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RESEARCH ARTICLE

Relationship Between Grip Strength and Prediabetes in a Large-Scale Adult Population

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Introduction: Prediabetes has been a growing health problem in China, and it is a high-risk state for developing diabetes and cardiovascular disease. In previous studies, low grip strength has been associated with diabetes. However, few population-based studies have examined the relationship between grip strength and prediabetes. Thus, the purpose of this study was to investigate whether grip strength is related to prediabetes in a large-scale adult population.

Methods: A total of 27,295 participants aged 20 to 90 years were included from the 2013–2016 Tianjin Chronic Low-grade Systemic Inflammation and Health Cohort Study. Grip strength was assessed using an electronic hand-grip dynamometer and the greatest force was normalized to body weight. Prediabetes was diagnosed based on the American Diabetes Association criteria. Multiple logistic regression analysis was conducted in 2018 to assess the relationship of grip strength to the prevalence of prediabetes, while controlling for age, BMI, smoking, drinking, physical activities, dietary patterns, and other confounders.

Results: Of the 27,295 participants, 28.5% (7,783) had prediabetes. After adjusting for potential confounders, a one unit increase in grip strength per body weight was associated with 52% lower odds of having prediabetes for men (OR=0.48, 95% CI=0.30, 0.74, $p<0.01$) and 62% lower odds of having prediabetes for women (OR=0.38, 95% CI=0.20, 0.70, $p<0.01$).

Conclusions: Increased grip strength is independently associated with lower prevalence of prediabetes in Chinese adults, suggesting that grip strength may be a useful marker for screening individuals at risk of prediabetes.

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INTRODUCTION

Prediabetes, typically an intermediate state of dysglycemia between normoglycemia and diabetes, is defined as an individual having an impaired fasting glucose or impaired glucose tolerance or HbA1c of 5.7%–6.4%, or all three, according to the latest guidelines of the American Diabetes Association.[1] In China, prediabetes has been a growing health problem. According to a 2013 national study, the prevalence of prediabetes was 35.7% among the Chinese adult population.[2] Moreover, accumulating epidemiologic evidence has indicated that

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prediabetes is a high-risk state for developing diabetes and cardiovascular diseases.[3,4] Hence, timely identification and efficient prevention of prediabetes is essential.

As a major site of insulin- and exercise-stimulated glucose disposal, skeletal muscle can interact with the pancreas and modulate insulin secretion.[5] Extensive studies have revealed that muscle strength training can improve insulin sensitivity,[6–8] which is the principal risk factor for developing prediabetes.[9] On the other hand, contracting skeletal muscle can secrete a variety of cytokines, called myokines, such as interleukin-6 and follistatin-like 1, which can directly participate in mediating glucose metabolism.[10] In addition, irisin, a novel myokine, has been shown to be involved in the regulation of glucose uptake and insulin resistance in emerging mechanism studies.[11,12] From the above context, as an indicator of an individual's overall strength and muscle mass,[13] grip strength (GS) may be a potential predictive factor for prediabetes.

To date, 11 cross-sectional studies[14–24] and five longitudinal studies[25–29] have reported that low GS is associated with type 2 diabetes mellitus. However, few studies have focused on the relationship between GS and prediabetes in the general population. Only one cross-sectional study reported that GS was adversely related to prediabetes among healthy-weight U.S. adults.[30] However, important confounding factors, such as physical activity (PA) and dietary patterns, were not considered in that study.

The purpose of this study is to investigate whether prediabetes is associated with GS among a large-scale adult population. Additionally, the present study took account of a number of potential confounders, including PA and dietary patterns.

METHODS

Study Population

The Tianjin Chronic Low-grade Systemic Inflammation and Health Cohort Study is a large prospective dynamic cohort study, the principal aim of which is to investigate the association between chronic low-grade systemic inflammation and the health status of the general population living in Tianjin, China. Full details of the Tianjin Chronic Low-grade Systemic Inflammation and Health Cohort Study are avaiable elsewhere.[31] The study protocol was approved by the medical ethics committee of the IRB of Tianjin Medical University, and written informed consent was obtained from all participants prior to participation.

