scientific reports

Check for updates

OPEN

Association between muscular strength, abdominal obesity, and incident nonalcoholic fatty liver disease in a Korean population

Jae Ho Park[1] & Hyun-Young Park[2]✉

This study aimed to examine the association between relative handgrip strength (rHGS) and nonalcoholic fatty liver disease (NAFLD) incidence, considering abdominal obesity (ABO) status. This nationwide Korean cohort included 24,297 participants without NAFLD at baseline. Participants were categorized into sex-specific tertiles of rHGS (low, mid, and high). Multivariate Cox proportional hazards regression models were used to evaluate NAFLD incidence in relation to rHGS levels and/or ABO status. Over 100,381 person-years of follow-up, 1,735 participants (10.81% men and 6.01% women) developed NAFLD. High rHGS was associated with a 29% and 60% risk reduction for incident NAFLD in men and women, respectively, compared with low rHGS, despite men having significantly higher rHGS than women. Conversely, ABO increased NAFLD risk by 2.3 and 3.8 times in men and women, respectively. Even among women with ABO, mid and high rHGS were associated with a 23% and 36% risk reduction in incident NAFLD, respectively, compared with low rHGS. However, there was no significant relationship between rHGS levels and NAFLD incidence in men with ABO. Higher rHGS levels may prevent NAFLD, particularly in women. In individuals with ABO, high rHGS markedly decreased NAFLD risk in women but not in men.

Keywords Nonalcoholic fatty liver disease, Muscular strength, Handgrip strength, Abdominal obesity, Prevention

Nonalcoholic fatty liver disease (NAFLD) is a chronic liver disorder characterized by abnormal lipid accumulation in liver cells, unrelated to excessive alcohol consumption. NAFLD encompasses a spectrum of conditions, ranging from simple steatosis and nonalcoholic fatty liver to nonalcoholic steatohepatitis, cirrhosis, and hepatocellular carcinoma[1]. Recent meta-analytical evidence indicates a marked global increase in NAFLD prevalence, from 25.26% in 1990–2006 to 38.20% in 2016–2019[2]. Owing to rapid economic growth and lifestyle changes including overnutrition and sedentary lifestyle, NAFLD prevalence in Korea has increased from 29 to 31% over the last decade[3]. Given that NAFLD is closely associated with cardiovascular disease (CVD), liver-related mortality, and all-cause mortality[4,5], effective prevention and management strategies are crucial.

Obesity is a significant risk factor for developing NAFLD. Meta-analytical evidence suggests a 3.5-fold increase in the risk of developing NAFLD with obesity, with a dose–response relationship observed between body mass index (BMI) and NAFLD risk[6]. Abdominal obesity (ABO) is an independent risk factor for incident NAFLD. Recent studies demonstrate that ABO is independently associated with increased NAFLD risk, regardless of general obesity status diagnosed by BMI[7] or metabolic syndrome status[8]. A previous computed tomography (CT) study revealed that total abdominal fat and visceral fat volumes were more strongly associated with hepatic fat infiltration than with subcutaneous fat volume[9]. Thus, ABO status needs to be monitored more closely than general obesity status to mitigate NAFLD risk. Moreover, in Korea, ABO prevalence has increased by 8.5% (from 20.8 to 29.3%) among men and by 3.2% (from 15.8 to 19.0%) among women over the past decade[10].

Muscular strength, the ability of a muscle or muscle group to exert maximal force in a single effort, is widely considered an essential component of healthy aging. Handgrip strength (HGS) testing is a simple, fast, inexpensive, and highly reliable method to assess whole-body muscular strength and muscle mass in clinical and research settings[11–13]. Recent cross-sectional studies have revealed an inverse association between HGS and NAFLD risk[14–16]. To our knowledge, few prospective cohort studies have investigated the longitudinal

[1]Division of Population Health Research, Department of Precision Medicine, National Institute of Health, Cheongju-si 28160, Korea. [2]National Institute of Health, 187 Osongsaengmyeong2-ro, Osong-eup, Heungdeok-gu, Cheongju-si 28159, Chungcheongbuk-do, Korea. ✉email: hypark65@korea.kr

relationship between HGS and NAFLD incidence. Moreover, given that ABO is an independent risk factor for NAFLD incidence, it is essential to investigate whether high relative HGS (rHGS) confers protective effects against NAFLD, particularly in participants with ABO. A recent cross-sectional study revealed a significant association between HGS and NAFLD risk in participants with ABO[15]; however, it did not consider potential sex-based differences in this association. Therefore, data from other prospective cohorts is necessary to examine sex-specific variations and deduce causal associations.

Therefore, the present study aimed to investigate the relationship between HGS and NAFLD incidence in a large nationwide Korean cohort. Furthermore, considering ABO status, we aim to examine whether high HGS is significantly associated with a reduced risk of NAFLD incidence, even in participants with ABO.

Methods

Study participants

The Korean Genome and Epidemiology Study (KoGES) is a consortium project comprising six prospective cohort studies aimed at investigating the environmental and genetic etiologies of non-communicable chronic diseases in Korea, including hypertension, diabetes mellitus, CVD, and cancer[17]. This longitudinal study used data from the Health Examinee (HEXA) study, an ongoing prospective population-based cohort consisting of urban residents in Korea. The baseline data of the KoGES_HEXA study included 173,202 participants aged 40–79 years, who visited general hospitals and health examination centers between 2004 and 2013. We used baseline and follow-up data from 2012 to 2016. All participants underwent face-to-face surveys and physical examinations conducted by trained medical staff. Detailed information on this cohort has been previously provided[17].

