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Dietary patterns and risk of non-alcoholic fatty liver disease in Korean adults: a prospective cohort study

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ABSTRACT

Objectives Dietary patterns can holistically provide insights into the association of food groups and nutrients with the disease. Several studies have evaluated the association of dietary patterns with the risk of non-alcoholic fatty liver disease (NAFLD) in Western populations. However, few studies focused on this topic were conducted on Korean adults. Therefore, in this cohort study, we aimed to investigate the association between dietary patterns and the risk of NAFLD among middle-aged Koreans.

Design The survey was performed at general hospitals and health examination centres in Korea. Dietary intake was assessed using a validated Food Frequency Questionnaire. The dietary patterns were identified using principal component analysis. The HR and 95% CI for NAFLD for each of the quartiles of the three dietary patterns were estimated using a Cox proportional hazards model.

Setting South Korean Community.

Participants 44 460 healthy Koreans (aged 40–69 years) who completed a follow-up survey from 2012 to 2016 in the Health Examinees study were included.

Results Men and women following a prudent pattern showed a 22% and 36% lower NAFLD risk, respectively (men: HR=0.78; women: HR=0.64). Men and women who highly adhered to the flour-based food and meat pattern had a 29% and 55% higher NAFLD risk, respectively (men: HR=1.29; women: HR=1.55).

Conclusion The prudent pattern induced a lower NAFLD risk, whereas the flour-based food and meat pattern induced a higher NAFLD risk. No significant difference was found between the white rice pattern and NAFLD risk.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study used a large prospective database in which reproducibility and validity have been evaluated.
- ⇒ This study considered the effect of cardiometabolic risk factors on non-alcoholic fatty liver disease (NAFLD) risk.
- ⇒ This nature of the factor analysis will cause bias, because the interpretation of the meaning and the number of factors is subjective.
- ⇒ The diagnosis method of NAFLD is not the gold-standard liver biopsies, but the method we used was regarded as an accurate and low-cost method for predicting NAFLD risk.
- ⇒ The median year of follow-up duration is 4.2 years might be too short for enabling the development of NAFLD.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a common chronic progressive liver disease characterised by excessive accumulation (at least 5%–10% of liver weight) of lipids, such as fatty acids, triacylglycerols and cholesterol esters, in the liver (steatosis); hepatocellular damage; or variable liver fibrosis (non-alcoholic steatohepatitis). Non-alcoholic steatohepatitis can lead to cirrhosis.[1 2] Meta-analyses have shown that the worldwide prevalence of NAFLD, regardless of the diagnostic method used, is approximately 30%. In recent years, the prevalence rate of NAFLD in Asia has become similar to those reported in Western countries, suggesting serious outcomes of this pandemic in Asian countries.[3 4] Park *et al* investigated a large number of epidemiological studies (85 studies, 65 of which had an ultrasound-based NAFLD diagnosis) in Korea; owing to the highly organised and efficient health screening programme,[5] the prevalence rate of NAFLD was 31.46%.[6] However, no reliable or effective treatment for NAFLD has been established yet. Thus, prevention should be prioritised because NAFLD affects individuals of all ages.[7] Although some treatment methods have been used in clinical trials, their effectiveness remains unclear.[8] Currently, no effective therapeutic drugs have been proven for NAFLD treatment.[9]

Farrell *et al* concluded that NAFLD is a lifestyle-related disease resulting from overnutrition,[10] which is a nutritional disorder caused by overeating and chronic intake of high saturated fat and fructose combined with a lack of physical activity.[11] In recent years, numerous reviews have suggested that dietary modification may inhibit NAFLD by modulating insulin resistance and oxidative stress.[12] The association of individual food or nutrient with NAFLD risk has been investigated.[13 14] Dietary patterns can provide insights into the association of food groups and nutrients with the disease. Although many studies have examined the relationship between dietary patterns and NAFLD risk, most have analysed Western populations.[15 16] Few cohort studies have been performed on the Korean population, the majority of which are observational and case–control studies.[17 18] Therefore, this study aimed to investigate the association between dietary patterns which were conducted by Korean adults and the risk of NAFLD for 4.2-year follow-up.

METHODS

Patient and public involvement

Patients and public were not involved in the design of the study.

Study design and study population

This cohort study was based on the Health Examinees study, a large-scale prospective community-based study on the Korean population. It was conducted between 2004 and 2013 at 38 general hospitals and health examination centres in 8 regions of Korea, and the baseline survey included 169 730 adults aged 40–69 years. Among them, 64 659 completed the follow-up survey from 2012 to 2016. We excluded participants (1) without a record of biomarker measurements or Food Frequency Questionnaire (FFQ) results (n=5642); (2) with fatty liver disease (acute liver disease, chronic hepatitis, cirrhosis, cholelithiasis, cholecystitis) or thyroid disease at baseline (n=7131); (3) with a history of the fatty liver-related disease (n=3663); (4) without records of height or weight (n=121); with an implausible total energy intake (men: <800 or ≥4000 kcal/day; women: <500 or ≥3500 kcal/day) (n=1302)[19]; and (5) with a high alcohol intake (men: >210 g/week; women: >140 g/week) (n=2371).[20] Finally, 11 868 men (mean age, 56 years) and 32 592 women (mean age, 52 years) were included (online supplemental figure S1).

Dietary assessment

Dietary intake at baseline was measured at baseline using a semiquantitative 106-item FFQ. Reproducibility and validity of the FFQ have been evaluated in the previous study by 12-day dietary records.[21] Participants reported their average consumption for each food item over the past year. The frequency of average food intake ranged from 'never or seldom' to 'three times or more every day' and was classified into nine categories. Nutrient intake was calculated by linking the consumption frequency and serving size of each food item to the Korean food composition tables.[22] The 106 food items in the FFQ were aggregated into 22 food groups (online supplemental table S1).

