

Supplementary Table 1. Association between fatty liver categories and coronary artery calcification among 99,729 participants with available waist circumference

	Categories of fatty liver			
	No excessive alcohol intake and no FLD	Excessive alcohol intake and no FLD	NAFLD	AFLD
Total				
Number	49,811	9,496	32,590	7,832
CAC score >0 (%)	4,246 (8.5)	1,398 (14.7)	4,994 (15.3)	1,630 (20.8)
Adjusted ORs (95% CIs) ^a				
Model 1	1.00 (reference)	1.41 (1.31-1.51)	1.56 (1.49-1.64)	1.92 (1.79-2.06)
Model 2	1.00 (reference)	1.25 (1.15-1.35)	1.10 (1.05-1.17)	1.21 (1.11-1.31)
Model 3	1.00 (reference)	1.25 (1.16-1.35)	1.11 (1.05-1.17)	1.21 (1.11-1.31)

^aEstimated from binomial logistic regression models. Multivariable model 1 was adjusted for age and sex; model 2: model 1 plus adjustment for center, year of screening exam, waist circumference, smoking status, physical activity, educational level, total calorie intake, family history of cardiovascular disease, diabetes, hypertension, LDL-cholesterol, and medication for dyslipidemia; model 3 model 2 plus adjustment for hsCRP, and HOMA-IR. Abbreviations: AFLD, alcoholic fatty liver disease; FLD, fatty liver disease; NAFLD, nonalcoholic fatty liver disease.

Supplementary Table 2. Baseline characteristics according to fatty liver categories

Characteristics	NAFLD		<i>P</i> value	AFLD		<i>P</i> value
	Non-obese	Obese		Non-obese	Obese	
Number	12,269	22,113		2,315	6,004	
Age (years) [*]	42.0 (7.9)	40.7 (7.6)	<0.001	43.3 (7.8)	41.5 (7.3)	<0.001
Male (%)	87.2	90.2	<0.001	96.2	97.8	<0.001
Current smoker (%)	28.6	32.1	<0.001	51.2	48.9	0.061
HEPA (%)	11.8	13.6	<0.001	15.7	16.1	0.637
High education level (%) ^c	86.9	86.7	<0.001	78.9	81.5	<0.001
Diabetes (%)	6.6	8.6	<0.001	12.3	11.4	0.260
Hypertension (%)	14.2	24.0	<0.001	22.6	34.1	<0.001
Family history of CVD (%)	12.5	12.1	0.391	13.7	12.9	0.347
Waist circumference (cm) ^d	84.0 (4.6)	93.9 (6.9)	<0.001	84.9 (4.4)	94.8 (6.7)	<0.001
Albumin (g/dL) ^a	4.7 (0.2)	4.7 (0.2)	<0.001	4.7 (0.3)	4.7 (0.2)	0.318
Platelet ($\times 10^9/L$) ^a	249.5 (50.1)	252.0 (50.9)	<0.001	244.8 (47.2)	244.9 (47.7)	0.923
Systolic BP (mmHg) ^a	112.3 (11.0)	117.8 (11.6)	<0.001	116.3 (11.2)	121.0 (11.9)	<0.001
Diastolic BP (mmHg) ^a	73.6 (9.0)	76.5 (9.5)	<0.001	77.3 (9.2)	79.6 (9.8)	<0.001
Glucose (mg/dl) ^a	99.2 (19.1)	101.7 (19.0)	<0.001	105.4 (25.3)	105.6 (22.0)	0.618
Total cholesterol (mg/dl) ^a	204.6 (35.3)	207.1 (35.8)	<0.001	208.2 (36.4)	210.9 (37.0)	0.003
LDL-C (mg/dl) ^a	136.0 (32.2)	139.0 (32.3)	<0.001	133.2 (33.3)	137.8 (33.1)	<0.001
HDL-C (mg/dl) ^a	50.4 (11.6)	46.6 (10.3)	<0.001	53.2 (13.5)	48.6 (11.2)	<0.001
Triglycerides (mg/dl) ^b	131 (95-183)	153 (112-213)	<0.001	150 (107-215)	173 (123-244)	<0.001
AST (U/l) ^b	21 (18-26)	24 (20-31)	<0.001	23 (19-29)	26 (21-34)	<0.001
ALT (U/l) ^b	25 (18-36)	33 (24-50)	<0.001	27 (19-37)	34 (24-50)	<0.001
GGT (U/l) ^b	29 (21-44)	38 (26-59)	<0.001	48 (31-81)	58 (39-90)	<0.001
HOMA-IR ^b	1.56 (1.11-2.17)	2.27 (1.60-3.25)	<0.001	1.56 (1.09-2.16)	2.27 (1.59-3.23)	<0.001
hsCRP (mg/l) ^b	0.6 (0.3-1.0)	0.8 (0.5-1.6)	<0.001	0.6 (0.3-1.0)	0.8 (0.5-1.6)	<0.001
Fib4 ^a	0.78 (0.3)	0.76 (0.3)	<0.001	0.90 (0.5)	0.85 (0.4)	<0.001
APRI ^a	0.25 (0.1)	0.30 (0.2)	<0.001	0.29 (0.2)	0.33 (0.2)	<0.001
Total energy intake	1080.7 (0-1595.8)	1152.9 (0-1700.1)	<0.001	1148.7 (0-1684.2)	1260.7 (0-1837.1)	<0.001

