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Relative Hand Grip and Back Muscle Strength, but Not Mean Muscle Strength, as Risk Factors for Incident Metabolic Syndrome and Its Metabolic Components: 16 Years of Follow-Up in a Population-Based Cohort Study

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Abstract: Muscle strength is associated with health outcomes and can be considered an important disease predictor. There are several studies examining the relationship between hand grip strength (HGS) and metabolic syndrome (MetS). However, no results have been reported for long term longitudinal studies. In this study, we investigated the relationship between mean HGS, back muscle strength (BMS), relative HGS and BMS, and MetS. A total of 2538 non-MetS subjects aged 40–69 years (1215 women and 1323 men) in the Korean Genome and Epidemiology Study (KoGES) Ansan cohort were followed for 16 years. The relationships between incident MetS (iMetS) and muscle strength were estimated using Cox proportional hazard regression models after adjusting for the confounding factors. Increases in standard deviation (SD) and the lower quartile groups for relative HGS and BMS were significantly associated with iMetS in men and women. Moreover, increases in SD and high quintile groups (decreased HGS group) for the delta change in the mean and relative HGS were significantly associated with iMetS in men only. In addition, SD increases for the relative HGS and BMS were significantly associated with iMetS components in men and women. The present study suggests that lower relative HGS and BMS are associated with high risk for the future development of MetS.

Keywords: metabolic syndrome; handgrip strength; back muscle strength; relative muscle strength; physical activity; public health

1. Introduction

Metabolic syndrome (MetS) is a risk factor for cardiovascular disease morbidity and type 2 diabetes mellitus, which can lead to serious disabilities and mortality [1]. Therefore, MetS has become one of the major public health problems worldwide. MetS, also termed insulin resistance syndrome, the deadly quartet, and syndrome X syndrome, is defined as having three or more of five cardiovascular risk factors, including central obesity, hyperglycemia, decreased high density lipoprotein (HDL), elevated triglyceride (TG), and elevated blood pressure [2]. The criteria for MetS usually utilize the three popular definitions provided by the World Health Organization (WHO), the National Cholesterol Education Program (NCEP) Adult Treatment Panel III, and the International Diabetes Federation [3]. MetS is rapidly increasing in Korean society (from 24.9% in 1998 to 29.2% in

2009, and 31.3% in 2007), especially in those in their 50s and older, with a high prevalence rate of more than 40% [4].

Muscle mass and strength generally increase in adolescents and young people and decrease naturally throughout middle and old age [5]. Handgrip strength (HGS) is a very useful tool because it is an easy and comfortable method for measuring muscle strength [6]. Although muscle mass and muscle strength are highly correlated, muscle strength decreases faster than muscle mass with age [7]. HGS may be a critical important disease predictor because HGS is associated with health outcomes, including type 2 diabetes mellitus (T2DM) [8], hypertension (HTN) [9], mortality [10], and cognitive impairment [11].

The use of a relative method for muscle strength is recommended when investigating the association between disease states, because body composition and body size are highly correlated with muscle strength [12,13]. Relative muscle strength is defined by four popular measuring methods, including body mass index (BMI), body weight, waist circumference (WC), and the waist-hip ratio (WHR) [14,15].

Until recently, most studies of HGS, relative HGS, and MetS have reported cross-sectional findings [4,16–25], with one follow-up investigation reported [26]. Moreover, adolescent studies have shown that weight relative HGS is associated with MetS [22]. In the median 4-year follow-up survey, weight relative HGS showed significant risk rates in the first and second quartiles for incident MetS (iMetS) in comparison with the high quartile group (1.76 times and 1.67 times for men and 1.28 times and 1.3 times for women, respectively) [26]. In addition, the results of various muscle strength measurements, such as upper body strength/weight and skeleton mass index (SMI), showed significant association with iMetS [27,28]. Cardiorespiratory fitness is inversely associated with iMetS [29]. To sum up these results, although direct comparison is difficult, the above findings confirm that muscle mass and MetS are related regardless of the muscle mass measurement method or area. Nevertheless, there is no comparison of the effects of HGS, body mass index (BMI), body weight, and WC relative to HGS on metabolic syndrome. Additionally, there were no reported effects of iMetS due to muscle mass changes during the follow-up period.

Back muscle strength (BMS) decreases with age, similar to HSG, and influences quality of life in older adults [30]. Moreover, the correlation coefficient of HGS and BMS is higher in men (0.67) than in women (0.55) [31]. However, there have been no reports of a relationship between back muscle strength and incident metabolic syndrome. Therefore, this study aimed to assess the relationship between HGS, BMS, BMI-, weight-, WC-relative HGS and BMS, HGS delta change, and iMetS in a 16-year, longitudinal large cohort.

2. Materials and Methods

2.1. Study Participants and Population

Participants were selected among participants from the Korean Genome and Epidemiology Study (KoGES), an ongoing prospective population-based study among the Ansan cohort of middle-aged and older adults in Korea. The Ansan cohort was initiated in 2001 and has been followed biennially during scheduled site visits for 16 years. At baseline, the initial cohort of 5012 participants aged 40 to 69 years were randomly recruited from Ansan city (2518 men and 2494 women). Data collected from the cohort included questionnaires, anthropometric measurements, blood tests, and clinical examinations by trained interviewers and examiners.

For the present study, 1186 out of 5012 participants were excluded at baseline (HGS and BMS (N = 351), body mass index (BMI; N = 1), WC (N = 7), cardiovascular disease (CVD; N = 82), and MetS (N = 743)). During the 16-year study period, 1288 out of 3826 participants were lost to follow-up due to a lack of participation. Finally, 2538 participants remained eligible for this investigation (Figure 1). The follow-up rate at the ninth examination was 50.6%. This study protocol was conducted according to the guidelines of the Declaration of Helsinki and approved by Institutional Review Board of the Korea University Ansan Hospital, and written informed consent was obtained from all study participants.

We obtained the delta change in HGS in baseline and at the eighth follow-up.

Figure 1. Participant flowchart.

2.2. Muscle Strength

HGS and BMS were measured at baseline using a digital grip dynamometer (Grip-D T.K.K.5401 and T.K.K.5102, TAKEI Science Instruments Co., Ltd., Nigata, Japan). The HGS was measured three or two times in each hand at resting intervals of one-minute. To measure BMS, the participants stood upright and were positioned with their hands on the knob while the values were measured three times by straightening the waist at resting intervals of one-minute. The average muscle strength was used for this study. Body mass index (BMI), body weight, and WC are well-known factors used for relative muscle strength [4,14–25]. Relative muscle strength was calculated as the muscle strength divided by BMI, body weight, and WC for analysis independent of body composition. For further analysis, muscle strength was divided into quartiles or quintiles according to gender. In each case, the highest quintile group was fixed as the reference group for relative muscle strength. For handgrip delta change analysis, we calculated the difference between eighth follow-up examination and baseline. Middle group of quintiles was fixed as the reference group, which is a group where the muscle strength does not change.

