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The Prevalence and Agreement of Sarcopenic Obesity Using Different Definitions and Its Association with Mild Cognitive Impairment

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Abstract.

Background: The consistent definition of sarcopenic obesity (SO) is limited, its association with mild cognitive impairment (MCI) has not been clarified.

Objective: This study aimed to evaluate the prevalence and agreement of SO using different definitions and the association between SO and MCI.

Methods: SO was diagnosed by the co-existence of sarcopenia defined by the Asia Working Group for Sarcopenia (AWGS) and obesity by body mass index (BMI), visceral fat area (VFA), waist circumference (WC), or body fat percentage (BF%). Cohen's kappa was used to assess the agreement between the different definitions. The association between SO and MCI was assessed using multivariable logistic regression.

Results: Among 2,451 participants, the prevalence of SO ranged from 1.7% to 8.0% under different definitions. SO defined by AWGS and BMI (AWGS+BMI) showed fair agreements with the other three criteria (κ ranged from 0.334 to 0.359). The other criteria showed good agreements with each other. The κ statistics were 0.882 for AWGS+VFA and AWGS+BF%, 0.852 for AWGS+VFA and AWGS+WC, and 0.804 for AWGS+BF% and AWGS+WC, respectively. When using different diagnoses of SO, compared with the health group, the adjusted ORs of MCI for SO were 1.96 (95% CI: 1.29-2.99, SO: AWGS+WC), 1.75 (95% CI: 1.14-2.68, SO: AWGS+VFA), 1.94 (95% CI: 1.29-2.93, SO: AWGS+BF%), and 1.45 (95% CI: 0.67-3.12, SO: AWGS+BMI), respectively.

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Conclusion: Using different obesity indicators combined with AWGS to diagnose SO, BMI had lower prevalence and agreement compared with other three indicators. SO was associated with MCI under different methods (WC, VFA, or BF%).

Keywords: Alzheimer's disease, cross-sectional study, diagnostic agreement, mild cognitive impairment, prevalence, sarcopenic obesity

INTRODUCTION

Dementia is a global public health problem and poses a substantial socioeconomic and medical burden [1]. Because of its rapidly growing trend and limited effective treatment for dementia, its prevention has been of great importance [2]. Mild cognitive impairment (MCI), as a transitional phase between normal cognitive aging and dementia, constitutes an important endpoint for identifying risk factors and could be utilized for the identification of at-risk persons for dementia [3].

Sarcopenia is a complex skeletal muscle disease in older populations and has been related to increased risk of multiple adverse health outcomes in geriatrics, including frequent falls, lowered quality of life, and cognitive impairment [4]. Meanwhile, obesity is an established risk factor for a range of chronic diseases and premature death [5]. Defined as the coexistence of sarcopenia and obesity, sarcopenic obesity (SO) has become a major issue among older populations and raising a significant health burden [6, 7]. Preliminary evidence suggested that SO is associated with cognitive impairment [8-11]. Due to inconsistent definitions for SO, especially the diagnosis of obesity, makes an accurate diagnosis of SO challenging. There are great differences in the agreement of different SO definitions. A previous study indicated that body mass index (BMI) has poor diagnostic agreement with other obesity indicators in the diagnosis of SO and visceral fat area (VFA) had a relatively good agreement with waist circumference (WC) and body fat percentage (BF%) [12]. The lack of a consistent definition of SO hinders assessment of the prevalence and relevance of SO. There is no evidence of the relationship between SO and MCI by using multiple definitions of obesity in the same study, and further comparison studies should be done.

This study aims to assess the prevalence and the agreement of SO in middle-aged and older Chinese adults under different definition as well as its relationship with MCI. The findings could help identify individuals at high risk of MCI, leading to more effective and targeted interventions.

