Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

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ORIGINAL RESEARCH

# Relative handgrip strength as a marker of metabolic syndrome: the Korea National Health and Nutrition Examination Survey (KNHANES) VI (2014–2015)

This article was published in the following Dove Press journal:
Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

Dongwon Yi[1,2]
Ah Reum Khang[1,2]
Hye Won Lee[1,2]
Seok Man Son[1,2]
Yang Ho Kang[1,2]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, Yangsan, Korea; [2]Research Institute for Convergence of Biomedical Science and Technology, Pusan National University Yangsan Hospital, Yangsan, Korea

Correspondence: Yang Ho Kang
Division of Endocrinology and Metabolism, Department of Internal Medicine, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, 20 Geumo-ro, Mulgeum-eup, Yangsan 50612, Korea
Tel +82 55 360 1444
Fax +82 55 360 1565
Email kangyh@pusan.ac.kr

**Purpose:** Muscles play an important role in energy metabolism. Several studies have investigated the association between muscle mass and metabolic syndrome (MetS), reporting conflicting results. However, studies concerning the association between muscle strength and MetS are limited. We aimed to investigate the association between relative handgrip strength (HGS) and MetS in Korean adults.

**Participants and methods:** We analyzed data from 5,014 Korean adults aged ≥20 years (2,472 men and 2,542 women) who participated in the Korea National Health and Nutrition Examination Survey (KNHANES) VI (2014–2015).

**Results:** The increasing quartiles of relative HGS (defined as the sum of both hands' HGS divided by body mass index) were inversely associated with the risk of MetS in both men and women (OR, 0.37; 95% CI, 0.30–0.45, vs OR, 0.19; 95% CI, 0.14–0.27, respectively) after multivariable adjustment for age, region of residence, smoking status, heavy alcohol consumption, regular exercise, family income, and education level. On multivariable logistic regression analyses, participants with the highest relative HGS had a significant decrease in relative risk of MetS, compared with those with the lowest relative HGS. The multivariable-adjusted ORs (with 95% CIs) for MetS in quartiles 1, 2, 3, and 4 were 1.00, 0.72 (0.55–0.94), 0.34 (0.26–0.46), and 0.22 (0.15–0.32) in men and 1.00, 0.50 (0.36–0.68), 0.26 (0.17–0.40), and 0.16 (0.09–0.27) in women, respectively.

**Conclusion:** Relative HGS showed a highly significant inverse association with the risk of MetS in Korean adults, and it can be a novel biomarker for assessing the risk of MetS.

**Keywords:** hand strength, metabolic syndrome X, adult, Korea, nutrition surveys

## Plain language summary

Handgrip strength (HGS) is a simple, convenient, and fast method for assessing total muscle strength. In recent studies, relative HGS, defined as the sum of both hands' HGS divided by body mass index, showed a strong correlation with cardiovascular biomarkers. Metabolic syndrome (MetS), a cluster of cardiometabolic risk factors, including central obesity, dyslipidemia, hypertension, and abnormal glucose tolerance, is associated with the risk of insulin resistance, type 2 diabetes mellitus, cardiovascular disease, and increased all-cause mortality. Therefore, we aimed to investigate the association between relative HGS and MetS. We analyzed data from 5,014 Korean adults aged ≥20 years (2,472 men and 2,542 women) who participated in the Korea National Health and Nutrition Examination Survey (KNHANES) VI (2014–2015). Relative HGS showed a highly significant inverse association with the risk of MetS, independent

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http://dx.doi.org/10.2147/DMSO.S166875

of age, health behaviors (smoking status, heavy alcohol consumption, and regular exercise), and sociodemographic factors (region of residence, family income, and education level). Relative HGS can be a novel biomarker for assessing the risk of MetS.

## Introduction

Sarcopenia is the age-related loss of muscle mass and strength,[1,2] leading to impaired physical performance, as well as frailty, in the elderly.[3] As muscle plays an important role in energy metabolism, sarcopenia is known to be associated with metabolic disorders, such as obesity, insulin resistance, type 2 diabetes mellitus, and hence, metabolic syndrome (MetS).[2,4–6] In general, the diagnosis of sarcopenia is mainly based on the measurement of appendicular skeletal muscle mass by dual-energy X-ray absorptiometry or bioelectrical impedance analysis.[7] However, previous studies have demonstrated that decline in muscle strength may be a better predictor of clinical outcomes than low muscle mass.[8,9]

Handgrip strength (HGS), a measurement of the maximum voluntary force of the hands, is a simple, convenient, and fast method for the assessment of total muscle strength, and it strongly correlates with leg strength.[7,10] HGS measured in a seated position or a standing position reflects the muscle strength of the upper limb, or the lower limbs/core muscle, respectively.[11] Therefore, recent consensus reports on the definition, diagnosis, and management of sarcopenia by various working groups, including the Asian Working Group for Sarcopenia (AWGS), the European Working Group on Sarcopenia in Older People, and the Foundation for the National Institutes of Health Sarcopenia Project, accepted HGS as one of the recommended tools in the diagnostic algorithm for sarcopenia.[7,10,12,13] The AWGS defined low muscle strength as HGS of <26 kg in men and <18 kg in women; however, the cutoff points of HGS varied among different studies, which should be stratified by the body mass index (BMI).[12] Therefore, muscle strength adjusted for BMI has been recommended to minimize the confounding effect of body size.[13,14] Epidemiological studies demonstrated the association between HGS and nutritional status,[15] frailty,[16] functional capacity,[17,18] diabetes mellitus,[19] MetS,[20] cardiovascular disease (CVD),[21] and mortality,[22,23] Furthermore, handgrip, as isometric muscle contraction, has been recently used to evaluate changes in key elements of cardiac afterload in pre and postmenopausal women.[24] However, different HGS indexes, such as dominant HGS (maximal HGS of the dominant hand), absolute HGS (summation of maximal HGS of each hand) with or without adjustment with weight (HGS/Wt) or height (HGS/Ht), have been used in each study, as there is no standard HGS index yet. In recent nationwide population-based studies, relative HGS, defined as absolute HGS divided by BMI (HGS/BMI), showed stronger correlation with cardiovascular biomarkers than absolute HGS and dominant HGS.[21,25]

MetS, a cluster of cardiometabolic risk factors, including central obesity, dyslipidemia, hypertension, and abnormal glucose tolerance, is associated with the risk of insulin resistance,[4] type 2 diabetes mellitus, CVD, and increased all-cause mortality.[26] Several studies have investigated the association between muscle mass and MetS, reporting conflicting results. However, to our knowledge, studies concerning the association between relative HGS and MetS have never been reported.

Therefore, we aimed to examine the relationship of relative HGS as a marker of muscle strength and MetS by using representative data from Korean adults who participated in the Korea National Health and Nutrition Examination Survey (KNHANES) VI 2014–2015.

## Participants and methods

### Study population

We analyzed data from the second and third years (2014–2015) of the KNHANES VI (2013–2015) study. KNHANES is a nationwide, population-based, cross-sectional study that has been conducted periodically since 1998 by the Korea Centers for Disease Control and Prevention to assess the health and nutritional status of the Korean civilian, noninstitutionalized population. Data were obtained using complex, stratified, multistage probability sampling to achieve representativeness of the population.[27–29] The survey has been conducted annually since 2008, and ~6,000–10,000 participants are included per year. Each survey consists of three sections: health interview, health examinations, and nutritional survey. In 2014 and 2015, the surveys were completed by 7,550 (77.8% of the total target population of 9,701) and 7,380 (77.6% of the total target population of 9,505) participants, respectively.

