Original Article

Comparative associations of non-alcoholic fatty liver disease and metabolic dysfunction-associated steatotic liver disease with risk of incident chronic kidney disease: a cohort study

Ji Hye Heo[1]^, Mi Yeon Lee[2], Seong Hwan Kim[3], Ming-Hua Zheng[4,5,6,7], Christopher D. Byrne[8,9], Giovanni Targher[10], Ki-Chul Sung[11]

[1]Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, Republic of Korea; [2]Division of Biostatistics, Department of R&D Management, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [3]Division of Cardiology, Department of Internal Medicine, Korea University Ansan Hospital, Ansan, Republic of Korea; [4]MAFLD Research Center, Department of Hepatology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China; [5]Wenzhou Key Laboratory of Hepatology, Wenzhou, China; [6]Institute of Hepatology, Wenzhou Medical University, Wenzhou, China; [7]Key Laboratory of Diagnosis and Treatment for the Development of Chronic Liver Disease in Zhejiang Province, Wenzhou, China; [8]Nutrition and Metabolism, Faculty of Medicine, University of Southampton, Southampton, UK; [9]Southampton National Institute for Health and Care Research, Biomedical Research Centre, University Hospital Southampton, Southampton, UK; [10]Metabolic Diseases Research Unit, IRCCS Sacro Cuore-Don Calabria Hospital, Negrar di Valpolicelle, Italy; [11]Division of Cardiology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Contributions: (I) Conception and design: KC Sung; (II) Administrative support: JH Heo; (III) Provision of study materials or patients: KC Sung; (IV) Collection and assembly of data: MY Lee; (V) Data analysis and interpretation: MY Lee; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Ki-Chul Sung, MD, PhD. Division of Cardiology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 29, Saemunan-ro, Jongno-gu, Seoul 03181, Republic of Korea. Email: kcmd.sung@samsung.com; Ji Hye Heo, MD, PhD. Department of Internal Medicine, Hallym University College of Medicine, 1, Hallymdaehak-gil, Chuncheon 24252, Republic of Korea. Email: jihyeheo02@gmail.com.

Background: We examined the comparative associations between non-alcoholic fatty liver disease (NAFLD) and metabolic dysfunction-associated steatotic liver disease (MASLD) definitions with risk of developing chronic kidney disease (CKD) and abnormal albuminuria.

Methods: We conducted a cohort study of 214,145 Korean adults with normal kidney function at baseline who underwent liver ultrasonography. Participants were further subdivided into no steatotic liver disease (no-SLD), NAFLD-only, MASLD-only, both NAFLD and MASLD, and SLD not categorized as NAFLD or MASLD groups. Cox proportional hazards models were used to analyze the risk of incident CKD and albuminuria.

Results: Compared with either the no-NAFLD or no-MASLD groups, the NAFLD and MASLD groups were associated with a higher risk of incident CKD (NAFLD: adjusted hazard ratio (HR), 1.18 [95% CI, 1.01-1.38]; MASLD: adjusted HR, 1.21 [95% CI, 1.04-1.39]). Among the five subgroups, both NAFLD and MASLD group had the strongest association with risk of incident CKD (adjusted HR, 1.21 [95% CI, 1.04-1.42]). The MASLD-only group had the strongest association with incident abnormal albuminuria, with an adjusted HR comparable to that of the both NAFLD and MASLD group (adjusted HR 1.96 [95% CI, 1.44-2.67] for the MASLD-only, and adjusted HR 1.98 [95% CI, 1.58-2.49] for the both NAFLD and MASLD group versus the no-SLD group). The NAFLD-only group was not independently associated with risk of CKD or abnormal albuminuria.

Conclusions: These findings suggest that MASLD definition identifies individuals at high risk of

^ ORCID: 0000-0001-5445-8007.

developing incident CKD or abnormal albuminuria better than NAFLD definition.

Keywords: Metabolic dysregulation; non-alcoholic fatty liver disease (NAFLD); metabolic syndrome; chronic kidney disease (CKD); albuminuria

Submitted Oct 26, 2023. Accepted for publication Mar 13, 2024. Published online Jun 14, 2024.
doi: 10.21037/hbsn-23-558
View this article at: https://dx.doi.org/10.21037/hbsn-23-558

Introduction

Background

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common cause of chronic liver disease worldwide, affecting up to ~30% of the general adult population (1-3). MASLD includes a spectrum of progressive liver conditions spanning from simple hepatic steatosis to steatohepatitis, advanced fibrosis, and cirrhosis (4,5). MASLD is strongly associated with greater insulin resistance, increased adiposity, and type 2 diabetes mellitus (T2DM), which may contribute to an increased risk of developing adverse hepatic and extra-hepatic clinical outcomes (4). In particular, MASLD is considered as a multisystem disease that is associated with an increased risk of developing chronic kidney disease (CKD) (6), cardiovascular disease (CVD) (7-9), T2DM (10), and even some extra-hepatic malignancies.

CKD is a major public health problem (affecting up to nearly 15% of the general adult population), and its global incidence is expected to further increase in the future (11). CKD is an established risk factor for CVD, and all CKD stages are associated with an increased risk of CVD events and mortality (12). Moreover, as CKD develops, it can lead to end-stage kidney disease requiring renal replacement therapy, and result in premature death (12). Therefore, identifying novel and modifiable risk factors for CKD is clinically important for reducing its long-term prognostic impact.

Rationale and knowledge gap

The recent terminology change from non-alcoholic fatty liver disease (NAFLD) to MASLD has been proposed to better emphasize the contribution of metabolic dysregulation in the pathophysiology of this common liver disease and its systemic adverse effects on liver-related and extra-hepatic outcomes (including CKD) (5,13). To date, NAFLD definition is diagnosed by excluding significant alcohol consumption and other competing causes of hepatic steatosis. In contrast, the newly proposed MASLD definition has its specific and positive diagnostic criteria (based on the presence of hepatic steatosis and coexisting metabolic dysfunction), and does not exclude a priori other competing causes of hepatic steatosis. Thus, since the diagnostic criteria for NAFLD and MASLD are not superimposable, some observational cohort studies have recently assessed the concordance (or even the superiority) of MASLD definition in identifying individuals at higher risk of all-cause mortality as well as fatal and nonfatal CVD events, compared with NAFLD definition (9,14,15). Currently, it is uncertain whether the MASLD definition identifies individuals who develop incident CKD more

Highlight box

Key findings
- This study revealed that both non-alcoholic fatty liver disease (NAFLD) and metabolic dysfunction-associated steatotic liver disease (MASLD) were associated with a higher risk of incident chronic kidney disease (CKD), with MASLD showing a slightly stronger association in relatively healthy middle-aged Korean adults.
- The MASLD had strong association with incident abnormal albuminuria while the NAFLD-only group was not independently associated with CKD or abnormal albuminuria.

What is known and what is new?
- The recently proposed MASLD has been suggested as a more accurate representation of the metabolic aspects of fatty liver disease when compared to NAFLD.
- Currently, it is uncertain whether the MASLD definition identifies individuals who develop incident CKD more accurately than the NAFLD definition.

