Alcohol Abstinence and the Risk of Atrial Fibrillation in Patients With Newly Diagnosed Type 2 Diabetes Mellitus: A Nationwide Population-Based Study

You-jung Choi,[1] Kyung-Do Han,[2] Eue-Keun Choi,[1,3] Jin-Hyeung Jung,[4] So-Ryoung Lee,[1] Seil Oh,[1,3] and Gregory Y.H. Lip[3,5,6]

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OBJECTIVE

To investigate the effects of alcohol abstinence on prevention of new-onset atrial fibrillation (AF) in patients with type 2 diabetes mellitus (T2DM).

RESEARCH DESIGN AND METHODS

A total of 1,112,682 patients newly diagnosed with T2DM between 2011 and 2014 were identified from the Korean National Health Insurance Service database. After excluding those with a history of AF, 175,100 patients were included. The primary outcome was new-onset AF.

RESULTS

During a mean follow-up of 4.0 years, AF occurred in 4,174 patients. Those with heavy alcohol consumption (alcohol intake ≥40 g/day) before T2DM diagnosis had a higher risk of AF (adjusted hazard ratio [aHR] 1.22; 95% CI 1.06–1.41) compared with patients with no alcohol consumption. After T2DM diagnosis, those with moderate to heavy alcohol consumption (alcohol intake ≥20 g/day) who abstained from alcohol had a lower risk of AF (aHR 0.81; 95% CI 0.68–0.97) compared with constant drinkers. Alcohol abstinence showed consistent trends toward lower incident AF in all subgroups and was statistically significant in men (aHR 0.80; 95% CI 0.67–0.96), those aged >65 years (aHR 0.69; 95% CI 0.52–0.91), those with CHA_2DS_2-VASc score <3 points (aHR 0.71; 95% CI 0.59–0.86), noninsulin users (aHR 0.77; 95% CI 0.63–0.94), and those with BMI <25 kg/m^2 (aHR 0.68; 95% CI 0.53–0.88).

CONCLUSIONS

In patients with newly diagnosed T2DM, alcohol abstinence was associated with a low risk of AF development. Lifestyle modifications, such as alcohol abstinence, in patients newly diagnosed with T2DM should be recommended to reduce the risk of AF.

With an increase in the aging population, the prevalence of atrial fibrillation (AF), which is the most common sustained arrhythmia worldwide, is increasing, and effective prevention strategies should be implemented to mitigate this public health problem (1,2). The prevalence of diabetes is also rapidly increasing, with an increase in the number of patients at high risk of cardiovascular disease (3). Diabetes, specifically type 2 diabetes

[1]Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea
[2]Department of Statistics and Actuarial Science, Soongsil University, Seoul, Republic of Korea
[3]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea
[4]Department of Biostatistics, The Catholic University of Korea, Seoul, Republic of Korea
[5]Liverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool Chest and Heart Hospital, Liverpool, U.K.
[6]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

Corresponding author: Eue-Keun Choi, choiek17@snu.ac.kr

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Y.-j.C. and K.-D.H. contributed equally to this study.

mellitus (T2DM), is a strong risk factor for atherosclerotic cardiovascular disease, and it also increases the risk of AF development by 28% (4). Therefore, a combined approach to target diabetes and cardiovascular disease is important.

Unhealthy lifestyle habits, including lack of regular physical activity, obesity, weight fluctuation, and smoking, have a close association with a higher risk of incident AF (5–7). However, the association between alcohol consumption and cardiovascular disease is still controversial (8). The cardioprotective effects of alcohol consumption have been touted since the 18th century, and the majority of the literature suggests that a small amount of alcohol is beneficial but excess drinking is detrimental to the cardiovascular system (9). Moreover, a recent clinical trial on secondary prevention of AF supported that a substantial reduction in alcohol consumption could reduce the recurrence of AF (10). Although the mechanism underlying the increased susceptibility to AF because of alcohol consumption is not clearly understood, there are several pathophysiological mechanisms for AF development resulting from alcohol, including alternations in calcium handling (11), hypertension (12), obesity, and sleep apnea (13).

On the basis of these considerations, we hypothesized that alcohol abstinence in a T2DM population at high risk of developing AF would reduce the risk of incident AF development. To test this hypothesis, we aimed to investigate whether changes in alcohol consumption behavior in moderate to heavy alcohol consumption (≥20 g/day) would influence new-onset AF in patients newly diagnosed with T2DM.