2.3. Covariates

Study participants completed questionnaires including demographic information, medical conditions, family history of diseases, and lifestyle. Briefly, BMI was calculated as body weight (kg) divided by height squared (m^2). Family history of diseases were defined as a positive parental history. Metabolic equivalent (MET) values were evaluated based on a compendium of leisure-time physical activity (LPA). Alcohol consumption was calculated using questionnaires, including type of drink, amount, and frequency. Smoking status was categorized as never, past, and current smoker. Blood test was measured using an ADVIA 1650 Auto Analyzer (Siemens Medical Solutions, Tarrytown, NY, USA).

2.4. Definitions of Metabolic Syndrome

MetS was defined according to the NCEP Adult Treatment Panel III [32]. MetS was defined with three of five criteria as follows: WC (≥ 90 cm for men and ≥ 80 cm for women, abdominal obesity based on Asia–Pacific criteria [33]), TG (≥ 150 mg/dL), high density lipoprotein (HDL) cholesterol (< 40 mg/dL and < 50 mg/dL for gender, respectively), presence of HTN (systolic/diastolic blood pressure (SBP/DBP, $\geq 130/85$ mmHg and/or the use of antihypertensive agents), and high fasting blood glucose (≥ 100 mg/dL or the use of antidiabetic agents).

2.5. Statistical Analysis

Baseline characteristics were demonstrated using generalized linear models for continuous variables and chi-square tests for categorical variables. To assess the risk of iMetS, we were used Cox proportional hazard regression models (HRs), 95% confidence intervals (CIs), and p values. The iMetS, according to the increase in the HGS, was shown as a linear trend p . Sensitivity analysis for adjusted Cox hazard ratios demonstrated a one standard deviation (SD) increase in mean HGS, BMS, and relative muscle strength, stratified by follow-up time, gender and age subgroups. The covariates adjusted for in multivariate models were as follows: age, family history of hypertension (yes, no), family history of T2DM (yes, no), job (homemaker, white collar, or blue collar), income (Korean Won (KRW) <1,000,000, 1,000,000 ≤ or KRW < 2,000,000, KRW 2,000,000 ≤ or <4,000,000, or KRW 4,000,000 ≤), education (<12 year and ≥12 year), marriage status (yes, no), smoker (never smoker, ex-smoker, or current smoker), alcohol consumption (g/day), exercise (METs), and menopause (yes, no). Statistical analyses were performed using SAS software (SAS 9.4, SAS Institute, Cary, NC, USA). Statistically significant was defined using a two-tailed $p < 0.05$.

3. Results

3.1. Demographic and Clinical Characteristics of the Study Participants According to Gender

The demographic and clinical characteristics of participants in this study are shown in Table S1. The gender ratio of this study included 47.9% women and 52.1% men in 2538 total subjects. The mean ages were 47.9 ± 7.0 for women and 47.8 ± 6.8 for men ($p = 0.727$). Men constituted higher percentages of ex- or current smokers than women (35.4% vs. 1.0% and 42.8% vs. 1.9%, respectively) ($p < 0.001$). Most women were homemakers (65.8%), followed by blue collar workers (30.0%), whereas most men were blue collar workers (69.7%), followed by white collar workers (23.7%) ($p < 0.001$). The average monthly income of the family was at a higher percentage of KRW 2 to 4 million (43.2% for women and 48.6% for men) and a lower percentage of KRW 1 million (15.1% for women and 7.3% for men) ($p < 0.001$). Men had a higher level of education than women (32.0% vs. 11.3%) ($p < 0.001$). Married status was higher in men than women (90.3% for women and 97.2% for men) ($p < 0.001$). In total, 19.4% of women had experienced menopause. Height, body weight, and alcohol consumption level were significantly higher in men than in women ($p < 0.001$). In five metabolic component factors, WC, TG, SBP, and DBP levels were significantly higher in men than in women ($p < 0.001$). HDL-cholesterol was significantly higher in women than in men ($p < 0.001$). Mean HGS, BMS, BMI-, Weight-, and WC-relative muscle strength levels were higher in men than in women ($p < 0.001$). Family history of DM (FHD, 15.8% for women and 13.3% for men), family history of HTN (FHH, 20.9% for women and 20.0% for men), BMI (24.4 ± 2.8 for women and 24.5 ± 2.7 for men), and exercise (127.0 ± 198.0 for women and 125.3 ± 198.7 for men) were not different between women and men.

3.2. Characteristics of Study Participants in Normal and Incident Metabolic Syndrome According to Gender

The baseline characteristics of the study participants in normal and iMetS, according to gender, are shown in Table 1. Men were significantly more likely to have experienced iMetS than women (41.4% vs. 36.4%) ($p < 0.001$).

In women, age was significantly higher in the iMetS than in the normal group (50.5 ± 7.9 vs. 46.4 ± 5.9) ($p < 0.001$). KRW 1 million of average family monthly income and menopause status in iMetS were higher in percentage (19.9% vs. 12.4% and 26.7% vs. 15.3%, respectively) ($p \leq 0.005$). The BMI and body weight level were higher in the iMetS than in the normal group. In contrast, married status in iMetS was lower by a few percentage points (87.8% vs. 91.7%), and the height level was higher in the normal group than in the iMetS group. In five metabolic component factors, WC, TG, SBP, and DBP levels were significantly higher in iMetS than in the normal group ($p < 0.001$). On the contrary, HDL-cholesterol was significantly higher in the normal group than in iMetS ($p < 0.001$).

BMI-relative, weight-, and WC-relative muscle strength levels were higher in iMetS than in the normal group ($p < 0.001$). In contrast, mean HGS and BMS were not significant between iMetS and normal group. Smoking (1.0% for normal vs. 0.9% for iMetS for ex-smokers and 1.6% for normal vs. 2.5% for iMetS for current smokers); family history of T2DM (14.5% for normal and 18.1% for iMetS); family history of HTN (20.1% for normal and 22.4% for iMetS); job (30.5% for normal and 29.2% for iMetS in blue collar workers, 4.7% for normal and 3.2% for iMetS in white collar workers, 64.8% for normal and 67.6% for iMetS in homemakers); education (12.4% for normal and 9.3% for iMetS); alcohol consumption (1.3 ± 4.7 for normal and 1.9 ± 6.4 for iMetS); exercise (127.3 ± 200.3 for normal and 126.5 ± 194.3 for iMetS) were not different between the iMetS and normal groups.

Table 1. Demographic and clinical characteristics in baseline according to non-MetS and incident MetS.

