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Association of muscle strength with cardiovascular risk in Korean adults

Findings from the Korea National Health and Nutrition Examination Survey (KNHANES) VI to VII (2014–2016)

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Abstract

There are few existing studies that examine the association between muscle strength and cardiovascular disease (CVD) risk stratified by sex. Evaluation of the handgrip strength is a simple, quick, and inexpensive method to measure muscle strength. This study assessed the association of handgrip strength with the risk of CVD in the Korean general population.

Data were derived from a subset of an ongoing nationally representative survey: the Korea National Health and Nutrition Examination Survey (KNHANES), 2014 to 2016, which included 8576 participants aged 40 to 79 years (men: 3807; women: 4769). Individual CVD risk was evaluated by calculating the atherosclerotic cardiovascular disease (ASCVD) risk score and the Framingham risk score (FRS) in subjects aged 40 to 79 years without prior CVD.

Multivariate linear regression analysis revealed a significant inverse association (in both men and women) between relative handgrip strength and cardiovascular risk factors, including blood pressure, levels of fasting glucose and triglycerides, waist circumstance, FRS, high sensitivity C-reactive protein levels, and ASCVD risk. A significant positive association between relative handgrip and a low level of high density cholesterol levels in both men and women was identified. In both men and women, subjects in the lowest quartile of handgrip strength had an increased risk of CVD compared with those within the highest quartile (odds ratio range 2.05–3.03).

The results of this study suggest that increased handgrip is associated with a lower degree of cardiovascular risk in both men and women. Longitudinal studies are needed to examine the association between muscle strength and cardiovascular risk.

Abbreviations: ACC = American College of Cardiology, AHA = American Heart Association, ASCVD = atherosclerotic cardiovascular disease, ATP = adult treatment panel, BMI = body mass index, CI = confidence interval, CVD = cardiovascular disease, DBP = diastolic blood pressure, FPG = fasting plasma glucose, FRS = Framingham risk score, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein cholesterol, hs-CRP = high sensitivity C-reactive protein, KNHANES = Korean National Health and Nutrition Examination Survey, MR = Mendelian randomization, NCEP = National Cholesterol Education Program, NHANES = National Health and Nutrition Examination Survey, OR = odds ratio, SBP = systolic blood pressure, TC = total cholesterol, TG = triglycerides, WC = waist circumference.

Keywords: cardiovascular disease, handgrip strength, muscle strength

1. Introduction

Cardiovascular disease (CVD) accounts for 17.5 million deaths globally each year and was the primary global cause of death in 2012.[1] Risk factors for CVD include behavioral risk factors (such as tobacco use, poor diet, alcohol misuse, and physical inactivity) and CVD risk factors (such as high blood pressure, obesity, high blood sugar, and high blood cholesterol).[1] In Korea, cerebrovascular and cardiovascular diseases are the first and second highest causes of mortality due to single-organ disease. While the total CVD mortality rate has significantly decreased over recent years, mortality due to ischemic heart disease has continued to increase over the last 30 years.[2]

Evaluation of handgrip strength is a simple, quick, and inexpensive method to measure muscle strength.[3] Generally, it is an alternative for muscular fitness and a marker of frailty; as a result, it is a strong predictor of all-cause mortality. Previous large longitudinal population studies have reported that handgrip strength is associated with cardiovascular mortality, myocardial infarction, and stroke.[4] Meta-analysis of prospective cohort studies had reported that for the lowest versus highest category of handgrip strength, the hazard ratios were 1.63 for cardiovascular diseases.[5] In the Swiss CoLaus study, it was reported that there was no association between absolute handgrip strength and cardiovascular disease amongst 2707 participants (50–75 years).[6] Recent Mendelian randomization (MR) studies have also shown conflicting results for the association between handgrip strength and CVD. Xu and Hao[7] reported an inverse

Editor: Heye Zhang.

This work was supported by the Soonchunhyang University Research Fund.

The authors have no conflicts of interest to disclose.

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Medicine (2018) 97:47(e13240)

Received: 29 July 2018 / Accepted: 22 October 2018

http://dx.doi.org/10.1097/MD.0000000000013240

causal relationship between handgrip strength and the risk of coronary artery disease or myocardial infarction (MI). However, other MR analyses did not find evidence for causality in the associations between handgrip and cardiovascular events.[3]

Few studies have attempted to explain whether there is a significant difference in the association between muscle strength and CVD, based on sex, but the results were confusing. Reduced relative handgrip strength was associated with an increased Framingham risk score (FRS) only in men, as reported in a Taiwanese study containing 927 participants (510 men and 417 women).[8] Furthermore, a recent UK Biobank study reported that handgrip strength was associated with cardiovascular mortality in men but not in women.[9]

There are few studies evaluating the association between handgrip strength and cardiovascular risk in the Korean population. Therefore, the purpose of this study was to analyze the association between muscle strength and cardiovascular risk factors, atherosclerotic cardiovascular disease (ASCVD) risk, and FRS in men and women using the data from the Korea National Health and Nutrition Examination Survey (KNHANES).