RESEARCH DESIGN AND METHODS

Data Sources and Study Population

In this study, we used the Korean National Health Insurance Service–Health Screening Cohort (NHIS-HEALS) database, which is the national health claims database linked with the National Health Screening Program database (14). The National Health Screening Program includes physical examinations, regular blood tests, and self-administered questionnaires on lifestyle behavior, including alcohol consumption behavior, smoking status, and amount of moderate- to vigorous-intensity physical activity. The Korean government established the NHIS-HEALS database in 2015 to provide integrated health claims data appropriate and useful for a wide range of health research efforts. In the NHIS database, diagnoses are recorded based on the ICD-10 Clinical Modification (ICD-10-CM) codes.

We identified 1,112,682 patients newly diagnosed with T2DM between 2011 and 2014 from the NHIS database. T2DM was defined on the basis of diagnostic codes of T2DM (E11–E14), either one recorded during hospitalization or at least two recorded in outpatient clinics and/or the prescription of insulin and/or at least one oral hypoglycemic agent (14). Oral hypoglycemic agents included metformin, sulfonylurea, meglitinides, thiazolidinedione, dipeptidyl peptidase 4 inhibitor, and α-glucosidase inhibitor.

This study was approved by the institutional review board of Seoul National University Hospital (E-1912-085-1089). This study was conducted in accordance with the Declaration of Helsinki. The NHIS-HEALS database has been made publicly available to facilitate wider use of the health screening database with anonymous and deidentified information; therefore, the requirement for informed consent was waived.

Alcohol Consumption Behavior

Alcohol consumption behavior was defined based on data on the frequency of alcohol intake per week and the amount of alcohol consumed per drinking episode obtained from a health screening self-administered questionnaire in the NHIS-HEALS database.

After excluding individuals with a history of AF, we reviewed information on alcohol consumption behavior of 175,100 patients within 2 years before the first diagnosis of T2DM (Fig. 1). Alcohol consumption behavior was divided into three groups according to the average amount of alcohol intake per day as follows: *1*) no alcohol consumption (0 g/day), *2*) mild alcohol consumption (<20 g/day), and *3*) moderate to heavy consumption (≥20 g/day).

Alcohol Consumption Behavior Change in Patients With Moderate to Heavy Alcohol Consumption

To evaluate the impact of alcohol abstinence on the risk of AF, we classified patients with moderate to heavy alcohol consumption before T2DM diagnosis (n = 20,809) into two groups according to average alcohol consumption within 2 years after the first diagnosis of T2DM: *1*) abstainers who became non- to mild drinkers (<20 g/day) and *2*) constant drinkers who continued to drink alcohol moderately or heavily (≥20 g/day) (Fig. 1). Among patients reporting no alcohol consumption (n = 112,271), those who did not drink after being newly diagnosed with T2DM were defined as nondrinkers.

Primary Outcome: New-Onset AF

The primary outcome was new-onset AF, which was defined as a new diagnosis with ICD-10-CM codes I480–I484 and I489 by either one record during hospitalization or at least two records in the outpatient clinic. Because of apparent differences in a pathophysiological mechanism in valvular and nonvalvular AF, we excluded patients diagnosed as having mitral stenosis (I050, I052, and I059) and those who had mechanical heart valves (Z952–Z954) from the analysis to identify new-onset AF with a mechanism other than those by valvular heart disease. This definition has been validated in previous studies (15). The study population was followed up until the occurrence of AF, death, or 31 December 2017, whichever came first. Death or emigration before the primary event was treated as a censoring event.

Definition of Covariates

Demographic findings and socioeconomic variables were based on the NHIS-HEALS database. ICD-10-CM codes, prescription, and use of health care services (claims data) were used to define the comorbidities of the study population (Supplementary Table 1).

BMI was defined as weight in kilograms divided by the square of height in meters (kg/m^2). Smoking status (non-, former, or current smoker) and amount of moderate- to vigorous-intensity physical activity were obtained using a health screening self-administered questionnaire. Regular physical activity was defined as moderate physical activity for >30 min, at least five times per week, or strenuous physical activity for >20 min, at least three times per week. Low-income status indicated the lowest

