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ORIGINAL RESEARCH

Metabolic Dysfunction–Associated Steatotic Liver Disease, Alcohol Consumption, and the Risk of Atrial Fibrillation: A Nationwide Population-Based Study

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BACKGROUND: The recent reclassification of steatotic liver disease into metabolic dysfunction–associated steatotic liver disease (MASLD) and metabolic dysfunction-associated alcohol-related liver disease has highlighted their potential cardiovascular implications. This study aimed to investigate the impact of MASLD and metabolic dysfunction-associated alcohol-related liver disease on the risk of newly diagnosed atrial fibrillation (AF).

METHODS: Data from 362 285 participants who underwent a health screening in 2009 to 2010, sourced from the Korean National Health Insurance database, were identified, and we retrospectively analyzed their data through 2019. Excluding those with other liver diseases and heavy alcoholics, 206 455 participants with a fatty liver index were included. The primary outcome was newly diagnosed AF; associated conditions, such as ischemic stroke and heart failure, were also investigated. Participants were classified into 4 groups based on their steatotic liver disease status and alcohol consumption levels.

RESULTS: Over a median follow-up of 9.6 years, 5335 participants were newly diagnosed with AF (2.74 per 1000 person-years). The risk of AF was significantly higher in patients with MASLD who did not consume alcohol (adjusted hazard ratio [aHR], 1.32 [95% CI, 1.23–1.41]; $P<0.001$) and in those with MASLD with alcohol or metabolic dysfunction–associated steatotic liver disease with increased alcohol intake (aHR, 1.48 [95% CI, 1.36–1.61]; $P<0.001$). Compared with all other alcohol consumers, regardless of steatotic liver disease status, nondrinking patients with MASLD had a significantly higher risk of AF (aHR, 1.11 [95% CI, 1.02–1.20]; $P=0.011$).

CONCLUSIONS: MASLD is associated with incident AF. These findings suggest that metabolic dysfunction plays a more significant role in AF occurrence than the direct toxic effects of alcohol.

Key Words: alcohol intake ■ atrial fibrillation ■ metabolic dysfunction ■ nonalcoholic fatty liver disease ■ steatotic liver disease

The global prevalence of steatotic liver disease (SLD) has rapidly increased.[1] Previously referred to as nonalcoholic fatty liver disease, it was diagnosed based on the exclusion of significant alcohol consumption and other liver conditions.[2] However, ambiguity in diagnostic criteria and the negative connotation of the term "fatty" prompted the need for revised terminology.[3] In 2023, the disease was reclassified into metabolic dysfunction–associated steatotic liver disease (MASLD), metabolic dysfunction–associated steatotic liver disease with increased alcohol intake (MetALD), and alcohol-related liver disease, based on the level

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CLINICAL PERSPECTIVE

What Is New?

- This study is the first to investigate the association between metabolic dysfunction–associated steatotic liver disease and incident atrial fibrillation using a nationwide population-based cohort.
- Patients with metabolic dysfunction–associated steatotic liver disease, whether or not they consume alcohol, have a significantly higher risk of developing atrial fibrillation compared with individuals without liver disease

What Are the Clinical Implications?

- Metabolic dysfunction in metabolic dysfunction–associated steatotic liver disease plays a more critical role in increasing atrial fibrillation risk than the direct toxic effects of alcohol consumption.

Nonstandard Abbreviations and Acronyms

FLI	fatty liver index
MetALD	metabolic dysfunction–associated steatotic liver disease with increased alcohol intake
SLD	steatotic liver disease

of alcohol consumed and underlying causes.[4] Recent studies have reported the cardiovascular implications of this updated SLD classification.[5,6] However, no research has investigated the association between atrial fibrillation (AF) and MASLD.

AF is the most common form of persistent cardiac arrhythmia and is associated with an increased risk of stroke, heart failure (HF), and mortality.[7] An association between the nonalcoholic fatty liver disease, the previous nomenclature, and AF has already been established.[8] Moreover, alcohol is a significant risk factor for AF.[9–11] However, no studies have investigated the relationship between AF, alcohol consumption, and the newly defined SLD criteria, which permit mild to moderate alcohol intake. Therefore, we aimed to examine the association between MASLD and MetALD, conditions that permit mild to moderate alcohol consumption, and the risk of AF, using large-scale claims data.

METHODS

Data Availability Statement

Data sharing is limited due to Korean government regulations. However, additional data can be accessed with approval and oversight from the Korean National Health Insurance Service.