Of these 14,930 subjects, those aged ≥20 years (n=11,752) were selected for analysis in this study. We excluded those who were pregnant; with fasting time of <8 hours; with missing laboratory data, including levels of lipids, fasting plasma glucose (FPG), and hemoglobin A1c (HbA1c); with missing data on HGS measurement; with chronic diseases, including liver cirrhosis, viral hepatitis, and chronic kidney disease; with a history of myocardial infarction or angina, stroke, or any kind of malignancy; and with abnormal laboratory data, including serum levels of aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than three times the upper limit of the reference range, creatinine ≥1.5 mg/dL,

and white blood cell count >10,000 cells/mL. Participants lacking sufficient sociodemographic data, including age, sex, waist circumference, BMI, blood pressure, region of residence, smoking and alcohol consumption, regular exercise, family income, and education level, were also excluded. Finally, a total of 5,014 participants (2,472 men and 2,542 women), with a weighted total of 39,679,327 participants (22,176,994 men and 17,502,333 women), were included in the analysis (Figure 1). All participants of the KNHANES provided written informed consent for their data to be used in the study. The study was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention (2013-12EXP-03-5, 2015-01-02-6C), and the Institutional Review Board of Pusan National University Yangsan Hospital determined that this study was exempt from requiring their approval (IRB No 05-2017-117).

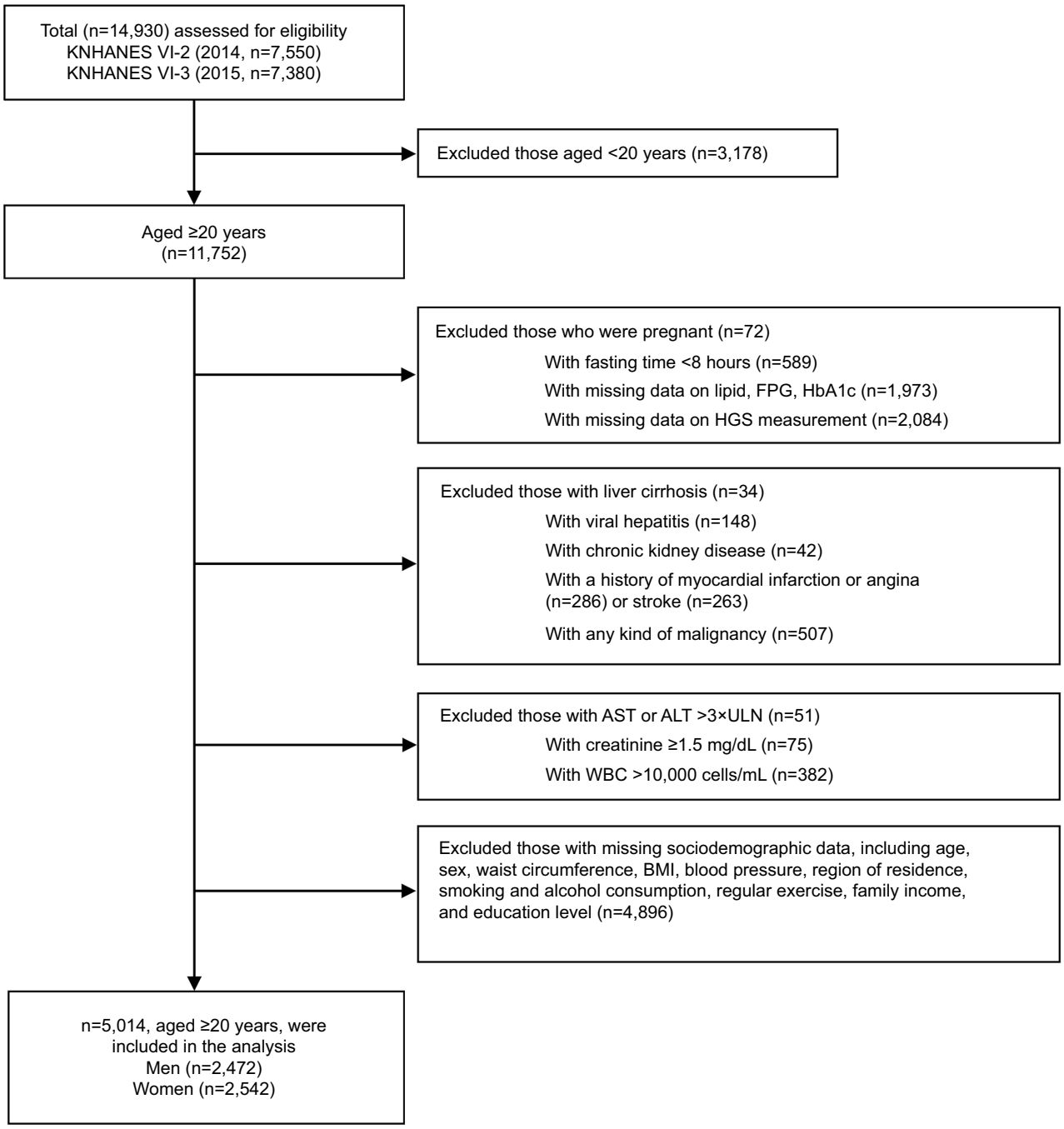


**Figure 1** Flowchart of participants throughout the study.
**Abbreviations:** KNHANES, Korea National Health and Nutrition Examination Survey; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; HGS, handgrip strength; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ULN, upper limit of normal; WBC, white blood cell; BMI, body mass index.

## Data collection

The health examinations included medical history taking, physical examination, and administration of a questionnaire on health-related behaviors, as well as anthropometric and biochemical measurements. Physical examinations were performed by trained medical staff following standardized procedures, and blood sampling was performed in all individuals aged ≥20 years. Participants were asked about health-related behaviors, including cigarette smoking, alcohol consumption, and regular exercise. Smoking status was indicated as "yes" when the participants had smoked more than five packs of cigarettes (100 cigarettes) during their lifetime and were smoking at the time of the survey. A standard drink was defined as a single glass of beer, wine, liquor, or the Korean traditional distilled liquor, Soju. One bottle of beer (355 mL) was counted as 1.6 standard drinks. The amount of alcohol per standard drink was calculated to be 10 g. Heavy alcohol drinking was indicated as "yes" when the participant had at least seven drinks at one time, more than twice a week, for men (at least five drinks for women). Regular exercise was indicated as "yes" when the participant performed moderate or strenuous exercise on a regular basis, regardless of indoor or outdoor exercise (>2 hours and 30 minutes per week for moderate exercise that causes slightly increased respiration and heart rate; >1 hour and 15 minutes for strenuous exercise that causes rapid respiration and a substantial increase in heart rate), or when the participant walked for a minimum of 30 minutes each day for 5 days/week. If they were being treated for any disease, they were asked for data on the diagnosis and a list of medications being taken. The completed questionnaires were reviewed by trained staff, and the records were entered into a database.

## Anthropometric and biochemical data

Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, with participants wearing light clothing and being barefooted. BMI was calculated as weight in kilograms divided by the square of height in meters. Blood pressure was measured on the right arm using a standard mercury sphygmomanometer (Baumanometer Wall Unit 33(0850), W.A. Baum Co. Inc., Copiague, NY, USA), with the participant in the sitting position. Systolic and diastolic blood pressure (SBP and DBP, respectively) readings were recorded twice at 5-minute intervals and averaged for analysis. Waist circumference was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest at the end of a normal expiration with the arms relaxed at the sides.

Blood samples were collected from the antecubital vein of each participant in the morning after overnight fasting for at least 8 hours, processed, transferred in cold storage (2°C–8°C) to the central laboratory of Neodin Medical Institute (Seoul, Korea), and analyzed within 24 hours. Measurements of FPG, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, total cholesterol, triglycerides, AST, ALT, blood urea nitrogen (BUN), and creatinine levels were performed using a Hitachi automatic analyzer 7600-210 (Hitachi Ltd, Tokyo, Japan). HbA1c levels were measured with a G8 automated high-performance liquid chromatography analyzer (Tosoh Corp, Tokyo, Japan).

