



# Association between sarcopenia and prediabetes among non-elderly US adults

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## Abstract

**Aim** To explore the specific association between sarcopenia and prediabetes based on large population samples.

**Methods** A total of 16,116 U.S. adults aged 20–59 with dual energy X-ray absorptiometry (DXA) was identified from the National Health and Nutrition Examination Surveys (NHANES). Sarcopenia was defined according to appendicular skeletal muscle mass (ASM) adjusted for body mass index (BMI). Multivariable binary logistic regression models were used to ascertain odds ratios (ORs) for developing prediabetes. Stratified analyses were also performed.

**Results** Prevalence of prediabetes was higher in the sarcopenia group ( $n = 1055$ ) compared with the non-sarcopenia group ( $n = 15,061$ ) (45.50% vs 28.74%,  $P < 0.001$ ). Sarcopenia was strongly associated with an increased risk of prediabetes after full adjustment (OR = 1.21, 95CI%: 1.05, 1.39,  $P = 0.009$ ). In the stratified analysis, this association remained significant independent of obesity, triglycerides, and low-density lipoprotein cholesterol levels. When sarcopenia subjects combined with obesity especially central obesity, the risk of prediabetes was the highest (OR = 2.63, 95CI%: 2.22, 3.11,  $P < 0.001$ ). Furthermore, a greater proportion of any of impaired glucose tolerance (IGT) individuals was observed in the sarcopenia group compared to the non-sarcopenia group among prediabetes population (41.72% vs 24.06%,  $P < 0.001$ ).

**Conclusions** Sarcopenia was positively associated with prevalent prediabetes especially IGT in the non-elderly. Moreover, synergistic interactions between the sarcopenia and obesity could greatly increase the risk of prediabetes.

**Keywords** Sarcopenia · Prediabetes · Obesity · NHANES

## Introduction

In recent years, the prevalence of prediabetes has shown a clear increasing trend. Up to 38% of U.S. adults could be diagnosed as prediabetes during 2017–2020 based only on fasting plasma glucose (FPG) and hemoglobin A1c (HbA1c) levels [1]. It is anticipated that around 470 million people will have prediabetes by 2030 [2]. A larger population with prediabetes is not only associated with rapid progression of diabetes mellitus (DM) and its complications [3–5] but also with high risk of cardiovascular disease, cognitive dysfunction, neoplasia, and mortality [2, 6, 7]. Hence, as

a typical metabolic disease, identification of its risk factors and prompt intervention are important.

In addition to the known classical risk factors of metabolic diseases such as hypertension, hyperlipidemia and obesity, increasing attention has recently been paid to the effect of skeletal muscle. Skeletal muscle, as the largest target organ for insulin action, is involved in energy metabolism in the whole body. Growing studies have proven that skeletal muscle loss, commonly known as sarcopenia, plays an essential role in the development of various metabolic diseases. Sarcopenia manifests as age-related loss of muscle mass, muscle strength, and function [8]. Although sarcopenia is most common among the elderly, with changes in modern lifestyle, its occurrence has gradually shown a younger trend [9]. Sarcopenia could exacerbate insulin resistance and become an independent risk factor for many diseases, including DM, metabolic syndrome, osteoporosis, and non-alcoholic fatty liver disease [10–13]. However,

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the specific association between sarcopenia and prediabetes risk still remains to be elucidated with a larger sample population.

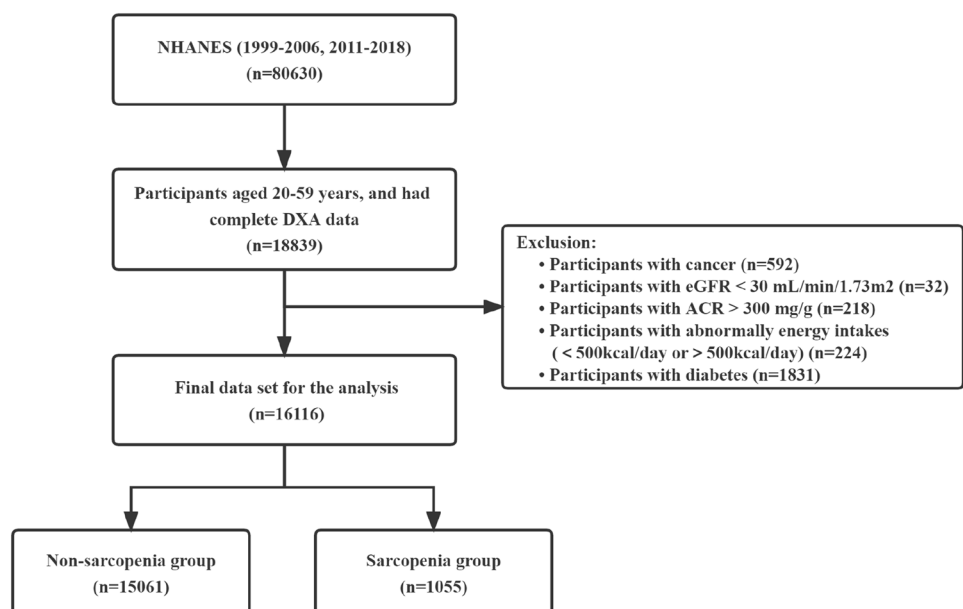
Dual-energy X-ray absorptiometry (DXA) is a relative ideal measurement method for diagnosing sarcopenia. Therefore, based on the aforementioned researches, this study aimed to clarify the association between prediabetes and sarcopenia evaluated by DXA. Furthermore, since obesity is a critical risk factor for prediabetes and closely associated with sarcopenia, we will also explore the joint effects of obesity and sarcopenia on prediabetes.