		Women (n = 1215)			Men (n = 1323)		
		Normal (n = 773, 63.6%)	iMetS (n = 442, 36.4%)		Normal (n = 775, 58.6%)	iMetS (n = 548, 41.4%)	
General Characteristics							
Age (year)		46.4 ± 5.9	50.5 ± 7.9	<0.001	47.5 ± 6.5	48.2 ± 7.3	0.062
Smoker	Ex-smoker	8 (1.0%)	4 (0.9%)	0.504	291 (37.5%)	178 (32.5%)	<0.001
	Current smoker	12 (1.6%)	11 (2.5%)		291 (37.5%)	275 (50.2%)	
Family history of T2DM	Yes	112 (14.5%)	80 (18.1%)	0.097	91 (11.7%)	85 (15.5%)	0.047
Family history of hypertension	Yes	155 (20.1%)	99 (22.4%)	0.332	132 (17.0%)	132 (24.1%)	0.002
Job	Blue color	236 (30.5%)	129 (29.2%)	0.363	543 (70.1%)	379 (69.2%)	0.594
	White color	36 (4.7%)	14 (3.2%)		185 (23.9%)	128 (23.4%)	
	Housekeeper	501 (64.8%)	299 (67.6%)		47 (6.1%)	41 (7.5%)	
Income (KRW)	<1 million	96 (12.4%)	88 (19.9%)	0.005	56 (7.2%)	41 (7.5%)	0.515
	1–2	238 (30.8%)	133 (30.1%)		213 (27.5%)	154 (28.1%)	
	2–4	347 (44.9%)	178 (40.3%)		388 (50.1%)	255 (46.5%)	
	4≤	92 (11.9%)	43 (9.7%)		118 (15.2%)	98 (17.9%)	
Education	<12 year	96 (12.4%)	41 (9.3%)	0.096	258 (33.3%)	165 (30.1%)	0.222
Marry Status	Yes	709 (91.7%)	388 (87.8%)	0.026	754 (97.3%)	532 (97.1%)	0.820
Menopause Status	Yes	118 (15.3%)	118 (26.7%)	<0.001	NA	NA	
Body Mass Index (kg/m ²)		23.6 ± 2.5	25.8 ± 2.8	<0.001	23.9 ± 2.6	25.4 ± 2.5	<0.001
Height (cm)		155.7 ± 5.1	154.5 ± 4.9	<0.001	167.8 ± 5.5	167.9 ± 5.8	0.635
Weight (kg)		57.3 ± 6.7	61.6 ± 7.2	<0.001	67.4 ± 8.4	71.6 ± 9.1	<0.001
Alcohol consumption (g/day)		1.3 ± 4.7	1.9 ± 6.4	0.072	17.0 ± 25.2	22.6 ± 30.2	<0.001
Leisure physical activity (Met)		127.3 ± 200.3	126.5 ± 194.3	0.945	124.0 ± 187.9	127.1 ± 213.1	0.781
Metabolic Components							
Waist circumference (cm)		73.6 ± 6.2	79.5 ± 6.6	<0.001	80.9 ± 6.7	85.4 ± 6.6	<0.001
HDL-cholesterol (mg/dL)		54.9 ± 11.9	49.8 ± 10.7	<0.001	49.6 ± 10.7	44.6 ± 8.9	<0.001
Triglycerides (mg/dL)		100.0 ± 52.0	133.1 ± 75.0	<0.001	132.4 ± 70.1	188.1 ± 109.2	<0.001
Systolic Blood Pressure (mmHg)		107.0 ± 13.8	118.7 ± 15.9	<0.001	114.0 ± 13.8	120.3 ± 15.7	<0.001
Diastolic Blood Pressure (mmHg)		70.8 ± 9.0	78.2 ± 9.9	<0.001	77.9 ± 10.0	82.0 ± 10.8	<0.001
Muscle Strength							
Hand grip Strength (HGS)							
Mean HGS (kg)		22.0 ± 3.8	21.4 ± 3.8	<0.001	35.4 ± 5.5	35.0 ± 5.8	0.216
BMI-relative Mean HGS		0.94 ± 0.19	0.84 ± 0.16	<0.001	1.49 ± 0.26	1.39 ± 0.24	<0.001
Weight-relative Mean HGS		0.39 ± 0.07	0.35 ± 0.06	<0.001	0.53 ± 0.09	0.49 ± 0.08	<0.001
WC-relative Mean HGS		0.30 ± 0.06	0.27 ± 0.05	<0.001	0.44 ± 0.08	0.41 ± 0.07	<0.001
Back Muscle Strength (BMS)							
Mean BMS (kg)		42.9 ± 12.3	42.5 ± 11.8	0.653	83.6 ± 19.2	84.3 ± 19.2	0.536
BMI-relative Mean BMS		1.83 ± 0.55	1.66 ± 0.46	<0.001	3.52 ± 0.82	3.34 ± 0.78	<0.001
Weight-relative Mean BMS		0.76 ± 0.22	0.69 ± 0.19	<0.001	1.25 ± 0.29	1.19 ± 0.28	<0.001
WC-relative Mean BMS		0.59 ± 0.17	0.54 ± 0.15	<0.001	1.04 ± 0.24	0.99 ± 0.23	<0.001

Abbreviation: iMetS, incident metabolic syndrome; T2DM, type 2 diabetes mellitus; KRW, Korean Won; BMI, body mass index; WC, waist circumference.

In men, current smoking, a family history of HTN, and a family history of T2DM were higher by percentage in iMetS than in the normal group (50.2% for iMetS vs. 37.5% for normal group, 24.1% for iMetS vs. 17.0% for normal group, and 11.7% for normal and 15.5%

for iMetS, respectively) ($p \leq 0.002$). The BMI and body weight levels were significantly higher in iMetS than in the normal group (25.4 ± 2.5 for iMetS vs. 23.9 ± 2.6 for normal group, and 71.6 ± 9.1 for iMetS vs. 67.4 ± 8.4 for the normal group, respectively, $p < 0.001$). For five metabolic component factors, WC, TG, SBP, and DBP levels were significantly higher in iMetS than in the normal group ($p < 0.001$). In contrast, HDL-cholesterol was significantly higher in the normal group than in iMetS ($p < 0.001$). BMI-, weight-, and WC-relative muscle strength mean and maximum levels were higher in iMetS than in the normal group ($p < 0.001$). In contrast, mean and maximum HGS and BMS were not significantly different between iMetS and normal group. Age (47.5 ± 6.5 vs. 48.2 ± 7.3 , $p = 0.062$); job (70.1% for normal and 69.2% for iMetS in blue collar workers, 23.9% for normal and 23.4% for iMetS in white collar workers, 6.1% for normal and 7.5% for iMetS in homemakers, $p = 0.594$); income (27.5% for normal and 28.1% for iMetS in KRW 1–2 million, 50.1% for normal and 46.5% for iMetS in KRW 2–4 million, 15.2% for normal and 17.9% for iMetS in more than KRW 4 million, $p = 0.515$); more than 12 years of education (33.3% for normal and 30.3% for iMetS, $p = 0.222$); married status (97.3% for normal and 97.1% for iMetS, $p = 0.820$); height (167.8 ± 5.5 for normal and 167.9 ± 5.8 for iMetS, $p = 0.635$); and exercise (124.0 ± 187.9 for normal and 127.1 ± 213.1 for iMetS, $p = 0.781$) were not different between the iMetS and normal groups.

