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Associations between sarcopenic obesity and the risk of cardiovascular-kidney-metabolic syndrome progression: insights from the China health and retirement longitudinal study

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Abstract

Background This study aimed to explore the association between sarcopenic obesity (SO) and advanced stages of cardiovascular-kidney-metabolic (CKM) syndrome, as well as to prospectively examine its relationship with cardiovascular events in CKM stages 0–3.

Methods Data were drawn from the China Health and Retirement Longitudinal Study (2011–2020) encompassing a median follow-up of 9.0 years for incident cardiovascular events. Sarcopenia was defined according to the Asian Working Group for Sarcopenia 2019 criteria. Non-sarcopenic participants with optimal body mass index or waist circumference served as the reference group. Outcome was major adverse cardiovascular events (MACEs) defined as a composite of all-cause death, cardiovascular problem, and stroke. Multivariable logistic regression and Cox proportional hazards models were employed to assess associations.

Results A total of 6,766 participants (age 60.0 ± 9.9 years, 46.9% male) were included. At baseline, SO was associated with a significantly higher likelihood of advanced CKM stages [OR (95% CI): 3.317 (2.533, 4.345)] compared to reference. Similarly, sarcopenic overweight [OR (95% CI): 3.171 (2.601, 3.865)] and sarcopenic abdominal obesity [OR (95% CI): 3.268 (2.662, 4.013)] were also linked to higher odds of advanced CKM stages. Over a median follow-up of 9.0 years, 1,322 participants (21.1%) from CKM stages 0–3 experienced MACEs. After adjusting for multiple covariates, SO was associated with an increased risk of MACEs [HR (95% CI): 2.248 (1.789, 2.824)] compared to reference. Similarly, sarcopenic overweight [HR (95% CI): 1.768 (1.465, 2.135)] and sarcopenic abdominal obesity [HR (95% CI): 1.730 (1.414, 2.115)] were also associated with an elevated risk of MACEs.

Conclusions SO was significantly associated with more advanced stages of the CKM spectrum. Furthermore, among individuals categorized with CKM stages 0–3 and without pre-existing cardiovascular disease, SO was independently associated with a substantially elevated risk of future MACEs.

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Keywords Cardiovascular-kidney-metabolic syndrome, Sarcopenic obesity, Sarcopenia, Cardiovascular disease

Introduction

Sarcopenic obesity (SO), characterized by the coexistence of reduced skeletal muscle mass and function alongside excess adiposity, is an increasingly prevalent condition, driven primarily by global population aging and the ongoing obesity epidemic [1]. A recent systematic review and meta-analysis published in 2021 (based on studies up to December 2020), encompassing 50 studies across various global populations, estimated an overall global prevalence of 11% among older adults (aged 60 years and older) [2]. Diagnosis of SO relies on established criteria for both sarcopenia and obesity, which often vary across expert guidelines, such as those from the European Working Group on Sarcopenia in Older People (EWGSOP) [3], the Asian Working Group for Sarcopenia (AWGS) [4], and the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project [5]. These guidelines typically incorporate criteria for low muscle mass, muscle strength, and/or physical performance, with specific cutoffs adapted for different ethnic populations.

While sarcopenia and obesity are distinct clinical entities, their co-occurrence as SO creates a complex pathophysiological milieu that significantly accelerates adverse health outcomes. This intricate link is underpinned by deeply intertwined inflammatory and metabolic pathways. Sarcopenia is increasingly recognized as a state of chronic low-grade inflammation, characterized by elevated pro-inflammatory cytokines (e.g., TNF-α, IL-6) that contribute to muscle protein degradation and insulin resistance [6–8]. Similarly, obesity, particularly with adipose tissue dysfunction, drives systemic inflammation and profound insulin resistance [9]. This metabolic dysregulation is central to conditions like metabolic syndrome and metabolic-associated fatty liver disease (MAFLD), which are strong drivers of cardiovascular disease and major adverse cardiovascular events (MACEs) [10]. When sarcopenia and obesity co-exist as SO, their combined effect is hypothesized to be synergistic, reinforcing these inflammatory and metabolic dysregulations. Beyond chronic inflammation and insulin resistance, other contributing factors include mitochondrial dysfunction (leading to reduced energy production and increased oxidative stress) and ectopic adiposity (fat infiltration into non-adipose tissues, impairing organ function) [1]. Indeed, prior research has shown that SO is associated with a significantly elevated risk of cardiovascular disease (CVD), with one study reporting a 23% increased risk compared to non-sarcopenic obesity [11].

The Cardiovascular-Kidney-Metabolic (CKM) syndrome is a newly proposed clinical framework that underscores the complex interplay between metabolic abnormalities, chronic kidney disease (CKD), and cardiovascular dysfunction [12]. More than a mere aggregation of comorbidities, CKM syndrome is understood as a progressive, multisystem condition characterized by interconnected pathophysiological processes leading to systemic organ damage and heightened cardiovascular risk [13]. Given its association with substantial morbidity and mortality, early identification of modifiable risk factors is critical for preventing or slowing CKM progression.

While SO has been increasingly recognized as a risk factor for various cardiometabolic conditions, including insulin resistance, metabolic syndrome, and cardiovascular diseases, its integrated and specific role within the comprehensive framework of CKM syndrome, particularly regarding its progression, remains to be fully elucidated. Addressing this gap is essential for improving risk stratification and informing targeted prevention strategies, particularly in aging populations.

To this end, the present study aimed to investigate the associations between SO and CKM syndrome progression among middle-aged and older Chinese adults. Utilizing data from the China Health and Retirement Longitudinal Study (CHARLS), we examined both the cross-sectional relationship between SO and advanced CKM stages (Stages 3 and 4) at baseline, and the prospective association between baseline SO and subsequent cardiovascular events in individuals at CKM Stages 0–3. These findings may provide novel insights into the interplay between body composition abnormalities and multisystem chronic disease progression in a rapidly aging population.