## Methods

### Study participants

Our study population was all drawn from the National Health and Nutrition Examination Surveys (NHANES) (1999–2006 and 2011–2018) since the primary variable dual energy X-ray absorptiometry (DXA) are included only in these data cycles. A total of 18,839 participants aged 20–59 years and with complete DXA data were studied. Next, we excluded partial population as follows: (1) participants with prior cancer diagnoses ( $n = 592$ ); (2) participants with severe renal dysfunction (estimate glomerular filtration rate (eGFR)  $< 30$  ml/min/1.73m<sup>2</sup>,  $n = 32$ ); (3) participants with macroalbuminuria (ACR  $\geq 300$  mg/g,  $n = 218$ ); (4) participants with abnormally energy intakes ( $< 500$  or  $> 5000$  kcal/day,  $n = 224$ ); (5) participants diagnosed with diabetes mellitus ( $n = 1831$ ). Finally, data of 16,116 participants were enrolled for the statistical analysis. See Fig. 1 for the flow diagram.

**Fig. 1** Flowchart of participant selection in this study



### DXA assessments and definition of sarcopenia

Whole body DXA scans were taken with a Hologic QDR-4500A fan-beam densitometer (Hologic, Inc., Bedford, Massachusetts). Participants who were pregnant, obese ( $> 136$  kg), tall ( $> 196$  cm), and administrated with radiographic contrast material (barium) in past 7 days were unable to attend the DXA examination. Appendicular skeletal muscle mass (ASM) was defined as the sum of the bone-free lean mass of both arms and legs. Afterwards, ASM was divided by body mass index (BMI) to further define sarcopenia. Since the target population in our study was U.S. adults from NHANES, we used the National Institutes of Health (NIH) definition of sarcopenia (ASM/BMI  $< 0.789$  for men and  $< 0.512$  for women) [14].

### Definition of prediabetes

Prediabetes was defined according to the American Diabetes Association (ADA) guidelines (2021) [15]. The diagnosis was confirmed when any one of the following criteria is met: (1) fasting plasma glucose (FPG) 100–125 mg/dL (5.6–6.9 mmol/L); (2) 2 h plasma glucose (2hPG) 140–199 mg/dL (7.8–11.0 mmol/L); (3) glycated hemoglobin A1c (HbA1c) 5.7–6.4% (39–47 mmol/mol). Prediabetes patients can be further classified as isolated impaired fasting glucose (i-IFG), isolated impaired glucose tolerance (i-IGT), and combined IFG and IGT. Any IFG and any IGT was considered any participants with IFG or IGT.

## Other variables

Categorical variables were defined based on relevant guidelines and literature. Smoking status was divided into three categories through self-report (current, past, and never smokers) [16]. The consumption of alcohol was dichotomized on the basis of having at least 12 drinks per year. Poverty–income ratio (PIR) was stratified into three categories [17]:  $\leq 1$  ( $\leq 100\%$  of the poverty threshold), 1–3 (100–300% of the poverty threshold),  $> 3$  ( $> 300\%$  of the poverty threshold). Total physical activity (PA) was calculated as the sum of the metabolic equivalents (METs) of three activity types (work/task activity, activities related to transportation, and muscle strengthening/recreational activities) per week. Then, participants were classified as recommended in the Physical Activity Guidelines for Americans ( $< 500$  MET-min/week;  $\geq 500$  MET-min/week) [18]. Hypertension, hypercholesterolemia, and cardiovascular disease (CVD) were defined by subject self-report. Obesity was characterized by three common criteria: (1) BMI  $\geq 30$  kg/m<sup>2</sup>; (2) waist circumference  $> 102$  cm for men and  $> 88$  cm for women; (3) highest quintile of body fat percent (BF%) assessed using DXA [19]. Obesity with low lean muscle mass (OLLMM) were also defined for the both presence of sarcopenic and obesity, and the participants were categorized into four groups: normal, only sarcopenic, only obesity, and OLLMM.

Partial continuous variables were calculated using the standard formulas. Homeostatic model for assessment of insulin resistance (HOMA-IR): fasting serum insulin ( $\mu\text{U/mL}$ )  $\times$  fasting plasma glucose (mmol/L)/22.5). Estimate glomerular filtration rate (eGFR) was estimated by the Modification of Diet in Renal Disease (MDRD) formula:  $175 \times \text{standardized (serum creatinine, mg/dl)}^{-1.154} \times \text{age}^{-0.203} \times 1.212$  [if African American]  $\times 0.742$  [if female]. Data on energy intake were calculated as proportion of energy from the total energy intake (grams of each nutrient  $\times$  energy coefficient / total energy  $\times 100$ ).

