

## Research Article



### OPEN ACCESS

**Received:** Nov 26, 2022

**Revised:** Dec 15, 2022

**Accepted:** Dec 19, 2022

**Published online:** Dec 23, 2022

#### Correspondence to

**So Young Bu**

Department of Food and Nutrition, College of Engineering, Daegu University, 201 Daegudae-ro, Gyeongsan 38453, Korea.

Tel: +82-53-850-6832

Email: busy@daegu.ac.kr

© 2022 The Korean Nutrition Society

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

#### ORCID iDs

So Young Bu 

<https://orcid.org/0000-0001-9801-5435>

#### Funding

This work was supported by the Daegu University General Research Grant, 2018 (20180493).

#### Conflict of Interest

There are no financial or other issues that might lead to conflict of interest.

# Association of energy intake with handgrip strength in Korean adults with non-alcoholic fatty liver disease

**So Young Bu** 

Department of Food and Nutrition, Daegu University, Gyeongsan, Korea

## ABSTRACT

**Purpose:** Recent studies have reported a significant association between skeletal muscle, muscle strength and non-alcoholic fatty liver disease (NAFLD). The effect of nutrient intake on the prediction of skeletal muscle mass and strength or its suggested correlation with metabolic diseases has been primarily reported in healthy individuals. The current study explores the association between energy intake and handgrip strength (HGS) in individuals with NAFLD.

**Methods:** Data were obtained from the Korea National Health and Nutrition Examination Surveys 2016-2018. Data from 12,469 participants were extracted and 1,293 men and 1,401 women aged 20 years and older were included in the analyses of patients with NAFLD. The presence of NAFLD was determined using the hepatic steatosis index. To estimate relative skeletal muscle strength, HGS was measured using a digital dynamometer and calculated by adjusting the body mass index of the dominant arm. Study subjects in the NAFLD and non-NAFLD groups were separately categorized according to quartiles of the calculated HGS.

**Results:** We found that individuals with low (EQ1) energy intake had lower odds of HGS compared to subjects with high (EQ4) energy intake, irrespective of their NAFLD status ( $p < 0.0001$ ). However, the HGS did not differ based on the level of protein or fat intake ratio. Additionally, the effect of energy intake on HGS was more pronounced in men than in women.

**Conclusion:** Energy intake was associated with the risk of weak HGS in men with NAFLD. The results indicate that energy intake may be a key factor in nutrition care for NAFLD patients with low muscle function.

**Keywords:** NAFLD; energy intake; skeletal muscle

## INTRODUCTION

Sarcopenia is a state characterized by decreased skeletal muscle mass and strength and its comorbidities increase the risk of metabolic disease and mortality [1,2]. Recent evidences suggest a significant relationship between skeletal muscle mass, metabolic disorders (e.g. obesity, non-alcoholic fatty liver disease [NAFLD]), and related dietary factors [3-5]. However, the effect of nutrient intake has not been incorporated in the prediction of skeletal muscle strength, and its relationship to muscle function has not been well established. In addition, the outcomes of studies that have investigated the role of a single nutrient supply

in augmenting muscle mass, or the effect of nutritional status on skeletal muscle health were still conflicting. For instance, the risk of sarcopenia was higher in overweight or obese individuals, and a higher body mass index (BMI) was positively correlated with lean body mass [4,6]. High protein intake increases fat-free mass and reduces insulin resistance [5], while another study reported an increased diabetes prevalence in study participants with high protein intake [7]. Our recent study reported a positive effect of total energy intake on skeletal muscle mass in Korean adults [8], though its relationship with muscle strength has not been reported.

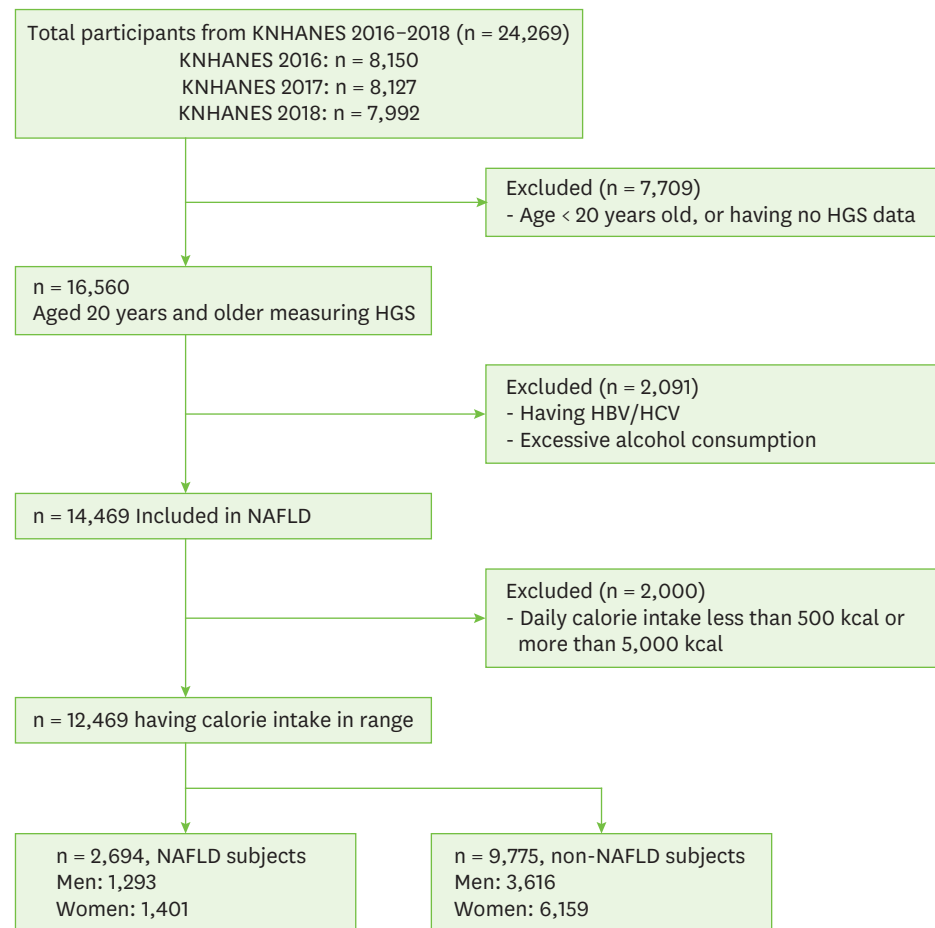
Among several metabolic complications, NAFLD is associated with higher energy intake. NAFLD has been reported to be significantly associated with high risk of sarcopenia, which may be related to low-energy intake [9-11]. Each study that reported the modulatory effect of diet and nutrient intake in association with NAFLD or with skeletal muscle strength separately exists [12-17]. For example, a Mediterranean diet was associated with a lower risk of developing frailty [14], and observational studies reported a shortage of energy intake in sarcopenia [17] and high fat intake (> 42%) and low micronutrient intake in patients with NAFLD [15]. However, the effects of energy intake on muscle strength in patients with NAFLD has not been reported. Recently, studies have reached a consensus that muscle strength predicts muscle health or frailty more precisely than muscle mass [18]. Handgrip strength (HGS) measurement is a convenient method for representing muscle strength and has been reported to be highly correlated with whole-body muscle mass [19]. Furthermore, HGS predicts the risk of many health problems, metabolic diseases, diabetes, and hypertension [20-22]. However, few studies have examined the relationship between muscle strength and NAFLD, and these studies observed the effect of nutrients on skeletal muscle mass or the association between muscle strength, mostly in healthy individuals.

Hence, the purpose of this study was to explore the association between energy intake and HGS as a functional index of muscle strength in patients with NAFLD.

## METHODS

### Data source and study participants

Data were obtained from 24,269 participants enrolled in the Korea National Health and Nutrition Examination Survey (KNHANES) between 2016 and 2018. Initially 16,560 individuals aged 20 years and older, whose HGS data were accessible were included. For classifying NAFLD, participants with excessive alcohol consumption (more than 210 g/week for men and more than 140 g/week for women) and with positive for hepatitis B or C viral marker were excluded [23]. Participants with a daily calorie intake of less than 500 kcal or more than 5,000 kcal were excluded. Upon considering the exclusion criteria, 12,469 individuals were included in the analysis (**Fig. 1**). The use of KNHANES 2018 data was approved by the Institutional Review Board (IRB) of the Korea Centers for Disease Control and Prevention (IRB No. 2018-01-03-P-A). IRB approval was not required for the use of KNHANES data between 2016 and 2017 under the Bioethics Act [24]. For the main analyses of patients with NAFLD, a total of 2,694 participants (1,293 men and 1,401 women), for comparison purpose, 9,775 participants (3,616 men and 6,159 women) without non-NAFLD were included in the analysis (**Fig. 1**).



