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Original Article

Handgrip Strength is Associated with Hypertension among Middle-Aged and Older Community-Dwelling Persons

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SUMMARY

Background: The incidence of hypertension is increasing worldwide, and handgrip strength (HGS) is an easily obtainable measure of physical health and muscle function. However, there is limited data available on the relationship between HGS and hypertension among community-dwelling persons in Japan. Therefore, we performed a population-based cohort study to examine whether relative HGS, defined by HGS/body mass index (BMI) ratio, was associated with hypertension.

Methods: A follow-up cohort study included 257 men aged 66 ± 9 years and 369 women aged 67 ± 8 years from a rural village (Nomura Cho, Seiyo City, in Ehime prefecture, Japan). Logistic regression models were used to evaluate the relative HGS as a significant predictor of hypertension.

Results: The median HGS was 36.4 (interquartile range: 31.3–40.7) kg in men and 21.9 (19.8–24.7) kg in women, while the mean HGS/BMI ratio was $1.62 \pm 0.33 \text{ m}^2$ in men and $1.04 \pm 0.21 \text{ m}^2$ in women. Of the participants, 120 men (46.7%) and 137 women (37.1%) had hypertension. The prevalence of hypertension was significantly decreased in relation to an increasing baseline relative HGS only among men. After adjustment for confounding factors, the respective odds ratios (95% confidence interval) of the three tertiles of the gender-specific relative HGS for hypertension were 1.00, 0.65 (0.35–1.22), and 0.27 (0.14–0.54) in men, and 1.00, 0.71 (0.42–1.19), and 0.56 (0.33–0.95) in women.

Conclusion: These results suggest that the relative HGS is significantly and negatively associated with an increased risk of hypertension in Japanese-community dwelling persons.

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1. Introduction

Handgrip strength (HGS) is a low-cost assessment tool and an easily obtainable measure of physical health and muscle function. It is a test commonly used as a satisfactory indicator of resistance training in epidemiological studies,^{1,2} and this measurement is widely applied to assess overall nutrition,³ functional capacity,⁴ the incidence of cardiovascular disease (CVD) and associated mortality,⁵ and adverse outcomes (mortality, physical functioning, hospital length of stay).⁶ However, it has been reported that the use of absolute HGS may introduce bias compared with relative HGS.⁷ Thus, the use of relative HGS (i.e., HGS adjusted for body mass index [BMI]) has been recommended to minimize the confounding effect of body size and proposed as an easy instrument for assessing metabolic health and cardiovascular risk in public health and clinical practice.^{7–10}

Hypertension is one of the leading causes of disability and death worldwide,¹¹ and it is established as a serious pre-medical condition that significantly increases the risk of CVD (e.g., heart, brain, kidney, and other diseases), type 2 diabetes, and all-cause mortality.¹² The development of hypertension is related to several modifiable lifestyle-related factors, such as unhealthy diets (excessive consump-

tion of salt, a diet high in saturated fat and trans fats, low intake of fruits and vegetables), lack of physical exercise, smoking, alcohol consumption, and being overweight or obese.¹¹ Moreover, insulin resistance is one of the key players in the pathophysiology of hypertension, and has even been postulated as being its underlying cause.¹³ Muscular fitness, measured by HGS or other methods, is associated with insulin resistance and glucose metabolism in adolescents, which indicates that an increasing HGS may be beneficial for the early prevention of insulin resistance.¹⁴ On the other hand, analyses of the association between HGS adjusted for BMI and blood pressure (BP) in a population are relatively scarce.

To address this hypothesis, we investigated the relationship between baseline relative HGS and potential risk factors and hypertension using a prospective cohort data from community-dwelling middle-aged and older individuals.

2. Methods

2.1. Participants

Data from the Nomura study, conducted between 2014 and 2017, were used in the present study.¹⁵ Community-dwelling middle-aged and older persons were recruited through a community-based annual check-up process from the Nomura Health and Wel-

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fare Center in a rural town located (Nomura-cho, Seiyo-city) in Ehime prefecture, Japan. Follow-up assessments were performed every three years. The study design and procedures were performed in accordance with ethical standards and the tenets of the Declaration of Helsinki. All participants provided written informed consent. The present study was approved by the ethics committee of Ehime University School of Medicine (Institutional Review Board Approval Number: 1402009).

