ORIGINAL RESEARCH

Does Moderate Drinking Increase the Risk of Atrial Fibrillation? The Norwegian HUNT (Nord-Trøndelag Health) Study

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***Background*—**Compelling evidence suggests that excessive alcohol consumption increases the risk of atrial fibrillation (AF), but the effect of light-moderate alcohol consumption is less certain. We investigated the association between alcohol consumption within recommended limits and AF risk in a light-drinking population.

***Methods and Results*—**Among 47 002 participants with information on alcohol consumption in a population-based cohort study in Norway, conducted from October 2006 to June 2008, 1697 validated AF diagnoses were registered during the 8 years of follow-up. We used Cox proportional hazard models with fractional polynomials to analyze the association between alcohol intake and AF. Population attributable risk for drinking within the recommended limit (ie, at most 1 drink per day for women and 2 drinks per day for men without risky drinking) compared with nondrinking was also calculated. The average alcohol intake was 3.8±4.8 g/d. The adjusted hazard ratio for AF was 1.38 (95% confidence interval, 1.06–1.80) when we compared participants consuming >7 drinks per week with abstainers. When we modeled the quantity of alcohol intake as a continuous variable, the risk increased in a curvilinear manner. It was higher with heavier alcohol intake, but there was virtually no association at <1 drink per day for women and <2 drinks per day for men in the absence of risky drinking. The population attributable risk among nonrisky drinkers was 0.07% (95% confidence interval, −0.01% to 0.13%).

***Conclusions*—**Although alcohol consumption was associated with a curvilinearly increasing risk of AF in general, the attributable risk of alcohol consumption within recommended limits among participants without binge or problem drinking was negligible in this population. **(*J Am Heart Assoc*. 2017;6:e007094. DOI: 10.1161/JAHA.117.007094.)**

Key Words: alcohol • atrial fibrillation • cohort study • epidemiology • HUNT • moderate alcohol

Excessive alcohol consumption is clearly responsible for adverse health outcomes, including various types of cardiovascular diseases.[1] Heavy alcohol consumption specifically increases the risk of cardiomyopathy, hypertension, and stroke, although light-moderate alcohol consumption tends to be associated with a reduced risk of ischemic heart diseases[2] and heart failure.[2–4]

In contrast to the effects of alcohol on the vasculature and on the myocardium, the effect of alcohol on atrial fibrillation (AF) is not as widely studied. Heavy drinking immediately increases risk of triggering atrial arrhythmias, like AF, sufficiently frequently to be termed the *holiday heart syndrome*.[5,6] However, whether light-moderate alcohol consumption is associated with increased risk of AF is less clear. Meta analyses and a recent study examining the long-term effect of the quantity of alcohol intake on AF risk have suggested a dose-response relationship, with a slightly increased risk even among light-moderate drinkers (ie,

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Accompanying Tables S1 through S8 are available at http://jaha.ahajournals.org/content/6/10/e007094/DC1/embed/inline-supplementary-material-1.pdf

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Clinical Perspective

What Is New?

- Alcohol intake is associated with atrial fibrillation risk in a curvilinear manner, with almost no increase up to 7 drinks per week and a steep increase at >14 drinks per week alcohol consumption.
- The population fraction of atrial fibrillation risk attributable to alcohol consumption, when consumed within recommended limits (up to 1 drink per day for women and 2 drinks per day for men, with no binge drinking), was essentially 0.

What Are the Clinical Implications?

- Light-moderate alcohol consumption within recommended limits (up to 1 drink per day for women and 2 drinks per day for men, without binge drinking) is not associated with a meaningfully increased risk of atrial fibrillation.
- Over recommended limits, however, alcohol intake increases the risk of atrial fibrillation.

consumers of up to 1–2 drinks per day).[6–10] However, meta-analyses that have addressed nonlinearity in their analyses have neither found clear evidence for a J-shape or threshold-type association nor could they rule out the existence of such a threshold.[9,10] Moreover, cohort studies have generally assessed only the overall quantity of alcohol intake on AF risk. Because binge drinking is a clear trigger for AF,[6,11] it may increase long-term risk of AF, even when the overall quantity does not exceed the recommended limits (ie, 1 drink for women and 2 drinks for men per day).[6,9,10] Furthermore, no previous study has estimated the population attributable risk of light-moderate alcohol intake for AF.

The objective of our study was to examine the association of light-moderate alcohol consumption with AF risk in a population-based cohort with a substantial number of light drinkers.

Methods

Study Population

In total, 93 860 individuals, aged 20 years or older and living in Nord-Trøndelag County in Norway, were invited to HUNT3 (the third wave of the Nord-Trøndelag Health Study), conducted between October 2006 and June 2008. A total of 50 803 (54.1%) of the invited attended a clinical examination conducted by trained nurses and answered self-administered questionnaires about their health status, medical history, and lifestyle. During the clinical examination, anthropometric characteristics, blood pressure were measured and nonfasting blood samples were taken. A more detailed description of the HUNT3 study can be found elsewhere.[12] Among those who participated, 47 002 people had no previous AF and provided valid answers on the questions about their alcohol consumption (Figure 1). Approximately 70% of those who were included in our study also reported their alcohol intake in the previous wave of HUNT (HUNT2) conducted between August 1995 and June 1997 (Figure 1).

The study was approved by the Regional Committee for Ethics in Medical Research (2015/2313/REK), the National Directorate of Health, and the Norwegian Data Inspectorate. All study participants provided written informed consent.

Measures

Alcohol consumption

Alcohol consumption was assessed with several overlapping self-administered questions.