Dietary pattern identification

Dietary patterns were derived from a principal component analysis, and varimax rotation was used across the population for greater interpretability. As shown in the scree plots (online supplemental figures S2 and S3), three factors with eigenvalues>1.5 were retained.[23] Each food group with an absolute factor loading≥0.2 was considered as a significant contributor to the corresponding factor. Factor scores were divided into quartiles, wherein Q1 and Q4 were regarded as the lowest and highest factor scores, respectively. Higher factor scores indicated better adherence to the dietary pattern. According to the characteristics of high factor loading for each factor, the dietary patterns were classified into prudent, flour-based food and meat, and white rice (table 1). The cumulative explained variance of the intake was 32.55% in men and 32.72% in women. The adequacy of the sample was assessed using the Kaiser-Meyer-Olkin test, and acceptable values were obtained (men: 0.77; women: 0.80).

NAFLD assessment

The fatty liver index (FLI), which included the triglyceride (TG) level, body mass index (BMI), gamma-glutamyl transferase (GGT) level and waist circumference (WC), was used to identify patients with NAFLD. The following formula was used to calculate FLI,[24 25] where an FLI of ≥60 was used to diagnose NAFLD:

$$FLI = \frac{e^{\left[\begin{array}{l}0.953\times\ln\left(TG\left[mg/dL\right]\right)+0.139\times BMI\left[kg/m^2\right]+\\0.718\times\ln\left(GGT\left[U/L\right]\right)+0.053\times WC\left[cm\right]-15.745\end{array}\right]}}{1+e^{\left[\begin{array}{l}0.953\times\ln\left(TG\left[mg/dL\right]\right)+0.139\times BMI\left[kg/m^2\right]+\\0.718\times\ln\left(GGT\left[U/L\right]\right)+0.053\times WC\left[cm\right]-15.745\end{array}\right]}}\times 100 \quad (1)$$

Covariate assessment

Sociodemographic data, including age, BMI, educational level, physical activity, alcohol consumption status and smoking status, were obtained from self-administered questionnaires. BMI was classified into three groups: <18.5 kg/m^2, ≥18.5 kg/m^2 and<25 kg/m^2, and≥25 kg/m^2. Educational level was categorised as follows: highest level was middle school, highest level was high school and lowest level was college. Physical activity was classified as active or inactive based on the responses to the questions, 'Do you regularly exercise to the point you are sweating'? and 'Is the exercise frequency more than 5 days per week'? Alcohol consumption status was classified as 'current drinker', or 'non-drinker'. Non-drinkers included participants with a history of drinking. Smoking status was categorised as 'current smoker', 'ex-smoker', or 'non-smoker'. Biochemical data, including fasting blood glucose (FBG), total cholesterol (TC), TG, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, systolic blood pressure (SBP) and diastolic blood pressure (DBP). All participants received a venous blood sample after fasting for >12 hours or overnight. FBG was measured using the hexokinase method. TC, TG and HDL serum concentrations were measured using an enzymatic calorimetric method. SBP and DBP were measured within 5 min using a standard mercury

Table 1 Factor loading matrix for the three dietary patterns as reported by the Health Examinees study (2004–2013) in Korea

	Men (n=11 868)			Women (n=32 592)		
Food group	Prudent pattern	Flour-based food and meat pattern	White rice pattern	Prudent pattern	Flour-based food and meat pattern	White rice pattern
Rice	–	–	0.946	–	–	0.930
Other grains	–	–	−0.928	–	–	−0.916
Noodles and dumplings	–	0.488	–	–	0.521	–
Wheat flour and bread	–	0.603	–	–	0.632	–
Potatoes	0.405	0.238	–	0.475	–	–
Sweets	–	0.262	–	–	0.386	–
Soybean pastes	0.437	–	–	0.475	–	–
Bean, tofu and soymilk	0.330	0.262	–	0.460	–	–
Nuts	–	0.228	–	0.221	–	–
Green and yellow vegetables	0.774	–	–	0.791	–	–
Light-coloured vegetables	0.736	–	–	0.711	–	–
Kimchi	0.521	–	–	0.458	–	–
Mushroom	0.621	–	–	0.622	–	–
Fruits	0.379	–	–	0.395	–	–
Red meat and its products	0.235	0.516	–	–	0.598	–
White meat and its products	–	0.514	–	–	0.548	–
Eggs	–	0.426	–	0.234	0.346	–
Fish and shellfish	0.598	0.290	–	0.587	0.270	–
Seaweeds	0.574	–	–	0.585	–	–
Milk and dairy products	–	0.331	–	0.317	–	–
Beverage	–	0.338	–	–	–	–
Coffee and tea	–	–	–	0.206	0.300	–
Variance explained (%)	17.09	8.89	6.57	17.52	8.33	6.87
Cumulative variance explained (%)	17.09	25.98	32.55	17.52	25.85	32.72

Absolute values<0.2 were excluded for simplicity.

sphygmomanometer (Baumanometer, Copiague, New York, USA). The average of the two measurements was used for data analyses.

Statistical analysis

All statistical analyses were performed using SAS V.9.4. Statistical significance was set at two-tailed p<0.05. Stratified analyses were conducted using STATA MP V.17.0 (StataCorp, College Station, Texas, USA). In this study, for each participant, the duration of follow-up were calculated from baseline to the follow-up examination or the date of examination with new onset of NAFLD, whichever occurred first. Normality of the variables was evaluated using the Kolmogorov-Smirnov normality test because the sample size was >2000 participants. All data analyses were separately performed for men and women. Continuous variables are expressed as mean±SE, and categorical variables are expressed as number (percentage). Cox proportional-hazards models were used to estimate the association between the three dietary patterns and NAFLD risk after adjusting for potential confounding variables at baseline: model 1, age; model 2, further adjusted for BMI, total energy intake, smoking status, drinking status, educational level and physical activity; and model 3, further adjusted for cardiometabolic risk factors (FBG, TC, LDL cholesterol, HDL cholesterol, SBP and DBP) measured at baseline to examine the effect of cardiometabolic risk factors on the association between dietary pattern and NAFLD risk. Stratified analyses according to age, BMI, physical activity and drinking status were conducted in both women and men, and an additional stratified analysis according to smoking status was conducted in men. The p value for interactions was calculated using the likelihood ratio test to assess the significance of the interaction between the covariates and dietary patterns on outcomes.

