Research Paper

Association of handgrip strength with the prevalence of metabolic syndrome in US adults: the national health and nutrition examination survey

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Correspondence to: Yuhong Zhao; email: zhaoyuhong@sj-hospital.orgKeywords: metabolic syndrome, handgrip strength, waist circumference, triglyceride, hypertensionReceived: December 11, 2019Accepted: March 30, 2020Published: May 4, 2020

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ABSTRACT

Objective: Aimed to find the cut-off point of handgrip strength and it's association with MetS.

Results: The relative handgrip strength was negatively associated with the prevalence of MetS. Of note, the odds ratios (ORs) with 95% confidence intervals (CIs) across tertiles of relative handgrip strength were 1 (reference), 0.45 (0.33, 0.62), and 0.13 (0.08, 0.20) in male participants after adjusting for demographic factors, calorie intake, and physical activity. Similar results were observed in female participants. The cutoff values of relative handgrip strength for male and female participants were 0.52 and 0.40, respectively.

Conclusions: Findings of this study suggest that a strong relationship exists between handgrip strength and prevalence of MetS in US adults, regardless of sex.

Methods: A total of 5 056 participants in the National Health and Nutrition Examination Survey were analysed in this study. Handgrip strength was measured by using a handgrip dynamometer. MetS was defined in accordance with the criteria of the scientific statement of the American Heart Association in 2009. Multivariable binary logistic regression was used to explore the association between handgrip strength and MetS.

INTRODUCTION

Metabolic syndrome (MetS) is a group of metabolic conditions that occur together and promote the development of cardiovascular disease and diabetes [1]. Moreover, MetS and its components are associated with cancers, such as colorectal cancer [2], prostate cancer [3], and primary liver cancer [4]. In parallel with changes towards a sedentary lifestyle and subsequent obesity worldwide, the prevalence of MetS has increased in recent decades. A previous study demonstrated that the prevalence of MetS in the United States (US) has increased from 32.9% in 2003-2004 to 34.7% in 2010-2012 [5]. Thus, considering the increasing burden of MetS, it is important to identify modifiable risk factors of MetS.

Handgrip strength is a simple and reliable measurement method, especially a good measurement of upper body strength, which is realized as an index for muscular fitness [6, 7]. And a strong evidence suggests that in addition to obesity, low level of fitness is a major contributor to a development of metabolic disease and metabolic syndrome [8, 9]. Furthermore, muscle strengthening activities are closely related with improved insulin sensitivity, meliorated dyslipidemia, and reduced blood pressure, all of those are principle components of metabolic syndrome [10-12]. In addition, skeletal muscle can secrete multiple peptides [13]. Many of these peptides contribute to metabolic homeostasis [14, 15]. Interleukin-15 from skeletal muscle negatively regulates fat mass [16]. Inhibition of myostatin suppresses body fat accumulation and

improves insulin sensitivity [17, 18]. These myokines appear to participated in maintenance of whole-body metabolic homeostasis. Muscles are target organs for insulin action [19]. Moreover, insulin resistance is a hallmark of MetS [20]. Muscles also secrete irisin [21] which could be a therapeutic tool in managing obesity and MetS [22]. Thus, it is plausible that muscle strength could play an important role in the development of MetS. Indeed, several previous studies found that high muscle strength was associated with lower prevalence of MetS [23-30]. Most of these studies were conducted in Asian countries. In the US, only the Aerobics Center Longitudinal Study demonstrated that lower muscle strength was associated with higher MetS prevalence in men [30]. Moreover, compared to participants with higher muscle strength, the odds ratios (ORs) were 2.20 (95% confidence interval (CI), 1.89-2.54) and 2.11 (95% CI, 1.62-2.74) for male participants aged <50 years and ≥ 50 years with lower muscle strength, respectively [30]. However, the Aerobics Center Longitudinal Study used the supine bench press and seated leg press to assess muscle strength [30] instead of handgrip strength, which is easier to use in both clinical and community settings [31]. Moreover, most of the previous studies were conducted in middle-aged and older participants or in men alone, which would limit the generalization of their findings. Studies have shown that BMI increased with the prevalence of MetS [32]. BMI can be a factor differentiating the course of many metabolic and adaptive processes in the body [33-36]. It can also be a factor conditioning a different response of the body to certain lifestyle elements that modifiers of metabolic risk factors [37]. We therefore accept the hypothesis that individuals with a different BMI also have a different response to the relationship between muscle strength and MetS.

