed relative grip strength) was calculated by dividing grip strength by BMI. Relative grip strength has been used elsewhere in sarcopenia screening[31,32], and was included to normalize grip as higher grip strength is linked to larger body size. The 6MWT has been used elsewhere in screening for sarcopenia[33] and is an appropriate test for patients with knee OA[34]. Therefore, it was included to distinguish between short and long distance walking function. The 6MWT was completed in the clinic, and assisted walking aids were used if patients normally used them for ambulation.

Quality of life, pain and function

Patient-reported health-related quality of life was assessed using an electronic version of the EuroQol Foundation EQ-5D-5L[35]. Patients rated their perceived level of problems across five health dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) from 1 (no problems) to 5 (extreme problems). Results were dichotomized into no problems (score of 1), and problems (score of 2-5). Patients rated their overall health on the EQ-5D-5L visual analogue scale (VAS) from 0 (worst health) to 100 (best heath). Patient-reported OA pain and function were assessed with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[36]. The WOMAC has patients rate 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, and normalized to a 0-100 scale.*Statistical analysis*

A clinical screening model was built using correlation and logistic regression analyses, and model strength was examined using receiver operating characteristic (ROC) and area under the curve (AUC) analyses. The association between independent variables of patient characteristics [age, sex, FM, waist

circumference, smoking status, and comorbidities (including type II diabetes, cardiovascular disease, dyslipidemia, hypertension, sleep apnea, and hand OA)] and muscle function [gait speed, grip strength, relative grip strength, 6MWT], and the dichotomous outcome variable of low muscle mass present or absent was examined using logistic regression[37]. Univariate correlation was first examined between the outcome variable of low muscle mass and each independent variable of patient characteristics and muscle function measures to identify candidate variables for the regression analysis. Candidate variables were selected if correlated p <0.1 with the outcome of low muscle mass (***Supplementary table 1.***). A multivariable logistic regression model was built using a backwards stepwise approach, including examination of interaction between independent variables. Odds ratios (OR) and 95% confidence intervals are reported for the univariate and multivariable models. The discriminating ability of the final model was examined using ROC analysis with the predicted probabilities, calculating AUC. Based on the findings from the final model, sex-specific cut-points were examined using separate ROC curves for males and females. Optimal cut-points were calculated using three parameters[38]: 1) Youden's index [maximum (sensitivity + specificity -1)], 2) the shortest distance to (0,1) [the upper left corner of the ROC curve[38]], and 3) similar values of sensitivity and specificity (an equivalent balance of both). Between-group comparisons were conducted using two-tailed Student's independent t-test. A p value of <0.05 was considered statistically significant. All analyses were conducted using IBM SPSS Statistics v24 (IBM Corp., Armonk, NY).

Results

Sample Characteristics

The study included 151 patients (58.9% female), mean age 65.1±7.9 years (range: 40.2-88.3 years), mean BMI 37.1±5.5 kg/m^2 (range 30.0-56.7), predominantly Caucasian (95%). **Table 1** provides a

summary description of this patient cohort, as reported previously[1]. Low muscle mass (low ASM/BMI) was present in n=18 females (20.2%) and n=23 males (37.1%).

Association with low muscle mass

Age, FM, waist circumference, smoking status, dyslipidemia, cardiovascular disease, hypertension, sleep apnea, hand OA, and grip strength were not correlated with low muscle mass. Sex, type II diabetes, gait speed, 6MWT, and relative grip strength were correlated ($p<0.1$) with low muscle mass, and included in the multivariable model. Although not correlated, age was included in the multivariable model due to its clinical and biological relevance with low muscle mass. The results of univariate and multivariable models are reported in **Table 2**. Only sex and relative grip strength remained after backwards stepwise selection in the final model (OR 15.09 and 0.01, respectively). Using the predicted probabilities from the final model, a ROC curve was plotted (**Figure 1a)** and AUC calculated (AUC 0.774, 95% confidence interval 0.692-0.856). ROC curves for sex-specific relative grip strength associated with low muscle mass were then explored (**Figures 1b and 1c**). This enabled discrimination of optimal cut-points for low relative grip strength associated with low muscle mass in this cohort (<0.65 kg/m^2 in females, and <1.1 kg/m^2 in males), facilitating clinical relevance for testing grip strength (which differs by sex). These cut-points were used to define low relative grip strength, present in n=32 females (35.9%) and n=28 males (45.2%). Sensitivity analyses for the cut-points to identify low muscle mass are reported in **Table 3.** Comparisons with previously published cut-points for low absolute[22,39,40] and relative grip strength[31] used for sarcopenia identification are provided in ***Supplementary Table 2***.