Table S2 shows the sex-adjusted correlation coefficient of relative HGS and metabolic components. BMI, Weight, and WC-relative HGS and BMS showed a higher correlation with metabolic components than means HGS. In particular, relative HGS showed higher correlation than relative BMS.

3.3. Cox Proportional Hazard Ratios for Incident Metabolic Syndrome According to Inverse One Standard Deviation Increase in Mean Hand Grip Strength, Back Muscle Strength, and Relative Muscle Strength in Gender

The MetS risk of inverse one SD increase in muscle strength and relative muscle strength was shown in Table 2, adjusted for the confounding factors.

Table 2. Adjusted hazard ratio (HR) of incident metabolic syndrome associated with inverse one standard deviation increase in mean hand grip strength, back muscle strength, and relative muscle strength according to gender.

	HGS		BMS	
	Univariate HR (95% CI) <i>p</i>	Multivariate HR (95% CI) <i>p</i> *	Univariate HR (95% CI) <i>p</i>	Multivariate HR (95% CI) <i>p</i> *
Women				
Mean (kg)	1.176 (1.066–1.296) 0.001	1.042 (0.938–1.157) 0.445	1.045 (0.951–1.149) 0.355	0.932 (0.845–1.028) 0.161
BMI-relative	1.680 (1.514–1.864) < 0.001	1.494 (1.337–1.671) < 0.001	1.352 (1.224–1.494) < 0.001	1.192 (1.072–1.324) 0.001
Weight-relative	1.618 (1.461–1.792) < 0.001	1.454 (1.306–1.620) < 0.001	1.297 (1.175–1.432) < 0.001	1.158 (1.044–1.283) 0.005
WC-relative	1.662 (1.501–1.841) < 0.001	1.447 (1.293–1.620) < 0.001	1.314 (1.190–1.451) < 0.001	1.135 (1.022–1.261) 0.019
Men				
Mean HGS (kg)	1.076 (0.984–1.176) 0.107	1.078 (0.982–1.182) 0.114	0.982 (0.903–1.069) 0.679	0.987 (0.905–1.076) 0.766
BMI-relative	1.454 (1.324–1.596) < 0.001	1.470 (1.335–1.618) < 0.001	1.203 (1.106–1.309) < 0.001	1.212 (1.113–1.320) < 0.001
Weight-relative	1.465 (1.338–1.604) < 0.001	1.472 (1.342–1.614) < 0.001	1.207 (1.110–1.313) < 0.001	1.212 (1.114–1.317) < 0.001
WC-relative	1.422 (1.298–1.559) < 0.001	1.431 (1.302–1.574) < 0.001	1.187 (1.091–1.292) < 0.001	1.190 (1.092–1.297) < 0.001

Abbreviation: HGS, handgrip strength; BMC, back muscle strength; HR, hazard ratio; CI, confidence interval; BMI, body mass index; WC, waist circumference. * Adjusted for baseline muscle strength plus age; family history of DM (yes, no); family history of hypertension (yes, no); job (homemaker, white collar, or blue collar); income (KRW < 1,000,000, KRW 1,000,000 ≤ or < 2,000,000, KRW 2,000,000 ≤ or < 4,000,000, or KRW 4,000,000 ≤); education (<12 years and ≥12 years); married status (yes, no); smoker (never smoker, ex-smoker, or current smoker); alcohol consumption (g/day); and leisure physical activity (METs). Women added menopause (yes, no).

In univariate analysis, the HR per inverse one SD increase in BMI-, weight-, and WC-relative HGS and BMS was associated with a lower risk of iMetS in women and men (HR = 1.187–0.168, $p < 0.001$). However, the HGS and BMS in both women and men were not associated with iMetS. After adjusting for confounders, the HR per inverse one SD increase in BMI-, weight-, and WC-relative HGS was associated with a lower risk of iMetS in women and men (HR = 0.135–0.494, $p < 0.005$). However, HGS and BMS were not

associated with iMetS in both women and men. For sensitivity analyses, we calculated the HR for inverse one standard deviation increase in mean HGS, BMS, and relative muscle strength, stratified by follow-up time (second, sixth, and ninth follow-up) and gender subgroups (Table S3). We were able to confirm that a similar trend was maintained during the follow-up period.

3.4. Cox Proportional Hazard Ratios for Incident Metabolic Syndrome According to Quartile Groups of Mean Hand Grip Strength, Back Muscle Strength, and Relative Muscle Strength by Gender

Participants were divided into quartile groups based on gender-specific HGS and BMC, and relative HGS and BMC (Table 3 and Table S4). In univariate analysis, HGS and BMS was not associated with iMetS in both women and men. However, BMI-, weight-, and WC-relative HGS and BMS were shown to have higher HR rates for iMetS in women and men (HR = 1.718–3.858, $p \leq 0.001$ in women and HR = 1.377–2.515, $p \leq 0.015$ for men), excluding the third quartile of the BMS of men. After adjusting for confounders, HGS and BMS was also not associated with iMetS in both women and men. However, the first, second, and third quartile of BMI-, weight-, and WC-relative HGS and BMS was shown to have higher HR values for iMetS in women and men (HR = 1.459–2.821, $p \leq 0.001$ for women and HR = 1.368–2.821, $p \leq 0.024$ for men), excluding the third quartile of the BMS of men. Additionally, the p value for linear trend was shown to be significant ($p < 0.001$).

Table 3. Adjusted hazard ratio (HR) of incident metabolic syndrome associated with quartile group of mean hand grip strength, back muscle strength, and relative muscle strength according to gender.