Methods

Data source and study population

The China Health and Retirement Longitudinal Study (CHARLS) is a nationally representative cohort survey conducted across 28 provinces in mainland China, covering 150 counties and 450 communities. Detailed methodologies, including study design and protocols for blood sample collection, have been described previously [14–16]. The baseline survey was initiated in 2011, with subsequent follow-up waves conducted in 2013, 2015, 2018, and 2020. Ethical approval was granted by the Institutional Review Board of Peking University (IRB00001052–11015). For this analysis, data from the 2011 and 2020 survey waves were used. Of the 17,705 individuals recruited at baseline in 2011, participants were excluded if they lacked baseline measurements for body mass index (BMI), waist circumference (WC), blood pressure, fasting plasma glucose, glycated hemoglobin (HbA1c),

high-density lipoprotein cholesterol (HDL-C), serum creatinine, or serum cystatin C; were missing data on sex or estimated glomerular filtration rate (eGFR); or lack of sarcopenia information. After applying these exclusion criteria, a final sample of 6,766 participants was included in the analysis (Fig. 1).

Assessment of obesity and sarcopenia status

Sarcopenia was defined based on the 2019 criteria established by the AWGS, which includes three components: reduced muscle strength, impaired physical performance, and decreased muscle mass [4].

Muscle strength was assessed via handgrip strength (HGS), measured using a Yuejian WL-1000 dynamometer. Participants completed three attempts per hand, and the highest value from either hand was used for analysis. Low muscle strength was defined as HGS < 28.0 kg for men and < 18.0 kg for women.

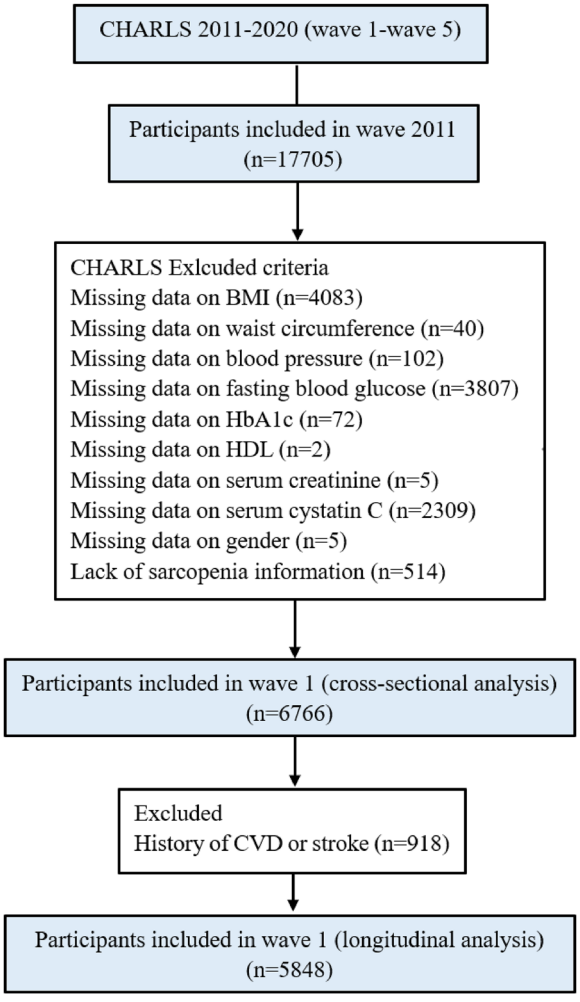

Fig. 1 A detailed flow chart of participant recruitment. BMI: body mass index; HbA1C: glycosylated hemoglobin; HDL-C: high-density lipoprotein-cholesterol

Physical performance was evaluated using the five-time chair stand test and a 2.5-meter walking test (converted to a 6-meter walk speed). According to AWGS 2019, poor physical performance was defined as a chair stand time ≥ 12.0 s or a walking speed < 1.0 m/s.

Muscle mass was estimated using a validated anthropometric equation suitable for Chinese populations, which demonstrated high agreement with dual-energy X-ray absorptiometry (DXA) [17]: ASM = 0.193×weight (kg) + 0.107×height (cm) − 4.157×sex − 0.037×age − 2.631, where sex was coded as 1 for men and 2 for women. Skeletal muscle index (SMI) was then calculated by adjusting ASM for height squared (SMI = ASM/height² in m²). Low muscle mass was defined as an SMI below the lowest sex-specific quintile of the study population [18–20], with cutoffs of < 7.76 kg/m² for men and < 6.15 kg/m² for women.

In this study, possible sarcopenia was characterized by either low muscle strength (HGS < 18 kg) or reduced physical performance (chair stand test ≥ 12 s), whereas confirmed sarcopenia required low muscle mass in combination with either criterion.

Obesity was assessed using both BMI and WC. General obesity was defined as BMI ≥ 28.0 kg/m², while overweight status corresponded to a BMI between 24.0 and 27.9 kg/m² [21]. Abdominal obesity was classified as WC ≥ 85 cm for men and ≥ 80 cm for women [22].

Participants were stratified into four categories based on the combination of obesity and sarcopenia status: Normal weight without possible sarcopenia or sarcopenia; Normal weight with possible sarcopenia or sarcopenia; Obesity without possible sarcopenia or sarcopenia; Obesity with possible sarcopenia or sarcopenia.

Definition of CKM syndrome stages and CKM conditions

Definitions of CKM Health Stages by the AHA Presidential Advisory Statement on CKM Syndrome [12]: Stage 0: No CKM health risk factors; Stage 1: Excess and/or dysfunctional adiposity; Stage 2: Metabolic risk factors and CKD; Stage 3: Subclinical CVD in CKM; Stage 4: Clinical CVD in CKM (algorithm is detailed in Table S1).

Clinical CVD was defined as any history of chronic heart failure, coronary heart disease, heart attack, or stroke [12]. Subclinical CVD was defined as having ≥ 20% of 10-year CVD risk or high-risk CKD [12] (algorithm is detailed in Table S2). The predicted 10-year CVD risk was calculated by the Framingham risk score (the algorithm is detailed in Table S3) [23].

The Chronic Kidney Disease Epidemiology Collaboration (CKDEPI) creatinine-cystatin C equation was used to calculate eGFR for CHARLS [24], as follows: eGFR ($mL/min/1.73m^2$) = $135 \times \min(Cr/\kappa, 1)^{\alpha} \times \max(Cr/\kappa, 1)^{-0.601} \times \min(Cys/0.8, 1)^{-0.375} \times \max(Cys/0.8, 1)^{-0.711} \times 0.995^{age} \times 0.969$[if female]. Where Cr refers to serum

creatinine measured in mg/dL and CysC refers to serum cystatin C measured in mg/liter. κ is 0.7 for females and 0.9 for males. α is − 0.248 for females and − 0.207 for males.