To the best of our knowledge, no epidemiological study has investigated the associations between handgrip strength and MetS in general US adults and considering BMI as a stratification factor. Thus, we used data from 2011-2012 and 2013-2014 survey cycles of the National Health and Nutrition Examination Survey (NHANES) to determine the associations between handgrip strength and MetS and identify cut-off points of handgrip strength associated with MetS in general US adults. In order to help individuals to identify the risk of MetS as quick as possible.

RESULTS

Characteristics of participants

According to the data from NHANES 2011-2012 and 2013-2014 cycles, 19 931 people joined the household questionnaire interview, and 14 984 people participated

in the handgrip strength test. Because of the design of NHANES, subsampling was required to reduce respondent burden and facilitate the scheduling and completion of examinations, the final analysed sample comprised 5 056 participants, of which 36.33% had MetS. The prevalence of MetS in men was 36.35% and that in women was 36.30% (P=0.9796). Baseline characteristics of the participants are shown in Table 1. With the increase in relative handgrip strength, age, BMI, waist circumference, triglyceride, fasting glucose, SBP, and the prevalence of MetS were decreased, and the proportion of male participants, DBP, tobacco and alcohol use, proportion of college graduation, percentage of >\$100 000 annual household income, energy intake per day, and proportion of high physical activity were increased.

Handgrip strength and MetS

The association between relative handgrip strength and components of MetS in the male and female participants is shown in Table 2. Multivariable binary logistic regression was used to estimate the OR value and 95% CI. Relative handgrip strength was negatively associated with the prevalence of MetS in male and female participants, the OR (95% CI) values across the tertiles of relative handgrip strength were 1 (Reference), 0.45 (0.33, 0.62), 0.13 (0.08, 0.20) for male participants (P for trend <0.0001) and 1 (Reference), 0.35 (0.27, 0.46), 0.12 (0.08, 0.18) for female participants (P for trend <0.0001) after adjusting for age, race, drinking and smoking status, education level, household income, total energy intake, and physical activity. We additionally analysed the association between handgrip strength and components of MetS, and the results were comparable in both male and female participants.

To analyse the effect of BMI on the association between handgrip strength and components of MetS, we categorized BMI to lower BMI (BMI < 30) and higher BMI (BMI \geq 30) groups. Supplementary Table 1 shows the results of the association between relative handgrip strength and components of MetS in male participants. Handgrip strength was negatively associated with the prevalence of MetS in male participants with BMI < 30 after adjusted by potential covariables. However, in male participants with BMI \geq 30, the negative association was lost. In female participants, handgrip strength was negatively associated with the prevalence of MetS, in both BMI < 30 group and BMI \geq 30 group (Supplementary Table 2).

The ROC curve was used to evaluate the performance of the adjusted model to analyse the association between relative handgrip strength and prevalence of MetS. The AUC with 95% CI for each adjusted model in both male and female participants is shown in Figure 1.

	Tertiles of handgrip strength per weight (kg/kg) (Range)					
	Level 1 (0.11, 0.41)	Level 2 (0.41, 0.53)	Level 3 (0.53, 1.13)	<i>P</i> for trend*		
No. of participants (%)	33.32	33.56	33.12			
Age (year)	49.92 (49.01, 50.84)	41.47 (40.56, 42.38)	35.29 (34.38, 36.20)	< 0.0001		
Male (%)	21.31	47.69	80.69	< 0.0001		
BMI (kg/m ²)	33.41 (33.15, 33.67)	26.51 (26.24, 26.77)	23.79 (23.53, 24.06)	< 0.0001		
Waist circumference (cm)	108.28(107.60, 108.96)	93.00 (92.32, 93.68)	85.16 (84.48, 85.84)	< 0.0001		
Triglyceride (mg/dL)	125.16 (120.18, 130.13)	116.84 (111.870, 121.82)	104.59 (99.63, 109.56)	< 0.001		
HDL cholesterol (mg/dL)	52.46 (51.76, 53.15)	53.76 (53.07. 54.46)	53.62 (52.93 54.32)	0.0204		
Fasting glucose (mg/dL)	112.39 (110.98, 113.81)	102.80 (101.38, 104.22)	99.40 (97.99, 100.82)	< 0.0001		
SBP (mm Hg)	123.43 (122.64, 124.22)	118.79 (118.00, 119.59)	117.28 (116.49,118.07)	< 0.0001		
DBP (mm Hg)	67.32 (66.70, 67.94)	67.07 (66.45, 67.69)	67.18 (66.57, 67.80)	0.7609		
Metabolic syndrome (%)	59.35	33.48	16.06	< 0.0001		
Smoke						
Every day (%)	34.21	31.63	47.26			
Somedays (%)	6.12	8.83	8.81			
Never (%)	59.67	59.54	43.93			
Drink						
Yes (%)	70.37	80.97	85.55			
No (%)	29.63	19.03	14.45			
Education						
≤High school (%)	43.95	42.74	46.80			
≥College (%)	56.05	52.26	53.20			
Annual household income (%)						
Low (<35 000)	40.56	29.91	30.45			
Medium (<100 000)	44.25	43.74	42.23			
High (≥100 000)	15.19	26.34	27.32			
	1899.01	2120.94	2388.95	-0.0001		
Energy intake (kcal/d)	(1845.31, 1952.71)	(2067.18, 2174.71)	(2335.31, 2442.59)	< 0.0001		
Physical activity (MET * h/wk) (%)						
Low (< 3500/year)	47.65	29.44	19.95			
Medium (< 10 000/year)	31.07	34.28	34.14			
High ($\geq 10\ 000$ /year)	21.28	36.28	45.91			