## Sociodemographic factors

The participants were asked to provide data on sociodemographic factors, including region of residence, family income, and education level. Region of residence was categorized as rural and urban. Among the 16 administrative districts where this survey was conducted, Seoul, Gyeonggi, and six other metropolitan cities (Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) were defined as urban areas. The remaining regions were defined as rural areas. Based on the national median household income, family income was categorized into quartiles as lowest (<25th percentile), medium-lowest (25th–49th percentile), medium-highest (50th–74th percentile), and highest (≥75th percentile). Meanwhile, education level was classified as elementary school or less, middle school graduate, high school graduate, and college graduate or higher.

## HGS measurement

HGS was measured using a digital hand dynamometer (Digital Grip Dynamometer, TKK 5401, Takei Scientific Instruments Co, Ltd, Tokyo, Japan). Grip strength was measured with the participant in a standing position and with the arms fully extended at the sides, not touching the body. The participants were asked to squeeze the dynamometer with as much force as possible, for <3 seconds, three times with each hand alternatively. At least 30 seconds of rest interval was allowed between each trial. Absolute HGS was calculated as the summation of the maximal reading from each hand and was expressed in kilograms. Relative HGS was defined as the absolute HGS divided by BMI.

## Definition of MetS

MetS was defined according to the combined definition from the International Diabetes Federation (IDF), the American Heart Association, and the National Heart, Lung, and Blood Institute.[30]

The presence of three or more of the following criteria was used to define MetS:

1. Central obesity, waist circumference (≥90 cm for men and ≥85 cm for women) based on the Korean abdominal obesity criteria for waist circumference[31]
2. Triglycerides ≥150 mg/dL or current use of triglyceride-lowering medication
3. HDL cholesterol <40 mg/dL in men and <50 mg/dL in women
4. SBP ≥130 mmHg or DBP ≥85 mmHg or current use of antihypertensive medication
5. FPG ≥100 mg/dL, current use of antihyperglycemic medication, or previous diagnosis of type 2 diabetes

## Statistical analysis

Statistical analysis was performed with SAS version 9.3 (SAS Institute, Inc, Cary, NC, USA), using sampling weights from the KNHANES to acquire nationally representative estimates. The data in this study were presented as weighted means or weighted proportions with standard errors for continuous or categorical variables, respectively. Due to significant differences in HGS by sex, data for men and women were separated for further analysis. Logarithmic transformation was used to analyze variables with skewed distributions, including levels of FPG, triglycerides, HbA1c, AST, ALT, and BUN. Adjusted variables included age, sex, region of residence, smoking status, heavy alcohol consumption, regular exercise, family income, and education level. MetS components and other clinical variables by sex were compared in participants with and without MetS using the linear regression model (PROC SURVEYREG in SAS) or chi-square test (PROC SURVEYFREQ in SAS). Age-adjusted regression coefficients were also calculated using PROC SURVEYREG in SAS. The participants were divided into four groups according to the quartiles of relative HGS distribution: first (0.6–3.1), second (3.1–3.5), third (3.5–4.0), and fourth (4.0–5.9) in men and first (0.9–2.0), second (2.0–2.3), third (2.3–2.6), and fourth (2.6–3.7) in women. The prevalence of MetS in each quartile was indicated as a percentage and compared using the chi-square test (PROC SURVEYFREQ in SAS). Finally, the ORs and corresponding 95% CIs for the highest quartile of relative HGS (fourth) were calculated as estimates of relative risk of MetS using the logistic regression model (PROC SURVEYLOGISTIC in SAS; with the lowest quartile [first] used as the reference category), which consisted of the unadjusted model, age-adjusted model (Model 1), and the multivariable-adjusted model (Model 2, adjusted for the earlier-mentioned variables). All tests for statistical significance were two tailed, and $p$-values <0.05 were considered significant.

# Results

## Clinical characteristics of the study population by sex in relation to the presence of MetS

Sex-specific characteristics of the 2,472 men and 2,542 women in relation to the presence of MetS are shown in Table 1. The mean age was 42.7±0.35 years for men and 42.2±0.34 years for women. The prevalence of MetS in the total population, in men, and in women was 21.7%, 27.6%, and 14.3%, respectively (not shown in Table 1). The mean age, BMI, and MetS components (waist circumference, SBP, DBP, FPG, and triglyceride levels) were significantly higher in both sexes with MetS, whereas the HDL cholesterol level was lower in both sexes with MetS. Moreover, HbA1c, AST, ALT, BUN, and creatinine levels were significantly higher in members of both sexes with MetS than in those without MetS.

Dominant HGS and absolute HGS were significantly higher in men with MetS than in those without MetS (43.9±0.4 kg vs 43.5±0.2 kg, $p$=0.001; and 85.6±0.7 kg vs 84.8±0.4 kg, $p$=0.001, respectively); there were no statistical differences in women. In contrast, relative HGS was significantly lower in both men and women with MetS than in those without MetS (3.24±0.02 vs 3.64±0.02, $p$<0.001, and 1.93±0.02 vs 2.35±0.01, $p$<0.001, respectively).

The proportion of urban residents in the MetS group was significantly lower in men (72.9% vs 73.4%; $p$=0.047), but not in women (72.0% vs 76.4%; $p$=0.095). The proportion of heavy alcohol consumption in the MetS group was significantly higher in men (35.1% vs 18.5%; $p$<0.001), but not in women (7.0% vs 5.8%; $p$=0.553). Moreover, the proportion of people doing regular exercise in the MetS group was significantly lower among women (55.6% vs 63.1%; $p$=0.009), but not among men (64.4% vs 67.1%; $p$=0.232). The prevalence of MetS significantly increased according to increasing quartiles of family income in women, but not in men. Furthermore, the prevalence of MetS significantly increased according to the increasing level of education in both sexes.

## Age-adjusted regression coefficients for relative HGS and clinical characteristics by sex

The regression coefficients adjusted for age between relative HGS and clinical variables are shown in Table 2. In both