Overall, 1,832 community-dwelling participants (818 men and 1,014 women) aged 20–95 were registered between April and November 2014. In this study, the analysis was restricted to participants aged ≥ 40 years with no missing baseline data. The initial dataset consisted of 1,720 participants (765 men and 955 women) aged 40 to 95 years, followed up three years later. Of the participants, those with antihypertensive medication at baseline ($N = 767$) and missing data ($N = 327$), especially no data on HGS and BP, were excluded. The final dataset comprised 626 participants (257 men and 369 women). The flowchart in Figure 1 describes the inclusion of participants.

2.2. Evaluation of risk factors

The present conditions of the participants, the physical activity level (e.g., exercise habits), information on medical history, and medications were obtained by interview using a structured questionnaire. Exercise habits was defined as present if the study subjects had engaged in at least 30 minutes of any type of moderate-to-vigorous physical activity such as brisk walking, playing golf, gardening, jogging, or playing tennis at least 2 days a week for 1 year or more. The BMI was calculated as body weight in kilograms divided by the square of body height in meters (kg/m^2). Smoking status was defined as the number of cigarette packs per day multiplied by the number of years the person smoked (pack-years). The participants were classified into never smokers, past smokers, light smokers (< 30 pack-years), and heavy smokers (≥ 30 pack-years). Drinking status was measured using the Japanese unit of measurement, corresponding to 22.9 g of ethanol. The participants were classified into never drinkers, light drinkers (< 1 unit/day), and daily drinkers (moderate: < 2 units/day; heavy: ≥ 2 units/day). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice with an appropriate-sized cuff on the right upper arm of the participants in a sitting position using an automatic oscillometric BP recorder (BP-103i; Colin, Aichi, Japan) after having rested for at least 5 min. The two values were subsequently averaged. Blood samples were collected in the morning after an overnight fast of at least 11 hours and triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), hemoglobin A1c (HbA1c), serum creatinine (Cr), and serum uric acid (SUA) were measured. We calculated the estimated glomerular filtration ratio (eGFR) using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equations modified by a Japanese coefficient (eGFR_{CKDEPI}): male, $\text{Cr} \leq 0.9 \text{ mg/dl}$: $141 \times (\text{Cr}/0.9)^{-0.411} \times 0.993^{\text{age}} \times 0.813$; $\text{Cr} > 0.9 \text{ mg/dl}$: $141 \times (\text{Cr}/0.9)^{-1.209} \times 0.993^{\text{age}} \times 0.813$ and female, $\text{Cr} \leq 0.7 \text{ mg/dl}$: $144 \times (\text{Cr}/0.7)^{-0.329} \times 0.993^{\text{age}} \times 0.813$; $\text{Cr} > 0.7 \text{ mg/dl}$: $144 \times (\text{Cr}/0.7)^{-1.209} \times 0.993^{\text{age}} \times 0.813$.¹⁶

2.3. Handgrip strength test

HGS was evaluated using the Takei Digital Hand Grip dynamometer (Japan). Previous studies have determined the reliability and validity of the Takei Digital Hand Grip.¹⁰ The participants hold the dynamometer in the hand, with the arm at right angles and the elbow by the side of the body. The handle of the dynamometer is adjusted

if required — the base should be placed on the first metacarpal bone (heel of palm) and the handle should rest on middle of four fingers. When ready, the participants hold the dynamometer with maximum isometric effort. This will be maintained for approximately 5 s. Other body movements are not allowed during the measurement. The mean of two right and left measurements was used for analysis.