Sarcopenic obesity identification and comparison of outcome measures

The new low relative grip strength cut-points were used in combination with low muscle mass to screen and identify a subgroup of the cohort with sarcopenic obesity, illustrated using the proposed sarcopenic

obesity screening algorithm in **Figure 2** (modified from the age-related sarcopenia screening algorithm of the European Working Group on Sarcopenia in Older Persons (EWGSOP2[22]). This was conducted to examine and validate the discrimination of these criteria to effectively screen and identify a subgroup of the cohort with sarcopenic obesity-related impairments. Based on this criteria, prevalence of sarcopenic obesity was 19.9% (95% CI 14.3-26.9%). In females, prevalence was 14.6% (95% CI 8.7-23.4%), compared to 27.4% in males (95% CI 17.9 -39.6%). When examined by age categories, prevalence was 16.2% in ages 40-64.9 years (95% CI 9.5-26.2%), and 23.4% in age ≥ 65 years (95% CI 15.3-34.0%). **Table 4** presents differences in physical function and patient-reported measures between those identified as having or not having sarcopenic obesity. The sarcopenic obesity group had slower gait speed (p=0.013), walked less distance in the 6MWT (p<0.001), and had lower absolute grip strength (p=0.012). Additionally, they had poorer health-related quality of life, with lower EQ-5D VAS scores (p=0.015), and more problems reported on the EQ-5D self-care dimension (washing and dressing themselves) (p=0.002).

Discussion

This study found that sex and relative grip strength were associated with low muscle mass in patients with advanced knee OA. The results suggest that relative grip strength may be promising as a clinical screening method to identify sarcopenic obesity in OA clinical practice. When sex-specific cut-points for low relative grip strength were discerned and examined using a modified clinical screening algorithm[22] (**Figure 2**), a subgroup of patients with sarcopenic obesity (low relative grip strength and low muscle mass) were identified that had mobility impairments (lower gait speed and walking endurance) and poorer quality of life (**Table 4**). This illustrates the potential efficacy of relative grip strength for identifying patients with knee OA who may require attention and treatment for sarcopenic obesity[23]. However, further validation in additional clinical studies will be important.

Relative grip strength is inexpensive and simple to administer. As measures of height, weight and grip strength (using a handgrip dynamometer) are low burden, it could be easily integrated into clinical OA assessments. Patients could be screened for low relative grip strength (below proposed sex-specific cut-points) following the proposed clinical screening algorithm for sarcopenic obesity in OA (**Figure 2**). If low relative grip strength is present, sarcopenic obesity would be suspected. The patient would then be sent for body composition assessment (e.g. using DXA), to confirm the presence of low muscle mass (low ASM/BMI) and the diagnosis of sarcopenic obesity[22]. Patients with confirmed sarcopenic obesity (having both low relative grip strength and low muscle mass) could then be recommended for appropriate treatment[23].

Our results indicate that gait speed and 6MWT were poorer discriminators of low muscle mass compared to relative grip strength. This could be due to the influence of OA on lower limb function and ambulation. Our results differed from those of El Ghoch et al[41] who examined clinical screening for low ASM/BMI in females with obesity. They reported gait speed was superior to grip strength or 6MWT when examined independently (using sensitivity analyses), however when examined in a multivariable model, only 6MWT was related to low ASM/BMI. This difference in findings between our studies could be due to their cohort not having knee OA, being all female, and no consideration of relative grip strength.

We did not find an association between absolute grip strength and low muscle mass in our cohort. While absolute grip strength has been used frequently in screening tool for low strength in sarcopenia[22,23,29,40], it may be less discriminative in adults with obesity[42]. Adjusting grip strength by BMI, weight, or FM may be preferable as it accounts for differences in strength with increasing body size[42,43]. Relative grip strength may have a stronger association with mobility impairment compared to absolute grip strength[43], although varied sex-differences have been

reported. In the Foundation for the National Institutes of Health (FNIH) Sarcopenia project[29,31,44,45], absolute and relative grip strength were equally associated with mobility impairment, however due to heterogeneity in females[45], absolute grip strength was preferred as it was considered simpler to assess[44]. Sallinen et al[42] found relative grip strength better identified mobility limitations in males, with a weaker relationship in females. This differed from findings by Sampaio et al[46], who found a stronger relationship between relative grip strength and fear of falling in women. Clearly, sex-differences may be present, requiring further investigation. However it is noteworthy that the cohorts in these studies did not all have obesity, and as they were community samples they may be under-representative of adults with mobility limitations.