**Table 1** Characteristics of men and women in relation to the presence of MetS

| Variables | Men (n=2,472/22,176,994) | | *p*-value | Women (n=2,542/17,502,333) | | *p*-value |
|---|---|---|---|---|---|---|
| | MetS (n=753/6,119,167) | Non-MetS (n=1,719/16,057,827) | | MetS (n=441/2,496,987) | Non-MetS (n=2,101/15,005,346) | |
| Age, years | 48.8 (0.55) | 40.5 (0.41) | <0.0001 | 54.0 (0.70) | 40.2 (0.34) | <0.0001 |
| Height, cm | 171.69 (0.30) | 172.21 (0.18) | <0.0001 | 156.74 (0.33) | 159.42 (0.15) | <0.0001 |
| Weight, cm | 78.84 (0.59) | 69.71 (0.29) | <0.0001 | 66.24 (0.68) | 56.22 (0.21) | <0.0001 |
| BMI, kg/m$^2$ | 26.64 (0.15) | 23.47 (0.08) | <0.0001 | 26.88 (0.22) | 22.13 (0.08) | <0.0001 |
| Waist circumference, cm | 92.22 (0.36) | 82.42 (0.22) | <0.0001 | 88.26 (0.46) | 74.56 (0.23) | <0.0001 |
| SBP, mmHg | 126.89 (0.61) | 115.52 (0.36) | <0.0001 | 124.25 (0.90) | 108.47 (0.34) | <0.0001 |
| DBP, mmHg | 83.79 (0.43) | 76.01 (0.27) | <0.0001 | 78.57 (0.59) | 71.16 (0.23) | <0.0001 |
| FPG, mg/dL | 111.65 (1.11) | 95.01 (0.43) | <0.0001 | 111.45 (1.63) | 91.28 (0.31) | <0.0001 |
| Total cholesterol, mg/dL | 197.47 (1.65) | 187.27 (0.92) | <0.0001 | 201.32 (2.29) | 185.83 (0.79) | <0.0001 |
| Triglyceride, mg/dL | 257.66 (7.33) | 129.93 (2.76) | <0.0001 | 189.87 (5.11) | 87.79 (1.18) | <0.0001 |
| HDL cholesterol, mg/dL | 41.89 (0.37) | 50.71 (0.31) | <0.0001 | 44.90 (0.52) | 58.73 (0.29) | <0.0001 |
| LDL cholesterol, mg/dL | 104.05 (1.88) | 110.57 (0.86) | <0.0001 | 118.45 (2.06) | 109.54 (0.70) | <0.0001 |
| HbA1c (%) | 5.95 (0.04) | 5.49 (0.02) | <0.0001 | 6.11 (0.06) | 5.42 (0.01) | <0.0001 |
| AST, IU/L | 26.91 (0.41) | 22.30 (0.23) | <0.0001 | 24.48 (0.61) | 18.81 (0.14) | <0.0001 |
| ALT, IU/L | 32.47 (0.86) | 22.67 (0.38) | <0.0001 | 25.03 (0.93) | 14.73 (0.21) | <0.0001 |
| BUN, mg/dL | 14.98 (0.19) | 14.51 (0.11) | <0.0001 | 14.53 (0.24) | 12.56 (0.09) | <0.0001 |
| Creatinine, mg/dL | 0.96 (0.01) | 0.95 (0.00) | <0.0001 | 0.72 (0.01) | 0.71 (0.00) | 0.001 |
| Dominant HGS, kg | 43.94 (0.35) | 43.47 (0.23) | 0.001 | 26.59 (0.32) | 26.52 (0.13) | 0.548 |
| Absolute HGS, kg | 85.64 (0.67) | 84.76 (0.43) | 0.001 | 51.25 (0.59) | 51.30 (0.25) | 0.784 |
| Relative HGS | 3.24 (0.02) | 3.64 (0.02) | <0.0001 | 1.93 (0.02) | 2.35 (0.01) | <0.0001 |
| Region of residence, % | | | 0.047 | | | 0.095 |
| Urban | 72.86 (2.32) | 73.37 (1.74) | | 72.02 (2.64) | 76.41 (1.63) | |
| Rural | 27.15 (2.32) | 26.63 (1.74) | | 27.98 (2.64) | 23.59 (1.63) | |
| Smoking status, % | | | 0.547 | | | 0.879 |
| Yes | 41.55 (2.27) | 39.92 (1.36) | | 6.03 (1.50) | 5.78 (0.65) | |
| No | 58.45 (2.27) | 60.08 (1.36) | | 93.97 (1.50) | 94.22 (0.65) | |
| Heavy alcohol consumption, % | | | <0.0001 | | | 0.553 |
| Yes | 35.12 (2.12) | 18.49 (1.21) | | 6.96 (1.50) | 8.00 (0.71) | |
| No | 64.88 (2.12) | 81.51 (1.21) | | 93.04 (1.50) | 92.00 (0.71) | |
| Regular exercise, % | | | 0.232 | | | 0.009 |
| Yes | 64.44 (1.99) | 67.13 (1.39) | | 55.55 (2.73) | 63.06 (1.27) | |
| No | 35.56 (1.99) | 32.87 (1.39) | | 44.45 (2.73) | 36.94 (1.27) | |
| Family income, percentile | | | 0.767 | | | <0.0001 |
| <25th | 7.96 (1.08) | 7.56 (0.73) | | 18.97 (2.11) | 8.20 (0.71) | |
| 25th–50th | 23.25 (1.88) | 21.84 (1.33) | | 26.29 (2.34) | 22.64 (1.31) | |
| 50th–75th | 31.47 (2.27) | 33.89 (1.55) | | 29.06 (2.53) | 32.24 (1.35) | |
| 75th–100th | 37.32 (2.27) | 36.72 (1.77) | | 25.68 (2.34) | 36.92 (1.58) | |
| Education level, % | | | <0.0001 | | | <0.0001 |
| Elementary school or less | 10.55 (1.14) | 6.17 (0.59) | | 32.68 (2.69) | 7.55 (0.60) | |
| Middle school graduate | 9.81 (1.29) | 5.85 (0.57) | | 13.98 (2.07) | 6.82 (0.61) | |
| High school graduate | 34.88 (2.07) | 42.79 (1.55) | | 34.78 (2.81) | 39.46 (1.29) | |
| College graduate or higher | 44.75 (2.28) | 45.19 (1.54) | | 18.57 (2.26) | 46.16 (1.36) | |

**Notes:** Data are presented as weighted means or weighted proportions (with standard errors) for continuous or categorical variables, respectively. The number of participants is presented as unweighted/weighted.

**Abbreviations:** MetS, metabolic syndrome; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, hemoglobin A1c; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; HGS, handgrip strength.

sexes, weight, BMI, waist circumference, SBP, DBP, FPG, triglycerides, HbA1c, AST, and ALT showed a significant negative correlation with relative HGS; however, height and HDL cholesterol showed a significant positive correlation with relative HGS. In women, total cholesterol and LDL cholesterol showed a significant negative correlation, while creatinine showed a significant positive correlation, with relative HGS.

**Table 2** Age-adjusted regression coefficients for relative handgrip strength and various characteristics by sex

| Variables | Men (n=2,472/22,176,994) | | | | Women (n=2,542/17,502,333) | | | |
|---|---|---|---|---|---|---|---|---|
| | Beta | 95% CI | | *p*-value | Beta | 95% CI | | *p*-value |
| | | Lower | Upper | | | Lower | Upper | |
| Height | 0.022 | 0.017 | 0.027 | <0.0001 | 0.028 | 0.024 | 0.031 | <0.0001 |
| Weight | –0.018 | –0.02 | –0.015 | <0.0001 | –0.016 | –0.018 | –0.013 | <0.0001 |
| BMI | –0.090 | –0.098 | –0.082 | <0.0001 | –0.066 | –0.071 | –0.061 | <0.0001 |
| Waist circumference | –0.032 | –0.035 | –0.029 | <0.0001 | –0.022 | –0.024 | –0.020 | <0.0001 |
| SBP | –0.005 | –0.007 | –0.003 | <0.0001 | –0.004 | –0.006 | –0.003 | <0.0001 |
| DBP | –0.004 | –0.007 | –0.001 | 0.006 | –0.003 | –0.005 | –0.001 | 0.011 |
| FPG | –0.441 | –0.613 | –0.269 | <0.0001 | –0.404 | –0.539 | –0.269 | <0.0001 |
| Total cholesterol | –0.001 | –0.001 | 0.0003 | 0.229 | –0.001 | –0.002 | –0.001 | 0.0001 |
| Triglyceride | –0.162 | –0.206 | –0.118 | <0.0001 | –0.168 | –0.203 | –0.134 | <0.0001 |
| HDL cholesterol | 0.011 | 0.008 | 0.014 | <0.0001 | 0.005 | 0.004 | 0.007 | <0.0001 |
| LDL cholesterol | 0.000005 | –0.001 | 0.001 | 0.990 | –0.001 | –0.002 | –0.001 | <0.0001 |
| HbA1c | –0.572 | –0.809 | –0.334 | <0.0001 | –0.692 | –0.891 | –0.493 | <0.0001 |
| AST | –0.229 | –0.321 | –0.137 | <0.0001 | –0.148 | –0.226 | –0.071 | 0.0002 |
| ALT | –0.286 | –0.340 | –0.232 | <0.0001 | –0.174 | –0.220 | –0.129 | <0.0001 |
| BUN | –0.002 | –0.010 | 0.005 | 0.529 | –0.006 | –0.012 | 0.0002 | 0.059 |
| Creatinine | 0.127 | –0.090 | 0.344 | 0.251 | 0.524 | 0.294 | 0.753 | <0.0001 |

**Notes:** The number of participants is presented as unweighted/weighted.
**Abbreviations:** BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, hemoglobin A1c; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen.