**Fig. 1. Inclusion and exclusion criteria for the study participants.**

NAFLD, non-alcoholic fatty liver disease. HGS, handgrip strength. HBV, hepatitis B virus. HCV, hepatitis C virus.

### Definition of NAFLD

The hepatic steatosis index was used to diagnose NAFLD in the study participants. NAFLD was defined using a previously reported model that calculated hepatic steatosis index [25] as  $8 \times \text{alanine aminotransferase (ALT)}/\text{aspartate aminotransferase (AST)} + \text{BMI} (+2 \text{ for diabetes}; +2 \text{ for female})$ . The prediction sensitivity and specificity of the hepatic steatosis index for NAFLD were 86% and 66%, respectively, in the Korean population [25].

### Anthropometric and biochemical data

Anthropometric, health-related, and biochemical parameters were obtained from all the participants. The data obtained were age, waist circumference (WC), systolic blood pressure (SBP) and diastolic blood pressure (DBP). Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, with participants wearing light clothing [24]. BMI was calculated as weight in kilograms divided by the square of height in meter squares. Blood pressure was measured on the right arm using a standard mercury sphygmomanometer (Baumanometer Wall Unit 33(0850), W.A. Baum Co. Inc., Copiague, NY, USA) in stable position. Blood pressure was measured twice at 5-min intervals and the averaged value were reported [24]. Enzymatic analysis was performed to measure serum parameters of metabolic status including fasting glucose, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, total triglycerides, ALT, AST, blood urea nitrogen, and

creatinine levels (using Hitachi Automatic Analyzer 7600, Japan). All analytic procedures were subjected to quality control inspection [24].

### Assessment of HGS

HGS was assessed using a digital grip strength dynamometer (T.K.K 5401; Takei, Niigata, Japan), in a standing position with the participants' arms in full extension. The participants were instructed to squeeze the dynamometer as strongly as possible, for at least 3 s. The right and left hands were alternately squeezed three times for a total of six measurements [24]. Relative HGS was calculated using a previously reported equation [10,20]: the absolute HGS value of a dominant arm divided by BMI. The quartiles of HGS were calculated for each sex, with Q1 and Q4 being the lowest and highest quartiles, respectively. Q1 was defined as the set of participants with low HGS.

### Dietary records

The dietary intake data of participants were assessed by trained survey researchers using the 24-h dietary recall method. The intake of each nutrient, including carbohydrates, fats, and proteins, was calculated using food composition tables issued by the National Rural Resources Development Institute (9th revision) [26]. In addition, the participants were asked whether the dietary intake recorded in their 24-h dietary recall was similar to their typical diet [24]. To minimize the variation due to one-day dietary assessment, the data that were similar to a participant's usual dietary intake were analyzed.

### Assessment of other covariates

Covariates include household income, education, physical activity, and the presence of hypertension, hyperglycemia or diabetes mellitus. Household income data were reported as quartiles of average household monthly income in the KNHANES: low, low-middle, middle-high, and high [24]. The data on education were categorized into two levels: less than a high school education or above. Hypertension was recognized by the SBP  $\geq$  140 mmHg, DBP  $\geq$  90 mmHg, or use of antihypertensive medications. Diabetes was assessed when participants had 8-h fasting glucose levels  $\geq$  126 mg/dL, were taking insulin, or had a medical diagnosis. Hypertriglyceridemia was defined by triglyceride levels  $\geq$  150 mg/dL, or use of triglyceride-lowering medications. The type of physical activity was classified as active or non-active considering the following criteria: doing mild or mid-strength physical activity for at least five days a week for a minimum 30 min were coded as "active" and the others coded as "non-active." The smoking status of participants was classified as either a "smoker" who have smoked more than five packs of cigarettes during the lifetime or as a "non-smoker" who never have smoked.

### Statistical analysis

Statistical analyses were performed using the SAS software (version 9.4, SAS Institute Inc., Cary, NC, USA). Values are reported as mean and standard error for continuous variables, and percentages for categorical variables. Due to substantial differences in HGS by sex, data for men and women were separated for further analysis. All analyses were performed as complex-sampling analyses, and a domain code was assigned to a subgroup of interest to minimize error estimates. The range of values for each HGS quartile was as follows: for NAFLD men, first quartile (Q1): HGS < 1.19, second quartile (Q2):  $1.19 \leq$  HGS < 1.40, third quartile (Q3):  $1.40 \leq$  HGS < 1.61, and fourth quartile (Q4):  $1.61 \leq$  HGS. For NAFLD women, Q1: HGS < 0.65, Q2:  $0.65 \leq$  HGS < 0.78, Q3:  $0.78 \leq$  HGS < 0.93, and Q4:  $0.93 \leq$  HGS. For non-NAFLD men, first quartile (Q1): HGS < 1.34, second quartile (Q2):  $1.34 \leq$  HGS < 1.56, third quartile (Q3):

1.56 ≤ HGS < 1.80, and fourth quartile (Q4): 1.80 ≤ HGS. For non-NAFLD women, Q1: HGS < 0.82, Q2: 0.82 ≤ HGS < 0.98, Q3: 0.98 ≤ HGS < 1.15, and Q4: 1.15 ≤ HGS. Linear regression analysis (PROC SURVEYREG) or chi-square test (PROC SURVEYFREQ) was conducted to test the differences in variables among the quartile groups of HGS. Multivariate linear regression models were designed and tested to characterize the association of energy nutrient intake and quartile of HGS by accounting age, household income, education level, WC and physical activity level. A logistic regression analysis was performed to estimate the odds ratio, 95% confidence intervals (CIs), and p-values for the trend of risk of low muscle strength by the level of total energy intake, in men and women separately, after adjusting for key covariates including age, WC, physical activity, household income, and education level. Statistical significance was set at  $p < 0.05$ .

## RESULTS

### Characteristics of study participants according to HGS

Patients with NAFLD and participants without NAFLD were separately grouped by quartiles of HGS, and the prevalence of NAFLD was compared according to the quartiles of HGS (**Supplementary Tables 1 and 2**). The mean age of the study population at Q1 was  $51.2 \pm 0.7$  years and  $56.3 \pm 0.6$  years for men and women, respectively in NAFLD patients and  $43.9 \pm 1.1$  years and  $59.2 \pm 1.0$  years for men and women, respectively in participants without NAFLD. The mean values of HGS at Q1, Q2, Q3, and Q4 were 1.02, 1.30, 1.50, and 1.77 for men, 0.52, 0.72, 0.85 and 1.05 for women, respectively in NAFLD patients, and 1.14, 1.46, 1.68, and 2.00 for men, 0.67, 0.90, 1.06 and 1.29 for women, respectively in participants without NAFLD. Both NAFLD patients and non-NAFLD participants have shown a tendency of decrease in mean BMI and WC from Q1 to Q4 ( $p < 0.0001$  for all). The range of the ratio having diabetes, hypertension, and hyperglyceridemia among Q1 to Q4 were 13.4–22.4%, 26.1–45.1%, 27.3–40.3% for men and 16.6–29.1%, 27.4–57.2%, 17.3–23.8% for women in NAFLD patients and 3.3–15.6%, 16.0–37.8%, 11.6–16.7% for men and 2.2–11.4%, 8.0–34.8%, 4.2–10.5% for women in individuals without NAFLD. The distribution of household income and education level in both NAFLD patients and participants without NAFLD differed according to quartiles of HGS.