The prevalence of sarcopenic obesity in this cohort was 19.9% when identified using the combination of low relative grip strength with low muscle mass. This prevalence is higher than projected in our previous study when gait speed or grip strength cut-points (developed in older adults) were used with low muscle mass to identify sarcopenic obesity (prevalence of 8.6%)[1]. Further, using the new proposed criteria, sarcopenic obesity was similarly identified in both younger (ages 40-64.9 years) and older (age ≥ 65 years) age categories (prevalence of 16.2% and 23.4%, respectively). This provides further indication that sarcopenic obesity identification in knee OA may need to be different from identification approaches used in age-related sarcopenia.

In our cohort, males had greater odds of low muscle mass compared to females when examined independently [OR 2.33 in males (females as reference category) *vs* OR 0.43 in females (males as reference category), p=0.023]. This could be related to steeper declines in aging-related muscle mass and strength[47,48] common in males associated with declining endocrine function during andropause[49]. Males may be more sensitive to aging-related increases in adiposity and muscle loss driven by OA-related inflammation and inactivity, compared to females. These sex differences were

magnified in the final model, with much higher OR for low muscle mass in males [OR 15.09 in males (females as reference category) *vs* 0.07 in females (males as reference category), $p<0.001$]. While this may be influenced by the higher prevalence of low muscle mass in males in our cohort (37.1% in males *vs* 20.2% in females), it may also indicate underlying sex-differences as discussed previously. Future studies will need to consider sex differences in the relationship between muscle function and low muscle mass, potentially leading to sex-specific screening approaches.

Interestingly, age was not correlated with low muscle mass in this study, supporting our understanding that sarcopenic obesity occurs across age categories and may be unique from age-related sarcopenia. Although we found type II diabetes was independently associated with low muscle mass (OR 2.43), similar to reports elsewhere[50], it did not contribute in the final model. Additionally, while the presence of hand OA can reduce grip strength[51], we did not find it associated with either absolute or relative grip strength in this cohort.

As a result of our analyses, we were able to propose cut-points for relative grip strength that balance sensitivity and specificity for identifying low muscle mass in this cohort of patients with knee OA and obesity. When compared to previously published cut-points for low absolute and relative grip strength used for sarcopenia screening and identification, the proposed cut-points have greater sensitivity (***Supplementary Table 2***). Whether higher sensitivity (correctly rule in patients who have sarcopenic obesity) or specificity (correctly rule out patients who do not have sarcopenic obesity) is important will need to be determined[20]. There may be a benefit to increased sensitivity, as preserving muscle mass and preventing further loss will likely be easier than increasing muscle mass. Measurement of low muscle mass[6] is still important for the diagnosis of sarcopenic obesity, and economic analyses of the costs of body composition assessments in comparison to the cost of misdiagnosis[52] will provide further clarity. Additionally, considering the implications of false positives and false negatives will be

critical for determination of the most relevant criteria and cut-points. While further external validation is required, our results provide initial confirmation that assessing low relative grip strength has value in screening for the presence of sarcopenic obesity. Further testing of these cut-points in other cohorts with knee OA and obesity will clarify their effectiveness and validity as a screening measure.

Strengths and limitations

This study provides an important contribution to the growing body of knowledge around sarcopenic obesity in adults with knee OA. Our findings are novel and have relevance to clinical practice, suggesting that screening using sex-specific relative grip strength can be conducted in OA treatment settings to identify patients who are likely to have sarcopenic obesity. The current work adds to the findings from our previous study[1], emphasizing the negative implications sarcopenic obesity has on physical function and quality of life in this clinical population. Although the same cohort data was used, the current investigation is distinct from the prior work[1]. These complementary studies were planned *a priori* in the protocol and design for this research.