## Clinical characteristics of subjects according to the quartiles of relative HGS by sex

The participants were classified according to quartiles of relative HGS, and their clinical characteristics were compared by sex (Tables 3 and 4). Age, height, weight, BMI, waist circumference, SBP, DBP, FPG, total cholesterol, triglyceride, LDL cholesterol, HbA1c, AST, ALT, BUN, creatinine, family income, and education level decreased across increasing quartiles of relative HGS in both sexes. In men, HDL cholesterol level and the proportion of smokers increased across increasing quartiles of relative HGS (Table 3). In women, HDL cholesterol level, the proportion of smokers, and regular exercise increased across increasing quartiles of relative HGS (Table 4).

## ORs for individual MetS components according to quartiles of relative HGS by sex

ORs and 95% CIs for individual MetS components according to increasing quartiles of relative HGS are presented in Table 5. In men, relative HGS was significantly and independently associated with all MetS components, including large waist circumference (OR, 0.21; 95% CI, 0.16–0.26), high blood pressure (OR, 0.69; 95% CI, 0.58–0.83), low HDL cholesterol (OR, 0.58; 95% CI, 0.47–0.70), elevated triglycerides (OR, 0.60; 95% CI, 0.50–0.70), and elevated FPG (OR, 0.67; 95% CI, 0.55–0.80). In women, relative HGS was also significantly and independently associated with all MetS components, including large waist circumference (OR, 0.08; 95% CI, 0.05–0.11), high blood pressure (OR, 0.72; 95% CI, 0.52–0.99), low HDL cholesterol (OR, 0.56; 95% CI, 0.45–0.71), elevated triglycerides (OR, 0.46; 95% CI, 0.35–0.59), and elevated FPG (OR, 0.48; 95% CI, 0.0.35–0.64). Overall, relative HGS was associated with risk of MetS in both men and women (OR, 0.37; 95% CI, 0.30–0.45, vs OR, 0.19; 95% CI, 0.14–0.27, respectively) after multivariable adjustment for age, region of residence, smoking status, heavy alcohol consumption, regular exercise, family income, and education level (Table 5).

## Prevalence and ORs for MetS according to quartiles of relative HGS by sex

The prevalence of MetS significantly decreased across increasing quartiles of relative HGS in men and women (first, 42.4%; second, 33.3%; third, 18.8%; and fourth, 11.4%; $p<0.0001$; vs first, 29.1%; second, 12.7%; third, 6.4%; and 3.0%; $p<0.001$, respectively) (Figure 2).

**Table 3** Differences in variables among the four groups classified according to the range of relative HGS in men

| Variables | Relative HGS (n=2,472/22,176,994) | | | | *p*-value |
|---|---|---|---|---|---|
| | First (0.6–3.1) | Second (3.1–3.5) | Third (3.5–4.0) | Fourth (4.0–5.9) | |
| Number | 837/6,291,194 | 614/5,465,706 | 590/5,934,923 | 431/4,485,171 | |
| Age, years | 47.59 (0.73) | 43.85 (0.64) | 40.69 (0.57) | 37.30 (0.61) | <0.0001 |
| Height, cm | 169.91 (0.29) | 171.38 (0.32) | 172.74 (0.26) | 175.05 (0.31) | <0.0001 |
| Weight, cm | 75.88 (0.58) | 72.96 (0.59) | 70.57 (0.45) | 68.41 (0.50) | <0.0001 |
| BMI, kg/m$^2$ | 26.17 (0.16) | 24.74 (0.15) | 23.60 (0.13) | 22.28 (0.14) | <0.0001 |
| Waist circumference, cm | 90.08 (0.39) | 86.31 (0.38) | 83.04 (0.34) | 79.49 (0.39) | <0.0001 |
| SBP, mmHg | 121.27 (0.57) | 119.99 (0.66) | 117.44 (0.65) | 114.97 (0.64) | <0.0001 |
| DBP, mmHg | 78.60 (0.47) | 79.23 (0.47) | 78.07 (0.49) | 76.33 (0.51) | <0.0001 |
| FPG, mg/dL | 103.14 (0.93) | 102.50 (1.02) | 96.79 (0.68) | 94.82 (0.82) | <0.0001 |
| Total cholesterol, mg/dL | 190.44 (1.48) | 192.30 (1.48) | 192.47 (1.78) | 183.73 (1.76) | <0.0001 |
| Triglyceride, mg/dL | 180.80 (5.62) | 182.30 (6.95) | 157.70 (5.82) | 132.27 (6.18) | <.00001 |
| HDL cholesterol, mg/dL | 45.98 (0.44) | 47.27 (0.49) | 49.03 (0.51) | 51.75 (0.64) | <0.0001 |
| LDL cholesterol, mg/dL | 108.30 (1.33) | 108.57 (1.71) | 111.91 (1.74) | 105.53 (1.71) | <0.0001 |
| HbA1c (%) | 5.75 (0.03) | 5.72 (0.04) | 5.51 (0.02) | 5.45 (0.03) | <0.0001 |
| AST, IU/L | 25.23 (0.40) | 23.62 (0.42) | 23.09 (0.39) | 21.81 (0.41) | <0.0001 |
| ALT, IU/L | 29.40 (0.84) | 26.46 (0.81) | 23.66 (0.63) | 20.65 (0.55) | <0.0001 |
| BUN, mg/dL | 15.18 (0.19) | 14.90 (0.17) | 14.25 (0.17) | 14.09 (0.19) | <0.0001 |
| Creatinine, mg/dL | 0.95 (0.01) | 0.95 (0.01) | 0.95 (0.01) | 0.96 (0.01) | 0.001 |
| Region of residence, % | | | | | 0.694 |
| Urban | 72.14 (2.21) | 75.22 (2.13) | 73.35 (2.50) | 72.15 (2.80) | |
| Rural | 27.86 (2.21) | 24.78 (2.13) | 26.65 (2.50) | 27.85 (2.80) | |
| Smoking status, % | | | | | 0.001 |
| Yes | 33.86 (1.91) | 41.21 (2.41) | 41.05 (2.27) | 47.57 (2.73) | |
| No | 66.14 (1.91) | 58.79 (2.41) | 58.95 (2.27) | 52.43 (2.73) | |
| Heavy alcohol consumption | | | | | 0.288 |
| Yes | 22.13 (1.69) | 23.74 (1.96) | 25.55 (2.14) | 20.31 (2.23) | |
| No | 77.87 (1.69) | 76.26 (1.96) | 74.45 (2.14) | 79.69 (2.23) | |
| Regular exercise, % | | | | | 0.700 |
| Yes | 64.81 (2.20) | 66.44 (2.12) | 66.30 (2.21) | 68.68 (2.64) | |
| No | 35.19 (2.20) | 33.56 (2.12) | 33.70 (2.21) | 31.32 (2.64) | |
| Family income, percentile | | | | | 0.003 |
| <25th | 10.93 (1.22) | 6.71 (1.06) | 6.82 (1.14) | 5.38 (1.25) | |
| 25th–50th | 24.60 (1.88) | 21.03 (1.98) | 18.72 (1.85) | 24.99 (2.53) | |
| 50th–75th | 27.34 (2.06) | 35.45 (2.23) | 37.14 (2.39) | 33.57 (2.76) | |
| 75th–100th | 37.12 (2.35) | 36.81 (2.48) | 37.32 (2.46) | 36.06 (2.78) | |
| Education level, % | | | | | <0.0001 |
| Elementary school or less | 12.07 (1.28) | 9.10 (1.37) | 3.75 (0.69) | 3.51 (0.99) | |
| Middle school graduate | 8.16 (1.01) | 7.85 (1.15) | 7.10 (1.08) | 3.93 (1.01) | |
| High school graduate | 35.25 (2.00) | 38.97 (2.46) | 41.11 (2.24) | 49.45 (2.87) | |
| College graduate or higher | 44.52 (2.17) | 44.08 (2.47) | 48.04 (2.32) | 43.11 (2.81) | |

**Notes:** Data are presented as weighted means or weighted proportions (with standard errors) for continuous or categorical variables, respectively. The number of participants is presented as unweighted/weighted.