METHODS

Participants

The Lifestyle and Healthy Aging of Chinese Square Dancer Study (HealthyDance Study) is an ongoing prospective cohort study among middle-aged and older adults who regularly participate in a square dance. The participants are recruited and enrolled in 7 prefecture-level cities (Wuhan, Yichang, Xiangyang, Shanghai, Xiamen, Beijing, and Chengdu) in China. Inclusion criteria were: 1) age $\geq$ 45 years; 2) regular participation in square dance, with frequency at least once a week; 3) permanent resident population in the survey area (living in the area for more than 6 months before the survey); 4) no participation in any clinical trial during the three months prior to the survey. Participants who 1) unable to complete the survey on their own; 2) were in the acute phase of severe diseases; 3) diagnosed by deafness, dumb or serious mental illness were excluded. Each survey participant completed a face-to-face interview and physical examinations. The Ethics Committee of Wuhan University of Science and Technology approved the study with registration code 202049, and written informed consent was obtained from all participants. Our study used the baseline data from the HealthyDance Study, ranging from August 2020 to December 2021. After excluding 523 participants without complete information on obesity, sarcopenia, MCI diagnoses, and 2 participants with dementia, 2,451 participants were included in the final analysis (Supplementary Figure 1).

Cognitive function

Different measures were used to assess cognitive function impairment in the baseline survey of the HealthyDance Study, including an auditory verbal learning test (AVLT), digit symbol substitution test (DSST), verbal fluency test (VFT), and trail-making test B (TMT-B). These tests encompass different cognitive domains (i.e., episodic memory, attention,

language fluency, and executive function). Clinical dementia rating (CDR) was used to evaluate dementia. All cognitive assessments were performed by uniformly trained researchers. MCI was ascertained by Petersen criteria [13], as follows: 1) self-reported memory decline; 2) lower score (less than 1.5 standard deviations below normative means) in any cognitive test (TMT-B, AVLT, DSST, and VFT); 3) intact daily functioning; 4) absence of dementia (CDR $\leq$ 0.5). Details of each cognitive test are disclosed in the Supplementary Material.

Body composition and SO ascertainment

Each participant underwent a standardized physical examination with measurements of height, WC, and blood pressure. Participants wore light clothing and trained workers use a non-stretching tape to measure WC, at the narrowest part of the waist. Body composition was assessed by using a multi-frequency octopolar bioelectrical impedance analysis (BIA) (Haikang H-Key350; Beijing Sihai Huachen Technology Co., Ltd.). H-Key350 measures five body segments (left arm, right arm, trunk, left leg, and right leg) at six different frequencies (1 kHz, 5 kHz, 50 kHz, 250 kHz, 500 kHz, and 1000 kHz). Participants wore lightweight clothes and stood barefoot on the body composition analyzer. The sole contacted the foot electrodes and held the hand electrodes. The arm formed a 15° Angle with the torso. Input personal information such as age, gender, height, etc., and click to start the detection. The measurement mainly includes the following parameters: weight, BMI, fat mass, muscle mass, BF%, fat-free mass, VFA, and appendicular skeletal muscle (ASM). Appendicular skeletal muscle index (ASMI) was calculated as ASM in kilograms divided by the square of height in meters (kg/m^2).

According to the Asia Working Group for Sarcopenia (AWGS) 2019, Sarcopenia was diagnosed with low muscle mass, strength, and physical performance [14]. The definitions of low muscle mass for men and women were ASMI < 7.0 kg/m^2 and < 5.7 kg/m^2, respectively. Handgrip strength was measured using a hand dynamometer (Jamar Hand Dynamometer, IL, USA). Participants were instructed to stand and measure the strength of both hands. Low muscle strength was defined as maximum grip strength of < 28 kg in men and < 18 kg in women. Short Physical Performance Battery (SPPB) assessed physical function, including a standing balance test, a walking speed test, and five timed repeated chair rises. Each test was scored from 0 to 4, and the SPPB score was obtained by summating the three test scores. Lower physical performance was defined as SPPB scores $\leq$ 9.

We used several methods to define obesity for the diagnosis of SO according to BMI, BF%, WC, and VFA [12]. In accordance with the recommended definition of obesity for Chinese, the cut-off point for BMI was $\geq$ 28 kg/m^2, and the cut-off points of BF% were $\geq$ 35% for women and $\geq$ 25% for men [15, 16]. VFA and WC were used to define central obesity (VFA > 100 cm^2; WC > 80 cm in women and > 90 cm in men) [17, 18].

SO is defined as the combination of sarcopenia with obesity. We combined AWGS 2019 criteria with four obesity-related variables to diagnose SO (i.e., AWGS+VFA, AWGS+WC, AWGS+BF%, and AWGS+BMI). Based on their sarcopenia and obesity status, participants were classified into four groups: healthy (non-sarcopenia and non-obesity), only obesity (non-sarcopenia), only sarcopenia (non-obesity), and SO.