First, participants reported how often they consumed alcohol in the past 12 months. Those who reported drinking alcohol at least once in the past month were further asked about their usual number of standard servings of beer (containing >3.5% alcohol by volume), wine, and spirits in the past 2 weeks. Participants were also asked how often they drank 5 drinks or more in one setting. In addition, the CAGE questionnaire was completed to assess problem drinking.[13] We categorized participants according to their average quantity of alcohol intake: (1) those who reported no alcohol consumption during the past year were classified as nondrinkers, (2) those who reported no alcohol consumption in a usual 2-week period, but consumed alcohol during the past year, were considered rare drinkers; (3) those who reported alcohol consumption during a usual 2-week period were categorized as consuming 3 or fewer drinks per week, (4) those consuming between >3 and 7 drinks per week, or (5) those consuming >7 drinks per week. Daily alcohol consumption (in grams) was also calculated, assuming 12 g alcohol in a standard drink.[14]

Binge drinking was defined as reporting the consumption of 5 or more units of alcohol in one sitting at least once per week. *Problem drinkers* were considered participants who endorsed at least 2 risky alcohol-related behaviors from the CAGE questionnaire.

We defined *nonrisky drinking* as no more than 7 drinks per week for women and no more than 14 drinks per week for men,[15] with no report of binge or problem drinking.

Participants who reported no alcohol consumption in HUNT3, but participated in HUNT2, were categorized as either long-term abstainers, if they were nondrinkers in HUNT2, or abstainers, who were former drinkers if they reported any alcohol intake 10 years earlier.

Atrial fibrillation

Study participants' AF diagnoses were retrieved from diagnosis registers at the 2 existing hospitals in Nord-Trøndelag

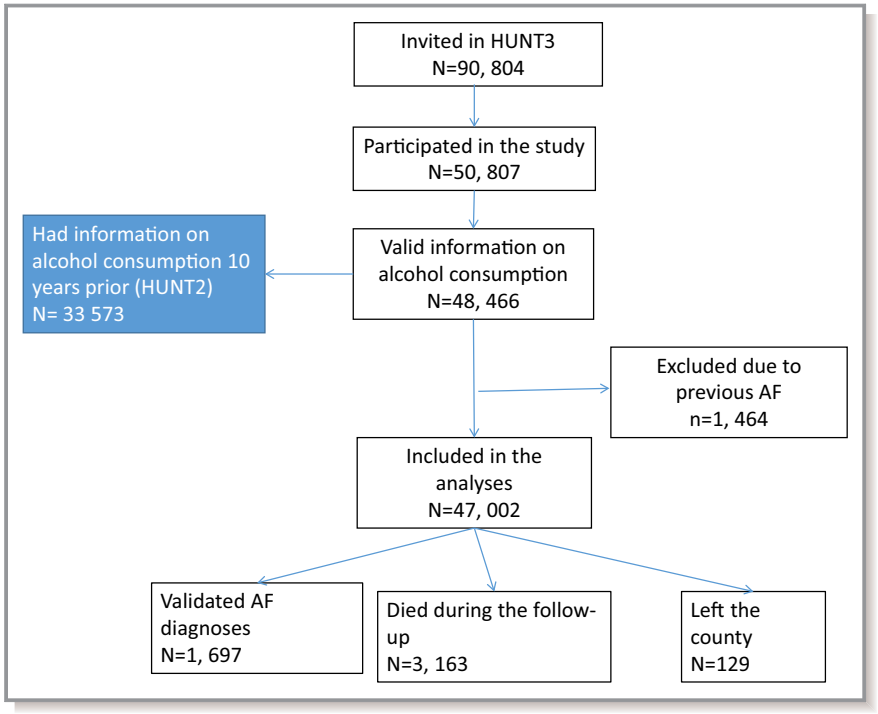

Figure 1. Flowchart of the selection of the study participants. AF indicates atrial fibrillation; and HUNT, Nord-Trøndelag Health.

County, Norway, between the day of the baseline examination in HUNT3 and November 30, 2015. The code I48 in the *International Classification of Diseases Tenth Revision*, was used to identify patients with AF. Subsequently, the hospital medical records of all study participants with a diagnosis of AF were reviewed. An individual was considered to have AF if the available ECG presented evidence for AF or atrial flutter, according to standard criteria.[16] If an ECG was unavailable, the text of the medical record was reviewed in depth. If a physician (V.M.) had described the ECG as showing AF or atrial flutter using standard criteria, the case was defined as AF. In doubtful cases, the information was evaluated separately by a specialist in cardiology (J.P.L.) and one in internal medicine (H.E.), and then discussed in a consensus meeting. Short episodes of AF in relation to cardiac surgery, myocardial infarction, or septic shock (n=19) were not considered as events in primary analyses.

Covariates

Demographic variables. Marital status was categorized as follows: (1) cohabiting, (2) single, or (3) widowed/divorced. Socioeconomic position was determined using the Erikson Goldthorpe Parocarero occupational group scale[17]; the reported last or present occupation was transformed to an Erikson Goldthorpe Parocarero category, as previously described.[17,18] Erikson Goldthorpe Parocarero categories were further categorized as follows: (1) higher-grade professionals, such as legislators, managers, senior officers, and physicians; (2) lower-grade professionals, such as technicians, managers of small businesses, and secretaries; (3) routine nonmanual workers, such as clerks, service workers, and shop assistants; and (4) manual workers, such as agricultural workers, fishery workers, machine operators, and construction workers.

Lifestyle variables. Participants were categorized according to the frequency and the intensity of their physical activity as follows: (1) physically inactive, if they reported light-to-moderate physical activity, at most 30 to 60 min/week; (2) moderately active, if they reported light-to-moderate physical activity, >60 min/week, and/or vigorous activity, up to a maximum of 60 min/week; and (3) physically active, if they reported vigorous activity, >60 min/week. Participants were categorized according to their smoking status as follows: (1) never, (2) former, (3) occasional, not daily, and (4) regular, daily smokers.

