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# Handgrip strength is inversely associated with metabolic syndrome and its separate components in middle aged and older adults: a large-scale population-based study

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ABSTRACT

*Background:* Muscle weakness is followed by insulin resistance which is associated with metabolic disorders leading to metabolic syndrome (MetS). Therefore, muscle strength decline may be associated with MetS. The aim of this study was to investigate the relationships between muscle strength and MetS and its separate components.
*Methods:* A cross-sectional study was performed in 17,703 participants aged 40 years and older living in Tianjin, China. Handgrip strength was measured using a handheld digital dynamometer. MetS was defined in accordance with the criteria of the American Heart Association scientific statements of 2009. Multiple logistic regression analyses were used to assess the association between handgrip strength and MetS and its separate components.
*Results:* The overall prevalence of MetS was 33.6%. The prevalence of MetS was significantly higher in men than in women (41.6% vs 22.9%, $P < 0.0001$). After adjustment for potential confounding factors (including sociodemographic variables, lifestyle factors, total energy intake, and family history of disease), the odds ratios (95% confidence interval) of MetS across decreasing handgrip strength 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, respectively ($P$ for all trend <0.0001). Similarly, handgrip strength was also observed to be negatively associated with separate components of MetS both in men and women.
*Conclusions:* Muscle strength is inversely associated with MetS and its separate components. Further prospective studies are needed to confirm this issue.



## 1. Introduction

Metabolic syndrome (MetS) is defined as having three or more of the following five metabolic risk factors: elevated waist circumference (WC), triglycerides (TG), reduced high-density lipoprotein (HDL) cholesterol, elevated blood pressure (BP), and elevated fasting blood glucose (FBG) [1]. Over the past few decades, there has been a steep increase in MetS throughout the world, especially in developing countries. Studies have shown that MetS is a strong predictor of type 2 diabetes, cardiovascular disease (CVD), and all-cause mortality [2–5]. Therefore, clarifying risk factors of MetS can contribute to numerous potential health benefits.

In this respect, physical fitness components related to health, such as muscular fitness, measured by muscle strength, may play a key role in

*Abbreviations:* MetS, metabolic syndrome; WC, waist circumference; TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; CVD, cardiovascular disease; IR, insulin resistance; TCLSIH, Tianjin Chronic Low-Grade Systemic Inflammation and Health; FFQ, food frequency questionnaire; BMI, body mass index; IPAQ, international physical activity questionnaire; CI, confidence interval; OR, odds ratios; SDs, standard deviations; ROC, Receiver Operating Characteristics; AUC, area under the curve; AWGS, Asian Working Group for Sarcopenia; EWGSOP, the European Working Group on Sarcopenia; HOMA-IR, homeostasis model assessment of insulin resistance.

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the treatment and prevention of MetS. It is well known that skeletal muscles are primary sites for glucose uptake and deposition [6]. Studies have shown that muscle-strengthening activities are closely related with improved insulin sensitivity, ameliorated dyslipidemia [7,8], and reduced blood pressure [9], all of which are principal risk factors for MetS. Furthermore, muscle strength decline is associated with myofiber lipid accumulation [10]. Excessive lipid deposition in skeletal muscles leads to lipotoxicity and insulin resistance (IR) development. IR thereby results in substantial whole-body metabolic disturbances [7,11,12].

In addition, skeletal muscle as a secretory organ can secrete multiple peptides (myokines) [13]. Many of these peptides (such as interleukin-15, myostatin, and irisin) contribute to metabolic homeostasis [14,15]. For example, a release of interleukin-15 from skeletal muscle negatively regulates fat mass [16]. Inhibition of myostatin suppresses body fat accumulation and improves insulin sensitivity [17,18]. Irisin is involved in the regulation of obesity and glucose homeostasis [19]. Because these myokines appear to participate in maintenance of whole-body metabolic homeostasis, and muscle strength is associated with myokines levels [20,21], we hypothesize that muscle strength decline may contribute to MetS. In this study, handgrip strength was selected as the primary measure of muscle strength, for that it is easy to use in both clinical and community settings [22]. It has been reported that handgrip strength could decline as early as age 40 [23,24]. Therefore, we focused on a population aged 40 years and older in a large sample of Chinese men and women.

To best of our knowledge, no study has evaluated the relationship between handgrip strength and MetS and its separate components in a large middle aged and older population. Thus, we performed this study to investigate the relationships between handgrip strength and MetS and its separate components.

## 2. Methods

### 2.1. Study Population

A large prospective dynamic cohort study [25], called the Tianjin Chronic Low-Grade Systemic Inflammation and Health (TCLSIH) Cohort Study, was carried out in a general adult population living in Tianjin, China. Detailed information on the study design and methods of the TCLSIH has been described previously [26,27]. This cross-sectional study used data from the TCLSIH Cohort Study ranging from 2013 to 2017. During the research period there were 19,877 participants who had received health examinations and handgrip test. We excluded participants who did not complete data collection on food frequency questionnaire (FFQ) ($n = 1884$), body mass index (BMI) ($n = 12$), International Physical Activity Questionnaire (IPAQ) ($n = 136$) or those with a history of cancer ($n = 142$). As a result of these exclusions, the final cross-sectional study population comprised 17,703 subjects [age 45.2 (51.3–59.2) years; median (interquartile range)]. The protocol of this study was approved by the Institutional Review Board of the Tianjin Medical University. Written informed consent was obtained from all participants.