### Energy nutrient intake by participants

To investigate the association between HGS and energy intake in NAFLD, individuals with and without NAFLD were separated by calculating the hepatic steatosis index score (**Tables 1 and 2**). Total energy, protein and fat intake gradually increased as the quartile of HGS increased in both men and women without NAFLD ( $p < 0.0001$ ). In men without NAFLD, carbohydrate intake was significantly increased by the HGS quartile ( $p = 0.0009$ ). Energy intake from alcohol consumption was significantly increased by HGS quartile in both men and women (**Table 1**). In patients with NAFLD, the total energy and nutrient intake increased as the HGS quartile increased (**Table 2**). The intake ratio of carbohydrates to total energy in men and women in Q1 were 62.1% and 69.3%, respectively, while the ratios tended to decrease to 59.0% and 63.7% in men and women in the highest HGS quartile. The intake ratio of protein to total energy at Q1 were 14.7% and 13.3% in both men and women, respectively, while the intake ratios of fat to total energy at Q1 were 19.4% and 15.8% in men and women, respectively. The intake ratios of both protein ( $p < 0.0001$ ) and fat ( $p = 0.0003$ ) relative to the total energy intake in women showed an increasing trend in a narrow range as the HGS quartile increased. The energy obtained from alcohol consumption was not significantly different by HGS quartile in men and women in the HGS quartile (**Table 2**).

**Table 1.** Energy intake by the quartile of HGS in participant without non-alcoholic fatty liver disease

Variables	Men (n = 3,616)					Women (n = 6,159)				
	Q1 (n = 904)	Q2 (n = 904)	Q3 (n = 904)	Q4 (n = 904)	p-trend	Q1 (n = 1,540)	Q2 (n = 1,539)	Q3 (n = 1,540)	Q4 (n = 1,540)	p-trend
Energy (kcal)	2,074.4 ± 35.1 <sup>1)</sup>	2,245.9 ± 33.9	2,323.5 ± 33.8	2,426.2 ± 30.5	<0.0001	1,584.8 ± 18.1	1,697.0 ± 19.8	1,746.0 ± 20.6	1,761.5 ± 18.6	<0.0001
Carbohydrate (g)	325.1 ± 5.2	335.9 ± 4.6	342.1 ± 5.0	351.2 ± 4.7	0.0014	262.0 ± 3.1	272.0 ± 3.2	268.8 ± 3.3	266.0 ± 3.1	0.1676
Protein (g)	72.4 ± 1.6	81.0 ± 1.6	85.7 ± 1.5	90.6 ± 1.5	<0.0001	55.0 ± 0.8	60.6 ± 0.9	63.4 ± 0.9	65.0 ± 0.9	<0.0001
Fat (g)	41.4 ± 1.4	50.1 ± 1.5	52.7 ± 1.4	57.4 ± 1.3	<0.0001	32.6 ± 0.8	37.2 ± 0.8	42.1 ± 0.9	44.6 ± 0.8	<0.0001
Carbohydrate (% Energy) <sup>2)</sup>	64.7 ± 0.6	61.8 ± 0.6	60.5 ± 0.5	59.1 ± 0.5	<0.0001	67.2 ± 0.4	64.8 ± 0.4	62.6 ± 0.4	61.2 ± 0.3	<0.0001
Protein (% Energy)	13.8 ± 0.2	14.4 ± 0.2	14.9 ± 0.2	15.0 ± 0.2	<0.0001	13.8 ± 0.1	14.3 ± 0.1	14.5 ± 0.1	14.8 ± 0.1	<0.0001
Fat (% Energy)	17.0 ± 0.4	19.1 ± 0.4	19.6 ± 0.3	20.8 ± 0.3	<0.0001	17.7 ± 0.3	19.2 ± 0.3	21.1 ± 0.3	22.2 ± 0.3	<0.0001
Alcohol intake (kcal) <sup>3)</sup>	53.0 ± 3.0	62.2 ± 2.8	62.5 ± 2.8	64.2 ± 2.6	0.0282	16.4 ± 1.2	22.5 ± 1.2	21.7 ± 1.2	26.7 ± 1.1	<0.0001
Alcohol intake (% Energy)	2.8 ± 0.2	3.0 ± 0.1	3.1 ± 0.2	3.0 ± 0.1	0.7838	1.1 ± 0.1	1.5 ± 0.1	1.4 ± 0.1	1.7 ± 0.1	<0.0001

HGS, handgrip strength.

<sup>1)</sup>Mean ± SE; <sup>2)</sup>Percent intake from total energy intake; <sup>3)</sup>Caloric intake from alcohol was calculated as follows: servings/day × 64 kcal/serving. For men, first quartile (Q1): HGS < 1.34, second quartile (Q2): 1.34 ≤ HGS < 1.56, third quartile (Q3): 1.56 ≤ HGS < 1.80, and fourth quartile (Q4): 1.80 ≤ HGS. For women, Q1: HGS < 0.82, Q2: 0.82 ≤ HGS < 0.98, Q3: 0.98 ≤ HGS < 1.15, and Q4: 1.15 ≤ HGS. The p values are from regression analysis in a complex sampling design for assessing the trend of difference among quartiles.

**Table 2.** Energy intake by the quartile of HGS in non-alcoholic fatty liver disease patients

Variables	Men (n = 1,293)					Women (n = 1,401)				
	Q1 (n = 323)	Q2 (n = 324)	Q3 (n = 322)	Q4 (n = 324)	p-trend	Q1 (n = 351)	Q2 (n = 349)	Q3 (n = 350)	Q4 (n = 351)	p-trend
Energy (kcal)	2,149.7 ± 46.3 <sup>1)</sup>	2,330.2 ± 54.9	2,283.9 ± 52.5	2,389.0 ± 48.7	0.0176	1,597.7 ± 57.0	1,667.7 ± 46.0	1,686.9 ± 41.8	1,734.2 ± 40.2	0.2477
Carbohydrate (g)	322.5 ± 8.5	328.7 ± 7.0	331.5 ± 7.8	341.6 ± 6.8	0.3089	269.2 ± 8.0	274.1 ± 7.8	270.5 ± 6.6	275.6 ± 7.4	0.9171
Protein (g)	79.6 ± 3.0	89.0 ± 2.5	85.7 ± 2.2	91.5 ± 2.6	0.0110	54.0 ± 2.2	58.1 ± 1.8	61.1 ± 1.9	63.8 ± 1.7	0.0014
Fat (g)	49.4 ± 2.3	59.1 ± 2.7	55.3 ± 2.3	58.8 ± 2.4	0.0129	30.5 ± 2.5	35.6 ± 1.9	37.2 ± 1.7	38.6 ± 1.3	0.0483
Carbohydrate (% Energy) <sup>2)</sup>	62.1 ± 0.7	58.6 ± 0.8	59.4 ± 0.8	59.0 ± 0.8	0.0027	69.3 ± 1.0	66.4 ± 0.8	65.0 ± 0.8	63.7 ± 0.7	<0.0001
Protein (% Energy)	14.7 ± 0.3	15.3 ± 0.3	15.2 ± 0.3	15.1 ± 0.3	0.5766	13.3 ± 0.2	14.0 ± 0.2	14.7 ± 0.3	14.9 ± 0.3	<0.0001
Fat (% Energy)	19.4 ± 0.5	21.7 ± 0.6	21.3 ± 0.6	21.3 ± 0.5	0.0929	15.8 ± 0.7	18.5 ± 0.6	19.1 ± 0.6	19.9 ± 0.5	<0.0001
Alcohol intake (kcal) <sup>3)</sup>	54.7 ± 4.0	54.1 ± 4.3	57.3 ± 4.1	66.3 ± 4.3	0.1597	10.4 ± 1.8	16.5 ± 2.0	18.1 ± 2.0	19.8 ± 2.3	0.0042
Alcohol intake (% Energy)	2.8 ± 0.2	2.4 ± 0.2	2.7 ± 0.2	3.2 ± 0.3	0.1701	0.9 ± 0.2	1.1 ± 0.2	1.3 ± 0.2	1.5 ± 0.2	0.3200

HGS, handgrip strength.

<sup>1)</sup>Mean ± SE; <sup>2)</sup>Percent intake from total energy intake; <sup>3)</sup>Caloric intake from alcohol was calculated as follows: servings/day × 64 kcal/serving. For men, first quartile (Q1): HGS < 1.19, second quartile (Q2): 1.19 ≤ HGS < 1.40, third quartile (Q3): 1.40 ≤ HGS < 1.61, and fourth quartile (Q4): 1.61 ≤ HGS. For women, Q1: HGS < 0.65, Q2: 0.65 ≤ HGS < 0.78, Q3: 0.78 ≤ HGS < 0.93, and Q4: 0.93 ≤ HGS. The p values are from regression analysis in a complex sampling design for assessing the trend of difference among quartiles.