CKD stages were classified according to Kidney Disease Improving Global Outcomes (KDIGO) (the algorithm is detailed in Table S4) [12].

Outcomes

The study's endpoints were MACEs during the follow-up period. MACEs were defined as a composite of all-cause death, cardiovascular problem, and stroke. All-cause mortality was defined as death from any cause during the follow-up period. Cardiovascular problem were diagnosed by the questions: "Have you been told by a doctor that you have been diagnosed with a heart attack, angina, coronary heart disease, heart failure, or other heart problems?". Stroke was diagnosed by the question: "Have you been told by a doctor that you have been diagnosed with a stroke?". Advanced CKM stages were defined as CKM stage 3 and 4.

Covariates

For the purposes of this investigation, the following information was gathered: Demographic data: age, gender, education level, marital status; Body measurements: systolic blood pressure (SBP), diastolic blood pressure (DBP), height, weight, BMI, and waist circumference; Lifestyle data: smoking and drinking status; Data on disease history and medication history: hypertension, hypertension medication, diabetes, diabetes medication, chronic heart failure, coronary heart disease, heart attack, stroke; Laboratory test data: HbA1C, fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), HDL-C, serum creatinine (Scr), and serum cystatin C.

Statistical analysis

Participants were classified into four groups based on their SO status. The distribution of continuous variables was evaluated for normality. Variables following a normal distribution were reported as means with standard deviations (mean ± SD), while non-normally distributed data were expressed as medians with interquartile ranges (IQR). Categorical variables were described using frequencies and percentages.

Group comparisons for continuous variables across the four sarcopenic obesity phenotypes were performed using one-way Analysis of Variance (ANOVA) for normally distributed data, or the Kruskal-Wallis H test for non-normally distributed data. For categorical variables, differences were assessed using the chi-square test or Fisher's exact test, as appropriate.

To investigate the relationship between SO status and advanced stages of CKM disease (Stages 3 and 4) at baseline, logistic regression models were utilized. Kaplan–Meier survival curves were generated to estimate the cumulative incidence of MACEs across SO groups, and statistical differences were evaluated using the log-rank test.

Both univariate and multivariate Cox proportional hazards models were applied to examine the association between SO status and the risk of cardiovascular events. Furthermore, subgroup analyses were conducted by age (< 60 vs. ≥60 years), sex, presence of diabetes, smoking status, hypertension, and presence of CKD to explore potential effect modification.

All statistical analyses were performed using SPSS version 21.0 and R version 4.3.2. A two-sided p-value < 0.05 was considered indicative of statistical significance.

Results

Baseline characteristics of participants classified by the sarcopenia and obesity

Table 1 summarizes the baseline characteristics of the study population stratified by sarcopenia and obesity status. A total of 6,766 participants were included in the analysis, with a mean age of 60.0 ± 9.9 years; 46.9% were male. Participants identified with sarcopenic overweight tended to be older, predominantly female, and less likely to report a history of smoking or alcohol use (all $P < 0.01$). In contrast, this group demonstrated a significantly higher prevalence of hypertension, diabetes, prediabetes, and metabolic syndrome (all $P < 0.01$). Moreover, individuals with sarcopenic overweight exhibited unfavorable cardiometabolic profiles, including elevated BMI, waist circumference, SBP, FBG, HbA1c, TC, and TG. In comparison, they had lower levels of HDL-C and eGFR (all $P < 0.01$).

Prevalence of CKM stages according to the sarcopenia and obesity status

The overall prevalence of CKM Stages 0 to 4 was 6.4%, 13.1%, 29.5%, 37.4%, and 13.6%, respectively (Table 1). Compared to individuals without sarcopenic overweight, those with sarcopenic overweight showed a significantly lower prevalence of early CKM stages (0–2) and a substantially higher prevalence of advanced stages (3–4) ($P < 0.001$; Fig. 2).

Association between SO status and advanced CKM stages at baseline

Logistic regression analysis revealed that SO was an independent and significant predictor of advanced CKM stages, even after adjusting for potential confounders such as age, sex, education level, marital status, smoking, and alcohol use (Table 2). Compared to individuals

Table 1 Baseline characteristics of individuals classified by the sarcopenia and overweight status