Clinical measurements. Height, weight, waist, and hip circumference, and blood pressure were measured in light clothing and without shoes. Body mass index was calculated as kilograms (weight) per meter squared (height). Nonfasting lipid levels were measured. Detailed descriptions of the

clinical examination and laboratory protocols can be found elsewhere.[12]

Symptoms of depression and anxiety were measured with the Norwegian version of the Hospital Anxiety and Depression Scale, which encompasses 7 questions with a 4-point Likert scale and contains subscales to assess anxiety and depression symptoms during the past week.[19]

Participants were also asked if they had specific chronic diseases, including hypertension, diabetes mellitus, angina pectoris, stroke, heart failure, chronic kidney disease, asthma, chronic bronchitis, emphysema, chronic obstructive pulmonary disease, psoriasis, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia, arthrosis, hypothyroidism, or hyperthyroidism.

Statistical Analyses

Descriptive statistics of the study participants are presented in Table 1. χ^2 Tests were used to compare categorical variables, and ANOVA was used to compare continuous variables, among the different alcohol intake categories.

Cox proportional hazard models were used to investigate the association between alcohol consumption and AF. Proportionality was tested using formal tests of interaction with time and ln(time) and with ln-ln curves. The covariate occupational group was included as a time-dependent covariate in the analyses because it did not satisfy the proportionality assumption. We found no evidence against proportionality for any other variables.

Quantity of alcohol intake was modeled as both a categorical and a continuous variable. In the base model, we adjusted for sex and used age as the underlying scale in the Cox regression. In the multivariable-adjusted model, we also adjusted for sociodemographic factors (marital status and socioeconomic position) and traditional risk factors for AF (smoking, physical activity, height, body mass index, and diabetes mellitus). In further analyses, we also examined whether other possible confounders, such as waist/hip ratio, anxiety, or depression, influenced the strength of the observed associations. Furthermore, we also examined the effect of adding systolic blood pressure to our multivariable-adjusted models because blood pressure can be considered both a possible confounder and a mediator of the association between alcohol consumption and AF. To detect possible nonlinear and threshold effects, we tested the best-fitting fractional polynomials for the multivariable-adjusted model.[20,21]

To examine whether binge drinking influenced the association between alcohol consumption and the risk of AF, we added binge drinking to the multivariable-adjusted model. We also investigated if risky drinking behavior influences the association by excluding women who reported consuming >7 and men who reported consuming >14 drinks per week, along with those who reported problem or binge drinking. The population attributable risk was calculated for alcohol consumption both with and without risky drinkers using the %par macro in SAS.[22] Beverage-specific analyses were conducted by examining the effect of a specific beverage while adjusting simultaneously for the other 2 types. To control for the sick-quitter bias, we examined whether exclusion of abstainers who were former drinkers influenced the association.

We conducted several additional sensitivity analyses to examine the robustness of our findings using alcohol intake dichotomized at 7 drinks per week: this cutoff was set a priori, and it corresponds to, on average, 1 drink per day alcohol intake. First, we excluded participants who reported any of the following forms of cardiovascular diseases: angina, myocardial infarction, heart failure, other heart disease, stroke, or brain hemorrhage. Second, to control for reverse causation, we excluded events registered in the first 5 years of the follow-up. Third, we repeated our models after excluding participants who reported ever having been diagnosed as having a chronic disease. Fourth, we addressed the effect of having diagnosed hypertension by excluding participants with a history of chronic hypertension. Fifth, we performed stratified analyses to examine potential effect modification by age (dichotomized at 50 years), sex, smoking, physical activity, body mass index, and systolic blood pressure (dichotomized at 140 Hg mm). Last, we also examined whether treating transient AF cases during the follow-up as events influenced the estimates.

To handle missing values for covariates, we used list-wise deletion. All analyses were performed using Stata/IC 12.0 for Windows and SAS Enterprise Guide 4.3.

Results

Quantity of Alcohol Intake

The average daily alcohol consumption in our sample was 3.8±4.8 grams, or just over 2 drinks per week. Overall, 23% of participants reported intake of >3 drinks per week. In general, those who reported >3 drinks per week were more likely to be younger and men, and were less likely to have any chronic disease (Table 1).

Among the 47 002 study participants, 1697 sustained an episode of AF during the follow-up (Figure 1). Alcohol consumption of >7 drinks per week was associated with an increased risk of AF when compared with nondrinkers (Table 2). AF risk was similar among nondrinkers, rare drinkers, and light drinkers. These associations remained essentially unchanged after additional adjustment for waist/hip ratio, anxiety, depression, or blood pressure (Table S1, Table 2).

Table 1. Baseline Characteristics of Study Participants According to the Quantity of Alcohol Intake