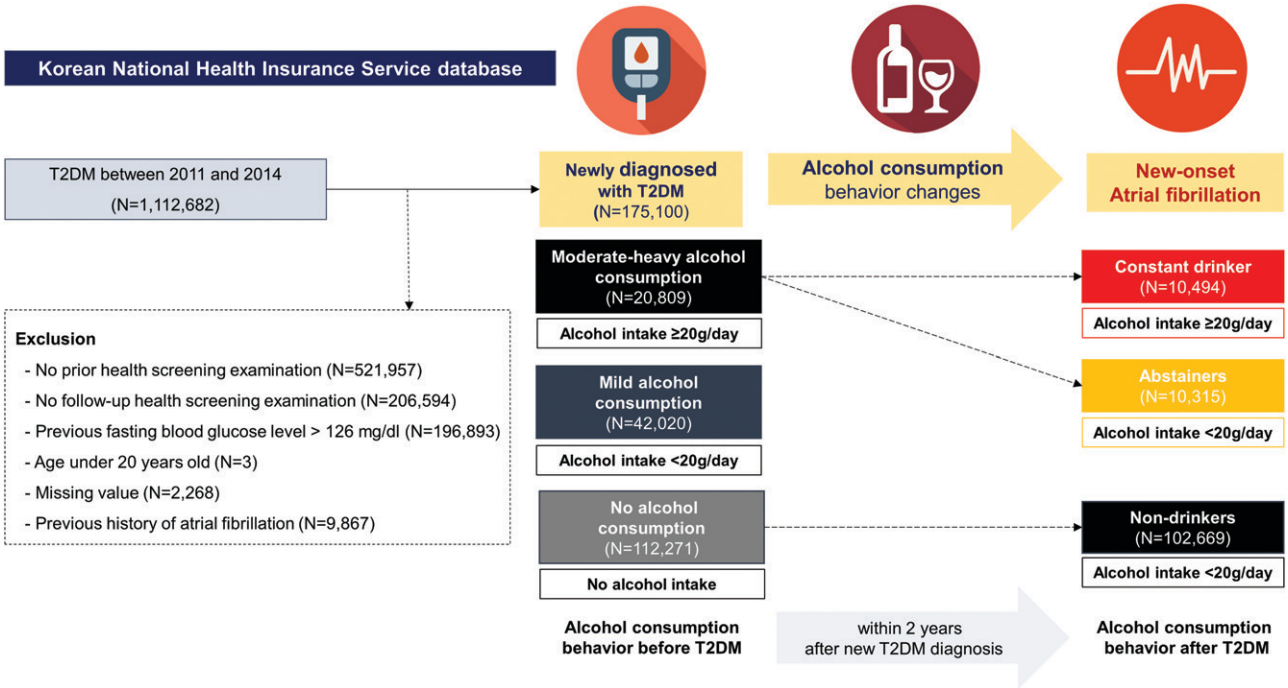


Figure 1—Flow of study population. Patients were divided into three groups based on the average amount of alcohol consumed before the first diagnosis of T2DM (alcohol consumption behavior): *1*) no alcohol consumption (0 g/day), *2*) mild alcohol consumption (<20 g/day), and *3*) moderate to heavy consumption (≥20 g/day). Alcohol consumption behavior change among those who drank a moderate to heavy amount (≥20 g/day) was defined as the average amount of alcohol consumed within 2 years after new diagnosis of T2DM: *1*) constant drinkers (≥20 g/day) and *2*) abstainers (<20 g/day); those who did not drink alcohol either before or after T2DM diagnosis were defined as *3*) nondrinkers.

quadrant (25%) of income level. The CHA_2DS_2-VASc score comprises congestive heart failure, hypertension, age (>65 years = 1 point; >75 years = 2 points), diabetes, previous stroke/transient ischemic attack (2 points), vascular disease (peripheral arterial disease, previous myocardial infarction, and aortic atheroma), and sex category (female sex).

Statistical Analyses

Baseline characteristics are presented as numbers and percentages for categorical variables and means ± SDs for continuous variables. For baseline comparisons, the Student *t* or Mann-Whitney *U* test was used for continuous variables, and the χ^2 or Fisher exact test was used for categorical variables.

The event rate of the primary outcome is presented as 1,000 person-years, determined by dividing the number of events by the total person-year period. Hazard ratios (HRs) and 95% CIs for AF development were analyzed using the Cox proportional hazards model. For multivariate analysis, model 1 was adjusted for age and sex, and model 2 was adjusted for age, sex, BMI, smoking status, regular physical activity, low-income status, CHA_2DS_2-VASc score, hypertension, dyslipidemia, stroke/transient ischemic attack, congestive heart failure, peripheral artery disease, thromboembolism, use of insulin, and number of oral hypoglycemic agents. Subgroup analysis was performed according to the following: sex, age (<65 or ≥65 years), CHA_2DS_2-VASc score (<3 or ≥3 points), use of insulin, smoking status (non-, former, or current smoker), and BMI (<25 and ≥25 kg/m^2).

Statistical significance was defined as a two-sided *P* value of <0.05. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc.) and R version 3.2.4 (R Core Team) software.

RESULTS

Baseline Characteristics of Patients Newly Diagnosed With T2DM

Overall, 175,100 patients (mean age 61.1 years; male 50.4%) were newly diagnosed with T2DM between 2011 and 2014. Before they were diagnosed with T2DM, there were a total of 112,271 (64.1%), 42,020 (24.0%), and 20,809 (11.9%) nondrinkers, mild drinkers, and moderate to heavy drinkers, respectively. Baseline characteristics according to alcohol consumption before diagnosis of T2DM are summarized in Supplementary Table 2.