Among the 173,202 participants, the following participants were excluded from the present study: those with a clinical history of CVD, hepatitis, liver cirrhosis, or any cancer ($n = 15,372$); those with incomplete data on parameters necessary for calculating the Framingham steatosis index (FSI) such as blood pressure (BP), triglyceride (TG), fasting blood glucose (FBG), aspartate aminotransferase (AST), or alanine aminotransferase (ALT) ($n = 37,125$); those without data on HGS and physical activity (PA) levels ($n = 76,973$); men and women with alcohol consumption > 30 g/day and > 20 g/day, respectively ($n = 6,907$; 5,623 men and 1,284 women); those without data on covariates ($n = 506$); and those diagnosed with NAFLD at baseline ($n = 12,022$). Overall, 24,297 participants (18,571 women) were included in the final analysis (Fig. 1). All the participants provided written informed consent. This study was approved by the Institutional Review Board of the National Institute of Health,

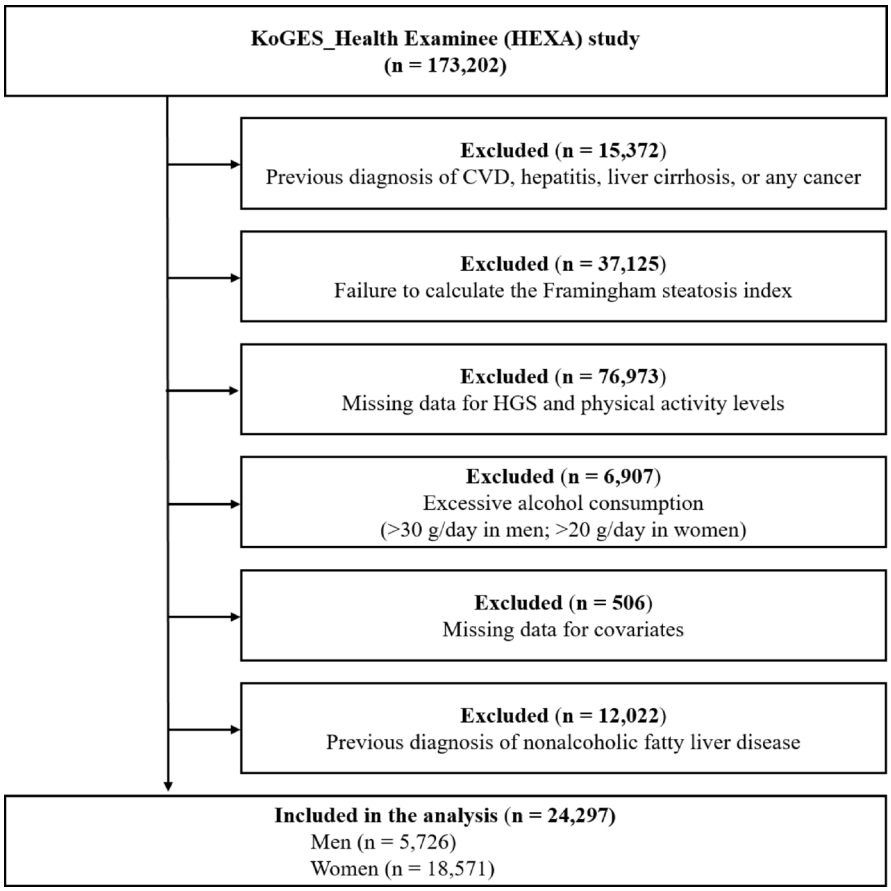

Fig. 1. Flow diagram illustrating participant inclusion and exclusion. *CVD* cardiovascular disease, *HGS* handgrip strength.

Korea Disease Control and Prevention Agency (Approval No. KDCA-2024-02-12-P-01). All research procedures were performed in accordance with the relevant guidelines and regulations.

Measurement of rHGS

Trained healthcare providers measured HGS using a digital grip strength dynamometer (T.K.K. 5401; Takei Scientific Instruments Co., Ltd., Tokyo, Japan). Participants were instructed to stand upright with their feet hip-width apart and to look forward, with their elbows fully extended, during the measurement. The dynamometer was held by the testing hand in a comfortable neutral position (not flexed or extended), with the index finger at a 90° flexion. Participants were then instructed to squeeze the grip continuously, exerting full force for at least 3 s, with approximately a 60-s interval. HGS was recorded as the mean of two trials for each hand, and the highest reading (in kg) from each hand was used as the absolute HGS. rHGS was calculated by dividing the absolute HGS (kg) by BMI (kg/m^2), as previously described[18,19]. Participants were categorized into sex-specific tertiles of rHGS (low, mid, and high). The ranges for each group were as follows: low (< 1.50 in men; <0.93 in women), mid (1.50–1.78 in men; 0.93–1.13 in women), and high (> 1.78 in men; >1.13 in women).

Definition of incident NAFLD

Incident NAFLD was defined as the occurrence of NAFLD during the follow-up period, without other liver-related diseases at baseline and significant alcohol consumption from baseline to follow-up. NAFLD occurrence was defined based on the FSI, with BMI, TG, AST, ALT, hypertension, and diabetes mellitus used to calculate it based on the following formula[20]:

$$FSI = 1/(1 + \exp(-x)) \times 100,$$

where x = −7.981 + 0.011 × age (years) − 0.146 × sex (female = 1, male = 0) + 0.173 × BMI (kg/m^2) + 0.007 × TG (mg/dL) + 0.593 × hypertension (yes = 1, no = 0) + 0.789 × DM (yes = 1, no = 0) + 1.1 × ALT:AST ratio ≥ 1.33 (yes = 1, no = 0).

Incident NAFLD was defined as an FSI ≥ 23 in the follow-up period[20], a diagnostic model externally validated in independent cohorts, including Korean patients[21–23]. For baseline characteristic comparison, participants were categorized into two groups based on new-onset NAFLD during the follow-up period: "non-NAFLD" (those without NAFLD) and "NAFLD" (those with NAFLD).

Covariates

Our analyses included sociodemographic and health-related factors such as age, sex, educational level, drinking and smoking habits, total leisure time spent in PA (PA time), regular resistance training (RT), BMI, waist circumference (WC), BP, hypertension, diabetes mellitus, and laboratory parameters. Educational level was categorized as elementary school graduates or lower, middle school or high school graduates, and college graduates or higher. Drinking and smoking habits were classified as "never," "former," and "current." PA time was defined as the total time (min/week) spent engaging in moderate-intensity leisure-time PA during a typical week, defined as participation in sports or engagement in exercises that resulted in sweating. Regular RT was defined as participation in an RT program for more than 1 day per week, with RT including any training program involving muscle contraction against external resistance such as body weight, weight machines, barbells, and dumbbells.