### The quantitative association between energy intake and HGS in NAFLD

We examined the association between total energy intake and the sarcopenia index within the same sex and HGS quartile (Table 3) by incorporating age as a covariate into the linear regression model. In men without NAFLD, total energy intake was positively associated with HGS ( $p < 0.0001$ ). Women without NAFLD in the highest HGS quartiles had a higher energy intake than those in the reference group ( $p = 0.0003$ ). In patients with NAFLD, total energy intake from the lowest HGS quartile to the highest HGS quartile was observed, but only in men ( $p = 0.0228$ ). When education level, household income, WC and physical activity were incorporated to the regression model, the quantitative association between muscle strength and energy intake in men with NAFLD remained significant ( $p = 0.0062$ ). Carbohydrate and fat intake were not significantly associated with HGS in men without NAFLD. Associations between the same parameters in women without NAFLD disappeared in the regression model adjusted for other covariates (Tables 4 and 5). In patients with NAFLD, a significantly

**Table 3.** Estimated change of total energy intake according to the quartile of HGS

Variables	NAFLD		Non-NAFLD	
	Men (n = 1,293)	Women (n = 1,401)	Men (n = 3,616)	Women (n = 6,159)
Model I <sup>1)</sup>				
Q1	Ref <sup>3)</sup>	Ref	Ref	Ref
Q2	-109.0 (-248.1, 30.5)	-18.4 (-134.0, 97.3)	-58.9 (-146.5, 28.8)	3.3 (-52.8, 59.5)
Q3	-49.1 (-195.8, 97.7)	-34.1 (-156.1, 88.0)	-105.7 (-198.8, -12.5)*	-22.8 (-76.2, 30.5)
Q4	-228.7 (-378.5, -79.0)**	-63.7 (-216.4, 89.0)	-230.2 (-330.1, -130.3)***	-101.4 (-171.1, -60.1)***
p for trend	0.0228	0.8599	< 0.0001	0.0003
Model II <sup>2)</sup>				
Q1	Ref	Ref	Ref	Ref
Q2	-131.9 (-274.1, 10.3)	-1.6 (-120.9, 117.7)	-78.8 (-169.1, 11.6)	-2.6 (-58.0, 52.9)
Q3	-92.5 (-243.8, 58.8)	-7.2 (-134.7, 120.4)	-121.5 (-218.4, -24.5)*	-26.4 (-81.3, 28.6)
Q4	-269.4 (-421.5, -117.4)***	-9.0 (-174.9, 156.8)	-234.2 (-341.8, -126.6)***	-87.1 (-144.6, -29.6)**
p for trend	0.0062	0.9993	0.0004	0.0094

HGS, handgrip strength; NAFLD, non-alcoholic fatty liver disease.

Beta coefficient with 95% confidence interval were shown. <sup>1)</sup>Model I: adjusted for age, <sup>2)</sup>Model II: Model I + education + household income + waist circumference + physical activity. For NAFLD men, first quartile (Q1): HGS < 1.19, second quartile (Q2): 1.19 ≤ HGS < 1.40, third quartile (Q3): 1.40 ≤ HGS < 1.61, and fourth quartile (Q4): 1.61 ≤ HGS. For NAFLD women, Q1: HGS < 0.65, Q2: 0.65 ≤ HGS < 0.78, Q3: 0.78 ≤ HGS < 0.93, and Q4: 0.93 ≤ HGS. For non-NAFLD men, first quartile (Q1): HGS < 1.34, second quartile (Q2): 1.34 ≤ HGS < 1.56, third quartile (Q3): 1.56 ≤ HGS < 1.80, and fourth quartile (Q4): 1.80 ≤ HGS. For non-NAFLD women, Q1: HGS < 0.82, Q2: 0.82 ≤ HGS < 0.98, Q3: 0.98 ≤ HGS < 1.15, and Q4: 1.15 ≤ HGS. <sup>3)</sup>The lowest quartiles within same sex was used as a reference group. \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001 compared to reference group (Q1) within same sex.

**Table 4.** Carbohydrate intake ratio according to the quartile of HGS

Variables	NAFLD		Non-NAFLD	
	Men (n = 1,293)	Women (n = 1,401)	Men (n = 3,616)	Women (n = 6,159)
Model I <sup>1)</sup>				
Q1	Ref <sup>3)</sup>	Ref	Ref	Ref
Q2	0.57 (-1.70, 2.85)	-0.04 (-2.09, 2.02)	-0.15 (-1.48, 1.18)	0.18 (-0.75, 1.11)
Q3	-0.74 (-2.99, 1.52)	1.19 (-0.89, 3.27)	0.05 (-1.33, 1.45)	0.91 (-0.46, 1.87)
Q4	2.75 (0.69, 4.82)**	2.18 (-0.07, 4.43)	1.25 (-0.22, 2.71)	1.25 (0.28, 2.21)*
p for trend	0.0046	0.1545	0.2379	0.0404
Model II <sup>2)</sup>				
Q1	Ref	Ref	Ref	Ref
Q2	0.85 (-1.47, 3.17)	-0.39 (-2.41, 1.62)	0.39 (-0.96, 1.73)	0.10 (-0.83, 1.03)
Q3	-0.11 (-2.39, 2.16)	0.53 (-1.63, 2.69)	0.76 (-0.67, 2.20)	0.69 (-0.28, 1.67)
Q4	3.11 (0.85, 5.37)**	0.84 (-1.52, 3.20)	1.96 (0.42, 3.49)	0.50 (-0.50, 1.49)
p for trend	0.0091	0.7183	0.0760	0.4984

HGS, handgrip strength; NAFLD, non-alcoholic fatty liver disease.

Beta coefficient with 95% confidence interval were shown. <sup>1)</sup>Model I: adjusted for age, <sup>2)</sup>Model II: Model I + education + household income + waist circumference + physical activity. For NAFLD men, first quartile (Q1): HGS < 1.19, second quartile (Q2): 1.19 ≤ HGS < 1.40, third quartile (Q3): 1.40 ≤ HGS < 1.61, and fourth quartile (Q4): 1.61 ≤ HGS. For NAFLD women, Q1: HGS < 0.65, Q2: 0.65 ≤ HGS < 0.78, Q3: 0.78 ≤ HGS < 0.93, and Q4: 0.93 ≤ HGS. For non-NAFLD men, first quartile (Q1): HGS < 1.34, second quartile (Q2): 1.34 ≤ HGS < 1.56, third quartile (Q3): 1.56 ≤ HGS < 1.80, and fourth quartile (Q4): 1.80 ≤ HGS. For non-NAFLD women, Q1: HGS < 0.82, Q2: 0.82 ≤ HGS < 0.98, Q3: 0.98 ≤ HGS < 1.15, and Q4: 1.15 ≤ HGS. <sup>3)</sup>The lowest quartiles within same sex was used as a reference group. \*p < 0.05, \*\*p < 0.01 compared to reference group (Q1) within same sex.

**Table 5.** Estimated change of fat intake according to the quartile of HGS

Variables	NAFLD		Non-NAFLD	
	Men (n = 1,293)	Women (n = 1,401)	Men (n = 3,616)	Women (n = 6,159)
Model I <sup>1)</sup>				
Q1	Ref <sup>3)</sup>	Ref	Ref	Ref
Q2	-0.14 (-1.64, 1.37)	0.13 (-1.38, 1.64)	0.09 (-0.34, 1.38)	-0.25 (-1.00, 0.50)
Q3	0.76 (-0.86, 2.38)	-0.29 (-1.81, 1.24)	0.43 (-0.52, 1.38)	-1.10 (-1.86, -0.34)**
Q4	-1.49 (-2.93, -0.04)*	-1.72 (-3.50, 0.07)	-0.29 (-1.18, 0.60)	-1.07 (-1.82, -0.33)**
p for trend	0.0264	0.1759	0.5176	0.0063
Model II <sup>2)</sup>				
Q1	Ref	Ref	Ref	Ref
Q2	-0.32 (-1.84, 1.19)	0.50 (-1.01, 2.00)	-0.09 (-0.94, 0.75)	-0.14 (-0.90, 0.62)
Q3	0.33 (-1.27, 1.93)	0.44 (-1.09, 1.98)	0.25 (-0.72, 1.22)	-0.83 (-1.62, -0.04)
Q4	-1.58 (-3.16, -0.01)	-0.38 (-2.44, 2.05)	-0.32 (-1.27, 0.63)	-0.32 (-1.10, 0.47)
p for trend	0.0769	0.7126	0.6933	0.1595

HGS, handgrip strength; NAFLD, non-alcoholic fatty liver disease.