Data Source and Study Population

We conducted a nationwide cohort study in the Republic of Korea using the claims data from the National Health Insurance Service. Using the National Health Screening Cohort database, we conducted our study on 362 285 individuals who underwent health screenings between 2009 and 2010.[12] The *International Classification of Diseases, 10th Revision* (*ICD-10*) and the fatty liver index (FLI) were used to diagnose and classify participants. Individuals with rheumatic mitral stenosis or prosthetic heart valve (n=1050), previous history of AF (n=6005), those diagnosed with liver diseases of a clearly different cause, including viral or autoimmune hepatitis, alcoholic liver disease, toxic liver disease, Wilson disease, and biliary cholangitis (n=109 737), were excluded. Heavy alcoholics (n=8364), defined as individuals who consumed >420 g of alcohol per week for men or >350 g of alcohol per week for women, were also excluded. Additionally, participants with a previous history of cancer (n=15 733), decompensated liver cirrhosis (n=4231), those with missing values that made it impossible to calculate the FLI (n=6732), or extreme aspartate transaminase/alanine transaminase ratios in the <1% or >99% range (n=3979) were excluded. Finally, 206 455 participants were included in the analysis for this study (Figure S1). This study was conducted according to the principles of the 2013 Declaration of Helsinki and was approved by the institutional review board of each participating hospital (institutional review board number: 9-2024-0142, DAUHIRB-24-157). Due to the retrospective nature of the study, the obligation for informed consent was waived.

Covariates

This study followed methodologies that were outlined in previous publications using claims data.[12,13] Demographic information was obtained through resident identification numbers, and income levels were divided into quartiles. Table S1 provides the operational definitions for comorbidities, including hypertension, diabetes, and dyslipidemia, and for outcomes such as AF, ischemic stroke, and HF. Incident AF was defined using the *ICD-10* code I48. A diagnosis was confirmed if the code appeared at least once during hospitalization or at least twice in outpatient clinic visits, consistent with definitions used in previous studies.[14,15] The Charlson Comorbidity Index was calculated according to established method.[16] Laboratory assessments included aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transferase, hemoglobin levels, and the estimated glomerular filtration rate. The estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease formula.

In addition, a self-reported questionnaire was used to gather data on current smoking status and regular exercise habits.

Definitions of Alcohol Consumption and SLD

Data on alcohol consumption were obtained from the health screening questionnaire, which included frequency (days per week) and intensity (number of drinks per occasion). These variables were used to assess individual drinking patterns. To ensure consistency, a standard drink was defined based on specific cup size for each type of alcohol. However, despite varying cup volumes, each cup was calibrated to contain approximately 10 g of pure alcohol. Weekly alcohol consumption was then calculated by multiplying drinking frequency by drinking intensity. SLD was defined using an FLI of ≥30, in line with international clinical guidelines for large-scale epidemiological studies, offering a noninvasive alternative to imaging-based diagnosis.[3,5] MASLD was diagnosed in individuals with SLD, mild alcohol consumption (<210 g per week for men and <140 g per week for women), and at least 1 of the following 5 established cardiometabolic risk factors: (1) body mass index ≥23 kg/m^2 or waist circumference ≥90 cm for men and ≥85 cm for women (based on Asian-specific criteria), (2) fasting blood glucose ≥100 mg/dL or current treatment for type 2 diabetes, (3) blood pressure ≥130/85 mm Hg or antihypertensive drug use, (4) serum triglycerides ≥150 mg/dL or lipid-lowering medication use, and (5) high-density lipoprotein cholesterol ≤40 mg/dL for men or ≤50 mg/dL for women or lipid-lowering medication use. MetALD was diagnosed in individuals with SLD who reported moderate alcohol consumption (210–420 g per week for men and 140–350 g per week for women), along with at least 1 of the 5 established cardiometabolic risk factors listed above.

Participants were categorized into 4 groups according to SLD status and alcohol consumption: no SLD without alcohol, MASLD without alcohol, no SLD with alcohol, and MASLD with alcohol and MetALD.

Study Outcomes

The primary outcome was newly diagnosed AF. Secondary outcomes included ischemic stroke and HF, which are commonly associated with an AF-related clinical event. Participants were followed up from the index date (the date of health screening) until the diagnosis of AF, death, or December 31, 2019, whichever occurred first.