The baseline data from 2013 to 2016 were used for the cross-sectional study. A flow chart detailing the derivation of sample is presented in Figure 1. A total of 33,003 participants received physical examinations, including GS test and a comprehensive lifestyle questionnaire, during the course of the research study (the assessment of GS and prediabetes for each participant was within a day). Individuals were excluded if data were missing regarding their age, BMI, GS, PA, and diets (n=695), or if they had a history of cardiovascular disease (n=1,694) or cancer (n=346). Additional participants were excluded if they already had type 2 diabetes mellitus at baseline (n=2,973). The final study population included 27,295 participants (14,235 males and 13,060 females).

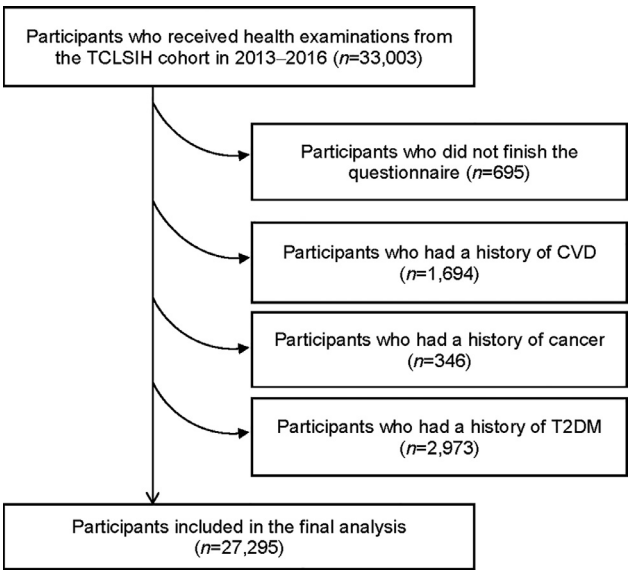

Figure 1. Flowchart of the study population selection process.
CVD, cardiovascular disease; T2DM, type 2 diabetes mellitus; TCLSIH, Tianjin Chronic Low-grade Systemic Inflammation and Health.

Measures

Muscle strength was measured with an electronic hand-grip dynamometer. Before the measurement, dynamometers were calibrated with a back-loading rig, with a consequent error range <0.1 kg. The dynamometer width was adjusted for optimal fit for each participant.[32] All participants were instructed to stand upright with the dynamometer beside but not against their body and squeeze the dynamometer with maximal effort. Tests were completed on both hands, with each hand tested twice, and the greatest force was used for the analyses. GS relative to body weight (normalized GS, kg/kg) was also calculated in terms of the involvement of body weight in the maximal performance of muscle strength.[33–35] The test variability for maximal force on the part of the same participant was <5%.

Venous blood samples for biochemical analysis were collected in siliconized vacuum plastic tubes. Fasting blood glucose was measured using the glucose oxidase method. Postprandial glucose levels were measured at 2 hours during a 75 g oral glucose tolerance test. HbA1c was quantified using a chromatography analyzer.[36] In accordance with the American Diabetes Association criteria, prediabetes was defined as impaired fasting glucose (a fasting plasma glucose level ≥5.6 mmol/L but ≤6.9 mmol/L), or impaired glucose tolerance (2-hour plasma glucose value in the oral glucose tolerance test of 7.8 mmol/L to 11.0 mmol/L), or HbA1c range of 5.7%–6.4%.[1]

Total cholesterol and triglycerides were measured with enzymatic methods, low-density lipoprotein cholesterol was determined by the polyvinyl sulfuric acid precipitation method, and high-density lipoprotein cholesterol was assessed by chemical precipitation. Systolic blood pressure and diastolic blood pressure

were measured in the upper right arm at the brachial artery by an automatic device, and were recorded as the mean of two measurements. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or taking antihypertensive medications.[37] Hyperlipidemia was defined as having total cholesterol ≥5.17 mmol/L, or triglycerides ≥1.7 mmol/L, or low-density lipoprotein cholesterol ≥3.37 mmol/L, or a history of hyperlipidemia, or current use of antihyperlipidemic medications.[38]

Anthropometric parameters, including height, weight, and waist circumference, were recorded for each participant using a standardized protocol. BMI was calculated as weight/height^2 (kg/m^2).