Beta coefficient with 95% confidence interval were shown. <sup>1)</sup>Model I: adjusted for age, <sup>2)</sup>Model II: Model I + education + household income + waist circumference + physical activity. For NAFLD men, first quartile (Q1): HGS < 1.19, second quartile (Q2): 1.19 ≤ HGS < 1.40, third quartile (Q3): 1.40 ≤ HGS < 1.61, and fourth quartile (Q4): 1.61 ≤ HGS. For NAFLD women, Q1: HGS < 0.65, Q2: 0.65 ≤ HGS < 0.78, Q3: 0.78 ≤ HGS < 0.93, and Q4: 0.93 ≤ HGS. For non-NAFLD men, first quartile (Q1): HGS < 1.34, second quartile (Q2): 1.34 ≤ HGS < 1.56, third quartile (Q3): 1.56 ≤ HGS < 1.80, and fourth quartile (Q4): 1.80 ≤ HGS. For non-NAFLD women, Q1: HGS < 0.82, Q2: 0.82 ≤ HGS < 0.98, Q3: 0.98 ≤ HGS < 1.15, and Q4: 1.15 ≤ HGS. <sup>3)</sup>The lowest quartiles within same sex was used as a reference group. \*p < 0.05, \*\*p < 0.01 compared to reference group (Q1) within same sex.

**Table 6.** Estimated change of protein intake according to the quartile of HGS

Variables	NAFLD		Non-NAFLD	
	Men (n = 1,293)	Women (n = 1,401)	Men (n = 3,616)	Women (n = 6,159)
Model I <sup>1)</sup>				
Q1	Ref <sup>3)</sup>	Ref	Ref	Ref
Q2	0.04 (-0.76, 0.84)	-0.07 (-0.88, 0.74)	0.15 (-0.44, 0.74)	-0.14 (-0.48, 0.20)
Q3	0.18 (-0.58, 0.95)	-0.70 (-1.39, 0.00)*	-0.19 (-0.67, 0.28)	-0.24 (-0.58, 0.10)
Q4	-0.36 (-1.15, 0.43)	-1.10 (-1.79, -0.41)**	-0.52 (-0.99, -0.05)	-0.49 (-0.87, -0.11)
p for trend	0.6375	0.0021	0.0391	0.0907
Model II <sup>2)</sup>				
Q1	Ref	Ref	Ref	Ref
Q2	-0.06 (-0.83, 0.72)	0.06 (-0.75, 0.86)	0.05 (-0.54, 0.65)	-0.07 (-0.41, 0.26)
Q3	0.00 (-0.78, 0.78)	-0.50 (-1.23, 0.23)	-0.32 (-0.81, 0.17)	-0.13 (-0.47, 0.21)
Q4	-0.67 (-1.53, -0.19)	-0.73 (-1.48, 0.02)	-0.62 (-1.11, -0.13)	-0.17 (-0.56, 0.21)
p for trend	0.3761	0.0878	0.0295	0.8294

HGS, handgrip strength; NAFLD, non-alcoholic fatty liver disease.

Beta coefficient with 95% confidence interval were shown. <sup>1)</sup>Model I: adjusted for age, <sup>2)</sup>Model II: Model I + education + household income + waist circumference + physical activity. For NAFLD men, first quartile (Q1): HGS < 1.19, second quartile (Q2): 1.19 ≤ HGS < 1.40, third quartile (Q3): 1.40 ≤ HGS < 1.61, and fourth quartile (Q4): 1.61 ≤ HGS. For NAFLD women, Q1: HGS < 0.65, Q2: 0.65 ≤ HGS < 0.78, Q3: 0.78 ≤ HGS < 0.93, and Q4: 0.93 ≤ HGS. For non-NAFLD men, first quartile (Q1): HGS < 1.34, second quartile (Q2): 1.34 ≤ HGS < 1.56, third quartile (Q3): 1.56 ≤ HGS < 1.80, and fourth quartile (Q4): 1.80 ≤ HGS. For non-NAFLD women, Q1: HGS < 0.82, Q2: 0.82 ≤ HGS < 0.98, Q3: 0.98 ≤ HGS < 1.15, and Q4: 1.15 ≤ HGS. <sup>3)</sup>The lowest quartiles within same sex was used as a reference group. \*p < 0.05, \*\*p < 0.01 compared to reference group (Q1) within same sex.

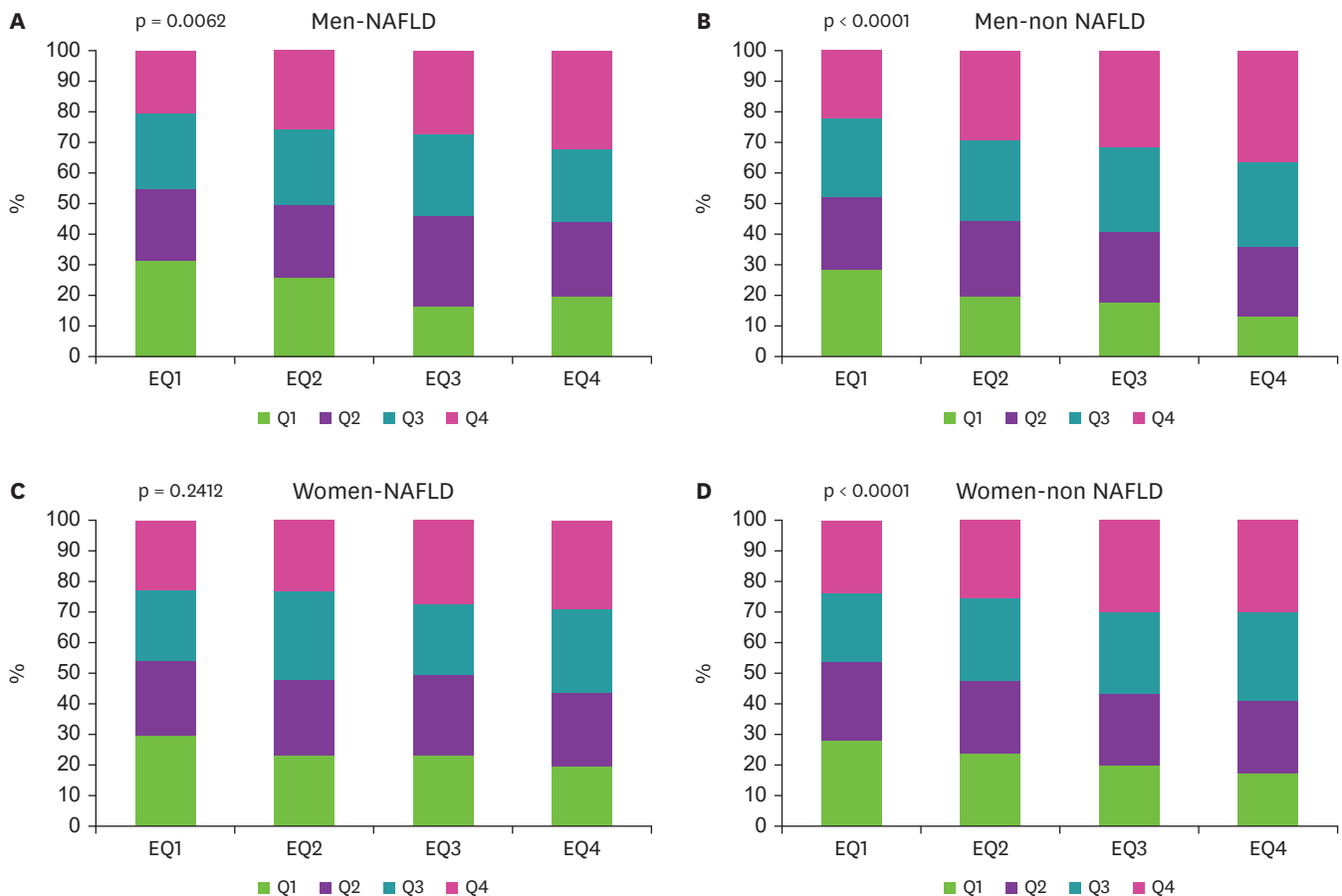
negative association between carbohydrate intake and HGS and fat intake and HGS was observed only in men, and the association remained after education level, household income, WC and physical activity were adjusted. Protein intake was associated with HGS only in women with NAFLD (p = 0.0021), but the significance disappeared after the addition of education level, household income, WC and physical activity to the regression model. No significant association was found in men with NAFLD. In participants without NAFLD, protein levels were not significantly associated with HGS in either men or women (Table 6).