Muscle Strength	Group	HGS		BMS	
		Women HR (95% CI) p *	Men HR (95% CI) p *	Women HR (95% CI) p *	Men HR (95% CI) p *
Mean (kg)	Q4	Reference	Reference	Reference	Reference
	Q3	0.880 (0.669–1.159) 0.363	1.032 (0.805–1.323) 0.801	1.135 (0.877–1.469) 0.336	0.897 (0.706–1.139) 0.372
	Q2	0.896 (0.685–1.173) 0.426	1.117 (0.875–1.426) 0.375	0.907 (0.688–1.197) 0.491	1.141 (0.903–1.441) 0.268
	Q1	0.897 (0.674–1.194) 0.456	1.173 (0.914–1.505) 0.211	0.895 (0.676–1.185) 0.439	0.968 (0.757–1.238) 0.794
p value for linear trend		0.506	0.166	0.224	0.72
BMI-relative	Q4	Reference	Reference	Reference	Reference
	Q3	1.801 (1.293–2.511) 0.001	1.369 (1.042–1.799) 0.024	1.787 (1.334–2.393) < 0.001	1.188 (0.921–1.531) 0.185
	Q2	2.209 (1.597–3.057) < 0.001	1.553 (1.188–2.030) 0.001	1.631 (1.213–2.193) 0.001	1.551 (1.215–1.980) < 0.001
	Q1	2.821 (2.028–3.923) < 0.001	2.401 (1.854–3.110) < 0.001	1.579 (1.163–2.143) 0.003	1.596 (1.247–2.041) < 0.001
p value for linear trend		<0.001	<0.001	0.009	<0.001
Weight-relative	Q4	Reference	Reference	Reference	Reference
	Q3	1.868 (1.350–2.585) < 0.001	1.486 (1.129–1.955) 0.005	1.649 (1.236–2.200) 0.001	1.193 (0.925–1.538) 0.174
	Q2	2.166 (1.572–2.986) < 0.001	1.858 (1.420–2.431) < 0.001	1.601 (1.197–2.141) 0.002	1.484 (1.165–1.890) 0.001
	Q1	2.700 (1.962–3.717) < 0.001	2.514 (1.940–3.258) < 0.001	1.531 (1.134–2.067) 0.005	1.642 (1.291–2.089) < 0.001
p value for linear trend		<0.001	<0.001	0.01	<0.001
WC-relative	Q4	Reference	Reference	Reference	Reference
	Q3	1.694 (1.229–2.335) 0.001	1.517 (1.156–1.991) 0.003	1.670 (1.258–2.217) < 0.001	1.006 (0.780–1.299) 0.962
	Q2	2.109 (1.536–2.896) < 0.001	1.743 (1.333–2.279) < 0.001	1.459 (1.092–1.950) 0.011	1.368 (1.076–1.739) 0.011
	Q1	2.242 (1.613–3.115) < 0.001	2.315 (1.783–3.006) < 0.001	1.485 (1.100–2.004) 0.010	1.460 (1.144–1.862) 0.002
p value for linear trend		<0.001	<0.001	0.03	<0.001

Abbreviation: HGS, hand grip strength; BMS, back muscle strength; HR, hazard ratio, CI; confidence interval; BMI, body mass index; WC, waist circumference. * Adjusted for baseline muscle strength plus age; family history of diabetes (yes, no); family history of hypertension (yes, no); job (homemaker, white collar, or blue collar); income (KRW < 1,000,000, KRW 1,000,000 ≤ or <2,000,000, KRW 2,000,000 ≤ or <4,000,000, or KRW 4,000,000 ≤); education (<12 year and ≥12 year), married status (yes, no); smoker (never smoker, ex-smoker, or current smoker); alcohol consumption (g/day); and leisure physical activity (METs). Women added menopause (yes, no).

3.5. Cox Proportional Hazard Ratios for Incident Metabolic Syndrome According to Delta Change of Mean Hand Grip Strength and Relative Hand Grip Strength in Gender

We obtained the delta change in HGS in baseline and at the which we used to confirm risk of iMetS (Tables 4 and 5).

Table 4. Adjusted hazard ratio (HR) of incident metabolic syndrome associated with invers one standard deviation increase in mean hand grip strength delta change and relative muscle strength according to gender.

Standardized Delta Change of HGS	Women		Men	
	HR (95% CI) <i>p</i> *	HR (95% CI) <i>p</i> §	HR (95% CI) <i>p</i> *	HR (95% CI) <i>p</i> §
Δ Mean (kg)	0.971 (0.865–1.091) 0.624	0.918 (0.816–1.031) 0.150	1.048 (0.946–1.160) 0.370	1.058 (0.953–1.176) 0.290
Δ BMI-relative	1.131 (1.009–1.269) 0.035	1.034 (0.916–1.168) 0.585	1.173 (1.060–1.297) 0.002	1.148 (1.033–1.276) 0.010
Δ Weight-relative	1.127 (1.003–1.267) 0.045	1.025 (0.907–1.159) 0.692	1.216 (1.099–1.345) < 0.001	1.174 (1.057–1.304) 0.003
Δ WC-relative	1.160 (1.033–1.302) 0.012	1.064 (0.942–1.201) 0.318	1.158 (1.046–1.283) 0.005	1.160 (1.041–1.291) 0.007

Abbreviation: HGS, hand grip strength; BMS, back muscle strength; HR, hazard ratio; CI, confidence interval; BMI, body mass index; WC, waist circumference. * Adjusted for baseline muscle strength. § Adjusted for baseline muscle strength plus age; family history of DM (yes, no); family history of hypertension (yes, no); job (homemaker, white collar, or blue collar); income (KRW < 1,000,000, KRW 1,000,000 ≤ or < 2,000,000, KRW 2,000,000 ≤ or < 4,000,000, or KRW 4,000,000 ≤); education (<12 years and ≥12 years); married status (yes, no); smoker (never smoker, ex-smoker, or current smoker); alcohol consumption (g/day); and leisure physical activity (METs). Women added menopause.

Table 5. Adjusted hazard ratio (HR) of incident metabolic syndrome associated with quintiles group of mean hand grip strength, back muscle strength, and relative muscle strength according to gender.