Detailed information on sociodemographic variables (gender, age), educational level, employment status, household income, smoking status, drinking status, a detailed personal and family history of physical illness, and current medications were obtained from a standardized questionnaire survey. Smoking status was classified into three categories: smoker, ex-smoker, and nonsmoker. Drinking status was defined as everyday, sometime, ex-drinker, and non-drinker. The levels of PA in the most recent week were assessed with a validated short Chinese version of the International Physical Activity Questionnaire.[39]

Dietary intake in the last month was evaluated using a 100-item validated self-administered food frequency questionnaire.[31] Detailed information is available elsewhere.[40] According to the factor analysis, dietary patterns were categorized as fruits and sweets dietary pattern (Factor 1), healthy dietary pattern (Factor 2), and animal foods dietary pattern (Factor 3).

Statistical Analysis

No variables had missing values. All statistical analyses were performed in 2018 using SAS, version 9.3 for Windows. The distributions of continuous variables, except normalized GS, were not normal, and therefore the natural logarithm was applied to normalize the data before analysis. Data were plotted as the geometric mean (95% CI) for continuous variables and percentage for categorical variables, whereas normalized GS was expressed as the mean (SD).

Differences between participants with and without prediabetes were tested using ANOVA and multiple logistic regression analysis for continuous and categorical variables respectively. Considering that distributions of GS per body weight were approximately normal for both men and women, normalized GS was used as a continuous variable in the analysis. Prediabetes was used as the dependent variable, and normalized GS was used as an independent variable. The relationship between normalized GS and prediabetes status was examined using multiple logistic regression by four different models, with the ORs and 95% CI for the prevalence of prediabetes per unit and SD change calculated as well. Model 1 was the crude model. Age and BMI were added in Model 2. Model 3 was adjusted for age, drinking status, total energy intake, educational levels, employment status, household income, hypertension, and hyperlipidemia. Model 4 was further adjusted for smoking status, PA, and dietary patterns in addition to all covariates mentioned above. Considering that gender is a dominant factor affecting GS, interaction terms were added to the model to investigate whether the relationship was different between men and women.

Two sensitivity analyses were performed. First, in terms of a non-linear association between BMI and cardiovascular disease[41] and kidney cancer risk,[42] participants were categorized into quartiles based on BMI: underweight (<18.5 kg/m^2), normal weight (18.5–23.9 kg/m^2), overweight (24.0–27.9 kg/m^2), and obese (≥28 kg/m^2).[43] Second, given that pregnancy is a risk factor of gestational diabetes, another sensitivity analysis was performed by excluding pregnant women (n=16). All tests were two-sided and p<0.05 was defined as statistically significant.

RESULTS

Of the 27,295 participants (mean age 41.6 [SD=1.17] years for men, 40.3 [SD=1.15] years for women), 7,783 (28.5%) had prediabetes based on the American Diabetes Association criteria. The prevalence of prediabetes in men and women was 34.3% and 22.2%, respectively.

The age-adjusted characteristics for the full sample across prediabetes status are shown in Table 1. Compared with participants not diagnosed with prediabetes, men with prediabetes were more likely to be older and have hypertension and hyperlipidemia. They had higher BMI, waist circumference, total cholesterol, triglycerides, low-density lipoprotein cholesterol, systolic blood pressure, diastolic blood pressure, fasting blood glucose, household income, and animal foods dietary pattern scores (all p-values<0.001), but lower levels of high-density lipoprotein cholesterol (p=0.02). Meanwhile, the proportions of current smokers and everyday drinkers were higher in individuals with prediabetes. However, these participants were less likely to be nonsmokers. Apart from these results, no significant difference was observed between the two groups. Comparisons between participants with and without prediabetes were generally similar among women. Nevertheless, women with prediabetes were less educated and less likely to be sometime drinkers, non-drinkers, and employed as professionals. No differences were observed in dietary patterns and smoking status between women with and without prediabetes.