Variables*	Total Population (N=47 002)	Alcohol Intake Categories				
		Abstainers (n=5302)	Rare Drinkers (n=6212)†	>0 and ≤3 Drinks/Week (n=24 792)	>3 and ≤7 Drinks/Week (n=8391)	>7 Drinks/Week (n=2305)
Categorical variables, % (n)						
Women	55 (25 885)	70 (3719)	69 (4271)	57 (14 216)	37 (3143)	23 (536)
Physical activity						
Inactive	22 (10 100)	26 (1327)	25 (1525)	20 (4959)	21 (1727)	24 (562)
Moderately active	42 (19 562)	52 (2624)	45 (27 849)	42 (10 282)	37 (3098)	34 (774)
Active	36 (16 808)	22 (1083)	30 (1832)	38 (9389)	42 (3545)	42 (959)
Smoking status						
Current‡	25 (11 415)	16 (830)	22 (1383)	24 (5902)	30 (2512)	35 (788)
Former	34 (14 850)	25 (1273)	28 (1707)	33 (7983)	36 (3012)	38 (875)
Never	42 (19 910)	59 (2986)	49 (2993)	43 (10 534)	33 (2780)	27 (617)
Living in a relationship	24 (11 128)	17 (891)	26 (1616)	23 (5639)	26 (2188)	35 (794)
Alcohol consumption						
Binge drinker§	3 (1552)	0 (0)	0 (0)	1 (152)	7 (582)	35 (818)
Problem drinker‖	9 (3001)	3 (40)	3 (101)	5 (1035)	17 (1157)	39 (668)
Has previous CVD¶	9 (4414)	17 (925)	11 (691)	8 (2039)	7 (582)	8 (177)
Has any chronic disease#	69 (24 929)	59 (3692)	59 (3678)	50 (12 518)	47 (3947)	48 (1094)
Continuous variables, mean (SD)						
Age, y (n=47 002)	52.3 (15.7)	62.3 (16.8)	53.5 (17.2)	51.2 (14.6)	49.5 (14.0)	47.6 (15.5)
BMI, kg/m^2 (n=46 683)	27.1 (4.4)	27.7 (4.9)	27.7 (5.0)	27.0 (4.3)	26.9 (3.9)	26.8 (3.9)
Cholesterol, mmol/L (n=45 678)	5.5 (1.1)	5.6 (1.2)	5.5 (1.2)	5.5 (1.1)	5.5 (1.1)	5.5 (1.1)
HDL-C, mmol/L (n=45 677)	1.3 (0.35)	1.3 (0.3)	1.3 (0.3)	1.4 (0.3)	1.4 (0.4)	1.3 (0.4)
BP, mm Hg						
Systolic (n=46 739)	130 (19)	135 (21)	130 (20)	129 (18)	131 (17)	133 (17)
Diastolic (n=46 739)	73 (11)	73 (12)	72 (11)	73 (11)	75 (11)	75 (12)
Anxiety score (n=36 563)	4.01 (3.3)	4.2 (3.7)	4.2 (3.6)	4.0 (3.2)	3.9 (3.2)	4.0 (3.3)
Depression score (n=36 777)	3.3 (2.9)	3.9 (3.2)	3.6 (3.1)	3.1 (2.8)	3.0 (2.7)	3.3 (2.9)

All *P* values from testing the differences in means (continuous variables) and proportions (categorical variables), according to alcohol consumption categories, were <0.01. BMI indicates body mass index; BP, blood pressure; CVD: cardiovascular disease; and HDL-C, high-density lipoprotein cholesterol.

*Categorical variables are presented as percentages (number of individuals), whereas continuous variables are presented as means (SDs).

†Occasional and regular smokers.

‡Defined as reporting the consumption of alcohol during the past year, but not during the past 2 weeks.

§Defined as reporting at least 1 episode of binge drinking during a week.

‖Defined on the basis of 2 or more positive answers on the CAGE questionnaire.

¶Defined as ever having acute myocardial infarction, angina pectoris, heart failure, other heart disease, and/or stroke/brain hemorrhage.

#Defined as ever having any of the following: hypertension, diabetes mellitus, angina pectoris, heart failure, other heart disease, stroke/brain hemorrhage, kidney disease, asthma, chronic bronchitis, emphysema, chronic obstructive pulmonary disease, cancer, epilepsy, rheumatoid arthritis, Bechterev disease, sarcoidosis, or osteoarthritis.

When we modeled alcohol consumption linearly as a continuous variable, the hazard ratio (HR) for a 1-drink increment was 1.03 (95% confidence interval [CI], 1.01–1.04).

However, the best-fitting fractional polynomial indicated a curvilinear association instead of a truly linear one (Figure 2). The cut point where risk deviated from the null occurred at ≈4 to 5 drinks per week consumption. The predicted HRs at an intake of 4 and 7 drinks per week were 1.02 (95% CI, 1.01–1.03) and 1.08 (95% CI, 1.03–1.15), respectively. The association appeared largely similarly among men and women (Table S2), but only 536 women reported consuming >7 drinks per week. The population proportion of AF incidence attributable to alcohol consumption was 1.6% (95% CI, 0.6%–2.7%) when we compared all drinkers with nondrinkers.

Table 2. HRs and 95% CIs for Atrial Fibrillation According to Weekly Alcohol Intake

Drinking Categories (Drinks/Week)	No. of Events/ Person-Years	Age- and Sex-Adjusted Model (n=47 002)		Multiadjusted Model (n=45 193)*		Multiadjusted Model+Binge Drinking (n=45 193)†		Multiadjusted Model+Blood Pressure (n=45 153)	
		HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Abstainers	347/41 694	Reference		Reference		Reference		Reference	
Rare drinkers‡	258/50 411	1.03 (0.88–1.21)	0.70	1.04 (0.88–1.24)	0.64	1.04 (0.88–1.24)	0.59	1.06 (0.89–1.26)	0.60
>0 and ≤3	725/205 234	0.94 (0.82–1.08)	0.40	1.00 (0.87–1.63)	0.96	1.00 (0.87–1.16)	0.98	1.02 (0.88–1.17)	0.88
>3 and ≤7	225/68 994	1.00 (0.83–1.19)	0.98	1.05 (0.87–1.28)	0.60	1.05 (0.87–1.80)	0.55	1.05 (0.87–1.27)	0.63
>7	77/18 434	1.25 (0.97–1.62)	0.08	1.38 (1.06–1.80)	0.02	1.38 (1.06–1.81)	0.02	1.38 (1.06–1.81)	0.02

CI indicates confidence interval; and HR, hazard ratio.
*Adjusted for sex, height, body mass index, marital status, socioeconomic position, physical activity, smoking, and diabetes mellitus.
†Binge drinking was defined as having 5+ drinks in one sitting at least once a week.
‡Rare drinking was defined as reporting alcohol consumption during the past year, but not during the past 2 weeks.