RESULTS

Table 1 presents the main contributors to the three dietary patterns. We found a similar distribution for men and women. The prudent pattern was characterised by high consumption of potatoes, soybean pastes, beans,

Table 2 General and biochemical characteristics of the participants with and without NAFLD

Characteristics	Men (n=11 868)			Women (n=32 592)		
	Non NAFLD	NAFLD	P value	Non NAFLD	NAFLD	P value
N	11 099	769	–	31 808	784	–
Age (years)	55.45±0.08	52.25±0.3	<0.0001	52.49±0.04	53.26±0.27	0.9952
Educational level, n (%)	–	–	0.9919	–	–	<0.0001
Middle school	2237 (20.34)	156 (20.53)	–	10 802 (34.31)	351 (45.82)	–
High school	4344 (39.5)	300 (39.47)	–	14 116 (44.83)	321 (41.91)	–
College or higher	4416 (40.16)	304 (40)	–	6567 (20.86)	94 (12.27)	–
Physical activity, n (yes, %)	2761 (24.95)	145 (18.98)	0.0002	6626 (20.88)	158 (20.26)	0.6701
Current drinking status, n (%)	7249 (65.51)	548 (71.54)	0.0007	9287 (29.34)	222 (28.53)	0.6267
Current smoking status, n (%)	2447 (22.12)	269 (35.16)	<0.0001	–	–	–
Total energy (kcal/day)	1816.69±4.35	1820.66±17.19	0.9169	1679.18±2.73	1674.73±17.61	0.4393
Percentage of energy from carbohydrates	72.1±0.06	71.54±0.23	0.1206	72.24±0.04	72.49±0.24	0.8534
Percentage of energy from fat	13.55±0.05	14.06±0.18	0.0682	13.49±0.03	13.14±0.18	0.6971
Percentage of energy from protein	13.08±0.02	13.1±0.08	0.9655	13.37±0.01	13.33±0.09	0.7126
Triglyceride (mg/dL)	118.99±0.58	145.25±2.31	<0.0001	106.13±0.34	143.46±2.89	<0.0001
GGT (U/L)	29.88±0.2	45.25±1.09	<0.0001	19.67±0.08	31.11±0.83	<0.0001
BMI (kg/m^2)	23.58±0.02	25.64±0.07	<0.0001	23.21±0.01	27.42±0.09	<0.0001
Waist circumference (cm)	83.36±0.06	88.12±0.2	<0.0001	77.11±0.04	86.74±0.22	<0.0001
FBG (mg/dL)	96.48±0.19	97.48±0.71	0.1298	91.52±0.09	95.44±0.69	<0.0001
TC (mg/dL)	189.73±0.32	193.24±1.21	0.0164	198.72±0.2	205.74±1.35	<0.0001
HDL cholesterol (mg/dL)	49.96±0.11	46.6±0.35	<0.0001	56.53±0.07	51.15±0.4	<0.0001
LDL cholesterol (mg/dL)	115.98±0.29	117.59±1.16	0.2079	120.96±0.18	125.9±1.24	0.0001
Systolic blood pressure (mm Hg)	123.9±0.13	126.27±0.51	<0.0001	119.88±0.08	126.39±0.55	<0.0001
Diastolic blood pressure (mm Hg)	77.21±0.09	78.88±0.34	<0.0001	74.02±0.05	77.9±0.34	<0.0001

BMI, body mass index; LDL cholesterol, low-density lipoprotein cholesterol; HDL cholesterol, high-density lipoprotein cholesterol; FBG, fasting blood glucose; GGT, gamma-glutamyl transferase; NAFLD, non-alcoholic fatty liver disease; TC, total cholesterol.

tofu, soymilk, green and yellow vegetables, light-coloured vegetables, kimchi, mushrooms, fruits, fish, shellfish and seaweed. The flour-based food and meat pattern was characterised by high intake of noodles and dumplings, wheat flour and bread, red meat and its products, white meat and its products, eggs, dairy products and beverages. The white rice pattern was characterised by high absolute factor loadings for rice and other grains.

Table 2 shows baseline and biochemical characteristic of the participants with and without NAFLD. A total of 44 460 participants were analysed, 769 men and 784 women were diagnosed with NAFLD. Compared with women, men were more likely to have NAFLD. In baseline characteristic, gender difference shows different results. Among men, participants with NAFLD participants were relatively younger, and exhibited lower physical activity, higher number of current drinkers and smokers than those without NAFLD (p<0.05). Among women, participants with NAFLD had lower education levels than those without NAFLD (p<0.0001). As for biochemical characteristics, participants with NAFLD had higher TG, GGT, BMI, WC, TC, SBP, DBP and lower HDL cholesterol than those without NAFLD (p<0.05).

Table 3 summarises the baseline characteristics of participants according to quartiles of the dietary patterns. Participants who exhibited high adherence to the prudent pattern were relatively older (men: 56.12 years; women: 52.76 years) than those with the low adherence to this pattern, whereas those who exhibited high adherence to the flour-based food and meat pattern were almost 3 years younger (men: 52.75 years; women: 49.71 years) than Q1 group. Furthermore, participants who highly adhered to the white rice pattern were almost 2 years younger than those who lowly adhered to this pattern (men: 53.58 years; women: 51.93 years). Additionally, compared with participants with poor dietary pattern adherence, those with high dietary pattern adherence had a higher educational level. Participants who adhered to the flour-based food and meat pattern had the highest educational level (higher than college, men: 48.64%; women: 30.41%). Those who highly adhered to the prudent pattern exhibited higher physical activity, whereas those who highly adhered to the flour-based food and meat and white rice patterns exhibited lower physical activity (p<0.0001). Similarly, as adherence to the dietary patterns increased, those who adhered to the