Standardized Delta Change in HGS		Women		Men	
		HR (95% CI) <i>p</i> *	HR (95% CI) <i>p</i> §	HR (95% CI) <i>p</i> *	HR (95% CI) <i>p</i> §
Δ Mean (kg)	Q1	1.105 (0.799–1.529) 0.545	1.181 (0.849–1.643) 0.323	1.425 (1.035–1.960) 0.030	1.349 (0.973–1.870) 0.073
	Q2	0.762 (0.536–1.082) 0.128	0.749 (0.526–1.068) 0.110	1.389 (1.011–1.907) 0.043	1.192 (0.864–1.646) 0.285
	Q3	Reference	Reference	Reference	Reference
	Q4	0.927 (0.661–1.301) 0.662	0.970 (0.689–1.365) 0.861	1.333 (0.967–1.837) 0.080	1.325 (0.959–1.832) 0.089
	Q5	0.864 (0.612–1.221) 0.408	0.776 (0.547–1.100) 0.155	1.560 (1.136–2.142) 0.006	1.500 (1.080–2.085) 0.016
Δ BMI-relative	Q1	0.938 (0.658–1.337) 0.725	1.184 (0.825–1.699) 0.359	1.057 (0.769–1.454) 0.732	1.102 (0.798–1.523) 0.556
	Q2	1.105 (0.784–1.559) 0.567	1.117 (0.789–1.581) 0.533	1.082 (0.789–1.485) 0.625	1.155 (0.840–1.589) 0.376
	Q3	Reference	Reference	Reference	Reference
	Q4	1.417 (1.006–1.997) 0.046	1.332 (0.942–1.885) 0.105	1.342 (0.986–1.826) 0.061	1.335 (0.978–1.821) 0.069
	Q5	1.305 (0.913–1.865) 0.144	1.258 (0.874–1.811) 0.217	1.504 (1.101–2.054) 0.010	1.502 (1.091–2.067) 0.013
Δ Weight-relative	Q1	0.842 (0.592–1.197) 0.337	1.028 (0.719–1.472) 0.878	1.066 (0.775–1.467) 0.693	1.157 (0.838–1.598) 0.376
	Q2	1.005 (0.715–1.413) 0.977	0.993 (0.705–1.399) 0.966	1.057 (0.768–1.454) 0.734	1.132 (0.821–1.560) 0.450
	Q3	Reference	Reference	Reference	Reference
	Q4	1.228 (0.872–1.730) 0.240	1.131 (0.796–1.606) 0.493	1.522 (1.119–2.069) 0.007	1.486 (1.089–2.029) 0.013
	Q5	1.313 (0.923–1.866) 0.130	0.869 (0.612–1.234) 0.433	1.531 (1.117–2.099) 0.008	1.530 (1.107–2.114) 0.010
Δ WC-relative	Q1	0.719 (0.510–1.015) 0.061	0.836 (0.594–1.175) 0.303	1.130 (0.824–1.550) 0.448	1.044 (0.756–1.443) 0.792
	Q2	0.812 (0.579–1.139) 0.227	Reference	1.100 (0.801–1.510) 0.557	1.028 (0.744–1.421) 0.866
	Q3	Reference	1.160 (0.831–1.617) 0.383	Reference	Reference
	Q4	1.134 (0.817–1.574) 0.452	1.007 (0.710–1.428) 0.968	1.378 (1.010–1.881) 0.043	1.292 (0.944–1.768) 0.109
	Q5	1.108 (0.785–1.564) 0.560	1.181 (0.849–1.643) 0.323	1.524 (1.114–2.085) 0.008	1.445 (1.048–1.992) 0.025

Abbreviation: HGS, hand grip strength; BMS, back muscle strength; HR, hazard ratio; CI, confidence interval; BMI, body mass index; WC, waist circumference. * Adjusted for baseline muscle strength. § Adjusted for baseline muscle strength plus age; family history of DM (yes, no); family history of hypertension (yes, no); job (homemaker, white collar, or blue collar); income (KRW < 1,000,000, KRW 1,000,000 ≤ or < 2,000,000, KRW 2,000,000 ≤ or < 4,000,000, or KRW 4,000,000 ≤); education (<12 years and ≥12 years); married status (yes, no); smoker (never smoker, ex-smoker, or current smoker); alcohol consumption (g/day); leisure physical activity (METs); and BMI. Women added menopause.

The MetS risk of increase in normalized delta change in muscle strength and relative muscle strength was shown in Table 4. After the adjustment of baseline muscle strength, the HRs per invers one SD increase in delta change in BMI-, weight-, and WC-relative HGS and BMS were associated with a high risk of iMetS in women and men (HR = 1.131–1.216, $p \leq 0.005$). However, the delta changes in HGS in both women and men were not associated with iMetS. In the full model, the HR per one SD increase in delta change in BMI-, weight-, and WC-relative HGS were associated with a high risk of iMetS in only men (HR = 1.148–1.174, $p \leq 0.010$). However, women were not associated with iMetS.

The participants were divided into quintile groups based on gender-specific HGS and relative HGS. The middle (third) quintile group was fixed as the reference group. The first quintiles group is the group with increased HGS during the follow-up period, whereas the last quintile group is that with decreased HGS (Table 5). After the adjustment of baseline muscle strength, the fourth quintile of BMI-relative HGS was associated with iMetS in women.

However, the other groups were not associated with iMetS in women. In men, the first, second, and fifth delta changes in mean HGS, and fifth delta changes in BMI- and WC-relative HGS, and fourth and fifth delta changes in weight-relative HGS were associated with iMetS. In the full model, the fifth delta change in HGS and BMI-, and WC-relative HGS, and the fourth and fifth delta changes in weight-HGS were also associated with iMetS (HR = 1.486–1.530, $p \leq 0.025$). Based on the comparison of the differences between baseline and the eighth follow-up muscle strength and LPA, HGS and relative HGS were significantly reduced in women ($p < 0.001$) and there was no difference in LPA. On the other hand, men showed significant increases in HGS, relative HGS, and LPA ($p < 0.05$; Supplementary Table S5). Similarly, we analyzed the effect of vigorous-LPA [34] and these delta changes on incident metabolic syndrome, but the results were not significant (data not shown).

3.6. Cox Proportional Hazard Ratios for Incident Metabolic Syndrome Components According to Mean Hand Grip Strength, Back Muscle Strength, and Relative Muscle Strength in Gender

We showed HR per one SD increase, 95% CIs, and p values for each one SD increase in muscle strength and relative muscle strength in the incidence of each MetS component adjusted for the confounding factors (Table 6 and Table S6).

Table 6. Adjusted hazard ratio (HR) of incident metabolic syndrome components associated with one standard deviation increase in mean hand grip strength, back muscle strength, and relative muscle strength according to gender.