Statistical Analysis

Continuous variables are presented as mean±SD, whereas categorical variables are presented as number and percentage. Group comparisons for continuous variables were conducted using the analysis of variance test, and for categorical variables, the χ^2 test was applied as appropriate. The incidence rates for the primary end point were calculated by dividing the number of events by the total follow-up time, and the results were expressed as rates per 1000 person-years. Kaplan-Meier survival curves were used to illustrate the cumulative incidence of both primary and secondary end points, with the log-rank test used for comparison. Continuous multivariable-adjusted associations between FLI, alcohol amount, and AF were presented as restricted cubic splines with 4 knots at the fifth, 35th, 65th, and 95th percentiles.

Multivariable Cox proportional hazards regression analysis was performed to determine independent risk factors for the primary end point, with results presented as hazard ratios (HRs) and 95% CIs. The proportional hazard assumption was evaluated using the Schoenfeld residuals test based on the logarithm of the cumulative hazard function derived from the Kaplan-Meier estimates. The results demonstrated that the assumption of proportional hazard risk over time was not violated. Propensity scores were also calculated to represent the probability of belonging to each group based on an individual's characteristics. This was achieved using a multinomial logistic regression model, incorporating all measured demographic characteristics. Subsequently, we performed an inverse probability of treatment weighting analysis to balance covariates among the 4 groups, with the no SLD without alcohol group serving as the reference. The analyses are repeated after inverse probability of treatment weighting, and results were presented as HRs and 95% CIs.

We performed 4 sensitivity analyses. First, we stratified the primary analysis based on age and sex. Second, we used a higher cutoff of FLI ≥60, instead of ≥30, to define SLD. Third, we repeated the main analysis using alternative biochemical models for hepatic steatosis, specifically the hepatic steatosis index ≥36.[17] Fourth, we divided participants into groups based on the amount of alcohol consumption and conducted the main analysis within these subgroups. Statistical analyses were performed using SAS software version 9.3 (SAS Institute) and R software version 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at a 2-sided *P* value of <0.05.

RESULTS

Baseline Characteristics of the Study Participants

Overall, 206 455 participants were included in this study, with a mean age of 58.4±8.6 years, and 47.9%

were women. Table 1 presents their participants' baseline clinical characteristics. Among the total population, 73 847 participants (35.8%) were classified as having SLD, including MASLD or MetALD. Of these, 38 311 (18.6%) were categorized into the MASLD without alcohol group. A total of 76 127 participants (36.9%) reported alcohol consumption, including 40 591 (19.7%) who were categorized in the no SLD with alcohol group. The MASLD with alcohol and MetALD group was predominantly men, whereas the MASLD without alcohol group had a slightly higher proportion of women. Participants in the MASLD with alcohol and MetALD group were younger than those in the MASLD without alcohol group. The MASLD group had higher prevalence rates of hypertension, diabetes, and dyslipidemia, and the MASLD without alcohol group had a higher proportion of participants with a Charlson Comorbidity Index score of ≥3. Smoking rates and the proportion of participants with regular physical activity at least once weekly were higher in the alcohol consumption group (Table 1).

Primary and Secondary End Points

The median follow-up duration was 9.6 (interquartile range, 9.2–10.2) years. During this follow-up period, the primary end point of newly diagnosed AF occurred in 5335 (2.6%) patients (2.74 per 1000 person-years). In our study, both FLI and alcohol consumption were statistically significant predictors of incident AF (Figure 1). The spline curve demonstrated that AF risk increased progressively with higher FLI (Figure 1A). Similarly, an increase in alcohol intake noticeably increased AF occurrence (Figure 1B). Furthermore, components of metabolic syndrome, specifically higher body mass index, waist circumference, and blood pressure, were associated with elevated AF risk (Figure S2).

Among all groups, the MASLD without alcohol group had the highest AF incidence rate (3.81 per 1000 person-years), followed by the MASLD with alcohol and MetALD group (3.23 per 1000 person-years). Both groups had significantly higher AF incidence than groups without SLD (log-rank $P<0.001$) (Table 2 and Figure 2A). Given the differences in alcohol consumption patterns between sexes, we conducted subgroup analyses for men and women. The SLD group had a significantly higher incidence of AF than the non-SLD group, with a slightly higher trend of AF incidence in the alcohol-consuming group than that in the non-alcohol group (Figures 2B and 2C).

After multivariable adjustment, using the no SLD without alcohol group as the reference, the AF risk in the MASLD without alcohol group was 1.32 times higher (95% CI, 1.23–1.41), and 1.48 times higher in the MASLD with alcohol and MetALD group (95% CI, 1.36–1.61) (Table 2). The no SLD with alcohol group showed no statistically significant difference compared with the reference group. These trends were consistent in the inverse probability of treatment weighting analysis.