2. Methods

2.1. Study population

KNHANES was conducted annually and was a rolling sampling survey, based on a complex stratified multistage probability cluster survey of a cross-sectional and nationally representative sample of individuals from the non-institutionalized civilian population of the Republic of Korea.

This study was performed using handgrip strength data from KNHANES VI–VII (2014–2016). The following participants were excluded from the study: individuals under the age of 40 years (n=9959); individuals over the age of 80 years (n=780); individuals with prior cardiovascular disease (stroke, myocardial infarction, and angina pectoris) (n=590); individuals with insufficient information to calculate either a ASCVD risk score (n=2020) or Framingham risk score (n=55); and those with data missing on handgrip strength for the right or the left hand (n=1100). After these participants were excluded, a total of 8576 participants (2014: 2483 participants; 2015: 2817 participants; and 2016: 3276 participants) remained eligible for the present study (Fig. 1).

2.2. Ethics statement and data available

The KNHANES studies are conducted according to the principles of the Declaration of Helsinki (Korea Center for Disease Control and Prevention Institutional Review Board No. 2013–07CON-03-4C, 2013-12EXP-03-5C, and 2015-01-02-6C). All participants in the survey signed an informed written consent form. Further information can be found in KNHANES VI/VII, which is available on the KNHANES website (http://knhanes.cdc.go.kr), in addition to other locations.[10] The data from KNHANES is available on request by email by visiting the Korea National Health and Nutrition Examination Survey

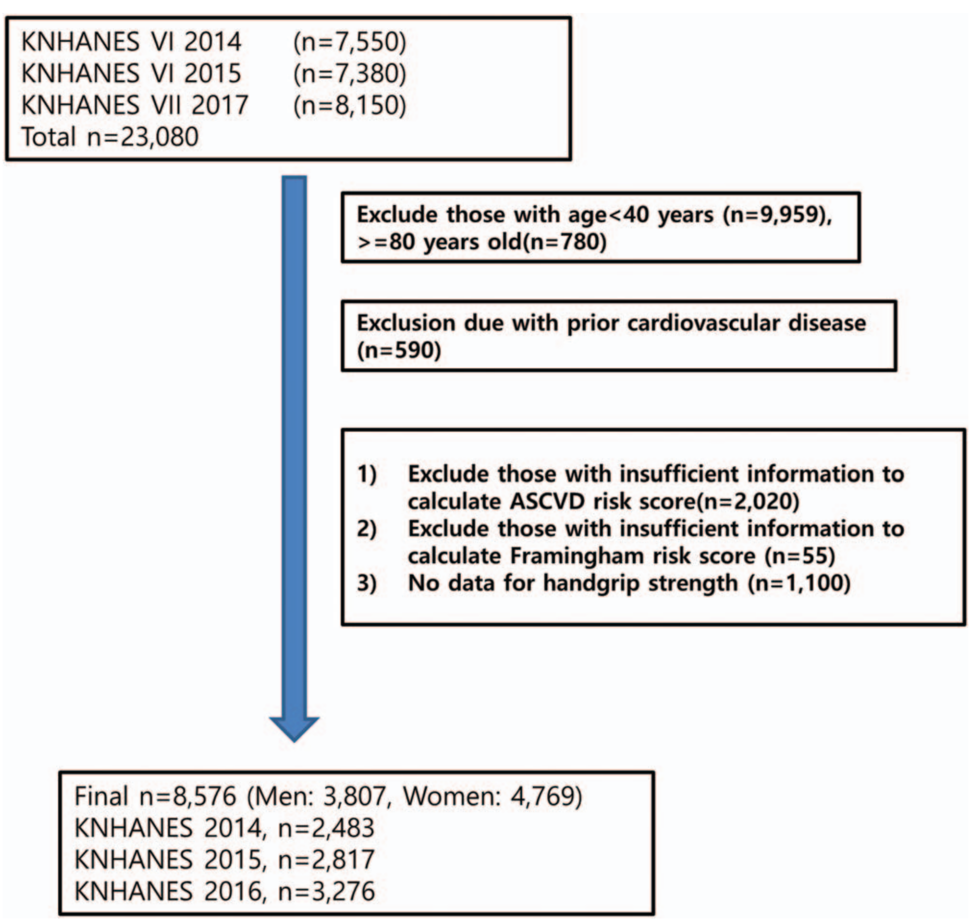

Figure 1. Participant flow diagram illustrating the number of patients excluded by various criteria, and the number of patient data sets analyzed.

website. These data are free of charge for the purposes of academic research.