What is the implication, and what should change now?
- Our findings suggest that the MASLD definition is more effective in identifying individuals at high risk of developing CKD or abnormal albuminuria compared to the NAFLD definition.

accurately than the NAFLD definition.

Objective

Therefore, in this large cohort study of South Korean apparently healthy adults undergoing health screening examinations, we examined the comparative associations between NAFLD and MASLD definitions and risk of developing incident CKD (stage ≥3) or abnormal albuminuria. We present this article in accordance with the STROBE reporting checklist (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-558/rc).

Methods

Kangbuk Samsung Health Study cohort study

This is a cohort study of Korean individuals aged 18 years and older who received annual or biannual comprehensive health checkups at the Kangbuk Samsung Hospital Health Checkup Centers in South Korea (16). All study participants who underwent thorough physical examinations at least twice between January 1, 2011, and December 31, 2018, as well as those who had at least one additional follow-up visit before December 31, 2020, were initially included in the current analysis (n=258,388). Then, we excluded 44,243 participants who had 1 or more exclusion criteria, as specified in Figure S1. Finally, a total of 214,145 participants with normal kidney function at baseline were included in the current study. This study was approved by the Institutional Review Board (IRB) of Kangbuk Samsung Hospital (Institutional Review Board No.: 2022-06-039) and the requirement for written informed consent was waived by the IRB because anonymous and de-identified information was used for the analyses. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Data collection and definition of outcomes

A standardized, self-administered questionnaire was used to gather information on demographic factors, family history, health practices, and medical history. During examinations, trained staff members performed anthropometric measures and blood sampling. An enzymatic colorimetric assay was used to measure fasting plasma glucose and lipid levels. A particle-enhanced immunoturbidimetric assay on a Modular Analytics P800 apparatus (Roche Diagnostics, Tokyo, Japan) was used to measure serum high-sensitivity C-reactive protein (hs-CRP). Fasting insulin was measured using an electrochemiluminescence immunoassay (Roche Diagnostics). Insulin resistance was estimated using the homeostasis model assessment [homeostatic model assessment of insulin resistance (HOMA-IR) score] as follows: fasting plasma insulin (IU/mL) × fasting glucose (mg/dL)/405. Serum creatinine was measured using the Jaffè method on an automated chemistry analyzer (Modular D2400, Roche, Tokyo, Japan). During the study period, the within-batch and overall coefficients of variation for the low- and high-quality control samples were 1.8% to 3.9% and 1.4% to 1.8%, respectively (17). In all participants, we calculated estimated glomerular filtration rate (eGFR) using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation (18). Incident CKD (stage ≥3) was defined as occurrence of eGFR <60 mL/min/1.73 m^2 over the follow-up period (19). Urine albumin and creatinine were measured with the quantitative Tina-quant Albumin Gen.2 and COBAS INTEGRA Creatinine Jaffe Gen.2 (Roche Diagnostics, Basel, Switzerland) using a quantitative analyzer, Cobas Integra 800. Urine albumin was measured using an immunoturbidimetric method and its analytical range was 3.0–210.0 mg/L. Urine creatinine was quantitated using the Jaffè-kinetic method, and its analytical range was 0.31–367 mg/dL. Specimens showing concentrations above the analytical measurement limits were repeatedly measured after 1:10 dilution with normal saline (20). Incident abnormal albuminuria was defined as occurrence of urinary albumin-to-creatinine ratio (ACR) ≥30 mg/g over the follow-up period.

Definitions of MASLD and NAFLD

For the diagnosis of MASLD and NAFLD, we used standard definitions (5,13). All participants underwent liver ultrasonography using a 3.5 MHz probe, and the presence of fatty liver was based on typical ultrasonographic features, such as hepatorenal echo contrast, liver brightness, or vascular blurring (21). MASLD was diagnosed by the coexistence of hepatic steatosis on ultrasonography with one or more of the following three metabolic conditions: overweight or obesity [defined as a body mass index (BMI) of 23 kg/m^2] (22), T2DM, or metabolic dysfunction defined by the presence of at least two of seven metabolic risk factors (i.e., a waist circumference ≥90 cm for men and ≥80 cm

for women; a serum triglyceride level ≥150 mg/dL; a high-density lipoprotein (HDL) cholesterol level <40 mg/dL in men or <50 mg/dL in women; systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or use of any anti-hypertensive medications; prediabetes status based on fasting glucose levels between 100 and 125 mg/dL or hemoglobin A1c between 5.7% and 6.4%; a HOMA-IR score ≥2.5, or a plasma hs-CRP level ≥0.2 mg/dL (5,9). Participants who did not meet these MASLD criteria were classified as having no-MASLD. Participants were considered to have NAFLD if they had evidence of hepatic steatosis on liver ultrasonography in the absence of significant alcohol consumption (conventionally defined as >30 g/day for men and >20 g/day for women) and other coexisting liver diseases, such as hepatitis B or C infections, which were detected by hepatitis B surface antigen and hepatitis C antibody tests. Participants were categorized as belonging to the no-NAFLD group if they had SLD but they did not meet the NAFLD criteria. Subsequently, participants were categorized into five subgroups according to their baseline SLD status to compare the risk of developing incident CKD or abnormal albuminuria as follows: the no-SLD group (i.e., the reference category); the NAFLD-only group; the MASLD-only group; the both NAFLD and MASLD group; the SLD group not categorized as NAFLD or MASLD, respectively.

Statistical analysis

Baseline characteristics of the study participants are expressed as means ± standard deviation (SD) for continuous variables and numbers (percentages) for categorical variables. The independent *t*-test and one-way analysis of variance were used to compare the continuous variables between the groups. The chi-square test was used to compare the categorical variables. The cumulative incidence rates of CKD and abnormal albuminuria were estimated by the Kaplan-Meier method. We performed Cox proportional hazards models to study the independent associations of MASLD, NAFLD or different SLD categories at baseline (as specified above) with the risk of developing incident CKD stage ≥3 (i.e., eGFR <60 mL/min/1.73 m^2) or abnormal albuminuria (ACR ≥30 mg/g) after adjustment for potential confounding factors. The two progressive multivariable-adjusted models used were as follows: model 1 was adjusted for age, sex, education level, smoking history, and regular exercise (≥3×/week, defined as a total of 75 min per week engaging in vigorous physical activities or 150 min per week of moderate physical activities), daily alcohol intake, prior history of coronary artery disease, and use of any anti-hypertensive medications (modelled as time-varying variable); and model 2 was further adjusted for eGFR levels at baseline in addition to the model 1's covariates.