Table 1. Participants characteristics according to categories of adjusted handgrip.

BMI, body mass index; DBP, diastolic blood pressure; MET, metabolic equivalent; SBP, systolic blood pressure. * *P* for trend was anayzed by variance or chis-guare test.

The AUC value of the adjusted model for male participants was 0.76 (95% CI: 0.74, 0.78) and that for female participants was 0.80 (95% CI: 0.79, 0.82). The cut-off values of relative handgrip strength were 0.52 and 0.40 for male and female participants, respectively.

DISCUSSION

In this cross-sectional study, we explored the associations between handgrip strength and MetS in general US adults. The results demonstrated that higher handgrip strength was associated with lower prevalence of MetS in both male and female participants after adjustments of age, race, drinking status, smoking status, educational level, household income, total energy intake, and physical activity. We further generated ROC curves to quantify the AUC and the cut-off points of handgrip strength associated with the prevalence of MetS in both male and female participants.

In this study, the prevalence rates of MetS were 36.4% and 36.3% in US men and women, respectively. The results were close to the last report using data from the 2011-2012 wave of the NHANES, which found that the prevalence rates of MetS in the US were 32.8% and 36.6% in men and women, respectively [5].

Handgrip strength is a simple and reliable measurement of upper body strength and muscle mass [29]. Moreover, compared to supine bench press and seated leg press, handgrip strength is much easier to assess. Thus, handgrip strength could be a flexible indicator