2.3. Definitions of CVD risk

CVD risk was evaluated using a variety of approaches, including the 10-year ASCVD risk score derived from the 2013 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines—this scoring system is applicable for subjects from 40 to 79 years of age.[11] The FRS was used as a measure to estimate the risk of cardiovascular disease over the next 10 years using the 2001 National Cholesterol Education Program (NCEP)-Adult Treatment Panel (ATP) III method.[12] In this study, we used traditional risk factors: age, sex, smoking habits, total cholesterol, HDL-C, and systolic blood pressure. In addition, individuals in the upper 10% of ACC/AHA ASCVD 10-year risk scores and the upper 20% of Framingham CVD risk scores were classified as a high risk group.[11,13]

2.4. Measurement of handgrip strength

Handgrip strength was measured 3 times in each hand, using a digital grip strength dynamometer (TKK 5401; Takei Scientific Instruments Co., Ltd., Tokyo, Japan). Trained medical technicians instructed the seated participants to hold the dynamometer with the distal interphalangeal finger joints of the hand at 90° to the handle and to squeeze the handle as firmly as they could. After participants had slowly stood up, handgrip strength was measured during expiration. Study participants conducted 3 attempts per hand, with a 1 minute rest period between each attempt to reduce the effect of repetition fatigue. Measures of grip strength were reported for both the left and right hands as an average of the 3 measurements on the respective hand.[14] Relative handgrip strength was defined as grip strength per unit of body mass index (BMI).

2.5. Measurement of clinical and laboratory parameters

Trained medical staff measured the height and weight of patients to the nearest 0.1 cm and 0.1 kg, respectively, following standardized procedures in mobile examination centers. BMI was calculated as weight divided by height squared (kg/m^2), and waist circumference (WC) was measured at the midpoint between the inferior margin of the last rib and the iliac crest in the horizontal plane, in accordance with World Health Organization guidelines.

Blood pressure was measured manually using mercury sphygmomanometers (Baumanometer Wall unit 33; W.A. Baum, Copiague, NY). Readings were taken 3 times on the patient's right arm in a rested and seated position. Final blood pressure values were calculated as an average of the second and third blood pressure readings.

All blood samples were measured in the fasting state and were analyzed within 24 hours after isolation. Fasting plasma glucose (FPG) level was measured using hexokinase ultraviolet (UV). Total cholesterol (TC) and triglyceride (TG) levels were measured using an enzymatic method, and high-density lipoprotein cholesterol (HDL-C) levels were measured using a homogeneous enzymatic colorimetric method. All cholesterol and glucose levels were measured using a Hitachi Automatic Analyzer 7600 (Hitachi, Tokyo, Japan). Hemoglobin A1c (HbA1c) level was measured using high performance liquid chromatography with Tosoh G8 (Tosoh. Corporation, Tokyo, Japan). High sensitivity C-reactive protein (hs-CRP) level was measured using Cobas (Roche, Berlin, Germany) immunoturbidimetry; hs-CRP level was measured only in the 2015 and 2016 cohorts.

2.6. Covariates

Data on smoking status, alcohol consumption, and physical activity were acquired on a self-reported questionnaire. Subjects were categorized as never smokers, past smokers, or current smokers. Current smokers were defined as those who have a self-reported history of >100 cigarettes in their lifetime and who are still smoking. Past smokers self-reported that they only had a history of smoking. Alcohol consumers were defined as participants who had consumed at least 1 glass of alcohol every month over the last year. Physically active participants were defined as those who had performed exercise for least 150 minutes per week, at a medium intensity of physical activity; 75 minutes per week, at a high intensity of physical activity; or a combination of medium and high-intensity physical activity (where 1 minute of high intensity activity = 2 minute of medium intensity activity).