(kcal/d) ^{b,e}						
CAC score >0 (%)	13.9	16.0	<0.001	20.7	20.7	0.959
CAC score 1-100 (%)	11.7	13.3	<0.001	16.3	16.9	0.548
CAC score >100 (%)	2.2	2.7	0.004	4.4	3.8	0.231
CAC score ^f	17(5-54)	19 (5-64)	0.364	23 (7-75)	21 (6-69)	0.109
FRS>10(%)	14.1	18.2	<0.001	27.5	28.9	0.210

Data are expressed as ^amean (standard deviation), ^bmedian (interquartile range), or percentage.

Abbreviations: AFLD, alcoholic fatty liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BP, blood pressure; EAC, excessive alcohol consumption; GGT, gamma-glutamyl transferase ; FLD, fatty liver disease; HDL-C, high-density lipoprotein-cholesterol; HEPA, health-enhancing physical activity; hsCRP, high sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; NAFLD, nonalcoholic fatty liver disease.

^c≥ College graduate; ^d among 99,729 participants with available waist circumference; ^e among 71,521 participants with plausible estimated energy intake levels (within three standard deviations from log-transformed mean energy intake); ^f among 12,933 participants with CAC score >0

Supplementary Table 3. Prevalence ratios^a (95% CI) of coronary artery calcification by fatty liver categories

	Categories of fatty liver			
	No excessive alcohol intake and no FLD	Excessive alcohol intake and no FLD	NAFLD	AFLD
Number	52,529	10,098	34,382	8,319
CAC score 1-100 (%)	3,757 (7.2)	1,217 (12.1)	4,379 (12.7)	1,394 (16.8)
Adjusted PR (95% CI) ^a				
Model 1	1.00 (reference)	1.37 (1.27-1.47)	1.54 (1.47-1.62)	1.84 (1.71-1.97)
Model 2	1.00 (reference)	1.24 (1.14-1.34)	1.11 (1.05-1.18)	1.21 (1.11-1.31)
Model 3	1.00 (reference)	1.24 (1.14-1.34)	1.12 (1.05-1.18)	1.21 (1.11-1.31)
CAC score >100 (%)	722 (1.4)	267 (2.6)	870 (2.5)	327 (3.9)
Adjusted PR (95% CI) ^a				
Model 1	1.00 (reference)	1.68 (1.44-1.96)	1.75 (1.57-1.95)	2.48 (2.14-2.86)
Model 2	1.00 (reference)	1.32 (1.12-1.56)	1.07 (0.95-1.21)	1.21 (1.03-1.43)
Model 3	1.00 (reference)	1.33 (1.12-1.57)	1.06 (0.94-1.19)	1.19 (1.01-1.41)

^aEstimated from multinomial logistic regression models using CAC scores as outcomes categorized as 0, 1–100, and >100. Multivariable model 1 was adjusted for age and sex; model 2: model 1 plus adjustment for center, year of screening exam, BMI, smoking status, physical activity, educational level, total calorie intake, family history of cardiovascular disease, diabetes, hypertension, LDL-cholesterol, and medication for dyslipidemia; model 3 model 2 plus adjustment for hsCRP, and HOMA-IR.

Abbreviations: AFLD, alcoholic fatty liver disease; CI, confidence intervals; FLD, fatty liver disease; NAFLD, nonalcoholic fatty liver disease; PR, prevalence ratio.