Results

Baseline characteristics of the study participants

The study included 214,145 participants, consisting of 130,984 (61.2%) men and 83,161 (38.8%) women, with a mean age of 37.9±7.4 years. The median follow-up duration was 6.1 years, and the mean follow-up duration was 6.1±2.1 years. Of all study participants, 48,175 (22.50%) had NAFLD, and 57,785 (26.98%) had MASLD. *Table 1* summarizes the baseline characteristics of the study participants, grouped by their SLD status. At baseline, 44,254 (20.7% of total) participants met both NAFLD and MASLD definitions (belonging to the both NAFLD and MASLD group), 13,531 (6.3%) were classified as having MASLD-only, while 3,921 (1.8%) were classified as having NAFLD-only. A total of 680 (0.32%) participants were defined as SLD not categorized as NAFLD or MASLD. By either definition, participants with SLD were older, and more likely to be men and current smokers than those without SLD. Furthermore, individuals belonging to the MASLD-only group had higher adiposity measures (BMI and waist circumference), blood pressure, fasting glucose, HbA1c, HOMA-IR, and plasma lipids than individuals without SLD or those with NAFLD alone. The prevalence of T2DM, hypertension, and dyslipidemia was also higher in the MASLD-only group. The proportion of high alcohol intake was the highest in the SLD not categorized as NAFLD or MASLD group.

Risk of incident CKD stage ≥3 according to different steatotic liver disease categories at baseline

In *Table 2*, we examined the associations between each baseline SLD category and the risk of incident CKD stage ≥3 (defined as the occurrence of eGFR <60 mL/min/1.73 m^2). During a median follow-up of 6.1 years, 829 (0.39%) individuals developed incident CKD stage ≥3. When the participants were subdivided into the no-MASLD and MASLD groups, patients with MASLD had a higher risk of developing incident CKD even after adjusting

Table 1 Baseline characteristics of the study participants stratified by different steatotic liver disease status

Variables	No-SLD (n=151,759, 70.87%)	NAFLD-only (n=3,921, 1.83%)	MASLD-only (n=13,531, 6.32%)	Both NAFLD and MASLD (n=44,254, 20.67%)	SLD not categorized as NAFLD or MASLD (n=680, 0.32%)	P value
Age (years)	37.2±7.26	38.14±6.95	40.3±7.14	39.65±7.6	39.09±7.02	<0.001
Male	77,001 (50.74)	2,881 (73.48)	12,922 (95.50)	37,599 (84.96)	581 (85.44)	<0.001
Current smoker	28,498 (18.78)	875 (22.32)	6,372 (47.09)	13,099 (29.60)	286 (42.06)	<0.001
High alcohol intake[†]	20,528 (13.53)	0 (0.00)	12,067 (89.18)	0 (0.00)	547 (80.44)	<0.001
Higher education level	113,262 (74.63)	3,066 (78.19)	10,008 (73.96)	33,960 (76.74)	511 (75.15)	<0.001
BMI (kg/m^2)	22.25±2.7	21.77±1.04	26.77±2.74	26.39±2.8	21.89±1.03	<0.001
Waist circumference (cm)	78.37±8.02	79.1±4.72	91.52±7.06	89.88±7.28	79.84±4.55	<0.001
Systolic BP (mmHg)	108.32±12.46	108.93±10.4	119.78±12	117.21±11.91	111.56±10.88	<0.001
Diastolic BP (mmHg)	68.99±9.22	69.67±7.99	77.78±9.53	75.34±9.21	72.06±8.4	<0.001
Fasting glucose (mg/dL)	92.07±10.03	92.19±7.25	102.37±20.2	99.21±17.61	92.8±7.76	<0.001
Hemoglobin A1c (%)	5.53±0.32	5.52±0.24	5.78±0.67	5.76±0.61	5.47±0.25	<0.001
HOMA-IR score	1 (0.68–1.44)	1.11 (0.8–1.52)	1.8 (1.25–2.6)	1.76 (1.22–2.54)	1.06 (0.71–1.49)	<0.001
ALT (U/L)	16 (12–22)	21 (15–30)	32 (23–47)	30 (21–45)	23 (17–32.5)	<0.001
AST (U/L)	19 (16–23)	20 (17–24)	26 (21–33)	24 (19–30)	22 (19–28)	<0.001
GGT (U/L)	17 (12–27)	22 (16–33)	53 (34–84)	35 (24–54)	31 (22–50)	<0.001
Triglycerides (mg/dL)	80 (59–111)	97 (73–125)	157 (112–222)	142 (103–197)	101 (77–135.5)	<0.001
HDL-cholesterol (mg/dL)	61.57±14.64	56.08±11.91	49.51±11.32	47.86±10.56	59.53±13.57	<0.001
LDL-cholesterol (mg/dL)	113.38±29.37	125.25±30.97	133.54±32.56	134.7±31.62	121.69±31.01	<0.001
Total cholesterol (mg/dL)	188.96±31.76	196.96±33.26	209.26±36.34	206.86±35.12	198.25±32.56	<0.001
Lipid-lowering medications	1,758 (1.16)	50 (1.28)	641 (4.74)	1,858 (4.20)	9 (1.32)	<0.001
hs-CRP (mg/dL)	0.04 (0.02–0.07)	0.04 (0.03–0.07)	0.08 (0.05–0.14)	0.08 (0.04–0.15)	0.04 (0.03–0.07)	<0.001
Type 2 diabetes	1,957 (1.29)	0 (0.00)	1,326 (9.80)	3,453 (7.80)	0 (0.00)	<0.001
Hypertension	10,006 (6.59)	138 (3.52)	3,589 (26.52)	8,340 (18.85)	37 (5.44)	<0.001
History of CAD	691 (0.46)	21 (0.54)	108 (0.80)	345 (0.78)	1 (0.15)	<0.001
History of dyslipidemia	10,574 (6.97)	420 (10.71)	3,202 (23.66)	9,037 (20.42)	86 (12.65)	<0.001
Regular exercise	19,897 (13.11)	370 (9.44)	1,642 (12.14)	4,983 (11.26)	68 (10.00)	<0.001
eGFR (mL/min/1.73 m^2)	103.54±13.56	101.74±12.7	98.18±12.86	98.47±13.24	101.37±12.31	<0.001
Urinary ACR (mg/g)	4.17 (2.92–6.49)	3.98 (2.9–6.22)	4.18 (2.79–7.43)	4.55 (3.04–7.66)	3.69 (2.65–4.86)	<0.001

Cohort size (n=214,145). Data are expressed as means ± SD, medians (interquartile ranges), or n (%). [†], high alcohol intake was defined as >30 g/day in men and >20 g/day in women, respectively. SLD, steatotic liver disease; NAFLD, non-alcoholic fatty liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease; BMI, body mass index; BP, blood pressure; HOMA-IR, homeostatic model assessment of insulin resistance; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; ACR, albumin-to-creatinine ratio; SD, standard deviation.