**Abbreviations:** HGS, handgrip strength; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, hemoglobin A1c; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen.

Participants with the highest relative HGS had a significant decrease in the relative risk for MetS compared with those with the lowest relative HGS in all logistic regression analyses, which consisted of Model 1 and Model 2 in both sexes. The multivariable-adjusted ORs (95% CIs) for MetS in quartiles 1, 2, 3, and 4 were 1.00, 0.72 (0.55–0.94), 0.34 (0.26–0.46), and 0.22 (0.15–0.32) in men and 1.00, 0.50 (0.36–0.68), 0.26 (0.17–0.40, and 0.16 (0.09–0.27) in women, respectively (Table 6).

## Discussion

This study investigated the association between relative HGS and MetS, and the principal finding was a strong inverse association, independent of age, health behaviors (smoking

**Table 4** Differences in variables among the four groups classified according to the range of relative HGS in women

| Variables | Relative HGS (n=2,542/17,502,333) | | | | *p*-value |
|---|---|---|---|---|---|
| | First (0.9–2.0) | Second (2.0–2.3) | Third (2.3–2.6) | Fourth (2.6–3.7) | |
| Number | 878/5,410,688 | 641/4,409,814 | 540/3,875,492 | 483/3,806,339 | |
| Age, years | 48.21 (0.62) | 41.65 (0.59) | 40.30 (0.62) | 36.12 (0.55) | <0.0001 |
| Height, cm | 155.77 (0.23) | 158.94 (0.26) | 160.22 (0.26) | 162.60 (0.26) | <0.0001 |
| Weight, cm | 61.18 (0.43) | 58.28 (0.41) | 55.70 (0.40) | 53.89 (0.36) | <0.0001 |
| BMI, kg/m$^2$ | 25.17 (0.16) | 23.03 (0.14) | 21.67 (0.13) | 20.36 (0.11) | <0.0001 |
| Waist circumference, cm | 82.57 (0.38) | 76.51 (0.39) | 73.70 (0.39) | 70.78 (0.39) | <0.0001 |
| SBP, mmHg | 116.35 (0.67) | 109.95 (0.65) | 108.53 (0.63) | 105.86 (0.53) | <0.0001 |
| DBP, mmHg | 74.05 (0.41) | 72.43 (0.43) | 71.10 (0.47) | 70.49 (0.47) | <0.0001 |
| FPG, mg/dL | 98.69 (0.80) | 94.16 (0.80) | 91.65 (0.53) | 90.27 (0.42) | <0.0001 |
| Total cholesterol, mg/dL | 195.43 (1.41) | 188.29 (1.62) | 185.74 (1.48) | 179.60 (1.50) | <0.0001 |
| Triglyceride, mg/dL | 121.44 (2.93) | 106.18 (2.97) | 95.06 (3.04) | 78.22 (2.17) | <0.0001 |
| HDL cholesterol, mg/dL | 53.73 (0.51) | 56.36 (0.49) | 58.16 (0.63) | 60.09 (0.59) | <0.0001 |
| LDL cholesterol, mg/dL | 117.41 (1.23) | 110.70 (1.42) | 108.56 (1.31) | 103.86 (1.32) | <0.0001 |
| HbA1c (%) | 5.71 (0.03) | 5.49 (0.03) | 5.45 (0.02) | 5.34 (0.01) | <0.0001 |
| AST, IU/L | 21.37 (0.32) | 19.40 (0.29) | 18.91 (0.27) | 18.09 (0.30) | <0.0001 |
| ALT, IU/L | 19.34 (0.52) | 16.43 (0.50) | 14.55 (0.4) | 13.13 (0.30) | <0.0001 |
| BUN, mg/dL | 13.71 (0.16) | 12.70 (0.16) | 12.58 (0.17) | 12.02 (0.16) | <0.0001 |
| Creatinine, mg/dL | 0.70 (0.00) | 0.71 (0.00) | 0.71 (0.00) | 0.73 (0.00) | <0.0001 |
| Region of residence, % | | | | | 0.953 |
| Urban | 76.59 (2.04) | 75.16 (2.41) | 75.93 (2.33) | 75.19 (2.91) | |
| Rural | 23.41 (2.04) | 24.84 (2.41) | 24.07 (2.33) | 24.81 (2.91) | |
| Smoking status, % | | | | | 0.036 |
| Yes | 4.31 (0.89) | 7.39 (1.30) | 4.32 (0.99) | 7.67 (1.33) | |
| No | 95.69 (0.89) | 92.61 (1.30) | 95.68 (0.99) | 92.33 (1.33) | |
| Heavy alcohol consumption, % | | | | | 0.989 |
| Yes | 8.00 (1.10) | 8.06 (1.28) | 7.52 (1.28) | 7.72 (1.33) | |
| No | 92.00 (1.10) | 91.94 (1.28) | 92.48 (1.28) | 92.28 (1.33) | |
| Regular exercise, % | | | | | <0.0001 |
| Yes | 54.86 (1.98) | 61.71 (2.32) | 66.33 (2.34) | 68.01 (2.36) | |
| No | 45.14 (1.98) | 38.29 (2.32) | 33.67 (2.34) | 31.99 (2.36) | |
| Family income, percentile | | | | | <0.0001 |
| <25th | 14.98 (1.39) | 10.21 (1.49) | 5.69 (1.13) | 5.84 (1.19) | |
| 25th–50th | 26.42 (2.00) | 22.23 (2.01) | 22.84 (2.16) | 19.91 (2.10) | |
| 50th–75th | 29.86 (1.89) | 33.85 (2.25) | 29.16 (2.27) | 34.81 (2.45) | |
| 75th–100th | 28.74 (2.00) | 33.71 (2.31) | 42.30 (2.50) | 39.43 (2.60) | |
| Education level, % | | | | | <0.0001 |
| Elementary school or less | 25.34 (1.66) | 7.43 (1.08) | 4.57 (0.91) | 1.93 (0.66) | |
| Middle school graduate | 9.89 (1.08) | 11.03 (1.53) | 5.39 (0.95) | 3.73 (0.89) | |
| High school graduate | 34.18 (1.92) | 40.66 (2.29) | 42.03 (2.45) | 39.90 (2.64) | |
| College graduate or higher | 30.59 (2.00) | 40.88 (2.51) | 48.01 (2.47) | 54.45 (2.65) | |

**Notes:** Data are presented as weighted means or weighted proportions (with standard errors) for continuous or categorical variables, respectively. The number of participants is presented as unweighted/weighted.

**Abbreviations:** HGS, handgrip strength; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, hemoglobin A1c; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen.

status, heavy alcohol consumption, and regular exercise), and sociodemographic factors (region of residence, family income, and education level), in a nationally representative sample of Korean adults. Meanwhile, dominant HGS and absolute HGS were significantly higher in subjects with MetS compared with the results in those without MetS, particularly in men, but not in women, thus showing conflicting results.