2.7. Statistical analyses

Based on statistical guidance from the Korean Center for Disease Control and Prevention, we used a complex sample analysis to utilize all weighting data from KNHANES. Due to the significant sex differences in handgrip strength, data of men and women were separated in this study. We adjusted age, education (≤ 6, >6, and ≤ 9, >9 and ≤ 12, 12+ years of school), alcohol consumption (yes, no), smoker (never, past, current), and physical activity (yes, no) as covariates. Differences in demographic and anthropometric characteristics were split by sex and compared using the Student *t* test or Chi square test, as appropriate. Results for hs-CRP were not normally distributed for the purposes of linear regression and were log transformed for analysis.

Complex samples multivariate linear regression analysis was performed to analyze the association between relative handgrip strength and FPG, HbA1c, TC, TG, HDL-C, WC, systolic blood pressure (SBP), diastolic blood pressure (DBP), hs-CRP, ASCVD risk, and FRS. Relative handgrip strength was divided into quartiles. Odds ratios were calculated by complex samples logistic regression analysis to examine associations between the quartile of relative handgrip strength and the presence of high CVD risk. We used the *medeff* module[15] in Stata to assess whether obesity mediates the association between handgrip strength and the risk of CVD. The *medeff* command estimates mediation effects, calculating the percentage of the indirect effects accounted for by the factors studied.

Statistical significance was defined when $P < .05$. Continuous and categorical variables were expressed as mean ± standard error and n (%), respectively. Analyses were performed using Stata version 13 (Stata Corp., College Station, TX). Graph was prepared using the R software suite, version 3.3.3 (The Comprehensive R Archive Network: http://cran.r-project.org).

3. Results

The demographic and clinical characteristics of the participants are shown in Table 1. Among a total of 8576 participants, 3807 (44.4%) were men, and 4769 (55.6%) were women. The average age of participants was 57.4 years (range: 40–79 years; average age, men: 57.8 years; average age, women: 57.0 years). The mean

Table 1

General characteristics and cardiovascular risk factors of study population (n=8576).

	Total (n=8576)	Men (n=3807)	Women (n=4769)	*P*
Age, y, n(%)				
40–49	2465 (36.5)	1054 (36.9)	1411 (36.1)	**.008**
50–59	2541 (33.6)	1102 (34.7)	1439 (32.5)	
60–69	2172 (19.1)	994 (18.6)	1178 (19.6)	
≥70	1398 (10.8)	657 (9.8)	741 (11.7)	
Education, y, n (%)				
≤6	2191 (20.4)	726 (14.9)	1465 (25.7)	**<.001**
6<, ≤9	1183 (13.0)	519 (12.1)	664 (13.8)	
9<, ≤12	2739 (35.6)	1193 (34.3)	1546 (36.9)	
12<	2325 (31.0)	1292 (38.7)	1033 (23.6)	
Non response	138	77	61	
Household income, n (%)				
1Q	1600 (15.1)	624 (12.6)	976 (17.8)	**<.001**
2Q	2182 (23.9)	979 (23.8)	1203 (24.2)	
3Q	2216 (28.0)	1005 (29.0)	1211 (27.2)	
4Q	2551 (32.6)	1187 (34.6)	1364 (30.8)	
Non response	27	12	15	
Smoking, n (%)				
Never	5147 (55.3)	714 (18.4)	4433 (92.3)	**<.001**
Former	1972 (24.1)	1820 (44.8)	152 (3.4)	
Current	1457 (20.6)	1273 (36.8)	184 (4.3)	
Drinking, n (%)				
No	4168 (44.1)	1102 (26.5)	3066 (61.7)	**<.001**
Yes	4408 (55.9)	2705 (73.5)	1703 (38.3)	
Physical exercise, n (%)				
No	4529 (49.9)	1861 (48.0)	2668 (53.8)	**<.001**
Yes	3891 (48.1)	1861 (52.0)	3891 (46.2)	
Non response	156	85	71	
BMI, n (%)				
Underweight	192 (2.1)	78 (1.6)	114 (2.7)	**<.001**
Normal weight	5296 (61.5)	2225 (57.7)	3071 (65.4)	
Overweight	2719 (32.0)	1355 (36.5)	1364 (27.5)	
Obesity	369 (4.4)	149 (4.2)	220 (4.5)	
BMI, kg/m^2, mean (SE)	24.16 (0.04)	24.50 (0.06)	23.80 (0.06)	**<.001**
WC, cm, mean (SE)	83.37 (0.13)	86.49 (0.16)	80.27 (0.19)	**<.001**
FPG, mg/dL, mean (SE)	102.96 (0.33)	105.97 (0.50)	99.94 (0.40)	**<.001**
HbA1c,%, mean (SE)	5.79 (0.01)	5.84 (0.02)	5.74 (0.01)	**<.001**
Blood lipid, mg/dL, mean (SE)				
TC	196.29 (0.49)	194.73 (0.74)	197.85 (0.59)	**.001**
TG	151.48 (1.93)	179.48 (3.53)	123.51 (1.50)	**<.001**
HDL-C	50.30 (0.16)	46.86 (0.21)	53.73 (0.23)	**<.001**
LDL-C	115.16 (0.53)	115.69 (0.74)	114.48 (0.66)	.199
Blood pressure, mmHg, mean (SE)				
SBP	120.10 (0.24)	121.93 (0.31)	118.28 (0.31)	**<.001**
DBP	77.13 (0.14)	79.46 (0.20)	74.81 (0.18)	**<.001**
Handgrip, mean (SE)				
Absolute right hand grip, kg	31.45 (0.13)	39.36 (0.15)	23.54 (0.10)	**<.001**
Absolute left hand grip, kg	30.12 (0.12)	37.98 (0.14)	22.26 (0.09)	**<.001**
Relative right hand grip, kg/kg/m^2	1.31 (0.01)	1.62 (0.01)	1.00 (0.01)	**<.001**
Relative left hand grip, kg/kg/m^2	1.26 (0.01)	1.57 (0.01)	0.95 (0.01)	**<.001**
Cardiovascular risk score				
ASCVD risk score, mean (SE)	8.06 (0.13)	10.73 (0.18)	5.39 (0.15)	**<.001**
FRS, mean (SE)	12.39 (0.16)	17.41 (0.25)	7.37 (0.13)	**<.001**
High risk group, n (%)	1903 (18.2)	1517 (30.0)	386 (6.3)	**<.001**