Table 3 General characteristics of the participants according to the quartiles of the three dietary patterns

	Men (n=11 868)					Women (n=32 592)				
	Quartile of dietary pattern score					Quartile of dietary pattern score				
	Q1	Q2	Q3	Q4	P value	Q1	Q2	Q3	Q4	P value
N	2967	2967	2967	2967	–	8148	8148	8148	8148	–
Prudent pattern										
Age (years)	54.27±0.15	54.96±0.15	55.63±0.15	56.12±0.15	<0.0001	51.89±0.09	52.64±0.09	52.73±0.08	52.76±0.08	<0.0001
Educational level, n (%)					0.0183					<0.0001
Middle school	600 (20.42)	617 (20.96)	633 (21.56)	543 (18.48)	–	2998 (37.18)	2969 (36.75)	2780 (34.46)	2406 (29.92)	–
High school	1173 (39.93)	1173 (39.84)	1159 (39.48)	1139 (38.75)	–	3426 (42.49)	3500 (43.32)	3605 (44.69)	3906 (48.58)	–
College or higher	1165 (39.65)	1154 (39.20)	1144 (38.96)	1257 (42.77)	–	1639 (20.33)	1611 (19.94)	1682 (20.85)	1729 (21.50)	–
Physical activity, n (yes, %)	584 (19.74)	673 (22.72)	727 (24.64)	922 (31.16)	<0.0001	1305 (16.05)	1565 (19.26)	1801 (22.17)	2113 (26.00)	<0.0001
Current drinking status, n (%)	1910 (64.48)	1990 (67.21)	1940 (65.70)	1957 (66.23)	0.1652	2509 (30.90)	2390 (29.43)	2349 (28.99)	2261 (27.95)	0.0005
Current smoking status, n (%)	715 (24.15)	713 (24.11)	676 (22.88)	612 (20.72)	0.0179	148 (1.82)	98 (1.21)	86 (1.06)	84 (1.04)	<0.0001
Total energy (kcal/day)	1619.30±7.77	1722.76±7.13	1842.18±7.51	2083.53±8.72	<0.0001	1425.39±4.61	1563.47±4.41	1719.24±4.61	2008.21±5.60	<0.0001
Percentage of energy from carbohydrates	74.41±0.11	72.93±0.10	71.66±0.11	69.25±0.12	<0.0001	74.89±0.07	73.22±0.07	71.63±0.07	69.22±0.08	<0.0001
Percentage of energy from fat	12.17±0.09	13.03±0.08	13.82±0.09	15.31±0.09	<0.0001	11.69±0.06	12.80±0.05	13.92±0.05	15.50±0.06	<0.0001
Percentage of energy from protein	11.46±0.03	12.51±0.03	13.38±0.04	14.96±0.05	<0.0001	11.68±0.02	12.79±0.02	13.73±0.02	15.27±0.03	<0.0001
Flour-based food and meat pattern										
Age (years)	58.08±0.13	55.83±0.15	54.33±0.15	52.75±0.16	<0.0001	55.49±0.08	53.21±0.08	51.62±0.08	49.71±0.08	<0.0001
Educational level, n (%)					<0.0001					<0.0001
Middle school	835 (28.50)	653 (22.20)	510 (17.34)	395 (13.42)	–	4181 (51.87)	3022 (37.48)	2310 (28.67)	1640 (20.32)	–
High school	1179 (40.24)	1202 (40.86)	1146 (38.97)	1117 (37.94)	–	2933 (36.39)	3615 (44.84)	3912 (48.55)	3977 (49.27)	–
College or higher	916 (31.26)	1087 (36.95)	1285 (43.69)	1432 (48.64)	–	946 (11.74)	1425 (17.68)	1835 (22.78)	2455 (30.41)	–
Physical activity, n (yes, %)	769 (25.98)	738 (24.97)	707 (23.90)	692 (23.40)	<0.0001	1885 (23.17)	1685 (20.73)	1653 (20.36)	1561 (19.20)	<0.0001
Current drinking status, n (%)	1847 (62.36)	1926 (65.16)	2006 (67.84)	2018 (68.27)	<0.0001	1554 (19.18)	2258 (27.81)	2654 (32.77)	3043 (37.51)	<0.0001
Current smoking status, n (%)	562 (19.01)	626 (21.17)	732 (24.74)	796 (26.96)	<0.0001	74 (0.91)	92 (1.13)	110 (1.36)	140 (1.73)	<0.0001
Total energy (kcal/day)	1517.24±5.91	1660.18±6.01	1855.63±6.52	2234.72±8.53	<0.0001	1416.63±4.31	1520.61±4.21	1696.06±4.35	2083.00±5.43	<0.0001
Percentage of energy from carbohydrates	76.83±0.08	73.78±0.08	70.97±0.09	66.66±0.11	<0.0001	76.86±0.06	74.00±0.06	71.20±0.06	66.91±0.07	<0.0001
Percentage of energy from fat	9.37±0.06	12.11±0.06	14.60±0.07	18.25±0.08	<0.0001	9.38±0.04	12.03±0.04	14.42±0.05	18.07±0.05	<0.0001
Percentage of energy from protein	12.08±0.04	12.62±0.04	13.29±0.04	14.32±0.05	<0.0001	12.54±0.03	12.92±0.03	13.53±0.03	14.48±0.03	<0.0001
White rice pattern										
Age (years)	55.64±0.15	55.92±0.15	55.83±0.15	53.58±0.16	<0.0001	51.80±0.08	54.05±0.08	52.25±0.08	51.93±0.08	0.0105
Educational level, n (%)					<0.0001					<0.0001