Among the total participants, 4910 (2.4%) developed ischemic stroke (2.52 per 1000 person-years), and 2414 (1.2%) developed HF (1.23 per 1000 person-years). In multivariable Cox regression analysis, compared with the reference group, both the MASLD without alcohol group (adjusted HR, 1.32 [95% CI, 1.23–1.41]) and the MASLD with alcohol and MetALD group (adjusted HR, 1.30 [95% CI, 1.19–1.42]) were statistically significant independent risk factors for ischemic stroke (Table S2). A similar trend was observed for HF (Table S3).

Impact of MASLD on AF Occurrence Compared With Alcohol Consumption

Both alcohol consumption and FLI have been associated with AF occurrence. Therefore, we analyzed the relative impact of MASLD on AF risk compared with alcohol consumption. To this end, we excluded participants without SLD who did not consume alcohol and designated all participants who consumed alcohol, regardless of SLD status (ie, no SLD with alcohol and MASLD with alcohol and MetALD groups), as the reference group. Compared with this reference, the MASLD without alcohol group had a 1.43-fold higher risk of future AF occurrence (95% CI, 1.43–1.53). This association remained statistically significant after adjusting for demographic, clinical, and laboratory covariates (adjusted HR, 1.11 [95% CI, 1.02–1.20]; $P=0.011$) (Table 3).

Sensitivity Analysis

We conducted 4 sensitivity analyses. First, a subgroup analysis stratified by age and sex is presented in Figure 3. Except for the female subgroup, the results in men and in those aged <65 and ≥65 years were consistent with those observed in the main analysis. Second, redefining SLD using a stricter threshold of FLI ≥60 yielded results similar to the main findings. Third, applying an alternative definition of hepatic steatosis using the hepatic steatosis index ≥36 score also produced consistent results. These 2 analyses supplemented the study's primary operational definition of FLI ≥30 (Tables S4 and S5). Fourth, when participants were stratified into mild and moderate alcohol consumption categories, the results remained analogous to those of the main analysis (Tables S6 and S7). Collectively, these findings suggest that the observed increase in AF risk is more strongly associated with MASLD than with the degree of alcohol consumption (Table 3).

DISCUSSION

Among the 362 285 participants in the cohort with available health screening data, we focused on 206 455