Several studies have investigated the association between HGS and MetS. However, the correlation has been found to be controversial in terms of sex and type of HGS index. The Hertfordshire Cohort Study of 2,677 UK men and women aged 59–73 years found that lower unadjusted HGS was significantly associated with increased odds of having MetS according to the criteria of the National Cholesterol

**Table 5** Adjusted ORs and 95% CIs for metabolic syndrome and individual components of subjects according to increasing quartiles of relative HGS by sex

| Variables | Relative HGS | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Men (n=2,472/22,176,994) | | | | | | | | | | | | |
| | n (%) | Unadjusted | | | | Model 1[$] | | | | Model 2[‡] | | | |
| | | OR | 95% CI | | p-value | OR | 95% CI | | p-value | OR | 95% CI | | p-value |
| | | | Lower | Upper | | | Lower | Upper | | | Lower | Upper | |
| Metabolic syndrome | 753/6,119,167 (27.59) | 0.331 | 0.276 | 0.396 | <0.0001 | 0.393 | 0.323 | 0.480 | <0.0001 | 0.367 | 0.299 | 0.450 | <0.0001 |
| Large waist circumference | 725/6,115,027 (27.57) | 0.231 | 0.185 | 0.287 | <0.0001 | 0.230 | 0.183 | 0.290 | <0.0001 | 0.206 | 0.161 | 0.264 | <0.001 |
| High blood pressure | 1,064/8,109,966 (36.57) | 0.532 | 0.455 | 0.621 | <0.0001 | 0.703 | 0.588 | 0.841 | <0.001 | 0.694 | 0.578 | 0.832 | <0.001 |
| Low HDL cholesterol | 557/4,874,111 (21.98) | 0.566 | 0.470 | 0.682 | <0.0001 | 0.588 | 0.478 | 0.724 | <0.0001 | 0.578 | 0.469 | 0.712 | <0.001 |
| Elevated triglyceride | 998/8,920,124 (40.22) | 0.581 | 0.501 | 0.673 | <0.0001 | 0.630 | 0.540 | 0.734 | <0.0001 | 0.598 | 0.508 | 0.704 | <0.001 |
| Elevated FPG | 988/7,701,692 (34.73) | 0.522 | 0.444 | 0.614 | <0.0001 | 0.693 | 0.579 | 0.829 | <0.0001 | 0.665 | 0.554 | 0.799 | <0.001 |
| **Variables** | **Women (n=2,542/17,502,333)** | | | | | | | | | | | | |
| | n (%) | Unadjusted | | | | Model 1[$] | | | | Model 2[‡] | | | |
| | | OR | 95% CI | | p-value | OR | 95% CI | | p-value | OR | 95% CI | | p-value |
| | | | Lower | Upper | | | Lower | Upper | | | Lower | Upper | |
| Metabolic syndrome | 441/2,496,987 (14.27) | 0.104 | 0.076 | 0.142 | <0.0001 | 0.190 | 0.135 | 0.267 | <0.0001 | 0.193 | 0.136 | 0.274 | <0.001 |
| Large waist circumference | 525/3,242,626 (18.53) | 0.061 | 0.044 | 0.086 | <0.0001 | 0.076 | 0.054 | 0.108 | <0.0001 | 0.076 | 0.053 | 0.110 | <0.001 |
| High blood pressure | 654/3,703,870 (21.16) | 0.256 | 0.197 | 0.334 | <0.0001 | 0.657 | 0.482 | 0.895 | 0.008 | 0.722 | 0.522 | 0.998 | 0.048 |
| Low HDL cholesterol | 852/5,387,795 (30.78) | 0.442 | 0.359 | 0.544 | <0.0001 | 0.545 | 0.435 | 0.683 | <0.0001 | 0.562 | 0.446 | 0.707 | <0.001 |
| Elevated triglyceride | 457/2,819,656 (16.11) | 0.306 | 0.241 | 0.389 | <0.0001 | 0.462 | 0.359 | 0.595 | <0.0001 | 0.457 | 0.352 | 0.593 | <0.001 |
| Elevated FPG | 580/3,390,651 (19.37) | 0.272 | 0.211 | 0.350 | <0.0001 | 0.478 | 0.360 | 0.635 | <0.0001 | 0.477 | 0.353 | 0.644 | <0.001 |

**Notes:** The number of participants is presented as unweighted/weighted. [$]Adjusted for age. [‡]Adjusted for age, region of residence, smoking status, heavy alcohol consumption, regular exercise, family income, and education level.
**Abbreviations:** HGS, handgrip strength; HDL, high-density lipoprotein; FPG, fasting plasma glucose.

Education Program Adult Treatment Panel III (NCEP-ATP III) (OR, 1.18; 95% CI, 1.07–1.30, $p<0.001$) and IDF (OR, 1.11; 95% CI, 1.01–1.22, $p=0.03$).[20] A cross-sectional study of 400 men aged 40–80 years in the Netherlands showed no significant association between HGS of the nondominant hand and MetS, regardless of visceral fat levels.[32] Another cross-sectional analysis of 1,971 Japanese adults aged ≥65 years showed that MetS according to the NCEP-ATP III criteria was associated with lower HGS in both sexes in the multivariable models; however, the association was no longer significant after adjustment for abdominal obesity in both sexes. Notably, HGS in the lowest quintile was classified as low muscle strength in this cited study.[6] Additionally, a study of 309 Korean subjects aged ≥40 years found that unadjusted HGS was not significantly associated with MetS in either men or women.[33]

One cross-sectional analysis of 1,216 Japanese men aged 20–79 years revealed that HGS/Wt was significantly lower in subjects with MetS compared with the result in those without MetS, according to new criteria in Japan, in the use of both right (0.56±0.10 vs 0.65±0.12, $p<0.0001$) and left hands (0.54±0.10 vs 0.62±0.11, $p<0.0001$).[34] In an Australian study of 1,195 men aged 35–81 years, a lower value of HGS divided by lean mass per arm was significantly associated with an increased prevalence of MetS according to the NCEP-ATP-III and IDF classification, independent of insulin resistance and abdominal fat accumulation.[35] In the Korean Longitudinal Study on Health and Aging, HGS/Wt showed a significant

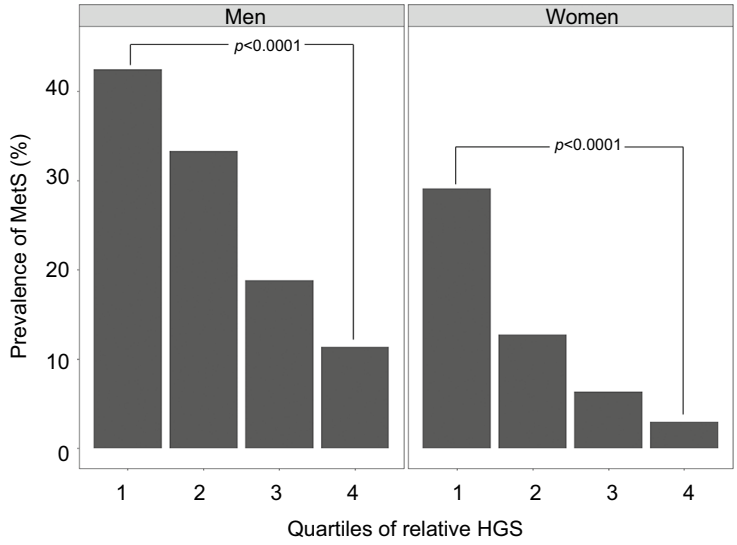


**Figure 2** Prevalence of MetS according to quartiles of relative handgrip strength.
**Notes:** Bar graphs express prevalence in percentages. Differences in prevalence among quartiles were analyzed using the chi-square test. 1, 1st quartile; 2, 2nd quartile; 3, 3rd quartile; 4, 4th quartile.
**Abbreviations:** MetS, metabolic syndrome; HGS, handgrip strength.