The crude and adjusted relationships between GS per body weight and prediabetes are presented in Table 2. Among men and women, the mean of normalized GS was 0.57 kg/kg (SD=0.10) and 0.44 kg/kg (SD=0.09), respectively. Notably, for all models, there was a significantly inverse association between normalized GS and the prevalence of prediabetes. After adjusting for all confounding factors, a one unit increase in normalized GS was associated with 52% lower odds of having prediabetes for men (OR=0.48, 95% CI=0.30, 0.74, p<0.01). Similarly, for women, a one unit increase in normalized GS was associated with 62% lower odds of having prediabetes (OR=0.38, 95% CI=0.20, 0.70, p<0.01). Furthermore, similar results were obtained per SD increase in

Table 1. Age-Adjusted Participant Characteristics by Prediabetes Status (n=27,295)

	Prediabetes status (men)			Prediabetes status (women)		
Characteristic	**No**	**Yes**	***p*-value[a]**	**No**	**Yes**	***p*-value[a]**
Subjects, *n*	9,351	4,884		10,161	2,899	
Age, years, m	39.9 (39.9, 40.0)[b]	40.2 (40.1, 40.2)	**<0.0001**	38.8 (38.8, 38.9)	38.6 (38.6, 38.7)	**<0.0001**
BMI, kg/m^2	25.0 (24.9, 25.1)	26.3 (26.2, 26.4)	**<0.0001**	22.4 (22.4, 22.5)	23.7 (23.6, 23.8)	**<0.0001**
WC, cm	86.6 (86.4, 86.8)	89.8 (89.5, 90.1)	**<0.0001**	74.6 (74.4, 74.7)	77.2 (76.8, 77.5)	**<0.0001**
TC, mmol/L	4.7 (4.7, 4.7)	4.9 (4.9, 5.0)	**<0.0001**	4.6 (4.6, 4.6)	4.8 (4.8, 4.8)	**<0.0001**
TG, mmol/L	1.3 (1.3, 1.3)	1.5 (1.5, 1.6)	**<0.0001**	0.9 (0.9, 0.9)	1.0 (1.0, 1.0)	**<0.0001**
LDL-C, mmol/L	2.8 (2.7, 2.8)	2.9 (2.9, 2.9)	**<0.0001**	2.6 (2.6, 2.6)	2.8 (2.7, 2.8)	**<0.0001**
HDL-C, mmol/L	1.2 (1.2, 1.2)	1.2 (1.2, 1.2)	**0.02**	1.5 (1.5, 1.5)	1.4 (1.4, 1.5)	0.21
SBP, mmHg	121.6 (121.3, 121.9)	124.9 (124.5, 125.3)	**<0.0001**	113.3 (113.1, 113.6)	118.0 (117.4, 118.5)	**<0.0001**
DBP, mmHg	77.4 (77.2, 77.6)	80.2 (79.9, 80.6)	**<0.0001**	71.0 (70.8, 71.2)	73.4 (73, 73.8)	**<0.0001**
FBG, mmol/L	4.8 (4.8, 4.8)	5.2 (5.2, 5.2)	**<0.0001**	4.7 (4.7, 4.7)	5.1 (5.1, 5.1)	**<0.0001**
PA, METs × hours/week	11.5 (11.2, 11.9)	11.3 (10.9, 11.7)	0.39	8.8 (8.5, 9.0)	8.8 (8.4, 9.3)	0.77
Total energy intake, kcal/day	2,073.0 (2,061.3, 2,084.8)	2,066.4 (2,049.9, 2,083.1)	0.54	1,917.9 (1,906, 1,929.8)	1,912.8 (1,889.7, 1,936.3)	0.71
Hypertension, %	22.2	41.9	**<0.0001**	8.1	29.2	**<0.0001**
Hyperlipidemia, %	48.0	66.9	**<0.0001**	29.9	57.8	**<0.0001**
"Fruits and sweets" dietary pattern, %	0.8 (0.8, 0.8)	0.8 (0.7, 0.8)	0.43	0.9 (0.8, 0.9)	0.8 (0.8, 0.9)	0.52
"Healthy" dietary pattern, %	0.9 (0.9, 0.9)	0.9 (0.9, 0.9)	0.43	0.7 (0.7, 0.7)	0.7 (0.7, 0.7)	0.66
"Animal foods" dietary pattern, %	0.9 (0.9, 0.9)	1.0 (1.0, 1.0)	**<0.0001**	0.6 (0.6, 0.6)	0.6 (0.6, 0.7)	0.16
Smoking status, %						
Smoker	36.0	40.3	**0.02**	1.38	1.96	0.10
Ex-smoker	7.84	12.1	0.07	0.73	0.58	0.21
Non-smoker	56.1	47.6	**<0.01**	97.9	97.5	0.50
Drinker status, %						
Everyday	6.4	12.3	**<0.0001**	0.55	1.19	0.09
Sometimes	73.9	68.5	0.09	40.5	38.5	**0.03**
Ex-drinker	9.6	8.9	0.33	10.3	7.43	0.16
Non-drinker	10.2	10.3	0.61	48.6	52.9	**<0.01**
Education (≥college graduate), %	72.9	60.8	0.96	70.3	47.1	**<0.0001**
Employment status, %						
Managers	44.2	44.8	0.95	43.1	37.0	0.20
Professionals	21.9	18.5	0.19	13.7	10.9	**<0.01**
Other	33.9	36.8	0.22	43.2	52.2	**<0.01**
Household income (≥10,000 yuan), %	35.6	38.4	**<0.0001**	34.8	31.5	0.86