	Men (N=2535)				Women (N=2521)			
	Tertiles of handgrip strength per body weight (kg/ kg) (range)				Tertiles of handgrip strength per body weight (kg/ kg) (range)			
	Level 1 (0.13, 0.48)	Level 2 (0.48, 0.60)	Level 3 (0.60, 1.13)		level 1 (0.11, 0.36)	Level 2 (0.36, 0.46)	Level 3 (0.46, 0.77)	
No. of participants (%)	31.80	34.33	33.86		33.44	34.73	31.83	
No. of participants with metabolic syndrome (%)	61.50	37.24	11.84	<0.0001	65.11	32.60	10.08	<0.0001
Crude model	Reference	0.37 (0.28, 0.50) ^b	0.08 (0.06, 0.12)	< 0.0001	Reference	0.26 (0.21, 0.32)	0.06 (0.04, 0.09)	< 0.0001
Adjusted model ^a	Reference	0.45 (0.33, 0.62)	0.13 (0.08, 0.20)	< 0.0001	Reference	0.35 (0.27, 0.46)	0.12 (0.08, 0.18)	< 0.0001
No. of participants with elevated waist circumference (%)	75.88	40.28	6.67	<0.0001	95.28	71.05	22.00	<0.0001
Crude model	Reference	0.21 (0.16, 0.28)	0.02 (0.02, 0.03)	< 0.0001	Reference	0.12 (0.08, 0.20)	0.01 (0.01, 0.02)	< 0.0001
Adjusted model ^a	Reference	0.22 (0.17, 0.29)	0.03 (0.02, 0.03)	< 0.0001	Reference	0.14 (0.09, 0.23)	0.02 (0.01, 0.03)	< 0.0001
No. of participants with elevated triglycerides (%)	56.85	40.68	22.90	<0.0001	53.63	29.76	16.44	<0.0001
Crude model	Reference	0.52 (0.39, 0.70)	0.23 (0.17, 0.30)	< 0.0001	Reference	0.37 (0.29, 0.47)	0.17 (0.12, 0.24)	< 0.0001
Adjusted model ^a	Reference	0.67 (0.46, 0.98)	0.39 (0.28, 0.53)	< 0.0001	Reference	0.52 (0.40, 0.69)	0.40 (0.28, 0.58)	< 0.0001
No. of participants with lower HDL (%)	29.14	25.21	17.47	< 0.0001	42.05	30.27	19.38	< 0.0001
Crude model	Reference	0.82 (0.63, 1.07)	0.51 (0.36, 0.73)	0.0004	Reference	0.60 (0.48, 0.74)	0.33 (0.26, 0.43)	< 0.0001
Adjusted model ^a	Reference	0.81 (0.61, 1.08)	0.51 (0.34, 0.76)	0.0013	Reference	0.49 (0.38, 0.6)	0.22 (0.15, 0.33)	< 0.0001
No. of participants with elevated blood pressure (%)	56.77	40.05	22.38	<0.0001	58.03	31.49	14.68	<0.0001
Crude model	Reference	0.51 (0.37, 0.70)	0.22 (0.17, 0.28)	< 0.0001	Reference	0.33 (0.27, 0.41)	0.13 (0.10, 0.16)	< 0.0001
Adjusted model ^a	Reference	0.70 (0.49, 0.99)	0.37 (0.28, 0.50)	< 0.0001	Reference	0.49 (0.34, 0.69)	0.33 (0.23, 0.48)	< 0.0001
No. of participants with elevated fasting glucose (%)	65.16	51.63	33.98	<0.0001	56.09	34.56	17.55	<0.0001
Crude model	Reference	0.57 (0.44, 0.74)	0.28 (0.22, 0.35)	< 0.0001	Reference	0.41 (0.32, 0.53)	0.17 (0.13, 0.22)	< 0.0001
Adjusted model ^a	Reference	0.71 (0.52, 0.96)	0.44 (0.32, 0.61)	< 0.0001	Reference	0.56 (0.42, 0.75)	0.33 (0.25, 0.45)	< 0.0001

Table 2. Association between handgrip and metabolic syndrome and its components in men and women.

a. Logistic regression adjusted for age, race, drinking status, smoking status, education level, income, total energy intake, and physical activity.

b. Odds ratio (95% confidence interval) (all such values).

HDL, high-density lipoprotein.

c. *P* for trend was analysed by multiple logistic regression analysis.

for screening MetS. A few previous studies have investigated the associations between handgrip strength and prevalence of MetS in different populations [24, 25, 27, 29]. A cross-sectional study conducted in Australian men found that the odds for the prevalence of MetS increased for lower muscle strength per body weight [24]. Another study conducted in Korea found that grip strength per body weight was lower in participants with MetS than in those without MetS [25]. A large Chinese population-based study also found that handgrip strength per body weight was inversely associated with MetS [27]. The ORs (95% CI) of MetS across decreasing handgrip strength per weight quartiles were 1.00 (reference), 1.87 (1.66, 2.11), 2.40 (2.13, 2.71), and 3.36 (2.97, 3.80) in men and 1.00 (reference), 1.80 (1.48, 2.21), 2.77 (2.29, 3.36), and 3.89 (3.22, 4.71) in women [27]. Most recently, another cross-sectional study including 488 male and 521 female participants found that low handgrip strength per body weight was associated with higher prevalence of MetS [29]. Compared with participants in the highest tertile of handgrip strength per weight, those in the lowest tertile had 2.52 (95% CI, 1.43-4.46) and 5.01 (95% CI, 1.66-15.08) times higher prevalence of MetS in male and female participants, respectively [29].

In line with previous studies, we found that higher handgrip strength per body weight was associated with lower prevalence of MetS after adjustments of confounding factors in the present study. The mechanisms that have been proposed to explain this association are mainly related to insulin resistance and inflammation. Muscles are major sites of insulinstimulated whole-body glucose disposal and muscle metabolism can influence whole-body glucose homeostasis and insulin sensitivity [38]. Meanwhile, insulin resistance is the most accepted unifying theory explaining the pathophysiology of MetS [39]. Moreover, low muscle strength and mass were associated with high level of inflammation markers, such as C-reactive protein [40] and neutrophillymphocyte ratio [41]. A chronic state of inflammation also appears to be a central mechanism underlying the pathophysiology of insulin resistance and MetS [42]. Previous studies also demonstrated that skeletal muscles could release factors such as irisin [21] and myonectin [43]. which can exert endocrine effects and consequently contribute to risk factors of MetS [44, 45]. Thus, lower muscle strength and mass could lead to the development of MetS.