We identified 447 study participants who reported nondrinking in HUNT3 but were former drinkers in HUNT2. Exclusion of these former drinkers did not influence the association between alcohol and AF (Table S3).

Risky Drinking and Beverage Type

Altogether, 4464 participants reported heavy episodic drinking at least once a week or were considered problem drinkers on the basis of their answers on the CAGE questionnaire. Adjustment for risky drinking did not substantially alter our results (Table 2). However, when we excluded individuals who reported problem or binge drinking or intake higher than the recommended limits (n=5140), the HRs for AF consistently approached 1 in both men and women (Figure 3A and 3B). The proportion of AF incidence attributable to alcohol intake within the recommended limit (ie, 1 drink per day for women and 2 drinks per day for men in the absence of risky drinking), compared with nondrinkers, was merely 0.07% (95% CI, −0.01% to 0.13%).

When we examined associations with intake of specific beverage types dichotomized at 7 drinks/week, the adjusted HRs were 1.31 (95% CI, 1.03–1.66) for beer, 1.31 (95% CI, 1.03–1.67) for wine, and 1.36 (95% CI, 1.07–1.73) for spirits.

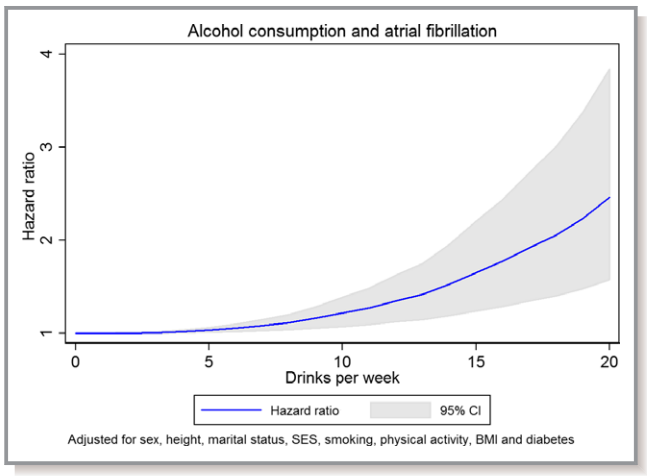

Figure 2. Alcohol consumption and atrial fibrillation risk. Data were adjusted for sex, height, marital status, socioeconomic status, smoking, physical activity, body mass index, and diabetes mellitus. CI indicates confidence interval; and HR, hazard ratio.

Sensitivity Analyses

The estimate was slightly lower after excluding the first 4 years of the follow-up: the adjusted HR, when comparing participants who reported consuming >7 drinks per week with participants who reported up to this amount, was 1.28 (95% CI, 1.05–1.53).

Excluding participants who at baseline reported a history of cardiovascular diseases (n=4414) did not influence the associations (Table S3). Including short-term AF (n=19) as an event during the follow-up gave exactly the same estimate as when not including it. There were 347 AF cases among the 22 073 individuals free from all chronic disorders at baseline: the association of alcohol consumption with AF risk among these participants was similar to that observed in the entire cohort (Table S3).

The association of alcohol and AF tended to be stronger among those who reported use of medication for hypertension than among those without hypertensive medication: the adjusted HRs (95% CIs) when comparing participants consuming >7 drinks per week with those who reported consuming fewer drinks were 1.64 (1.16–2.33) and 1.19 (0.88–1.65), respectively. Estimates were similar in the 2 groups when we stratified our analyses for systolic blood pressure ≥140 or <140 mm Hg (Table S4). We did not find evidence for effect modification by sex, age, smoking, physical activity, or body mass index (Tables S2, S5 through S8).

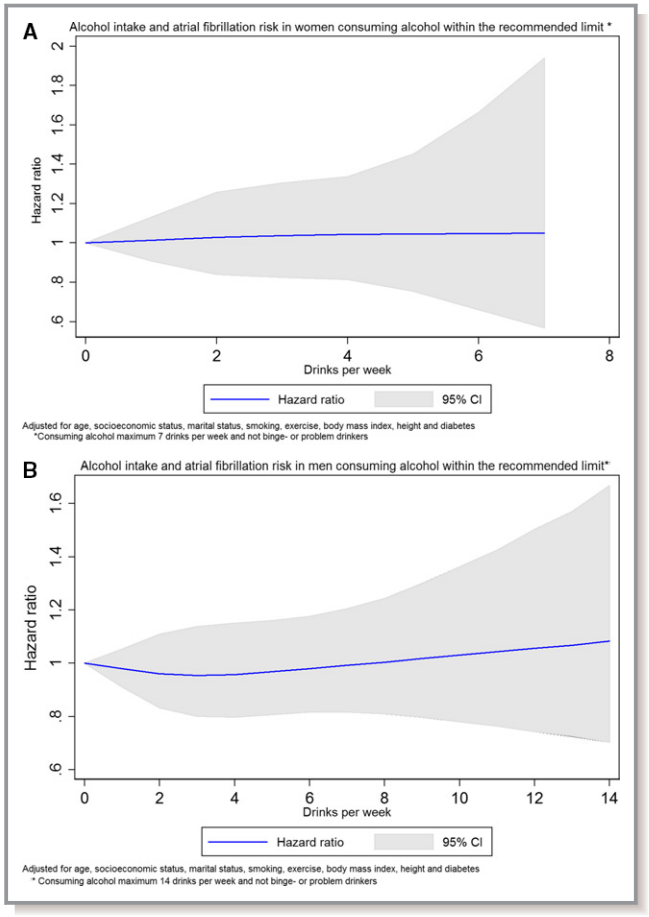

Figure 3. Alcohol consumption within recommended limits and the risk of atrial fibrillation among women (A) and men (B). Recommended limits were a maximum of 7 and 14 drinks per week for women and men, respectively, with no binge or problem drinking. Data were adjusted for age, socioeconomic status, marital status, smoking, exercise, body mass index, height, and diabetes mellitus. CI indicates confidence interval; and HR, hazard ratio.