Note: Boldface indicates statistical significance (p<0.05). Data are shown using the measure shown for each characteristic (95% CI) where appropriate.
[a]Analysis of variance or logistic regression analysis.
[b]Geometric mean (95% CI) (all such values).
DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PA, physical activity; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; WC, waist circumference.

Table 2. Adjusted Relationships of Grip Strength per Body Weight With Prediabetes (n=27,295)

	Men (mean=0.57 kg/kg)		Women (mean=0.44 kg/kg)	
Grip strength per body weight	**OR (95% CI)**	***p* for trend[a]**	**OR (95% CI)**	***p* for trend[a]**
Per unit increase				
Model 1[b]	0.05 (0.04, 0.07)	**<0.0001**	0.004 (0.002, 0.01)	**<0.0001**
Model 2[c]	0.48 (0.31, 0.75)	**<0.01**	0.33 (0.18, 0.61)	**<0.001**
Model 3[d]	0.14 (0.09, 0.20)	**<0.0001**	0.07 (0.04, 0.13)	**<0.0001**
Model 4[e]	0.48 (0.30, 0.74)	**<0.01**	0.38 (0.20, 0.70)	**<0.01**
Per SD increase (0.10 for men; 0.09 for women)				
Model 1[b]	0.74 (0.71, 0.76)	**<0.0001**	0.62 (0.59, 0.65)	**<0.0001**
Model 2[c]	0.93 (0.89, 0.97)	**<0.01**	0.91 (0.86, 0.96)	**<0.001**
Model 3[d]	0.82 (0.78, 0.85)	**<0.0001**	0.79 (0.76, 0.83)	**<0.0001**
Model 4[e]	0.93 (0.89, 0.97)	**<0.01**	0.92 (0.87, 0.97)	**<0.01**

Note: Boldface indicates statistical significance (p<0.05).
[a]Multiple logistic regression analysis.
[b]Crude model.
[c]Adjusted for age and BMI.
[d]Adjusted for age, drinking status, total energy intake, educational levels, employment status, household income, hypertension (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or history of hypertension) and hyperlipidemia (total cholesterol ≥5.17 mmol/L, or triglycerides ≥1.7 mmol/L, or low-density lipoprotein cholesterol ≥3.37 mmol/L, or history of hyperlipidemia, or current use of antihyperlipidemic medications).
[e]Adjusted for Model 3 covariates plus BMI, smoking status, physical activity, and dietary patterns.

normalized GS. These results suggested a robust association between normalized GS and prediabetes among men and women, independently of PA and other confounders. In addition, there was no significant interaction between gender and GS with respect to prevalence of prediabetes in the final multivariate model (p=0.10 for interaction).

When participants were categorized into quartiles based on BMI, the sensitivity analysis yielded similar results to the main analysis (data not shown). Moreover, exclusion of pregnant women did not show a substantial change in the main results (data not shown).

DISCUSSION

The crude results of this study indicated that lower GS per body weight was associated with a higher prevalence of prediabetes in both men and women. After adjustment for age, smoking status, drinking status, PA, dietary patterns, and other confounding factors, the association remained significant. These results support the hypothesis that GS has potential utility as a screening tool to detect prediabetes early in Chinese adults.

Until now, prior studies have demonstrated an association between GS and diabetes.[16,27] However, population-based studies focusing on the relationship between GS and the prevalence of prediabetes are rare. Only a cross-sectional study by Mainous et al.[30] explored this problem with data of 1,314 healthy-weight American adults from the 2011–2012 National Health and Nutrition Examination Survey. Their study found that GS was lower for individuals with prediabetes than those with normoglycemia. Nevertheless, not all confounding factors were examined and only gender is considered as a confounding factor in their study; thus, the real relationship between GS and prediabetes could not be deduced from their results. Potential confounders in this study were chosen based on the prior literature[21,26] and consideration of related biological relationships.