Furthermore, the ROC curves were generated to determine the cut-off points of handgrip strength per body weight associated with MetS. Results suggested that the cut-off points were 0.52 and 0.40 kg/kg of handgrip strength per body weight in men and women, respectively. The results were in line with a previous study that analysed 17,703 Chinese adults and found that the optimal cut-off values were 0.56 and 0.40 in men and women, respectively [27]. Another study found that the cut-off points were 2.57 and 2.35 kg/kg

bench press and leg press per body weight in US men aged < 50 years and ≥ 50 years [30]. However, to the best of our knowledge, this is the first study that used handgrip strength, which is easier to employ in both clinical and community settings, to calculate cut-off points of muscle strength associated with MetS.

Some limitations are notable in this study. Firstly, given the nature of observational study design, the mechanism underlying the associations cannot be illuminated. Secondly, even though we have adjusted confounding factors, we cannot rule out the possibility that unmeasured factors might contribute to the associations observed. Thirdly, selection bias may exist because lots of participates were excluded from the study. However, NHANES is unique in collecting person-level demographic, health, and nutrition information from personal interviews (interview) and a standardized physical examination in a mobile examination center (MEC). The examination includes objective measures of health status, including height, weight, blood pressure, and the collection of blood and urine specimens for laboratory testing. For some of these components, subsampling was required to reduce respondent burden and facilitate the scheduling and completion of examinations. In addition, weights were assigned to each component during sampling and analysis process. So sample representativeness was not been affected. Furthermore, considering the different definitions of MetS between studies, the comparability and generality of this study was limited. Finally, this study was conducted in a population of US adults, which could limit the generalizability of results to other populations.



Figure 1. Receiver operating characteristic curve for the adjusted model to analyse the association between relative handgrip strength and prevalence of MetS in US male (A) and female (B) participants.

In conclusion, findings from this study show that relative handgrip is negatively associated with the prevalence of MetS which defined by a joint multinational interim statement in men with BMI < 30 and women. Handgrip strength per weight lower than 0.52 (kg/ kg) in men and 0.40 (kg/ kg) in women may increase the risk of MetS. Enhancing muscle strength activities may be a new perspective for prevent MetS. Handgrip strength test may be a simple way to identify MetS. And further random controlled trial studies and cohort studies were needed.

MATERIALS AND METHODS

Study population

NHANES, a program of studies conducted by the Centers for Disease Control and Prevention's (CDC) and National Center for Health Statistics (NCHS), was designed to assess the health and nutritional status of adults and children in the US. NHANES uses a complex, multistage, probability sampling design to select participants representative of the non-institutionalized civilian, US population. Household interviews and physical and laboratory examinations were included in the survey [46]. Handgrip strength data are available for 2011-2012 and 2013-2014 survey cycles. Participants aged ≥ 20 years were included. All adults provided written consent to participate in NHANES, which was reviewed and approved by the NCHS Research Ethics Review Board.

Handgrip strength

Handgrip strength was measured using a Takei Digital Grip Strength Dynamometer (T.K.K. 5401) to the nearest 0.1 kg. Participants were asked to remove hand and wrist jewellery and adjust the grip size of the dynamometer until the second joint of the index finger was at 90°. After a practice trial, each hand of the participants would be tested three times, alternating hands between trials with a 60-s rest between measurements on the same hand. Participants stood straight with their feet and hip apart and arms fully extended alongside with palms facing their thighs. The participant's hand, which was in line with the wrist and forearm, quickly and forcefully squeezed the dynamometer handle at their maximum strength. The complete handgrip strength testing protocol is described in the NHANES muscle strength procedure manual (https://wwwn.cdc.gov/nchs/nhanes). To avoid the potential bias effect of body weight on the estimation of handgrip strength, relative handgrip strength (handgrip/body weight) was calculated to assess the handgrip strength.