### Relative risk of low muscle strength according to energy intake in NAFLD

Because the quartile of HGS was associated with the change in total energy intake in both men and women, we further examined the risk of weak HGS, as predicted by the quartile level of total energy intake. When energy intake and HGS were stratified by quartiles, energy intake showed a strong positive relationship with HGS in men and women without



NAFLD ( $p < 0.0001$ ; **Fig. 2**). In patients with NAFLD, the association was significant only in men ( $p = 0.0062$ ), and the trends of the association was not significant in women (**Fig. 2**). **Table 7** shows the odds ratio for the risk of falling in the lowest quartile of HGS in men and women based on the quartile scale of total energy intake. A higher total energy intake was associated with a lower risk of weak muscle strength (Q1) only in men with NAFLD (odds ratio [OR] for the lowest quartile, 0.56; 95% CI, 0.41–0.78;  $p$  for trend = 0.0036). Age and other covariates were further adjusted in the model, and the association between the total energy intake and the prevalence of falling in the weakest HGS quartile with low energy intake was still significant in men (OR for the highest quartile, 0.58; 95% CI, 0.42–0.81;  $p$  for trend = 0.0160). No association was observed between the quartile scale of energy intake and the risk of weak HGS in women with NAFLD (**Table 7**). The association between the total energy intake and the risk of weak HGS was significant at all levels of energy intake in men and women without NAFLD, with OR for the highest quartile, 0.47 (95% CI, 0.38–0.58;  $p < 0.0001$ ) and 0.62 (95% CI, 0.53–0.72;  $p < 0.0001$ ), respectively, and the significance of the association remained after adjusting for other covariates (**Table 7**).



**Fig. 2. Prevalence of low muscle strength according to energy intake in healthy participants and patients with NAFLD.** Energy intake and HGS was stratified by quartile scale and analyzed their association. The energy intake showed a strong negative relationship with HGS in men with NAFLD and men and women without NAFLD. NAFLD, non-alcoholic fatty liver disease; HGS, handgrip strength.

**Table 7.** Adjusted ORs with 95% CIs of low muscle function by quartile of total energy intake

Variables	NAFLD		Non-NAFLD	
	Men (n = 1,293)	Women (n = 1,401)	Men (n = 3,616)	Women (n = 6,159)
<b>Model I<sup>1)</sup></b>				
EQ1	1.00	1.00	1.00	1.00
EQ2	0.80 (0.54, 1.06)	0.81 (0.61, 1.07)	0.67 (0.56, 0.81)	0.82 (0.70, 0.96)
EQ3	0.61 (0.44, 0.85)	0.78 (0.57, 1.06)	0.59 (0.48, 0.72)	0.66 (0.57, 0.77)**
EQ4	0.56 (0.41, 0.78)*	0.65 (0.47, 0.88)	0.47 (0.38, 0.58)***	0.62 (0.53, 0.72)***
p for trend	0.0036	0.0519	< 0.0001	< 0.0001
<b>Model II<sup>2)</sup></b>				
EQ1	1.00	1.00	1.00	1.00
EQ2	0.78 (0.55, 1.08)	0.82 (0.62, 1.10)	0.71 (0.59, 0.86)	0.84 (0.72, 0.98)
EQ3	0.62 (0.44, 0.87)	0.79 (0.58, 1.07)	0.68 (0.55, 0.83)	0.72 (0.62, 0.83)**
EQ4	0.58 (0.42, 0.81)*	0.77 (0.56, 1.06)	0.60 (0.49, 0.74)**	0.76 (0.65, 0.89)
p for trend	< 0.0001	0.3399	< 0.0001	< 0.0001
<b>Model III<sup>3)</sup></b>				
EQ1	1.00	1.00	1.00	1.00
EQ2	0.87 (0.62, 1.23)	0.87 (0.65, 1.18)	0.72 (0.59, 0.88)	0.90 (0.77, 1.06)
EQ3	0.73 (0.52, 1.03)	0.94 (0.68, 1.30)	0.68 (0.55, 0.84)	0.80 (0.69, 0.93)
EQ4	0.60 (0.43, 0.83)**	0.87 (0.63, 1.21)	0.60 (0.49, 0.75)**	0.80 (0.68, 0.94)
p for trend	0.0160	0.7780	< 0.0001	0.0080

OR, odds ratio; CI, confidence interval; NAFLD, non-alcoholic fatty liver disease.

OR with 95% CI were shown. <sup>1)</sup>Model I: no adjustment, <sup>2)</sup>Model II: adjusted for age, <sup>3)</sup>Model III: Model I + education + household income + waist circumference + physical activity. Total energy intake was categorized into quartile scale; for NAFLD men, first quartile (EQ1): total energy intake < 1,662.2 kcal, second quartile (EQ2): 1,662.2 kcal ≤ total energy intake < 2,180.3 kcal, third quartile (EQ3): 2,180.3 kcal ≤ total energy intake < 2,741.3 kcal, fourth quartile (EQ4): 2,741.3 kcal ≤ total energy intake, for women, EQ1: total energy intake < 1,187.8 kcal, EQ2: 1,187.8 kcal ≤ total energy intake < 1,532.7 kcal, EQ3: 1,532.7 kcal ≤ total energy intake < 2,009.5 kcal, EQ4: 2,009.5 kcal ≤ total energy intake, for non-NAFLD men, first quartile (EQ1): total energy intake < 1,638.6 kcal, second quartile (EQ2): 1,638.6 kcal ≤ total energy intake < 2,115.0 kcal, third quartile (EQ3): 2,115.0 kcal ≤ total energy intake < 2,700.6 kcal, fourth quartile (EQ4): 2,700.6 kcal ≤ total energy intake, for non-NAFLD women, EQ1: total energy intake < 1,235.7 kcal, EQ2: 1,235.7 kcal ≤ total energy intake < 1,601.9 kcal, EQ3: 1,601.9 kcal ≤ total energy intake < 2,051.7 kcal, EQ4: 2,051.7 kcal ≤ total energy intake.

\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001 compared to reference group of total energy intake (EQ1) within same sex or total subjects.

## DISCUSSION

In this study, energy intake was associated with increased HGS in healthy individuals who did not have NAFLD, the reference group that we used. Total energy intake and major nutrient intake had a weak or no linear relationship with muscle strength in patients with NAFLD, while a significant linear relationship existed in healthy individuals. In the logistic regression model, after adjusting for age and other covariates, energy intake was positively associated with HGS in patients with NAFLD. In addition, trends of a higher prevalence of weak muscle strength due to low energy intake in patients with NAFLD were more pronounced in men.

