

SUPPLEMENTARY MATERIALS

S1. Exclusion criteria

A total of 81,851 subjects were excluded on the basis of the following criteria (**Figure 1**): excessive alcohol consumption (men ≥ 30 g/day; women ≥ 20 g/day) (n = 31,625); liver steatogenic medication (n = 971); history of hepatitis and medication for hepatitis treatment (n = 5,762); serologic positivity for hepatitis B or hepatitis C virus (n = 6,376); liver cirrhosis based on ultrasound (n = 25); history of CVD (n = 933); history of cancer (n = 3,012); diabetes at baseline (n = 2,606), as some glucose-lowering medications have BP-lowering effects [1]; history of hysterectomy, bilateral oophorectomy, radiation or chemotherapy-related menopause (n = 2,307); hypertension at baseline (n = 36,086); and missing information on hypertension, alcohol consumption, or metabolic parameters (n = 13,225). Some participants met more than one exclusion criterion, and the final sample yielded 153,342 participants without hypertension at baseline, comprising 85,789 women and 67,553 men.

S2. Data collection and measurement

Current average alcohol consumption per day was assessed using the frequency of alcohol consumption per week and the amount of alcohol consumed per drinking day. Physical activity levels were assessed using the validated Korean version of the International Physical Activity Questionnaire short form [2]. Physical activity levels were categorized into three groups: inactive, minimally active, and health-enhancing physical activity (HEPA) [2]. HEPA was defined as follows: (1) vigorous activity ≥ 3 days/week, with $\geq 1,500$ accumulated metabolic equivalent (MET)-min/week, or (2) a combination of walking and moderate- or vigorous-intensity activities over 7 days for a total of $\geq 3,000$ MET-min/week.

The homeostatic model assessment of insulin resistance (HOMA-IR) index was determined using the following equation: fasting blood insulin (mU/mL) \times fasting blood glucose (mmol/L)/22.5; the cutoff value of 2.5 was used to define insulin resistance [3]. Glycated hemoglobin (HbA1c) levels were measured using a Cobas Integra 800 (Roche Diagnostics, Rotkreuz, Switzerland) with a

turbidimetric inhibition immunoassay for hemolyzed whole blood. The intra- and inter-assay coefficients of variation were 2.3% and 2.4 %, respectively.

Being metabolically healthy was defined as having none of the following metabolic abnormalities [4]: 1) fasting glucose level ≥ 100 mg/dL or current use of glucose-lowering agents, 2) Blood pressure (BP) $\geq 130/80$ mmHg or current use of BP-lowering agents, 3) elevated triglyceride level (≥ 150 mg/dL) or current use of lipid-lowering agents, 4) low high-density lipoprotein-cholesterol (HDL-C) (< 40 mg/dL in men or < 50 mg/dL in women), 5) abdominal obesity (waist circumference ≥ 90 cm for men and ≥ 85 cm for women), or 6) insulin resistance, defined as a HOMA-IR score ≥ 2.5 .

Two noninvasive fibrosis indices were used to further assess NAFLD severity: the Fibrosis-4 Index for Liver Fibrosis (FIB-4) and NAFLD fibrosis score (NFS). The FIB-4 index was calculated using the following formula: $FIB-4 = (\text{age [years]} \times \text{aspartate transaminase [AST; U/L]}) / (\text{platelet count} [\times 10^9/\text{L}] \times \text{alanine aminotransferase [ALT; U/L]}^{1/2})$. The cutoff values of the FIB-4 index were used to define low (FIB-4 < 1.30), intermediate (FIB-4 $1.30-2.67$), and high (FIB-4 ≥ 2.67) probabilities of advanced fibrosis [5]. The NFS was calculated on the basis of the following published formula: $NFS = -1.675 + 0.037 \times \text{age (years)} + 0.094 \times \text{body mass index (BMI; kg/m}^2) + 1.13 \times \text{impaired fasting glycemia or diabetes (yes = 1, no = 0)} + 0.99 \times \text{AST/ALT ratio} - 0.013 \times \text{platelet} (\times 10^9/\text{L}) - 0.66 \times \text{albumin (g/dL)}$. [6] The NFS scores were categorized into three groups: high (NFS > 0.676), intermediate (NFS 0.676 to -1.455), and low (NFS < -1.455) [6].

S3. Supplementary tables

eTable 1. Absolute and relative estimates of stage 2 hypertension incidence for population strata defined by sex and NAFLD status among young adults under the age of 40 years (n = 153,342)

eTable 2. Development of stage 1 hypertension for population strata defined by sex and NAFLD status among young adults under the age of 40 years after further adjustment for HOMA-IR

eTable 3. Development of stage 1 hypertension for population strata defined by sex and NAFLD severity status based on ultrasound among young adults under the age of 40 years after further adjustment for HOMA-IR

eTable 4. Absolute and relative estimates of stage 2 hypertension incidence for population strata defined by sex and NAFLD severity status based on ultrasound among young adults under the age of 40 years (n = 153,342)

eTable 5. Development of stage 1 hypertension by NAFLD status or NAFLD severity based on ultrasound among metabolically healthy young adults under the age of 40 years (n = 91,628)

eTable 6. Development of stage 1 hypertension for population strata defined by sex and NAFLD severity status based on NFS among young adults under the age of 40 years

eTable 7 Development of stage 1 hypertension for population strata defined by sex and NAFLD severity status based on FIB-4 among young adults under the age of 40 years

eTable 1. Absolute and relative estimates of stage 2 hypertension incidence for population strata defined by sex and NAFLD status among young adults under the age of 40 years (n = 153,342)