Chi-squared test was used for categorical variable. And Student *t* test was used for continuous variables.
ASCVD=atherosclerotic cardiovascular disease, BMI=body mass index, DBP=diastolic blood pressure, FPG=fasting plasma glucose, FRS=Framingham risk score, HDL-C=high-density lipoprotein cholesterol, SBP=systolic blood pressure, SE=standard error, TC=total cholesterol, TG=triglycerides, WC=waist circumference.
Significant values were expressed in bold.

of absolute right handgrip strength was 29.8 kg (men: 38.1 kg, women: 23.2 kg), and the mean of absolute left handgrip strength was 28.5 kg (men: 36.8 kg, women: 21.9 kg).

General characteristics and cardiovascular risk factors of the weighted samples are presented in Table 1. Age, education, household income, smoking status, alcohol consumption, physical exercise, BMI, WC, levels of FPG, HbA1c, TC, TG, and HDL-C, BP, absolute and relative handgrip strength, ASCVD risk score, FRS, and the percentage of patients at high-risk of CVD differed significantly between men and women.

Table 2

The association between continuous relative hand grip strength and cardiovascular risk factor using multivariate linear regression.

	Relative right hand grip		Relative left hand grip	
	β (95% CI)	P	β (95% CI)	P
Men (n=3807)				
FPG	−9.76 (−12.91, −6.61)	**<.001**	−13.53 (−16.94,−10.12)	**<.001**
HbA1c	−0.33 (−0.44,−0.23)	**<.001**	−0.43 (−0.55,−0.31)	**<.001**
TC	−2.71 (−7.24, 1.83)	0.241	−2.83 (−7.45, 1.79)	.229
TG	−54.04 (−71.12,−36.95)	**<.001**	−57.56 (−73.57,−41.55)	**<.001**
HDL−C	7.14 (5.75, 8.53)	**<.001**	8.02 (6.58, 9.46)	**<.001**
WC	−12.21 (−13.20,−11.21)	**<.001**	−13.07 (−14.11,−12.04)	**<.001**
SBP	−3.59 (−5.35,−1.84)	**<.001**	−2.98 (−4.74,−1.22)	**.001**
DBP	−2.20 (−3.46,−0.94)	**.001**	−1.94 (−3.19,−0.68)	**.003**
ASCVD risk	−3.57 (−4.21,−2.92)	**<.001**	−4.06 (−4.76,−3.36)	**<.001**
FRS	−5.20 (−6.19,−4.21)	**<.001**	−5.82 (−6.88,−4.75)	**<.001**
ln(hs-CRP)	−0.45 (−0.59,−0.31)	**<.001**	−0.53 (−0.68,−0.38)	**<.001**
Women (n=4769)				
FPG	−11.57 (−15.26,−7.87)	**<.001**	−12.59 (−16.72,−8.46)	**<.001**
HbA1c	−0.36 (−0.48,−0.25)	**<.001**	−0.42 (−0.55,−0.29)	**<.001**
TC	−8.38 (−13.45,−3.31)	**.001**	−8.79 (−14.07,−3.52)	**<.001**
TG	−47.88 (−59.79,−35.96)	**<.001**	−52.50 (−65.25,−39.76)	**<.001**
HDL-C	7.72 (5.85, 9.58)	**<.001**	7.90 (5.89, 9.91)	**<.001**
WC	−16.48 (−17.75,−15.21)	**<.001**	−17.27 (−18.60,−15.94)	**<.001**
SBP	−6.36 (−8.71,−4.01)	**<.001**	−6.97 (−9.53,−4.41)	**<.001**
DBP	−2.92 (−4.35,−1.49)	**<.001**	−3.41 (−4.93,−1.90)	**<.001**
ASCVD risk	−2.75 (−3.46,−2.03)	**<.001**	−2.26 (−3.03,−1.50)	**<.001**
FRS	−3.17 (−3.84,−2.50)	**<.001**	−3.04 (−3.76,−2.33)	**<.001**
ln(hs-CRP)	−0.88 (−1.03,−0.73)	**<.001**	−0.96 (−1.13,−0.80)	**<.001**