## Statistical analysis

Given the complex sampling design of NHANES, all analyses were performed according to analytic guidelines using R (v.3.4.3) software packages and EmpowerStats software (<http://www.empowerstats.com/en/>). Continuous variables are expressed as weighted mean  $\pm$  standard error and categorical variables as number and percentage. A chi-square test was conducted to compare the prevalence of prediabetes among different groups. Logistic regression models were used to assess the association between sarcopenia and risk of prediabetes. Four models were created to adjust for confounding factors in a stepwise manner. The variables incorporated into multivariable models were either demographic and socioeconomic factors or established risk factors

for prediabetes [20, 21]. Model 1 was unadjusted. Model 2 was adjusted for sociodemographic factors, including age, sex, race, PIR, and educational level. Model 3 was further adjusted for lifestyle factors, including smoking status, alcohol consumption, total energy intake, carbohydrate intake, and PA. Model 4 was additionally adjusted for metabolic risk factors, including CVD, BMI, triglycerides (TG), total cholesterol (TC), systolic blood pressure (SBP), and eGFR. Age, total energy intake, carbohydrate intake, BMI, TG, TC, SBP and eGFR were adjusted as continuous variables, other variables were entered into the models as categorical variables, all variables are detailed in Table 1. Moreover, considering that obesity, hypertension, and lipid disorders are the established risk factors for both prediabetes and diabetes, analyses stratified according to BMI, waist circumference, SBP, DBP, TC, TG, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were performed to determine the independent effect of sarcopenia on prediabetes. In addition, we further screened the prediabetes population with complete glucose data from the 16,116 participants. Chi-square tests were used to compare the prevalence rates of prediabetes types (IFG, IGT, combined IFG and IGT, any IFG, and any IGT) between the sarcopenia group and the non-sarcopenia group. Statistical significance was set at  $P < 0.05$  (two-tails).

## Results

### Participant characteristics

Baseline characteristics of the participants are shown by the presence or absence of sarcopenia (Table 1). As expected, the weighted mean age and standard error of sarcopenia group was  $41.87 \pm 0.42$ , and significantly older than the non-sarcopenia group ( $37.79 \pm 0.18$ ). Sarcopenia group presented a higher proportion of males and obese subjects. In addition, we observed higher levels of blood pressure, lipids, blood glucose, and lower levels of education, socioeconomic, PA, and total energy intake in sarcopenia participants ( $P < 0.001$ ). However, sarcopenia group had lower proportions of current smokers (18.48% vs 22.91%) and alcoholic drinkers (58.39% vs 69.44%).

### Associations between sarcopenia and prediabetes

The prevalence of prediabetes was 45.50% in sarcopenia group and 28.74% in non-sarcopenia group, Group differences in prevalence are shown in Fig. 2A for visualization. Subsequently, four models were established to elucidate the association between sarcopenia and the risk of prediabetes. In the unadjusted Model 1, compared to the non-sarcopenia participants, the sarcopenia group showed a significantly