Supplementary Table 4. Coronary artery calcium score ratios^a (95% CI) by fatty liver categories with coronary artery calcification

	Categories of fatty liver			
	No excessive alcohol intake and no FLD	Excessive alcohol intake and no FLD	NAFLD	AFLD
Total				
Number	52,529	10,098	34,382	8,319
CAC score >0 (%)	4,479 (8.5)	1,484 (14.7)	5,249 (15.3)	1,721 (20.7)
Adjusted CAC score ratio ^a				
Model 1	1.00 (reference)	2.28 (1.94-2.67)	2.71 (2.44-3.01)	4.55 (3.90-5.31)
Model 2	1.00 (reference)	1.68 (1.42-1.98)	1.22 (1.09-1.37)	1.54 (1.30-1.83)
Model 3	1.00 (reference)	1.68 (1.42-1.98)	1.21 (1.08-1.36)	1.53 (1.29-1.82)

$P=0.054$ for overall interaction between obesity and by fatty liver category for coronary artery calcification (model 3).

Compared with NAFLD, CAC score ratio (95% CIs) in AFLD was 1.27 (1.08-1.49) ($p=0.004$).

^aEstimated from robust Tobit regression models used with natural log(CAC + 1) as the outcome. Multivariable model 1 was adjusted for age and sex; model 2: model 1 plus adjustment for center, year of screening exam, BMI, smoking status, physical activity, educational level, total calorie intake, family history of cardiovascular disease, diabetes, hypertension, LDL-cholesterol, and medication for dyslipidemia; model 3 model 2 plus adjustment for hsCRP, and HOMA-IR.

Abbreviations: AFLD, alcoholic fatty liver disease; FLD, fatty liver disease; NAFLD, nonalcoholic fatty liver disease.

Supplementary Table 5. Association between fatty liver categories and coronary artery calcification after including 1,605 CVD patients at baseline.

	Categories of fatty liver			
	No excessive alcohol intake and no FLD	Excessive alcohol intake and no FLD	NAFLD	AFLD
Total				
Number	53,109	10,249	34,767	8,426
CAC score >0 (%)	4,667 (8.8)	1,553 (15.0)	5,413 (15.6)	1,769 (21.0)
Adjusted ORs (95% CIs) ^a				
Model 1	1.00 (reference)	1.39 (1.29-1.49)	1.56 (1.49-1.63)	1.90 (1.77-2.03)
Model 2	1.00 (reference)	1.24 (1.14-1.33)	1.10 (1.05-1.16)	1.20 (1.11-1.30)
Model 3	1.00 (reference)	1.24 (1.15-1.33)	1.10 (1.04-1.16)	1.20 (1.11-1.30)
Non-obese (BMI <25 kg/m²)				
Number	51,503	8,583	16,469	3,087
CAC score >0 (%)	5,556 (10.8)	1,493 (17.4)	3,072 (18.7)	789 (25.6)
Adjusted ORs (95% CIs) ^a				
Model 1	1.00 (reference)	1.44 (1.32-1.57)	1.37 (1.28-1.47)	1.76 (1.56-1.98)
Model 2	1.00 (reference)	1.30 (1.18-1.43)	1.10 (1.02-1.18)	1.26 (1.11-1.43)
Model 3	1.00 (reference)	1.30 (1.18-1.43)	1.11 (1.03-1.19)	1.27 (1.11-1.45)
Obese (BMI ≥ 25 kg/m²)				
Number	13,455	4,179	30,516	8,179
CAC score >0 (%)	2,248 (16.7)	937 (22.4)	6,507 (21.3)	2,155 (26.4)
Adjusted ORs (95% CIs) ^a				
Model 1	1.00 (reference)	1.18 (1.04-1.33)	1.30 (1.20-1.40)	1.49 (1.36-1.64)
Model 2	1.00 (reference)	1.10 (0.96-1.24)	1.05 (0.97-1.14)	1.13 (1.02-1.25)
Model 3	1.00 (reference)	1.09 (0.96-1.24)	1.05 (0.96-1.13)	1.12 (1.01-1.24)

P = 0.059 for overall interaction between obesity and by fatty liver category for coronary artery calcification (model 3).

Compared with NAFLD, ORs (95% CIs) in AFLD was 1.09 (1.01-1.17) (*p* = 0.021).

^aEstimated from binomial logistic regression models. Multivariable model 1 was adjusted for age and sex; model 2: model 1 plus adjustment for center, year of screening exam, BMI, smoking status, physical activity, educational level, total calorie intake, family history of cardiovascular disease, diabetes, hypertension, LDL-cholesterol, and medication for dyslipidemia; model 3 model 2 plus adjustment for hsCRP, and HOMA-IR.

Abbreviations: AFLD, alcoholic fatty liver disease; FLD, fatty liver disease; NAFLD, nonalcoholic fatty liver disease.

