**Obesity Measures and Definitions of Sarcopenic Obesity in Singaporean Adults – the Yishun Study (accepted after revision J Frailty & Aging)**

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**Running Head:** Sarcopenic Obesity and Obesity Definitions

**Abbreviation List:** ALMI: Appendicular Lean Mass Index; AWGS: Asian Working Group for Sarcopenia; FM/FFM: Fat Mass to Fat-Free Mass ratio; FMI: Fat Mass Index; GPAQ: Global Physical Activity Questionnaire; GS: Gait Speed; HGS: Handgrip Strength; KES: Knee Extensor Strength; LASA: Longitudinal Aging Study Amsterdam; MNA: Mini Nutritional Assessment; PBF: Percentage Body Fat; RBANS: Repeatable Battery for the Assessment of Neuropsychological Status; SO: Sarcopenic Obesity; SPPB: Short Physical Performance Battery; TUG: Timed Up-and-Go; WC: Waist Circumference

**ABSTRACT**

**Background:** The prevalence of sarcopenic obesity (SO) and its effects on functional disability are of particular concern. Due to the lack of a uniform obesity definition, there is marked variability in reported SO prevalence and inconsistent data on observed adverse health outcomes.

**Objectives:** We compare SO prevalence and the associations of SO with physical function using sarcopenia according to current Asian Working Group for Sarcopenia (AWGS) guidelines and with different obesity measures. We recommend that the most optimal SO diagnostic formulation would be one that is most significantly associated with reduced physical function.

**Design:** 535 healthy, community-dwelling Singaporeans were recruited (21-90 years old, 57.9% women). We assessed anthropometry, body composition, and questionnaire-based physical and cognitive factors, and estimated SO prevalence with obesity defined according to waist circumference (WC), percentage body fat (PBF), fat mass index (FMI) and fat mass/fat-free mass ratio (FM/FFM). Muscle function was compared among phenotypes and obesity definitions using ANOVA. Differences across obesity measures were further ascertained using multiple linear regressions to determine their associations with the Short Physical Performance Battery (SPPB).

**Results:** Overall prevalence of SO was 7.6% (WC-based), 5.1% (PBF-based), 2.7% (FMI-based), and 1.5% (FM/FFM-based). The SO phenotype consistently performed poorer than the obese group (*p*<0.05) except for FM/FFM-based measure, and performed poorer than the sarcopenic group in SPPB (*p*<0.05) only in the PBF and FMI-based measures. SO was significantly associated with SPPB in the PBF and FMI models (*p*<0.05). Total variance explained by the different regression models was highest for the FMI definition.

**Conclusions:** Our findings suggest FMI as the most preferred measure for obesity and support its use as a diagnostic criteria for sarcopenic obesity.

**Keywords:** Sarcopenic Obesity; Sarcopenia; Obesity; Prevalence; Muscle Strength; Skeletal Muscle Mass; Singapore

**INTRODUCTION**

The rising tide of obesity prevalence is currently a global public health problem of epidemic proportions in all ages. At the same time, population ageing will double the number of persons aged 65 years and over worldwide in the next three decades, reaching 1.5 billion in 2050 (1),many of whom will be physically frail and disabled from the progressive loss of muscle mass and function (sarcopenia) (2). Obesity, the excessive accumulation of body fat, is an important factor in the development of metabolic syndrome and cardiovascular disease (3),and is also an important contributing cause of muscle loss. The two conditions have overlapping causes and feedback mechanisms that are interconnected and mutually-aggravating (3). Coexistence of both, a condition known as sarcopenic obesity (SO), has been shown to act synergistically to exacerbate metabolic impairment, disability, cardiovascular disease and mortality more so than either condition alone (3,4).

