Supplementary materials

Alcohol abstinence and the risk of atrial fibrillation in patients with newly diagnosed type 2 diabetes mellitus: a nationwide population-based study

Short title: Alcohol abstinence and the risk of atrial fibrillation

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Supplementary Table S1. Definition of comorbidities

Diagnosis	ICD 10th Revision-Clinical Modification code and definition	Diagnostic definition
Congestive heart failure	I50	-
Hypertension	I10-I13, I15 and minimum 1 prescription of anti-hypertensive drug (thiazide, loop diuretics, aldosterone antagonist, alpha-/beta-blocker, calcium-channel blocker, angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker)	Systolic blood pressure ≥140 mmHg or Diastolic blood pressure ≥90 mmHg
Dyslipidemia	E78 and minimum 1 prescription of lipid-lowering drug	Fasting total cholesterol ≥240 mg/dl
Stroke	I63, I64	-
Transit ischemic attack	G458, G459	-
Thromboembolism	I74, I26, I802	-
Peripheral artery disease	I70, I73	-
Myocardial infarction	I21, I22	-

ICD indicates International Classification of Disease.

Supplementary Table S2. Baseline characteristics according to the amount of alcohol consumption before the first diagnosis type 2 diabetes mellitus.

Variables	Amount of alcohol consumption		
	Non-drinkers	**Mild alcohol consumption (< 20 g/day)**	**Moderate-Heavy alcohol consumption (≥20 g/day)**
Number, n (%)	112271 (64.1)	42020 (24.0)	20809 (11.9)
Age, years	63.4 ± 10.6	57.3 ± 11.5	56.3 ± 10.8
< 65 years-old, n (%)	58924 (52.5)	30694 (73.05)	16289 (78.3)
65-75 years-old, n (%)	37987 (33.8)	8928 (21.3)	3663 (17.6)
≥ 75 years-old, n (%)	15360 (13.7)	2398 (5.7)	857 (4.1)
Male sex, n (%)	36263 (32.3)	32333 (77.0)	19650 (94.4)
Body mass index, kg/m^2	25.1 ± 3.52	25.3 ± 3.4	25.5 ± 3.43
BP measurements			
Systolic BP, mmHg	126.7 ± 14.8	125.9 ± 14.0	127.9 ± 14.1
Diastolic BP, mmHg	77.0 ± 9.5	78.0 ± 9.5	79.5 ± 9.6
Comorbidities, n (%)			
Congestive heart failure	4843 (4.3)	1086 (2.6)	469 (2.3)
Hypertension	24284 (21.6)	8324 (19.8)	5031 (24.2)
Dyslipidaemia	67820 (60.4)	23408 (55.7)	11325 (54.4)
stroke/transit ischaemic attack	4972 (4.5)	1420 (3.4)	684 (3.3)
Thromboembolism	964 (0.9)	290 (0.69)	131 (0.6)
Peripheral artery disease	23276 (20.7)	6443 (15.3)	3184 (15.3)
Myocardial infarction	2090 (1.9)	708 (1.7)	307 (1.5)
Triglyceride, mg/dL	35.3 ± 44.5	53.5 ± 67.3	90.0 ± 114.8
Serum glucose, mg/dL	112.3 ± 26.3	116.2 ± 30.4	119.5 ± 32.0
Aspartate aminotransferase, U/L	28.4 ± 24.1	30.1 ± 21.7	35.5 ± 42.4
Alanine aminotransferase, U/L	28.7 ± 29.2	32.8 ± 28.0	36.1 ± 42.9
Smoking status, n (%)			
Never	87834 (78.2)	17535 (41.7)	4914 (23.6)
Ex-smoker	14213 (12.7)	13153 (31.3)	7384 (35.5)
Current smoker	10224 (9.1)	11332 (27.0)	8511 (40.9)
Low income, n (%)	24553(21.9)	7921(18.9)	3785 (18.2)
Regular physical activity, n (%)	23303(20.8)	10742(25.6)	4892 (23.5)
Insulin user, n (%)	15377 (13.7)	6048 (14.4)	3122 (15.0)
Oral hypoglycemic agent, n (%)			
Single	72518 (64.6)	26456 (63.0)	12979 (62.4)
Dual combination	29456 (26.2)	11445 (27.2)	5749 (27.6)