Table 1. Baseline Characteristics of Study Population

Variables		No SLD without alcohol (n=92017)	MASLD without alcohol (n=38311)	No SLD with alcohol (n=40591)	MASLD with alcohol and MetALD (n=35536)	*P* value
Sex (%)	Men	24343 (26.5)	17389 (45.4)	29616 (73.0)	32510 (91.5)	<0.001
	Women	67674 (73.5)	20922 (54.6)	10975 (27.0)	3026 (8.5)	
Age, y, mean±SD		59.2±9.0	60.8±8.8	56.3±7.8	56.1±7.3	<0.001
Income level (%)	1st quartile	14683 (16.0)	5948 (15.5)	4735 (11.7)	3814 (10.7)	<0.001
	2nd quartile	20556 (22.3)	8106 (21.2)	7882 (19.4)	5977 (16.8)	
	3rd quartile	26197 (28.5)	11796 (30.8)	11344 (27.9)	9957 (28.0)	
	4th quartile	30581 (33.2)	12461 (32.5)	16630 (41.0)	15788 (44.4)	
Residence area (%)	Rural	32552 (35.4)	14400 (37.6)	11647 (28.7)	10901 (30.7)	<0.001
	Urban	59465 (64.6)	23911 (62.4)	28944 (71.3)	24635 (69.3)	
Hypertension (%)		33802 (36.7)	22128 (57.8)	12846 (31.6)	17884 (50.3)	<0.001
Diabetes (%)		7970 (8.7)	7588 (19.8)	3124 (7.7)	5747 (16.2)	<0.001
Dyslipidemia (%)		29698 (32.3)	21491 (56.1)	9455 (23.3)	15261 (42.9)	<0.001
Charlson Comorbidity Index (%)	0	46590 (50.6)	16152 (42.2)	24982 (61.5)	20715 (58.3)	<0.001
	1	25755 (28.0)	10775 (28.1)	10099 (24.9)	9006 (25.3)	
	2	11348 (12.3)	5660 (14.8)	3584 (8.8)	3436 (9.7)	
	≥3	8324 (9.0)	5724 (14.9)	1926 (4.7)	2379 (6.7)	
Body mass index, kg/m^2, mean±SD		22.7±2.3	26.5±2.6	22.5±2.1	25.7±2.3	<0.001
Waist, cm, mean±SD		77.0±6.6	88.2±6.3	78.6±6.1	88.0±5.9	<0.001
Systolic blood pressure, mm Hg, mean±SD		122.3±15.3	128.6±15.1	122.8±14.4	129.0±14.4	<0.001
Diastolic blood pressure, mm Hg, mean±SD		75.4±9.7	79.2±9.7	76.6±9.6	80.8±9.7	<0.001
Fasting blood glucose, mg/dL, mean±SD		96.2±20.0	104.9±27.8	97.4±20.2	105.7±27.0	<0.001
Total cholesterol, mg/dL, mean±SD		199.7±36.2	209.4±39.6	194.8±33.5	205.3±36.2	<0.001
Triglycerides, mg/dL, mean±SD		105.3±48.8	187.0±94.3	98.3±43.1	190.2±99.6	<0.001
HDL cholesterol, mg/dL, mean±SD		56.7±23.9	50.3±28.0	57.8±19.8	51.1±20.1	<0.001
LDL cholesterol, mg/dL, mean±SD		122.6±34.7	123.3±39.9	117.7±33.4	117.3±38.5	<0.001
Aspartate aminotransferase, U/L, mean±SD		23.2±8.1	26.7±13.5	23.7±7.9	27.8±14.5	<0.001
Alanine aminotransferase, U/L, mean±SD		19.8±10.3	28.5±17.5	20.1±9.4	29.2±17.7	<0.001
γ-Glutamyl transpeptidase, U/L, mean±SD		19.3±11.1	37.3±33.7	25.9±15.6	58.9±52.4	<0.001
Hemoglobin, g/dL, mean±SD		13.2±1.3	13.9±1.5	14.1±1.4	14.9±1.3	<0.001
Glomerular filtration rate, mL/min per 1.73 m^2, mean±SD		79.1±28.6	76.0±28.8	79.9±32.4	78.8±35.2	<0.001
Smoking (%)	Nonsmoker	79295 (86.2)	29029 (75.8)	19836 (48.9)	11603 (32.7)	<0.001
	Ex-smoker	6666 (7.2)	5156 (13.5)	10720 (26.4)	11956 (33.6)	
	Smoker	6056 (6.6)	4126 (10.8)	10035 (24.7)	11977 (33.7)	
Alcohol drinking (%)		182 (0.2)	179 (0.5)	40591 (100.0)	35536 (100.0)	<0.001
Amount of alcohol drinking, g/wk, mean±SD		0.0±0.0	0.0±0.0	91.5±85.4	128.9±101.2	<0.001
Regular exercise (%)	No	67349 (83.2)	28442 (83.2)	22845 (67.5)	19501 (65.1)	<0.001
	1–2 times/wk	13598 (16.8)	5760 (16.8)	10975 (32.5)	10445 (34.9)	
	3–4 times/wk	6733 (7.3)	2505 (6.5)	4255 (10.5)	3740 (10.5)	
	≥5 times/wk	4337 (4.7)	1604 (4.2)	2516 (6.2)	1850 (5.2)	
Fatty liver index, mean±SD		13.1±7.8	48.7±14.8	15.0±7.8	52.9±16.4	<0.001

HDL indicates high-density lipoprotein; LDL, low-density lipoprotein; MASLD, metabolic dysfunction–associated steatotic liver disease; MetALD, metabolic dysfunction–associated steatotic liver disease with increased alcohol intake; and SLD, steatotic liver disease.

participants, excluding those whose conditions could interfere with the analysis of the association between MASLD and incident AF. Participants without SLD, regardless of alcohol consumption, did not exhibit a high risk of new-onset AF. However, patients with MASLD and MetALD had higher risks of AF and AF-related diseases, including stroke and HF. Our results showed that metabolic dysfunction and the resulting SLD are strongly associated with AF occurrence. Notably, the AF risk for patients with MASLD who do not consume alcohol was