Although the diagnosis of sarcopenia has been increasingly harmonized by consensus working groups such as the Asian Working Group for Sarcopenia (AWGS) (2), the lack of a uniform obesity definition in the context of SO has led to great variation in the methods and cut-offs applied to define obesity, resulting in marked variability in reported SO prevalence as well as conflicting data on observed adverse health outcomes (5). Obesity is officially considered a disease that requires clinical treatment, however, there are currently no universally-accepted definitions for it (3). Commonly used measures include the body mass index (BMI), waist circumference (WC), percentage body fat (PBF), fat mass index (FMI) and fat mass to fat-free mass (FM/FFM) ratio. BMI provides a good indication of disease risk, but does not distinguish between fat and fat-free mass, thus making its clinical value questionable (3,5,6). WC indicates central obesity and serves as a surrogate measure of visceral adiposity (5-7), while PBF gives an objective indication of total body fat and its distribution (5). FM and FFM are the most frequently used adiposity indexes for SO classification (7), with the FM/FFM ratio deemed clinically-suitable in the diagnosis of SO (6). However, each of these measures assesses a different construct of obesity and are not interchangeable (5). To better understand its underlying physiological processes, and to determine disease prevalence and design clinical interventions, it is necessary to progress towards a unified criteria for the diagnosis and classification of obesity.

Aside from the wide heterogeneity of obesity measures used in studies, inconsistent observations of associations between SO and disease risk (7) may also result from the criteria used for defining sarcopenia in most studies, which other than muscle mass did not always consider muscle strength and physical function (3,5). Muscle strength and function have been shown to decline more rapidly with age and contribute more significantly to physical decline and frailty than muscle mass.

The primary aim of the present study was to propose the most optimal SO diagnostic formulation by comparing the association of SO with physical function using different obesity measures (WC, PBF, FMI and FM/FFM). We hypothesize that the most optimal diagnostic formulation would be one that is most significantly associated with physical functional impairment. The secondary aim was to compare and describe estimates of SO prevalence among community-dwelling younger and older adults in the Singapore population using AWGS guidelines for sarcopenia diagnosis and the different obesity definitions.

**METHODS**

*Setting*

Community-dwelling adults (≥21 years) were recruited from the town of Yishun, one of the largest north-residential towns in Singapore, residential population of 220,320 (50.6% females), with 12.2% older adults (≥65 years), similar to the overall Singapore residential population of 4,026,210 (51.1% females), with 14.4% older adults (≥65 years) (8).

*Participants*

Random sampling was employed to obtain a representative sample of approximately 300 male and 300 female participants, filling quotas of 20-40 participants in each sex- and age-group (10-year age-groups between 21-60; 5-year age-groups after 60). Detailed recruitment methods and exclusion criteria have been reported previously (9). Ethics approval was obtained from the National Healthcare Group DSRB (2017/00212). All respondents signed informed consent before participating in the study.

*Questionnaires*

Participants answered questionnaires pertaining to education level, housing type (a proxy for socio-economic status), living arrangement, marital status, smoking and drinking (more than four days a week), a health and medical questionnaire indicating medical conditions and comorbidities, a mini nutritional assessment (MNA) (10), a global physical activity questionnaire (GPAQ) (11) and the LASA physical activity questionnaire (12).

*Anthropometry*

Body weight to the nearest 0.1 kg and height to nearest millimeter were measured using a digital balance and stadiometer (Seca, GmbH & Co. KG, Hamburg, Germany). Waist and hip circumferences were measured using a non-elastic, flexible measuring tape around the navel and widest part of the hips respectively. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. ‘Obesity’ according to waist circumference (WC) was defined as ≥90 and ≥80 cm for men and women respectively (13).

*Cognitive Assessment*

Global cognition and cognitive domains including immediate and delayed memory, visuospatial, language and attention were assessed using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (14).

*Body Composition*

Bone mineral density, total percentage body fat (PBF), fat mass (FM), fat-free mass (FFM) and appendicular lean mass (ALM) were measured using DXA (Discovery WI, Hologic, Inc., Marlborough, USA). Fat mass index (FMI) and appendicular lean mass index (ALMI) were calculated as FM (kg) and ALM (kg) divided by height (m) squared, where FM equals to total body fat mass and ALM equals to the sum of lean mass in the upper and lower limbs. FM/FFM ratio was calculated by taking FM (kg) divided by FFM (kg). ‘Obesity’ according to PBF, FMI and FM/FFM were defined using the upper two quintiles of PBF and FMI, and a ratio of >0.80 for FM/FFM (6).