Characteristic	Total	Normal weight		Overweight		P value
		Nonsarcopenic	Possible sarcopenia or sarcopenia	Nonsarcopenic	Possible sarcopenia or sarcopenia	
n	6766	1625	2437	1248	1456	
Age, years	60.0 ± 9.9	53.4 ± 6.5	66.3 ± 8.8	52.5 ± 5.9	63.0 ± 8.5	< 0.001
Gender						< 0.001
Male, n(%)	3176 (46.9)	853 (52.5)	1279 (52.5)	496 (39.7)	548 (37.6)	
Female, n(%)	3590 (53.1)	772 (47.5)	1158 (47.5)	752 (60.3)	908 (62.4)	
Ever smoke, n(%)	2664 (39.4)	742 (45.7)	1103 (45.3)	379 (30.4)	440 (30.2)	< 0.001
Ever drink, n(%)	2181 (32.2)	633 (39.0)	787 (32.3)	386 (30.9)	375 (25.8)	< 0.001
Educational level						< 0.001
Below primary school, n(%)	3300 (48.8)	638 (39.3)	1489 (61.1)	407 (32.6)	766 (52.6)	
Primary school, n(%)	1429 (22.6)	348 (21.4)	573 (23.5)	264 (21.2)	344 (23.6)	
Middle school, n(%)	1292 (19.1)	418 (25.7)	275 (11.3)	368 (29.5)	231 (15.9)	
High school or above, n(%)	645 (9.5)	221 (13.6)	100 (4.1)	209 (16.7)	115 (7.9)	
Marital status						< 0.001
Married, n(%)	5859 (86.6)	1494 (91.9)	1940 (79.6)	1185 (95.0)	1240 (85.2)	
Other, n(%)	907 (13.4)	131 (8.1)	497 (20.4)	63 (5.0)	216 (14.8)	
Hypertension, n(%)	3835 (56.7)	642 (39.5)	1359 (55.8)	763 (61.1)	1071 (73.6)	< 0.001
Diabetes, n(%)	1178 (17.4)	177 (10.9)	385 (15.8)	258 (20.7)	358 (24.6)	< 0.001
Prediabetes, n(%)	2915 (43.1)	663 (40.8)	1017 (41.7)	570 (45.7)	665 (45.7)	0.005
MetS, n(%)	2943 (43.5)	391 (24.1)	670 (27.5)	810 (64.9)	1072 (73.6)	< 0.001
BMI, kg/m2	23.4 ± 3.9	21.4 ± 1.8	20.7 ± 2.1	27.1 ± 3.1	27.1 ± 3.0	< 0.001
Waist circumference, cm	84.0 ± 12.7	78.5 ± 9.6	78.7 ± 10.4	91.2 ± 11.1	92.9 ± 12.5	< 0.001
SBP, mmHg	130.9 ± 21.9	123.2 ± 18.5	131.5 ± 22.8	130.8 ± 20.1	138.7 ± 22.3	< 0.001
FBG, mg/dl	110.0 ± 36.3	104.7 ± 25.1	109.3 ± 38.7	112.7 ± 37.9	115.7 ± 40.2	< 0.001
HBA1C,%	5.3 ± 0.8	5.1 ± 0.6	5.2 ± 0.8	5.3 ± 0.8	5.4 ± 1.0	< 0.001
TC, mg/dl	193.4 ± 38.9	190.6 ± 38.2	189.8 ± 37.5	196.5 ± 41.1	199.8 ± 39.3	< 0.001
TG, mg/dl	105.3 (74.3, 154.0)	94.7 (69.0, 134.5)	92.0 (68.1, 131.9)	126.1 (89.8, 187.6)	128.3 (91.6, 186.8)	< 0.001
HDL-C, mg/dl	51.1 ± 15.1	54.2 ± 15.8	54.6 ± 15.3	46.5 ± 13.4	45.7 ± 12.5	< 0.001
eGFR, mL/min/1.73m^2	84.9 ± 17.8	91.6 ± 15.4	78.4 ± 17.0	93.4 ± 16.1	81.3 ± 17.3	< 0.001
CKM stage, n(%)						< 0.001
Stage 0	436 (6.4)	268 (16.5)	168 (6.9)	0 (0.0)	0 (0.0)	
Stage 1	888 (13.1)	326 (20.1)	263 (10.8)	196 (15.7)	103 (7.1)	
Stage 2	1996 (29.5)	546 (33.6)	486 (19.9)	562 (45.0)	402 (27.6)	
Stage 3	2528 (37.4)	394 (24.2)	1158 (47.5)	329 (26.4)	647 (44.4)	
Stage 4	918 (13.6)	91 (5.6)	362 (14.9)	161 (12.9)	304 (20.9)	

MetS: metabolic syndrome; BMI: body mass index; SBP: systolic blood pressure; FBG: fasting blood glucose; HbA1C: glycosylated hemoglobin; TC, total cholesterol; TG, triglyceride; HDL-C: high-density lipoprotein-cholesterol; eGFR, estimated glomerular filtration rates; CKM: cardiovascular-kidney-metabolic

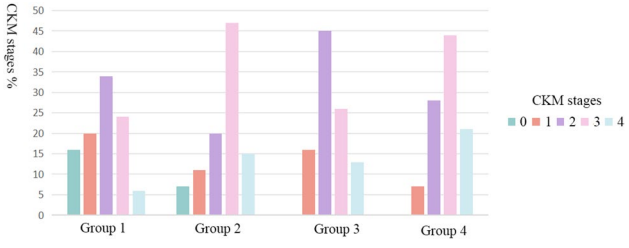

Fig. 2 Prevalence of CKM stages according to the sarcopenia and obesity status. Group 1: normal weight and without possible sarcopenia or sarcopenia; Group 2: normal weight and with possible sarcopenia or sarcopenia; Group 3: overweight and without possible sarcopenia or sarcopenia; Group 4: overweight and with possible sarcopenia or sarcopenia

without SO, those with sarcopenic obesity exhibited markedly higher odds of progressing to advanced CKM stages [OR (95% CI): 3.317 (2.533–4.345)]. Similarly, participants with sarcopenic overweight [OR (95% CI): 3.171 (2.601–3.865)], and participants with sarcopenic abdominal obesity [OR (95% CI): 3.268 (2.662–4.013)] also demonstrating significantly elevated risk.

Association between baseline SO status and incident cardiovascular disease in individuals with CKM stages 0–3

During a median follow-up period of 9.0 years, a total of 1,213 participants (20.7%) across CKM Stages 0–3 experienced MACEs. The Kaplan–Meier survival curves demonstrated a increase in MACEs incidence in participants

Table 2 Odds ratios of advanced CKM stages at baseline in the sarcopenic overweight groups, sarcopenic obesity groups, and sarcopenic abdominal obesity groups

Sarcopenic overweight	Case, *n* (%)	OR (95% CI)		
		Model 1	Model 2	Model 3
Group 1	485 (29.8)	Reference	Reference	Reference
Group 2	1520 (62.4)	3.896 (3.407, 4.456)***	1.196 (0.992, 1.441)	1.206 (0.999, 1.456)
Group 3	490 (39.3)	1.519 (1.301, 1.775)***	2.800 (2.320, 3.378)***	2.844 (2.353, 3.438)***
Group 4	951 (65.3)	4.426 (3.804, 5.150)***	3.097 (2.544, 3.770)***	3.171 (2.601, 3.865)***
Sarcopenic obesity	**Case, n (%)**	**OR (95% CI)**		
		Model 1	**Model 2**	**Model 3**
Group 5	827 (32.9)	Reference	Reference	Reference
Group 6	2188 (62.91)	3.464 (3.110, 3.859)***	1.162 (0.993, 1.361)	1.176 (1.004, 1.378)*
Group 7	148 (41.5)	1.446 (1.153, 1.814)**	2.734 (2.096, 3.566)***	2.699 (2.068, 3.522***
Group 8	283 (68.2)	4.379 (3.504, 5.471)***	2.270 (2.499, 4.278)***	3.317 (2.533, 4.345)***
Sarcopenic abdominal obesity	**Case, n (%)**	**OR (95% CI)**		
		Model 1	**Model 2**	**Model 3**
Group 9	351 (29.3)	Reference	Reference	Reference
Group 10	1058 (62.8)	4.088 (3.488, 4.792)***	1.253 (1.016, 1.546)*	1.270 (1.028, 1.570)*
Group 11	624 (37.3)	1.439 (1.227, 1.687)***	2.830 (2.335, 3.431)***	2.876 (2.368, 3.493)***
Group 12	1413 (64.0)	4.294 (3.689, 4.997)***	3.203 (2.612, 3.927)***	3.268 (2.662, 4.013)***