Table 2 Associations between MASLD or NAFLD status (or different SLD groups) at baseline and risk of developing incident chronic kidney disease (stage ≥3)

Status of liver steatosis	PY	Event	Incident rate (10^4 PY), (95% CI)	Model 1	Model 2
According to the presence or absence of NAFLD or MASLD					
No-MASLD (n=156,360)	944,550.12	432	4.57 (4.16–5.03)	1.0 (reference)	1.0 (reference)
MASLD (n=57,785)	350,981.42	397	11.31 (10.25–12.48)	1.36 (1.17–1.57)	1.21 (1.04–1.39)
No-SLD (n=151,759)	916,334.73	427	4.66 (4.24–5.12)	1.0 (reference)	1.0 (reference)
NAFLD (n=48,175)	294,667.40	323	10.96 (9.83–12.22)	1.35 (1.15–1.57)	1.18 (1.01–1.38)
SLD not categorized as NAFLD (n=14,211)	84,529.41	79	9.35 (7.50–11.65)	1.06 (0.82–1.36)	1.07 (0.83–1.39)
According to different SLD subgroups					
No-SLD (n=151,759)	916,334.73	427	4.66 (4.24–5.12)	1 (reference)	1.0 (reference)
NAFLD-only (n=3,921)	24,087.54	4	1.66 (0.62–4.42)	0.36 (0.13–0.97)	0.45 (0.17–1.20)
MASLD-only (n=13,531)	80,401.56	78	9.7 (7.77–12.11)	1.09 (0.84–1.41)	1.09 (0.85–1.41)
Both NAFLD and MASLD (n=44,254)	270,579.86	319	11.79 (10.56–13.16)	1.4 (1.20–1.64)	1.21 (1.04–1.42)
SLD not categorized as NAFLD or MASLD (n=680)	4,127.85	1	2.42 (0.34–17.2)	0.38 (0.05–2.72)	0.52 (0.07–3.70)

Cohort size, n=214,145. CKD stage ≥3 was defined as occurrence of eGFR <60 mL/min/1.73 m^2 (as estimated by using the CKD-EPI equation). Model 1: adjusted for age, sex, education level, smoking status, regular exercise (3 times/week), alcohol intake, and prior history of coronary artery disease, and use of any anti-hypertensive medications (as time-varying variable). Model 2: adjusted for age, sex, education level, smoking history, regular exercise (3 times/week), alcohol intake, prior history of coronary artery disease, use of any anti-hypertensive medications (as time-varying variable), and levels of eGFR at baseline. MASLD, metabolic dysfunction-associated steatotic liver disease; NAFLD, non-alcoholic fatty liver disease; SLD, steatotic liver disease; PY, person years; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; EPI, Epidemiology Collaboration.

for potential confounding factors including also baseline eGFR levels, compared to the no-MASLD group [adjusted model 2: hazard ratio (HR) =1.21; 95% confidence interval (CI): 1.04–1.39]. Furthermore, when participants were subdivided into the no-SLD, the NAFLD, and the SLD not categorized as NAFLD groups, only the NAFLD group was significantly associated with a higher risk of developing incident CKD, compared to the no-SLD group (adjusted model 2: HR =1.18; 95% CI: 1.01–1.38).

When the study participants were subdivided into five groups according to their SLD status at baseline (as also shown in *Table 2*), the both NAFLD and MASLD group was significantly associated with a higher risk of developing incident CKD compared with the no-SLD group (adjusted model 2: HR =1.21; 95% CI: 1.04–1.42), even after adjusting for potential confounders. The MASLD-only group also tended to have a higher risk of incident CKD than the no-SLD group, although the HR did not achieve statistical significance (adjusted model 2: HR =1.09; 95% CI: 0.85–1.41). Conversely, the NAFLD-only group was not independently associated with the risk of incident CKD compared with the no-SLD group (adjusted model 2: HR =0.45; 95% CI: 0.17–1.20). When we analyzed the risk of CKD according to SLD status by sex, we found the same pattern as the result of the total study population for both sexes (Table S1).

As shown in *Figure 1*, the cumulative incidence rates of CKD stage ≥3 were significantly greater in participants with SLD by either definition than in those with no-SLD. When participants were categorized by the combination of the two criteria, the cumulative incidence rates of CKD were the highest in the both NAFLD and MASLD group, followed by the MASLD-only group, and then the other groups (being the lowest risk observed in the NAFLD-only group).

Risk of incident abnormal albuminuria according to different steatotic liver disease categories at baseline

We examined the associations between each baseline category of SLD and the risk of developing abnormal albuminuria (defined as occurrence of urinary ACR ≥30 mg/g) in a subset of individuals who had data on