**Table 1** Baseline and clinical characteristics of the study population according to sarcopenic status

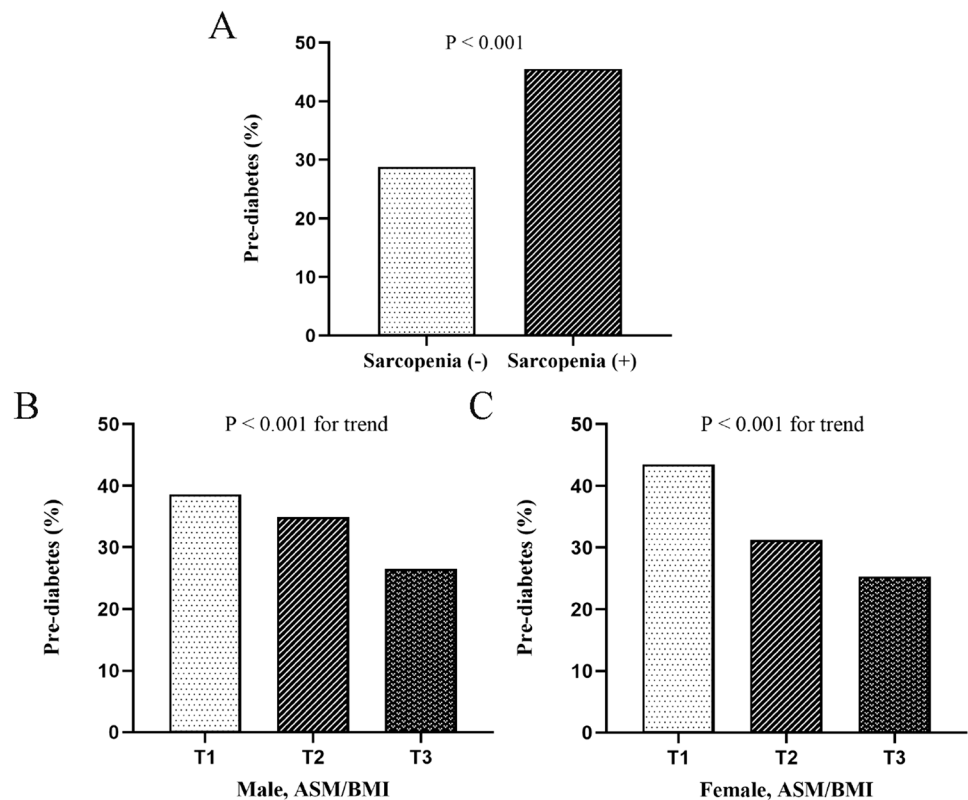
Characteristic	Non-sarcopenia ( <i>n</i> = 15,061)	Sarcopenia ( <i>n</i> = 1055)	<i>p</i> value
Age (years)	37.79 ± 0.18	41.87 ± 0.42	< 0.001
Male, <i>n</i> (%)	7663 (50.88)	599 (56.78)	< 0.001
Race, <i>n</i> (%)			< 0.001
Mexican American	2596 (17.24)	444 (42.09)	
Other Hispanic	1122 (7.45)	126 (11.94)	
Non-Hispanic White	6330 (42.03)	281 (26.64)	
Non-Hispanic Black	3142 (20.86)	73 (6.92)	
Other race	1871 (12.42)	131 (12.42)	
Education level, <i>n</i> (%)			< 0.001
Less than high school	2972 (19.73)	411 (38.96)	
High school	3371 (22.38)	250 (23.70)	
More than high school	8718 (57.88)	394 (37.35)	
PIR, <i>n</i> (%)			< 0.001
≤ 1	2599 (17.26)	265 (25.12)	
> 1, ≤ 3	5291 (35.13)	444 (42.09)	
> 3	5941 (39.45)	255 (24.17)	
Not recorded	1230 (8.17)	91 (8.63)	
Smoking status, <i>n</i> (%)			< 0.001
Current	3451 (22.91)	195 (18.48)	
Past	2822 (18.74)	227 (21.52)	
Never	8788 (58.35)	633 (60.00)	
Alcohol consumption, <i>n</i> (%)			< 0.001
Yes	10,459 (69.44)	616 (58.39%)	
No	3624 (24.06)	352 (33.36%)	
Not recorded	978 (6.49)	87 (8.25%)	
Nutritional intake			
Total energy, kcal/day	2236.78 ± 9.18	2031.83 ± 28.52	< 0.001
Carbohydrate, % of energy	48.49 ± 0.13	49.70 ± 0.47	0.017
Protein, % of energy	15.59 ± 0.05	15.97 ± 0.19	0.050
Fat, % of energy	33.78 ± 0.11	32.90 ± 0.40	0.032
Physical activity (MET-min/week), <i>n</i> (%)			< 0.001
< 500	9461 (62.82)	586 (55.55)	
≥ 500	2697 (17.91)	128 (12.13)	
Not recorded	2903 (19.27)	341 (32.32)	
ASM, kg	20.86 ± 0.08	18.30 ± 0.31	< 0.001
ASM/BMI	0.91 ± 0.00	0.62 ± 0.01	< 0.001
BMI (kg/m <sup>2</sup> )	27.22 ± 0.07	32.85 ± 0.27	< 0.001
Waist circumference (cm)	93.46 ± 0.20	106.00 ± 0.65	< 0.001
HOMA-IR, <i>n</i> (%)			< 0.001
< 2.5	4277 (28.40)	183 (17.35)	
≥ 2.5	2576 (17.10)	296 (28.06)	
Not recorded	8208 (54.50)	576 (54.60)	
FPG (mmol/L)	5.08 ± 0.01	5.27 ± 0.02	< 0.001
HbA1c (%)	5.25 ± 0.01	5.40 ± 0.01	< 0.001
SBP (mmHg)	117.68 ± 0.17	122.26 ± 0.63	< 0.001
DBP (mmHg)	71.76 ± 0.18	74.18 ± 0.51	< 0.001
TC (mmol/L)	5.02 ± 0.01	5.15 ± 0.04	0.002
TG (mmol/L)	1.55 ± 0.02	1.80 ± 0.04	< 0.001
HDL-C (mmol/L)	1.38 ± 0.01	1.27 ± 0.02	< 0.001

**Table 1** (continued)

Characteristic	Non-sarcopenia (n = 15,061)	Sarcopenia (n = 1055)	p value
LDL-C (mmol/L), n (%)			0.004
< 4.14	5995 (39.80)	403 (38.20)	
≥ 4.14	656 (4.36)	69 (6.54)	
Not recorded	8410 (55.84)	583 (55.26)	
ALT (U/L)	25.64 ± 0.18	30.32 ± 0.75	< 0.001
AST (U/L)	24.81 ± 0.14	26.04 ± 0.49	0.023
eGFR (ml/min/1.73 m <sup>2</sup> )	95.23 ± 0.33	102.11 ± 1.02	< 0.001
Hypertension, n (%)	3269 (21.71)	331 (31.37)	< 0.001
Hypercholesterolemia, n (%)	2788 (18.51)	272 (25.78)	< 0.001
CVD, n (%)	330 (2.19)	51 (4.83)	< 0.001