Group 1: normal weight and without possible sarcopenia or sarcopenia; Group 2: normal weight and with possible sarcopenia or sarcopenia; Group 3: overweight and without possible sarcopenia or sarcopenia; Group 4: overweight and with possible sarcopenia or sarcopenia

Group 5: without obesity and without possible sarcopenia or sarcopenia; Group 6: without obesity and with possible sarcopenia or sarcopenia; Group 7: with obesity and without possible sarcopenia or sarcopenia; Group 8: with obesity and with possible sarcopenia or sarcopenia

Group 9: without abdominal obesity and without possible sarcopenia or sarcopenia; Group 10: without abdominal obesity and with possible sarcopenia or sarcopenia; Group 11: with abdominal obesity and without possible sarcopenia or sarcopenia; Group 12: with abdominal obesity and with possible sarcopenia or sarcopenia

Model 1: unadjusted; Model 2: adjusted for age and gender; Model 3: adjusted for age, gender, education, marital, smoking, and drinking

OR, odds ratio; CI, confidence interval

'***': $P < 0.001$; '**': $P < 0.01$; '*': $P < 0.05$

with sarcopenic obesity, sarcopenic overweight or sarcopenic abdominal obesity, with the log-rank test indicating a statistically significant difference ($P < 0.001$; Fig. 3). Results from the Cox proportional hazards regression analysis are presented in Table 3. Specifically, individuals with sarcopenic obesity had a significantly increased risk of MACEs [HR (95% CI): 2.248 (1.789, 2.824)] compared to controls. Similarly, patients with sarcopenic overweight [HR (95% CI): 1.768 (1.465, 2.135)], and patients with sarcopenic abdominal obesity [HR (95% CI): 1.730 (1.414, 2.115)] also had a significantly increased risk of MACEs.

Subgroup analyses

Subgroup analyses were conducted to assess potential effect modification in the association between SO status and the risk of MACEs. A statistically significant interaction were identified between SO and diabetes status (P for interaction = 0.017), and between SO and hypertension (P for interaction < 0.001), even after adjusting for all relevant confounders (Table 4). In contrast, no significant interactions were found between SO and age ($P = 0.330$), gender ($P = 0.936$), smoking status ($P = 0.497$), or CKD ($P = 0.727$) indicating the association between SO and MACEs was consistent across these subgroups. Results from subgroups with wide confidence intervals should be interpreted as exploratory and require validation in larger, adequately powered studies.

Discussion

In this nationally representative cohort of middle-aged and older adults, SO was independently associated with an elevated risk of advanced CKM stages at baseline. Moreover, over a median follow-up of 9.0 years, individuals with SO and but without baseline cardiovascular disease demonstrated a significantly increased incidence of MACEs. These results underscore the clinical importance of early detection and targeted management of SO to mitigate CKM progression and reduce future cardiovascular risk.

SO is characterized by the coexistence of reduced skeletal muscle mass and strength alongside adiposity [25]. As individuals age, body composition shifts towards decreased muscle mass and increased fat accumulation, particularly visceral fat [26]. In older adults, obesity, especially central and visceral obesity, is a well-established risk factor for various cardiometabolic disorders, including insulin resistance, type 2 diabetes, dyslipidemia, and CVD [11]. Similarly, diminished muscle mass and strength have been linked to CVD risk factors such as arterial stiffness, impaired glucose metabolism, and metabolic syndrome [11]. When obesity is accompanied by low muscle mass, this combined condition, SO, may confer synergistic adverse effects, amplifying the health risks associated with either condition alone [27]. SO has been implicated in a range of clinical complications, including frailty, fractures, cardiovascular disease, cancer, as well as higher rates of hospitalization and mortality [1].

Accumulating evidence suggests that SO is closely linked to elevated risks of CVD, MetS, type 2 diabetes mellitus (T2DM), and CKD. Evidence suggests that SO markedly increases the likelihood of cardiometabolic abnormalities such as insulin resistance, metabolic

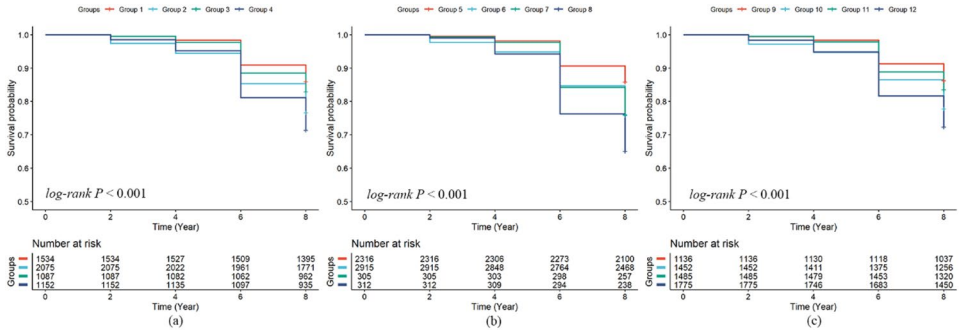

Fig. 3 Cumulative incidence curve (K-M curves) of MACEs in participants with CKM Stages 0–3. (**a**) Group 1: normal weight and without possible sarcopenia or sarcopenia; Group 2: normal weight and with possible sarcopenia or sarcopenia; Group 3: overweight and without possible sarcopenia or sarcopenia; Group 4: overweight and with possible sarcopenia or sarcopenia (**b**) Group 5: without obesity and without possible sarcopenia or sarcopenia; Group 6: without obesity and with possible sarcopenia or sarcopenia; Group 7: with obesity and without possible sarcopenia or sarcopenia; Group 8: with obesity and with possible sarcopenia or sarcopenia (**c**) Group 9: without abdominal obesity and without possible sarcopenia or sarcopenia; Group 10: without abdominal obesity and with possible sarcopenia or sarcopenia; Group 11: with abdominal obesity and without possible sarcopenia or sarcopenia; Group 12: with abdominal obesity and with possible sarcopenia or sarcopenia