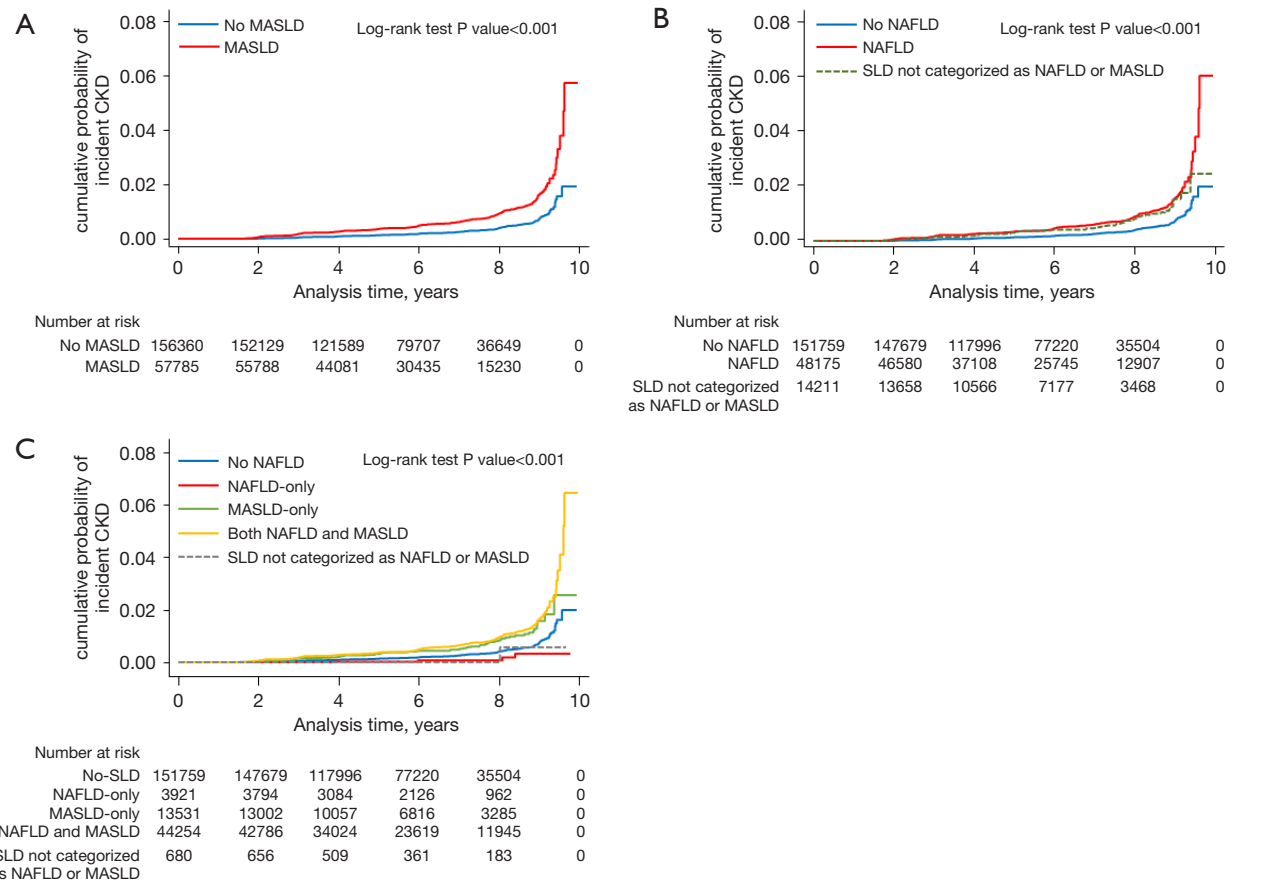

Figure 1 Cumulative incidence rates of chronic kidney disease stage ≥3 by Kaplan-Meier methods according to presence and combination of NAFLD and/or MASLD. MASLD, metabolic dysfunction-associated steatotic liver disease; CKD, chronic kidney disease; NAFLD, non-alcoholic fatty liver disease; SLD, steatotic liver disease.

albuminuria both at baseline and at follow-up (n=8,322) (*Table 3*). During the follow-up period, 876 (10.5%) subjects developed incident abnormal albuminuria. When the participants were subdivided into the no-MASLD and MASLD groups, multivariable Cox proportional hazards analyses showed that MASLD was associated with a 1.98-fold increase in the risk of developing incident abnormal albuminuria after adjusting for potential confounders (adjusted model 2: HR =1.98; 95% CI: 1.61–2.44 versus the no-MASLD group). When the participants were categorized into the no-SLD, NAFLD, and SLD not categorized as NAFLD groups, both the NAFLD group and the SLD not categorized as NAFLD group were associated with a higher risk of developing incident abnormal albuminuria, compared with the no-SLD group (adjusted model 2: HR =1.93; 95% CI: 1.54–2.41 for the NAFLD group, and HR =1.89; 95% CI: 1.39–2.57 for the SLD not categorized as NAFLD group versus the no-SLD group).

When the study participants were subdivided into five subgroups according to their SLD status at baseline (as also shown in *Table 3*), the MASLD-only group and the both NAFLD and MASLD group were associated with the highest risks of developing abnormal albuminuria compared with the no-SLD group (adjusted model 2: HR =1.96; 95% CI: 1.44–2.67 for the MASLD-only group and HR =1.98; 95% CI: 1.58–2.49 for the both NAFLD and MASLD group versus the no-SLD group). When we analyzed the risk of developing abnormal albuminuria according to SLD status by sex, we found the same pattern as the result of the total study population for both sexes (Table S2).

The cumulative incidence rates of abnormal albuminuria were significantly greater in participants with SLD by either definition than in those without (*Figure 2*). When participants

Table 3 Associations between MASLD or NAFLD status (or different SLD groups) at baseline and risk of developing incident abnormal albuminuria

Status of liver steatosis	PY	Event	Incident rate (10^4 PY), (95% CI)	Model 1	Model 2
According to the presence or absence of NAFLD or MASLD					
No-MASLD (n=5,729)	22,068.65	214	0.97 (0.85–1.11)	1.0 (reference)	1.0 (reference)
MASLD (n=2,593)	10,828.90	224	2.07 (1.81–2.36)	1.97 (1.6–2.42)	1.98 (1.61–2.44)
No-SLD (n=5,536)	21,402.62	209	0.98 (0.85–1.12)	1.0 (reference)	1.0 (reference)
NAFLD (n=2,006)	8,168.70	163	2 (1.71–2.33)	1.91 (1.53–2.39)	1.93 (1.54–2.41)
SLD not categorized as NAFLD (n=780)	3,326.23	66	1.98 (1.56–2.53)	1.89 (1.39–2.56)	1.89 (1.39–2.57)
According to different SLD subgroups					
No-SLD (n=5,536)	21,402.62	209	0.98 (0.85–1.12)	1.0 (reference)	1.0 (reference)
NAFLD-only (n=153)	493.14	4	0.81 (0.3–2.16)	1.02 (0.38–2.75)	1.02 (0.38–2.75)
MASLD-only (n=740)	3,153.33	65	2.06 (1.62–2.63)	1.96 (1.44–2.67)	1.96 (1.44–2.67)
Both NAFLD & MASLD (n=1,853)	7,675.56	159	2.07 (1.77–2.42)	1.97 (1.57–2.47)	1.98 (1.58–2.49)
SLD not categorized as NAFLD or MASLD (n=40)	172.90	1	0.58 (0.08–4.11)	0.68 (0.09–4.84)	0.67 (0.09–4.81)

Cohort size, n=8,322. Abnormal albuminuria was defined as occurrence of urine ACR ≥30 mg/g. Model 1: adjusted for age, sex, education level, smoking status, regular exercise (3 times/week), alcohol intake, and prior history of coronary artery disease, and use of any anti-hypertensive medications (as time-varying variable). Model 2: adjusted for age, sex, education level, smoking history, regular exercise (3 times/week), alcohol intake, prior history of coronary artery disease, use of any anti-hypertensive medications (as time-varying variable), and levels of eGFR at baseline. MASLD, metabolic dysfunction-associated steatotic liver disease; NAFLD, non-alcoholic fatty liver disease; SLD, steatotic liver disease; PY, person years; CI, confidence interval; ACR, albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate.

were categorized by the combination of the two criteria, the cumulative incidence rates of abnormal albuminuria were the highest in the MASLD-only group, followed by the both NAFLD and MASLD group, and then the no-SLD group, the NAFLD-only group, and the SLD not categorized as NAFLD or MASLD group, in that order.

Discussion

In this large-scale retrospective longitudinal cohort study, including 214,145 Korean adult individuals with normal kidney function at baseline, we assessed the comparative associations between NAFLD and MASLD definitions with the risk of developing incident CKD (stage ≥3) or abnormal albuminuria. Our results showed that individuals with MASLD or NAFLD had a significantly higher risk of developing incident CKD and abnormal albuminuria over a median follow-up of 6.1 years. This risk remained significant even after adjusting for multiple potential confounding factors, such as age, sex, education level, smoking, regular exercise, alcohol intake, prior history of CAD, use of any anti-hypertensive medications (modelled as time-varying variable), and baseline levels of eGFR. In addition, and most importantly, when the study participants were subdivided into five subgroups according to their SLD status at baseline, patients with NAFLD without coexisting metabolic abnormalities at baseline (i.e., the NAFLD-only group) did not have any significant risk of developing incident CKD or abnormal albuminuria, while those with MASLD alone had a significantly higher risk of developing kidney dysfunction (especially abnormal albuminuria) during the follow-up period. The risk of developing incident CKD or abnormal albuminuria was an even greater among participants who had both NAFLD and MASLD at baseline (i.e., the both NAFLD and MASLD group). Collectively, these findings indicate that MASLD definition can identify individuals at high risk of developing incident CKD or abnormal albuminuria better than NAFLD definition.