Covariates

Information on age, sex, marital status, education, employment, family income, smoking status, drinking status, living arrangement, and physical activity was obtained by standardized questionnaires. Marital status was categorized as married or others (single, divorced, or widowed). Education level was categorized as primary school and below, middle school and high school, and college or above. Employment status was classified as retired or paid employment. Annual household income (in Chinese Yuan) was categorized as < 20,000, 20,000-40,000, or > 40,000. Smoking status was classified as current smoker or non-smoker (never or past smoker). Alcohol status was classified as a current drinker or non-drinker (never or past drinker). Living arrangement was classified as living alone or living with others. The Physical Activity Scale for the Elderly (PASE) was used to assess whether the physical activity in the most recent week met the recommendations of WHO Guidelines 2020 on Physical Activity and Sedentary Behavior [19]. Physical activity (light, moderate, and vigorous-intensity physical activity)$\geq$150 min/week, moderate-intensity physical activity $\geq$ 150 min/week, or vigorous-intensity physical activity $\geq$ 75 min/week were considered to have met the recommended amount. Cardiovascular disease was assessed through self-report and physician diagnoses. Hypertension was ascertained

through self-report and/or blood pressure (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg). Diabetes was defined as fasting blood glucose ≥ 7.0 mmol/L and/or random blood glucose ≥ 11.1 mmol/L and/or self-reported.

Statistical analysis

Participants' characteristics were presented as the numbers (percentages) for categorical variables and as the mean (standard deviation [SD]) for continuous variables by SO (AWGS+VFA) groups (healthy, obesity, sarcopenia, and SO). Differences between the four groups were compared by using one-way variance analysis for continuous variables and the Chi-squared test for categorical variables. The agreement between different definitions of SO was assessed using Cohen kappa statistics and classified into four categories: poor (<0.20), fair (0.20–0.40), moderate (0.41–0.60), good (0.61–0.80), and very good (0.81–1.00) [20]. In addition, we performed sensitivity analyses to estimate the agreement when stratified by age (≤60 versus > 60 years).

Association between SO and MCI was evaluated using multivariable logistic regression model, and odds ratio (OR) and 95% confidence interval (CI) were calculated. Two models were constructed in our study: Model 1 was adjusted for age and sex; Model 2 was further adjusted for employment status, living alone, income, education level, marital status, smoking status, alcohol intake, physical activity, hypertension, diabetes, and cardiovascular disease. We calculated the adjusted means (95% CI) of multidimensional cognitive test results by SO groups and evaluated differences using general linear models. All the analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC, USA), and a two-sided p-value<0.05 was considered statistically significant.

RESULTS

Characteristics of participants

A total of 2,451 participants (mean age, 62.1 years [SD, 6.1 years]; 2,203 were women [89.9%]; 1,580 were 60 years of age or older [64.5%]) were included in this study. Under the definition of AWGS+VFA, 181 (7.4%) participants had SO, 134 (5.5%) had only sarcopenia, 1,098 (44.8%) had only obesity, and 1,038 (42.3%) were healthy. The characteristics of the four groups are shown in Table 1. Compared with the healthy group, those with SO were more likely to be older, living alone, primary school and below, never or past smoker, retired, and having diabetes (all $p < 0.05$).

A total of 335 (13.7%) participants were diagnosed with MCI. Regardless of the definition of obesity used, the prevalence of MCI was highest in the SO population compared to other groups (Supplementary Table 1).

Prevalence of group and agreement of definitions

Among the four definitions, the prevalence of SO was the highest when using AWGS+BF% (8.0%), followed by using AWGS+WC (7.8%) and AWGS+VFA (7.4%). The prevalence was the lowest (1.7%) when using the AWGS+BMI approach (Table 2). The agreements between different methods were shown in Table 3. SO defined by AWGS and BMI (AWGS+BMI) showed only fair diagnostic agreements with other criteria (κ ranged from 0.334 to 0.359). The other three criteria showed very good diagnostic agreements with each other. The κ statistics were 0.882 for AWGS+VFA and AWGS+BF%, 0.852 for AWGS+VFA and AWGS+WC, and 0.804 for AWGS+BF% and AWGS+WC, respectively. Age-stratified analysis showed that the agreements were even lower (κ<0.4) using AWGS+BMI in elderly (>60 years) women (Supplementary Table 2).