	WC	HDL	TG	HTN	DM
	HR (95% CI) p *	HR (95% CI) p *	HR (95% CI) p *	HR (95% CI) p *	HR (95% CI) p *
Women					
HGS (kg)	1.040 (0.913–1.185) 0.554	0.902 (0.796–1.021) 0.103	0.924 (0.835–1.022) 0.124	1.046 (0.940–1.163) 0.409	0.818 (0.702–0.953) 0.010
BMI-relative HGS	0.579 (0.503–0.667) <0.001	0.875 (0.773–0.990) 0.034	0.829 (0.747–0.919) <0.001	0.826 (0.739–0.923) 0.001	0.650 (0.552–0.765) <0.001
Weight-relative HGS	0.530 (0.462–0.608) <0.001	0.880 (0.778–0.995) 0.042	0.846 (0.765–0.937) 0.001	0.833 (0.748–0.928) 0.001	0.693 (0.592–0.811) <0.001
WC-relative HGS	0.647 (0.562–0.745) <0.001	0.861 (0.759–0.976) 0.020	0.833 (0.748–0.927) 0.001	0.841 (0.751–0.942) 0.003	0.655 (0.556–0.772) <0.001
BMS (kg)	1.088 (0.962–1.231) 0.180	0.924 (0.819–1.043) 0.202	0.957 (0.869–1.054) 0.373	1.028 (0.932–1.134) 0.579	0.916 (0.792–1.059) 0.235
BMI-relative BMS	0.740 (0.646–0.849) <0.001	0.901 (0.798–1.018) 0.094	0.879 (0.797–0.970) 0.010	0.893 (0.804–0.991) 0.033	0.772 (0.660–0.904) 0.001
Weight-relative BMS	0.711 (0.621–0.813) <0.001	0.907 (0.804–1.024) 0.114	0.900 (0.817–0.993) 0.035	0.905 (0.817–1.003) 0.056	0.820 (0.705–0.955) 0.011
WC-relative BMS	0.820 (0.717–0.938) 0.004	0.900 (0.796–1.018) 0.094	0.892 (0.808–0.986) 0.026	0.911 (0.820–1.012) 0.082	0.800 (0.684–0.935) 0.005
Men					
HGS (kg)	1.073 (0.805–1.430) 0.632	0.963 (0.875–1.060) 0.441	1.007 (0.907–1.119) 0.891	0.927 (0.843–1.018) 0.114	0.925 (0.824–1.037) 0.182
BMI-relative HGS	0.416 (0.302–0.572) <0.001	0.813 (0.739–0.894) <0.001	0.870 (0.787–0.962) 0.007	0.793 (0.723–0.869) <0.001	0.689 (0.612–0.775) <0.001
Weight-relative HGS	0.322 (0.237–0.437) <0.001	0.826 (0.754–0.905) <0.001	0.861 (0.781–0.949) 0.003	0.780 (0.712–0.854) <0.001	0.691 (0.617–0.774) <0.001
WC-relative HGS	0.448 (0.329–0.610) <0.001	0.826 (0.751–0.909) <0.001	0.863 (0.780–0.954) 0.004	0.812 (0.740–0.891) <0.001	0.700 (0.622–0.787) <0.001
BMS (kg)	1.268 (0.967–1.663) 0.086	1.054 (0.963–1.153) 0.251	1.015 (0.919–1.120) 0.772	0.942 (0.861–1.031) 0.196	1.093 (0.982–1.216) 0.103
BMI-relative BMS	0.665 (0.502–0.882) 0.005	0.941 (0.862–1.027) 0.174	0.924 (0.840–1.015) 0.100	0.847 (0.776–0.923) <0.001	0.890 (0.802–0.988) 0.028
Weight-relative BMS	0.560 (0.421–0.745) <0.001	0.954 (0.876–1.040) 0.290	0.917 (0.836–1.005) 0.065	0.841 (0.771–0.917) <0.001	0.894 (0.807–0.991) 0.033
WC-relative BMS	0.698 (0.527–0.925) 0.012	0.953 (0.872–1.041) 0.287	0.916 (0.832–1.008) 0.071	0.859 (0.787–0.938) 0.001	0.904 (0.813–1.004) 0.059

Abbreviation: HR, hazard ratio; CI, confidence interval; WC, waist circumference; HDL, high density lipoprotein; TG, triglyceride; HTN, hypertension; DM, diabetes mellitus; HGS, hand grip strength; BMS, back muscle strength. * Adjusted for baseline muscle strength plus age; family history of DM (yes, no); family history of hypertension (yes, no); job (homemaker, white collar, or blue collar); income (KRW < 1,000,000, KRW 1,000,000 ≤ or < 2,000,000, KRW 2,000,000 ≤ or < 4,000,000, or KRW 4,000,000 ≤); education (<12 years and ≥12 years); married status (yes, no); smoker (never smoker, ex-smoker, or current smoker); alcohol consumption (g/day); leisure physical activity (METs); and BMI. Women added menopause.

In univariate analysis, the HR per one SD increase for incident WC, incident dyslipidemia (HDL-cholesterol and TG), incident HTN, and incident DM in women and men was associated with a lower risk in BMI-, weight-, and WC-relative HGS and BMS (HR = 0.492–0.666, $p < 0.001$ for women, and HR = 0.334–0.698, $p \leq 0.011$ for men in incident WC; HR = 0.863–0.892, $p \leq 0.044$ for women, and HR = 0.803–0.818, $p < 0.001$ for men in incident HDL-cholesterol; HR = 0.806–0.875, $p \leq 0.005$ for women, and HR = 0.879–0.900, $p \leq 0.032$ for men in incident TG; HR = 0.739–0.836, $p < 0.001$ for women, and HR = 0.788–0.877, $p \leq 0.003$ for men in incident HTN; HR = 0.610–0.769, $p < 0.001$ for women, and HR = 0.687–0.891, $p \leq 0.029$ for men in incident DM), excluding HSG and BMS in both women and men, weight-relative HGS of women, and relative BMS of men.

After adjusting for confounders, the HR for all the metabolic components was not associated with HGS and BMS in both men and women. The HR for incident WC, incident dyslipidemia (HDL-cholesterol and TG), incident HTN, and incident DM in women and men was associated with a lower risk in BMI-, weight-, and WC-relative HGS (HR = 0.530–0.647, $p < 0.001$ for women, and HR = 0.322–0.448, $p < 0.001$ for men in incident WC; HR = 0.861–0.880, $p \leq 0.042$ for women, and HR = 0.813–0.826, $p < 0.001$ for men in incident HDL-cholesterol; HR = 0.829–0.846, $p \leq 0.001$ for women, and HR = 0.870–0.863, $p \leq 0.007$ for men in incident TG; HR = 0.826–0.841, $p \leq 0.003$ for women, and HR = 0.780–0.812, $p < 0.001$ for men in incident HTN; HR = 0.650–0.693, $p < 0.001$ for women, and HR = 0.689–0.700, $p < 0.001$ for men in incident DM). The HR for incident WC, HTN, and DM in women and men was associated with a lower risk in BMI-, weight-, and WC-relative BMS (HR = 0.711–0.820, $p \leq 0.004$ for women, and HR = 0.560–0.698, $p \leq 0.012$ for men in incident WC; HR = 0.893, $p = 0.033$ for women, and HR = 0.841–0.859, $p \leq 0.001$ for men in incident HTN; HR = 0.772–0.820, $p \leq 0.011$ for women, and HR = 0.890–0.894, $p \leq 0.033$ for men in incident DM), excluding weight- and WC-relative BMS for women, and WC-relative BMS for men. The HR for incident TG in women was only associated with a lower risk in BMI-, weight-, and WC-relative BMS (HR = 0.879–0.900, $p \leq 0.035$).