Metabolic syndrome

MetS was defined according to the joint scientific statement of harmonizing the MetS criteria as participants presented three or more of the following components [47]: (1) waist circumference \geq 88 cm in women and \geq 102 cm in men; (2) elevated plasma triglycerides \geq 150 mg/dl (1.7 mmol/L), or treatment for elevated triglycerides; (3) reduced high-density lipoprotein cholesterol <40 mg/dl (1.0 mmol/L) in men, and <50 mg/dl (1.3 mmol/L) in women, or treatment for reduced high-density lipoprotein cholesterol; (4) evaluated blood pressure (BP): systolic blood pressure (SBP) \geq 130 mm Hg and/or diastolic blood pressure (DBP) \geq 85 mm Hg, or antihypertensive drug treatment; (5) high fasting glucose \geq 100 mg/dl, or drug treatment for elevated glucose.

Assessment and definition of other variables

Age, gender, race, education, household income, diet, physical activity, and tobacco and alcohol use were self-reported. Race was classified as Mexican American, other Hispanic, Non-Hispanic White, Non-Hispanic Black, and other Race. Education level was categorized into high school and lower (\leq 3) and college graduate and above (4-5). Household income was categorized as low (< 3500/year), medium (< 100000/year), and high (\geq 100000/year).

Standing height was measured to the nearest 0.1 cm by a stadiometer platform. A digital weighing scale was used to measure weight to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured at the horizontal plane of the iliac crest to the nearest millimetre, using a measuring tape [48].

Seated resting BP was obtained by a trained physician using a Baumanometer[®] calibrated mercury true gravity wall model sphygmomanometer and Baumanometer[®] Calibrated V-Lok® cuffs. All participants sat all the way to the back of the height-adjustable chair to keep the spine straight and rested quietly for 5 min prior to BP measurement. The arm was bare and unrestricted by clothing with the palm turned upward. The elbow was slightly flexed, and the midpoint of the upper arm was at the level of the heart. Three consecutive BP readings were obtained by auscultation. A fourth attempt was performed if a BP measurement was interrupted or incomplete. All BP determinations (systolic and diastolic) were performed in the NHAES Mobile Examination Center.

Physical activity was assessed using the Global Physical Activity Questionnaire. Participants were asked to report the frequency and duration of leisure-time physical activities in a typical week. According to physical activity guidelines [49], vigorous-intensity activity and moderateintensity activity were translated to metabolic equivalent values; therefore, the total physical activity (metabolic equivalent value per week) for each participant was calculated. Dietary intake was assessed via two 24-h recall interviews. Energy intake was later quantified for each food recorded during the survey.

Statistical analysis

Participants' baseline characteristics have been presented as least square means (with 95% confidence interval, CI) for continuous variables. Categorical variables were presented as percentages. Relative handgrip strength was categorized into sex-specific tertiles and sex-BMIspecific tertiles in separate models. Multivariable logistic regression was used to estimate the ORs with 95% CIs of associations between tertiles of relative handgrip strength and MetS with each component. The linear trend across increasing tertiles was tested using the median value of each tertile as a continuous variable based on logistic regression. The crude model was unadjusted. To estimate the potential differences in confounding effects, we adjusted for covariates including age, race, drinking and smoking status, education level, household income, total energy intake, and physical activity. The area under receiver operating characteristic (ROC) curve (AUC) with 95% CI was calculated to assess the performance of the multivariable logistic model. The cutoff value of relative handgrip strength associated with MetS was quantified by ROC curve.

All models were estimated using appropriate SAS survey procedures and NHANES strata, cluster, and sampling probability weights to account for the NHANES complex survey design and to produce unbiased national estimates. Sampling probability weights were appropriately constructed based on NHANES guidance. All data management and analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). Two-sided P<0.05 was considered significant.

Research data (data sharing and collaboration)

NHANES is an open database. All the data from this study could be acquired through the website <u>https://www.cdc.gov/nchs/nhanes/</u>.

AUTHOR CONTRIBUTIONS

Yuhong Zhao, Yang Xia, and Chao Ji designed and conducted this study; Chao Ji and Yang Xia managed and analysed the data and wrote the manuscript as cofirst authors. Qijun Wu and Shuhui Tong revised the manuscript. Yuhong Zhao had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of data analysis. All authors approved the final manuscript.

ACKNOWLEDGMENTS

The authors thank Yang Xia and Qijun Wu for their help and support for this study.

CONFLICTS OF INTEREST

On behalf of all authors, the corresponding author states that there is no conflicts of interest.