### 2.2. Assessment of Metabolic Syndrome

Waist circumference was measured at the umbilical level with participants standing and breathing normally. BP was measured twice from the upper left arm using an automatic device (Andon, Tianjin, China) after 5 min of rest in a seated position. The mean of these 2 measurements was taken as the BP value. Blood samples for the analysis of FBG and lipids were collected in siliconized vacuum plastic tubes. FBG was measured by the glucose oxidase method, TG were measured by enzymatic methods, and HDL was measured by the chemical precipitation method using reagents from Roche Diagnostics on an automatic biochemistry analyzer (Roche Cobas 8000 modular analyzer, Mannheim, Germany).

Metabolic syndrome was defined in accordance with the criteria of the American Heart Association scientific statements of 2009 [1]. Participants were considered to have MetS when they presented three or more of the following components: 1) Elevated WC for Chinese individuals (≥85 cm in males; ≥80 cm in females). 2) Elevated TG (≥1.7 mmol/L), or drug treatment for elevated TG. Drug treatment was determined by self-report medications (hypolipidemic agents) or by medical records (lipid-modifying agents). 3) Reduced HDL (<1.0 mmol/L in males; <1.3 mmol/L in females) or drug treatment for reduced HDL. Drug treatment was determined by self-report medications (hypolipidemic agents) or by medical records (lipid-modifying agents). 4) Elevated BP (SBP ≥130 mmHg and/or diastolic blood pressure (DBP) ≥85 mmHg) or antihypertensive drug treatment. 5) Elevated FBG (≥ 5.56 mmol/L) or drug treatment for elevated glucose.

### 2.3. Measurement of Muscle Strength

Muscle strength was assessed by handgrip strength, measured using a hand-held dynamometer (EH101; CAMRY, Guangdong, China). Participants were tested by the trained technicians under the same conditions. Dynamometer width was adjusted for optimal fit for each participant according to instructions on the dynamometer. Participants were instructed to stand upright and with the dynamometer beside but not against their body. The evaluator gave verbal encouragement to elicit maximal performance from the participants during measurement. Participants were asked to perform 2 maximum force trials for each hand and the greatest force was used as the final score. Handgrip strength was normalized to body weight to account for the proportion of strength relative to body weight [handgrip strength (kg)/body weight (kg)] [28,29].

### 2.4. Assessment of Other Variables

Physical activity in the most recent week was assessed using the short form of the IPAQ [30]. Dietary intake was assessed using a validated FFQ [27] that included 100 food items (the initial version of the FFQ included 81 food items [31] with specified serving sizes). The mean daily intake of total energy was estimated with the use of the nutrient composition of all food items on the FFQ. The Chinese food composition tables [32] were used as the nutrient database.

Information about education levels, household income, smoking and drinking status were gathered using a standardized, structured interview questionnaire. A detailed personal and family history of physical illness and current medications was noted from "yes" or "no" responses to relevant questions. Height and body weight were measured using a standard protocol, and BMI was calculated as weight/height$^2$ (kg/m$^2$).

### 2.5. Statistical Analysis

All statistical analyses were performed using the Statistical Analysis System 9.3 edition for Windows (SAS Institute Inc., Cary, NC). Descriptive data is presented as the mean (95% confidence interval (CI)) for continuous variables, and as percentages for categorical variables. Baseline characteristics were examined by analysis of covariance for continuous variables or by multiple logistic regression analysis for categorized variables between participants with and without MetS after adjustment for age and sex. Furthermore, we defined a reference value for handgrip strength to identify persons with a "low handgrip strength". The reference values were pragmatically expressed as 2 standard deviations (SDs) below the sex-specific mean value taken from 5344 women and 5653 men younger than 40 years [33].

For main analysis, the prevalence of MetS and components of MetS were used as dependent variables, and quartiles of handgrip strength were used as independent variables. Multiple logistic regression models were used to evaluate the association between handgrip strength and