Risk of AF According to Alcohol Consumption Behavior Before T2DM Diagnosis

During a mean follow-up period of 4.0 years, new-onset AF was observed in 4,174 patients with T2DM. The risk of AF was different depending on the amount and frequency of alcohol consumption before T2DM diagnosis (Supplementary Table 3). Compared with no alcohol consumption, heavy alcohol consumption (average amount of alcohol consumed ≥40 g/day) was associated with a high risk of AF development (adjusted HR [aHR] 1.22; 95% CI 1.06–1.41). Drinking more than or equal to three times a week was significantly associated with AF development (aHR 1.13; 95% CI 1.03–1.25). Mild or moderate alcohol consumption (<40 g/day) and drinking fewer than three times a week was not statistically significantly associated with AF development compared with no alcohol consumption.

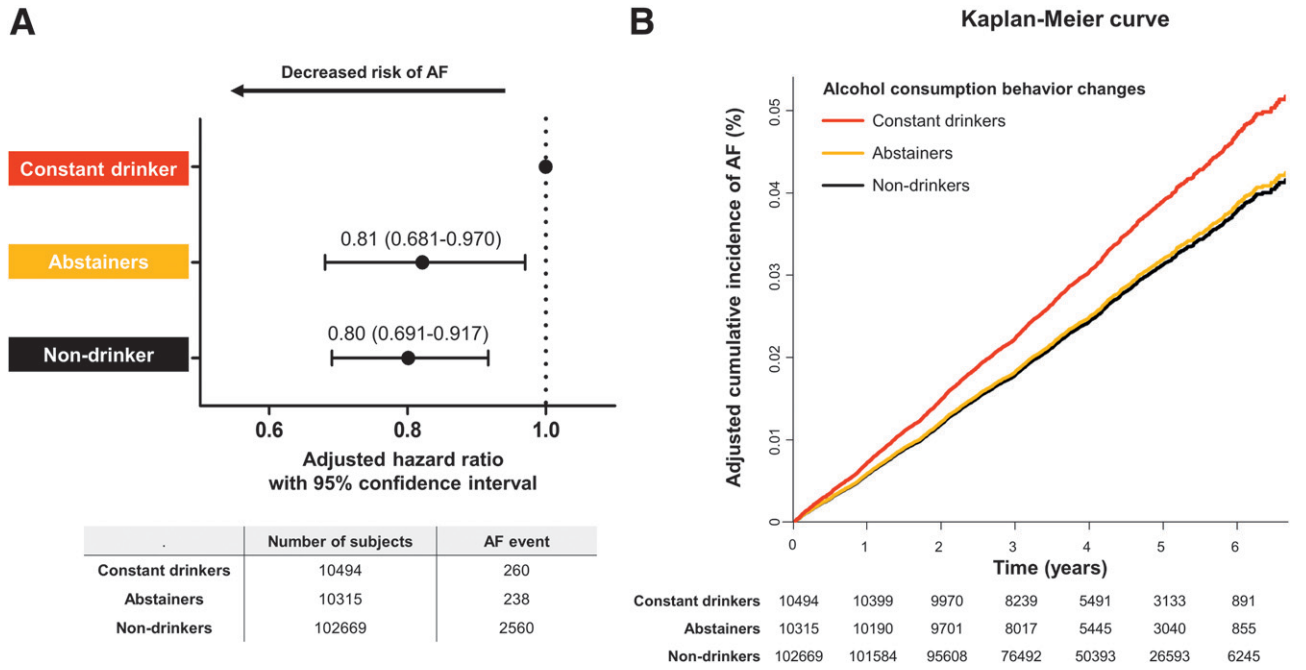
Table 1—Baseline characteristics according to alcohol consumption behavior change after the first diagnosis of T2DM