*Functional Performance*

Muscle function, as a gauge of functional deterioration and impairment, was measured using objective and validated assessments including handgrip strength (HGS) (15), knee extensor strength (KES) (16), usual gait speed (GS) (17), the Short Physical Performance Battery (SPPB) (18) and the Timed Up-and-Go (TUG) (19).HGS was assessed using the Jamar Plus+ Digital Hand Dynamometer (Patterson Medical, Evergreen Boulevard, Cedarburg, USA), and the highest of four readings (two trials per arm) recorded. KES was assessed using a spring gauge strapped 10 cm above the ankle joint, and the highest of four readings (two trials per leg) recorded. GS was measured using the 6 m GAITRite Walkway (CIR Systems Inc., Sparta. New Jersey, USA) with a 2 m lead in and out phase, and the average speed (three trials) recorded. TUG measures the progress of balance, sit-to-stand and walking. The average timing (two trials) was recorded. A composite score was calculated for SPPB, which comprises three components: balance, gait speed and repeated chair stands.

*Sarcopenia*

Sarcopenia was assessed using the AWGS criteria (2). Poor physical function was defined as GS <1.0 m/s, low muscle mass as ALMI <7.0 and <5.4 kg/m2, and muscle strength by HGS <28 and <18 kg for men and women respectively. Presence of low muscle mass and poor muscle strength and/or physical performance constitutes ‘sarcopenia’ (2). Participants with both sarcopenia and obesity were classified as ‘sarcopenic obese (SO)’. Those who had neither were classified as ‘normal’.

*Statistical Analysis*

SPSS version 22 (Chicago, Illinois, USA) was used for analysis. Prevalence of SO were extrapolated to the general population weights by age groups. The four phenotypes – ‘Normal’, ‘Obese’, ‘Sarcopenic’ and ‘Sarcopenic Obese’ – were compared against muscle function measures using one-way analysis of variance (ANOVA) with Bonferroni correction for post-hoc comparison. To further ascertain the impact of obesity definitions on physical function, univariate and multiple linear regressions were performed to determine their associations with SPPB. Statistical significance was set at *p*<0.05.

**RESULTS**

A total of 542 participants (57.9% females) aged 21-90 years were recruited. Due to incomplete data from seven participants, data from 535 participants were analyzed (**Figure 1.**). Of these, 81.9% were Chinese, 8.6% Malays, 6.7% Indians, and 2.8% from other races. Mean age was 58.6 (18.8) years. The descriptive statistics are presented in **Table 1.** and **2.**

Cut-off values for obesity using the sex-specific upper two quintiles of PBF and FMI were 31.0% and 7.63 kg/m2 for men, and 41.4% and 9.93 kg/m2 for women. Overall population-adjusted prevalence of sarcopenic obesity (SO) was 7.6% (WC-based: men 7.2%; women 7.9%), 5.1% (PBF-based: men 4.4%; women 5.7%), 2.7% (FMI-based: men 2.2%; women 3.2%), and 1.5% (FM/FFM-based; men 0%; women 2.9%). Population-adjusted prevalence of SO for older adults (≥60 years) was 21.6% (WC-based), 16.1% (PBF-based), 9.5% (FMI-based) and 3.7% (FM/FFM-based; **Table 3.**).

*Participant Characteristics and Sarcopenic Obesity*

Across all four obesity measures, the SO phenotypes had higher age compared to the overall sample (**Table 4.**). Individuals with the lowest education levels, smallest housing types, lived alone, were widowed, had diabetes, hypertension or high cholesterol, or had one or more medical conditions were more likely to have SO. Individuals who smoked were more likely to have SO using the PBF and FMI phenotypes, while individuals who drank were more likely to have SO using the WC, PBF and FMI phenotypes. The FM/FFM-based definition did not identify any males with SO (0%).