Discussion

In this population-based cohort study in a light-drinking population, alcohol consumption of >7 drinks per week was associated with an increased risk of AF. The association between the quantity of alcohol consumption and AF risk was curvilinear, indicating a steeper increase in risk with higher alcohol intake. The threshold at which AF risk clearly increased above that of nondrinkers occurred at ≈4 to 5 drinks per week. Among consumers within recommended limits, we observed no meaningful increase in AF risk.

Comparison With Previous Studies

Results from previous studies on the link between alcohol consumption and AF risk are somewhat inconsistent. Although some large cohort studies have not observed an association between alcohol consumption and AF risk,[23–26] others report a higher risk of AF among drinkers.[27,28] Meta-analyses have concluded that alcohol consumption is associated with an increased risk of AF, especially at levels >14 drinks per week when compared with nondrinkers. Dose-response analyses suggested an ≈8% risk increase for a 1-drink increment, albeit assuming a simple linear relationship.[7–10] In this study, we found an ≈40% higher risk of AF among consumers of >7 drinks per week relative to nondrinkers, and the linear model showed a 4% risk increase for a drink increment.

Ongoing controversy exists about whether the risk of AF is elevated among light-moderate drinkers or whether the association exhibits a threshold in risk, with no risk increase below a certain amount of alcohol intake. Meta-analyses that have investigated light-moderate drinkers as a separate group in categorical analyses found no evidence for a higher AF risk among them.[7,10] This is in line with our findings, because we did not observe an increased AF risk with an alcohol intake <7 drinks per week in our categorical analyses. Indeed, our results suggest that a simple linear model is likely to overestimate the risk of AF associated with drinking <7 drinks per week. Other studies that have used flexible modeling approaches to detect possible nonlinear or threshold-type associations have also suggested that the association may not be simply linear, although they have not defined a specific risk threshold.[9,10] When we modeled the association with fractional polynomials, we observed a curvilinear relationship with no deviance from one in the predicted risk function until some 4 to 5 drinks per week, but a steep increment in risk at >14 drinks per week.

Binge drinking is clearly an important trigger for AF.[6,29] Short-term, extensive alcohol consumption can trigger cardiac arrhythmias by altering the electrophysiological properties of the myocardium and influencing both sympathetic and parasympathetic activity.[6,11] The few prospective studies that have examined the effect of binge drinking found an increased risk of AF among binge drinkers.[7,28] When we accounted for both the overall amount of intake and binge or problem drinking, we found essentially no association of alcohol consumption with risk of AF among light drinkers, who reported no problem behaviors. The risk for AF that could be attributed to consumption within the recommended limits was virtually 0. Thus, our results suggest that, in contradiction to the conclusion of a recent review,[6] there may be a level and pattern of alcohol intake that does not increase risk of AF.

There are several possible mechanisms through which long-term alcohol consumption may influence the atria.[6] Studies show that long-term, excessive alcohol intake can cause atrial remodeling with fibrosis,[6,30] but no structural changes are seen among light-moderate drinkers (ie, those who consume <14 drinks per week).[30] Excessive alcohol

intake may change the electrophysiological properties of the myocardium, causing a long-term decrease of the refractory period.[6,30] It also has a direct cardiotoxic effect,[31] increases inflammation,[32] and is associated with an increased risk of hypertension.[6,33,34] In contrast, regular, low-dose alcohol intake had direct cardioprotective effects by protecting the myocardium from ischemic injury through the activation of the protein kinase cascades.[35]

Strengths and Limitations

The HUNT Study was conducted in a socioeconomically and genetically homogeneous population with a low net migration rate.[12] Because most of the population consumes modest amounts of alcohol, attributable to the restricted accessibility of alcoholic beverages and a strong promotion of alcohol-free public places,[36] nondrinking has been a culturally accepted norm in the country.[37] This tends to normalize abstention and may reduce the likelihood that drinkers and nondrinkers differ in unmeasured factors that are also associated with AF risk. These findings were compared with other Western countries, where moderate drinking is the cultural norm and moderate drinkers are often socially more active and have a healthier lifestyle than abstainers.[38] Furthermore, we controlled our analyses for a wide range of possible confounders, and found that the estimates remained largely robust. As in any observational design, it is possible that there are unmeasured confounders, but these factors need to be strongly associated with both alcohol consumption and AF to influence our estimates meaningfully.

Most study participants took part in the previous HUNT Study, 10 years before baseline, where alcohol intake was also assessed. Thus, using these prospectively collected data, we had the option to control for the "sick quitter" bias (ie, the increased ill-health risk among the abstainers may be attributable to the fact that many of the abstainers were previous drinkers who stopped drinking alcohol because of their health condition).

Because of the low average alcohol consumption, our power was limited to study excessive alcohol intake. Alcohol consumption and many covariates were self-reported, which might decrease the accuracy of their assessment. Self-reported alcohol consumption usually underestimates overall alcohol intake, especially in higher intake categories. However, alcohol intake was correlated, albeit weakly, with high-density lipoprotein[39] levels (r=0.14 among men and r=0.18 among women), indicating that the rank ordering of the self-reported consumption was likely to be valid. Last, only AF cases that were registered in hospital records were detected and, thus, it is possible that some AF cases were missed. Nonetheless, because ECGs of all the potential AF cases were validated by experts, it is unlikely that false-positive cases occurred, which are generally a greater threat to validity in similar studies than false-negative ones.[40,41] Because the study was conducted in a fairly rural area of Norway with homogeneous Norwegian ethnicity, our findings cannot be generalized directly to urban centers or to other ethnic groups.