Although the final model in this study provided moderate discriminatory power (AUC 0.774), the discerning power of strength and function measures may have limitations in heterogeneous OA populations where OA-severity[53] and comorbid conditions such as type II diabetes[54] may alter the relationship between strength, function and muscle mass. Males and females were analyzed together in our regression model due to the limited sample, but nascent indications of sex-differences require further investigation in larger samples. Further studies with larger samples are needed to compare body composition by sarcopenic obesity status (stratified by sex), to clarify whether height influence is magnified by ASM/BMI adjustments, potentially confounding associations with strength. The primarily Caucasian sample and cross-sectional approach are further study limitations, and causal or explanatory relationships between variables cannot be extrapolated from this study. Proposed cut-offs

for relative grip strength were not validated internally using bootstrapping or externally with other samples, so further validation is important. No blood tests were conducted, so examination of associations with biomarkers were not explored.

Conclusion

Sex and relative handgrip strength were associated with low muscle mass in this cohort of patients with obesity and end-stage knee OA. Cut-points for low relative grip strength of <0.65 kg/m^2 in females and <1.1 kg/m^2 in males are proposed to screen patients with knee OA who should then have a body composition assessment to confirm the presence of low muscle mass and the identification of sarcopenic obesity. This approach shows promise as a screening method to discern patients with knee OA and sarcopenic obesity-related impairments in physical function and quality of life, but further validation is required.**Authors' contributions:** KG, LJW, CMP and MF contributed to the conception and design of the study. KG prepared the first draft, and KG, LJW, CMP and MF contributed to the manuscript revision and approval of the final version.

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Table and Figure Legends

Table 1. Description of patient cohort, n=151 adults with knee OA and obesity.

Table 2. Univariable associations and final model of patient characteristics and muscle function measures associated with low muscle mass.

Table 3. Sensitivity analyses of proposed relative grip strength cut-points to identify low muscle mass in n=151 adults with knee OA

Table 4. Differences in physical performance and patient-reported measures by sarcopenic obesity status (identified using the proposed screening algorithm) in n=151 patients with knee OA

FIGURE 1a. Receiver operating characteristic curve and area under the curve (AUC) of predicted probabilities from final logistic regression model to identify low muscle mass in n=151 adults with knee osteoarthritis. Model includes sex and relative grip strength (grip/BMI).

Low muscle mass was classified as ASM/BMI <0.512 kg/m^2 in females and <0.789 kg/m^2 in males.
(ASM = appendicular skeletal muscle mass, BMI = body mass index, CI = confidence interval)

FIGURES 1b. and 1c. Receiver operating characteristic curves and area under the curves (AUC) for relative grip strength, stratified by sex, to identify low muscle mass in n=151 adults with knee osteoarthritis.

- In females (1b): A cut-point of <0.65 kg/m^2 for relative grip strength had maximal Youden index at 0.454, shortest distance to upper left corner at 0.38, and a balance of 72.2% sensitivity and 73.2% specificity.
- In males (1c): A cut-point of <1.1 kg/m^2 for relative grip strength had maximal Youden index at 0.457, shortest distance to upper left corner at 0.38, and a balance of 73.9% sensitivity and 71.8% specificity.

Relative grip strength was calculated by grip strength divided by BMI.
Low muscle mass was classified as ASM/BMI <0.512 kg/m^2 in females and <0.789 kg/m^2 in males.
(ASM = appendicular skeletal muscle mass, BMI = body mass index, CI = confidence interval)

FIGURE 2. Proposed clinical screening algorithm for sarcopenic obesity in adults with knee OA and obesity (modified from the EWGSOP2[18] algorithm).

(DXA = dual-energy x-ray absorptiometry, EWGSOP = European Working Group on Sarcopenia in Older Persons)

Supplementary Table 1. Bivariate correlations in sample (n=151).