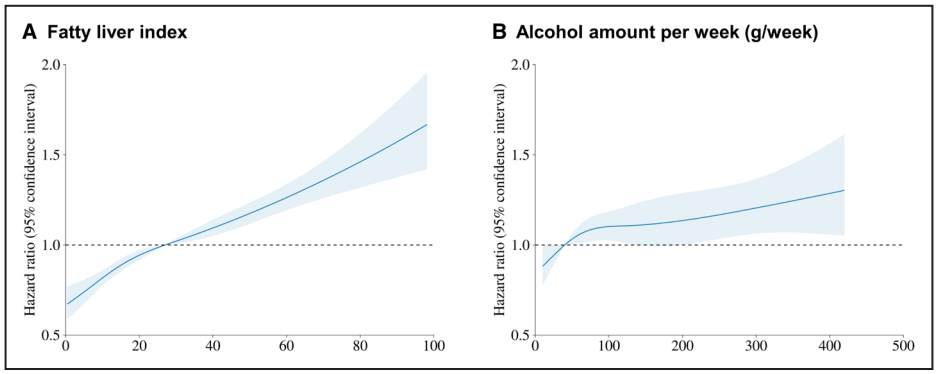

Figure 1. Restricted cubic spline (hazard ratio with 95% CI) for AF about FLI and alcohol amount per week (grams per week).
A, Gradual increase in AF risk as FLI increases, starting from around FLI=30. **B**, AF risk remained stable at lower levels of alcohol intake but increased as alcohol consumption became higher. AF indicates atrial fibrillation; and FLI, fatty liver index.

statistically significantly higher than other participants who consumed alcohol, regardless of SLD status. This suggests that rather than the direct toxic effect of alcohol itself, it is the metabolic dysfunction caused by alcohol consumption that could contribute to AF risk.

AF is the most common form of persistent cardiac arrhythmia and is associated with an increased risk of stroke, HF, and mortality.[7] The association between AF incidence and metabolic syndrome is well established.[18,19] However, the relationship between SLD and AF remains unclear. A meta-analysis of 6 studies reported that SLD increased the risk of incident AF by 19%.[20] However, another meta-analysis assessing the association between SLD and AF risk found that SLD only increased AF risk in patients with type 2 diabetes.[21] This study raised questions about the association between AF and SLD in nondiabetic groups, because it was based on only 3 cohort studies. Furthermore, these studies were limited by their small sample sizes or the heterogeneity of MASLD diagnostic criteria, which restricted the interpretation of the results.[21] A recent large-scale cohort study involving patients with biopsy-proven MASLD reported a significant association between MASLD and incident AF, which is consistent with our findings.[22]

The exact mechanisms by which MASLD induces AF remains unclear. However, several potential mechanisms can be inferred from previous studies. Patients with MASLD exhibited greater autonomic dysfunction than the control groups, as evidenced by reduced heart rate variability and baroreceptor reflex sensitivity.[23,24] Furthermore, small-sized preclinical studies have found an association between MASLD and left atrial enlargement, as well as increased left ventricular mass index, factors that may impair diastolic function, elevate left atrial pressure, and contribute to AF development.[25–27] Electrical–mechanical delays within and between the atria have also been observed in patients with MASLD,

Table 2. HRs and 95% CIs for Newly Diagnosed Atrial Fibrillation Across Different Groups Based on SLD Status and Alcohol Consumption

Group	No.	Events	Follow-up duration (person-years)	Incidence rate (per 1000 person-years)	Crude HR (95% CI, *P* value)	Adjusted HR* (95% CI, *P* value)	IPTW HR (95% CI, *P* value)
No SLD without alcohol	92017	2068	874020	2.37	1 (Reference)	1 (Reference)	1 (Reference)
MASLD without alcohol	38311	1374	360987	3.81	1.61 (1.50–1.72, *P*<0.001)	1.32 (1.23–1.41, *P*<0.001)	1.30 (1.22–1.39, *P*<0.001)
No SLD with alcohol	40591	819	383094	2.14	0.91 (0.84–0.99, *P*=0.020)	1.01 (0.93–1.10, *P*=0.792)	0.98 (0.91–1.05, *P*=0.517)
MASLD with alcohol and MetALD	35536	1074	332362	3.23	1.38 (1.28–1.48, *P*<0.001)	1.48 (1.36–1.61, *P*<0.001)	1.43 (1.33–1.53, *P*<0.001)

HR indicates hazard ratio; IPTW, inverse probability of treatment weighting; MASLD, metabolic dysfunction–associated steatotic liver disease; MetALD, metabolic dysfunction–associated steatotic liver disease with increased alcohol intake; and SLD, steatotic liver disease.
*The model was adjusted for age, sex, income level, residence area, Charlson Comorbidity Index, hemoglobin level, glomerular filtration rate, smoking, and regular exercise status.