Associations of sarcopenia and obesity status with MCI

The odds of sarcopenic obesity and MCI among different body composition groups with different adiposity measures were shown in Table 4. Compared with healthy participants, those with SO or obesity had higher odds of MCI when using AWGS+VFA as the definition. After adjustment for sex and age (Model 1), the odds for MCI were significantly higher in the SO group (OR 2.08, 95% CI: 1.38-3.14) and obesity group (OR 1.45, 95% CI: 1.11-1.89), compared with the health group. In Model 2, the ORs of the SO group and obesity group for MCI were 1.75 (95% CI: 1.14-2.68) and 1.35 (95% CI: 1.02-1.78), respectively. Compared with the health group, the sarcopenia group was also associated with increased odds of MCI, although the association was not statistically significant (OR 1.57, 95% CI: 0.93-2.63).

Moreover, we examined the associations of SO with the odds of MCI using different diagnoses. Similar results were yielded using the AWGS+WC approach to define SO. The SO group (OR 1.96,

Table 1
Characteristics of participants according to different body composition groups

	Healthy	Only Obesity	Only Sarcopenia	Sarcopenic Obesity	p[a]
N (n, %)	1038 (42.4)	1098 (44.8)	134 (5.5)	181 (7.4)	
Age, y, mean (SD)	61.33 (6.1)	62.12 (5.9)	64.32 (6.1)	64.82 (6.0)	<0.001
Female (%)	913 (88.0)	1036 (94.4)	99 (73.9)	155 (85.6)	<0.001
Living alone, n (%)	55 (5.3)	81 (7.4)	16 (11.9)	17 (9.4)	0.009
Marital status, n (%)					
Married	935 (90.1)	946 (86.2)	112 (83.6)	155 (85.6)	0.014
Others [b]	103 (9.9)	152 (13.8)	22 (16.4)	26 (14.4)	
Educational level, n (%)					
Primary school and below	78 (7.5)	105 (9.6)	9 (6.7)	32 (17.7)	<0.001
Middle and high school	816 (78.6)	883 (80.4)	106 (79.1)	136 (75.1)	
College or above	144 (13.9)	109 (10.0)	19 (14.2)	13 (7.2)	
Annual household income per capita, n (%)					
<20,000 CNY	216 (20.8)	281 (25.6)	21 (15.7)	35 (19.3)	0.001
20,000-40,000 CNY	436 (42.0)	485 (44.2)	57 (42.5)	92 (50.8)	
>40,000 CNY	386 (37.2)	332 (30.2)	56 (41.8)	54 (29.8)	
Smoking, n (%)					
Never or past smoker	963 (93.4)	1044 (95.2)	118 (88.1)	173 (95.6)	0.005
Current smoker	69 (6.7)	53 (4.8)	16 (11.9)	8 (4.4)	
Alcohol intake, n (%)					
Never or past drinker	860 (82.9)	960 (87.4)	109 (81.3)	156 (86.2)	0.015
Current drinker	178 (17.2)	138 (12.6)	25 (18.7)	25 (13.8)	
Meeting physical activity recommendation, n (%)	879 (84.7)	954 (86.9)	97 (72.4)	142 (78.5)	<0.001
Retired, n (%)	862 (83.0)	913 (83.2)	108 (80.6)	162 (89.5)	0.123
Hypertension, n (%)	429 (41.3)	647 (58.9)	62 (46.3)	102 (56.4)	<0.001
Diabetes, n (%)	94 (9.1)	100 (9.1)	14 (10.5)	21 (11.6)	0.692

Data were expressed as the mean (SD), or n (%).SD, standard deviation. Sarcopenia was defined by Asia Working Group for Sarcopenia. Obesity was defined by visceral fat area. Sarcopenic obesity was defined as the presence of obesity and sarcopenia. [a]p-value for a chi-square test or one-way variance analysis. [b]Other marital status included single, divorced, or widowed.