Supplementary Table 2. Sensitivity and specificity comparison of proposed relative grip strength cut-points with other published cut-points

TABLE 1. Description of patient cohort, n=151 adults with knee OA and obesity

	Females (n=89) mean (SD) or n (%)	Males (n=62) mean (SD) or n (%)
Demographics		
Age (years)	64.9 (8.5)	65.5 (7.1)
Type of comorbidities:		
Type II diabetes	14 (15.7)	14 (22.6)
Dyslipidemia	28 (31.4)	20 (32.2)
Cardiovascular disease	5 (5.6)	5 (8.1)
Hypertension	55 (61.8)	27 (43.5)
Sleep apnea	25 (28.1)	21 (33.9)
Cancer	11 (12.3)	11 (17.7)
Hand osteoarthritis	37 (41.6)	18 (29.0)
Anthropometrics and body composition		
Height (cm)	161.6 (6.6)	176.0 (7.5)
Weight (kg)	98.6 (16.1)	112.3 (17.4)
BMI (kg/m^2)	37.8 (5.6)	36.0 (5.4)
Waist circumference (cm)	119.3 (12.1)	123.7 (11.3)
FM (kg)	49.5 (11.0)	43.8 (11.2)
FM (%)	50.3 (4.3)	39.4 (5.2)
LM (kg)	45.8 (7.0)	62.4 (8.1)
ASM (kg)	21.6 (3.9)	29.7 (4.4)
ASM/height^2 (kg/m^2)	8.3 (1.3)	9.7 (1.2)
ASM/BMI (kg/m^2)	0.574 (0.076)	0.83 (0.114)
Physical performance and strength		
Gait speed (m/s)	1.06 (0.31)	1.12 (0.24)
6MWT (m)	321.5 (115.3)	366.0 (117.9)
Grip strength, absolute (kg)	27.3 (6.1)	40.8 (9.8)
Grip strength, relative to BMI (kg/m^2)	0.73 (0.17)	1.15 (0.31)

ASM = appendicular skeletal muscle mass, BMI = body mass index, FM = fat mass, LM = lean mass, OA = osteoarthritis, 6MWT = six-minute walk test

[Δ]mobility aids include cane (n=26), walker (n=8) or wheelchair (n=1)

TABLE 2. Univariable associations and final model of patient characteristics and muscle function measures associated with low muscle mass[*]

	Univariable association with low muscle mass[*]		**[ϕ]Final model for association with low muscle mass[*]**	
Identifying variable	**OR (95% CI)**	***p* value**	**OR (95% CI)**	***p* value**
Age	1.01 (0.97 – 1.06)	0.586		
Sex, male[Δ]	2.33 (1.12 – 4.83)	0.023	**15.09 (4.66 – 48.84)**	**<0.001**
Type II diabetes	2.43 (1.03 – 5.72)	0.042		
Gait speed	0.22 (0.06 – 0.84)	0.026		
Relative grip strength[†]	0.23 (0.06 – 0.88)	0.031	**0.01 (0.001 – 0.08)**	**<0.001**
6MWT	0.99 (0.99 – 1.0)	0.021		

[*]Identified as ASM/BMI, kg/m^2 (<0.512, <0.789) in females and males, respectively
[ϕ]age, sex, type II diabetes, gait speed, relative grip strength and 6MWT were all included in the final model
[Δ]Female as reference category
[†]grip strength/BMI
95% CI = 95% confidence interval

TABLE 3. Sensitivity analyses of proposed relative grip strength[†] cut-points to identify low muscle mass[*] in n=151 adults with knee OA

	True+ n	False+ n	True- n	False- n	Sensitivity % (CI)	Specificity % (CI)	PPV % (CI)	NPV % (CI)	+LR (CI)	-LR (CI)
Females										
<0.65 kg/m^2	13	19	52	5	72.2 (51.5-92.9)	73.2 (62.9-83.5)	40.6 (23.6-57.6)	91.2 (83.9-98.6)	2.70 (1.67-4.36)	0.379 (0.178-0.809)
Males										
<1.1 kg/m^2	17	11	28	6	73.9 (56.0-91.8)	71.8 (57.7-85.9)	60.7 (42.6-78.8)	82.3 (69.5-95.2)	2.62 (1.5-4.57)	0.363 (0.178-0.743)

[†]grip strength/BMI

[*] low muscle mass identified by ASM/BMI, kg/m^2 (<0.512, <0.789) in females and males, respectively

CI = 95% confidence interval, NPV = negative predictive value, PPV = positive predictive value, + LR = positive likelihood ratio, - LR = negative likelihood ratio, + = positive, - = negative

TABLE 4. Differences in physical performance and patient-reported measures by sarcopenic obesity[†] status (identified using the proposed screening algorithm) in n=151 patients with knee OA