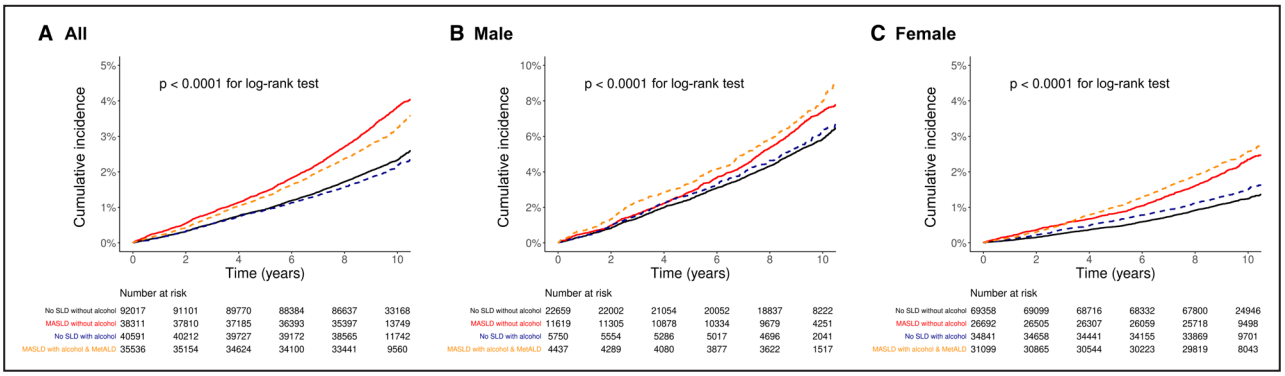

Figure 2. Kaplan-Meier curve for the association between SLD and AF.
A, In the total population, participants with MASLD (regardless of alcohol consumption) had a significantly higher incidence of AF than those without SLD. **B**, Among men, the SLD group showed higher AF incidence than the non-SLD group, with a slightly higher trend in alcohol users than nonusers. **C**, Similar findings were observed in women; AF incidence was higher in the SLD group, particularly among those consuming alcohol. AF indicates atrial fibrillation; MASLD, metabolic dysfunction–associated steatotic liver disease; MetALD, metabolic dysfunction–associated steatotic liver disease with increased alcohol intake; and SLD, steatotic liver disease.

suggesting potential electrical remodeling.[26] In patients with nonalcoholic fatty liver disease, activation of the hepatic intracellular transcription factor-signaling pathway (nuclear factor-κB) in the liver can trigger the transcription of various inflammatory cytokines and promote low-grade systemic inflammation, potentially contributing to AF onset.[28–30] Furthermore, MASLD is associated with increased epicardial fat mass, which has been independently linked to higher arrhythmia recurrence rates following AF ablation, suggesting an indirect role of MASLD in AF progression.[31]

Alcohol is a known risk factor for new-onset AF. A meta-analysis reported a dose–response relationship between alcohol consumption and the incidence of AF.[11] Notably, unlike HF and other cardiovascular diseases, even the consumption of 1.2 drinks per day has been associated with an increased risk of incident AF.[9] Another large cohort study indicated that frequent drinking, rather than binge drinking, was more likely to induce AF.[10] However, these studies did not clearly elucidate the mechanisms by which low levels of alcohol consumption induce AF. Our findings suggest that liver injury associated with metabolic dysfunction may play a more prominent role in AF development than the direct toxic effects of alcohol itself, particularly in individuals who do not engage in heavy alcohol consumption. This highlights the importance of metabolic dysfunction management as a crucial strategy for AF prevention, alongside efforts to reduce alcohol consumption. More intensive treatment of metabolic dysfunction could reduce the AF incidence and subsequently reduce the risk of related cardiocerebrovascular events such as HF and stroke.

This study has some limitations. First, SLD was defined using noninvasive biochemical scores rather than biopsy or abdominal imaging. However, the method we used to define SLD has already been extensively validated in numerous studies,[5,6,17,32] and the usefulness of noninvasive biomarkers for defining SLD in large epidemiological studies is recognized by international guidelines.[3] Second, selection bias may have occurred because the study included only participants with available health screening data from the overall population. Furthermore, being an observational study, it is limited in establishing causality. However, we attempted to mitigate these issues by including only participants appropriate for the SLD analysis based on predefined exclusion criteria and by setting

Table 3. HRs and 95% CIs for Newly Diagnosed Atrial Fibrillation in MASLD Without Alcohol Compared With All Participants Consuming Alcohol Regardless of SLD Status

Group	No.	Events	Follow-up duration (person-years)	Incidence rate (per 1000 person-years)	Crude HR (95% CI, *P*-value)	Adjusted HR* (95% CI, *P* value)
Alcohol consumption (regardless of SLD)	76 127	1893	715 455	2.65	1 (Reference)	1 (Reference)
MASLD without alcohol	38 311	1374	360 987	3.81	1.43 (1.34–1.53, *P*<0.001)	1.11 (1.02–1.20, *P*=0.011)

HR indicates hazard ratio; MASLD, metabolic dysfunction–associated steatotic liver disease; and SLD indicates steatotic liver disease.
*The model was adjusted for age, sex, income level, residence area, Charlson Comorbidity Index, hemoglobin level, glomerular filtration rate, smoking, and regular exercise status.