Triple combination	10297 (9.2)	4119 (9.8)	2081 (10.0)
CHA_2DS_2-VAS score, point	2.87 ± 1.28	2.02 ± 1.08	1.82 ± 0.98
≥3 points, n (%)	62187 (55.4)	11189 (26.6)	4172 (20.1)
CHA_2DS_2-VAS score, n (%)			
1	13533 (12.1)	15890 (37.8)	9814 (47.2)
2	36551 (32.6)	14941 (35.6)	6823 (32.8)
3	30764 (27.4)	7163 (17.1)	2878 (13.8)
4	19047 (17.0)	2740 (6.5)	920 (4.4)
5	8574 (7.6)	938 (2.2)	263 (1.3)
6	2835 (2.5)	290 (0.69)	91 (0.44)
7	760 (0.68)	50 (0.12)	18 (0.09)
8	194 (0.17)	8 (0.02)	2 (0.01)
9	13 (0.01)	0 (0)	0 (0)

All variables were significantly different among the groups (All p <0.001).

BP indicates blood pressure. The CHA_2DS_2-VASc stands for congestive heart failure, hypertension, age (>65 years = 1 point, >75 years = 2 points), DM, previous stroke/transient ischemic attack (2 points), vascular disease (peripheral arterial disease, previous myocardial infarction, aortic atheroma), and sex category (female sex).

Supplementary Table S3. The relative risk of atrial fibrillation according to the amount and frequency of alcohol consumption at baseline

Variables	Total number	Atrial fibrillation	Follow-up duration*	Unadjusted HR (95% CI)	Adjusted (Model 1) HR (95% CI)	Adjusted (Model 2) HR (95% CI)
Drinking amount per day						
None	112271	2782	446418	1 (Reference)	1 (Reference)	1 (Reference)
Mild (< 20 g/day)	42020	894	169904	0.84 (0.78–0.91)	0.99 (0.91–1.07)	1.00 (0.92–1.09)
Moderate (20–39 g/day)	12581	268	51338	0.84 (0.74–0.95)	1.06 (0.93–1.21)	1.05 (0.92–1.20)
Heavy (≥ 40 g/day)	8228	230	33113	1.11 (0.97–1.27)	1.24 (1.08–1.43)	1.22 (1.06–1.41)
Drinking frequency per week						
0	112271	2782	446418	1 (Reference)	1 (Reference)	1 (Reference)
1 or 2 days	39476	747	160544	0.75 (0.69–0.81)	0.96 (0.88–1.05)	0.97 (0.89–1.06)
More than or equal 3 days	23353	645	93810	1.10 (1.01–1.20)	1.13 (1.03–1.24)	1.13 (1.03–1.25)

*Follow-up duration present as person-years.

Model 1: adjusted for age and sex.

Model 2: adjusted for age, sex, body mass index, smoking status, regular physical activity, low income, CHA_2DS_2-VASc score, hypertension, dyslipidemia, chronic heart failure, peripheral arterial disease, stroke/transit ischemic attack, thromboembolism, the use of insulin, and the number of oral hypoglycemic agents.

Supplementary Table S4. Risk of atrial fibrillation according to alcohol consumption behavior change after the first diagnosis of type 2 diabetes mellitus

Variables	Total number	AF	Follow-up duration*	Unadjusted	Adjusted (Model 1)	Adjusted (Model 2)
				HR (95% CI)	HR (95% CI)	HR (95% CI)
Constant drinkers	10494	260	42590	1 (Reference)	1 (Reference)	1 (Reference)
Abstainers	10315	238	41860	0.93 (0.78–1.11)	0.83 (0.69–0.99)	0.81 (0.68–0.97)
Non-drinkers	102669	2560	407666	1.03 (0.91–1.17)	0.79 (0.69–0.91)	0.80 (0.69–0.92)

*Follow-up duration was presented as person-years.

Model 1: adjusted for age and sex

Model 2: adjusted for age, sex, body mass index, smoking status, regular physical activity, low income, CHA_2DS_2-VAS score, hypertension, dyslipidemia, chronic heart failure, peripheral arterial disease, stroke/transit ischemic attack, thromboembolism, the use of insulin, and the number of oral hypoglycemic agents.