Continued

Table 3 Continued

	Men (n=11 868)					Women (n=32 592)				
	Quartile of dietary pattern score					Quartile of dietary pattern score				
	Q1	Q2	Q3	Q4	P value	Q1	Q2	Q3	Q4	P value
Middle school	520 (17.65)	611 (20.82)	633 (21.57)	629 (21.38)	–	2331 (28.92)	3649 (45.27)	2347 (29.10)	2826 (35.04)	–
High school	1122 (38.09)	1180 (40.20)	1180 (40.22)	1162 (39.50)	–	3816 (47.34)	3247 (40.28)	3804 (47.17)	3570 (44.27)	–
College or higher	1304 (44.26)	1144 (38.98)	1121 (38.21)	1151 (39.12)	–	1914 (23.74)	1165 (14.45)	1914 (23.73)	1668 (20.68)	–
Physical activity, n (yes, %)	884 (29.87)	754 (25.48)	740 (24.99)	528 (17.89)	<0.0001	1806 (22.22)	1699 (20.88)	1806 (22.24)	1473 (18.13)	<0.0001
Current drinking status, n (%)	1877 (63.54)	1977 (66.81)	1967 (66.41)	1976 (66.85)	0.0191	2360 (29.09)	2045 (25.19)	2570 (31.71)	2534 (31.30)	<0.0001
Current smoking status, n (%)	520 (17.60)	590 (19.95)	768 (25.93)	838 (28.41)	<0.0001	53 (0.65)	80 (0.99)	122 (1.50)	161 (1.99)	<0.0001
Total energy (kcal/day)	2124.55±7.91	1757.96±6.24	1672.84±7.96	1712.42±8.69	<0.0001	1991.93±4.69	1772.47±3.89	1498.84±5.02	1453.06±5.54	<0.0001
Percentage of energy from carbohydrates	72.56±0.10	73.97±0.1	71.03±0.12	70.69±0.13	<0.0001	73.64±0.06	74.81±0.06	70.50±0.07	70.02±0.09	<0.0001
Percentage of energy from fat	13.42±0.08	11.97±0.08	14.23±0.09	14.72±0.10	<0.0001	12.44±0.05	11.13±0.05	15.04±0.06	15.29±0.07	<0.0001
Percentage of energy from protein	12.77±0.04	12.48±0.04	13.79±0.05	13.27±0.05	<0.0001	12.61±0.02	12.7±0.02	13.99±0.03	14.17±0.03	<0.0001

prudent dietary pattern had the least number of current drinkers and smokers, and those who adhered to the other two dietary patterns correlated with the number of alcohol drinkers and smokers.

Online supplemental table S2 shows results of biochemical analyses. High adherence to the prudent pattern was associated with a lower TC level in men (p<0.0001) than those in lower adherence to this pattern. Conversely, high adherence to the flour-based food and meat pattern was associated with a higher TC level in men (p<0.0001) than those with lowest pattern score. Adherence to the white rice pattern was positively associated with the TC level.

Table 4 shows HRs of NAFLD according to quartiles of the dietary patterns (person-years: men=57 016; women=1 59 0730.7), over a median follow-up of 4.2 years. After adjusting for age, BMI, total energy intake, smoking status, drinking status, educational level, physical activity and cardiometabolic risk factors, high adherence to the prudent pattern was positively associated with a lower risk of NAFLD than those in Q1 group (men: HR=0.78, 95% CI: 0.63 to 0.97, p for trend=0.0159; women: HR=0.64, 95% CI: 0.52 to 0.80, p for trend<0.0001) than those in lowest pattern scores. Conversely, compared with adherence to the lowest quartile group, high adherence to the flour-based food and meat pattern was positively associated with higher NAFLD risk (men: HR=1.29, 95% CI: 1.00 to 1.67, p for trend=0.0282; women: HR=1.55, 95% CI: 1.22 to 1.97, p for trend=0.0003). Differences in dietary patterns had a greater effect on the incidence of NAFLD in women than in men. The white rice pattern showed no significant difference between men and women (men: p for trend=0.4862; women: p for trend=0.3194); however, compared with adherence to the lowest quartile in women, the second quartile exhibited a significantly lower NAFLD risk (HR=0.78, 95% CI: 0.63 to 0.96).

The results of the stratified analyses were in accordance with the subgroups based on major potential confounders (figures 1 and 2). Men with high adherence to the prudent pattern aged<56 years (HR=0.68, 95% CI: 0.52 to 0.89) and current alcohol drinkers (HR=0.71, 95% CI: 0.55 to 0.92) had low NAFLD risk than those in lowest quartile of the prudent group. Conversely, those in the highest quartile of the flour-based food and meat pattern and those aged<56 years who were not current drinkers had a significantly increased NAFLD risk (HR=1.43, 95% CI: 1.05 to 1.96; HR=1.89, 95% CI: 1.20 to 2.98) than Q1 group of this pattern. Women in the highest quartile of the prudent pattern had low NAFLD risk if their BMI was ≥25 kg/m^2 or if they were non-drinkers (HR=0.73, 95% CI: 0.57 to 0.93; HR=0.60, 95% CI: 0.46 to 0.78) than those in Q1 group. Conversely, women in the highest quartile of the flour-based food and meat pattern with a BMI≥25 kg/m^2 (HR=1.70, 95% CI: 1.31 to 2.21) or non-drinkers (HR=1.57, 95% CI: 1.18 to 2.09) had high NAFLD risk than those in Q1 group. However, no interactions among the three dietary patterns and subgroups were found between the men and women (p>0.05).