	Person-years (PY)	Incident cases	Incidence density (/ 10 ³ PY)	Age adjusted HR (95% CI)	Multivariable-adjusted HR ^a (95% CI)	HR (95% CI) ^b in a model with time-dependent variables
Women (n = 85,789)						
No NAFLD	423,216	420	1.0	1.00 (reference)	1.00 (reference)	1.00 (reference)
NAFLD	26,737	135	5.0	4.79 (3.94-5.81)	2.17 (1.75-2.68)	2.06 (1.69-2.51)
Men (n = 67,553)						
No NAFLD	241,449	666	2.8	1.00 (reference)	1.00 (reference)	1.00 (reference)
NAFLD	121,177	765	6.3	2.09 (1.89-2.32)	1.34 (1.19-1.50)	1.47 (1.30-1.65)

The *P*-value for the interaction of sex, menopausal status, and NAFLD status with the risk of hypertension was <0.001 (Multivariable-adjusted model).

^a Estimated from Cox proportional hazards models; multivariable Model 1 was adjusted for age, center, year of screening examination, alcohol consumption, smoking status, physical activity, education level, hyperlipidemia medication, and BMI

^b Estimated from Cox proportional hazard models with NAFLD status, smoking status, alcohol consumption, physical activity, BMI, and hyperlipidemia medication, as time-dependent categorical variables, and baseline age, center, year of screening examination, and education level as time-fixed variables
Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; NAFLD, nonalcoholic fatty liver disease

eTable 2. Development of stage 1 hypertension for population strata defined by sex and NAFLD status among young adults under the age of 40 years after further adjustment for HOMA-IR

	Multivariable-adjusted HR ^a (95% CI)
Women	
No NAFLD	1.00 (reference)
NAFLD	1.64 (1.53-1.76)
Men	
No NAFLD	1.00 (reference)
NAFLD	1.23 (1.19-1.27)

The *P*-value for the interaction of sex and NAFLD status with the risk of hypertension was <0.001 (Multivariable-adjusted model).

^a Estimated from Cox proportional hazards models; multivariable model was adjusted for age, center, year of screening examination, alcohol consumption, smoking status, physical activity, education level, lipid-lowering medication, BMI and HOMA-IR.

Abbreviation: BMI, body mass index; CI, confidence interval; HOMA-IR, homeostatic model for insulin resistance; HR, hazard ratio; NAFLD, nonalcoholic fatty liver disease

eTable 3. Development of stage 1 hypertension for population strata defined by sex and NAFLD severity status based on ultrasound among young adults under the age of 40 years after further adjustment for HOMA-IR

	Multivariable-adjusted HR ^a (95% CI)
Women	
No NAFLD	1.00 (reference)
NAFLD, mild	1.66 (1.55-1.78)
NAFLD, moderate/severe	0.96 (0.64-1.44)
<i>p</i> for trend	<0.001
Men	
No NAFLD	1.00 (reference)
NAFLD, mild	1.23 (1.19-1.27)
NAFLD, moderate/severe	1.17 (1.02-1.33)
<i>p</i> for trend	<0.001

The *P*-value for the interaction of sex and NAFLD status with the risk of hypertension was <0.001 (Multivariable-adjusted model).

^a Estimated from Cox proportional hazards models; multivariable model was adjusted for age, center, year of screening examination, alcohol consumption, smoking status, physical activity, education level, lipid-lowering medication, BMI and HOMA-IR.

Abbreviation: BMI, body mass index; CI, confidence interval; HOMA-IR, homeostatic model for insulin resistance; HR, hazard ratio; NAFLD, nonalcoholic fatty liver disease

eTable 4. Absolute and relative estimates of stage 2 hypertension incidence for population strata defined by sex and NAFLD severity status based on ultrasound among young adults under the age of 40 years (n = 153,342)

	Person-years (PY)	Incident cases	Incidence density (/ 10 ³ PY)	Age adjusted HR (95% CI)	Multivariable-adjusted HR ^a (95% CI)	HR (95% CI) ^b in a model with time-dependent variables
Women (n = 85,789)						
No NAFLD	423,216	420	1.0	1.00 (reference)	1.00 (reference)	1.00 (reference)
NAFLD, mild	23,696	107	4.5	4.21 (3.41-5.21)	2.12 (1.69-2.66)	2.01 (1.63-2.48)
NAFLD, moderate/severe	3,041	28	9.2	9.90 (6.75-14.51)	2.62 (1.73-3.97)	2.45 (1.73-3.45)
<i>P</i> for trend				< 0.001	< 0.001	< 0.001
Men (n = 67,553)						
No NAFLD	241,449	666	2.8	1.00 (reference)	1.00 (reference)	1.00 (reference)
NAFLD, mild	97,828	568	5.8	1.90 (1.70-2.13)	1.32 (1.17-1.49)	1.45 (1.28-1.64)
NAFLD, moderate/severe	23,349	197	8.4	2.93 (2.50-3.44)	1.45 (1.21-1.72)	1.55 (1.31-1.82)
<i>P</i> for trend				< 0.001	< 0.001	< 0.001

The *P* value for the interaction of sex and NAFLD categories for the risk of hypertension was <0.001 (Multivariable-adjusted model).