*PIR* poverty-income ratio, *ASM* appendicular skeletal muscle mass, *BMI* body mass index, *HOMA-IR* Homeostatic model for assessment of insulin resistance, *FPG* fasting plasma glucose, *HbA1c*, hemoglobin A1c *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *eGFR* estimate glomerular filtration rate, *CVD* cardiovascular disease, *CI* confidence interval. Data were adjusted for complex survey designs

**Fig. 2** Prevalence of prediabetes according to sarcopenic status or ASM/BMI values. **A** Comparison between sarcopenic group and nonsarcopenic group. **B** Comparison among the ASM/BMI tertile groups in male. **C** Comparison among the ASM/BMI tertile groups in female



higher risk of prediabetes (OR = 2.07, 95CI%: 1.82, 2.35,  $P < 0.001$ ). With progressive adjustment for covariates, the effect of sarcopenia on the risk of incident prediabetes was gradually reduced. However, statistically significant differences were consistently indicated. After being fully adjusted with 3 categories of factors including sociodemographic, lifestyle factors, and metabolic risk factors

(Model 4), sarcopenia still increased the risk of prediabetes (OR = 1.21, 95CI%: 1.05, 1.39,  $P = 0.009$ ). See Table 2 for detailed results.

Since sarcopenia was defined by ASM/BMI in our study, we further investigated the prevalence rates and risk situations of prediabetes among the tertile groups of ASM/BMI. The results revealed that the prevalence of prediabetes all

**Table 2** The association between sarcopenia and risk of prediabetes through multiple regression models

	Non-Sarcopenia	Sarcopenia OR (95% CI)	<i>p</i> value
No. of prediabetes cases/participants	4329/15061	480/1055	
Unadjusted Model 1	reference	2.07 (1.82–2.35)	<0.001
Adjusted Model 2	reference	1.56 (1.36–1.78)	<0.001
Adjusted Model 3	reference	1.55 (1.35–1.77)	<0.001
Adjusted Model 4	reference	1.21 (1.05–1.39)	0.009

Model 1: adjusted for none

Model 2: adjusted for age, sex, race, poverty-income ratio, and educational level

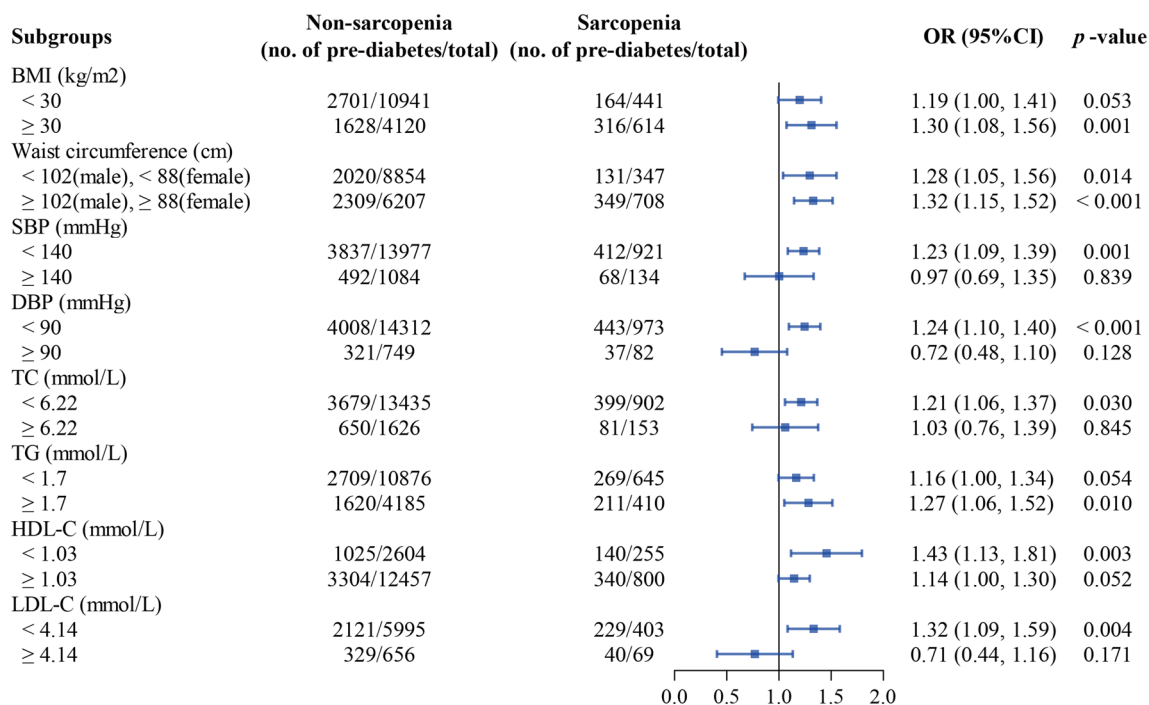
Model 3: Model 2+adjusted for smoking status, alcohol consumption, total energy intake, carbohydrate intake, and physical activity