2.4. Criteria for the clinical diagnosis of hypertension

Normotension was defined as not receiving antihypertensive medication and having an SBP < 120 mmHg and DBP < 80 mmHg. Prehypertension was defined as not receiving antihypertensive medication and having an SBP of 120–139 mmHg and/or DBP 80–89 mmHg. Hypertension was defined as receiving antihypertensive medication and/or having an SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg according to the definitions of the 7th Report of the Joint National Committee.¹⁷

2.5. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistical Version 26 (Statistical Package of Social Science Japan, Tokyo, Japan). All values are expressed as the mean \pm standard deviation (SD), unless otherwise specified. Data for HGS, triglycerides, and HbA1c were skewed, and are expressed as medians (interquartile ranges), and log-transformed for analysis. Participants were divided into two groups according to gender. Areas under the receiver operating characteristic (ROC) curves were determined for the HGS and HGS/BMI ratio to identify the predictors of hypertension. An ROC curve is a plot of sensitivity (true positive) versus 1 – specificity (false positive) for different cutoff points of a parameter. Area under the ROC curve is a summary of the overall diagnostic accuracy of the test including standard errors. Participants were divided into three groups according to tertiles of the baseline HGS/BMI ratio (first, second, and third) by gender. Differences among the three groups divided according to the tertiles of the baseline HGS/BMI ratio were analyzed by ANOVA for continuous variables or the chi-squared (χ^2) test for categorical

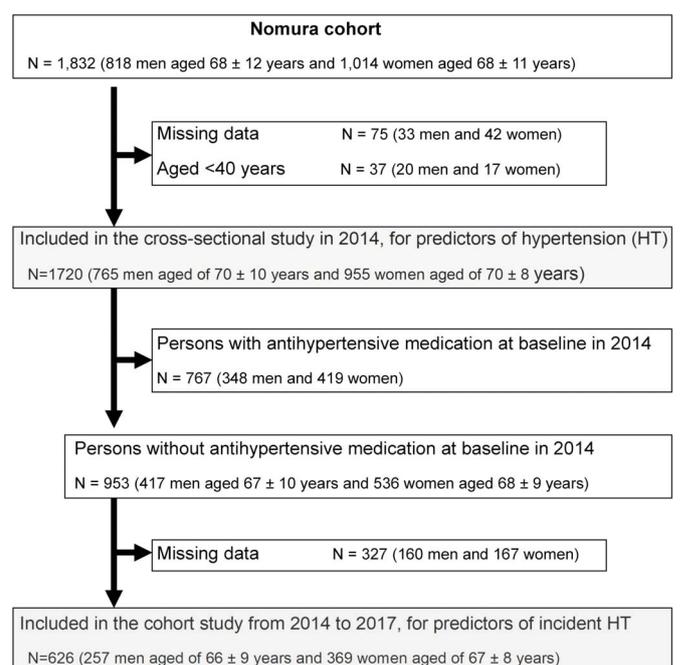


Figure 1. Flowchart. For the longitudinal analyses, only participants without antihypertensive medication at baseline in 2014 were included ($N = 626$).

variables. Multiple logistic linear regression analysis was used to evaluate the contribution of the baseline HGS/BMI ratio and confounding factors (i.e., gender, age, smoking status, drinking status, exercise habits, presence of CVD, triglycerides, HDL-C, LDL-C, use of antidyslipidemic medication, HbA1c, use of antidiabetic medication, eGFR, and SUA) on the incidence of hypertension in the cohort study. Moreover, a similar analysis was performed on participants over the age of 60 years to minimize the effect of age on HGS assessment. A *p*-value < 0.05 denoted statistically significant differences.

3. Results

3.1. Baseline characteristics of participants by gender

A total of 257 men aged 66 ± 9 years (range: 40–88 years) and 369 women aged 67 ± 8 years (range: 41–85 years) were included. The median HGS was 36.4 (interquartile range: 31.3–40.7) kg in men and 21.9 (19.8–24.7) kg in women, while the mean HGS/BMI ratio

was 1.62 ± 0.33 m² in men and 1.04 ± 0.21 m² in women. Gender-specific characteristics of the participants are illustrated in Table 1. The BMI, HGS, HGS/BMI ratio, smoking status, drinking status, DBP, triglycerides, use of antidiabetic medication, and SUA were significantly higher in men than in women. However, HDL-C, LDL-C, use of antidyslipidemic medication, and eGFR were significantly lower in men. There were no gender differences regarding age, exercise habits, SBP, HbA1c levels or eGFR.