**Table 1**
Age- and sex-adjusted participant characteristics by metabolic syndrome status[a].

| | Metabolic syndrome status | | $P$ value[b] |
|---|---|---|---|
| | No (n = 11,762) | Yes (n = 5941) | |
| Age (y) | 49.5 (49.3, 49.6)[c] | 53.4 (53.2, 53.7) | <0.0001 |
| Sex (men, %) | 50.1 | 70.7 | <0.0001 |
| Handgrip strength (kg) | 34.3 (34.2, 34.4) | 33.9 (33.8, 34.1) | <0.0001 |
| BMI (kg/m$^2$) | 24.1 (24.0, 24.2) | 26.9 (26.8, 27.0) | <0.0001 |
| WC (cm) | 81.9 (81.8, 82.0) | 90.1 (89.8, 90.3) | <0.0001 |
| TG (mmol/L) | 1.07 (1.06, 1.08) | 1.99 (1.97, 2.01) | <0.0001 |
| HDL (mmol/L) | 1.44 (1.43, 1.45) | 1.14 (1.13, 1.15) | <0.0001 |
| SBP (mmHg) | 119.3 (119.0, 119.6) | 132.4 (131.9, 132.8) | <0.0001 |
| DBP (mmHg) | 75.4 (75.2, 75.5) | 84.1 (83.8, 84.4) | <0.0001 |
| FBG (mmol/L) | 4.93 (4.92, 4.95) | 5.70 (5.68, 5.73) | <0.0001 |
| Physical activity (Mets × hours/week) | 11.2 (11.0, 11.5) | 10.3 (9.90, 10.6) | <0.0001 |
| Energy intake (kcal/d) | 1947.3 (1932.1, 1962.7) | 1978.2 (1967.6, 1989.0) | <0.001 |
| Smoking status (%) | | | |
| Non-smoker | 74.1 | 60.9 | <0.01 |
| Smoker | 19.2 | 28.2 | <0.001 |
| Ex-smoker | 6.66 | 11.0 | <0.001 |
| Drinking status (%) | | | |
| Non-drinker | 29.5 | 24.7 | 0.001 |
| Everyday | 6.51 | 10.8 | <0.0001 |
| Sometime | 55.6 | 55.0 | 0.47 |
| Ex-drinker | 8.47 | 9.51 | <0.05 |
| Education level (≥College graduate, %) | 52.7 | 43.1 | <0.0001 |
| Household income (≥10,000 Yuan, %) | 34.8 | 30.9 | <0.0001 |
| Family history of diseases (%) | | | |
| CVD | 40.9 | 39.7 | 0.18 |
| Hypertension | 55.5 | 59.7 | <0.0001 |
| Hyperlipidemia | 0.54 | 0.37 | 0.32 |
| Diabetes | 25.9 | 31.3 | <0.0001 |

[a] BMI, body mass index; WC, waist circumference; TG, triglycerides; HDL, high-density lipoprotein-cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; CVD, cardiovascular disease.
[b] Analysis of covariance or multiple logistic regression analysis.
[c] Mean (95% confidence interval) (all such values).

MetS and components of MetS. Analyses were performed in a sex specific manner because of significant differences in muscle strength and prevalence of MetS. For crude model, the analysis was conducted without any adjustment. For multiple-adjusted model, we adjusted for age, smoking status, drinking status, physical activity, educational levels, household income, total energy intake, and family history of diseases (including CVD, hypertension, hyperlipidemia, and diabetes). The final multivariate logistic analysis was performed with the forced entry of all factors considered to be potential covariates that may influence the relationship between handgrip strength and MetS. A linear trend across

**Table 2**
Relationships between handgrip strength and metabolic syndrome and its components in men[a].

| | Quartiles of handgrip strength per body weight (kg/kg) (range) | | | | $P$ for trend[b] |
|---|---|---|---|---|---|
| | Level 4 (0.62–1.00) | Level 3 (0.55–0.62) | Level 2 (0.49–0.55) | Level 1 (0.20–0.49) | |
| | 2525 | 2525 | 2525 | 2525 | |
| No. of metabolic syndrome | 657 | 1006 | 1160 | 1379 | |
| Crude | 1.00 (reference) | 1.88 (1.67, 2.12)[c] | 2.42 (2.15, 2.72) | 3.42 (3.04, 3.85) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.87 (1.66, 2.11) | 2.40 (2.13, 2.71) | 3.36 (2.97, 3.80) | <0.0001 |
| Metabolic syndrome components | | | | | |
| No. of elevated WC | 1325 | 1872 | 2165 | 2300 | |
| Crude | 1.00 (reference) | 2.60 (2.31, 2.92) | 5.45 (4.76, 6.25) | 9.26 (7.92, 10.9) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.42 (1.21, 1.66) | 2.07 (1.73, 2.48) | 2.09 (1.68, 2.60) | <0.0001 |
| No. of elevated TG | 825 | 1056 | 1124 | 1202 | |
| Crude | 1.00 (reference) | 1.48 (1.32, 1.66) | 1.65 (1.48, 1.85) | 1.87 (1.67, 2.10) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.53 (1.36, 1.72) | 1.78 (1.58, 2.00) | 2.20 (1.95, 2.48) | <0.0001 |
| No. of reduced HDL | 395 | 559 | 601 | 653 | |
| Crude | 1.00 (reference) | 1.53 (1.33, 1.77) | 1.68 (1.46, 1.94) | 1.88 (1.64, 2.16) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.58 (1.37, 1.83) | 1.81 (1.57, 2.10) | 2.14 (1.85, 2.48) | <0.0001 |
| No. of elevated BP | 1035 | 1266 | 1359 | 1581 | |
| Crude | 1.00 (reference) | 1.45 (1.30, 1.62) | 1.68 (1.50, 1.88) | 2.41 (2.15, 2.70) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.38 (1.23, 1.54) | 1.53 (1.37, 1.72) | 1.97 (1.75, 2.22) | <0.0001 |
| No. of elevated FBG | 498 | 634 | 769 | 912 | |
| Crude | 1.00 (reference) | 1.37 (1.20, 1.56) | 1.78 (1.57, 2.03) | 2.30 (2.03, 2.62) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.31 (1.14, 1.50) | 1.61 (1.41, 1.84) | 1.86 (1.63, 2.13) | <0.0001 |

[a] WC: waist circumference; TG, triglycerides; HDL, high-density lipoprotein-cholesterol; BP, blood pressure; FBG, fasting blood glucose; CVD, cardiovascular disease.
[b] Multiple logistic regression analysis.
[c] Adjusted odds ratios (95% confidence interval) (all such values).
[d] Adjusted for age, smoking status, drinking status, physical activity, educational levels, household income, total energy intake, and family history of diseases (including CVD, hypertension, hyperlipidemia, and diabetes).

the quartiles of muscle strength was tested by using the median value of each category as an ordinal variable. Finally, receiver operating characteristics (ROC) curves were performed to quantify sensitivity, specificity, area under the curve (AUC), and cut-off points of handgrip strength associated with the MetS. All tests were two-tailed and $P < 0.05$ was defined as statistically significant.