syndrome (MetS), and dysregulated glucose and lipid metabolism [28–31]. A systematic review of cross-sectional studies reported that older adults with SO are at significantly higher risk for CVD [32]. Longitudinal data from the China Health and Retirement Longitudinal Study (CHARLS) further confirmed that both definite and possible SO were positively associated with increased CVD incidence [27]. A large-scale UK Biobank cohort study demonstrated that individuals with SO faced the highest risk for both CVD events and CVD-related mortality [33]. Another meta-analysis of more than 167,000 older adults found a robust association between SO and increased incidence of CVD [34]. A recent cohort study demonstrated that a higher sarcopenia index (indicating better muscle health) was negatively associated with the risk of stroke in elderly hypertensive patients, even after extensive adjustment for confounders [35]. The coexistence of sarcopenia and obesity also appears to significantly elevate the prevalence of MetS. Several studies, including national cohorts from Taiwan and Korea, have demonstrated that individuals with both conditions are more likely to meet the diagnostic criteria for MetS than those with either condition alone [36–40]. In particular, data from CHARLS indicated a strong positive association between SO and MetS prevalence, as well as a link to cardiometabolic multimorbidity [41, 42]. Regarding glycemic disorders, a systematic review of 11 cross-sectional studies showed that SO increases the risk of developing T2DM by approximately 38% compared to excess weight alone [43]. Supporting this, a longitudinal study of 36,304 diabetes-free individuals identified presarcopenic obesity as the phenotype with the greatest risk of future diabetes onset [44]. Emerging evidence also connects SO with kidney dysfunction, particularly in individuals with T2DM. In a study of patients with diabetes, those with SO experienced over a 30% decline in estimated glomerular filtration rate (eGFR) and had faster progression of renal impairment compared to those with either sarcopenia or obesity alone [45]. Furthermore, a retrospective cohort study involving T2DM patients found that SO was independently associated with a higher risk of incident CKD [46].

In our study, participants with SO exhibited significantly poorer overall health status and a greater burden of cardiovascular risk factors. Those classified as having sarcopenic overweight were generally older and demonstrated a higher prevalence of hypertension, diabetes, prediabetes, and metabolic syndrome. They also presented with elevated levels of BMI, waist circumference, SBP, FBG, HbA1c, TC, and TG, alongside reduced levels of HDL-C and eGFR. SO was positively associated with more advanced stages of the CKM spectrum. Notably, even among individuals without established cardiovascular disease, SO was independently related to a higher risk of MACEs during follow-up. We also incorporated the concept of "possible sarcopenia" as defined by the 2019 AWGS criteria. Findings revealed that obese individuals with possible sarcopenia had significantly higher odds of progressing to advanced CKM stages and were at increased risk of experiencing MACEs compared to those without sarcopenia. This underscores the potential benefits of early intervention targeting initial muscle loss in mitigating CKM deterioration. To further delineate the impact of adiposity, we evaluated body composition using both BMI and waist circumference. Among individuals with sarcopenia, those with a BMI ≥ 28.0 kg/m^2 had 3.317 times the odds of reaching advanced CKM stages, while those with BMI ≥ 24.0 kg/m^2 had 3.171 times the odds, relative to non-sarcopenic controls. Similarly, sarcopenic individuals with abdominal obesity showed a 3.268-fold increased likelihood of advanced CKM stages. In terms of cardiovascular outcomes among CKM stage

Table 3 Hazard ratios of maces in the sarcopenic overweight groups, sarcopenic obesity groups, and sarcopenic abdominal obesity groups in participants with CKM stages 0–3

Sarcopenic overweight	Case, *n* (%)	HR (95% CI)		
		Model 1	Model 2	Model 3
Group 1	215 (14.0)	Reference	Reference	Reference
Group 2	484 (23.3)	1.739 (1.481, 2.041)***	1.290 (1.071, 1.553)**	1.310 (1.087, 1.579)**
Group 3	185 (17.0)	1.230 (1.011, 1.497)*	1.271 (1.043, 1.548)*	1.277 (1.047, 1.556)*
Group 4	329 (28.6)	2.156 (1.815, 2.560)***	1.736 (1.439, 2.094)***	1.768 (1.465, 2.135)***
Trend test		1.204 (1.143, 1.268)***	1.172 (1.111, 1.237)***	1.177 (1.115, 1.242)***
Sarcopenic obesity	**Case, n (%)**	**HR (95% CI)**		
		Model 1	**Model 2**	**Model 3**
Group 5	327 (14.1)	Reference	Reference	Reference
Group 6	704 (24.2)	1.785 (1.566, 2.035)***	1.343 (1.146, 1.575)***	1.365 (1.163, 1.602)***
Group 7	73 (23.9)	1.744 (1.353, 2.247)***	1.817 (1.409, 2.345)***	1.807 (1.400, 2.333)***
Group 8	109 (34.9)	2.679 (2.157, 3.328)***	2.211 (1.761, 2.776)***	2.248 (1.789, 2.824)***
Trend test		1.383 (1.298, 1.474)***	1.310 (1.223, 1.405)***	1.315 (1.226, 1.409)***
Sarcopenic abdominal obesity	**Case, n (%)**	**HR (95% CI)**		
		Model 1	**Model 2**	**Model 3**
Group 9	156 (13.7)	Reference	Reference	Reference
Group 10	322 (22.2)	1.680 (1.388, 2.035)***	1.266 (1.024, 1.566)*	1.289 (1.041, 1.596)*
Group 11	244 (16.4)	1.211 (0.991, 1.481)	1.241 (1.014, 1.519)*	1.245 (1.016, 1.525)*
Group 12	491 (27.7)	2.134 (1.783, 2.556)***	1.702 (1.393, 2.079)***	1.730 (1.414, 2.115)***
Trend test		1.218 (1.155, 1.283)***	1.026 (1.020, 1.032)***	1.172 (1.109, 1.239)***