Anthropometric data, including height, body weight, and WC, were measured by trained healthcare providers using standardized methods. BMI (kg/m^2) was calculated as body weight (kg) divided by height squared (m^2). ABO was defined as a WC of ≥ 90 cm in men and ≥ 85 cm in women[24]. Trained healthcare providers also measured BPs using standard methods, with systolic BP (SBP) and diastolic BP (DBP) obtained by averaging two readings from the arm with the highest SBP after the participant rested for 5 min in a seated position. Blood samples were collected after an overnight fasting of 8 h. Biochemical assays were performed to determine levels of total cholesterol (T-Chol), high-density lipoprotein cholesterol (HDL-C), TG, FBG, AST, and ALT. Hypertension was defined based on a previous diagnosis by a physician, current use of antihypertensive drugs, SBP ≥ 140 mmHg, or DBP ≥ 90 mmHg. Diabetes mellitus was defined based on a previous diagnosis by a physician, current use of antidiabetic medications (including insulin and oral hypoglycemic agents), FBG ≥ 126 mg/dL, or glycated hemoglobin ≥ 6.5%. Detailed information on the biochemical analyses is described in a previous study[17].

Statistical analysis

All statistical analyses were conducted using SAS software (version 9.4; SAS Institute, Cary, North Carolina, United States). Participant characteristics are presented as descriptive statistics. Continuous variables are presented as mean ± standard deviation, whereas categorical variables are expressed as absolute frequencies and percentages (%). Chi-squared tests were used to determine intergroup differences in educational level; drinking and smoking habits; regular RT; and the prevalence of ABO, hypertension, and diabetes mellitus. Independent *t*-tests and one-way analysis of variance (ANOVA) were used to compare age, PA time, HGS, rHGS, BMI, WC, SBP, DBP, T-Chol, HDL-C, TG, FBG, AST, ALT, and FSI between groups. When ANOVA showed significant differences between groups, Scheffe tests were used for post-hoc comparisons.

Multivariate Cox proportional hazards regression models were used to assess hazard ratios (HRs) and 95% confidence intervals (CIs) for incident NAFLD. Models were adjusted for age, sex, drinking, smoking, educational level, T-Chol and ALT levels, PA time, hypertension, and diabetes mellitus. Subgroup analyses were performed for each sex to investigate the association between rHGS levels and incident NAFLD, considering age (< 65 and ≥ 65 years), educational level (≤ middle school and ≥ high school), current drinking status (no and yes), smoking status (never and ever), PA time (< 150 and ≥ 150 min/week), hypertension status (no and yes), and diabetes mellitus status (no and yes). The *p*-value for interaction was estimated to assess the consistency of associations across subgroups. All tests were two-tailed, and statistical significance was set at a *p*-value of < 0.05.

Results

A total of 24,297 participants (18,571 women) were enrolled in the present study. The mean follow-up period was 4.13 ± 1.12 (range 1.33–7.68) years. Over 100,381 person-years of follow-up, 1,735 participants (7.14%) developed NAFLD. Table 1 presents the baseline characteristics of the study participants. Men had a higher mean age than women, and the prevalence of a high educational level (≥ college), current drinking and smoking, regular RT, ABO, hypertension, and diabetes mellitus was higher in men than in women. Men also exhibited markedly higher PA time, HGS, rHGS, BMI, WC, SBP, DBP, levels of TG, FBG, AST, and ALT, and FSI, but lower levels of T-Chol and HDL-C.

The baseline characteristics of study participants based on sex and new-onset NAFLD during the follow-up period are presented in Supplementary Table 1. The incidence of NAFLD was significantly higher in men (10.81%) than in women (6.01%) ($p < 0.0001$). In both sexes, compared with the non-NAFLD group, the NAFLD group exhibited markedly higher BMI, WC, SBP, DBP, FSI, levels of T-Chol, TG, FBG, and ALT, and prevalence of ABO, hypertension, and diabetes mellitus, but lower rHGS and HDL-C level. In men, the NAFLD group showed a significantly lower mean age but higher HGS and proportion of current smokers than the non-NAFLD group. In women, the NAFLD group showed markedly higher mean age and AST levels, but lower proportions of a high educational level (≥ college) and current drinkers compared with the non-NAFLD group.

The baseline characteristics of participants based on sex-specific tertiles of rHGS are presented in Supplementary Table 2. Compared to the lower rHGS group, the high-rHGS group was younger, with lower BMI, WC, SBP, and DBP, as well as T-Chol, TG, FBG, AST, ALT, and FSI levels, and had lower proportions of participants with low education level (≤ elementary school), ABO, hypertension, and diabetes mellitus. The

Variables	Men ($n = 5726$)	Women ($n = 18,571$)	p-value
Age (years)	55.56 ± 8.38	52.55 ± 7.64	< 0.0001
Educational level, n (%)			
≤Elementary school	440 (7.68)	2873 (15.47)	< 0.0001
Middle/high school	2938 (51.31)	11,636 (62.66)	
≥College	2348 (41.01)	4062 (21.87)	
Drinking habit, n (%)			
Never drinker	1447 (25.27)	12,483 (67.22)	< 0.0001
Ex-drinker	429 (7.49)	299 (1.61)	
Current drinker	3850 (67.24)	5789 (31.17)	
Smoking habit, n (%)			
Never smoker	1841 (32.15)	18,112 (97.53)	< 0.0001
Ex-smoker	2533 (44.24)	190 (1.02)	
Current smoker	1352 (23.61)	269 (1.45)	
PA time (min/week)	219.78 ± 267.03	169.30 ± 223.42	< 0.0001
RT, n (%)	966 (16.87)	2620 (14.11)	< 0.0001
HGS (kg force)	38.36 ± 8.31	23.61 ± 5.50	< 0.0001
rHGS (HGS/BMI)	1.65 ± 0.37	1.03 ± 0.26	< 0.0001
BMI (kg/m^2)	23.44 ± 2.23	23.07 ± 2.50	< 0.0001
WC (cm)	83.04 ± 6.65	76.60 ± 7.31	< 0.0001
SBP (mmHg)	123.02 ± 13.15	119.61 ± 14.19	< 0.0001
DBP (mmHg)	76.18 ± 8.85	73.43 ± 9.13	< 0.0001
T-Chol (mg/dL)	192.00 ± 32.52	199.62 ± 34.57	< 0.0001
HDL-C (mg/dL)	51.13 ± 11.68	57.40 ± 12.74	< 0.0001
TG (mg/dL)	112.18 ± 50.15	100.27 ± 47.94	< 0.0001
FBG (mg/dL)	94.18 ± 15.77	90.40 ± 12.96	< 0.0001
AST (IU/L)	22.97 ± 8.10	21.40 ± 8.26	< 0.0001
ALT (IU/L)	21.44 ± 11.27	17.85 ± 10.64	< 0.0001
FSI	10.43 ± 5.48	7.72 ± 5.13	< 0.0001
ABO, n (%)	911 (15.91)	2586 (13.92)	< 0.001
Hypertension, n (%)	1337 (23.35)	3537 (19.05)	< 0.0001
Diabetes mellitus, n (%)	344 (6.01)	703 (3.79)	< 0.0001