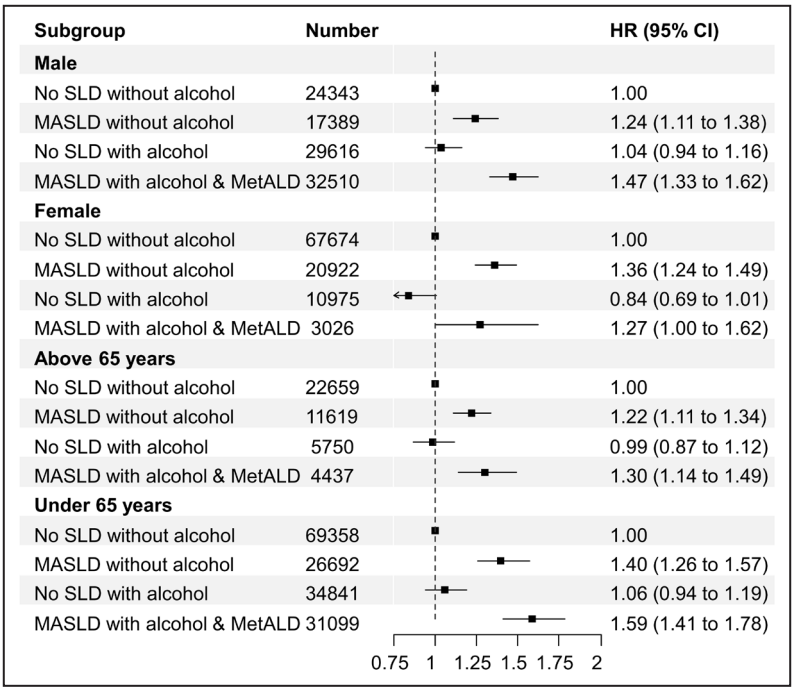

Figure 3. Subgroup analysis based on sex and age.
HRs with 95% CIs for incident atrial fibrillation are shown according to SLD status and alcohol consumption, stratified by sex (men, women) and age (<65 years, ≥65 years). The associations between MASLD and incident atrial fibrillation were generally consistent across subgroups, except in women, where the results showed a less clear trend. HR indicates hazard ratio; MASLD, metabolic dysfunction–associated steatotic liver disease; MetALD, metabolic dysfunction–associated steatotic liver disease with increased alcohol intake; and SLD, steatotic liver disease.

the primary outcome as new-onset AF. Third, using a low cutoff of FLI ≥30 may have led to the inclusion of individuals without SLD. However, sensitivity analyses using alternative definitions of SLD, such as FLI ≥60 and the hepatic steatosis index, also supported MASLD as a significant risk factor for new-onset AF. Fourth, because the study was based on data from a National Health Screening Program, we could not account for various factors potentially influencing SLD and AF, such as genetic polymorphisms and lifestyle and dietary habits, and the self-reported alcohol consumption data may also have been subject to inaccuracies. Additionally, SLD status was assessed only at baseline, and changes during the follow-up could not be captured, which may have influenced the results. Furthermore, we excluded individuals with heavy alcohol use due to the lack of a standardized definition for alcohol-related liver disease in claims-based data sets. Definitions based on alcohol-related liver disease, such as heavy drinking alone or combined with hepatic steatosis, often led to misclassification or have yielded small sample sizes insufficient for robust comparisons. This was further supported by the relatively small number of heavy drinkers among eligible participants. Last, because this study was conducted in a Korean population, additional research is needed to assess the generalizability of these findings to Western populations.

CONCLUSIONS

In this nationwide population-based study, we found that MASLD was significantly associated with incident AF. By distinguishing alcohol consumption levels, the new definition suggested that the metabolic dysfunction, as reflected by SLD, may be more significantly associated with AF occurrence than the direct toxic effects of alcohol itself.

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Disclosures

None.

Supplemental Material

Tables S1–S7
Figures S1–S2

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