Supplementary Table 6. Association of fatty liver categories and their severity based on APRI with coronary artery calcification

	Reference	NAFLD		AFLD	
		Low	Intermediate/high	Low	Intermediate/high
Fibrosis severity based on APRI					
Number	52,529	32,166	2,213	7,513	806
CAC score >0 (%)	4,479 (8.5)	4,854 (15.1)	395 (17.9)	1,530 (20.4)	191 (23.7)
Adjusted ORs (95% CIs) ^a					
Model 1	1.00	1.54 (1.46-1.61)	1.98 (1.75-2.25)	1.86 (1.74-2.00)	2.32 (1.92-2.79)
Model 2	1.00	1.10 (1.04-1.16)	1.06 (0.92-1.21)	1.19 (1.10-1.29)	1.20 (0.99-1.46)
Model 3	1.00	1.10 (1.04-1.16)	1.06 (0.92-1.21)	1.19 (1.10-1.29)	1.20 (0.99-1.46)

Compared with low-APRI NAFLD, ORs (95% CIs) in intermediate/high APRI NAFLD was 0.96 (0.84-1.10) (p = 0.558, model 3).

Compared with low-APRI AFLD, ORs (95% CIs) in intermediate/high APRI AFLD was 1.01 (0.83-1.23) (p = 0.948, model 3)

^aEstimated from binomial logistic regression models comparing FLD and APRI categories to reference category (no excessive alcohol use and no fatty liver). Multivariable model 1 was adjusted for age and sex; model 2: model 1 plus adjustment for center, year of screening exam, BMI, smoking status, physical activity, educational level, total calorie intake, family history of cardiovascular disease, diabetes, hypertension, LDL-cholesterol, and medication for dyslipidemia; model 3 model 2 plus adjustment for hsCRP, and HOMA-IR.

Abbreviations: AFLD, alcoholic fatty liver disease; CI, confidence intervals; FLD, fatty liver disease; NAFLD, nonalcoholic fatty liver disease.

Supplementary Table 7. Coronary artery calcium score ratios^a (95% CI) by fatty liver categories and their severity based on FIB-4 and APRI with coronary artery calcification

	Reference	NAFLD		AFLD	
		Low	Intermediate/high	Low	Intermediate/high
Fibrosis severity based on FIB-4					
Number	52,529	32,512	1,865	7,527	791
CAC score >0 (%)	4,479 (8.5)	4,482 (13.8)	767 (41.1)	1,367 (18.2)	354 (44.8)
Adjusted CAC score ratio ^a					
Model 1	1.00	2.67 (2.40-2.98)	3.11 (2.41-4.02)	4.31 (3.66-5.09)	6.35 (4.48-9.02)
Model 2	1.00	1.19 (1.06-1.34)	1.32 (1.03-1.70)	1.43 (1.20-1.72)	2.14 (1.50-3.05)
Model 3	1.00	1.18 (1.05-1.33)	1.31 (1.02-1.69)	1.42 (1.19-1.71)	2.12 (1.49-3.03)
Fibrosis severity based on APRI					
Number	52,529	32,166	2,213	7,513	806
CAC score >0 (%)	4,479 (8.5)	4,854 (15.1)	395 (17.9)	1,530 (20.4)	191 (23.7)
Adjusted CAC score ratio ^a					
Model 1	1.00	2.60 (2.34-2.90)	4.77 (3.59-6.35)	4.33 (3.69-5.09)	7.04 (4.64-10.68)
Model 2	1.00	1.20 (1.07-1.35)	1.14 (0.85-1.52)	1.51 (1.27-1.81)	1.53 (1.00-2.35)
Model 3	1.00	1.20 (1.06-1.34)	1.11 (0.83-1.49)	1.50 (1.26-1.79)	1.50 (0.97-2.31)

Compared with low-Fib4 NAFLD, CAC score ratio (95% CIs) in intermediate/high FIB-4 NAFLD was 1.11 (0.86-1.42) (p = 0.415, model 3).

Compared with low-Fib4 AFLD, CAC score ratio (95% CIs) in intermediate/high FIB-4 AFLD was 1.49 (1.04-2.15) (p = 0.032, model 3).

Compared with low-APRI NAFLD, CAC score ratio (95% CIs) in intermediate/high APRI NAFLD was 0.93 (0.70-1.23) (p = 0.608, model 3).