Table 4 Adjusted HRs and 95% CI of non-alcoholic fatty liver disease according to the quartiles of the three dietary patterns

	Men (n=11 868)					Women (n=32 592)				
	Quartile of dietary pattern score					Quartile of dietary pattern score				
Characteristics	**Q1**	**Q2**	**Q3**	**Q4**	**P trend**	**Q1**	**Q2**	**Q3**	**Q4**	**P value**
Prudent pattern										
Person-years, sum	14 536.6	14 122	14 099.5	14 257.9	–	39 283.8	39 337.1	39 555.6	41 527.2	–
Cases, n	219	194	182	174	–	204	203	201	176	–
Crude HR	1.00 (ref)	0.96 (0.79 to 1.16)	0.91 (0.75 to 1.10)	0.84 (0.69 to 1.02)	0.0661	1.00 (ref)	1.02 (0.84 to 1.24)	0.99 (0.81 to 1.20)	0.75 (0.61 to 0.92)	0.0023
Model 1	1.00 (ref)	0.97 (0.80 to 1.18)	0.95 (0.78 to 1.16)	0.89 (0.73 to 1.08)	0.2358	1.00 (ref)	1.00 (0.82 to 1.22)	0.97 (0.80 to 1.18)	0.74 (0.61 to 0.91)	0.0018
Model 2	1.00 (ref)	0.97 (0.80 to 1.18)	0.90 (0.74 to 1.11)	0.80 (0.65 to 0.99)	0.0289	1.00 (ref)	1.00 (0.82 to 1.21)	0.94 0.77 to 1.15)	0.64 (0.51 to 0.80)	<0.0001
Model 3	1.00 (ref)	0.97 (0.80 to 1.18)	0.88 (0.72 to 1.07)	0.78 (0.63 to 0.97)	0.0159	1.00 (ref)	0.97 (0.80 to 1.19)	0.92 (0.75 to 1.12)	0.64 (0.52 to 0.80)	<0.0001
Flour-based food and meat pattern										
Person-years, sum	14 748	14 332.1	14 159.9	13 776	–	41 115.6	39 959.9	39 173.9	39 454.3	–
Cases, n	176	180	212	201	–	192	189	200	203	–
Crude HR	1.00 (ref)	1.10 (0.89 to 1.35)	1.34 (1.10 to 1.64)	1.38 (1.13 to 1.69)	0.0006	1.00 (ref)	1.06 (0.87 to 1.30)	1.19 (0.97 to 1.45)	1.16 (0.95 to 1.41)	0.1207
Model 1	1.00 (ref)	0.99 (0.80 to 1.22)	1.14 (0.93 to 1.40)	1.11 (0.90 to 1.37)	0.2033	1.00 (ref)	1.15 (0.94 to 1.41)	1.35 (1.11 to 1.66)	1.39 (1.13 to 1.70)	0.0011
Model 2	1.00 (ref)	1.03 (0.83 to 1.27)	1.23 (0.99 to 1.52)	1.24 (0.96 to 1.60)	0.0636	1.00 (ref)	1.30 (1.06 to 1.59)	1.48 (1.19 to 1.82)	1.62 (1.27 to 2.07)	0.0001
Model 3	1.00 (ref)	1.02 (0.83 to 1.27)	1.27 (1.02 to 1.58)	1.29 (1.00 to 1.67)	0.0282	1.00 (ref)	1.25 (1.02 to 1.53)	1.46 (1.18 to 1.80)	1.55 (1.22 to 1.97)	0.0003
White rice pattern										
Person-years, sum	13 825.7	14 233.6	14 347.3	14 609.4	–	39 413.4	39 921.2	39 426.5	40 942.6	–
Cases, n	168	178	202	221	–	190	184	185	225	–
Crude HR	1.00 (ref)	0.98 (0.80 to 1.21)	1.10 (0.90 to 1.35)	1.14 (0.94 to 1.40)	0.1395	1.00 (ref)	0.95 0.77 to 1.16)	0.97 (0.79 to 1.18)	1.06 (0.88 to 1.29)	0.2686
Model 1	1.00 (ref)	0.99 (0.80 to 1.22)	1.12 (0.91 to 1.37)	1.04 (0.85 to 1.28)	0.8077	1.00 (ref)	0.89 (0.72 to 1.09)	0.95 (0.78 to 1.17)	1.06 (0.88 to 1.29)	0.1592
Model 2	1.00 (ref)	0.92 (0.74 to 1.15)	1.00 (0.80 to 1.24)	0.93 (0.74 to 1.15)	0.5723	1.00 (ref)	0.78 (0.64 to 0.97)	0.83 (0.67 to 1.03)	0.91 (0.74 to 1.13)	0.5311
Model 3	1.00 (ref)	0.92 (0.74 to 1.14)	1.04 (0.83 to 1.30)	0.92 (0.74 to 1.15)	0.4862	1.00 (ref)	0.78 (0.63 to 0.96)	0.85 (0.69 to 1.06)	0.95 (0.77 to 1.17)	0.3194

Model 1: age; model 2: further adjusted for body mass index at baseline, total energy intake, smoking status, drinking status, educational level and physical activity; model 3: further adjusted for the baseline measurements of cardiometabolic risk factors (fasting blood glucose, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, systolic blood pressure and diastolic blood pressure).