Variable	Nondrinkers (n = 102,669)	Abstainers (n = 10,315)	Constant drinkers (n = 10,494)
Age, years	63.9 ± 10.4	57.2 ± 11.1	55.3 ± 10.3
<65	52,255 (50.9)	7,705 (74.7)	8,584 (81.8)
65–75	35,783 (34.9)	2,071 (20.1)	1,592 (15.2)
≥75	14,631 (14.3)	539 (5.2)	318 (3.0)
Male sex	30,073 (29.3)	9,439 (91.5)	10,211 (97.3)
BMI, kg/m^2	25.1 ± 3.5	25.3 ± 3.5	25.7 ± 3.4
BP measurement, mmHg			
Systolic	126.7 ± 14.9	126.8 ± 14.1	129.0 ± 14.0
Diastolic	76.9 ± 9.5	78.6 ± 9.5	80.4 ± 9.6
Comorbidities			
Congestive heart failure	4,582 (4.5)	295 (2.9)	174 (1.7)
Hypertension	22,240 (21.7)	2,233 (21.7)	2,798 (26.7)
Dyslipidemia	62,350 (60.7)	5,600 (54.3)	5,725 (54.6)
Stroke/transient ischemic attack	4,654 (4.5)	448 (4.4)	236 (2.3)
Thromboembolism	902 (0.9)	79 (0.8)	1,095 (0.8)
Peripheral artery disease	21,648 (21.1)	1,651 (16.0)	1,533 (14.6)
Myocardial infarction	1,943 (1.9)	194 (1.9)	113 (1.1)
Total cholesterol, mg/dL	185.9 ± 40.4	184.4 ± 40.8	188.5 ± 40.7
Serum glucose, mg/dL	111.9 ± 26.0	117.0 ± 31.0	121.9 ± 32.8
AST, units/L	28.1 ± 23.4	33.1 ± 36.4	37.8 ± 47.4
ALT, units/L	28.4 ± 28.6	34.4 ± 33.1	37.7 ± 50.7
Smoking status			
Never	82,964 (80.8)	3,115 (30.2)	1,799 (17.1)
Former	11,644 (11.3)	3,586 (34.8)	3,798 (36.2)
Current	8,061 (7.9)	3,614 (35.0)	4,897 (46.7)
Low income	22,494 (21.9)	1,993 (19.3)	1,792 (17.1)
Regular physical activity	21,019 (20.5)	2,513 (24.4)	2,379 (22.7)
Insulin user	14,241 (13.9)	1,974 (19.1)	1,148 (10.9)
Oral hypoglycemic agent			
Single	66,334 (64.6)	6,266 (60.8)	6,713 (64.0)
Dual combination	26,864 (26.2)	2,858 (27.7)	2,891 (27.6)
Triple combination	9,471 (9.2)	1,191 (11.6)	890 (8.5)
CHA_2DS_2-VASc points	2.93 ± 1.28	1.91 ± 1.04	1.73 ± 0.91
≥3	58,965 (57.4)	2,425 (23.5)	1,747 (16.7)
CHA_2DS_2-VASc score*			
1	10,714 (10.4)	4,546 (44.1)	5,268 (50.2)
2	32,990 (32.1)	3,344 (32.4)	3,479 (33.2)
3	28,805 (28.1)	1,622 (15.7)	1,256 (12.0)
4	18,211 (17.7)	552 (5.35)	368 (3.51)
5	8,259 (8.04)	175 (1.7)	88 (0.84)
6	2,753 (2.68)	60 (0.58)	31 (0.3)
7	732 (0.71)	14 (0.14)	4 (0.04)
8	193 (0.19)	2 (0.02)	0 (0)
9	12 (0.01)	0 (0)	0 (0)

Data are presented as n (%) or mean ± SD. All variables were significantly different among the groups (all $P < 0.001$). *CHA_2DS_2-VASc score includes congestive heart failure, hypertension, age (>65 = 1 point; >75 = 2 points), diabetes, previous stroke/transient ischemic attack/thromboembolism (2 points), vascular disease (peripheral arterial disease, previous myocardial infarction, and aortic atheroma), and sex category (female sex).

Baseline Characteristics According to Alcohol Consumption Behavior Change

According to alcohol consumption behavior change within 2 years after new diagnosis of T2DM, abstainers and constant drinkers were younger (mean age 57.2 ± 11.1 and 55.3 ± 10.3 years, respectively) and more commonly male (91.5% and 97.3%, respectively) compared with nondrinkers (mean age 63.9 ± 10.4 years; male 29.3%). Nondrinkers had more underlying comorbidities, such as congestive heart failure, dyslipidemia, stroke/transient ischemic attack, and peripheral arterial disease compared with abstainers and constant drinkers (Table 1).



.	Number of subjects	AF event
Constant drinkers	10494	260
Abstainers	10315	238
Non-drinkers	102669	2560

Constant drinkers	10494	10399	9970	8239	5491	3133	891
Abstainers	10315	10190	9701	8017	5445	3040	855
Non-drinkers	102669	101584	95608	76492	50393	26593	6245

Figure 2—The risk of AF according to alcohol consumption behavior change after diagnosis of T2DM. *A*: Forest plot of aHRs (adjusted for age, sex, BMI, smoking status, regular physical activity, low income, CHA_2DS_2-VASc score, hypertension, dyslipidemia, chronic heart failure, peripheral arterial disease, stroke/transient ischemic attack, thromboembolism, use of insulin, and number of oral hypoglycemic agents) with 95% CIs of the risk of AF in abstainers and nondrinkers compared with constant drinkers. *B*: Kaplan-Meier curve estimates of the cumulative incidence of AF according to alcohol consumption behavior change.