AF indicates atrial fibrillation; HR, hazard ratio; CI, confidence interval.

Supplementary Table S5. Subgroup analysis according to changes in smoking habit and body mass index.

Variables	Total number	AF	Follow-up duration*	Unadjusted	*P* value†	Adjusted (Model 1)	*P* value†	Adjusted (Model 2)	*P* value†
				HR (95% CI)		HR (95% CI)		HR (95% CI)	
Change in smoking status					0.119		0.459		0.491
None → None									
Constant drinkers	4648	132	18915	1 (Reference)		1 (Reference)		1 (Reference)	
Abstainers	5118	131	20752	0.90 (0.71–1.15)		0.82 (0.65–1.05)		0.80 (0.62–1.01)	
Non-drinkers	91189	2265	362141	0.90 (0.75–1.07)		0.81 (0.67–0.98)		0.78 (0.64–0.94)	
None → Current									
Constant drinkers	366	13	1503	1 (Reference)		1 (Reference)		1 (Reference)	
Abstainers	322	5	1354	0.42 (0.15–1.19)		0.37 (0.13–1.04)		0.36 (0.13–1.02)	
Non-drinkers	1315	32	5256	0.70 (0.37–1.34)		0.48 (0.24–0.98)		0.48 (0.23–0.97)	
Current → None									
Constant drinkers	949	18	3796	1 (Reference)		1 (Reference)		1 (Reference)	
Abstainers	1583	40	6404	1.32 (0.76–2.30)		1.21 (0.69–2.11)		1.10 (0.63–1.93)	
Non-drinkers	3419	106	13264	1.69 (1.03–2.78)		1.20 (0.71–2.02)		1.12 (0.66–1.89)	
Current → current									
Constant drinkers	4531	97	18377	1 (Reference)		1 (Reference)		1 (Reference)	
Abstainers	3292	62	13350	0.88 (0.64–1.21)		0.81 (0.59–1.12)		0.81 (0.58–1.11)	
Non-drinkers	6746	157	27005	1.10 (0.86–1.42)		0.76 (0.58–1.00)		0.76 (0.58–1.00)	
Body mass index change (kg/m$^{2)}$					0.445		0.525		0.445
< 25 → < 25									

Constant drinkers	3878	110	15558	1 (Reference)	1 (Reference)	1 (Reference)
Abstainers	4126	94	16523	0.81 (0.61–1.06)	0.71 (0.54–0.94)	0.69 (0.52–0.91)
Non-drinkers	43561	1089	172309	0.90 (0.74–1.09)	0.77 (0.62–0.96)	0.75 (0.60–0.93)
< 25 → ≥ 25						
Constant drinkers	487	12	1949	1 (Reference)	1 (Reference)	1 (Reference)
Abstainers	483	13	1965	1.08 (0.49–2.37)	1.03 (0.47–2.26)	1.02 (0.46–2.26)
Non-drinkers	4309	107	16936	1.03 (0.57–1.87)	0.78 (0.39–1.54)	0.78 (0.39–1.54)
≥ 25 → < 25						
Constant drinkers	734	19	3043	1 (Reference)	1 (Reference)	1 (Reference)
Abstainers	891	16	3694	0.70 (0.36–1.35)	0.64 (0.33–1.25)	0.62 (0.32–1.21)
Non-drinkers	10074	281	40221	1.12 (0.71–1.79)	0.98 (0.59–1.61)	0.95 (0.58–1.57)
≥ 25 → ≥ 25						
Constant drinkers	5395	119	22040	1 (Reference)	1 (Reference)	1 (Reference)
Abstainers	4815	115	19678	1.08 (0.84–1.40)	0.98 (0.76–1.27)	0.96 (0.74–1.24)
Non-drinkers	44725	1083	178201	1.13 (0.93–1.36)	0.83 (0.67–1.03)	0.80 (0.65–1.00)

*Follow-up duration was presented as person-years. †*P* for interaction.

Model 1: adjusted for age and sex

Model 2: adjusted for age, sex, body mass index, smoking status, regular physical activity, low income, CHA_2DS_2-VASc score, hypertension, dyslipidemia, chronic heart failure, peripheral arterial disease, stroke/transit ischemic attack, thromboembolism, the use of insulin, and the number of oral hypoglycemic agents.