ASCVD=atherosclerotic cardiovascular disease, BMI=body mass index, CI=confidence interval, DBP=diastolic blood pressure, FPG=fasting plasma glucose, FRS=Framingham risk score, HDL-C=high-density lipoprotein cholesterol, hs-CRP=high sensitivity C-reactive protein, SBP=systolic blood pressure, TC=total cholesterol, TG=triglycerides, WC=waist circumference.
Bold numbers highlight the statistical significance.
Adjusted for age, education, drinking alcohol, smoking status, and physical activity.

After adjustment for age, education, physical activity, alcohol consumption, and smoking status, the relative handgrip strength was inversely associated with the levels of FPG, HbA1c, and TG, WC, SBP, and DBP in both men and women ($P<.05$). Relative handgrip strength was directly associated with HDL-C levels in both men and women ($P<.05$). In women alone, the relative handgrip strength was inversely associated with measured total cholesterol levels. Multiple linear regression using ASCVD risk, FRS, and ln (hs-CRP) as dependent variables revealed that relative handgrip strength was a significant predictor for the risk of CVD (ASCVD β coefficient=(−4.06–[−2.26]), FRS β coefficient=(−5.82–[−3.04]), and ln(hs-CRP) β=(−0.96–[−0.45]); for all factors, $P<.001$) (Table 2).

Among men, the OR for lowest quartile relative to the highest quartile of handgrip strength for having a high risk of CVD was 2.51 for right hand (95% confidence interval [CI]: 1.84–3.43) and 2.92 for left hand (95% CI: 2.08–4.10). Among women, the OR for lowest quartile relative to the highest quartile of handgrip strength of having high risk of CVD was 3.03 for right hand (95% CI 1.57–5.84) and 2.05 for left hand (95% CI 1.17–3.59) compared with those in the highest quartile of relative handgrip strength (Fig. 2).

In men, 47% and 51% of the effect of handgrip strength on risk of ASCVD was mediated by BMI (right and left hand, respectively), while 45% and 50% of the effect of handgrip strength on the risk of ASCVD was mediated by WC (right and left hand, respectively). In women, 34% and 39% of the effect of handgrip strength on the risk of CVD was mediated by BMI (right and left hand, respectively). Furthermore, 48% and 54% of the effect of handgrip strength on the risk of CVD was mediated by WC (right and left hand, respectively).

4. Discussion

In this cross-sectional study, we show that lower handgrip strength is associated with a high risk of CVD. Amongst the risk factors, FPG, HbA1c, TG, and HDL-C levels, SBP, DBP, and WC were found to be associated with handgrip strength. To the best of our knowledge, this study is the first to investigate the association between relative handgrip strength and risk of ASCVD in Korean population. It is also the first report, to identify the involvement of BMI and WC in the relationship between handgrip strength and risk of ASCVD in middle aged-elderly adults using mediation analysis.