	Sarcopenic obesity identified by low strength[a] and low muscle mass[b] **SO n=30** Compared to NSO n=121
Physical performance and strength measures:	
Gait speed (m/s)	-0.14 (-0.25 - -0.03)*
Gait speed, female	-0.13 (-0.3 - 0.0)
Gait speed, male	-0.18 (-0.3 - -0.05)*
Grip strength (kg)	-5.2 (-9.3 - -1.2)*
Grip strength, female	-6.0 (-9.5 - -2.6)*
Grip strength, male	-9.9 (-14.9 - -4.9)*
6MWT (m)	-81.5 (-127.4 - -35.6)*
6MWT, female	-54.1 (-122.3 - 14.1)
6MWT, male	-127.0 (-186.2 - -67.7)*
Patient-reported measures:	
WOMAC pain 0-20	1.0 (-0.4 - 2.4)
WOMAC stiffness 0-8	0.2 (-0.5 - 0.8)
WOMAC function 0-68	1.7 (-3.0 - 6.5)
WOMAC total 0-100	3.0 (-3.6 - 9.6)
EQ-5D VAS, 0-100	-9.0 (-16.2 - -1.8)*
EQ-5D self-care dimension[$]	29.3*

Values presented are mean differences (CI) in group classified as SO compared to group classified as NSO, unless otherwise indicated

†identified with both low strength and low muscle mass

[a]low strength identified by relative grip strength <0.65 kg/m^2 in females and <1.1 kg/m^2 in males

[b]low muscle mass identified by ASM/BMI, kg/m^2 (<0.512, <0.789) in females and males, respectively

[$]difference in proportion (%) of SO group reporting problems compared to NSO group (no between-group differences were present in other EQ-5D dimensions)

*p<0.05

CI = 95% confidence interval, NSO = not sarcopenic obesity, SO = sarcopenic obesity

Figure 1a.

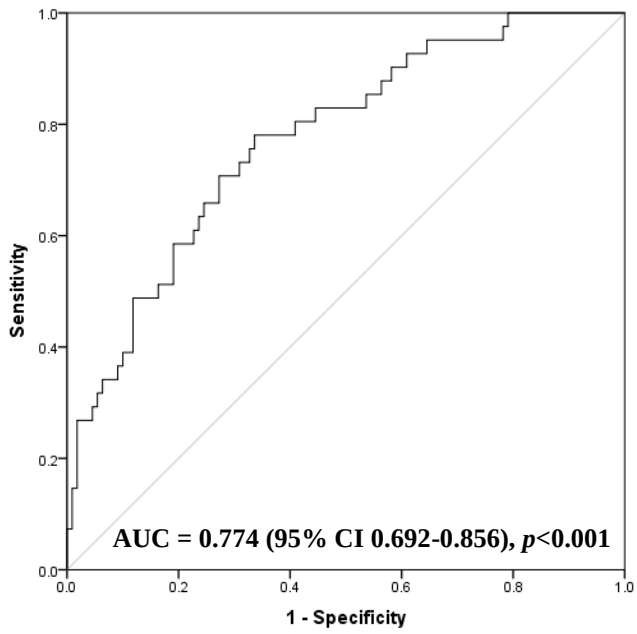


Figure 1b.

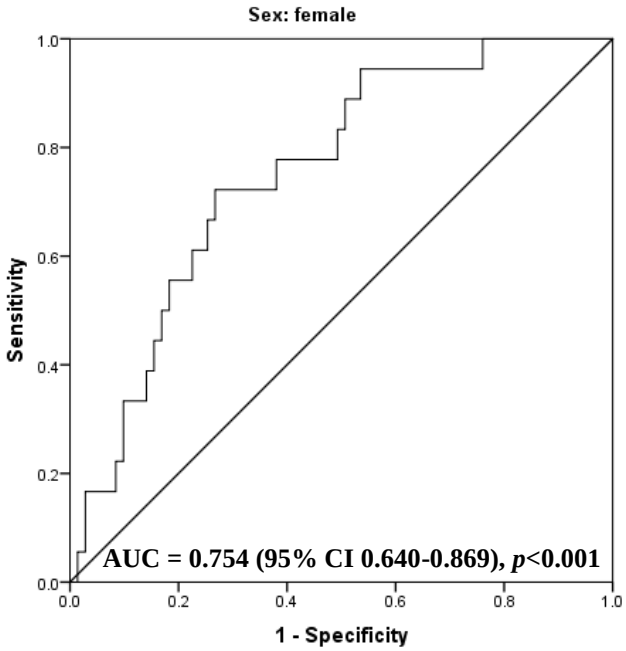


Figure 1c.