Compared with low-APRI AFLD, CAC score ratio (95% CIs) in intermediate/high APRI AFLD was 1.00 (0.65-1.54) (p = 0.939, model 3)

^aEstimated from robust Tobit regression models used with natural log(CAC + 1) as outcome comparing FLD and FIB-4 categories to reference category (no excessive alcohol use and no fatty liver). Multivariable model 1 was adjusted for age and sex; model 2: model 1 plus adjustment for center, year of screening exam, BMI, smoking status, physical activity, educational level, total calorie intake, family history of cardiovascular disease, diabetes, hypertension, LDL-cholesterol, and medication for dyslipidemia; model 3 model 2 plus adjustment for hsCRP, and HOMA-IR.

Abbreviations: AFLD, alcoholic fatty liver disease; CI, confidence intervals; FLD, fatty liver disease; NAFLD, nonalcoholic fatty liver disease.

Supplementary Table 8. Association between fatty liver categories and coronary artery calcification in clinically relevant subgroups.

Subgroup	No excessive alcohol intake and no FLD	Excessive alcohol intake and no FLD	NAFLD	AFLD	<i>p</i> -value for interaction
Age					0.001
< 40 years (N =50,753)	reference	1.35 (1.15-1.59)	1.32 (1.19-1.47)	1.41 (1.21-1.65)	
≥ 40 years (N = 54,575)	reference	1.18 (1.09-1.28)	1.05 (0.99-1.11)	1.13 (1.04-1.22)	
Sex					0.471
Women (N =23,662)	reference	1.33 (0.92-1.91)	0.99 (0.85-1.15)	1.16 (0.66-2.02)	
Men (N = 81,666)	reference	1.25 (1.16-1.35)	1.12 (1.06-1.18)	1.21 (1.12-1.31)	
Current smoking					0.255
No (N = 72,418)	reference	1.27 (1.15-1.41)	1.12 (1.05-1.20)	1.28 (1.15-1.43)	
Yes (N = 28,978)	reference	1.22 (1.09-1.36)	1.04 (0.95-1.14)	1.12 (1.00-1.25)	
HEPA					0.314
No (N=88,454)	reference	1.21 (1.11-1.32)	1.09 (1.03-1.15)	1.21 (1.11-1.32)	
Yes (N = 16,336)	reference	1.35 (1.16-1.57)	1.18 (1.05-1.33)	1.16 (0.98-1.37)	
HOMA					0.582
< 2.5 (N = 86,723)	reference	1.25 (1.15-1.35)	1.10 (1.03-1.16)	1.23 (1.13-1.35)	
≥ 2.5 (N = 18,605)	reference	1.26 (0.99-1.61)	1.09 (0.94-1.25)	1.12 (0.95-1.32)	
HsCRP					0.752
<1.0 mg/l (N=77,416)	reference	1.26 (1.16-1.37)	1.12 (1.06-1.20)	1.22 (1.11-1.34)	
≥1.0 mg/l (N=27,912)	reference	1.19 (1.02-1.39)	1.06 (0.96-1.17)	1.17 (1.02-1.33)	

^aEstimated from binomial logistic regression models. Multivariable model was adjusted for age, sex, center, year of screening exam, BMI, smoking status, physical activity, educational level, total calorie intake, family history of cardiovascular disease, diabetes, hypertension, LDL-cholesterol, medication for dyslipidemia, hsCRP, and HOMA-IR.

Abbreviations: AFLD, alcoholic fatty liver disease; HEPA, health-enhancing physical activity; HOMA-IR, homeostasis model assessment of insulin resistance; hsCRP, high sensitivity C-reactive protein; NAFLD, nonalcoholic fatty liver disease.

Supplementary information

There are three different hospitals under Samsung medical center including Samsung Seoul Hospital, Kangbuk Samsung Hospital and Samsung Changwon hospital (https://en.wikipedia.org/wiki/Samsung_Medical_Center). Whilst the previous study of 4731 adults on the association between NAFLD and CAC was conducted using data from Samsung Seoul Hospital,[1] our study was performed using data from Kangbuk Samsung Health Study. The sample size of our study is bigger and the study population is much younger than the former cohort (mean age 41.2 vs 52.2 years). In South Korea, the Industrial Safety and Health Law requires annual or biennial health screening exams of all employees, offered free of charge. In our cohort, 93.6 % of participants (N=97,607) were employees of various companies and local governmental organizations and their spouses.

Reference

- 1 Sinn DH, Kang D, Chang Y, Ryu S, Gu S, Kim H, *et al*. Non-alcoholic fatty liver disease and progression of coronary artery calcium score: a retrospective cohort study. Gut 2017;**66**:323-9.