Table 1. Baseline characteristics of study participants. *PA time* total time of regular participation in any sport or exercise to the point of sweating, *RT* resistance training, *HGS* handgrip strength, *rHGS* relative handgrip strength, *BMI* body mass index, *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *T-Chol* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *TG* triglyceride, *FBG* fasting blood glucose, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *FSI* Framingham steatosis index, *ABO* abdominal obesity.

	N	rHGS (HGS/BMI)	PA time (min/week)	Total person-years	No. of NAFLD (%)	Event rate (1000-person year)	Crude model	Adjusted model
							HR (95% CI)	HR (95% CI)
Total								
Low	8098	0.89 ± 0.26	170.33 ± 226.84	33,783.15	853 (10.53)	25.25	1 (reference)[c]	1 (reference)[c]
Mid	8100	1.17 ± 0.27	186.84 ± 239.68	33,592.19	520 (6.42)	15.48	0.61 (0.54–0.68)****	0.64 (0.57–0.71)****
High	8099	1.47 ± 0.39	186.42 ± 239.11	33,005.37	362 (4.47)	10.97	0.45 (0.40–0.51)****	0.50 (0.44–0.57)****
Men								
Low (< 1.50)	1908	1.27 ± 0.22	211.86 ± 255.69	7,990.14	248 (13.00)	31.04	1 (reference)[b]	1 (reference)[a]
Mid (1.50–1.78)	1909	1.64 ± 0.08	227.12 ± 273.41	7,955.21	203 (10.63)	25.52	0.82 (0.68–0.98)*	0.80 (0.67–0.97)*
High (> 1.78)	1909	2.03 ± 0.26	220.34 ± 271.55	7,789.54	168 (8.80)	21.57	0.72 (0.59–0.88)**	0.71 (0.58–0.88)**
Women								
Low (< 0.93)	6190	0.77 ± 0.13	157.53 ± 215.59	25,793.01	605 (9.77)	23.46	1 (reference) [c]	1 (reference)[c]
Mid (0.93–1.13)	6191	1.03 ± 0.06	174.42 ± 226.86	25,636.99	317 (5.12)	12.36	0.52 (0.45–0.60)****	0.56 (0.49–0.64)****
High (> 1.13)	6190	1.30 ± 0.22	175.96 ± 227.18	25,215.82	194 (3.13)	7.69	0.34 (0.29–0.40)****	0.40 (0.34–0.47)****

Table 2. Hazard ratios for the new-onset NAFLD according to sex-specific tertiles of rHGS. Adjusted for age, sex, drinking, smoking, educational level, T-Chol, ALT, PA time, hypertension, and diabetes mellitus. *NAFLD* nonalcoholic fatty liver disease, *rHGS* relative handgrip strength, *HGS* handgrip strength, *BMI* body mass index, *PA time* total time of regular participation in any sport or exercise to the point of sweating, *HR* hazard ratio, *CI* confidence interval, *T-Chol* total cholesterol, *ALT* alanine aminotransferase. [a]$p < 0.01$ in the test for trend of HRs; [b]$p < 0.001$ in the test for trend of HRs; [c]$p < 0.0001$ in the test for trend of HRs. *$p < 0.05$; **$p < 0.01$; ****$p < 0.0001$.

	N	rHGS (HGS/BMI)	PA time (min/week)	Total person-years	No. of NAFLD (%)	Event rate (1,000-person year)	Crude model	Adjusted model
							HR (95% CI)	HR (95% CI)
Total								
non-ABO	20,800	1.20 ± 0.39	183.00 ± 235.04	85,696.46	1077 (5.18)	12.57	1 (reference)	1 (reference)
ABO	3497	1.07 ± 0.38	170.49 ± 237.24	14,684.24	658 (18.82)	44.81	3.50 (3.18–3.85)****	3.23 (2.92–3.56)****
Men								
non-ABO	4815	1.67 ± 0.37	218.82 ± 265.35	19,912.35	430 (8.93)	21.59	1 (reference)	1 (reference)
ABO	911	1.54 ± 0.37	224.84 ± 275.83	3822.54	189 (20.75)	49.44	2.30 (1.94–2.73)****	2.30 (1.94–2.74)****
Women								
non-ABO	15,985	1.06 ± 0.26	172.21 ± 224.01	65,784.12	647 (4.05)	9.84	1 (reference)	1 (reference)
ABO	2586	0.91 ± 0.21	151.35 ± 218.92	10,861.70	469 (18.14)	43.18	4.27 (3.79–4.80)****	3.82 (3.38–4.32)****

Table 3. Hazard ratios for the new-onset NAFLD according to ABO and sex. Adjusted for age, sex, drinking, smoking, educational level, T-Chol, ALT, PA time, hypertension, and diabetes mellitus. *NAFLD* nonalcoholic fatty liver disease, *ABO* abdominal obesity, *rHGS* relative handgrip strength, *HGS* handgrip strength, *BMI* body mass index, *PA time* total time of regular participation in any sport or exercise to the point of sweating, *HR* hazard ratio, *CI* confidence interval, *T-Chol* total cholesterol, *ALT* alanine aminotransferase. ****$p < 0.0001$.

high-rHGS group showed higher PA time, HGS, rHGS, and HDL-C and higher proportions of participants with current drinking, smoking, and regular RT engagement status.