Model 4: Model 3+adjusted for cardiovascular disease, body mass index, triglycerides, total cholesterol, systolic blood pressure, and estimate glomerular filtration rate

exhibited a downward trend with the increasing ASM/BMI tertiles for both men and women (*P* for trend <0.001) (Fig. 2B–C). Nevertheless, after full adjustment for confounding factors (same as the above Model 4), only the third tertile of ASM/BMI significantly decreased the prediabetes risk compared to the first tertile in men (OR=0.77, 95CI%: 0.67, 0.89, *P*<0.001) and no significant differences were found among tertiles groups in woman (*P*>0.05) (Table S1).

### Stratified analysis association between sarcopenia and the risk of prediabetes

To further elucidate the independent effect of sarcopenia on prediabetes risk, we performed stratified analysis of the abovementioned factors and they were stratified based on cardiovascular risk indicators [22]. Figure 3 shows that among all stratification subgroups, compared with non-sarcopenia group, the sarcopenia group exhibited higher prediabetes rates and was consistent with the trend in overall prevalence of prediabetes. After fully adjusting the covariates (similar to Model 4), the association between sarcopenia and the risk of prediabetes remained stable in some subgroups, such as the obese subgroup defined by BMI (OR = 1.30, 95CI%: 1.08, 1.56, *P* = 0.001), the non-obese subgroup (OR = 1.19, 95CI%: 1.00, 1.41, *P* = 0.001), the centrally obese subgroup defined by waist circumference (OR = 1.32, 95CI%: 1.15, 1.52, *P* < 0.001), and the non-obese subgroup (OR = 1.28, 95CI%: 1.05, 1.56, *P* = 0.014). For subgroups stratified by TG and HDL-C levels, the above risk association still persisted (Fig. 3). Of notice, although differences in partial stratified analysis did not attain strict statistical significance (*P* = 0.052–0.054), strong trends in prediabetes risk were still considered evident. In addition, we observed no significant association between sarcopenia and increased risk of prediabetes across some high-risk subgroups (SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, TC ≥ 6.22 mmol/L, LDL-C ≥ 4.14 mmol/L, *P* > 0.05).



**Fig. 3** Stratified analysis based on cardiovascular risk indicators for the association between sarcopenia and prediabetes risk

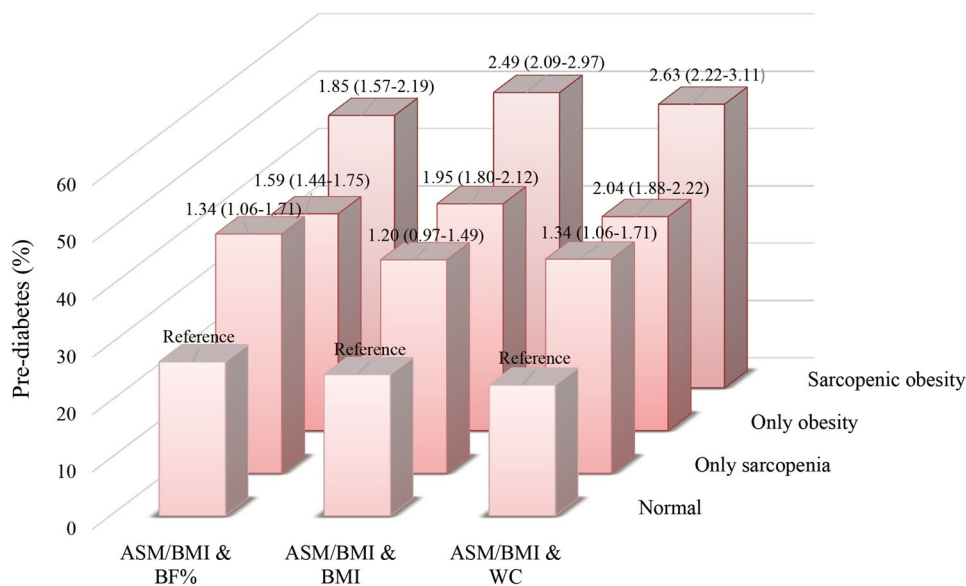
### Overall effects of OLLMM on prediabetes

Regardless of the criteria used to define obesity, we found highest prevalence of prediabetes in the OLLMM groups with 47.47% (obesity defined by BF%), 49.43% (defined by waist circumference) and 51.47% (defined by BMI), respectively (Fig. 4). The prevalence of prediabetes was close among the only sarcopenia and the only obesity groups. Consistent with our expectations, after adjustment for confounders in logistic regression models, clear difference in risk between four groups could be observed. Compared to the reference group (normal group), the only sarcopenia group, the only obesity group and the OLLMM group exhibited a tendency for an increased risk of prediabetes progressively. Of these, the risk of prediabetes was most pronounced in the sarcopenia obesity group, especially when obesity defined by waist circumference (OR = 2.63, 95CI%: 2.22, 3.11,  $P < 0.001$ ) (Fig. 4).