Our results are in accordance with those of several previous studies. Data from the National Health and Nutrition Examination Survey (NHANES) supported a correlation between higher relative muscular strength and a more-favorable CVD biomarker profile (SBP and levels of HDL-C, TG, plasma insulin, and glucose) in 4221 participants aged ≥20 years.[16] Lee et al[8] identified that relative handgrip strength (calculated by controlling handgrip strength by BMI), had a significant association with cardiovascular risk factors (SBP, TG, HDL-C, and uric acid in men; HDL-C and fasting glucose in women) in 927 subjects aged 53 years and older (510 men and 417 women) in Taiwan. In a study with 5520 Chinese participants, Li et al[17] identified that relative handgrip strength (normalized to BMI) was associated with favorable levels of HDL-C, LDL-C, TG, and total cholesterol in both sexes; in men alone, relative handgrip strength was associated with a lower risk of impaired fasting glucose levels. A study by Leong et al[4] suggested that handgrip strength was inversely associated with cardiovascular mortality, myocardial infarction and stroke, and grip strength was a stronger predictor of cardiovascular mortality than SBP (this

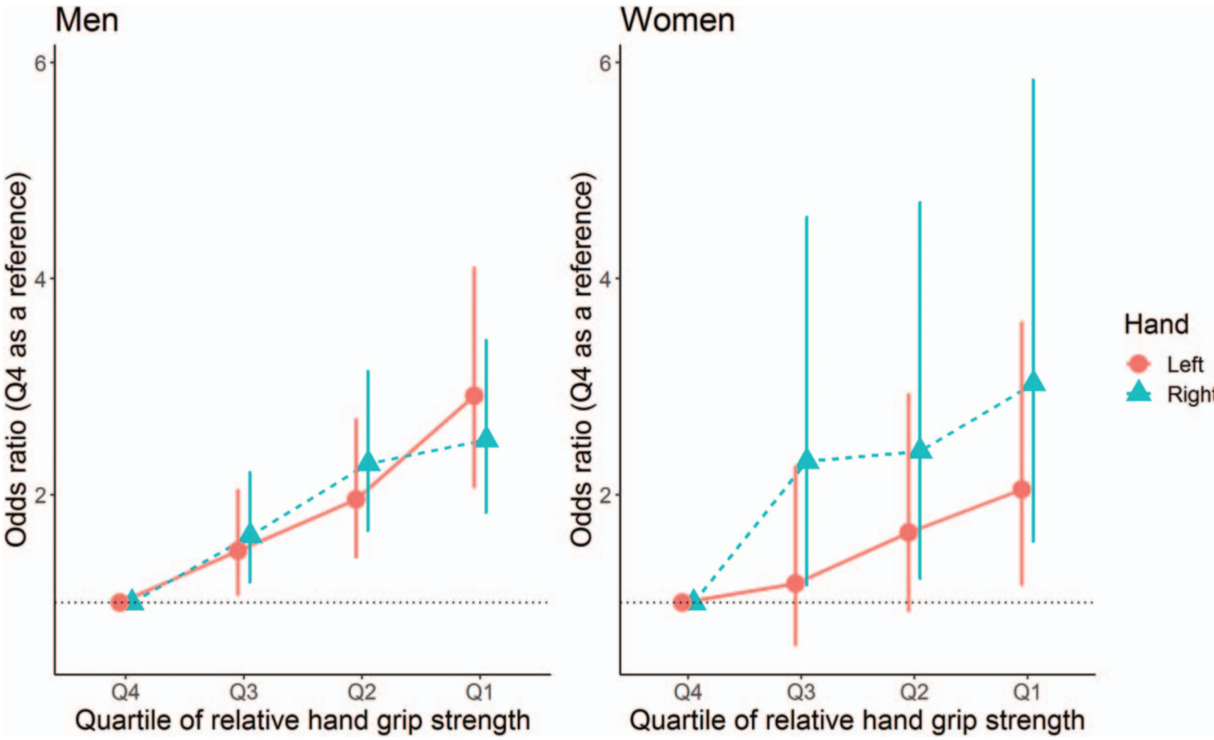

Figure 2. Association between relative hand grip strength quartile and risk of cardiovascular disease using multivariate logistic regression. Adjusted for age, education, alcohol consumption, smoking status, and physical activity. Q=quartile. Men quartiles: Quartile 1 (right: <1.37; left: <1.32), Quartile 2 (right: ≥1.37, <1.57; left: ≥1.32, <1.52), Quartile 3 (right: ≥1.57, <1.80; left: ≥1.52, <1.73), and Quartile 4 (right: ≥1.80, left: ≥1.73). Women quartiles: Quartile 1 (right: <0.82; left: <0.77), Quartile 2 (right: ≥0.82, <0.98; left: ≥0.77, <0.93), Quartile 3 (right: ≥0.98, <1.15; left: ≥0.93, <1.08), and Quartile 4 (right: ≥1.15; left: ≥1.08).