Table 2
The prevalence of sarcopenia, obesity, and sarcopenic obesity based on different definitions

Number (%)	Definition 1[a]	Definition 2[b]	Definition 3[c]	Definition 4[d]
Sarcopenic Obesity	181 (7.4)	192 (7.8)	196 (8.0)	42 (1.7)
Only Sarcopenia	134 (5.5)	123 (5.0)	119 (4.9)	273 (11.1)
Only Obesity	1098 (44.8)	1170 (47.7)	1063 (43.4)	234 (9.6)
Healthy	1038 (42.4)	966 (39.4)	1073 (43.8)	1902 (77.6)

Data were expressed as n (%). [a]Sarcopenia: AWGS; Obesity: VFA; Sarcopenic Obesity: AWGS+VFA. [b]Sarcopenia: AWGS; Obesity: WC; Sarcopenic Obesity: AWGS+WC. [c]Sarcopenia: AWGS; Obesity: BF%; Sarcopenic Obesity: AWGS+BF%. [d]Sarcopenia: AWGS; Obesity: BMI; Sarcopenic Obesity: AWGS+BMI.

Table 3
Cohen's kappa (κ) agreement for sarcopenic obesity using different criteria of obesity

	AWGS+WC	AWGS+VFA	AWGS+BF%
AWGS+VFA	0.852	–	–
AWGS+BF%	0.804	0.882	–
AWGS+BMI	0.340	0.359	0.334

AWGS, Asia Working Group for Sarcopenia; BF%, body fat percentage; WC, waist circumference; BMI, body mass index; VFA, visceral fat area. Cohen's kappa for different numbers of diagnostic agreement of sarcopenic obesity between different diagnostic methods. Kappa values were classified into four categories: poor agreement (< 0.20), fair agreement (0.20–0.40), moderate agreement (0.41–0.60), good agreement (0.61–0.80), and very good agreement (0.81–1.00).

95% CI: 1.29-2.99) and the obesity group (OR 1.37, 95% CI: 1.03-1.82) were associated with higher odds of MCI, compared with the health group. When using the definition of AWGS+BF%, only SO was associated with the odds of MCI (OR 1.94, 95% CI: 1.29-2.93). Nevertheless, SO defined by

Table 4
Association between different definitions of body composition and risk of mild cognitive impairment

	Healthy	Only Obesity	Only Sarcopenia	Sarcopenic Obesity
Definition 1[a] (VFA)				
Model 1	1 (ref)	1.45 (1.11, 1.89)	1.58 (0.96, 2.59)	2.08 (1.38, 3.14)
Model 2	1 (ref)	1.35 (1.02, 1.78)	1.57 (0.93, 2.63)	1.75 (1.14, 2.68)
Definition 2[b] (WC)				
Model 1	1 (ref)	1.53 (1.16, 2.01)	1.42 (0.82, 2.45)	2.35 (1.57, 3.53)
Model 2	1 (ref)	1.37 (1.03, 1.82)	1.34 (0.76, 2.37)	1.96 (1.29, 2.99)
Definition 3[c] (BF%)				
Model 1	1 (ref)	1.40 (1.07, 1.82)	1.23 (0.70, 2.14)	2.26 (1.52, 3.36)
Model 2	1 (ref)	1.27 (0.96, 1.68)	1.13 (0.63, 2.02)	1.94 (1.29, 2.93)
Definition 4[d] (BMI)				
Model 1	1 (ref)	1.57 (1.08, 2.26)	1.57 (1.12, 2.20)	1.94 (0.92, 4.06)
Model 2	1 (ref)	1.43 (0.97, 2.10)	1.50 (1.06, 2.14)	1.45 (0.67, 3.12)

Values are odds ratio (95% confidence interval). [a]Definition 1: Using AWGS to define sarcopenia and VFA to define obesity. Combined AWGS and VFA to define sarcopenic obesity. [b]Definition 2: Using AWGS to define sarcopenia and WC to define obesity. Combined AWGS and WC to define sarcopenic obesity. [c]Definition 3: Using AWGS to define sarcopenia and BF% to define obesity. Combined AWGS and BF% to define sarcopenic obesity. [d]Definition 4: Using AWGS to define sarcopenia and BMI to define obesity. Combined AWGS and BMI to define sarcopenic obesity. Model 1: adjusted for age, and sex. Model 2: adjusted for model 1 + employment status, living alone, income, education level, marital status, smoking status, alcohol intake, physical activity, hypertension, diabetes, and cardiovascular disease.

AWGS+BMI was not significantly related to odds of MCI (OR 1.45, 95% CI: 0.67-3.12), statistically.