Previous epidemiological and intervention studies have reported a relationship between nutrient intakes and muscle mass and strength [12-14,16,17]. These studies have investigated the effects of single nutrients mainly proteins and other micronutrients, on muscle parameters. However, these studies could not monitor the whole diet of their participants and yielded inconclusive results [27,28]. Total energy intake, which may reflect the overall food intake status, has been shown to a strong relationship with muscle mass and strength [8,16,17]. For example, decreased energy intake is related to the risk of malnutrition or undernutrition, which has been reported to be strongly associated with low walk speed and low HGS [16]. In the current study, only total energy intake showed a significant linear relationship with HGS in patients with NAFLD. No individual macronutrients were found to be associated with HGS. Carbohydrate and fat intake showed a linear relationship but this association was not reproduced in the analysis based on the category of intake amount. Protein intake was not associated with HGS in patients with NAFLD in this study. Although the benefit of adequate protein intake has received considerable attention owing to its ability

to stimulate skeletal protein synthesis and contribute to muscle integrity [29,30], studies on protein intake and frailty have revealed conflicting results. Several studies have reported inverse associations between protein intake (adjusted for energy intake) and frailty [13,31], whereas some other studies, no such association was found [12]. In line with our findings, studies suggest that higher energy intake, but not protein intake specifically, is associated with less frailty, as assessed by muscle weakness, slowness, and fatigue [13,32]. In addition, inadequate energy intake rather than low protein intake was associated with sarcopenia in Japanese patients with diabetes aged 65 years and older [17]. The link between low energy intake and low muscle strength can be explained by the relationship between energy intake and muscle metabolism; energy restriction causes the breakdown of muscle protein to compensate for the deficit of energy consumption [33]. In this study, the range of protein intake of the participants was 15–25% and nearly met the recommended level or the level that was previously proven to be beneficial to health. Clinical trials have shown that protein intake has a beneficial effect on the course of NAFLD and attenuates NASH development [34]. A study which investigated overweight adults reported that moderate protein intake of up to 25% of the total calories had a positive influence on weight loss and insulin sensitivity [35]. Hence, the nutritional intake of NAFLD should be adequate and adjusted to maintain optimal metabolism. Guidelines published by American Association for the Study of Liver Diseases recommended low-energy intake for NAFLD, partially for weight-loss [23]. However, based on the previous and current findings of a higher prevalence of low muscle mass and strength in NAFLD, practicing low energy intake for patients with NAFLD should be cautiously approached and the risks due to an energy-restricted diet among NAFLD should be recognized.

The results of this study showed that the association between energy intake and HGS was significant only in men. Based on the results of this study, women tended to consume a higher percentage of energy from carbohydrates than men who had consumed carbohydrates within the acceptable macronutrient distribution ranges of the Dietary Reference Intakes for Koreans [36]. The tendency toward a high carbohydrate intake ratio rather than a balanced low-calorie diet may shadow the effect of energy intake or a certain diet on health outcomes, including HGS. In addition, the gender-specific findings of this study are in line with the data of our previous study, which revealed that the association between skeletal muscle mass and total energy intake in men was more pronounced than that in women [8]. In addition, studies on Chinese and Korean populations revealed that the beneficial effects of a Mediterranean diet or vegetable-oriented diet on skeletal muscle mass were more favorable in men than in women [37,38].

In this study we measured the HGS as a functional indicator of muscle strength. Grip strength measurement is a quick test and a well validated tool to predict frailty as a surrogate measure of body strength. The recently updated guidelines from the European Working Group on Sarcopenia in Older People suggested muscle strength as the key characteristic of sarcopenia and the main parameter for its diagnosis [19]. In addition, nutritional status including nutritional screening, commonly involves the measurement of muscle quality in patients with NAFLD as well as healthy individuals. Weak muscle strength predicted fracture, falling, cardiovascular disease, and all-cause mortality more precisely than low skeletal mass [21]. In the current study, muscle strength was inversely associated with the prevalence of NAFLD regardless of age. Such an inverse relationship between HGS and BMI observed in this study seems paradoxical because BMI, in many cases of nutritional epidemiology, reflects long-term energy intake. However, BMI seems to be a poor indicator of muscle

strength, probably because it does not reflect body composition. This aspect is particularly relevant to this study because the age distribution of the participants was skewed to 50 years and older; these age groups typically experience declines in both height and muscle mass that occur with age [12,13,16]. Although older age was significantly related to low muscle strength and function, adjustment for age could not modulate the association between HGS and energy intake in this study. This finding can be explained in part by age-related changes in metabolic, hormonal, and inflammatory factors that affect muscle loss, leading to anabolic resistance and loss of muscle mass [3,29].

Our study had several limitations. Because of the cross-sectional nature of the current study, causality between energy intake and HGS in patients with NAFLD could not be determined. In addition, the data of patients with NAFLD from a nationwide survey could be different from the phenomena observed in a clinical setting, and a single 24-h dietary recall may not support an estimate of a long-term habitual diet. With the current KNHANES data, we could not confirm whether the association between energy intake and HGS in both patients with NAFLD and healthy individuals is independent of muscle mass; the KNHANES data used in this study only provided HGS without information on skeletal muscle mass. Nevertheless, accumulating evidence [2,19] suggests that alterations in muscle strength are correlated with changes in muscle strength and function. Taken together with our recent study, changes in skeletal muscle may mediate the association between total energy intake and muscle strength. Finally, energy requirement based on the daily physical activity level of participants should have been incorporated into the estimation of total energy intake in this study. Although physical activity level through exercise was incorporated in both linear and logistic regression models in this study, information regarding the daily physical activity of study participants was limited to the KNHANES data. Hence, the data from this nation-wide survey need to be further validated with a study investigating participants' physical activity in detail and a longitudinal prospective study in the future.

## SUMMARY

We demonstrated an association between energy intake and HGS in Korean patients with NAFLD from a nationwide survey of the Korean population. As in healthy non-NAFLD participants, low energy intake was significantly associated with an increased prevalence of weak muscle strength in patients with NAFLD, independent of age and other covariates, and this association was more prominent in men than in women. This finding needs to be confirmed by further investigations using prospective design to assess the possible causal relationship between energy intake and muscle strength in NAFLD. In addition, nutritional assessment and intervention for patients with NAFLD need to be considered multilaterally, especially for individuals who are lean or experience muscle loss.

## SUPPLEMENTARY MATERIALS

### Supplementary Table 1

Characteristics of participants without non-alcoholic fatty liver disease according to the quartile of HGS

[Click here to view](#)

## Supplementary Table 2

Characteristics of non-alcoholic fatty liver disease patients according to the quartile of HGS

[Click here to view](#)

## REFERENCES

1. Doherty TJ. Invited review: aging and sarcopenia. *J Appl Physiol* (1985) 2003; 95(4): 1717-1727.  
[PUBMED](#) | [CROSSREF](#)
2. Lang T, Streeter T, Cawthon P, Baldwin K, Taaffe DR, Harris TB. Sarcopenia: etiology, clinical consequences, intervention, and assessment. *Osteoporos Int* 2010; 21(4): 543-559.  
[PUBMED](#) | [CROSSREF](#)
3. Lee CG, Boyko EJ, Strotmeyer ES, Lewis CE, Cawthon PM, Hoffman AR, et al. Association between insulin resistance and lean mass loss and fat mass gain in older men without diabetes mellitus. *J Am Geriatr Soc* 2011; 59(7): 1217-1224.  
[PUBMED](#) | [CROSSREF](#)
4. Blundell JE, Caudwell P, Gibbons C, Hopkins M, Näslund E, King NA, et al. Body composition and appetite: fat-free mass (but not fat mass or BMI) is positively associated with self-determined meal size and daily energy intake in humans. *Br J Nutr* 2012; 107(3): 445-449.  
[PUBMED](#) | [CROSSREF](#)
5. Johnston CS, Sears B, Perry M, Knurick JR. Use of novel high-protein functional food products as part of a calorie-restricted diet to reduce insulin resistance and increase lean body mass in adults: a randomized controlled trial. *Nutrients* 2017; 9(11): 1182.  
[PUBMED](#) | [CROSSREF](#)
6. Hopkins M, Finlayson G, Duarte C, Whybrow S, Ritz P, Horgan GW, et al. Modelling the associations between fat-free mass, resting metabolic rate and energy intake in the context of total energy balance. *Int J Obes* 2016; 40(2): 312-318.  
[PUBMED](#) | [CROSSREF](#)
7. Tinker LF, Sarto GE, Howard BV, Huang Y, Neuhauser ML, Mossavar-Rahmani Y, et al. Biomarker-calibrated dietary energy and protein intake associations with diabetes risk among postmenopausal women from the Women's Health Initiative. *Am J Clin Nutr* 2011; 94(6): 1600-1606.  
[PUBMED](#) | [CROSSREF](#)
8. Jang BY, Bu SY. Total energy intake according to the level of skeletal muscle mass in Korean adults aged 30 years and older: an analysis of the Korean National Health and Nutrition Examination Surveys (KNHANES) 2008–2011. *Nutr Res Pract* 2018; 12(3): 222-232.  
[PUBMED](#) | [CROSSREF](#)
9. Lee YH, Kim SU, Song K, Park JY, Kim DY, Ahn SH, et al. Sarcopenia is associated with significant liver fibrosis independently of obesity and insulin resistance in nonalcoholic fatty liver disease: nationwide surveys (KNHANES 2008-2011). *Hepatology* 2016; 63(3): 776-786.  
[PUBMED](#) | [CROSSREF](#)
10. Lee SB, Kwon YJ, Jung DH, Kim JK. Association of muscle strength with non-alcoholic fatty liver disease in Korean adults. *Int J Environ Res Public Health* 2022; 19(3): 1675.  
[PUBMED](#) | [CROSSREF](#)
11. Park SH, Kim DJ, Plank LD. Association of grip strength with non-alcoholic fatty liver disease: investigation of the roles of insulin resistance and inflammation as mediators. *Eur J Clin Nutr* 2020; 74(10): 1401-1409.  
[PUBMED](#) | [CROSSREF](#)
12. Bollwein J, Diekmann R, Kaiser MJ, Bauer JM, Uter W, Sieber CC, Volkert D. Distribution but not amount of protein intake is associated with frailty: a cross-sectional investigation in the region of Nurnberg. *Nutr J* 2013; 12: 109.  
[PUBMED](#) | [CROSSREF](#)
13. Rahi B, Colombet Z, Gonzalez-Colaço Harmand M, Dartigues JF, Boirie Y, Letenneur L, et al. Higher protein but not energy intake is associated with a lower prevalence of frailty among community-dwelling older adults in the French three-city cohort. *J Am Med Dir Assoc* 2016; 17(7): 672.e7-672.e11.  
[PUBMED](#) | [CROSSREF](#)
14. Talegawkar SA, Bandinelli S, Bandeen-Roche K, Chen P, Milanesechi Y, Tanaka T, et al. A higher adherence to a Mediterranean-style diet is inversely associated with the development of frailty in community-dwelling elderly men and women. *J Nutr* 2012; 142(12): 2161-2166.  
[PUBMED](#) | [CROSSREF](#)