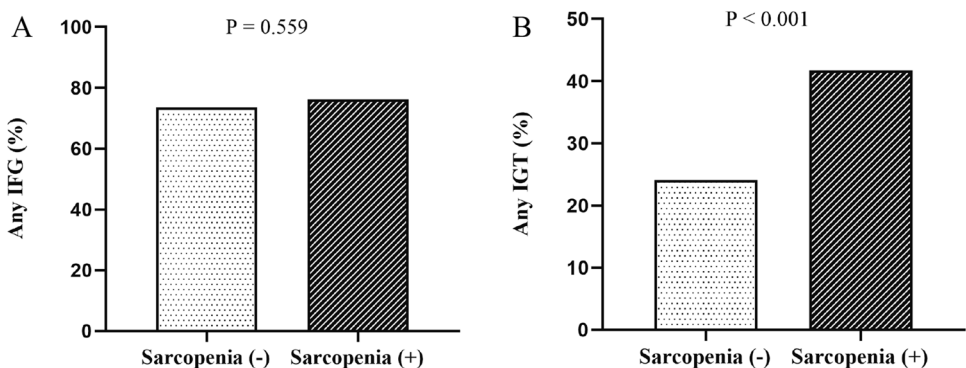
### Preliminary assessment of the association between sarcopenic and type of prediabetes

To explore the association between sarcopenic and the type of prediabetes, we screened 1568 participants with prediabetes and complete blood glucose data (including FPG, 2hPG and HbA1c) from above study populations. 1417 were non-sarcopenic participants and 151 were sarcopenic participants. See Table S2 for baseline characteristics between groups. The prevalence of i-IFG, i-IGT, and combined IFG & IGT was 59.84%, 10.37%, and 13.69% in the nonsarcopenic group and 48.34%, 13.91%, and 27.81% in the sarcopenic group, respectively. Notably, the prevalence of any IGT was significantly different between the sarcopenic group and the nonsarcopenic group (41.72% vs 24.06%,  $P < 0.001$ ) (Fig. 5). Any IFG prevalence was similar across groups (76.16% vs 73.54%,  $P = 0.559$ ).

**Fig. 4** Prediabetes prevalence and odds ratios by 4 groups (the normal, only sarcopenia, only obesity, and OLLMM groups)



**Fig. 5** The prevalence of different types of prediabetes in the sarcopenic and nonsarcopenic population. **A** Prevalence of “any IFG” in prediabetes patients **B** Prevalence of “any IGT” in prediabetes patients



## Discussion

Our study is the first to clarify the specific association between sarcopenic status and prediabetes risk through such a large sample size. The association was evident even after adjustment for multiple confounders, or in the partial stratified analyses. Additionally, the synergistic effect of sarcopenia and obesity was also confirmed. The risk of developing prediabetes was roughly doubled in OLLMM participants compared to individuals only with sarcopenia. Finally, we noted that sarcopenia might have more effects on postprandial plasma glucose and increased the prevalence of IGT.

At present, numerous studies have proved that the loss of muscle mass is closely associated with abnormal metabolic state [23]. However, most studies just focused on examining the association of sarcopenia with T2DM and diabetes-related complications, there are only few clinical studies on the association between sarcopenia and prediabetes. Previously, one study on an Indian population found patients with prediabetes had lower skeletal muscle mass and contractile quality as compared to the general population, suggesting the change of skeletal muscle mass and function might become a sensitive indicator of abnormalities in glucose metabolism [24]. However, the small sample size is a major limitation and there were differences between study populations. A prospective study from the United States demonstrated that decreased fat-free mass was associated with increased incidence of prediabetes [25]. Markedly though, fat-free mass could not completely substitute for skeletal muscle mass. In our study accurate skeletal muscle mass measurements were conducted using DXA and our results highlighted an association between sarcopenic status and prediabetes. In addition, a study using data from NHANES III showed that with each 10% increase in skeletal mass index (estimated skeletal muscle mass/total body weight), there was a relative reduction in prediabetes prevalence of 23% (95% CI: 11, 33). This is similar to our results, but some differences also existed. In our study, we found a 23% relative reduction in the prediabetes prevalence in the highest tertile of ASM/BMI compared to the lowest tertile only in males, but not in females. This discrepancy with our results may arise from the estimated skeletal muscle mass rather than exact values or different approaches with adjustment for potential confounders. An important point to note was that the included population in our study were all non-elderly aged 20–59, which may reduce the age-bias to some extent, since advanced age is strongly associated with metabolic status and skeletal muscle mass. Additionally, smoking is one of the known risk factor for sarcopenia; however, the current smokers were fewer in the sarcopenia group. This is in line

with previous study using data from the Korean National Health and Nutrition Examination Surveys [26]. This may be related to the lower sample size in the sarcopenia group.