## 3. Results

In this study, the overall prevalence of MetS was 33.6% (5941 of 17,703). The prevalence of MetS was significantly higher in men than in women (41.6% compared with 22.9%, $P < 0.0001$).

Age and sex adjusted baseline characteristics of participants by MetS status are presented in Table 1. Compared with participants without MetS, participants with MetS were older, have higher BMI, WC, TG, SBP, DBP, FBG, and total energy intake, but lower levels of handgrip strength, physical activity, and HDL (All $P < 0.001$). The proportion of men, current smokers, ex-smokers, everyday drinkers, ex-drinkers, and family history of hypertension and diabetes were significantly higher in the MetS group than in the non-MetS group (All $P < 0.05$). The proportion of non-smokers, non-drinkers, educational level of college graduate, and household income of higher than 10,000 Yuan were significantly lower in the MetS group than in the non-MetS group (All $P < 0.0001$). Otherwise, no significant difference was observed between participants with MetS and without MetS.

The mean value of handgrip strength was 44.7 ± 7.11 kg for men and 25.9 ± 4.73 kg for women in the young reference population. We defined low handgrip strength as handgrip strength below 2 SDs of mean value. Thus, the reference value of low handgrip strength was 30.5 kg for men and 16.4 kg for women. The values are approximately comparable to values defined as low muscle strength by the Asian Working Group for Sarcopenia (AWGS) and the European Working Group on Sarcopenia (EWGSOP) [33,34].

The prevalence for components of MetS in descending order were 64.2%, 43.3%, 32.0%, 24.8%, and 23.0%, respectively, for elevated WC, BP, TG, reduced HDL, and elevated FBG. Abnormal levels of WC were observed most frequently among those classified as having the MetS (94.6%).

Tables 2 and 3 present the crude and adjusted relationships between quartiles of handgrip strength and MetS and its components in men and women. In the final multivariate models, lower handgrip strength is significantly associated with higher MetS prevalence, the adjusted odds ratios (OR) (95% CI) for MetS across quartiles of handgrip strength were 1.00 (reference), 1.87 (1.66, 2.11), 2.40 (2.13, 2.71), and 3.36 (2.97, 3.80) ($P$ for trend <0.0001) in men (Table 2) and 1.00 (reference), 1.80 (1.48, 2.21), 2.77 (2.29, 3.36), and 3.89 (3.22, 4.71) ($P$ for trend <0.0001) in women (Table 3) respectively. In addition, after adjustment for potential confounders, handgrip strength was also inversely associated with components of MetS both in men (Table 2) and women (Table 3).

Handgrip strength associated with the prevalence of MetS was tested for its ability to detect MetS by ROC curves (Fig. 1). The AUC values of handgrip strength for the detection of MetS are provided in Table 4. In men, the optimal cut-off value was 0.56 kg/kg body weight (AUC = 0.65). The corresponding sensitivity and specificity for predicting the MetS was 65.3% and 56.2%. In women, the optimal cut-off value was 0.40 kg/kg body weight (AUC = 0.71). The corresponding sensitivity and specificity for predicting the MetS was 63.0% and 67.5%.

## 4. Discussion

The findings of this study were derived from a comprehensive study in a large sample of Chinese men and women aged 40 years and older. In this cross-sectional study, we found that muscle strength is inversely associated with MetS and its components including elevated WC, TG, BP, and FPG, and reduced HDL, even after adjustment for potential confounding factors.

The overall prevalence of MetS in our population was 33.6%. This is similar to a value in a recent report from a Chinese population-based study [35], but is higher than a value reported in a systematic review of data which showed that a pooled estimate of MetS prevalence is 25% in Middle-East countries [36]. What's more, the prevalence rate in the present study is comparable to that reported in the United States, according to the data from the Third National Health and Nutrition Examination Survey (NHANES III) (4448 (29.8%) of 14,916 subjects)