Associations of sarcopenia and obesity status with multiple cognitive domains

The adjusted means (95% CI) of multiple cognitive domains tests scores under different definitions were presented according to SO groups (Table 5). When using AWGS+VFA as the definition, the SO group had the lower scores in AVLT (24.4 versus 26.7, $p < 0.05$), VFT (16.0 versus 16.8, $p < 0.05$), and DSST (27.4 versus 29.0, $p < 0.05$), and spent more time on TMT-B (74.1 versus 61.9, $p < 0.05$) compared with the healthy group. Additionally, participants with SO (AWGS+VFA) had poorer performance in AVLT (24.4 versus 26.5, $p < 0.05$), VFT (16.0 versus 16.7, $p < 0.05$), and TMT-B (74.1 versus 63.9, $p < 0.05$) compared with the only obesity group. Consistent results were obtained between the healthy and SO group when using AWGS+WC or AWGS+BF% in the diagnosis of SO. However, when SO was defined by AWGS+BMI, statistically significant differences were only found in the DSST test (26.0 versus 28.6, $p < 0.05$), compared with the healthy group.

Secondary analyses

The results of the secondary analyses are presented in Supplementary Table 3. Age-stratified analyses showed that the results were consistent in middle-aged (45-60 years) or older (>60 years) participants. Stratified by sex, SO (AWGS+VFA) was associated with a higher risk of MCI in females. We found a statistically significant association between SO (AWGS+VFA) and MCI in middle-aged (45-60 years) women, but not in older women (>60 years). In addition, the association remained similar when we excluded premenopausal females.

DISCUSSION

In this cross-sectional study, we explored the prevalence and agreement of SO according to different diagnostic criteria as well as its association with MCI in middle-aged and older Chinese adults. We found that the AWGS+BMI identified the lowest prevalence of SO and had poor agreements with other criteria, while other definitions (AWGS+VFA, AWGS+WC, and AWGS+BF%) yielded consistent prevalence and had relatively good agreements. When using different definitions of SO, compared with the healthy participants, SO was associated with a 1.96-fold (AWGS+WC), 1.75-fold (AWGS+VFA), and 1.94-fold (AWGS+BF%) increased odds of MCI, respectively. Moreover, SO was associated with four cognitive domains under these definitions (AWGS+WC, AWGS+VFA, or AWGS+BF%, all $p < 0.05$).

In our study, the prevalence of MCI was 13.7%, which is similar to a previous study that reported a prevalence of MCI in adults aged 60 years or older

Table 5
Adjusted means (95% CI) of domain specific cognitive scores or time of each group with different definitions

	Healthy	Only Obesity	Only Sarcopenia	Sarcopenic Obesity
Definition 1 (VFA)				
AVLT, score	26.7 (24.8, 28.5)	26.5 (24.6, 28.3)	25.3 (22.9, 27.6)	24.4 (22.2, 26.6)[a,b]
VFT, score	16.8 (16.1, 17.6)	16.7 (15.9, 17.5)	16.1 (15.1, 17.1)	16.0 (15.0, 16.9)[a,b]
DSST, score	29.0 (27.5, 30.6)	28.0 (26.4, 29.6)[a]	27.6 (25.6, 29.6)	27.4 (25.6, 29.3)[a]
TMT-B, seconds	61.9 (56.7, 67.2)	63.9 (58.6, 69.2)	66.6 (59.8, 73.3)	74.1 (67.8, 80.4)[a,b,c]
Definition 2 (WC)				
AVLT, score	27.0 (25.2, 28.9)	26.4 (24.6, 28.2)	26.2 (23.8, 28.7)	24.0 (21.9, 26.2)[a,b]
VFT, score	16.9 (16.1, 17.7)	16.8 (15.9, 17.5)	16.3 (15.3, 17.3)	15.9 (15.0, 16.8)[a,b]
DSST, score	29.4 (27.9, 31.0)	28.0 (26.5, 29.6)[a]	28.4 (26.3, 30.4)	27.1 (25.3, 29.0)[a]
TMT-B, seconds	61.4 (56.0, 66.7)	63.3 (58.1, 68.5)	65.7 (58.7, 72.7)	73.5 (67.4, 79.7)[a,b,c]
Definition 3 (BF%)				
AVLT, score	26.8 (25.0, 28.7)	26.4 (24.5, 28.2)	25.2 (22.8, 27.6)	24.5 (22.3, 26.7)[a,b]
VFT, score	17.0 (16.2, 17.8)	16.5 (15.8, 17.3)[a]	16.5 (15.5, 17.5)	15.7 (14.8, 16.6)[a,b]
DSST, score	29.1 (27.5, 30.6)	28.0 (26.4, 29.6)[a]	28.5 (26.4, 30.5)	26.9 (25.1, 28.8)[a]
TMT-B, seconds	62.0 (56.7, 67.2)	63.7 (58.5, 69.0)	64.1 (57.2, 71.1)	75.1 (68.9, 81.4)[a,b,c]
Definition 4 (BMI)				
AVLT, score	26.3 (24.5, 28.2)	27.8 (25.7, 29.95)[a,c]	24.7 (22.7, 26.8)[a,b]	24.6 (21.1, 28.0)
VFT, score	16.8 (16.0, 17.5)	16.7 (15.8, 17.55)	16.0 (15.2, 16.9)[a]	16.0 (14.5, 17.4)
DSST, score	28.6 (27.1, 30.2)	28.1 (26.3, 29.90)	27.8 (26.1, 29.5)	26.0 (23.0, 28.9)[a]
TMT-B, seconds	62.4 (57.2, 67.6)	64.3 (58.2, 70.42)[c]	70.8 (65.0, 76.7)[a,b]	69.3 (59.4, 79.2)