^a Estimated from Cox proportional hazards models; multivariable model was adjusted for age, center, year of screening examination, alcohol consumption, smoking status, physical activity, education level, lipid-lowering medication, and BMI.

^b Estimated from Cox proportional hazard models with NAFLD categories, smoking, alcohol consumption, physical activity, BMI, medication for lipid-lowering as time-dependent categorical variables and baseline age, center, year of screening examination, and education level as time-fixed variables.

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; NAFLD, nonalcoholic fatty liver disease

eTable 5. Development of stage 1 hypertension by NAFLD status or NAFLD severity based on ultrasound among metabolically healthy young adults under the age of 40 years (n = 91,628)

	Multivariable-adjusted HR ^a (95% CI)		<i>P</i> for interaction
	Among metabolically healthy young women (n = 64,412)	Among metabolically healthy young men (n = 27,216)	
By NAFLD			<0.001
No NAFLD	1.00 (reference)	1.00 (reference)	
NAFLD	1.64 (1.40-1.92)	1.22 (1.14-1.31)	
By NAFLD severity			<0.001
No NAFLD	1.00 (reference)	1.00 (reference)	
NAFLD, mild	1.62 (1.38-1.90)	1.22 (1.14-1.32)	
NAFLD, moderate/severe	2.26 (1.01-5.04)	1.21 (0.96-1.53)	
<i>P</i> for trend	< 0.001	< 0.001	

^a Estimated from Cox proportional hazards models; multivariable Model 1 was adjusted for age, center, year of screening examination, alcohol consumption, smoking status, physical activity, education level, hyperlipidemia medication, and BMI
Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; NAFLD, nonalcoholic fatty liver disease

eTable 6. Development of stage 1 hypertension for population strata defined by sex and NAFLD severity status based on NFS among young adults under the age of 40 years

	Person-years (PY)	Incident cases	Incidence density (/ 10 ³ PY)	Multivariable-adjusted HR ^a (95% CI)
Women				
No NAFLD	408,384.8	5,691	13.9	1.00 (reference)
NAFLD, low NFS	23,403.5	1,010	43.2	1.63 (1.51-1.76)
NAFLD, intermediate / high NFS	561.8	24	42.7	1.73 (1.48-2.03)
<i>p</i> for trend				<0.001
Men				
No NAFLD	208,576.0	10,727	51.4	1.00 (reference)
NAFLD, low NFS	91,121.4	8,194	89.9	1.46 (1.38-1.54)
NAFLD, intermediate / high NFS	1,944.8	233	119.8	1.16 (1.13-1.18)
<i>p</i> for trend				<0.001

The *P*-value for the interaction of sex and NAFLD status with the risk of hypertension was <0.001 (Multivariable-adjusted model).

^a Estimated from Cox proportional hazards models; multivariable model was adjusted for age, center, year of screening examination, alcohol consumption, smoking status, physical activity, education level, lipid-lowering medication, and BMI.

Abbreviation: BMI, body mass index; CI, confidence interval; HR, hazard ratio; NAFLD, nonalcoholic fatty liver disease; NFS, NAFLD fibrosis score

eTable 7 Development of stage 1 hypertension for population strata defined by sex and NAFLD severity status based on FIB-4 score among young adults under the age of 40 years

	Person-years (PY)	Incident cases	Incidence density (/ 10 ³ PY)	Multivariable-adjusted HR ^a (95% CI)
Women				
No NAFLD	408,384.8	5,691	13.9	1.00 (reference)
NAFLD, low FIB-4	23,815.9	1,027	43.1	1.64 (1.53-1.76)
NAFLD, intermediate / high FIB-4	149.4	7	46.9	1.59 (0.76-3.33)
<i>p</i> for trend				<0.001
Men				
No NAFLD	208,576.0	10,727	51.4	1.00 (reference)
NAFLD, low FIB-4	92,190.1	8,345	80.5	1.23 (1.19-1.27)
NAFLD, intermediate / high FIB-4	879.3	83	94.4	1.19 (0.96-1.47)
<i>p</i> for trend				<0.001

The *P*-value for the interaction of sex and NAFLD status with the risk of hypertension was <0.001 (Multivariable-adjusted model).

^a Estimated from Cox proportional hazards models; multivariable model was adjusted for age, center, year of screening examination, alcohol consumption, smoking status, physical activity, education level, lipid-lowering medication, and BMI.

Abbreviation: BMI, body mass index; CI, confidence interval; FIB-4, fibrosis-4 index; HR, hazard ratio; NAFLD, nonalcoholic fatty liver disease

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