**Table 3**
Relationships between handgrip strength and metabolic syndrome and its components in women[a].

| | Quartiles of handgrip strength per body weight (kg/kg) (range) | | | | $P$ for trend[b] |
|---|---|---|---|---|---|
| | Level 4 (0.49–1.20) | Level 3 (0.43–0.49) | Level 2 (0.37–0.43) | Level 1 (0.10–0.37) | |
| | 1901 | 1899 | 1902 | 1901 | |
| No. of metabolic syndrome | 176 | 327 | 513 | 723 | |
| Crude | 1.00 (reference) | 2.04 (1.68, 2.48)[c] | 3.62 (3.01, 4.37) | 6.01 (5.03, 7.22) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.80 (1.48, 2.21) | 2.77 (2.29, 3.36) | 3.89 (3.22, 4.71) | <0.0001 |
| Metabolic syndrome components | | | | | |
| No. of elevated WC | 422 | 775 | 1105 | 1397 | |
| Crude | 1.00 (reference) | 2.42 (2.10, 2.79) | 4.86 (4.22, 5.60) | 9.71 (8.38, 11.3) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 2.20 (1.91, 2.55) | 3.97 (3.42, 4.59) | 6.79 (5.82, 7.93) | <0.0001 |
| No. of elevated TG | 202 | 295 | 429 | 525 | |
| Crude | 1.00 (reference) | 1.55 (1.28, 1.88) | 2.45 (2.05, 2.94) | 3.21 (2.69, 3.84) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.39 (1.15, 1.69) | 1.95 (1.62, 2.35) | 2.18 (1.81, 2.63) | <0.0001 |
| No. of reduced HDL | 419 | 512 | 580 | 665 | |
| Crude | 1.00 (reference) | 1.31 (1.13, 1.52) | 1.55 (1.34, 1.80) | 1.90 (1.65, 2.20) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.32 (1.14, 1.53) | 1.58 (1.37, 1.84) | 1.96 (1.68, 2.28) | <0.0001 |
| No. of elevated BP | 366 | 526 | 669 | 863 | |
| Crude | 1.00 (reference) | 1.59 (1.37, 1.86) | 2.28 (1.96, 2.64) | 3.49 (3.02, 4.04) | <0.0001 |
| Multiple adjusted [d] | 1.00 (reference) | 1.35 (1.15, 1.58) | 1.55 (1.32, 1.81) | 1.89 (1.61, 2.22) | <0.0001 |
| No. of elevated FBG | 185 | 261 | 347 | 471 | |
| Crude | 1.00 (reference) | 1.48 (1.21, 1.81) | 2.07 (1.71, 2.51) | 3.06 (2.55, 3.68) | <0.0001 |
| Multiple adjusted[d] | 1.00 (reference) | 1.28 (1.04, 1.57) | 1.51 (1.24, 1.85) | 1.83 (1.51, 2.24) | <0.0001 |

[a] WC: waist circumference; TG, triglycerides; HDL, high-density lipoprotein-cholesterol; BP, blood pressure; FBG, fasting blood glucose; CVD, cardiovascular disease.
[b] Multiple logistic regression analysis.
[c] Adjusted odds ratios (95% confidence interval) (all such values).
[d] Adjusted for age, smoking status, drinking status, physical activity, educational levels, household income, total energy intake, and family history of diseases (including CVD, hypertension, hyperlipidemia, and diabetes).

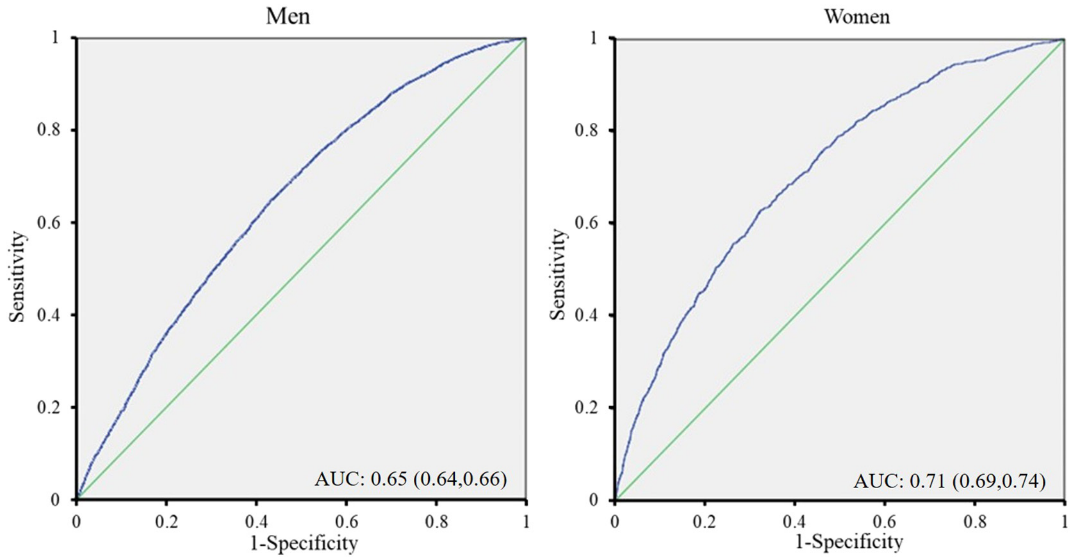


**Fig. 1.** Receiver operating characteristic (ROC) curves of the normalized handgrip strength [measured as handgrip strength (kg)/body weight (kg)], to detect subjects with metabolic syndrome in both sexes. AUC: area under the curve (95% confidence interval).

[37]. Similar to its significant prevalence in developed countries, MetS has been emerging as a serious health problem in developing countries. Western lifestyle may have contributed to this phenomenon.