Table 2 presents the inverse association between sex-specific tertiles of rHGS and the risk of incident NAFLD after adjusting for covariates. In men, compared with participants in the low-rHGS group, those in the mid- and high-rHGS groups had a 20% ($p < 0.05$) and 29% ($p < 0.01$) risk reduction for incident NAFLD (p for trend < 0.01). In women, compared with individuals in the low-rHGS group, those in the mid- and high-rHGS groups were associated with a 44% and 60% risk reduction for incident NAFLD, respectively (all $p < 0.0001$; p for trend < 0.0001).

As shown in Table 3, compared with the non-ABO group, ABO increased the risk of incident NAFLD by 2.3 and 3.8 times in men and women, respectively, after adjusting for covariates (all $p < 0.0001$). We further examined whether high rHGS was related to a reduced risk of developing NAFLD after adjustment for covariates, even in participants with ABO (Fig. 2). Among male participants without ABO, compared with those in the low-rHGS group, those in the high-rHGS group had a 28% risk reduction of incident NAFLD ($p < 0.01$), whereas there was no significant relationship between rHGS and the risk of developing NAFLD in men with ABO. Among female participants without ABO, compared with those in the low-rHGS group, those in the mid- and high-

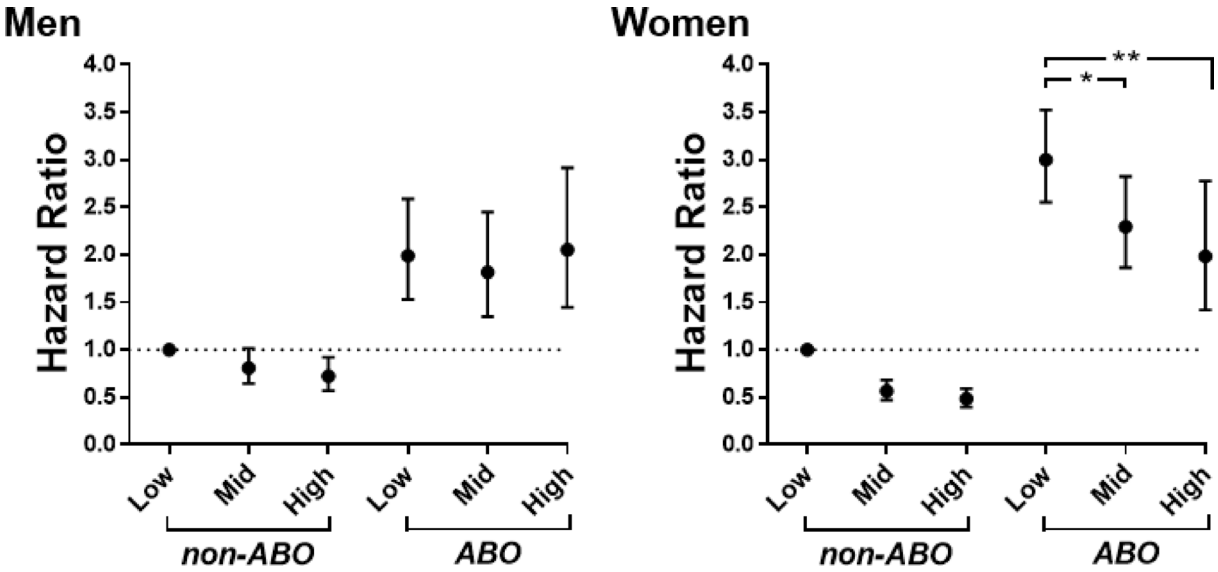

Fig. 2. Hazard ratios for new-onset NAFLD based on sex-specific tertiles of rHGS and ABO. Adjusted for age, drinking, smoking, educational level, T-Chol, ALT, PA time, hypertension, and diabetes mellitus. *NAFLD* nonalcoholic fatty liver disease, *rHGS* relative handgrip strength, *ABO* abdominal obesity, *T-Chol* total cholesterol, *ALT* alanine aminotransferase, *PA time* total time of regular participation in any sport or exercise to the point of sweating. $^{*}p < 0.05$; $^{**}p < 0.01$.

rHGS groups were related to a 43% and 51% risk reduction of developing NAFLD, respectively (all $p < 0.0001$). Importantly, even in women with ABO, compared with those in the low-rHGS group, those in the mid- and high-rHGS groups were associated with a 23% ($p < 0.05$) and 36% ($p < 0.01$) risk reduction in incident NAFLD, respectively.

Subgroup analyses were conducted for each sex to investigate whether the association between higher rHGS and NAFLD risk reduction was consistent in various subgroups, including age, educational level, current drinking habits, smoking status, PA time, hypertension status, and diabetes mellitus status. In men, the significance of the relationship between high rHGS and NAFLD risk reduction differed in some subgroups (Supplementary Table 3). The protective benefit of high rHGS against developing NAFLD was significant only in male participants aged < 65 years ($p < 0.01$), non-drinkers ($p < 0.01$), ever-smokers ($p < 0.001$), those engaged in PA for < 150 min/week ($p < 0.001$), those with middle school education or lower ($p < 0.05$), those without hypertension ($p < 0.0001$), and those without diabetes mellitus ($p < 0.01$). In men, significant interactions were observed for smoking status (p for interaction < 0.05), PA time (p for interaction < 0.05), and hypertension (p for interaction < 0.01). In women, the benefit of high rHGS in preventing NAFLD was consistent across all subgroups, except for smoking status, where statistical significance was not observed in those who had ever smoked ($p = 0.13$) (Supplementary Table 4). However, there was no significant interaction with smoking status (p for interaction = 0.52). Although a significant interaction was observed for hypertension status (p for interaction < 0.001), high rHGS conferred a protective benefit against NAFLD in both subgroups (no and yes).

Discussion

To the best of our knowledge, the present study is the first to investigate the risk of incident NAFLD by simultaneously considering both rHGS and ABO status in a nationwide prospective cohort in Korea. Our findings indicate that maintaining a higher rHGS may confer a preventive effect against NAFLD, with this effect being greater in women than in men. Additionally, among individuals with ABO, having high rHGS significantly decreased the risk of developing NAFLD in women but not in men.