Results of stratified analysis by traditional cardiovascular risk factors suggested that sarcopenia might be an independent risk factor for prediabetes. Nevertheless, no statistically significant results were observed in hypertensive subgroups and partial hyperlipidemic subgroups. This might be related to the small sample size in the above subgroups. Also, the possibility that the effect of blood pressure, TG, and HDL-C on the prediabetes were more significant than sarcopenia cannot be excluded. In line with most studies, the results of our study further revealed that the prevalence of dysglycemia was highest and can reach as high as 50% in OLLMM populations. Especially in a recent publication, authors stated that the prevalence of OLLMM was high worldwide and OLLMM patients had higher risk of developing metabolic diseases [27]. This is similar to our results and again demonstrated the ubiquitous and synergistic effect between sarcopenia and obesity. Of course, the synergistic effect on prediabetes was not limited to glucose metabolism. OLLMM is also associated with increased risk of metabolic syndrome, non-alcoholic fatty liver disease, hypertension, and arteriosclerotic cardiovascular disease [28–30]. Therefore, the increased risk of prediabetes in sarcopenic obese individuals is multifactorial.

All the above-mentioned risk results could not be separated from an important pathologic link—insulin resistance (IR) [31]. Previous study showed that skeletal insulin resistance was a vital link between sarcopenia and dysglycemia [32], and the mechanism might involve mitochondrial dysfunction in skeletal muscle, enhanced oxidative stress response, dysregulated myokine secretion, and chronic low-grade inflammation [33–35]. As insulin resistance continues to develop, muscle strength and muscle mass may decline further, leading to a vicious cycle. It was also clear from our study that sarcopenic patients exhibited higher HOMA-IR values. In addition, obesity, especially central obesity, is a strong risk factor for the development of IR. Similarly, our findings showed that participants with the co-existence of sarcopenia and central obesity defined by waist circumference were at highest risk of prediabetes. Central obesity was related to the accumulation of visceral adipose tissue, which showed a more pronounced IR and thus obviously increased risk of metabolic diseases [36, 37]. A notable result was that sarcopenia group had lower amount of energy intake, however had higher BMI. Table 1 shows that compared with non-sarcopenic counterparts, sarcopenic patients exhibited a higher percentage of energy from carbohydrates. Further, while sarcopenia group had higher amount of unrecorded PA, sarcopenic patients showed a higher percentage of low PA among patients with a documented PA assessment



and had low metabolic rate [38, 39]. Therefore, sarcopenic patients were more likely to have a higher BMI.

After refining the specific types of prediabetes, we found a reduction in muscle mass might be more relevant to the abnormal increase in postprandial blood glucose level. As we all know, skeletal muscle is responsible for approximately 80% of dietary glucose and served as a buffer for the body's blood glucose balance [40]. When skeletal muscle mass decreases or even develops into sarcopenia, the decrease in glucose metabolism and the delay of glucose absorption could occur simultaneously in the muscle tissue, predisposing to increased postprandial glucose [41]. Multiple studies have also confirmed that muscle strength training and increased lean muscle mass can effectively improve glucose tolerance [42, 43]. In contrast, impaired fasting glucose level is mainly associated with metabolism in liver [44, 45]. Therefore, in the present study, insignificantly different proportions of patients with IFG were noted among the groups.

There are several implications in our study. First, we showed a definite association between sarcopenia and prediabetes through large sample populations. This suggested that we should be vigilant for the excess loss of muscle even not in old age and avoid a sedentary lifestyle. Strengthening exercise could positively influence occurrence and development of prediabetes. Secondly, the coexistence of sarcopenia and obesity will significantly increase the risk of developing prediabetes. Therefore, fat reduction is particularly important for patients with low skeletal muscle mass and obesity, especially abdominal obesity. Finally, our study highlighted the close association between the loss of muscle mass and postprandial glucose levels. Since postprandial hyperglycemia contributed more to the development of chronic diabetes complications, keeping the focus on postprandial glucose control of sarcopenic patients would be of greater clinical significance.

There are also limitations to the study. One is that our study was cross-sectional, so it was difficult to address causality. In addition, we could only estimate the prevalence of prediabetes in sarcopenic subjects, not incidence. Another one is that although sarcopenia can be diagnosed by muscle mass, the assessment of muscle function is equally important to define sarcopenia and should be further included in our future researches.

In conclusion, Sarcopenia could increase the risk of prediabetes especially IGT in the non-elderly. The risk association between the two exists independently of obesity, TG, and HDL-C. Additionally, OLLMM patients exhibited the highest prevalence of prediabetes. Based on the above results, focusing on muscular exercise and weight control might be effective in preventing prediabetes.

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## Declarations

**Conflict of interest** The authors declare no conflict of interest.

**Ethical approval** The studies involving human participants were reviewed and approved by NCHS of the CDC.

**Informed consent** The patients/participants provided their written informed consent to participate in this study.

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