Several studies have investigated the relationship between muscle strength and MetS. Most of the studies have, however, included a relative small sample size, or mainly focused on older adults [38–41]. Sayer et al. reported that impaired grip strength is associated with the individual features of the metabolic syndrome including higher fasting TG, BP and WC as well as with the overall summary definitions of MetS in men and women aged 59–73 years [40]. Vieira DC, et al. showed that elderly women with MetS have lower functional capacity, and muscle strength as compared to women without MetS [38]. In addition, Yang EJ, et al. found a significant association between reduced muscle strength and MetS, particularly in older men, after controlling for confounding factors [41]. Our analyses showed that handgrip strength was inversely independent associated with MetS and its separate components in both men and women which were consisted with above findings.

In our study, association of MetS with reduced handgrip strength remained significant even after controlling for confounding factors, such as demographics, lifestyle, total energy intake, and family history of disease. This finding suggests that muscle weakness in MetS cannot be explained solely by energy intake or physical inactivity but, rather, may have a specific pathophysiological pathway.

On the one hand, skeletal muscle, as a target organ for insulin action, plays an important role in insulin sensitivity and insulin resistance, which are important factors in the pathophysiology of metabolic disorders [42,43]. Moreover, skeletal muscle can release hundreds of factors which can exert endocrine effects. These factors were classified as myokines such as irisin and myonectin [34,44]. Impaired secretion and action of myokines, may contribute to a higher level of proinflammatory adipokines that promotes pathological process such as type 2 diabetes, cardiovascular disease and MetS [45,46]. Therefore, it is plausible that skeletal muscle could have protective effects and counteract the harmful effects of proinflammatory adipokines for MetS by secreting various myokines.

**Table 4**
Threshold of handgrip strength associated with metabolic syndrome[a].

| | Optimal cut-off value (kg/kg body weight) | Sensitivity | Specificity | AUC (95%CI) |
|---|---|---|---|---|
| Men | 0.56 | 65.3% | 56.2% | 0.65 (0.64, 0.66) |
| Women | 0.40 | 63.0% | 67.5% | 0.71 (0.69, 0.74) |

[a] AUC: area under the ROC curve; CI: confidence interval.

Compared with previous studies the present study has several advantages. Firstly, this was a large population-based analysis using well-examined data, which strengthens the statistical reliability of the results. Secondly, we adjusted statistically for as many other potential confounding factors as possible, such as sociodemographic variables, lifestyle factors, socioeconomic status, and family history of diseases. To appreciate these advantages, several limitations should be taken into consideration. Firstly, we cannot demonstrate a causal relation because of the cross-sectional study design. Secondly, although we adjusted for a considerable number of potentially confounding factors, we cannot exclude the possibility that MetS is affected by other variables such as hormone levels, which is intrinsically related to muscle strength. Thirdly, serum insulin levels were not measured in the present study. Therefore, homeostasis model assessment of insulin resistance (HOMA-IR) (an indirect marker of IR) cannot be calculated. Further studies are needed to confirm whether handgrip strength is associated with MetS by mediating insulin-signaling pathway. Finally, the study population was comprised of middle aged and older Asians, which limits the generalizability of results to other populations.

In conclusion, this study suggests that handgrip strength is inversely associated with MetS and its components in adult men and women aged 40 years and older. Future prospective and intervention studies should examine the association between muscle strength and MetS and determine if increasing muscle strength reduces the likelihood of MetS.

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## Declarations of Interest

None.

## Authors' Contributions

The authors' responsibilities were as follows: J. S. H., J. H., B. Z., G. D. and K. N designed research. H. W., M. L., V. T. Q. C., J. W., Q. Z., L. L., G. M., Z. Y., X. B., Y. G., S. Z., S. S., M. Z., Q. J. and K. S. conducted research. H. W. and K. N analyzed data; and H. W. wrote the paper. H.W. and K.N. revised the manuscript for important intellectual contents. K. N had primary responsibility for final content. All authors approved the final manuscript.

## References


[1] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640–5. https://doi.org/10.1161/CIRCULATIONAHA.109.192644.

[2] Younis A, Younis A, Tzur B, Peled Y, Shlomo N, Goldenberg I, et al. Metabolic syndrome is independently associated with increased 20-year mortality in patients with stable coronary artery disease. Cardiovasc Diabetol 2016;15:149. https://doi.org/10.1186/s12933-016-0466-6.

[3] Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005;365:1415–28. https://doi.org/10.1016/S0140-6736(05)66378-7.

[4] Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. J Am Coll Cardiol 2010;56:1113–32. https://doi.org/10.1016/j.jacc.2010.05.034.

[5] Grundy SM. Metabolic syndrome update. Trends Cardiovasc Med 2016;26:364–73. https://doi.org/10.1016/j.tcm.2015.10.004.

[6] Lundell LS, Massart J, Altintas A, Krook A, Zierath JR. Regulation of glucose uptake and inflammation markers by FOXO1 and FOXO3 in skeletal muscle. Mol Metab 2018. https://doi.org/10.1016/j.molmet.2018.09.011.

[7] Cheng YJ, Gregg EW, De Rekeneire N, Williams DE, Imperatore G, Caspersen CJ, et al. Muscle-strengthening activity and its association with insulin sensitivity. Diabetes Care 2007;30:2264–70. https://doi.org/10.2337/dc07-0372.

[8] Mizgier ML, Casas M, Contreras-Ferrat A, Llanos P, Galgani JE. Potential role of skeletal muscle glucose metabolism on the regulation of insulin secretion. Obes Rev 2014;15:587–97. https://doi.org/10.1111/obr.12166.