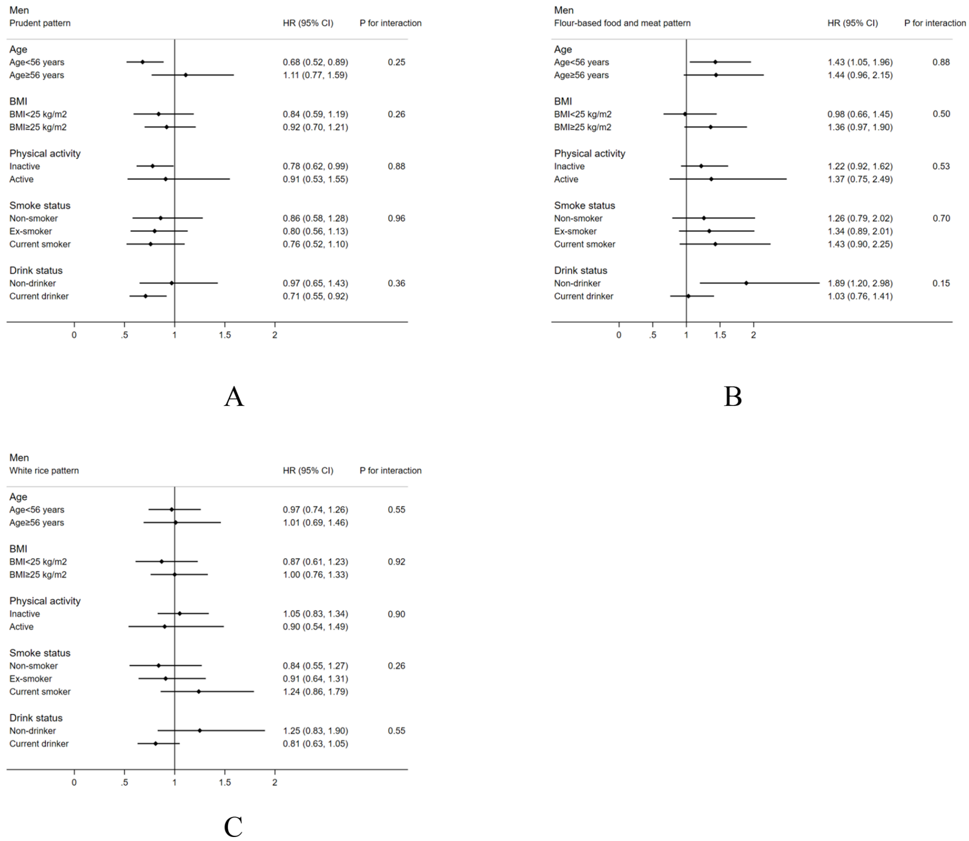

Figure 1 Stratified analysis of the three dietary patterns and non-alcoholic fatty liver disease risk in men. (A) Prudent pattern, (B) flour-based food and meat pattern and (C) white rice pattern. This multivariable model was adjusted for age, body mass index at baseline, total energy intake, smoking status, drinking status, educational level and physical activity. The p value for interactions was calculated using the likelihood ratio test.

DISCUSSION

In this large-scale prospective cohort study on Korean adults, we identified prudent, flour-based food and meat, and white rice dietary patterns. We found that a greater adherence to the prudent pattern may lower NAFLD risk, whereas the flour-based food and meat pattern may higher NAFLD risk.

Our findings are consistent with those of previous studies that reported a beneficial effect of the prudent dietary pattern on NAFLD risk.[26 27] The prudent pattern, similar to the dietary guidelines for Americans, was characterised by high consumption of green and yellow vegetables, light-coloured vegetables, kimchi, mushrooms, potatoes, beans, tofu, soymilk and fish. Its beneficial effect on NAFLD risk may result from consumption of vegetables, fruits and fish.[28 29] Vegetables and fruits contain numerous dietary fibres, carotenoids and polyphenols, which lower the total energy intake, change the gut microbiome and promote intestinal homeostasis to prevent NAFLD.[30 31] Fish consumption is a major factor that influences this dietary pattern. Fish are rich in monounsaturated fatty acids and ω–3 and ω–6 polyunsaturated fatty acids (PUFAs), which reduce hepatic steatosis by modulating the lipid profile and glycaemic control.[32 33] Additionally, ω–3 PUFAs can enhance mitochondrial fatty acid β-oxidation and reduce hepatic inflammation, preventing NAFLD.[33]

The flour-based food and meat pattern was characterised by high consumption of noodles, dumplings, wheat flour, potatoes, sweets, nuts, red meat, white meat and dairy products. Our findings are consistent with those of previous studies reporting a positive association between flour-based food and meat patterns and NAFLD risk. Among them, the 'fast-food type pattern' (Greek population study, Kalafati *et al.*), 'noodle/meat-rich dietary pattern' (Korean adults, Park *et al*) and 'animal food dietary pattern' (Chinese adults, Zhang *et al*) emphasised the consumption of high-rich carbohydrate food and meat, similar to the flour-based food and meat pattern in the current study. The positive association between this dietary pattern and NAFLD risk observed in the current study has several possible explanations. First, the dietary patterns identified in this study included high egg intake. A previous study based on the 2005–2010 National Health and Nutrition Examination Survey indicated adverse effects of egg consumption on NAFLD development.[34] Second, high adherence to this dietary pattern rich in saturated fat, trans fat, ratio of ω–6: ω–3 and animal fat protein intake, possibly increasing NAFLD severity.[30 32 35] Wan *et al* indicated that unbalanced dietary ratios of the