Risk of AF According to Alcohol Consumption Behavior Change After T2DM Diagnosis

Compared with constant drinkers (average amount of alcohol consumed ≥20 g/day), abstainers (average amount of alcohol consumed <20 g/day) who previously engaged in moderate to heavy drinking after T2DM diagnosis (aHR 0.81; 95% CI 0.68–0.97) and nondrinkers (aHR 0.80; 95% CI 0.69–0.92) showed a significantly lower risk of new-onset AF (Fig. 2 and Supplementary Table 4). The risk of new-onset AF in the abstainer group was comparable to that in the nondrinker group ($P = 0.762$).

Subgroup Analysis

In the subgroup analysis, alcohol abstinence showed consistent trends toward lower incident AF compared with constant drinking across all subgroups (Table 2). Despite the small number in each subgroup, there were statistically significant differences for men (aHR 0.80; 95% CI 0.67–0.96), those aged <65 years (aHR 0.69; 95% CI 0.52–0.91) and ≥65 years (aHR 0.79; 95% CI 0.64–0.97), those with CHA_2DS_2-VAS score <3 points (aHR 0.71; 95% CI 0.59–0.86), noninsulin users (aHR 0.77; 95% CI 0.63–0.94), and those with low BMI (<25 kg/m^2) (aHR 0.68; 95% CI 0.53–0.88). Subgroup analysis according to changes in smoking habits and BMI also had no statistically significant interaction (Supplementary Table 5).

CONCLUSIONS

To our knowledge, this is the first study showing the beneficial effects of alcohol abstinence in preventing cardiovascular disease, specifically new-onset AF, in patients with T2DM. Our principal findings are as follows: *1*) heavy and frequent drinking patterns were both associated with a high risk of incident AF; *2*) alcohol abstainers who previously engaged in moderate to heavy drinking after T2DM diagnosis had a lower risk of AF development compared with those who still engaged in constant moderate to heavy drinking; *3*) those abstaining from alcohol had a low risk of incident AF, similar to that of nondrinkers, despite a history of moderate to heavy alcohol consumption before T2DM diagnosis; and *4*) subgroup analyses showed consistent trends in all relevant patient subgroups.

AF is common in patients with diabetes, and both conditions will be more prevalent in the future because of the aging population. Experimental and clinical evidence suggests that diabetes and AF are strongly pathologically interconnected (16,17). Mutual mechanisms that can explain an increased risk of AF with diabetes include structural remodeling of the left atrium in the form of atrial dilation and fibrosis (18), and electromechanical (19) and autonomic remodeling (20). Considering that diabetes has been associated with worse AF symptoms, lower quality of life, and increased risk of death and hospitalization, our main finding, that is, alcohol abstinence in patients with T2DM could lower the risk of developing AF, is an important consideration in the holistic approach to AF care (21,22).

Alcohol consumption is highly prevalent in the U.S. and has increased over the past few decades, reaching 2.35 gallons of ethanol per capita in 2018 (23). In Korea, the prevalence of high-risk alcohol consumption is 15.1%, with the highest prevalence of 28.3% found in middle-aged men (45–64 years) (24). Considering that the liver significantly metabolizes alcohol, this may have an impact on controlling