*Muscle Function (ANOVA)*

The sarcopenic and SO phenotypes consistently performed poorer than the normal group in functional measures and across obesity definitions (*p*<0.05, **Table 5.**), except for the FM/FFM-based definition. The SO phenotype also persistently performed poorer than the obese group (*p*<0.05), except for the FM/FFM-based definition. Using the PBF-based and FMI-based definitions, the SO phenotype performed poorer than the sarcopenic phenotype in SPPB and TUG (*p*<0.05).

*Multiple Linear Regression for SPPB*

We adjusted for age, gender (covariates with theoretical relevance), education level, housing type, living arrangement, number of medical conditions, diabetes, hypertension, high cholesterol, GPAQ activity level and RBANS global cognition (statistically significant covariates in univariate analysis; *p*<0.05). Using the WC-based, PBF-based, FMI-based and FM/FFM-based definitions, the total variance explained by the regression models were 22.4% [F(12, 469)=12.575, *p*<0.001], 23.1% [F(12, 469)=13.026, *p*<0.001], 23.7% [F(12, 469)=13.416, *p*<0.001] and 22.4% [F(12, 469)=12.575, *p*<0.001] respectively (**Table 6.**).

**DISCUSSION**

In this study, we present reference values for waist circumference (WC), percentage body fat (PBF), fat mass index (FMI) and fat mass to fat-free mass (FM/FFM) ratio, as well as sex-specific cut-off values for PBF and FMI, to define alternative phenotypic representations of sarcopenic obesity (SO). We describe the corresponding SO prevalences using AWGS guidelines for sarcopenia, across the age groups of healthy adults. Our estimated prevalence of SO for adults aged ≥21 years and ≥60 years were 7.6% and 21.6% (WC-based), 5.1% and 16.1% (PBF-based), 2.7% and 9.5% (FMI-based), and 1.5% and 3.7% (FM/FFM-based) respectively.

Comparatively, a recent study on 200 cognitively-intact and functionally-independent community-dwelling adults in Singapore (≥50 years) reported a prevalence of 10.5% and 10.0% based on WC-based and PBF-based definitions of SO respectively (5), slightly lower than the 15.4% and 10.7% in the present study (≥50 years). Notably, the authors used the original AWGS criteria to define sarcopenia (20), with lower cut-offs for muscle strength and gait speed and thus lower detection rates compared to the updated AWGS criteria (2). Another study involving 591 healthy volunteers in Korea found a prevalence of 10.9% (40-59 years) and 18.0% (≥60 years) using the PBF-based definition (4), higher than the 2.1% (40-59 years) and 16.1% (≥60 years) in the present study. However, their criteria did not include the functional components of sarcopenia (2), and their population-derived cut-offs for low muscle mass were much higher at 8.81 and 7.36 kg/m2 compared to AWGS’ 7.0 and 5.4 kg/m2 used in the present study (2,20).

Using one-way analysis of variance (ANOVA) with Bonferroni correction for post-hoc comparisons, the SO phenotype consistently performed poorer than the obese-only group in all measures of muscle/physical function for the WC, PBF and FMI-based definitions of SO. Compared to the sarcopenic-only group, the SO phenotype performed worse in the SPPB and TUG assessments for the PBF-based and FMI-based SO definitions. Physical function impairment in the absence of disability likely represents the shared core of sarcopenia and physical frailty. Such functional deterioration with deficits in gait speed, balance, and muscle strength, can be objectively assessed through the SPPB (21). Given that the SPPB is considered one of the most reliable and valid assessments for functional performance (5,18,21), our findings suggest PBF and FMI to be the preferred obesity measures for defining SO. Furthermore, Multiple linear regression results for SPPB revealed that only FMI-based and PBF-based definitions of SO were significantly associated with poorer SPPB scores, and the total variance explained by the different regression models was highest for the FMI definition, followed by PBF, and then WC and FM/FFM, suggesting FMI to be the most preferred obesity measure followed by PBF.