Using the NAFLD definition, previous published studies have repeatedly reported that NAFLD is associated with an increased prevalence and incidence of CKD (23-26).

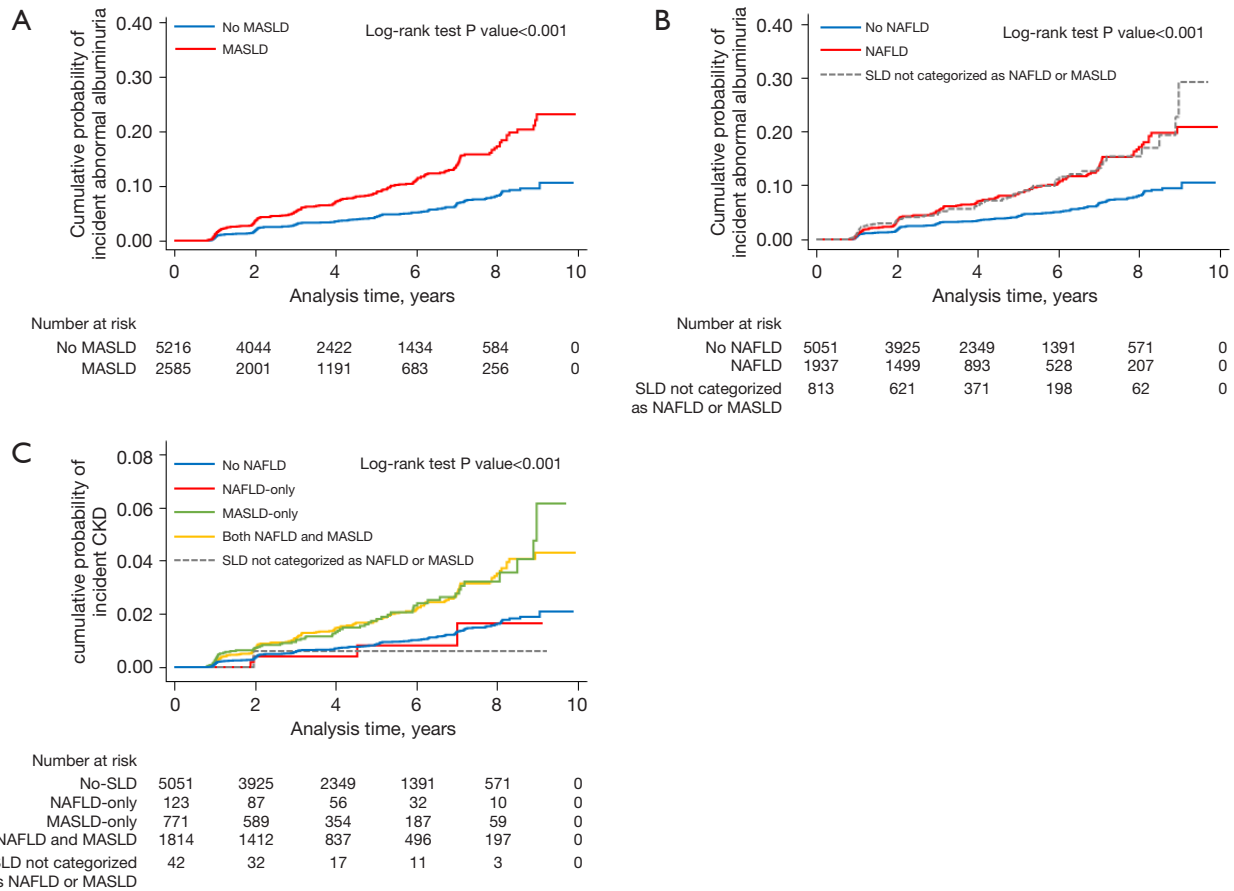

Figure 2 Cumulative incidence rates of abnormal albuminuria by Kaplan-Meier methods according to presence and combination of NAFLD and/or MASLD. MASLD, metabolic dysfunction-associated steatotic liver disease; NAFLD, non-alcoholic fatty liver disease; SLD, steatotic liver disease.

However, a consensus of international experts has recently proposed a terminology change from NAFLD to MASLD, thus further emphasizing the key role of metabolic dysregulation in the pathophysiology of this common and burdensome liver disease. This proposal was also made in response to the possible criticisms regarding the use of the adjective "non-alcoholic" in the NAFLD's term (27). Although there is a high concordance between NAFLD and MASLD diagnostic criteria in "real-word" data, these two conditions may be at least partly discordant (28-30). So, it is crucial to better establish the natural course of hepatic and extrahepatic clinical outcomes in each subgroup of individuals with SLD—the MASLD-only, the NAFLD-only, and the both NAFLD and MASLD groups—in comparison with individuals without SLD. This could help to improve the identification of subjects who may develop adverse clinical outcomes associated with their baseline SLD status, and to start early prevention and treatments tailored to specific types of SLD.

By applying the newly proposed MASLD definition, a new subgroup of individuals with hepatic steatosis without coexisting metabolic dysfunction and other competing causes of hepatic steatosis (the NAFLD-only group) can be identified. Interestingly, in our study we showed that the NAFLD-only group was not independently associated with an increased risk of developing CKD stage ≥3 or abnormal albuminuria during the follow-up. Similarly, we also showed that the SLD not categorized as NAFLD or MASLD group, which includes individuals who have SLD (that is largely attributable to significant alcohol consumption or other concomitant liver diseases) in the absence of metabolic dysregulation, did not show any significant risk of developing incident CKD or abnormal albuminuria, compared to the no-SLD group. At first

glance, these findings suggest that coexisting metabolic abnormalities such as diabetes, obesity and dyslipidemia, rather than fatty liver alone, may play a predominant role in the development of kidney dysfunction. However, the fact that the both NAFLD and MASLD group had the highest risk of developing incident CKD and abnormal albuminuria over the follow-up also suggests that some other hepatic mediators released by the steatotic/inflamed liver (besides coexisting metabolic disorders) might synergistically interact, thus increasing the risk of kidney dysfunction over time.

In this study, we found that only the both NAFLD and MASLD group exhibited the highest risk of developing incident CKD, although the MASLD-only group also had a tendency towards an increased risk of CKD. Conversely, the MASLD-only group and the both NAFLD and MASLD group had the highest risk of developing abnormal albuminuria, and this risk was comparable between the two groups. It could be partly explained by the fact that the follow-up duration of the study was relatively short to observe an eGFR decline among our relatively young participants, whereas it was sufficient to observe the occurrence of abnormal albuminuria. Since abnormal albuminuria typically precedes the progressive decline in renal function, it is possible to hypothesize that a longer follow-up duration would have revealed a significantly higher risk of incident CKD also in the MASLD-only group compared to the no-SLD group.