FUNDING

This study was supported by grants from the National Key Research and Development Program of China [No. 2017YFC0907402 to Yuhong Zhao], Natural Science Foundation of China [No. 81903302 to Yang Xia], and China Postdoctoral Science Foundation Funded Project [No. 2018M641753 to Yang Xia], and 345 Talent Project of Shengjing Hospital of China Medical University [No. M0294 to Yang Xia].

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SUPPLEMENTARY MATERIALS

Supplementary Tables

Supplementary Table 1. The association between handgrip and metabolic syndrome and its components in men.

	Men (BMI<30)				Men (>=30)			
	Tertiles of handgrip strength per body weight (kg/				Tertiles of handgrip strength per body weight (kg/			
	kg) (range)					kg) (range)		
	Level1	Level2	Level3		Level1	Level2	Level3	
	(0.20, 0.53)	(0.53, 0.64)	(0.64, 1.13)		(0.14, 0.39)	(0.40, 0.48)	(0.48, 0.87)	
No. of participants (%)	30.85	34.89	34.26		29.48	34.04	36.48	
No. of participants with metabolic syndrome (%)	38.74	20.71	7.00	<0.0001	74.99	72.73	61.56	0.0043
Crude model	Reference	0.41 (0.27, 0.63) ^b	0.12 (0.08, 0.18)	< 0.0001	Reference	0.89 (0.52, 1.54)	0.53 (0.31, 0.92)	0.0209
Adjusted model ^a	Reference	0.59 (0.35, 0.98)	0.24 (0.14, 0.41)	< 0.0001	Reference	0.90 (0.49, 1.66)	0.89 (0.51, 1.57)	0.7150
No. of participants with elevated waist circumference (%)	34.76	16.94	1.81	<0.0001	98.48	98.10	79.56	<0.0001
Crude model	Reference	0.38 (0.26, 0.57)	0.04 (0.01, 0.09)	< 0.0001	Reference	0.80 (0.26, 2.41)	0.06 (0.02, 018)	< 0.0001
Adjusted model ^a	Reference	0.47 (0.32, 0.70)	0.06 (0.02, 0.15)	< 0.0001	Reference	0.52 (0.19, 1.45)	0.05 (0.02, 0.11)	< 0.0001
No. of participants with elevated triglycerides (%)	45.21	32.56	18.55	<0.0001	66.33	58.35	50.86	0.0049
Crude model	Reference	0.58 (0.40, 0.84)	0.28 (0.18, 0.44)	< 0.0001	Reference	0.74 (0.44, 1.15)	0.53 (0.29, 0.96)	0.0382
Adjusted model ^a	Reference	0.80 (0.50, 1.30)	0.52 (0.29, 0.92)	0.0239	Reference	0.70 (0.44, 1.09)	0.83 (0.44, 1.57)	0.6532
No. of participants with lower HDL (%)	23.81	17.59	15.20	< 0.0001	39.76	29.67	36.96	0.3933
Crude model	Reference	0.68 (0.46, 1.00)	0.58 (0.36, 0.92)	0.0209	Reference	0.64 (0.35, 1.15)	0.89 (0.52, 1.53)	0.7373
Adjusted model ^a	Reference	0.76 (0.52, 1.10)	0.67 (0.38, 1.16)	0.1376	Reference	0.66 (0.33, 1.31)	0.79 (0.42, 1.49)	0.5198
No. of participants with elevated blood pressure (%)	45.21	30.41	20.60	<0.0001	62.75	62.24	46.45	0.0007
Crude model	Reference	0.53 (0.37, 0.75)	0.32 (0.24, 0.42)	< 0.0001	Reference	0.98 (0.63, 1.54)	0.51 (0.33, 0.81)	0.0056
Adjusted model ^a	Reference	0.79 (0.50, 1.24)	0.64 (0.41, 0.99)	0.0388	Reference	1.16 (0.64, 2.10)	0.96 (0.53, 1.75)	0.8161
No. of participants with elevated fasting glucose (%)	53.77	43.18	29.80	<0.0001	74.77	68.64	61.81	0.0117
Crude model	Reference	0.66 (0.46, 0.95)	0.36 (0.27, 0.48)	< 0.0001	Reference	0.74 (0.40, 1.36)	0.55 (0.33, 0.91)	0.0225
Adjusted model ^a	Reference	0.88 (0.58, 1.35)	0.58 (0.42, 0.81)	0.0026	Reference	0.94 (0.52, 1.70)	0.0.97 (0.55, 1.73)	0.9568

a. Logistic regression adjusted for age, race, drinking status, smoking status, education level, income, total energy intake and physical activity.

b. Odds ratio (95% confidence interval) (all such values).