Table 2—Subgroup analysis

Variable	*n* of patients		Follow-up duration, person-years	Unadjusted		Adjusted			
						Model 1†		Model 2‡	
	Total	AF		HR (95% CI)	*P**	HR (95% CI)	*P**	HR (95% CI)	*P**
Sex group					0.728		0.261		0.350
Male									
Constant drinkers	10,211	255	41,499	1 (reference)		1 (reference)		1 (reference)	
Abstainers	9,439	222	38,361	0.94 (0.79–1.13)		0.83 (0.69–0.99)		0.80 (0.67–0.96)	
Nondrinkers	30,073	930	118,248	1.28 (1.12–1.47)		0.83 (0.71–0.95)		0.80 (0.69–0.92)	
Female									
Constant drinkers	283	5	1,091	1 (reference)		1 (reference)		1 (reference)	
Abstainers	876	16	3,499	1.00 (0.37–2.72)		0.90 (0.33–2.46)		0.86 (0.31–2.34)	
Nondrinkers	72,596	1,630	289,418	1.23 (0.51–2.95)		0.69 (0.29–1.68)		0.66 (0.27–1.61)	
Age group, years					0.429		0.329		0.267
<65									
Constant drinkers	8,584	156	35,200	1 (reference)		1 (reference)		1 (reference)	
Abstainers	7,705	135	31,745	0.96 (0.76–1.21)		0.97 (0.77–1.22)		0.92 (0.73–1.16)	
Nondrinkers	52,255	684	212,466	0.73 (0.61–0.86)		0.80 (0.66–0.98)		0.75 (0.61–0.92)	
≥65									
Constant drinkers	1,910	104	7,390	1 (reference)		1 (reference)		1 (reference)	
Abstainers	2,610	103	10,115	0.72 (0.55–0.95)		0.71 (0.54–0.93)		0.69 (0.52–0.91)	
Nondrinkers	50,414	1,876	195,200	0.68 (0.56–0.83)		0.82 (0.66–1.00)		0.79 (0.64–0.97)	
CHA_2DS-VASc points					0.552		0.142		0.144
< 3									
Constant drinkers	8,747	180	35,709	1 (reference)		1 (reference)		1 (reference)	
Abstainers	7,890	137	32,390	0.84 (0.67–1.05)		0.81 (0.65–1.01)		0.78 (0.63–0.98)	
Nondrinkers	43,704	600	176,686	0.68 (0.57–0.80)		0.74 (0.61–0.88)		0.71 (0.59–0.86)	
≥3									
Constant drinkers	1,747	80	6,881	1 (reference)		1 (reference)		1 (reference)	
Abstainers	2,425	101	9,471	0.92 (0.68–1.20)		0.91 (0.68–1.22)		0.87 (0.65–1.17)	
Nondrinkers	58,965	1,960	230,980	0.73 (0.58–0.91)		0.95 (0.75–1.20)		0.90 (0.71–1.14)	
Insulin use					0.547		0.605		0.639
Nonuser									
Constant drinkers	9,346	228	38,077	1 (reference)		1 (reference)		1 (reference)	
Abstainers	8,341	175	34,184	0.85 (0.70–1.04)		0.77 (0.63–0.94)		0.77 (0.63–0.94)	
Nondrinkers	88,428	2,085	353,409	0.99 (0.86–1.13)		0.78 (0.67–0.91)		0.77 (0.66–0.89)	
User									
Constant drinkers	1,148	32	4,513	1 (reference)		1 (reference)		1 (reference)	
Abstainers	1,974	63	7,676	1.16 (0.76–1.77)		1.05 (0.69–1.62)		1.03 (0.67–1.58)	
Nondrinkers	14,241	475	54,257	1.23 (0.86–1.76)		0.98 (0.67–1.43)		0.95 (0.65–1.39)	
Smoking status					<0.001		0.213		0.222
Nonsmoker									
Constant drinkers	1,799	60	7,336	1 (reference)		1 (reference)		1 (reference)	
Abstainers	3,115	80	12,598	0.78 (0.56–1.08)		0.77 (0.55–1.07)		0.73 (0.52–1.02)	
Nondrinkers	82,964	1,975	330,168	0.73 (0.57–0.95)		0.70 (0.53–0.92)		0.66 (0.51–0.87)	
Former									
Constant drinkers	3,798	90	15,375	1 (reference)		1 (reference)		1 (reference)	
Abstainers	3,586	91	14,559	1.07 (0.80–1.43)		0.95 (0.71–1.27)		0.92 (0.68–1.23)	
Nondrinkers	11,644	396	45,237	1.50 (1.19–1.88)		1.02 (0.80–1.29)		0.99 (0.78–1.26)	
Current									
Constant drinkers	4,897	110	19,880	1 (reference)		1 (reference)		1 (reference)	
Abstainers	3,614	67	14,703	0.82 (0.61–1.12)		0.76 (0.56–1.03)		0.75 (0.56–1.02)	
Nondrinkers	8,061	189	32,261	1.06 (0.84–1.34)		0.73 (0.57–0.94)		0.73 (0.57– 0.95)	
BMI, kg/m^2					0.191		0.104		0.073
<25									
Constant drinkers	4,612	129	18,601	1 (reference)		1 (reference)		1 (reference)	
Abstainers	5,017	110	20,217	0.79 (0.61–1.01)		0.71 (0.55–0.91)		0.68 (0.53–0.88)	
Nondrinkers	53,635	1,370	212,530	0.93 (0.78–1.12)		0.81 (0.67–0.99)		0.79 (0.65–0.96)	