**Table 6** Adjusted ORs and 95% CIs for metabolic syndrome according to quartiles of relative HGS by sex

| **Men (n=2,472/22,176,994)** | **Relative HGS** | | | | |
|---|---|---|---|---|---|
| | **Quartile 1 (0.6–3.1)** | **Quartile 2 (3.1–3.5)** | **Quartile 3 (3.5–4.0)** | **Quartile 4 (4.0–5.9)** | |
| | **n=837/6,291,194** | **n=614/5,465,706** | **n=590/5,934,923** | **n=431/4,485,171** | ***p*-value** |
| Unadjusted | Reference | 0.678 (0.529–0.869) | 0.315 (0.239–0.414) | 0.174 (0.121–0.250) | <0.0001 |
| Model 1[§] | Reference | 0.753 (0.583–0.972) | 0.378 (0.283–0.504) | 0.233 (0.159–0.341) | <0.0001 |
| Model 2[‡] | Reference | 0.719 (0.551–0.940) | 0.343 (0.256–0.460) | 0.219 (0.149–0.321) | <0.0001 |
| **Women (n=2,542/17,502,333)** | **Quartile 1 (0.9–2.0)** | **Quartile 2 (2.0–2.3)** | **Quartile 3 (2.3–2.6)** | **Quartile 4 (2.6–3.7)** | |
| | **n=878/5,410,688** | **n=641/4,409,814** | **n=540/3,875,492** | **n=483/3,806,339** | ***p*-value** |
| Unadjusted | Reference | 0.355 (0.263–0.478) | 0.165 (0.111–0.246) | 0.075 (0.044–0.128) | <0.0001 |
| Model 1[§] | Reference | 0.490 (0.357–0.673) | 0.248 (0.163–0.378) | 0.152 (0.088–0.260) | <0.0001 |
| Model 2[‡] | Reference | 0.495 (0.358–0.683) | 0.261 (0.170–0.400) | 0.155 (0.090–0.268) | <0.0001 |

**Notes:** The number of participants is presented as unweighted/weighted. [§]Adjusted for age. [‡]Adjusted for age, region of residence, smoking status, heavy alcohol consumption, regular exercise, family income, and education level.
**Abbreviation:** HGS, handgrip strength.

inverse association only in men, but not in women, and the effect was stronger in men aged 65–74 years.[36] In contrast, another cross-sectional study revealed that lower HGS/Wt was significantly associated with an increased risk of MetS in 1,679 community-dwelling elderly Japanese men and women aged ≥50 years.[37]

These discrepancies in the findings regarding the association between HGS and MetS may have existed for several reasons. First, different HGS indexes were used for each study, including dominant HGS and absolute HGS with or without adjustment for weight or height. In our study, dominant HGS and absolute HGS were significantly higher in men with MetS than in those without MetS, whereas there were no statistical differences in women. However, relative HGS was significantly lower in both sexes with MetS than in those without MetS, showing consistent results. Second, differences in characteristics of the subjects, including ethnicity, genetic background, body size, and sociocultural factors, may have influenced the results. Third, differences in statistical issues, such as sample sizes and the methodology for statistical analysis, may also account for some of the discrepancies. Finally, differences in the effect of muscle strength on metabolism between both sexes may have also contributed to the results.

Relative HGS (absolute HGS/BMI) has been proposed as a novel cardiometabolic marker in recent studies, showing consistent results. A previous study of nationally representative data from the KNHANES study involving 4,221 participants aged ≥20 years found that relative HGS was more strongly associated with CVD biomarkers than absolute HGS.[21] In another nationwide population-based study of 927 Taiwanese participants aged ≥53 years, relative HGS showed a stronger correlation with CVD biomarkers than dominant HGS.[38] Furthermore, in a study of 730 Czech children aged 4–14 years, relative HGS was a useful marker to identify sarcopenic obesity. Considering these findings, relative HGS, which not only reflects the maximal HGS of each hand but also minimizes the confounding effect of body size, would be the best marker of cardiometabolic risk among various HGS indexes so far.

The negative association between relative HGS and risk of MetS is mediated by insulin resistance, as evidenced by previous studies, which showed an inverse association between HGS and insulin resistance.[20,21] Several possible mechanisms may underlie the negative relationship between relative HGS and insulin resistance. Skeletal muscle glycogen synthesis is essential for glucose disposal, and intramuscular triglyceride levels have been known to be negatively associated with insulin resistance.[39] Moreover, reduced expression of glucose transporter 4 by a decreased number and volume of muscles results in increased insulin resistance in skeletal muscle.[40] Furthermore, lower plasma levels of insulin-like growth factor-1[41] and higher levels of inflammatory markers, including interleukin-6, tumor necrosis factor-α, and C-reactive protein, are linked to muscle dysfunction,[42] leading to MetS.[43] A previous experimental research found that strength training enhanced insulin action in skeletal muscle in patients with type 2 diabetes, independent of increases in muscle mass. Muscle biopsy in the strength training group revealed increased protein content of glucose transporter 4, insulin receptor, protein kinase B, and glycogen synthase, as well as increased total activity of glycogen synthase.[44] Further controlled experimental studies are required to clarify the mechanism underlying the association between muscle strength and MetS.

In our study, the prevalence of MetS was significantly higher in men as expected. Interestingly, the proportion of smokers increased across increasing quartiles of relative HGS in both sexes, which could be attributed to several explanations. Firstly, there were no significant differences in the proportion of smokers in relation to the presence of MetS in both sexes. Secondly, anthropometric and biochemical factors might have more impact on relative HGS than smoking status. Thirdly, further analysis of occupation, such as the proportion of blue-collar workers, might account for some of these conflicting results. Lastly, in women, the proportion of smokers was very low, which might explain the inconsistent pattern across increasing quartiles of relative HGS. In contrast, family income and education level significantly decreased across increasing quartiles of relative HGS in both sexes. Taken together, our findings suggest that relative HGS, but not absolute or dominant HGS, is a more appropriate marker of MetS, and sociodemographic factors should be considered in public health interventions, including the prevention, evaluation, and management of MetS.

This study has several strengths. Firstly, to our knowledge, this is the first large-scale study that investigated the association between relative HGS and MetS using recent data from a nationally representative sample; therefore, our findings could be generalized to the entire Korean population. Secondly, high-quality measurements of HGS through the use of an isokinetic dynamometer with a standardized protocol were included in this study, which contributed to increased accuracy, compared with the methods used in previous studies. Lastly, we included all available clinical variables from the data, as well as the covariates of health behaviors and sociodemographic factors, in the analysis to determine the association between relative HGS and MetS independent of potential confounders.

The study has potential limitations. We could not determine a causal relationship between relative HGS and MetS due to the cross-sectional study design. In addition, measurement of muscle mass, the main diagnostic component of sarcopenia, was not performed in this study; thus, we could not compare the efficacy of relative HGS with that of muscle mass as a marker of MetS. Moreover, the associations between muscle mass and HGS or MetS were not evaluated.

## Conclusion

We demonstrated a strong inverse association between relative HGS and MetS, independent of age, health behaviors, and socioeconomic factors, in Korean adults. Therefore, relative HGS is a novel biomarker for assessing risk of MetS, superior to other HGS indexes. However, additional prospective or interventional studies are required to confirm the causal relationship between relative HGS and MetS and to determine whether interventions in subjects with low relative HGS are effective in preventing adverse health outcomes.

## Acknowledgment

We thank the Department of Biostatistics, Clinical Trial Center, Biomedical Research Institute, Pusan National University Hospital.

## Disclosure

The authors report no conflicts of interest in this work.

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