3.2. Results of the ROC curve analyses to identify optimal obesity indices for distinguishing participants with hypertension

Figure 2 shows the AUC for the BMI, HGS, and HGS/BMI ratio for hypertension in both genders using ROC analyses. The HGS/BMI ratio with BMI showed a significant predictive ability for incident hypertension in both genders; for men, the HGS/BMI ratio exhibited the strongest ability.

Table 1
Baseline characteristics of participants categorized by gender.

| Baseline characteristics (N=626) | Men (N = 257) | Women (N = 369) | <i>p</i> -value* |
|--|---------------------|-------------------|------------------|
| Age (years) | 66 ± 9 | 67 ± 8 | 0.102 |
| BMI (kg/m ²) | 22.5 ± 2.6 | 21.8 ± 2.9 | 0.002 |
| Handgrip strength | 36.4 (31.3–40.7) | 21.9 (19.8–24.7) | < 0.001 |
| Handgrip strength/BMI ratio | 1.62 ± 0.33 | 1.04 ± 0.21 | < 0.001 |
| Smoking status: never/past/light/heavy (%) | 37.4/37.0/8.2/17.5 | 96.5/1.9/0.5/1.1 | < 0.001 |
| Drinking status: never/light/moderate/heavy (%) | 24.1/23.7/12.1/40.1 | 68.6/24.7/3.8/3.0 | < 0.001 |
| Exercise habits, N (%) | 95 (37.0) | 136 (36.9) | 1.000 |
| Cardiovascular disease (%) | 10 (3.9) | 9 (2.4) | 0.347 |
| Systolic blood pressure (mmHg) | 130 ± 16 | 131 ± 18 | 0.825 |
| Diastolic blood pressure (mmHg) | 79 ± 10 | 75 ± 9 | < 0.001 |
| Antihypertensive medication (%) | 0 | 0 | ---- |
| Triglycerides (mg/dl) | 89 (65–129) | 81 (61–112) | 0.005 |
| HDL cholesterol (mg/dl) | 64 ± 16 | 70 ± 17 | < 0.001 |
| LDL cholesterol (mg/dl) | 118 ± 30 | 129 ± 29 | < 0.001 |
| Antidyslipidemic medication (%) | 20 (7.8) | 78 (21.1) | < 0.001 |
| Hemoglobin A1c (%) | 5.6 (5.4–5.9) | 5.6 (5.4–5.8) | 0.746 |
| Antidiabetic medication (%) | 20 (7.8) | 6 (1.6) | < 0.001 |
| Estimated GFR (ml/min/1.73 m ² /year) | 74.7 ± 9.1 | 75.5 ± 9.6 | 0.242 |
| Serum uric acid (mg/dl) | 6.0 ± 1.2 | 4.5 ± 1.0 | < 0.001 |

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; GFR, glomerular filtration ratio. Data are presented as the mean ± standard deviation, with the exception of data for handgrip strength, triglycerides, and hemoglobin A1c, which are skewed and are presented as the median (interquartile range).

**p*-value: Student’s *t*-test for the continuous variables or the χ^2 test for the categorical variables. Values in bold typeface are statistically significant (*p* < 0.05).