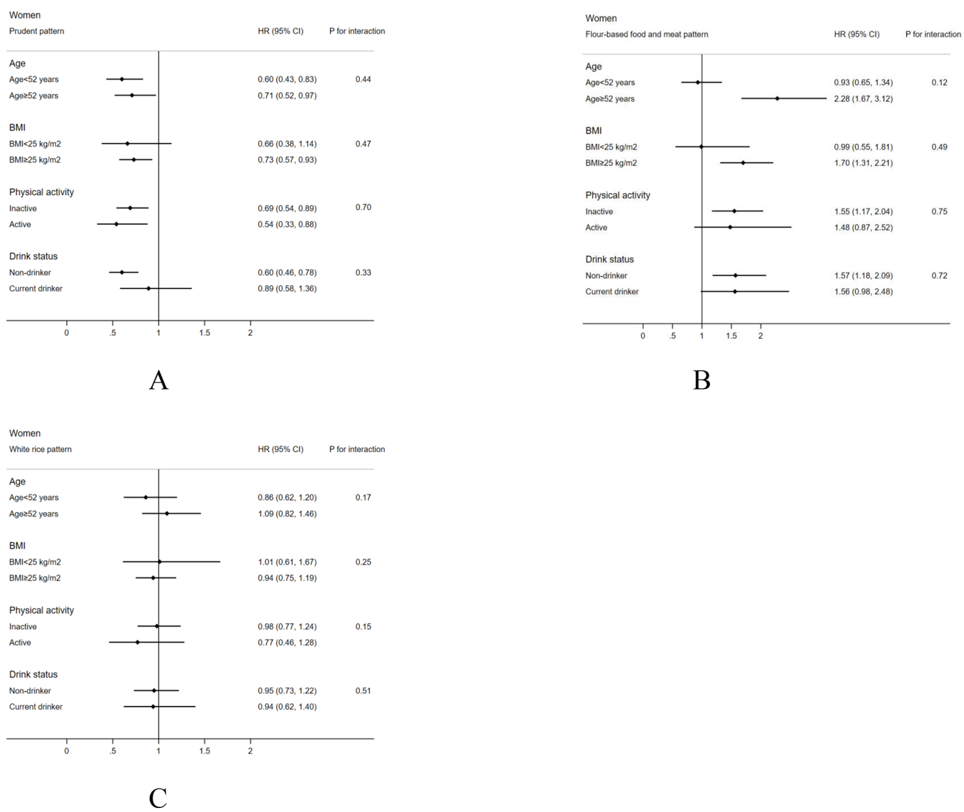

Figure 2 Stratified analysis of the three dietary patterns and NAFLD in women. (A) Prudent pattern, (B) flour-based food and meat pattern,and (C) white rice pattern. This multivariable model was adjusted for age, body mass index at baseline, total energy intake, smoking status, drinking status, educational level and physical activity. The P value for interactions was calculated using the likelihood ratio test.

ratio of ω–6: ω–3 may exacerbate disease-causing physiological conditions in NAFLD risk models.[36] Roumans *et al* showed that saturated fatty acids, damage the liver by increasing de novo liver lipogenesis and lipolysis of adipose tissue, leading to hepatic steatosis.[35] Third, the flour-based food and meat pattern had a higher carbohydrate consumption rich in fructose. Excessive fructose intake (100–220 g/day) has been proposed as a risk factor for NAFLD because it drives de novo lipogenesis in the liver, leading to liver fat accumulation.[37] However, Chung *et al*'s cross-sectional study in Korea agreed in part with our results, as no significant association was found.[18] This discrepancy may result from differences in study types. Our study was a cohort study, which implies that the participants followed the dietary pattern for a few years, whereas Chung *et al.*'s study was a cross-sectional study, which did not show causation.[18]

Based on findings from prudent dietary pattern and the flour-based food and meat pattern, there appear to be gender differences in the effect of dietary patterns on NAFLD risk. The effect of dietary patterns on NAFLD risk was more sensitive in women than men. This may be partially explained by the dietary pattern component difference. For example, in prudent pattern, the factor loadings of vegetable and fruit were bigger in women than men. In the flour-based food and meat pattern, compared with men, women had bigger factor loadings of noodles, weal and bread, and meat, which were rich in carbohydrates and saturated fat. Various studies have indicated the adverse effects of these nutrients on NAFLD.[30 32 35 38] Furthermore, although the effects of these two dietary patterns were completely opposite, the total energy both higher in greater adherence to dietary patterns than those in lower group; in contrast, the difference was the energy sources, which seems that the role of energy from food source is more important than total energy on NAFLD.[30] A systematic review was agree with this speculation that food source may mediate the effect of nutrients on NAFLD development.[39]

The white rice pattern was characterised by high rice consumption in the present study. Chung *et al* also identified a similar dietary pattern, named the 'simple meal pattern', and reported no association with NAFLD risk.[18] However, the mechanism is still unclear. A cross-sectional study, which conducted by Japan, was partly agree with our results.[40] They observed a positive association between rice consumption and NAFLD risk in women, but not found association in men. The difference in this study maybe due to the type of rice consume. In addition, owing to regional dietary differences, this is a special but common dietary pattern, mostly in Asian populations. Few studies have been conducted on this association in Western populations.

Subgroup analysis revealed that for men, the effects of the prudent pattern and the flour-based food and meat patterns on NAFLD risk were only found in those aged<56 years old. A review mentioned that age is an important factor in the development of chronic diseases.[41] For example, variability in lifestyle is more pronounced among younger groups than older groups, which may explain this.[41] Lifestyle is regard as a most relevant factor in the development of NAFLD.[42] For women, compared with participants with BMI<25 kg/m^2, participants with BMI≥25 kg/m^2 were more sensitive to the effect of the flour-based food and meat patterns on NAFLD risk. This may be explained by participants with BMI≥25 kg/m^2 may greater adhered to the flour-based food and meat patterns and consumed more high caloric food than those with BMI<25 kg/m^2. Besides that, BMI is widely considered as a risk factor for the development of NAFLD, which also may explain this.[43]

The present study has several limitations. First, we used non-invasive indices instead of gold-standard liver biopsies to diagnose NAFLD. Nevertheless, as reported by Bedogni *et al* in 2006, the FLI used in this study is an accurate and low-cost method for predicting new cases of NAFLD in the general population.[24 25] Second, factor analysis has drawbacks because the interpretation of meaning and the number of factors is subjective, which leads to bias.[44] Nonetheless, compared with other statistical methods, this method is beneficial for exploring the effects of dietary patterns.[23] Third, the follow-up duration (median: 4.2 years) might possibly be too short for enabling the development of NAFLD. Fourth, we focused only on the baseline data of the dietary patterns, which may have changed during the follow-up period. Finally, due to the lack of information on duration of abstinence, we could not consider the effect of duration of abstinence on NAFLD.

The present study also has several strengths. To the best of our knowledge, this is the first prospective study to assess the association between dietary patterns and NAFLD risk among Korean adults. Moreover, regarding the variables in the adjustment models, we considered the effect of cardiometabolic risk factors on NAFLD risk.[45]

In conclusion, our findings indicate that a greater adherence to a prudent pattern decreases NAFLD risk, whereas a greater adherence to a flour-based food and meat pattern increases NAFLD risk. Our findings will serve as a guide for the prevention or delay of NAFLD in Korean adults. Nevertheless, further randomised controlled trials are required to confirm these findings.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. Written informed consent was obtained from all participants. The local Institutional Review Board (IRB) of the ethics committee of the Korean Genome and Epidemiology Study of the Korea National Institute of Health (IRB no. E-1503- 103-657) approved this study, which was conducted in accordance with the guidelines of the Declaration of Helsinki. Participants gave informed consent to participate in the study before taking part.

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