Conclusions

Overall, the quantity of alcohol consumption was associated with an increased risk of AF, even among moderate drinkers. However, alcohol consumption within recommended limits (ie, drinking no more than 1 drink per day for women and 2 drinks per day for men, without binging and problem drinking) did not substantially increase the risk of AF.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Hazard ratios and 95% confidence intervals for atrial fibrillation according to weekly alcohol intake after further adjustment for anxiety-depression and waist-hip ratio

Drinking categories	Multi-adjusted model* + anxiety-depression† (n=34 925)		Multiadjsted model* + waist-hip ratio (n=45 030)	
	HR (95% CI)	P	HR (95% CI)	P
Abstainers	Reference		Reference	
Rare-drinkers‡‡	0.94 (0.77-1.14)	0.52	1.04 (0.88-1.25)	0.60
>0 and ≤3 drinks week^{-1}	0.95 (0.80-1.11)	0.50	1.01 (0.87-1.17)	0.87
>3 and ≤7 drinks week^{-1}	1.06 (0.81-1.24)	0.95	1.07 (0.88-1.30)	0.49
>7 drinks week^{-1}	1.38 (1.03-1.83)	0.03	1.38 (1.06-1.88)	0.02

no: number; HR: hazard ratio; CI: confidence intervals.

*Adjustment was made for sex, height, body mass index, marital status, socioeconomic position, physical activity, smoking and diabetes.

†Assessed with the Hospital Anxiety and Depression Scale

‡Rare drinking was defined as reporting alcohol consumption during the last year, but not during the last two weeks.

Table S2. Sex-specific hazard ratios and 95% confidence intervals for atrial fibrillation according to alcohol consumption categories

Drinking categories	Women (n=24 827)		Men (n=20 495)	
	No. of events/Person years	HR (95% CI)*	No. of events/Person years	HR (95% CI)*
Abstainers	234/29 651	Reference	113/12 043	Reference
Rare-drinkers†	131/35 153	0.93 (0.73-1.17)	127/15 258	1.25 (0.95-1.63)
>0 and ≤3 drinks week^{-1}	268/118 391	0.98 (0.78-1.20)	457/86 843	1.10 (0.88-1.37)
>3 and ≤7 drinks week^{-1}	50/25 780	1.08 (0.77-1.51)	175/43 214	1.09 (0.85-1.42)
>7 drinks week^{-1}	10/4304	1.34 (0.71-2.56)	67/14 130	1.46 (1.06-2.01)

no: number; HR: hazard ratio; CI: confidence intervals. P for homogeneity of HRs=0.88 with the dichotomized alcohol intake variable.

*Adjustment was made for height, body mass index, marital status, socioeconomic position, physical activity, smoking and diabetes.

†Rare drinking was defined as reporting alcohol consumption during the last year, but not during the last two weeks.

Table S3. Hazard ratios and 95% confidence intervals for atrial fibrillation according to weekly alcohol intake after excluding former drinkers, individuals with cardiovascular diseases and individuals with common chronic disorders

Drinking categories	Excluding former drinkers (n=31 976)		Excluding participants with previous cardiovascular diseases (n=41 056)		Excluding individuals with chronic disorders (n=22 073)	
	No. of events/ Person years	HR (95% CI)*	No. of events/ Person years	HR (95% CI)*	No. of events/ Person years	HR (95% CI)*
Abstainers	314/ 31 889	Reference	206/ 35 135	Reference	83/ 17 728	Reference
Rare-drinkers‡‡	225/ 35 641	1.06 (0.89-1.28)	184/ 45 230	1.19 (0.97-1.48)	87/ 27 471	1.15 (0.85-1.58)
>0 and ≤3 drinks week^{-1}	639/ 148 765	1.02 (0.87-1.19)	530/ 189 417	1.07 (0.89-1.29)	296/ 128 760	1.05 (0.80-1.37)
>3 and ≤7 drinks week^{-1}	190/ 48 048	1.06 (0.86-1.30)	169/ 64 446	1.06 (0.84-1.35)	120/ 45 313	1.21 (0.88-1.66)
>7 drinks week^{-1}	57/ 11 205	1.26 (0.93-1.71)	57/ 17 091	1.36 (0.99-1.87)	32/ 12 160	1.15 (0.75-1.78)

No: number; HR: hazard ratio; CI: confidence intervals.

*Adjustment was made for sex, height, body mass index, marital status, socioeconomic position, physical activity, smoking and diabetes.

† Adjustment was made for sex, height, body mass index, marital status, socioeconomic position, physical activity and smoking.

‡Rare drinking was defined as reporting alcohol consumption during the last year, but not during the last two weeks.

Table S4. Hazard ratios and 95% confidence intervals for atrial fibrillation according to alcohol consumption categories, stratified by blood pressure

Drinking categories	Systolic blood pressure < 140 Hgmm (n=37 374)		Systolic blood pressure ≥ 140 Hgmm (n=9 651)	
	No. of events/ Person years	HR (95% CI)*	No. of events/ Person years	HR (95% CI)*
Abstainers	158/26 316	Reference	188/15 056	Reference
Rare-drinkers†	143/36 368	1.20 (0.94-1.53)	114/13 776	0.90 (0.70-1.15)
>0 and ≤3 drinks week^{-1}	364/154 049	1.00 (0.80-1.23)	359/50 223	1.03 (0.84-1.26)
>3 and ≤7 drinks week^{-1}	101/51 126	0.94 (0.71-1.24)	120/17 605	1.16 (0.89-1.52)
>7 drinks week^{-1}	43/12 724	1.68 (1.17-2.42)	34/5 595	1.10 (0.74-1.64)

Hgmm: millimeter mercury; no: number; HR: hazard ratio; CI: confidence intervals. P for homogeneity of HRs=0.41 with the dichotomized alcohol intake variable.