4. Discussion

In this study, we studied relationship between mean and relative HGS and BMS and iMetS using a 16-year follow-up of the population-based cohort. The present study revealed that BMI-, weight-, and WC-relative HGS and BMS at baseline were independently associated with iMetS in men and women. In addition, the changes in muscle strength over 16 years was significant in iMetS in men. Unfortunately, baseline LPA and these changes were not associated with iMetS. The results of changes in muscle strength and LPA that had not been previously demonstrated were shown here. Additionally, we showed that iMetS components were strongly associated with a one standard deviation increase in relative HGS and BMS both in women and men.

Muscle strength can be measured in various areas, such as the knee, elbow, hand, leg, and back [15,35,36]. Additionally, it can be measured by an isokinetic dynamometer, cardiorespiratory fitness, dual-energy X-ray absorptiometry (DEX), and bioelectrical impedance analysis (BIA) [37]. Several studies have been reported, varying by the measurement site and measurement method, but there are few studies compared to those for HGS due to problems such as the measurement difficulty, high test cost, and challenges in validation [37,38]. Therefore, HGS is being used to research muscle strength in clinical and epidemiological studies [8]. Body composition and body size-independent measurements for muscle strength are important. The use of a relative method is recommended when investigating the relationship between diseases such as T2DM, HTN, MetS, and dementia [8–11]. Therefore, BMI-, weight-, and WC-relative muscle strength are frequently used methods for normalizing muscle strength [15].

The relevance of MetS components, iMetS, and HGS has also been reported in previous reports. Lower HGS was associated with incident T2DM [15,39,40], and meta-analysis results using the results of 10 observational cohort studies also demonstrated its relevance to DM [8]. Weak HGS is associated with HTN [9,41]. The results of HGS and MetS

showed contradictory results. In women, all results showed no association results [17,18]. Some of the results showed significant results in men [24]. Weight- [16,20,21,23] and BMI-relative [4,17–19] HGS were consistently associated with MetS both men and women. In addition, weight-relative HGS was associated with iMetS in both men and women [26]. In our results, BMI-, weight-, and WC-relative HGS were related to iMetS. The mean HGS was not significant. Moreover, sarcopenia is the age-related loss of skeletal muscle mass, quality, and strength [42]. The results of the meta-analysis using the results of 13 observational studies also demonstrated its relevance to MetS (2.01 fold) [43]. The development of MetS by HGS change has not been reported. Our results show that the decrease in HGS in men was significantly associated with iMetS.

Unfortunately, LPA was not relevant to the iMetS in our results. These results can be explained through previous reports that aerobic exercise does not significantly affect HGS. Therefore, resistance exercise is needed to improvement HGS [44,45]. In addition, in a four-year follow-up study, iMetS did not differ by moderate-LPA, but was only 0.36-fold lower in groups with a vigorous LPA of more than 7.5 METs per week for more than 60 min [34]. Another study showed an association with a 0.54-fold increase in MetS of more than 990 MET-minutes per week [46]. The baseline average leisure activity of the subjects in this study was 127.0 MET-minutes per week for women and 125.3 MET-minutes per week for men, showing very low LPA compared to previous studies. The difference between baseline and eighth follow-up HGS and relative HGS were significantly reduced in women. LPA was not different in women. On the other hand, men showed significant increases in HGS, relative HGS, and LPA. In our results, men showed high iMetS and decreased HGS. It is thought that increased or maintained LPA offset the effects of iMetS on HGS, while decreased LPA reduces HGS, increasing iMetS.

As the pace of aging increases, interest in dementia is also increasing. A recent meta-analysis has shown that MetS groups have 2.95-fold higher progression from MCI to dementia than in normal groups [47]. Therefore, the prevention of MetS is considered an important preventive factor for chronic diseases as well as the dementia of aging. In addition, HGS is used for the diagnosis of sarcopenia and frailty [48]. Sarcopenia is emerging as a large problem in old age. Only persistent LPA can maintain or increase muscles, which is essential for improving the quality of health, life, and living in aging [18,42].

MetS is not a disease. It is clustering of risk factors. MetS is a public problem because it leads to cardiovascular disease morbidity, T2DM, serious disabilities, and mortality [10]. Interpretation is also very complex and not fully elucidated because the development of MetS is a combination of five components [49]. Recent GWAS results have given us a partial understanding of their varying pathophysiology [50]. The relevant genes included genes related to T2DM (APOC1, FADS2, NEU2, SLC18A1, CMIP, PABPC4, etc.); HTN (blood pressure; NEU2, CMIP, CELF1, JMJD1C, ARID1A, CEP68, etc.); lipid regulation (ZPR1, CETP, LPL, CD300LG, TRIB1, ANGPTL4, etc.), and obesity (APOC1, FTO, BAZ1B, CELF1, PABPC4, PCCB, etc.). The analysis contained most genes traditionally thought to be the cause of metabolic syndrome [49,51]. Moreover, results of pathway analysis using these significant genes showed involvement of immunity pathway [51], inflammation [52], endosomal/vacuolar and ER-phagosome [53], and regulation of lipids and lipoprotein [54].

Recently, gender difference was confirmed in the longitudinal study [26]. However, our results did not show the relative HGS of genders and baseline and the interaction of BMS. Interestingly, in the delta change of relative HGS, women were not significant in DM development, but men showed significance with iMetS. As a result, it is thought that in-depth research between genders will be needed.

This study had some limitations. First, this study was limited to Koreans and, due to ethnic differences, it is difficult to generalize the results of our research. Second, a more accurate measurement of exercise is needed because the amount of exercise was calculated by the questionnaires. Third, muscle mass, muscle strength, and function may be different in various outcomes, so more research on this is needed.

5. Conclusions

The results of this study show that BMI-, weight-, WC-relative HGS and BMS are more sensitive indicators for iMetS than mean HGS and BMS. From the results of this study, it is possible to elucidate, to some extent, the relationship between the development of MetS through HGS and BMS. Studies are needed to confirm the exact mechanism and the associations of relative HGS and BMS with MetS. Nevertheless, our results suggest that relative HGS and BMS can be conveniently used as the simplest predictive method for screening and preventing subjects at risk of metabolic syndrome.

Supplementary Materials: The following are available online at <https://www.mdpi.com/article/10.3390/app11115198/s1>, Table S1. Baseline characteristics according to gender; Table S2. Sex adjusted partial correlation coefficient of relative hand grip strength and metabolic components. Table S3. Sensitivity analysis for adjusted Cox hazard ratios for one standard deviation of relative hand grip strength and back muscle strength stratified by follow up time, gender and age subgroups; Table S4. Univariate hazard ratio (HR) of incident metabolic syndrome associated with quartile group of mean hand grip strength, back muscle strength, and relative muscle strength according to gender; Table S5. Change in handgrip, relative handgrip, and leisure physical activity at baseline and eighth follow-up; Table S6. Univariate hazard ratio (HR) of incident metabolic syndrome components associated with one standard deviation increase in mean hand grip strength, back muscle strength, and relative muscle strength according to gender.

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