As there are currently no approved medications for the treatment or prevention of NAFLD, lifestyle modifications such as dietary changes, weight loss, and regular PA have been recommended for its management. Particularly, regular RT, which involves working muscle groups against external resistance, has been recommended for improving body composition, insulin resistance, BP, and muscular fitness[25]. Previous research has reported that RT significantly improves intrahepatic lipid and liver enzyme levels in patients with NAFLD, even at lower levels of energy consumption and training intensity than aerobic exercise training[26]. A recent cross-sectional study found that adding regular RT while meeting the PA guideline (≥ 150 min/week of moderate-intensity PA) can further decrease NAFLD risk[27]. However, few prospective cohort studies have examined the association between performing regular RT or having higher muscular strength, a major outcome of RT, and the risk of developing NAFLD in individuals initially without the condition. Accordingly, we investigated the longitudinal relationship between rHGS and incident NAFLD in a Korean population.

In our study, we observed an inverse dose–response relationship between rHGS and incident NAFLD in both sexes, even after adjusting for covariates, including total PA time. This finding aligns with a previous study that reported an inverse relationship between HGS and NAFLD incidence in a Chinese population[28]. Recent cross-

sectional studies in Korea[14,15] and the United States[16] have also shown that higher HGS is negatively correlated with NAFLD risk. Although the potential mechanisms linking skeletal muscle weakness and incident NAFLD are not fully understood, systemic inflammation and insulin resistance have been proposed as main factors. First, as skeletal muscle is a primary insulin-responsive organ, muscle weakness and myosteatosis may lead to increased hepatic free fatty acid (FFA) uptake, hepatic gluconeogenesis, and decreased FFA oxidation by reducing insulin response and energy expenditure[29]. Second, chronic inflammation has also been implicated as a crucial underlying factor in both muscle weakness and NAFLD. Liver fat accumulation has been associated with increased levels of markers of systemic inflammation and oxidative stress, such as interleukin 6 (IL-6), C-reactive protein (CRP), urinary isoprostanes, and intercellular adhesion molecule 1[30]. Conversely, recent meta-analyses have shown that higher levels of muscular strength or long-term RT are associated with lower systemic inflammatory markers including CRP, IL-6, and tumor necrosis factor-alpha (TNF-α)[31,32]. Overall, our findings and those of previous studies suggest that higher levels of muscular strength through regular RT may confer preventive advantages against NAFLD by improving systemic inflammation and insulin resistance.

ABO is a well-known independent risk factor for incident NAFLD. It is associated with an increased risk not only of NAFLD but also of hypertension, diabetes mellitus, CVD, and even cancer. This increased risk is attributed to the promotion of pro-inflammatory activity, dysregulation of adipokines, worsening insulin sensitivity, and abnormal glucose regulation[33,34]. Recent studies have highlighted that ABO is independently associated with an increased risk of developing NAFLD, regardless of metabolic syndrome[8] or general obesity status[7]. In our study, we found that compared with the non-ABO group, having ABO increased the risk of incident NAFLD by 2.3 and 3.8 times in men and women, respectively, after adjusting for covariates. This is consistent with the findings of a previous meta-analysis of cross-sectional studies, which reported that ABO increased the risk of NAFLD by 2.5 times[35]. Additionally, a recent prospective cohort study reported that ABO is a major risk factor for moderate-to-advanced liver fibrosis development in patients with NAFLD[36]. Consequently, there is a growing interest in preventive and therapeutic strategies targeting ABO to not only prevent NAFLD but also halt further liver fibrosis progression.

Considering that ABO markedly increases the risk of developing NAFLD, it is crucial to investigate whether higher levels of muscular strength confer protective effects against NAFLD, even in individuals with ABO. To the best of our knowledge, few studies have simultaneously considered muscular strength levels and ABO status when investigating NAFLD risk. Thus, we examined whether maintaining higher muscular strength could prevent NAFLD development, even in individuals with ABO. Our study found that even among female participants with ABO, those with mid and high rHGS showed a 23% and 36% risk reduction in developing NAFLD, respectively, compared to those with low rHGS. This aligns with recent cross-sectional studies reporting an inverse association between higher HGS and CRP levels and NAFLD risk in participants with ABO[15,37]. Moreover, a previous randomized controlled trial has shown that increasing muscular strength through regular RT can significantly reduce circulating systemic inflammatory markers including TNF-α and CRP in obese women, independently of changes in body composition[38]. Taken together, higher muscular strength may prevent NAFLD development, independent of ABO status, by improving chronic inflammation. However, the abovementioned cross-sectional study did not consider potential sex-based differences in the relationship between muscular strength and NAFLD risk in participants with ABO[15], therefore, data from prospective cohorts are needed to verify potential variations between sexes and deduce causal relationships.

In our prospective study, in individuals with ABO diagnosed by WC, having a high rHGS was associated with decreased risk of incident NAFLD in women but not in men. The underlying mechanisms for this difference are not yet fully understood. Studies using CT scans to measure abdominal fat area, which is considered the gold standard for body composition analysis, have shown that men have significantly more visceral fat area but less subcutaneous fat area than women, regardless of general obesity status[39,40]. As visceral fat volume is more strongly associated with hepatic fat infiltration than subcutaneous fat volume[9], the generally higher visceral fat volume in men may offset the protective benefit of high rHGS against NAFLD development. Thus, it may be necessary to simultaneously increase muscular strength and decrease visceral fat volume to effectively mitigate NAFLD risk. Since our study indirectly evaluated ABO status using WC, it is unclear whether the abdominal fat distribution difference is due to sex-based differences. In contrast, another study reported that HGS is inversely related to the incidence of NAFLD in both male and female patients, with ABO diagnosed using WC[28]. Considering these contradictory results, further prospective studies using advanced imaging techniques such as CT or magnetic resonance imaging (MRI) are needed to clarify whether sex-based differences in abdominal fat distribution influence the association between muscular strength and NAFLD risk.