Abbreviations: CI, confidence interval; AVLT, auditory verbal learning test; VFT, verbal fluency test; DSST, digit symbol substitution test; TMT-B, trail-making test B. Note: Data were expressed as the adjusted mean (95% CI) and adjusted for age, sex, employment status, living alone, income, education level, marital status, smoking status, alcohol intake, physical activity, hypertension, diabetes, and cardiovascular disease. [a]Compare with the Non- Sarcopenia and Non-Obesity group, $P < 0.05$. [b]Compare with the Only Obesity (Non- Sarcopenia) group, $P < 0.05$. [c]Compare with the Only Sarcopenia (Non-Obesity) group, $P < 0.05$.

in China of 15.5% [21]. The prevalence of SO was 1.7%-8.0% when using different obesity indicators combined with AWGS in the diagnosis of SO. A previous study also affirmed a similar range of prevalence (0.1%-7.9%) [12]. In addition, we found that regardless of the definition used, the prevalence of MCI was higher in the SO group compared with other groups. This result highlights that MCI tends to be more prevalent in SO individuals than in the sarcopenia group and obesity group. A cross-sectional study observed significant differences between different diagnostic criteria for SO, which used appendicular lean mass, appendicular lean mass index, and handgrip strength to define sarcopenia and BMI, WC, fat mass index, and fat mass to define obesity [22]. Another study used uniform sarcopenia criteria and different measures of obesity to diagnose SO found that BMI has poorer agreement with other obesity indicators (VFA, WC, and BF%) [12], which is consistent with our results. Despite the use of a uniform definition of sarcopenia, different definitions for obesity remain causing differences in the diagnosis of SO. Therefore, it is important to reach a consensus on obesity definitions in SO diagnosis.

In line with our study, previous results have found that SO was associated with increased odds of MCI. A cross-sectional study with 353 adults demonstrated that SO had the worst performance on global cognition when using BMI or BF% to define obesity and sarcopenia diagnosis guidelines to define sarcopenia [8]. Another cross-sectional study identified the positive association between SO and cognitive impairment, which used BF% and ASMI to diagnose SO [9]. The longitudinal National Health and Aging Trends Survey study found that SO (grip strength and BMI) was associated with cognitive impairment [10]. Another study using grip and BMI to define SO also found that SO was associated with MCI and dementia [11]. However, the lack of consensus on the diagnosis criteria of SO impedes the comparability of the findings of different studies. Existed differences among different definitions of SO may also hinder assessment of the prevalence and relevance of SO. In this study, we examined the associations between SO and MCI by using different diagnostic criteria of SO in the same population. We found that SO was associated with increased odds of MCI when using different obesity indicators (VFA, WC, and BF%) except for BMI.