Continued on p. 1399

Table 2—Continued

Variable	*n* of patients		Follow-up duration, person-years	Unadjusted		Adjusted			
						Model 1†		Model 2‡	
	Total	AF		HR (95% CI)	*P**	HR (95% CI)	*P**	HR (95% CI)	*P**
≥25									
Constant drinkers	5,882	131	23,989	1 (reference)		1 (reference)		1 (reference)	
Abstainers	5,298	128	21,643	1.08 (0.85–1.38)		0.99 (0.77–1.26)		0.96 (0.75–1.23)	
Nondrinkers	49,034	1,190	195,136	1.12 (0.93–1.34)		0.83 (0.68–1.02)		0.80 (0.65–0.99)	

**P* for interaction. †Model 1: adjusted for age and sex. ‡Model 2: adjusted for age, sex, BMI, smoking status, regular physical activity, low income, CHA_2DS_2-VASc score, hypertension, dyslipidemia, chronic heart failure, peripheral arterial disease, stroke/transient ischemic attack, thromboembolism, use of insulin, and number of oral hypoglycemic agents.

blood glucose levels among patients with diabetes (25). Furthermore, alcohol is high in carbohydrates and calories, which increase blood glucose levels and stimulate patients' appetite, leading to increased glucose levels as a result of overeating.

>The lowering of AF risk through alcohol abstinence could be explained by several mechanisms. First, alcohol could affect the autonomic nervous system, including sympathetic effects and vagal stimulation, which are considered important triggers for AF (26). Second, alcohol is well known to cause direct cardiac toxicity, triggering AF by rendering the myocardium in the atria more susceptible to AF, and binge and frequent drinking could lead to cardiac inflammation (27). Previous observational studies have linked regular alcohol consumption (as compared with no alcohol consumption) with dose-related increases in left atrial size (28), impairments in atrial mechanical and reservoir function (29), and adverse electrical remodeling (30). Alcohol is also associated with systolic hypertension, which increases the risk of AF by the activation of the renin-angiotensin system, increased vascular reactivity, and inhibition of endothelial nitric oxide production (12).

The effect of mild alcohol consumption (usually defined as <10–20 g/day) is associated with lower incidence, in a U-shaped pattern, of cardiovascular disease (31,32). As one of the major cardiovascular diseases, AF showed tendencies with regard to alcohol consumption similar to those of other cardiovascular diseases. Among middle-aged patients with diabetes, mild alcohol consumption did not seem to be associated with an increased risk of AF, but excessive alcohol consumption was associated with an increased risk of AF (33). Consistently, our findings showed that frequent drinking and heavy alcohol consumption led to a significantly higher risk of AF development, whereas less frequent or mild alcohol consumption did not lead to a higher risk of AF development. However, the association between mild alcohol consumption and dose-dependent risk of AF has been reported in several large meta-analyses (34–36). In the most recent meta-analysis of seven prospective studies with 79,019 men and women, Larsson et al. (36) reported that all studies demonstrated a linear dose-dependent pattern of association between the risk of AF and alcohol consumption, even a mild amount, with an overall 8% increase in the risk of AF per 1 drink/day increment in alcohol consumption. Additional studies are needed to determine the association between mild alcohol consumption and the risk of AF in patients with cardiovascular diseases, leading to a higher risk of AF.

Our findings suggest that regular alcohol consumption is a potentially modifiable risk factor for AF in patients with T2DM. For patients with diabetes, lifestyle modification is an important and effective nonpharmaceutical strategy to prevent cardiovascular disease, as much as controlling serum glucose levels with medication. Alcohol abstinence should be considered part of the overall management strategy for preventing AF development in patients with T2DM (37). Indeed, lifestyle modification (addressing excessive alcohol consumption) is part of the Atrial fibrillation Better Care (ABC) pathway for holistic AF care, which is advocated in the new 2020 European Society of Cardiology guidelines (38). The ABC pathway has been shown to improve adverse clinical outcomes in AF populations (39).

There are limitations to the current study. First, this was an observational study, which did not allow ascertainment of causality. However, we tried to show the time-sequential changes to demonstrate the cause-effect associations of alcohol consumption behavior change with data from the serial health examination program database. Second, this study was conducted in the Korean population; it is unclear whether the results could be extrapolated to the non-Asian population. Considering that ADH1B*2 variant alleles are predominant among East Asians, the effect of abstinence on the risk of AF would be more prominent (40). Therefore, it may be necessary to conduct a large-scale multiethnic study, including various high-risk populations, to generalize the effects of alcohol abstinence in preventing AF development. Finally, this study, based on the NHIS database, did not provide detailed information on the characteristics of patients with T2DM, such as serial HbA_{1c} levels, genetic mutations, and combined diabetes-related complications.

In summary, in patients with newly diagnosed T2DM, alcohol abstinence in those with moderate to heavy alcohol consumption before diagnosis was associated with a low risk of AF development. Lifestyle modification, such as alcohol abstinence, in patients newly

diagnosed with T2DM should be recommended to reduce the risk of AF.

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