That said, our findings suggest that newly proposed MASLD criteria can identify individuals at risk of developing incident CKD (stage ≥3) and abnormal albuminuria better than the old NAFLD criteria. Therefore, our findings corroborate and expand the results of other recent cohort studies supporting the superiority of MASLD definition for identifying patients with more advanced liver fibrosis, and those at higher risk of incident CVD events and all-cause mortality (9,14,16,31-33). When it comes to the risk of CKD, Sun *et al.* using cross-sectional data from 12,571 participants in the National Health and Nutrition Examination Survey (NHANES)-III 1988–1994 who underwent liver ultrasonography and did not have viral hepatitis, were the first to show that individuals with MASLD had significantly lower eGFR levels and a greater prevalence of stage 3–5 CKD than those with NAFLD (34). Furthermore, these authors also found that severe MASLD (as assessed by the NAFLD fibrosis score, i.e., a non-invasive biomarker of advanced fibrosis) was associated with a nearly 1.3-fold higher risk of prevalent CKD than that of individuals without MASLD, even after adjustment for sex, age, ethnicity, alcohol intake and pre-existing T2DM (34). In a retrospective cohort study involving 16,938 Japanese adult individuals, Hashimoto *et al.* showed that MASLD on ultrasound had a higher risk of developing CKD (defined as an eGFR of <60 mL/min/1.73 m^2 and/or proteinuria), whereas SLD without metabolic dysregulation was not independently associated with incident CKD (35). In another cohort study of 13,159 Japanese individuals with baseline liver ultrasound data who were followed for a 10-year period, Tanaka *et al.* also reported that MASLD was associated with incident CKD (defined as eGFR <60 mL/min/1.73 m^2 or positivity for urinary protein on dipsticks) and predicted independently the risk for CKD development better than NAFLD (36). However, unlike our study, the investigators did not measure urinary albumin extraction and plasma hs-CRP levels. Finally, in a retrospective nationwide cohort study of 268,946 middle-aged Korean adults undergoing National Health Insurance Service health examinations, Jung *et al.* also confirmed that MASLD identified a higher proportion of individuals at risk of developing incident CKD [defined as eGFR <60 mL/min/1.73 m^2 or proteinuria (≥ trace) compared to NAFLD] (37). However, the major limitations of this retrospective cohort study were that the authors did not have any data on albuminuria and the diagnosis of fatty liver was only based on the fatty liver index (FLI), which may have resulted in under- or over-estimation of the true prevalence of SLD. In this regard, our result can robustly support the superior utility of MASLD in identifying patients at high risk for metabolic dysfunction, the hepatic and extra-hepatic complications (38-40).

Although the precise reasons why MASLD predicts the development of kidney dysfunction better than NAFLD are not fully understood, the putative mechanisms linking MASLD and CKD involve a number of shared risk factors that contribute to kidney-liver crosstalk (41). These signals include metabolic risk factors (for example, those associated with insulin resistance, abdominal obesity, hypertension, and T2DM), liver-related proinflammatory mediators, intestinal dysbiosis and certain genetic risk factors [as extensively reviewed in (28)]. Thus, it is also conceivable that the newly proposed definition of MASLD is more closely aligned with the underlying pathophysiological mechanisms of kidney damage than that of NAFLD (28).

Our cohort study has some important limitations that should be mentioned. Firstly, although we did not directly measure GFR, we used the most widely accepted serum

creatinine-based equation for estimating GFR in both large epidemiological studies and clinical practice. In addition, both eGFR and albuminuria were measured only once. Secondly, because our study participants were Korean individuals, the results may not be generalizable to other ethnic groups. Thirdly, we did not assess the severity of liver fibrosis by using either vibration-controlled transient elastography or other non-invasive imaging methods (42). Fourthly, as discussed above, considering that our study participants were relatively young, the follow-up length of the study (median of 6.1 years) might be insufficient also to detect a significant and independent association between the MASLD-only status and incident CKD. However, it may help to rule out other serious comorbidities typically seen in older adults that may increase the risk of CKD, thus making it easier to detect a possible direct link between SLD and CKD development. Finally, we cannot exclude residual confounding due to unmeasured risk factors (e.g., changes in SLD status over the follow-up) or factors that we could not include in the model because of multicollinearity (e.g., diabetes, dyslipidemia, and obesity). Despite these limitations, we believe that the most important strengths of our study are that we analyzed data from a large cohort of healthy individuals who underwent liver ultrasonography to diagnose hepatic steatosis; we measured both eGFR levels and albuminuria, and we adjusted the data for multiple potential confounders, including also the use of any anti-hypertensive medications (modelled as time-varying variable), and baseline eGFR levels.

Conclusions

In conclusion, this large Korean cohort study provides strong evidence to the notion that MASLD can identify patients at risk of developing incident CKD (stage ≥3) or abnormal albuminuria more accurately than NAFLD. Our results also suggest that the NAFLD-only status (including persons with SLD without any coexisting metabolic dysregulation) is not independently associated with the risk of developing incident CKD or abnormal albuminuria. The clinical implication for these findings is that patients with MASLD may benefit from more intensive surveillance and treatment of cardiometabolic risk factors to decrease the risk of CKD. It suggests that the applying the MASLD definition may help to integrate SLD into multidisciplinary care and new clinical trials for patients with metabolic disease (43). Further prospective studies from different countries are needed to study the comparative associations of MASLD or NAFLD definitions with the risk of developing kidney dysfunction. Additionally, a better understanding of the different mechanisms potentially implicated in the link between MASLD and NAFLD definitions with the risk of kidney dysfunction is warranted to develop personalized therapeutic strategies for patients with different SLD subtypes.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-558/rc

Data Sharing Statement: Available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-558/dss

Peer Review File: Available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-558/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-558/coif). M.H.Z. serves as an unpaid editorial board member of *Hepatobiliary Surgery and Nutrition*. G.T. is supported in part by grants from the University School of Medicine of Verona, Verona, Italy. C.D.B. was supported in part by the Southampton National Institute for Health and Care Research Biomedical Research Centre (NIHR203319), UK. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board (IRB) of Kangbuk Samsung Hospital (Institutional Review Board No.: 2022-06-039) and the requirement for written informed consent was waived by the IRB because anonymous and de-identified information was used for the analyses.