[9] Bentley DC, Nguyen CHP, Thomas SG. High-intensity handgrip training lowers blood pressure and increases heart rate complexity among postmenopausal women: a pilot study. Blood Press Monit 2018;23:71–8. https://doi.org/10.1097/MBP.0000000000000313.

[10] Baker JF, Mostoufi-Moab S, Long J, Zemel B, Ibrahim S, Taratuta E, et al. Intramuscular fat accumulation and associations with body composition, strength, and physical functioning in patients with rheumatoid arthritis. Arthritis Care Res (Hoboken) 2018;70:1727–34. https://doi.org/10.1002/acr.23550.

[11] DeFronzo RA, Gunnarsson R, Bjorkman O, Olsson M, Wahren J. Effects of insulin on peripheral and splanchnic glucose metabolism in noninsulin-dependent (type II) diabetes mellitus. J Clin Invest 1985;76:149–55. https://doi.org/10.1172/JCI111938.

[12] Kewalramani G, Bilan PJ, Klip A. Muscle insulin resistance: assault by lipids, cytokines and local macrophages. Curr Opin Clin Nutr Metab Care 2010;13:382–90. https://doi.org/10.1097/MCO.0b013e32833aabd9.

[13] Li F, Li Y, Duan Y, Hu CA, Tang Y, Yin Y. Myokines and adipokines: involvement in the crosstalk between skeletal muscle and adipose tissue. Cytokine Growth Factor Rev 2017;33:73–82. https://doi.org/10.1016/j.cytogfr.2016.10.003.

[14] Ouchi N, Ohashi K, Shibata R, Murohara T. Protective roles of adipocytokines and myokines in cardiovascular disease. Circ J 2016;80:2073–80. https://doi.org/10.1253/circj.CJ-16-0663.

[15] Zhao Y, Li N, Li Z, Zhang D, Chen L, Yao Z, et al. Conditioned medium from contracting skeletal muscle cells reverses insulin resistance and dysfunction of endothelial cells. Metabolism 2018;82:36–46. https://doi.org/10.1016/j.metabol.2017.12.008.

[16] Nielsen AR, Hojman P, Erikstrup C, Fischer CP, Plomgaard P, Mounier R, et al. Association between interleukin-15 and obesity: interleukin-15 as a potential regulator of fat mass. J Clin Endocrinol Metab 2008;93:4486–93. https://doi.org/10.1210/jc.2007-2561.

[17] McPherron AC, Lawler AM, Lee SJ. Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member. Nature 1997;387:83–90. https://doi.org/10.1038/387083a0.

[18] Liu XH, Bauman WA, Cardozo CP. Myostatin inhibits glucose uptake via suppression of insulin-dependent and -independent signaling pathways in myoblasts. Physiol Rep 2018;6:e13837. https://doi.org/10.14814/phy2.13837.

[19] Lee MJ, Lee SA, Nam BY, Park S, Lee SH, Ryu HJ, et al. Irisin, a novel myokine is an independent predictor for sarcopenia and carotid atherosclerosis in dialysis patients. Atherosclerosis 2015;242:476–82. https://doi.org/10.1016/j.atherosclerosis.2015.08.002.

[20] Bang HS, Seo DY, Chung YM, Oh KM, Park JJ, Arturo F, et al. Ursolic acid-induced elevation of serum irisin augments muscle strength during resistance training in men. Korean J Physiol Pharmacol 2014;18:441–6. https://doi.org/10.4196/kjpp.2014.18.5.441.

[21] Chang JS, Kim TH, Nguyen TT, Park KS, Kim N, Kong ID. Circulating irisin levels as a predictive biomarker for sarcopenia: a cross-sectional community-based study. Geriatr Gerontol Int 2017;17:2266–73. https://doi.org/10.1111/ggi.13030.

[22] Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum Jr A, Orlandini A, et al. Prognostic value of grip strength: findings from the prospective urban rural epidemiology (PURE) study. Lancet 2015;386:266–73. https://doi.org/10.1016/S0140-6736(14)62000-6.

[23] Gomez-Cabello A, Carnicero JA, Alonso-Bouzon C, Tresguerres JA, Alfaro-Acha A, Ara I, et al. Age and gender, two key factors in the associations between physical activity and strength during the ageing process. Maturitas 2014;78:106–12. https://doi.org/10.1016/j.maturitas.2014.03.007.

[24] Leong DP, Teo KK, Rangarajan S, Kutty VR, Lanas F, Hui C, et al. Reference ranges of handgrip strength from 125, 462 healthy adults in 21 countries: a prospective urban rural epidemiologic (PURE) study. J Cachexia Sarcopenia Muscle 2016;7:535–46. https://doi.org/10.1002/jcsm.12112.

[25] Checkoway H, Pearce N, Dement JM. Design and conduct of occupational epidemiology studies: I. Design aspects of cohort studies. Am J Ind Med 1989;15:363–73.

[26] Sun S, Wu H, Zhang Q, Wang C, Guo Y, Du H, et al. Subnormal peripheral blood leukocyte counts are related to the lowest prevalence and incidence of metabolic syndrome: Tianjin chronic low-grade systemic inflammation and health cohort study. Mediators Inflamm 2014;2014:412386. https://doi.org/10.1155/2014/412386.