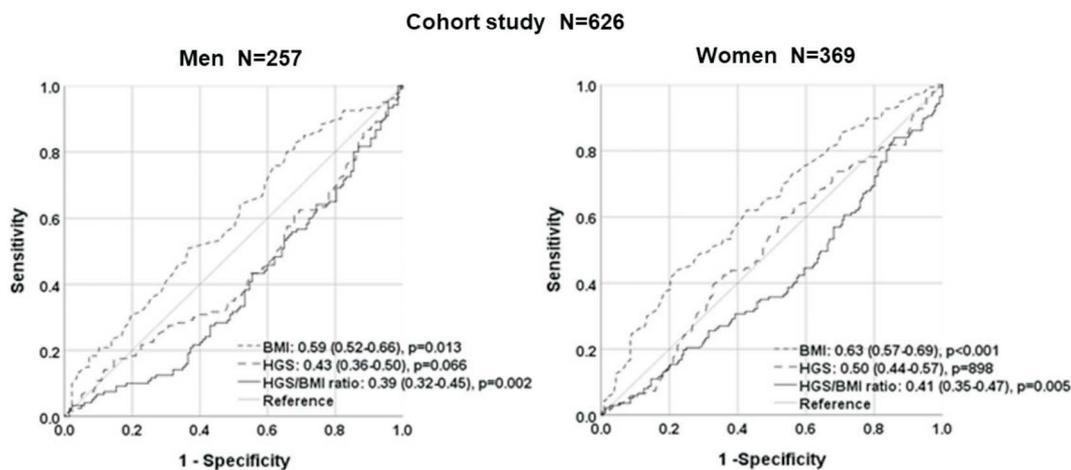


Figure 2. The receiver operating characteristic curves of the body mass index (BMI), handgrip strength (HGS), and HGS/BMI ratio for hypertension in both genders.

3.3. Baseline characteristics of participants by tertiles of the baseline HGS/BMI ratio

As shown in Table 2, HGS, drinking status, HDL-C, and eGFR were significantly increased with an increased tertile of the HGS/BMI ratio. However, age, BMI, SBP, triglycerides, HbA1c, and use of anti-diabetic medication were significantly lower.

3.4. Relationship between tertiles of the baseline HGS/BMI ratio and BP status

As shown in Figure 3, of the participants in the cohort study, 120 men (46.7%) and 137 women (37.1%) had hypertension. The prevalence of hypertension was significantly decreased in relation to an increasing baseline HGS/BMI ratio only among men.

3.5. Odds ratios (OR) (95% confidence interval [CI]) of tertiles of the baseline HGS/BMI ratio for hypertension

As shown in Table 3, we further investigated whether baseline HGS/BMI ratio may explain hypertension independent of other confounding factors. For this purpose, a multiple logistic regression analysis using hypertension as an objective variable and various confounding factors (e.g., baseline age, smoking status, drinking status, exercise habits, history of CVD, triglycerides, HDL-C, LDL-C, use of antidyslipidemic medication, HbA1c, eGFR, and SUA) as explanatory variables was performed with participants categorized by gender (Table 3). The respective OR (95% CI) of the three tertiles of the gender-specific HGS/BMI ratio for hypertension were 1.00, 0.65 (0.35–1.22), and 0.27 (0.14–0.54) in men, and 1.00, 0.71 (0.42–1.19), and 0.56 (0.33–0.95) in women.

3.6. OR (95% CI) of tertiles of the baseline HGS/BMI ratio for hypertension in participants aged of ≥ 60 years

In Table 4, a similar analysis was performed on participants over

the age of 60. Only in men, HGS/BMI ratio was negatively associated with the development of hypertension.

4. Discussion

In the present study, we demonstrated that relative HGS, defined by the HGS/BMI ratio, was prospectively associated with the prevalence of hypertension among both genders, independent of confounding factors. The principal finding was that the baseline HGS/BMI ratio was significantly associated with favorable cardio-metabolic risk measures, including BMI, drinking status, SBP, triglycerides, HDL-C, HbA1c, and eGFR in the cohort study. The findings of the present study were consistent with those of previous investigations.^{7,15} Notably, this study showed that the baseline HGS/BMI ratio is an important determinant of health outcomes and provides information relevant to the prevention of CVD risk factors. These data reinforce the importance of muscle strength as a modifiable determinant of cardiometabolic risk in both genders. To our knowledge, few epidemiologic studies have investigated the relationship between the baseline HGS/BMI ratio and hypertension in middle-aged and older community-dwelling Japanese persons.