On the whole, our results indicate that FMI is the most preferred measure of obesity for defining SO. PBF gives an objective indication of total body fat, but does not discern between visceral and subcutaneous fat (5). While WC provides an estimate of visceral adiposity which is associated with higher morbidity than its subcutaneous counterpart (22), it is not adjusted for height and is thus insensitive to body size (5-7). In corroboration with the literature, fat mass was previously reported to be the most frequently used adiposity index for the classification of SO, and its adjustment to height squared (FMI) has been the preferred method to account for differences in body size across age and between the sexes (6). In terms of physical performance, FMI is also considered an accurate indicator of total body adiposity that could improve the predictive value of SO in functional deterioration (6,7). In addition, FMI was found to be a better screening tool in the prediction of metabolic syndrome in Chinese men and women (23) and more accurately assessed obesity in Mexican Americans (24) compared to BMI or PBF.

The FM/FFM definition did not identify any men with SO. This is similar to the findings of previous studies, where using the FM/FFM definition led to markedly disproportionate low numbers of men identified with SO (6,7,25). Women inherently have much higher relative fat mass than men (26), and conversely, men have higher relative fat-free mass (total body water, muscle and bone mass) than women at all ages (26,27). This is primarily due to the hormonal differences between men and women; men have higher testosterone levels which exhibits anabolic effects on muscle and bone (28), while higher estrogen levels in women promote subcutaneous fat deposition especially in the hips, thighs and chest (29). In addition, approximately 75% of skeletal muscle tissue is composed of water (30). Thus, with higher muscle mass, men inadvertently hold more total body water, further contributing to the discrepancy in fat mass and fat-free mass between men and women. To address the underlying gender-bias of the FM/FFM criteria and improve its accuracy in identifying gender-specific obesity and SO prevalence, different cut-off values for men and women (lower cut-off values for men) should be explored.

A recent study on 1235 adults with type 2 diabetes (T2D) in Singapore (≥45 years)reported a SO prevalence of 19.4% using the FM/FFM-based definition, higher than the 2.3% reported in this study, although the criteria for diagnosing SO in that study did not include the AWGS functional components for sarcopenia, which could possibly have inflated the proportions identified with SO (6). Furthermore, previous studies have shown a close link between sarcopenia and obesity through insulin resistance (3). Visceral fat accumulation (which promotes secretion of pro-inflammatory cytokines) is a contributing factor to the loss of skeletal muscle (which is the largest insulin-responsive tissue). Obesity and sarcopenia have a synergistic effect on promoting insulin resistance which could exacerbate T2D (4). In addition, patients with T2D exhibit insulin resistance, systemic inflammation and metabolic complications that could in turn perpetuate excess adiposity accumulation and loss of muscle mass (3), leading to a vicious cycle of worsening insulin resistance, T2D, sarcopenia and obesity (4).

The strengths of this study are its population-based nature, thoroughness of data collection and application of up-to-date and evidence-based consensus. It also has a few limitations. It presents cross-sectional data on obesity, muscular health and function of Singaporeans, which precludes inferences on causality. Agreement amongst the obesity definitions was also not investigated, though it has previously been established that different obesity definitions intrinsically measure different constructs and are therefore not interchangeable (5). While the AWGS criteria is for older adults, we also applied the same criteria to estimate prevalence of SO in younger adults, and so this would have been underestimate. Finally, the participants were community-dwelling adults; thus, the findings may not be generalizable to hospitalized, institutionalized or disabled individuals.

**CONCLUSIONS**

This study presents new and much-needed data that help to better define and document sarcopenic obesity across age groups of healthy, community-dwelling Asian adults. To address the variability in sarcopenic obesity prevalence and conflicting data on its associations with adverse health consequences, a universally-accepted obesity definition is of utmost importance. Our findings suggest that FMI is the most preferred method for measuring obesity, and support its use as a diagnostic criteria for sarcopenic obesity.

**DISCLOSURE STATEMENT**

The authors declare no conflict of interest.

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BWJP, SLW, MUJ, TPN contributed to the research design. BWJP, LKL, KAJ, WTS, DHMN, QLLT, KKC conducted the research. BWJP, LKL, KAJ, WTS, DHMN, QLLT, KKC analyzed data and performed statistical analysis. BWJP, SLW, TPN wrote the paper. BWJP, SLW, TPN had primary responsibility for final content. All authors have read and approved the final version.

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