[27] Wu H, Wei M, Zhang Q, Du H, Xia Y, Liu L, et al. Consumption of chilies, but not sweet peppers, is positively related to handgrip strength in an adult population. J Nutr Health Aging 2016;20:546–52. https://doi.org/10.1007/s12603-015-0628-3.

[28] McGrath R, Vincent BM, Al Snih S, Markides KS, Peterson MD. The association between muscle weakness and incident diabetes in older Mexican Americans. J Am Med Dir Assoc 2017;18:452.e7–452.e12. https://doi.org/10.1016/j.jamda.2017.01.017.

[29] Peterson MD, Zhang P, Choksi P, Markides KS, Al Snih S. Muscle weakness thresholds for prediction of diabetes in adults. Sports Med 2016;46:619–28. https://doi.org/10.1007/s40279-015-0463-z.

[30] Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ). http://www.ipaq.ki.se/scoring.pdf; 2005, Accessed date: 25 May 2018.

[31] Jia Q, Xia Y, Zhang Q, Wu H, Du H, Liu L, et al. Dietary patterns are associated with prevalence of fatty liver disease in adults. Eur J Clin Nutr 2015;69:914–21. https://doi.org/10.1038/ejcn.2014.297.

[32] Yang Y, Wang G, Pan X. Chinese food composition tables. 2nd ed. Beijing: Peking University Medical Press; 2009.

[33] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. Age Ageing 2010;39:412–23. https://doi.org/10.1093/ageing/afq034.

[34] Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian working Group for Sarcopenia. J Am Med Dir Assoc 2014;15:95–101. https://doi.org/10.1016/j.jamda.2013.11.025.

[35] Song K, Du H, Zhang Q, Wang C, Guo Y, Wu H, et al. Serum immunoglobulin M concentration is positively related to metabolic syndrome in an adult population: Tianjin chronic low-grade systemic inflammation and health (TCLSIH) cohort study. PLoS One 2014;9:e88701. https://doi.org/10.1371/journal.pone.0088701.

[36] Ansarimoghaddam A, Adineh HA, Zareban I, Iranpour S, HosseinZadeh A, Kh F. Prevalence of metabolic syndrome in middle-east countries: meta-analysis of cross-sectional studies. Diabetes Metab Syndr 2018;12:195–201. https://doi.org/10.1016/j.dsx.2017.11.004.

[37] Gathirua-Mwangi WG, Monahan PO, Murage MJ, Zhang J. Metabolic syndrome and total cancer mortality in the third national health and nutrition examination survey. Cancer Causes Control 2017;28:127–36. https://doi.org/10.1007/s10552-016-0843-1.

[38] Vieira DC, Tibana RA, Tajra V, Nascimento Dda C, de Farias DL, Silva Ade O, et al. Decreased functional capacity and muscle strength in elderly women with metabolic syndrome. Clin Interv Aging 2013;8:1377–86. https://doi.org/10.2147/CIA.S50333.

[39] Atlantis E, Martin SA, Haren MT, Taylor AW, Wittert GA, Members of the Florey Adelaide Male Ageing S. Inverse associations between muscle mass, strength, and the metabolic syndrome. Metabolism 2009;58:1013–22. https://doi.org/10.1016/j.metabol.2009.02.027.

[40] Sayer AA, Syddall HE, Dennison EM, Martin HJ, Phillips DI, Cooper C, et al. Grip strength and the metabolic syndrome: findings from the Hertfordshire cohort study. QJM 2007;100:707–13. https://doi.org/10.1093/qjmed/hcm095.

[41] Yang EJ, Lim S, Lim JY, Kim KW, Jang HC, Paik NJ. Association between muscle strength and metabolic syndrome in older Korean men and women: the Korean longitudinal study on health and aging. Metabolism 2012;61:317–24. https://doi.org/10.1016/j.metabol.2011.07.005.

[42] Warren JL, Bulur S, Ovalle F, Windham ST, Gower BA, Fisher G. Effects of acute hyperinsulinemia on skeletal muscle mitochondrial function, reactive oxygen species production, and metabolism in premenopausal women. Metabolism 2017;77:1–12. https://doi.org/10.1016/j.metabol.2017.08.004.

[43] Barlow J, Solomon TPJ. Conditioned media from contracting skeletal muscle potentiates insulin secretion and enhances mitochondrial energy metabolism of pancreatic beta-cells. Metabolism 2019;91:1–9. https://doi.org/10.1016/j.metabol.2018.11.004.

[44] Millar PJ, Levy AS, McGowan CL, McCartney N, MacDonald MJ. Isometric handgrip training lowers blood pressure and increases heart rate complexity in medicated

hypertensive patients. Scand J Med Sci Sports 2013;23:620–6. https://doi.org/10.1111/j.1600-0838.2011.01435.x.

[45] Li K, Liao X, Wang K, Mi Q, Zhang T, Jia Y, et al. Myonectin predicts the development of type 2 diabetes. J Clin Endocrinol Metab 2018;103:139–47. https://doi.org/10.1210/jc.2017-01604.

[46] Otaka N, Shibata R, Ohashi K, Uemura Y, Kambara T, Enomoto T, et al. Myonectin is an exercise-induced myokine that protects the heart from ischemia-reperfusion injury. Circ Res 2018;123:1326–38. https://doi.org/10.1161/CIRCRESAHA.118.313777.