study included 139,691 participants aged 35–70 years). In recent survey, handgrip strength was inverse association with metabolic syndrome in Korean adults.[18]

Previous studies have reported differences in the association of handgrip strength and CVD risk between men and women. Yates et al[9] argued that stratification analysis by sex was more beneficial than considering sex a confounder since there is very little overlap between men and women in the distribution of handgrip strength. Yates et al[9] also illustrated that in the UK population, handgrip strength was not associated with cardiovascular mortality in women, whereas in men, a weak handgrip was associated with an increased cardiovascular mortality (230,670 women and 190,057 men). A previous study involving 647 elderly people (≥65 years) in Korea identified that weight-adjusted handgrip strength was associated with increased cardiovascular risk in men only, and the effect was weaker in older men (≥75 years) than in those aged 65 to 74 years.[19] They hypothesized that the reason for these differences between sexes was that women had lower general muscle strength and a homogenous level of function compared with men.[19] Lee et al[8] reported that relative handgrip strength was associated with FRS in men but not in women, although relative handgrip strength was associated with hs-CRP levels in both sexes. This may be because FRS underestimates the cardiovascular risk of women; consequently, hs-CRP level was a better indicator of cardiovascular health. We also analyzed the subjects by sex and showed no difference in the association between handgrip strength and cardiovascular risk (ASCVD risk score, FRS, and hs-CRP levels) based on sex.

Relative handgrip strength (absolute strength corrected for a measure of body size, such as BMI) was recommended because body size may be a confounding factor in evaluating the association between handgrip strength and cardiovascular disease.[16] In contrast to relative handgrip strength, Li et al[17] found that absolute strength (non-adjusted) was paradoxically associated with cholesterol levels. In Switzerland, a study using the absolute handgrip strength data of 3468 adults (aged 50–75 years) revealed that handgrip strength showed only moderate associations with cardiovascular risk markers.[20] Some studies have reported no association between handgrip strength and cardiovascular risk when handgrip strength was categorized as low or normal according to fragility criteria.[6] In addition, it has been suggested that relative handgrip strength is a better tool for CVD risk assessment than dominant handgrip strength.[8]

The underlying mechanism for the relationships between muscle strength and risk factors for CVD has not been clearly explored. A previous study on a Spanish population of young children (ages 8–11 years) has reported that 35.1% and 39.3% of the effect of muscular fitness (measured by handgrip and standing long jump test) on the cardiometabolic risk index was mediated by BMI in boys (n=587) and girls (n=571).[21] A recent study has also shown that cardiorespiratory fitness and WC mediate the association between muscular strength (measured by handgrip strength) and the cardiometabolic risk index in 370 participants drawn from a population of Spanish first year college students.[22] The adiponectin receptors, AdipoR1 and AdipoR2, are most abundantly found in the skeletal muscles and liver, respectively. Interaction of adiponectin with its receptor may result in anti-hyperglycemic, anti-atherogenic, and anti-inflammatory effects, which may hamper the development of CVD.[23] In this study, the mediation effect of BMI and WC was about 30% to 50%.

The study presented here has significant advantages. This study utilizes a large-scale nationally representative population sample, which has allowed for stratification by sex and the investigation of a number of key cardiovascular biomarkers, such as ASCVD, FRS, and hs-CRP levels. In addition, this is the first report to suggest that general and abdominal obesity has a mediation effect in the association between handgrip strength and ASCVD amongst the middle-aged and elderly. Finally, to improve the reliability of our sampling, we limited the study population by excluding those with a prior CVD history to prevent reverse causality.

This study has several limitations. A major limitation of this study was the cross-sectional design. Therefore, we could not study the occurrence of CVD as in the cohort study. Second, the only participants were Korean, so extrapolation of our findings to other ethnicities may be limited. Third, we have used handgrip strength as the sole indicator of muscular strength. Fourth, one of outcome variables of this study, ASCVD risk score and FRS are not biomarkers. Diagnostic, prognostic, or predictive biomarkers of CVD were not investigated in the study except hs-CRP. Finally, due to the limitations of our data, we could not conduct extensive experiments such as machine learning (regression convolutional neural network).

5. Conclusion

This study shows that relative handgrip strength is significantly associated with more favorable cardiovascular biomarker levels in both men and women. Furthermore, general and central obesity was mediator for the relationship between handgrip strength and ASCVD. More longitudinal research studies are required amongst the general population to determine the true validity of handgrip strength as a diagnostic tool to identify cardiovascular disease risk.

Author contributions

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