Group 1: normal weight and without possible sarcopenia or sarcopenia; Group 2: normal weight and with possible sarcopenia or sarcopenia; Group 3: overweight and without possible sarcopenia or sarcopenia; Group 4: overweight and with possible sarcopenia or sarcopenia

Group 5: without obesity and without possible sarcopenia or sarcopenia; Group 6: without obesity and with possible sarcopenia or sarcopenia; Group 7: with obesity and without possible sarcopenia or sarcopenia; Group 8: with obesity and with possible sarcopenia or sarcopenia

Group 9: without abdominal obesity and without possible sarcopenia or sarcopenia; Group 10: without abdominal obesity and with possible sarcopenia or sarcopenia; Group 11: with abdominal obesity and without possible sarcopenia or sarcopenia; Group 12: with abdominal obesity and with possible sarcopenia or sarcopenia

Model 1: unadjusted; Model 2: adjusted for age and gender; Model 3: adjusted for age, gender, education, marital, smoking, and drinking

HR, hazard ratio; CI, confidence interval

'***': $P < 0.001$; '**': $P < 0.01$; '*': $P < 0.05$

0–3 participants, those with BMI ≥ 28.0 kg/m² exhibited a 2.248-fold increased risk of MACEs, compared to 1.768-fold for BMI ≥ 24.0 kg/m² and 1.730-fold for those with abdominal obesity, further emphasizing the compounded risk posed by excess adiposity in the context of sarcopenia.

The mechanisms linking SO to the development of CKM syndrome are complex, involving both physiological alterations and the accumulation of behavioral risk factors. Several pathophysiological processes, such as endothelial dysfunction, autonomic dysregulation, chronic low-grade inflammation, insulin resistance, and reduced peripheral perfusion due to arterial stiffness, have been implicated in the connection between decreased muscle strength and CVD incidence [19]. First, one major pathway involves impaired insulin signaling. As skeletal muscle plays a central role in glucose uptake and homeostasis [47], loss of muscle mass may hinder glucose disposal and enhance local inflammation, thereby increasing the risk of diabetes [48]. Muscle dysfunction is also associated with a broad spectrum of metabolic disorders, including metabolic syndrome and insulin resistance [47]. Additionally, visceral adiposity contributes to metabolic dysfunction by increasing the production of adipocytokines such as resistin, leptin, and adiponectin, which are linked to heightened insulin resistance, diminished pancreatic β-cell function, and elevated blood glucose levels—all of which contribute to cardiometabolic comorbidities [49]. Secondly, inflammation is another critical mediator. Both sarcopenia and obesity are characterized by chronic systemic inflammation [50, 51]. In SO, excessive visceral fat and impaired muscle function synergistically promote a proinflammatory environment [42], marked by elevated circulating cytokines. This inflammatory milieu contributes to the progression of diabetes and CVD [49]. Moreover, sarcopenia is often accompanied by mitochondrial dysfunction and oxidative stress in muscle tissue, which generates reactive oxygen species that can damage vascular endothelial cells and myocardial tissue [27]. A cross-sectional study found that individuals with abdominal obesity and low muscle strength exhibited elevated levels of proinflammatory cytokines, which are well-known predictors of cardiovascular events [52]. Third, physical inactivity and conventional cardiovascular risk factors also play a contributory role in this association. In a prospective cohort of 3,366 older adults without pre-existing CVD, the elevated risk of cardiovascular events linked to SO, was attenuated from 23% to 18% after adjusting for physical activity levels, and further decreased to 6% after accounting for traditional CVD risk markers [11]. This suggests that SO may promote sedentary behavior and worsen cardiometabolic profiles, thereby amplifying the risk of cardiovascular complications.

Our findings indicate that middle-aged and older individuals with SO face a significantly elevated risk of CKM progression compared to those without this condition. With the global aging population expanding, both SO

Table 4 Subgroup and interaction analyses of the hazard ratios of maces in the sarcopenic obesity groups (defined by BMI = 28.0 kg/m^2) in participants with CKM stages 0–3

Variable		Count (%)	HR (95% CI)	*P* for interaction
Age				0.330
<60	Group 1	297 (14.0)	Reference	
	Group 2	116 (18.4)	1.291 (1.038, 1.606)*	
	Group 3	72 (24.5)	1.829 (1.410, 2.372)***	
	Group 4	39 (33.1)	2.433 (1.734, 3.414)***	
≥60	Group 1	30 (15.1)	Reference	
	Group 2	588 (25.7)	1.746 (1.207, 2.528)**	
	Group 3	1 (9.1)#	0.680 (0.093, 4.992)	
	Group 4	70 (36.1)	2.679 (1.740, 4.124)***	
Gender				0.936
Male	Group 1	168 (14.5)	Reference	
	Group 2	361 (25.1)	1.360 (1.085, 1.704)**	
	Group 3	30 (39.7)	2.259 (1.530, 3.337)***	
	Group 4	31 (31.6)	1.985 (1.340, 2.940)**	
Female	Group 1	159 (13.7)	Reference	
	Group 2	343 (23.3)	1.357 (1.081, 1.704)**	
	Group 3	43 (21.1)	1.580 (1.128, 2.215)**	
	Group 4	78 (36.4)	2.338 (1.750, 3.122)***	
Diabetes				0.017
No	Group 1	280 (13.9)	Reference	
	Group 2	577 (23.9)	1.323 (1.108, 1.578)**	
	Group 3	47 (20.3)	1.564 (1.246, 2.134)**	
	Group 4	73 (31.9)	2.010 (1.533, 2.636)***	
Yes	Group 1	47 (15.8)	Reference	
	Group 2	127 (25.5)	1.517 (1.034, 2.226)*	
	Group 3	26 (35.1)	2.361 (1.456, 3.828)***	
	Group 4	36 (43.4)	2.793 (1.772, 4.404)***	
Smoking				0.497
No	Group 1	176 (13.0)	Reference	
	Group 2	391 (22.9)	1.443 (1.164, 1.790)***	
	Group 3	47 (21.0)	1.654 (1.198, 2.284)**	
	Group 4	84 (35.7)	2.502 (1.901, 3.292)***	
Yes	Group 1	151 (15.8)	Reference	
	Group 2	313 (25.9)	1.262 (0.993, 1.603)	
	Group 3	26 (32.1)	2.258 (1.486, 3.430)***	
	Group 4	25 (32.5)	1.668 (1.074, 2.592)*	
Hypertension				< 0.001
No	Group 1	137 (10.6)	Reference	
	Group 2	247 (20.4)	1.479 (1.141, 1918)**	
	Group 3	13 (14.8)	1.540 (0.870, 2.726)	
	Group 4	12 (19.0)	1.600 (0.879, 2.913)	
Yes	Group 1	190 (18.6)	Reference	
	Group 2	457 (26.8)	1.259 (1.028, 1.543)*	
	Group 3	60 (27.6)	1.569 (1.170, 2.105)**	
	Group 4	97 (39.0)	2.039 (1.573, 2.643)***	
CKD				0.727
No	Group 1	313 (13.8)	Reference	
	Group 2	605 (23.6)	1.368 (1.159, 1.616)***	
	Group 3	72 (24.2)	1.856 (1.435, 2.402)***	
	Group 4	96 (34.4)	2.310 (1.819, 2.933)***	
Yes	Group 1	14 (25.0)	Reference	
	Group 2	99 (28.1)	0.994 (0.525, 1.883)	