An important strength of the present study is the use of a large nationwide cohort representative of the general Korean population aged 40–79 years. Furthermore, to the best of our knowledge, this is the first study to investigate the risk of incident NAFLD while considering the combined effects of rHGS and ABO status in Korea. Despite its strengths, the study has several limitations. First, because we only included Korean participants, the generalizability of our findings to other populations is limited. Second, although FSI has been externally validated in the Korean population using MRI[21], it is possible that the actual incidence of NAFLD was either underestimated or overestimated. Since early-grade hepatic steatosis may be difficult to screen through this indirect index[41], it needs to be diagnosed using MRI or magnetic resonance spectroscopy. Third, self-reported questionnaires were used to assess PA time and RT regularity, which may have introduced recall bias. Fourth, our subgroup analyses consisted of some subgroups with a small sample size which may have introduced type I error. Fifth, the assessment of ABO status using WC in our study could not provide specific information on abdominal fat distribution. Last, we could not consider the impact of other potential confounders such as dietary habits or genetic predisposition.

Conclusion

Our study indicates that maintaining high rHGS may confer a preventive effect against NAFLD, with a stronger impact observed in women than in men. Moreover, among individuals with ABO, having a high rHGS significantly reduced the risk of developing NAFLD in women but not in men. However, as our study indirectly evaluated ABO status, further research is necessary to investigate whether sex-based differences in abdominal fat distribution affect the protective effect of high muscular strength against NAFLD development.

Data availability

The data in this study were obtained from the Korean Genome and Epidemiology Study (KoGES; 6635-302), National Institute of Health, Korea. The relevant data request process and contact information can be found by following this link: https://www.nih.go.kr/ko/main/contents.do?menuNo=300566.

Received: 17 May 2024; Accepted: 28 April 2025
Published online: 21 May 2025

References

1. De, A. & Duseja, A. Natural history of simple steatosis or nonalcoholic fatty liver. *J. Clin. Exp. Hepatol.* **10**, 255–262 (2020).
2. Younossi, Z. M. et al. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology* **77**, 1335–1347 (2023).
3. Im, H. J., Ahn, Y. C., Wang, J. H., Lee, M. M. & Son, C. G. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. *Clin. Res. Hepatol. Gastroenterol.* **45**, 101526. https://doi.org/10.1016/j.clinre.2020.06.022 (2021).
4. Ma, W. et al. Association of NAFLD with cardiovascular disease and all-cause mortality: a large-scale prospective cohort study based on UK biobank. *Ther. Adv. Chronic Dis.* **13**, 20406223221122478. https://doi.org/10.1177/20406223221122478 (2022).
5. Simon, T. G., Roelstraete, B., Khalili, H., Hagström, H. & Ludvigsson, J. F. Mortality in biopsy-confirmed nonalcoholic fatty liver disease: results from a nationwide cohort. *Gut* **70**, 1375–1382 (2021).
6. Li, L. et al. Obesity is an independent risk factor for non-alcoholic fatty liver disease: evidence from a meta-analysis of 21 cohort studies. *Obes. Rev.* **17**, 510–519 (2016).
7. Zhao, D., Cui, H., Shao, Z. & Cao, L. Abdominal obesity, chronic inflammation and the risk of non-alcoholic fatty liver disease. *Ann. Hepatol.* **28**, 100726. https://doi.org/10.1016/j.aohep.2022.100726 (2023).
8. Kuang, M. et al. Abdominal obesity phenotypes are associated with the risk of developing non-alcoholic fatty liver disease: insights from the general population. *BMC Gastroenterol.* **22**, 311. https://doi.org/10.1186/s12876-022-02393-9 (2022).
9. Jang, S. et al. Correlation of fatty liver and abdominal fat distribution using a simple fat computed tomography protocol. *World J. Gastroenterol.* **17**, 3335–3341 (2011).
10. Yang, Y. S., Han, B. D., Han, K., Jung, J. H. & Son, J. W. Obesity fact sheet in Korea, 2021: trends in obesity prevalence and obesity-related comorbidity incidence stratified by age from 2009 to 2019. *J. Obes. Metab. Syndr.* **31**, 169–177 (2022).
11. Chan, J., Lu, Y. C., Yao, M. M. S. & Kosik, R. O. Correlation between hand grip strength and regional muscle mass in older Asian adults: an observational study. *BMC Geriatr.* **22**, 206. https://doi.org/10.1186/s12877-022-02898-8 (2022).
12. Vaidya, S. M. & Nariya, D. M. Handgrip strength as a predictor of muscular strength and endurance: a cross-sectional study. *J. Clin. Diagn. Res.* **15**, YC01–YC04 (2021).
13. Wind, A. E., Takken, T., Helders, P. J. M. & Engelbert, R. H. H. Is grip strength a predictor for total muscle strength in healthy children, adolescents, and young adults? *Eur. J. Pediatr.* **169**, 281–287 (2010).
14. Lee, S. B., Kwon, Y. J., Jung, D. H. & Kim, J. K. Association of muscle strength with non-alcoholic fatty liver disease in Korean adults. *Int. J. Environ. Res. Public Health*. **19**, 1675. https://doi.org/10.3390/ijerph19031675 (2022).
15. Rho, H. S. & Choi, W. S. Low muscle strength as risk factor for non-alcoholic fatty liver disease in different metabolic conditions. *Korean J. Fam Med.* **45**, 89–95 (2024).
16. Zhao, X., Shi, X., Gu, H., Zhou, W. & Zhang, Q. Association between handgrip strength, nonalcoholic fatty liver disease, advanced hepatic fibrosis and its modifiers: evidence from the NHANES database of the USA. *J. Gastroenterol. Hepatol.* **38**, 1734–1742 (2023).
17. Kim, Y., Han, B. G. & KoGES group. Cohort profile: the Korean Genome and Epidemiology Study (KoGES) consortium. *Int. J. Epidemiol.* **46**, e20. https://doi.org/10.1093/ije/dyv316 (2017).
18. Lee, S. B., Moon, J. E. & Kim, J. K. Association of handgrip strength with diabetes mellitus in Korean adults according to sex. *Diagnostics* **12**, 1874. https://doi.org/10.3390/diagnostics12081874 (2022).
19. Park, J. H., Lim, N. K. & Park, H. Y. Relative handgrip strength is inversely associated with hypertension in consideration of visceral adipose dysfunction: a nationwide cross-sectional study in Korea. *Front. Physiol.* **13**, 930922. https://doi.org/10.3389/fphys.2022.930922 (2022).
20. Long, M. T. et al. Development and validation of the Framingham steatosis index to identify persons with hepatic steatosis. *Clin. Gastroenterol. Hepatol.* **14**, 1172–1180e2 (2016).
21. Jung, T. Y., Kim, M. S., Hong, H. P., Kang, K. A. & Jun, D. W. Comparative assessment and external validation of hepatic steatosis formulae in a community-based setting. *J. Clin. Med.* **9**, 2851. https://doi.org/10.3390/jcm9092851 (2020).
22. Zhu, J. et al. Validation of simple indexes for nonalcoholic fatty liver disease in Western China: a retrospective cross-sectional study. *Endocr. J.* **65**, 373–381 (2018).
23. Motamed, N. et al. The ability of the Framingham steatosis index (FSI) to predict non-alcoholic fatty liver disease (NAFLD): a cohort study. *Clin. Res. Hepatol. Gastroenterol.* **45**, 101567. https://doi.org/10.1016/j.clinre.2020.10.011 (2021).
24. Lee, S. Y. et al. Appropriate waist circumference cutoff points for central obesity in Korean adults. *Diabetes Res. Clin. Pract.* **75**, 72–80 (2007).
25. Garber, C. E. et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med. Sci. Sports Exerc.* **43**, 1334–1359 (2011).
26. Hashida, R. et al. Aerobic vs. resistance exercise in non-alcoholic fatty liver disease: a systematic review. *J. Hepatol.* **66**, 142–152 (2017).
27. Park, J. H., Lim, N. K. & Park, H. Y. Protective effect of leisure-time physical activity and resistance training on nonalcoholic fatty liver disease: a nationwide cross-sectional study. *Int. J. Environ. Res. Public. Health*. **19**, 2350. https://doi.org/10.3390/ijerph19042350 (2022).
28. Xia, Y. et al. Longitudinal associations between hand grip strength and non-alcoholic fatty liver disease in adults: a prospective cohort study. *Front. Med.* **8**, 752999. https://doi.org/10.3389/fmed.2021.752999 (2021).
29. Li, A. A., Kim, D. & Ahmed, A. Association of sarcopenia and NAFLD: an overview. *Clin. Liver Dis.* **16**, 73–76 (2020).
30. Fricker, Z. P. et al. Liver fat is associated with markers of inflammation and oxidative stress in analysis of data from the Framingham Heart Study. *Clin. Gastroenterol. Hepatol.* **17**, 1157–1164e4 (2019).