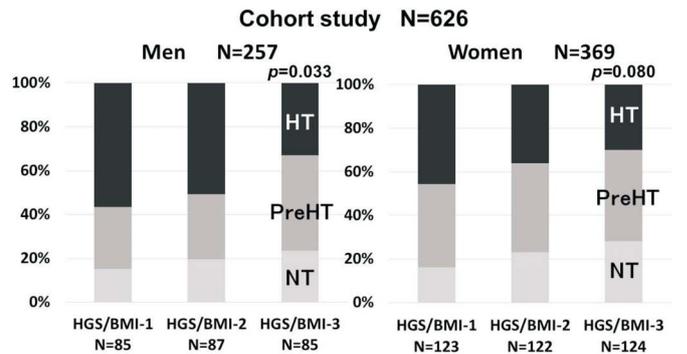


Figure 3. Relationship between tertiles of the baseline HGS/BMI ratio and BP status. In the cohort study, the prevalence of hypertension was significantly decreased only among men (p = 0.033).

Table 2

Characteristics of participants categorized by tertiles of baseline handgrip strength/body mass index ratio in the cohort study.

| Cohort study | Tertiles of baseline handgrip strength/body mass index(m ²) | | | p-value* | |
|---|---|---------------------------|---------------------------|--------------------|---------------------------|
| | Men (N = 257) | 1st 0.68–1.50 (N = 85) | 2nd 1.51–1.77 (N = 87) | | 3rd 1.78–2.47 (N = 85) |
| Women (N = 369) | 0.38–0.94 (N = 123) | 0.95–1.10 (N = 122) | 1.11–1.66 (N = 124) | | |
| Characteristics | | | | | |
| Age (years) | | 70 ± 8 | 67 ± 7 | 62 ± 8 | < 0.001 |
| Body mass index (kg/m ²) | | 23.6 ± 2.9 | 21.9 ± 2.4 | 20.6 ± 2.3 | < 0.001 |
| Handgrip strength (kg) | | 21.6 (18.6–28.1) | 24.8 (21.5–35.8) | 29.2 (24.7–40.2) | < 0.001 |
| Smoking status [‡] : never/past/light/heavy (%) | | 76.9/13.9/2.9/6.3 | 71.8/18.2/2.4/7.7 | 67.9/16.7/5.7/9.6 | 0.272 |
| Drinking status [‡] : never/light/moderate/heavy (%) | | 57.5/25.0/7.2/10.6 | 49.8/22.5/6.7/21.1 | 44.0/25.4/7.7/23.0 | 0.026 |
| Exercise habits, N (%) | | 87 (41.8) | 80 (38.3) | 64 (30.6) | 0.053 |
| History of cardiovascular disease (%) | | 10 (4.8) | 6 (2.9) | 3 (1.4) | 0.132 |
| Systolic blood pressure (mmHg) | | 135 ± 16 | 130 ± 16 | 127 ± 17 | < 0.001 |
| Diastolic blood pressure (mmHg) | | 77 ± 10 | 77 ± 10 | 76 ± 11 | 0.827 |
| Antihypertensive medication, N (%) | | 0 | 0 | 0 | 1.000 |
| Triglycerides (mg/dl) | | 95 (72–131) | 82 (65–119) | 75 (56–101) | < 0.001 |
| HDL cholesterol (mg/dl) | | 60 ± 13 | 68 ± 17 | 73 ± 18 | < 0.001 |
| LDL cholesterol (mg/dl) | | 127 ± 30 | 125 ± 29 | 122 ± 30 | 0.222 |
| Antidyslipidemic medication, N (%) | | 39 (18.8) | 34 (16.3) | 25 (12.0) | 0.155 |
| Hemoglobin A1c (%) | | 5.7 (5.5–5.9) | 5.7 (5.4–5.9) | 5.6 (5.4–5.8) | < 0.001 |
| Antidiabetic medication, N (%) | | 17 (8.2) | 9 (4.3) | 0 | < 0.001 |
| Estimated GFR (ml/min/1.73 m ²) | | 73.1 ± 11.0 | 75.1 ± 7.9 | 77.3 ± 8.5 | < 0.001 |
| Serum uric acid (mg/dl) | | 5.2 ± 1.2 | 5.2 ± 1.4 | 5.1 ± 1.4 | 0.643 |

Data are presented as the mean ± standard deviation, with the exception of data for handgrip strength, triglycerides, and hemoglobin A1c, which are skewed and are presented as the median (interquartile range).