Table 4 (continued)

Variable		Count (%)	HR (95% CI)	*P* for interaction
	Group 3	1 (14.3)#	0.695 (0.090, 5.401)	
	Group 4	13 (39.4)	1.384 (0.607, 3.152)	

Group 1: without obesity and without possible sarcopenia or sarcopenia; Group 2: without obesity and with possible sarcopenia or sarcopenia; Group 3: with obesity and without possible sarcopenia or sarcopenia; Group 4: with obesity and with possible sarcopenia or sarcopenia

Adjusted for age, gender, education, marital, smoking, and drinking

HR, hazard ratio; CI, confidence interval

'***': $P < 0.001$; '**': $P < 0.01$; '*': $P < 0.05$

#Due to an extremely low number of events ($n = 1$), this estimate should be interpreted with extreme caution and is likely unreliable

and CKM syndrome are becoming increasingly prevalent, posing a substantial public health challenge in geriatric care. Given the modifiable nature of SO, early detection and intervention are crucial. Public health strategies should prioritize routine screening for SO among older adults to facilitate timely prevention and management. Promoting healthy aging requires a dual focus: preventing excess fat accumulation while preserving skeletal muscle mass and strength. Such integrated strategies hold promise for reducing the burden of CKM-related complications in aging populations.

It is important to acknowledge several limitations of this study. First, due to its observational design, causality between SO and increased cardiovascular risk cannot be firmly established. Second, the reliance on self-reported cardiovascular events may introduce recall bias or lead to potential misclassification. Third, although multiple confounders were accounted for in the analysis, the influence of residual or unmeasured confounding factors cannot be entirely excluded. Forth, while the AWGS 2019 criteria are widely accepted, their primary validation is for individuals aged ≥ 60 years. Our study included participants aged 50 and above, which may introduce some misclassification bias, particularly in the younger participants (50–59 years). Future research should aim to develop or validate age-specific diagnostic criteria for sarcopenia in middle-aged populations. Fifth, in some of our combined analyses with obesity, we grouped 'possible sarcopenia' and 'confirmed sarcopenia' together. This approach may have blurred the distinction between early muscle loss and advanced sarcopenia in those specific analyses, potentially diluting the true effect sizes. Future studies with larger cohorts are warranted to fully explore the independent and interactive effects of these distinct sarcopenia stages with different obesity phenotypes. Sixth, our study did not collect detailed information on several critical confounders known to influence both sarcopenia and cardiovascular health, including physical activity levels, comprehensive dietary patterns, and specific medication adherence (e.g., statin use). Future research should endeavor to collect and adjust for these important lifestyle and therapeutic variables to provide more precise estimates of these associations. Our study was subject to a high exclusion rate (approximately 62%) due to missing data from the initially recruited cohort. Future research should prioritize robust data collection to minimize missingness and employ sophisticated statistical methods to account for missing data and mitigate selection bias. Our reliance on BMI for obesity definition, which does not distinguish between fat and lean mass, creates a risk of misclassification, particularly in older adults. Furthermore, the anthropometric equation used to estimate ASM also depends on weight and height, the same components of BMI. This inherent overlap introduces a potential circularity and a heightened risk of 'double misclassification' for the sarcopenic obesity phenotype. Such methodological dependencies may affect the accuracy of our classification and the validity of reported associations with CKM progression and MACEs. While these methods were necessitated by data availability in our large cohort, future studies should employ more precise and independent body composition assessments (e.g., DXA-derived fat mass and lean mass) to provide a more robust and less circular definition of sarcopenic obesity and to confirm these findings. Lastly, as the study population consisted exclusively of middle-aged and older Chinese adults, the applicability of these findings to other age groups or ethnic backgrounds may be limited.

Conclusions

Our study found that SO was significantly associated with more advanced stages of the CKM spectrum. Furthermore, among individuals categorized with CKM stages 0–3 and without pre-existing cardiovascular disease, SO was independently associated with a substantially elevated risk of future MACEs. These findings highlight the importance of considering early identification and management strategies for SO, as addressing both obesity and muscle health may be crucial for potentially mitigating CKM syndrome progression and related adverse cardiovascular outcomes. Further interventional studies are warranted to establish the efficacy of specific interventions.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13098-025-02032-9.

Supplementary Material 1.

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Author contributions
Yijing Xin: designed the study, performed the statistical analysis, and drafted and wrote the manuscript. Yanmin Yang: reviewed and revised the manuscript. Xifeng Qian performed the statistical analysis and revised the manuscript.

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Data availability
The data from the China Health and Retirement Longitudinal Study is openly available at https://charls.pku.edu.cn/en/index.htm.

Declarations

Ethics approval and consent to participate
Peking University has obtained ethical approval for CHARLS (IRB00001052–11015). Clinical trial number: not applicable.

Competing interests
The authors declare no competing interests.

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