BMI, body mass index.

c. *P* for trend was analysed by multiple logistic regression analysis.

	Women (BMI<30) Tertiles of handgrip strength per body weight (kg/ kg) (range)				Women (BMI>=30)			
					Tertiles of handgrip strength per body weight (kg/ kg) (range)			
	Level1 (0.14, 0.42)	Level2 (0.42, 0.50)	Level3 (0.50, 0.77)	-	Level1 (0.11, 0.29)	Level2 (0.29, 0.35)	Level3 (0.35, 0.69)	_
No. of participants (%)	35.66	32.60	31.74		32.70	34.04	33.26	
No. of participants with metabolic syndrome (%)	41.10	16.41	6.73	<0.0001	71.87	64.21	48.55	<0.0001
Crude model	Reference	0.28 (0.18, 0.45) ^d	0.10 (0.06, 0.18)	< 0.0001	Reference	0.70 (0.47, 1.06)	0.37 (0.26, 0.53)	< 0.0001
Adjusted model ^a	Reference	0.59 (0.36, 0.98)	0.31 (0.16, 0.60)	0.0003	Reference	0.84 (0.54, 1.31)	0.65 (0.44, 0.98)	0.0402
No. of participants with elevated waist circumference (%)	71.74	41.30	12.83	<0.0001	100.00	99.92	99.73	0.1573
Crude model	Reference	0.28 (0.21, 0.36)	0.06 (0.04, 0.09)	< 0.0001	Reference	-	-	-
Adjusted model ^a	Reference	0.36 (0.27, 0.50)	0.09 (0.05, 0.14)	< 0.0001	Reference	-	-	-
No. of participants with elevated triglycerides (%)	43.25	21.15	12.99	<0.0001	56.94	51.19	30.13	< 0.0001
Crude model	Reference	0.57 (0.32, 1.02)	0.38 (0.22, 0.66)	< 0.0001	Reference	0.98 (0.58, 1.65)	0.53 (0.30, 0.92)	< 0.0001
Adjusted model ^a	Reference	0.73 (0.47, 1.13)	0.59 (0.35, 1.00)	0.0184	Reference	0.97 (0.70, 1.33)	0.56 (0.36, 0.85)	0.0087
No. of participants with lower HDL (%)	23.74	22.76	18.45	0.0039	51.30	45.23	41.19	0.1446
Crude model	Reference	0.95 (0.64, 1.39)	0.73 (0.53, 0.99)	0.0502	Reference	0.78 (0.50, 1.23)	0.72 (0.50, 1.04)	0.0833
Adjusted model ^a	Reference	0.80 (0.53, 1.20)	0.59 (0.38, 0.91)	0.0170	Reference	0.67 (0.41, 1.12)	0.55 (0.35, 0.85)	0.0087
No. of participants with elevated blood pressure (%)	42.79	21.20	12.79	<0.0001	63.94	48.36	38.73	<0.0001
Crude model	Reference	0.36 (0.26, 0.50)	0.20 (0.15, 0.26)	< 0.0001	Reference	0.53 (0.34, 0.82)	0.36 (0.23, 0.55)	< 0.0001
Adjusted model ^a	Reference	1.00 (0.59, 1.70)	0.98 (0.56, 1.73)	0.9459	Reference	0.56 (0.32, 0.97)	0.56 (0.32, 0.98)	0.0465
No. of participants with elevated fasting glucose (%)	39.23	24.19	13.88	<0.0001	62.77	51.98	47.12	<0.0001
Crude model	Reference	0.50 (0.35, 0.70)	0.25 (0.19, 0.33)	< 0.0001	Reference	0.64 (0.42, 0.98)	0.53 (0.34, 0.81)	0.0058
Adjusted model ^a	Reference	0.92 (0.59, 1.43)	0575 (0.38, 0.85)	0.0186	Reference	0.77 (0.50, 1.19)	0.97 (0.60, 1.59)	0.9570

Supplementary Table 2. The association between handgrip and metabolic syndrome and its components in women.

a. Logistic regression adjusted for age, race, drinking status, smoking status, education level, income, total energy intake and physical activity.

b. Odds ratio (95% confidence interval) (all such values).

BMI, body mass index.

c. *P* for trend was analysed by multiple logistic regression analysis.