References

1. Eslam M, El-Serag HB, Francque S, et al. Metabolic (dysfunction)-associated fatty liver disease in individuals of normal weight. Nat Rev Gastroenterol Hepatol 2022;19:638-51.
2. Han E, Han KD, Lee YH, et al. Fatty Liver & Diabetes Statistics in Korea: Nationwide Data 2009 to 2017. Diabetes Metab J 2023;47:347-55.
3. Chan KE, Koh TJL, Tang ASP, et al. Global Prevalence and Clinical Characteristics of Metabolic-associated Fatty Liver Disease: A Meta-Analysis and Systematic Review of 10 739 607 Individuals. J Clin Endocrinol Metab 2022;107:2691-700.
4. Mantovani A, Scorletti E, Mosca A, et al. Complications, morbidity and mortality of nonalcoholic fatty liver disease. Metabolism 2020;111S:154170.
5. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol 2023;79:1542-56.
6. Huh JH, Kim JY, Choi E, et al. The fatty liver index as a predictor of incident chronic kidney disease in a 10-year prospective cohort study. PLoS One 2017;12:e0180951.
7. Zhou XD, Targher G, Byrne CD, et al. An international multidisciplinary consensus statement on MAFLD and the risk of CVD. Hepatol Int 2023;17:773-91.
8. Kim JH, Moon JS, Byun SJ, et al. Fatty liver index and development of cardiovascular disease in Koreans without pre-existing myocardial infarction and ischemic stroke: a large population-based study. Cardiovasc Diabetol 2020;19:51.
9. Sung KC, Yoo TK, Lee MY, et al. Comparative Associations of Nonalcoholic Fatty Liver Disease and Metabolic Dysfunction-Associated Fatty Liver Disease With Coronary Artery Calcification: A Cross-Sectional and Longitudinal Cohort Study. Arterioscler Thromb Vasc Biol 2023;43:482-91.
10. Seo IH, Lee HS, Lee YJ. Fatty liver index as a predictor for incident type 2 diabetes in community-dwelling adults: longitudinal findings over 12 years. Cardiovasc Diabetol 2022;21:209.
11. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020;395:709-33.
12. Kalantar-Zadeh K, Jafar TH, Nitsch D, et al. Chronic kidney disease. Lancet 2021;398:786-802.
13. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology 2023;78:1966-86.
14. Lee H, Lee YH, Kim SU, et al. Metabolic Dysfunction-Associated Fatty Liver Disease and Incident Cardiovascular Disease Risk: A Nationwide Cohort Study. Clin Gastroenterol Hepatol 2021;19:2138-2147.e10.
15. Kim KS, Hong S, Ahn HY, et al. Metabolic Dysfunction-Associated Fatty Liver Disease and Mortality: A Population-Based Cohort Study. Diabetes Metab J 2023;47:220-31.
16. Yoo TK, Lee MY, Kim SH, et al. Comparison of cardiovascular mortality between MAFLD and NAFLD: A cohort study. Nutr Metab Cardiovasc Dis 2023;33:947-55.
17. Kim Y, Kang J, Chang Y, et al. Coronary artery calcium and risk of chronic kidney disease in young and middle-aged adults. Nephrol Dial Transplant 2023;38:1439-47.
18. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.
19. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139:137-47.
20. Lim S, Yu HJ, Lee S, et al. Evaluation of the URiSCAN 2 ACR Strip to estimate the urine albumin/creatinine ratios. J Clin Lab Anal 2018;32:e22289.
21. Sung KC, Wild SH, Byrne CD. Development of new fatty liver, or resolution of existing fatty liver, over five years of follow-up, and risk of incident hypertension. J Hepatol 2014;60:1040-5.
22. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-63.
23. Byrne CD, Targher G. NAFLD as a driver of chronic kidney disease. J Hepatol 2020;72:785-801.
24. Musso G, Gambino R, Tabibian JH, et al. Association of non-alcoholic fatty liver disease with chronic kidney disease: a systematic review and meta-analysis. PLoS Med 2014;11:e1001680.
25. Tao Z, Li Y, Cheng B, et al. Influence of Nonalcoholic

Fatty Liver Disease on the Occurrence and Severity of Chronic Kidney Disease. J Clin Transl Hepatol 2022;10:164-73.
26. Mantovani A, Petracca G, Beatrice G, et al. Non-alcoholic fatty liver disease and risk of incident chronic kidney disease: an updated meta-analysis. Gut 2022;71:156-62.
27. Eslam M, Newsome PN, Sarin SK, et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol 2020;73:202-9.
28. Wang TY, Wang RF, Bu ZY, et al. Association of metabolic dysfunction-associated fatty liver disease with kidney disease. Nat Rev Nephrol 2022;18:259-68.
29. Targher G. Concordance between MAFLD and NAFLD diagnostic criteria in 'real-world' data. Liver Int 2020;40:2879-80.
30. Lin S, Huang J, Wang M, et al. Comparison of MAFLD and NAFLD diagnostic criteria in real world. Liver Int 2020;40:2082-9.
31. Kim D, Konyn P, Sandhu KK, et al. Metabolic dysfunction-associated fatty liver disease is associated with increased all-cause mortality in the United States. J Hepatol 2021;75:1284-91.
32. van Kleef LA, Ayada I, Alferink LJM, et al. Metabolic dysfunction-associated fatty liver disease improves detection of high liver stiffness: The Rotterdam Study. Hepatology 2022;75:419-29.
33. Yamamura S, Eslam M, Kawaguchi T, et al. MAFLD identifies patients with significant hepatic fibrosis better than NAFLD. Liver Int 2020;40:3018-30.
34. Sun DQ, Jin Y, Wang TY, et al. MAFLD and risk of CKD. Metabolism 2021;115:154433.
35. Hashimoto Y, Hamaguchi M, Okamura T, et al. Metabolic associated fatty liver disease is a risk factor for chronic kidney disease. J Diabetes Investig 2022;13:308-16.
36. Tanaka M, Mori K, Takahashi S, et al. Metabolic dysfunction-associated fatty liver disease predicts new onset of chronic kidney disease better than fatty liver or nonalcoholic fatty liver disease. Nephrol Dial Transplant 2023;38:700-11.
37. Jung CY, Koh HB, Park KH, et al. Metabolic dysfunction-associated fatty liver disease and risk of incident chronic kidney disease: A nationwide cohort study. Diabetes Metab 2022;48:101344.
38. Alharthi J, Gastaldelli A, Cua IH, et al. Metabolic dysfunction-associated fatty liver disease: a year in review. Curr Opin Gastroenterol 2022;38:251-60.
39. Eslam M, Sarin SK, Wong VW, et al. The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. Hepatol Int 2020;14:889-919.
40. Méndez-Sánchez N, Bugianesi E, Gish RG, et al. Global multi-stakeholder endorsement of the MAFLD definition. Lancet Gastroenterol Hepatol 2022;7:388-90.
41. Pan Z, Alqahtani SA, Eslam M. MAFLD and chronic kidney disease: two sides of the same coin? Hepatol Int 2023;17:519-21.
42. European Association for Study of Liver; Asociacion Latinoamericana para el Estudio del Higado. EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis. J Hepatol 2015;63:237-64.
43. Eslam M, Ahmed A, Després JP, et al. Incorporating fatty liver disease in multidisciplinary care and novel clinical trial designs for patients with metabolic diseases. Lancet Gastroenterol Hepatol 2021;6:743-53.

Cite this article as: Heo JH, Lee MY, Kim SH, Zheng MH, Byrne CD, Targher G, Sung KC. Comparative associations of non-alcoholic fatty liver disease and metabolic dysfunction-associated steatotic liver disease with risk of incident chronic kidney disease: a cohort study. HepatoBiliary Surg Nutr 2024;13(5):801-813. doi: 10.21037/hbsn-23-558