Some previous studies have explored the relationship between sarcopenia, obesity, and MCI. A longitudinal study showed that sarcopenia is associated with worse cognitive impairment among elderly adults, which used AWGS to diagnose sarcopenia

[23]. In our study, the sarcopenia group was associated with increased odds of MCI compared with the healthy group, although the association was not statistically significant. Additionally, according to previous studies, not all obesity indicators were positively correlated with cognitive impairment. Higher BMI in midlife was positively associated with dementia but inversely with dementia in later life [24]. Another study did not find any associations between obesity (BMI $\geq$30 kg/m^2) and cognition [25]. BMI may not be a suitable measure in obesity diagnosis among older adults because it does not reflect the fat distribution and does not discriminate well between skeletal muscle and fat. A meta-analysis showed that high WC could increase the risk of cognitive impairment [26]. In addition, a study found that the prevalence of abdominal obesity was higher than BMI-defined obesity in China [27], so simply using BMI to define obesity may be not applicable to Chinese population. A cross-sectional study suggested that higher BF% and visceral adiposity were associated with reduced cognitive scores [28]. A cross-sectional study indicated that central obesity, regardless of BMI, had poor cognitive outcomes, whereas high BMI without central obesity had better cognitive outcomes [29]. Central obesity may better predict obesity and cognitive function than BMI. In our results, when using the central obesity indicators (WC and VFA) and BF% as the definition, both the obesity and SO group were associated with MCI, and SO had higher odds of MCI than obesity. In addition, the SO (WC, VFA, and BF%) group had poorer cognitive function (episodic memory, attention, language fluency, and executive function) than the healthy group under different diagnosis criteria (WC, VFA, and BF%).

Several shared pathways have been proposed to explain the observed association. First, inflammation and insulin resistance are common in sarcopenia, obesity, and cognitive impairment. Body fat activates inflammatory processes and leads to insulin resistance [30]. Muscle catabolism could also cause insulin resistance and inflammation [31]. Excess fat contributes to fat redistribution, causing ectopic fat infiltration, especially in the skeletal muscles [32]. Skeletal muscle fat infiltration, sarcopenia, and obesity could make a larger vicious cycle, which leads to further inflammation and insulin resistance [33]. Inflammation and insulin resistance would accelerate cognitive decline [34, 35]. Second, previous study has found that growth hormone secretion was depressed in SO individuals [36]. Hormones is associated with cognitive function. Especially in females, the precipitous loss of estrogens and progestogens at menopause makes them at a higher risk of Alzheimer's disease than males, and sex hormones have brain-protective effects [37]. Owing to the specific mechanism between SO and MCI has not been elucidated, more research is needed.

Strengths and limitations

The main strength of our study is to compare the detection rates and agreement of SO and explore the relationship between SO and MCI by using multiple definitions of obesity in the same study. Additionally, we used a battery of cognitive tests for various cognitive domains to evaluate cognitive function in multiple dimensions in this study. This study also has some limitations. First, we used BIA to evaluate body composition instead of the gold standard method [38, 39]. Although previous studies have found that the results of BIA measurements are similar to those of magnetic resonance imaging or dual-energy X-ray absorptiometry [40, 41], there are some limitations to BIA measurements [42-44]. Therefore, these gold standard methods should be adopted in future studies to further verify our conclusions. Second, the participants in our study were Han Chinese and female. All participants in this study regularly participated in square dancing, resulting individuals with severe sarcopenia might be less. Thus, the results could not be directly generalized to other populations. Meanwhile, our results are worth being replicated in other ethnicities. Third, causal inferences between SO and cognition should be drawn with caution because of the cross-sectional design. Finally, residual confounding and potential bias may still exist due to the study's observational nature.

Conclusion

When using different obesity indicators combined with AWGS to diagnose SO, BMI had lower prevalence and agreement compared with other indicators (WC, VFA, and BF%). SO was associated with MCI when using different obesity indicators (WC, VFA, and BF%) except for BMI. How to define SO and the relationship between obesity classification and cognition will be an important direction of future research. With deepened appreciation of SO and its potential cognitive consequences, developing effective prevention and treatment strategies is imperative.

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Shuang Rong is an Editorial Board Member of this journal but was not involved in the peer-review process, nor had access to any information regarding its peer-review.

DATA AVAILABILITY

The datasets used to support the findings of this study are available from the corresponding author.

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: https://dx.doi.org/10.3233/JAD-221232.

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