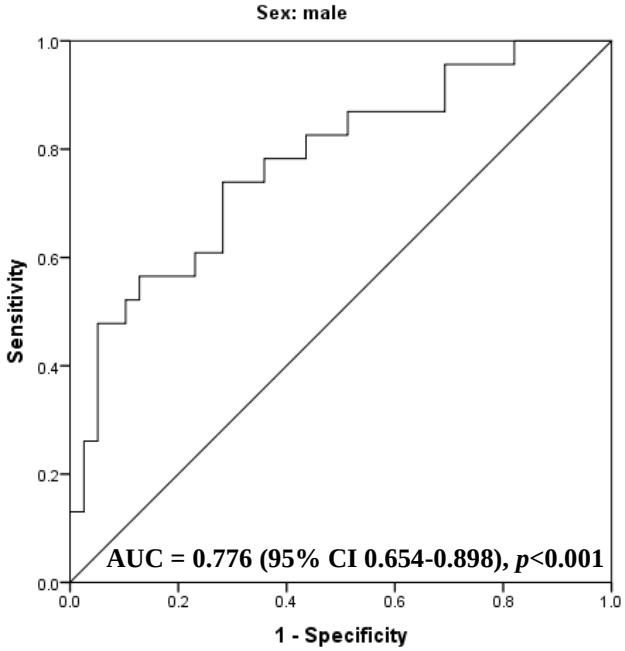
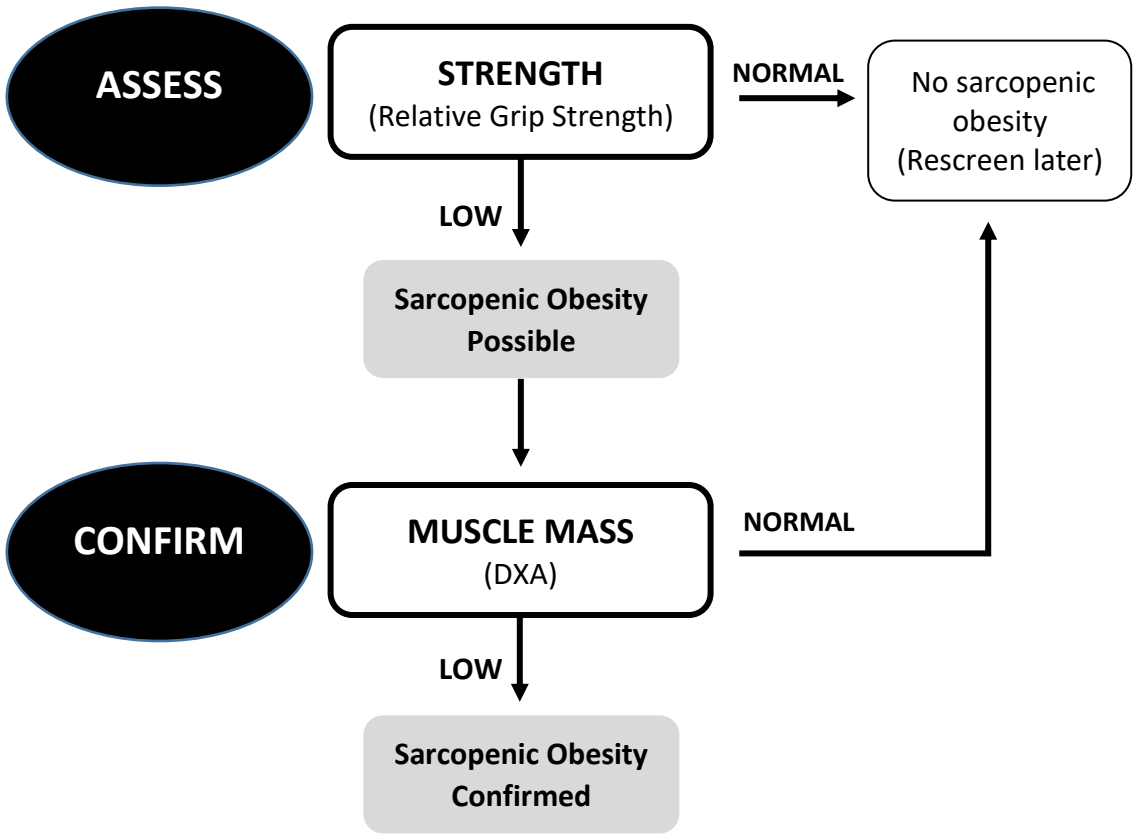


Figure 2.