15. Vranešić Bender D, Nutrizio M, Jošić M, Ljubas Kelečić D, Karas I, Premužić M, et al. Nutritional status and nutrition quality in patients with non-alcoholic fatty liver disease. *Acta Clin Croat* 2017; 56(4): 625-634.  
[PUBMED](#) | [CROSSREF](#)
16. Mendes J, Afonso C, Moreira P, Padrão P, Santos A, Borges N, et al. Association of anthropometric and nutrition status indicators with hand grip strength and gait speed in older adults. *JPEN J Parenter Enteral Nutr* 2019; 43(3): 347-356.  
[PUBMED](#) | [CROSSREF](#)
17. Okamura T, Miki A, Hashimoto Y, Kaji A, Sakai R, Osaka T, et al. Shortage of energy intake rather than protein intake is associated with sarcopenia in elderly patients with type 2 diabetes: a cross-sectional study of the KAMOGAWA-DM cohort. *J Diabetes* 2019; 11(6): 477-483.  
[PUBMED](#) | [CROSSREF](#)
18. Newman AB, Kupelian V, Visser M, Simonsick EM, Goodpaster BH, Kritchevsky SB, et al. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. *J Gerontol A Biol Sci Med Sci* 2006; 61(1): 72-77.  
[PUBMED](#) | [CROSSREF](#)
19. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019; 48(1): 16-31.  
[PUBMED](#) | [CROSSREF](#)
20. Ji C, Zheng L, Zhang R, Wu Q, Zhao Y. Handgrip strength is positively related to blood pressure and hypertension risk: results from the National Health and nutrition examination survey. *Lipids Health Dis* 2018; 17(1): 86.  
[PUBMED](#) | [CROSSREF](#)
21. Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A Jr, Orlandini A, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet* 2015; 386(9990): 266-273.  
[PUBMED](#) | [CROSSREF](#)
22. Nascimento DD, Prestes J, de Sousa Diniz J, Beal PR, Alves VP, Stone W, et al. Comparison of field- and laboratory-based estimates of muscle quality index between octogenarians and young older adults: an observational study. *J Exerc Rehabil* 2020; 16(5): 458-466.  
[PUBMED](#) | [CROSSREF](#)
23. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology* 2018; 67(1): 328-357.  
[PUBMED](#) | [CROSSREF](#)
24. Korea Disease Control and Prevention Agency. Analysis guideline for the seventh Korea National Health and Nutrition Examination Survey (2016–2018). Cheongju: Korea Disease Control and Prevention Agency; 2021.
25. Lee JH, Kim D, Kim HJ, Lee CH, Yang JI, Kim W, et al. Hepatic steatosis index: a simple screening tool reflecting nonalcoholic fatty liver disease. *Dig Liver Dis* 2010; 42(7): 503-508.  
[PUBMED](#) | [CROSSREF](#)
26. Rural Development Administration. 9th revision Korean food composition table. Jeonju: Rural Development Administration; 2016.
27. Paddon-Jones D, Leidy H. Dietary protein and muscle in older persons. *Curr Opin Clin Nutr Metab Care* 2014; 17(1): 5-11.  
[PUBMED](#) | [CROSSREF](#)
28. Mithal A, Bonjour JP, Boonen S, Burckhardt P, Degens H, El Hajj Fuleihan G, et al. Impact of nutrition on muscle mass, strength, and performance in older adults. *Osteoporos Int* 2013; 24(5): 1555-1566.  
[PUBMED](#) | [CROSSREF](#)
29. Beasley JM, Shikany JM, Thomson CA. The role of dietary protein intake in the prevention of sarcopenia of aging. *Nutr Clin Pract* 2013; 28(6): 684-690.  
[PUBMED](#) | [CROSSREF](#)
30. Cermak NM, Res PT, de Groot LC, Saris WH, van Loon LJ. Protein supplementation augments the adaptive response of skeletal muscle to resistance-type exercise training: a meta-analysis. *Am J Clin Nutr* 2012; 96(6): 1454-1464.  
[PUBMED](#) | [CROSSREF](#)
31. Kobayashi S, Asakura K, Suga H, Sasaki S; Three-generation Study of Women on Diets and Health Study Group. High protein intake is associated with low prevalence of frailty among old Japanese women: a multicenter cross-sectional study. *Nutr J* 2013; 12(1): 164.  
[PUBMED](#) | [CROSSREF](#)



32. Schoufour JD, Franco OH, Kieffe-de Jong JC, Trajanoska K, Stricker B, Brusselle G, et al. The association between dietary protein intake, energy intake and physical frailty: results from the Rotterdam Study. *Br J Nutr* 2019; 121(4): 393-401.  
[PUBMED](#) | [CROSSREF](#)
33. Newman AB, Lee JS, Visser M, Goodpaster BH, Kritchevsky SB, Tylavsky FA, et al. Weight change and the conservation of lean mass in old age: the Health, Aging and Body Composition Study. *Am J Clin Nutr* 2005; 82(4): 872-878.  
[PUBMED](#) | [CROSSREF](#)
34. Tricò D, Biancalana E, Solini A. Protein and amino acids in nonalcoholic fatty liver disease. *Curr Opin Clin Nutr Metab Care* 2021; 24(1): 96-101.  
[PUBMED](#) | [CROSSREF](#)
35. Arciero PJ, Gentile CL, Pressman R, Everett M, Ormsbee MJ, Martin J, et al. Moderate protein intake improves total and regional body composition and insulin sensitivity in overweight adults. *Metabolism* 2008; 57(6): 757-765.  
[PUBMED](#) | [CROSSREF](#)
36. The Korean Nutrition Society. Dietary reference intakes for Koreans. Seoul: The Korean Nutrition Society; 2020.
37. Jang BY, Bu SY. A vegetable and fish dietary pattern is positively associated with skeletal muscle mass in Korean men. *Clin Nutr Res* 2019; 8(1): 1-16.  
[PUBMED](#) | [CROSSREF](#)
38. Tian HY, Qiu R, Jing LP, Chen ZY, Chen GD, Chen YM. Alternate Mediterranean diet score is positively associated with skeletal muscle mass index in middle-aged adults. *Br J Nutr* 2017; 117(8): 1181-1188.  
[PUBMED](#) | [CROSSREF](#)