For instance, abundant evidence has shown that exercise training could improve handgrip strength[44] and particularly, regular PA could prevent the age-associated loss of muscle strength.[45] Additionally, physical training could increase peripheral insulin sensitivity.[46] In addition to PA, low education was found to be associated with low GS.[47] Further, education has a substantial influence on health and low levels of education are associated with a higher incidence of type 2 diabetes mellitus, presumably because of a less healthy lifestyle.[48] Thus, PA and education were considered to be potentially significant confounders, and adjustments were made for them in the multivariate model. In the present study, after adjusting for these variables in the final multivariate model analysis, the adverse association between GS per body weight and prediabetes remained significant both in men and women, suggesting that the relationship between GS and prediabetes is independent of PA and other confounding factors. The magnitude of association was similar in men and women.

Although the precise mechanisms behind the relationship of GS to prediabetes are not fully understood, these findings can be partly explained by the following aspects. Evidence has shown that insulin resistance and defective glucose sensing at the β cell are two determinants in the pathophysiology for abnormal glucose metabolism.[49] On the one hand, muscle strength training has been shown to increase the protein content of glucose transporter-4 and improve insulin resistance.[50] Skeletal muscle is responsible for most of the whole body insulin- and exercise-stimulated glucose uptake through glucose transporter-4 translocation to the plasma membrane.[51] On the other hand, contracting skeletal muscle can secrete a variety of myokines that can mediate glucose metabolism. Irisin, a recently discovered myokine, has been demonstrated to contribute to glucose homeostasis through functions in muscle, liver, and adipose tissue.[11] Additionally, irisin also has anti-apoptotic actions on pancreatic β-cells via v-akt murine thymoma viral oncogene homolog/β-cell lymphoma 2 signaling and stimulates β-cell proliferation, insulin biosynthesis, and secretion in a protein kinase A–dependent manner.[52] Therefore, it is plausible to suggest a relationship between GS and prediabetes because GS is well established as an indicator of muscle function.[13] Further studies are needed to explore the exact mechanisms underlying the relationship.

Limitations

This present study has several advantages. First, it appears to be the first to explore the association between GS and prediabetes in a large-scale Chinese adult population. Well-examined data used in this recent large population-based analysis strengthens the statistical reliability of the results. Second, contrary to the previous study, this study controlled for potential cofounders as much as possible, such as sociodemographic variables, drinking status, PA, and dietary patterns. However, several limitations should be noted. First, as with all cross-sectional studies, a limitation of the study is the inability to unravel the direction of causation. Second, although some potential confounding factors were adjusted, there are still many unknown factors, which could influence GS and prediabetes. Some potential confounders mentioned before (e.g., PA) may partly act as mediators and thus the adjustment for them may induce statistical bias. Nevertheless, after exclusion of these variables (Model 3), the analysis did not show a significant change in the main results, indicating a robust association between GS and prediabetes. Third, because Tianjin is a municipality directly under the central government, these results may only be generalized to residents in cities. More studies are required to determine the relationship between GS and prediabetes in rural areas.

CONCLUSIONS

The present study showed that normalized GS was inversely associated with prediabetes among men and women. These results suggested that as a simple and inexpensive technique, GS might be a useful marker to help identify adults at risk of prediabetes. In clinical or public health practice, low GS per body weight may cue primary care physicians to the need for blood test screening regardless of different patient characteristics. Interventions toward preserving muscle strength may help reduce the rate of prediabetes in this population. Further large prospective epidemiologic studies are necessary to investigate the impact of skeletal muscle strength on the incidence of prediabetes in the future.

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SH, YG, and KN designed the study and wrote the manuscript. YG, ZL, QZ, LL, GM, ZY, HW, XB, VC, SZ, ML, YW, LW, LZ, XW, CT, JF, SS, MZ, QJ, and KS provided assistance for data acquisition. SH, ZS, and KN carried out data analysis and interpretation. KN provided the critical revision of the manuscript for important intellectual content.

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