*Adjustment was made for sex, height, body mass index, marital status, socioeconomic position, physical activity, smoking and diabetes.

†Rare drinking was defined as reporting alcohol consumption during the last year, but not during the last two weeks.

Table S5. Hazard ratios and 95% confidence intervals for atrial fibrillation according to alcohol consumption categories, stratified by age

Drinking categories	≤50 years (n=26 260)		>50 years (n=20 742)	
	No. of events/ Person years	HR (95% CI)*	No. of events/ Person years	HR (95% CI)*
Abstainers	3/9938	Reference	344/31 756	Reference
Rare-drinkers†	11/22 188	2.25 (0.49-10.3)	247/28 223	1.02 (0.86-1.23)
>0 and ≤3 drinks week^{-1}	47/97 242	1.66 (0.39-6.98)	678/107 992	1.02 (0.87-1.18)
>3 and ≤7 drinks week^{-1}	18/33 877	1.41 (0.32-6.25)	207/35 117	1.10 (0.91-1.34)
>7 drinks week^{-1}	7/9322	1.81 (0.37-9.18)	70/9112	1.45 (1.09-1.91)

no: number; HR: hazard ratio; CI: confidence intervals. P for homogeneity of HRs=0.94 with the dichotomized alcohol intake variable.

*Adjustment was made for sex, height, body mass index, marital status, socioeconomic position, physical activity, smoking and diabetes.

†Rare drinking was defined as reporting alcohol consumption during the last year, but not during the last two weeks.

Table S6. Hazard ratios and 95% confidence intervals for atrial fibrillation according to alcohol consumption categories stratified by smoking

Drinking categories	Current smoker (n=11 415)		Former smoker (n=14 851)		Never smoked (n=19 910)	
	No. of events/ Person years	HR (95% CI)*	No. of events/ Person years	HR (95% CI)*	No. of events/ Person years	HR (95% CI)*
Abstainers	41/6 599	Reference	98/9 803	Reference	191/23 705	Reference
Rare-drinkers†	42/11 330	1.08 (0.69-1.70)	94/13 613	1.06 (0.79-1.42)	109/24 461	1.02 (0.80-1.30)
>0 and ≤3 drinks week^{-1}	155/48 756	1.17 (0.81-1.70)	299/65 712	0.92 (0.72-1.18)	257/87 707	1.06 (0.86-1.32)
>3 and ≤7 drinks week^{-1}	51/20 507	1.12 (0.71-1.76)	114/24 770	1.06 (0.79-1.43)	53/23 007	1.07 (0.77-1.50)
>7 drinks week^{-1}	20/6244	1.58 (0.89-2.81)	44/7 017	1.41 (0.96-2.06)	12/4 951	1.32 (0.74-2.37)

no: number; HR: hazard ratio; CI: confidence intervals. P for homogeneity of HRs=0.84 with the dichotomized alcohol intake variable.

*Adjustment was made for sex, height, body mass index, marital status, socioeconomic position, physical activity, smoking and diabetes.

†Rare drinking was defined as reporting alcohol consumption during the last year, but not during the last two weeks.

Table S7. Hazard ratios and 95% confidence intervals for atrial fibrillation according to alcohol consumption categories, stratified by physical activity

Drinking categories	No or light physical activity (n= 29 662)*		Physically active (n= 16 808)*	
	No. of events/ Person years	HR (95% CI)†	No. of events/ Person years	HR (95% CI)†
Abstainers	284/30 889	Reference	31/8916	Reference
Rare-drinkers‡	217/34 755	1.04 (0.87-1.26)	36/15 107	1.09 (0.67-1.95)
>0 and ≤3 drinks week^{-1}	509/126 126	0.96 (0.82-1.13)	202/77 826	1.31 (0.88-1.95)
>3 and ≤7 drinks week^{-1}	146/77 826	1.00 (0.81-1.26)	79/39 852	1.39 (0.89-2.17)
>7 drinks week^{-1}	53/10 772	1.48 (1.08-2.02)	24/7 576	1.50 (0.85-2.64)

no: number; HR: hazard ratio; CI: confidence intervals. P for homogeneity of HRs=0.61 with the dichotomized alcohol intake variable.

*Physically active was defined as doing vigorous physical activity at least 60 minutes per a week.

†Adjustment was made for sex, height, body mass index, marital status, socioeconomic position, physical activity, smoking and diabetes.

‡Rare drinking was defined as reporting alcohol consumption during the last year, but not during the last two weeks.

Table S8. Hazard ratios and 95% confidence intervals for atrial fibrillation according to alcohol consumption categories, stratified by body mass index

Drinking categories	BMI ≤ 25 kg/m^2 (n= 15 795)		BMI >25 kg/m^2 (n= 31 207)	
	No. of events/ Person years	HR (95% CI)*	No. of events/ Person years	HR (95% CI)*
Abstainers	69/ 13 009	Reference	278/ 28 685	Reference
Rare-drinkers†	63/ 16 072	1.42 (0.99-2.05)	195/ 34 339	0.97 (0.80-1.18)
>0 and ≤3 drinks week^{-1}	160/ 71 237	1.27 (0.93-1.75)	565/ 133 997	1.01 (0.85-1.18)
>3 and ≤7 drinks week^{-1}	49/ 22 265	1.43 (0.95-2.17)	176/ 46 729	1.10 (0.89-1.37)
>7 drinks week^{-1}	19/5937	2.27 (1.31-3.93)	58/ 12 497	1.49 (1.10-2.02)

BMI: body mass index; No: number; HR: hazard ratio; CI: confidence intervals. P for homogeneity of HRs=0.46 with dichotomized alcohol intake variable.

*Adjustment was made for sex, height, body mass index, marital status, socioeconomic position, physical activity, smoking and diabetes.

†Rare drinking was defined as reporting alcohol consumption during the last year, but not during the last two weeks.