31. Kim, S. D. & Yeun, Y. R. Effects of resistance training on C-reactive protein and inflammatory cytokines in elderly adults: a systematic review and meta-analysis of randomized controlled trials. *Int. J. Environ. Res. Public Health*. **19**, 3434. https://doi.org/10.3390/ijerph19063434 (2022).
32. Tuttle, C. S. L., Thang, L. A. N. & Maier, A. B. Markers of inflammation and their association with muscle strength and mass: a systematic review and meta-analysis. *Ageing Res. Rev.* **64**, 101185. https://doi.org/10.1016/j.arr.2020.101185 (2020).
33. Neeland, I. J. et al. Visceral and ectopic fat, atherosclerosis, and cardiometabolic disease: a position statement. *Lancet Diabetes Endocrinol.* **7**, 715–725 (2019).
34. Bansal, S., Vachher, M., Arora, T., Kumar, B. & Burman, A. Visceral fat: a key mediator of NAFLD development and progression. *Hum. Nutr. Metab.* **33**, 200210. https://doi.org/10.1016/j.hnm.2023.200210 (2023).
35. Pang, Q. et al. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. *World J. Gastroenterol.* **21**, 1650–1662 (2015).
36. Julián, M. T. et al. Abdominal obesity and dsyglycemia are risk factors for liver fibrosis progression in NAFLD subjects: a population-based study. *Front. Endocrinol.* **13**, 1051958. https://doi.org/10.3389/fendo.2022.1051958 (2023).
37. de Lima, T. R., González-Chica, D. A., Sui, X. & Santos Silva, D. A. The independent and joint associations among muscle strength, abdominal obesity and cardiometabolic variables among adults. *Eur. J. Sport Sci.* **22**, 1122–1131 (2022).
38. Phillips, M. D. et al. Resistance training reduces subclinical inflammation in obese, postmenopausal women. *Med. Sci. Sports Exerc.* **44**, 2099–2110 (2012).
39. Kim, J. A., Choi, C. J. & Yum, K. S. Cut-off values of visceral fat area and waist circumference: diagnostic criteria for abdominal obesity in a Korean population. *J. Korean Med. Sci.* **21**, 1048–1053 (2006).
40. Kong, M. et al. Assessing visceral obesity and abdominal adipose tissue distribution in healthy populations based on computed tomography: a large multicenter cross-sectional study. *Front. Nutr.* **9**, 871697. https://doi.org/10.3389/fnut.2022.871697 (2022).
41. McHenry, S., Park, Y., Browning, J. D., Sayuk, G. & Davidson, N. O. Dallas steatosis index identifies patients with nonalcoholic fatty liver disease. *Clin. Gastroenterol. Hepatol.* **18**, 2073–2080 (2020).

Author contributions

J.H.P. conceived the study, conducted the investigation, performed formal analysis, developed the software, validated the data, performed data visualization, drafted the original manuscript, and contributed to its review and editing. H.-Y.P. conceived the study, contributed to the methodology, curated the data, supervised the project, managed resources, acquired funding, and reviewed and edited the manuscript. All authors have read and approved the final version of the manuscript and agree with the order of presentation.

Funding

This research was supported by the National Institute of Health (NIH) research project (Grant Nos. 2024-NI-003-00 and 2024-NI-003-01).

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the National Institute of Health, Korea Disease Control and Prevention Agency (Approval No. KDCA-2024-02-12-P-01). The participants provided their written informed consent to participate in this study.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-00377-9.

Correspondence and requests for materials should be addressed to H.-Y.P.