* p-value: Student’s t-test for the continuous variables or the χ^2 test for the categorical variables. Values in bold typeface are statistically significant (p < 0.05).

Table 3

Odds ratios (95% confidence interval) of tertiles of baseline handgrip strength/body weight ratio for hypertension in the cohort studies.

| Cohort study | Tertiles of handgrip strength/body mass index (m ²) | | | p-value |
|-------------------------------------|---|---------------------|-------------------------|-------------------|
| | 1st | 2nd | 3rd | |
| Men (N = 257) | 0.68–1.50 (N = 85) | 1.51–1.77 (N = 87) | 1.78–2.47 (N = 85) | |
| Characteristics | | | | |
| Hypertension, N (%) | 48 (56.5%) | 44 (50.6%) | 28 (32.9%) | 0.006 |
| Unadjusted | 1 (referent) | 0.79 (0.43–1.44) | 0.38 (0.20–0.71) | 0.005 |
| Age-adjusted | 1 (referent) | 0.87 (0.46–1.63) | 0.43 (0.22–0.87) | 0.032 |
| Multivariable-adjusted [†] | 1 (referent) | 0.74 (0.37–1.47) | 0.33 (0.15–0.72) | 0.010 |
| Multivariable-adjusted [‡] | 1 (referent) | 0.65 (0.35–1.22) | 0.27 (0.14–0.54) | < 0.001 |
| Women (N = 369) | 0.38–0.94 (N = 123) | 0.95–1.10 (N = 122) | 1.11–1.66 (N = 124) | |
| Characteristics | | | | |
| Hypertension, N (%) | 56 (45.5%) | 44 (36.1%) | 37 (29.8%) | 0.037 |
| Unadjusted | 1 (referent) | 0.68 (0.40–1.13) | 0.51 (0.30–0.86) | 0.037 |
| Age-adjusted | 1 (referent) | 0.70 (0.42–1.17) | 0.61 (0.35–1.07) | 0.190 |
| Multivariable-adjusted [†] | 1 (referent) | 0.73 (0.43–1.26) | 0.70 (0.37–1.30) | 0.426 |
| Multivariable-adjusted [‡] | 1 (referent) | 0.71 (0.42–1.19) | 0.56 (0.33–0.95) | 0.094 |

Multivariable-adjusted for all confounding factors by multiple logistic regression analysis ([†]: forced entry method; [‡]: stepwise method). The numbers in bold indicate statistical significance.

Table 4

Odds ratios (95% confidence interval) of tertiles of baseline handgrip strength/body weight ratio for hypertension in participants aged of ≥ 60 years.

| Cohort study, age ≥ 60 years | Tertiles of handgrip strength/body mass index (m ²) | | | p-value |
|-------------------------------------|---|---------------------|--------------------|--------------|
| | 1st | 2nd | 3rd | |
| Men (N = 200) | 0.68–1.50 (N = 79) | 1.51–1.77 (N = 65) | 1.78–2.47 (N = 56) | |
| Characteristics | | | | |
| Hypertension, N (%) | 43 (54.4) | 34 (52.3) | 18 (32.1) | 0.024 |
| Multivariable-adjusted [†] | 1 (referent) | 0.90 (0.42–1.93) | 0.38 (0.16–0.92) | 0.050 |
| Multivariable-adjusted [‡] | 1 (referent) | 0.85 (0.43–1.66) | 0.33 (0.16–0.70) | 0.007 |
| Women (N = 311) | 0.38–0.94 (N = 113) | 0.95–1.10 (N = 112) | 1.11–1.66 (N = 86) | |
| Characteristics | | | | |
| Hypertension, N (%) | 50 (44.2%) | 43 (38.4%) | 30 (34.9%) | 0.389 |
| Multivariable-adjusted [†] | 1 (referent) | 0.81 (0.46–1.42) | 0.78 (0.40–1.52) | 0.695 |
| Multivariable-adjusted [‡] | 1 (referent) | 0.80 (0.47–1.36) | 0.71 (0.40–1.27) | 0.482 |

Multivariable-adjusted for all confounding factors by multiple logistic regression analysis ([†]: forced entry method; [‡]: stepwise method). The numbers in bold indicate statistical significance.