ASSESS
STRENGTH
(Relative Grip Strength)
NORMAL
No sarcopenic obesity
(Rescreen later)
LOW
Sarcopenic Obesity Possible
CONFIRM
MUSCLE MASS
(DXA)
NORMAL
LOW
Sarcopenic Obesity Confirmed

Supplementary Table 1. Bivariate correlations in sample (n=151)

	Low muscle mass$^{\Delta}$	Age (years)	Sex	Diabetes$^{\downarrow}$	Gait speed (m/s)	Relative grip† (kg/m^2)	6MWT (m)
Low muscle mass$^{\Delta}$	---	0.054	0.187*	0.168*	-0.174*	-0.152*	-0.175*
Age (years)		---	0.023	0.03	-0.132*	-0.079	-0.11*
Sex (male, female)			---	0.087	0.092	0.531**	0.176*
Diabetes$^{\downarrow}$ (yes, no)				---	-0.072	-0.052	-0.13
Gait speed (m/s)					---	0.235**	0.552**
Relative grip†(kg/m^2)						---	0.320**
6MWT (m)							---

Kendall's tau-b, two-tailed, was used for all correlations, except between gait speed and age where Pearson's correlation was used as both variables were normally distributed.

$^{\Delta}$identified as dichotomous outcome, present if ASM/BMI <0.512 kg/m^2 in females and <0.789 kg/m^2 in males

$^{\downarrow}$type II diabetes

†grip strength divided by body mass index

*p<0.05

**p≤0.001

Supplementary Table 2. Sensitivity and specificity of proposed relative grip strength cut-points to identify low muscle mass* in the sample cohort (n=89 females, n=62 males) compared to other published cut-points for low absolute or relative grip strength used in sarcopenia screening and identification

Cut-point in Females	Source	True + n	False + n	True - n	False - n	Sensitivity % (CI)	Specificity % (CI)
Relative grip strength† <0.65 kg/m^2	Proposed from current study	13	19	52	5	72.2 (51.5-92.9)	73.2 (62.9-83.5)
Relative grip strength† <0.56 kg/m^2	Cawthon et al.[31]	5	7	64	13	27.8 (7.1-48.5)	90.1 (83.2-97.1)
Absolute grip strength ≤ 21 kg	Beaudart et al.[39]	5	8	63	13	27.8 (7.1-48.5)	88.7 (81.4-96.1)
Absolute grip strength < 20 kg	Cruz-Jentoft et al.[40]	3	6	65	15	16.7 (0-33.9)	91.5 (85.1-98.0)
Absolute grip strength <16 kg	Cruz-Jentoft et al.[22]	0	0	71	18	0	1
Cut-point in Males	**Source**	**True + n**	**False + n**	**True - n**	**False - n**	**Sensitivity % (CI)**	**Specificity % (CI)**
Relative grip strength† <1.1 kg/m^2	Proposed from current study	17	11	28	6	73.9 (56.0-91.8)	71.8 (57.7-85.9)
Relative grip strength† <1.0 kg/m^2	Cawthon et al.[31]	13	9	30	10	56.5 (36.3-76.9)	76.9 (63.7-90.1)
Absolute grip strength ≤ 32 kg	Beaudart et al.[39]	8	4	35	15	34.8 (15.3-54.2)	89.7 (80.2-99.3)
Absolute grip strength < 30 kg	Cruz-Jentoft et al.[40]	6	4	35	17	26.1 (8.1-44.0)	89.7 (80.2-99.3)
Absolute grip strength <27 kg	Cruz-Jentoft et al.[22]	3	1	38	20	13.0 (0-26.8)	97.4 (92.5-1)

* low muscle mass identified by ASM/BMI, kg/m^2 (<0.512, <0.789) in females and males, respectively

† grip strength/BMI

CI = 95% confidence interval, EWGSOP = European Working Group on Sarcopenic in Older Persons, FNIH+ = positive, - = negative