Several previous cross-sectional and prospective studies found the link between muscle strength and hypertension. However, this relationship remained unclear. According to the data of 927 Taiwanese individuals aged ≥ 53 years (510 men and 417 women), relative HGS was significantly associated with favorable cardiometabolic risk factors, including BP.⁷ In a total of 1,009 Korean adults (488 men and 521 women), lower relative HGS was significantly associated with higher prevalence of hypertension in men, but not in women.¹⁸ Based on the data of 5,014 Korean adults aged ≥ 20 years (2,472 men and 2,542 women), relative HGS was linked to a significant decrease in the relative risk of hypertension in both genders.⁹ Nevertheless, there are some conflicting reports. Greater absolute HGS was found to be associated with higher BP.^{2,19} Among 4,597 participants (2,184 men and 2,413 women) in the National Health and Nutrition Examination Survey (USA), increased HGS was associated with higher DBP in both men and women; in men, especially those overweight and obese, greater HGS was associated with a higher risk of hypertension.²⁰ In a survey of 89,655 Chinese individuals aged 13–17 years, Dong et al. indicated that high HGS was associated with increased BP also after adjustment for BMI.² A cohort study conducted by Taekema et al.¹⁹ reported that higher HGS was associated with higher SBP in those aged > 85 years. Notably, in middle-age participants, HGS was not significantly associated with BP. Moreover, it was demonstrated that these relationships disappeared after adjusting for confounding factors, including BMI.²¹ The association may be modified by the

smoking status, drinking status, physical activity, cholesterol levels, and glucose levels, and especially mediated by BMI.²² Thus, many studies investigating the relationship between HGS and hypertension have yielded conflicting results. Our study observed that the crude association of a high relative HGS (i.e., HGS/BMI ratio) at baseline with the prevalence of hypertension was significant after adjustment for confounding factors in the prospective studies.

The mechanisms that lead to hypertension in individuals with low relative HGS remain unclear. There are several possible explanations for the association between low relative HGS and hypertension. This association appears to be mediated by increasing insulin resistance and inflammation, as these two factors are both associated with low muscular fitness.¹⁴ In addition, higher muscle fitness was associated with the release of several cytokines and peptides (i.e., myokines) into the circulation, which reduce arterial stiffness.²³ Additionally, some evidence supports that HGS is probably associated with other risk factors for hypertension, such as metabolic syndrome or CVD biomarkers, including triglycerides, HDL, LDL, HbA1c, SUA, and serum adiponectin levels.^{7,10,24}

We must acknowledge several limitations of this study. Firstly, we must consider the effect of antidiabetic and hyperglycemic medication on the present findings. Secondly, the measurements of baseline HGS and characteristics are based on a single assessment, which may have introduced a misclassification bias. Thirdly, the cohort study involved a relatively small sample size due to the pre-

sence of untraceable cases, reflected by the observed discrepancies in the sequential measurements of confounders between 2014 and 2017. The persons included in the cohort were slightly younger and healthier than those excluded, and this may have caused an underestimation of incident hypertension at the 3-year follow-up. Fourthly, as there is a wide range of target ages, the effects of age-related decrease in HGS^{25–27} and increase in blood pressure must be considered. Thus, the generalizability of the obtained results may be limited.

5. Conclusion

Our study showed that the baseline HGS/BMI ratio is strongly and inversely associated with hypertension in the general population in the cohort study. The underlying mechanism of this relationship is unclear; however, it appears to be independent of confounding factors, such as age, exercise habit, smoking status, drinking status, LDL-C, eGFR, SUA, and medication. Thus, the HGS/BMI ratio may provide an important marker for the assessment of risk and a therapeutic target for hypertension.

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Competing interests

The authors declare that they have no competing interests.

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