

How Does Alcohol Intake Relate to the Risk of Atrial Fibrillation?

Andreas J. Zimmermann and David Conen MD MPH

Department of Medicine, University Hospital, Petersgraben 4, 4031 Basel, Switzerland.

Abstract

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide. The close relationship between acute excesses of alcohol and the occurrence of AF even in healthy individuals has been known for several decades. More recently, a significant relationship has been consistently observed between elevated consumption of alcoholic beverages on a regular basis and an increased risk of developing AF. However, the amount of alcohol needed to confer an increased risk of AF is rather elevated, approximately two alcoholic beverages per day in women and four to five alcoholic beverages per day in men, suggesting that on a population level, alcohol is not a major contributor to the global AF epidemic.

Introduction

Atrial fibrillation (AF) is a highly prevalent cardiac arrhythmia, and approximately 2.3 million people are currently diagnosed with AF in the United States.¹ This number is expected to increase to 12.1 million by 2050.¹ The main factors involved in this major increase in AF prevalence and incidence are the aging of the population, the increasing rates of obesity, a better survival after a first cardiovascular event and improved diagnostic tools for detection of asymptomatic AF. Furthermore, several studies in various populations have consistently shown that in the presence of AF the risk of death increases approximately twofold, the risk of stroke approximately fivefold and the risk of congestive heart failure more than tenfold, underscoring the importance of the arrhythmia as a public health problem.²⁻⁵

For all these reasons, AF prevention and avoidance of precipitating factors is of primordial importance in order to reduce the public health burden of AF.

Blood pressure and obesity have been consistently shown to be two major, potentially modifiable AF risk factors,⁶⁻⁸ such that improved weight control and blood pressure reduction are important tools for AF prevention.⁹ In this context, alcohol consumption has also been associated with the occurrence of AF and other cardiovascular outcomes. Given the important health effects of elevated alcohol consumption, it is important to understand its effects on the occurrence of AF. This review therefore aims to review the current evidence on how alcohol consumption relates to the risk of developing AF and to summarize potential mechanistic factors for this relationship.

Acute Effects of Alcohol on Atrial Fibrillation

An increased risk of atrial arrhythmias (mainly AF) after acute alcohol excesses has been suspected for several decades.¹⁰ In a case series among habitual users of alcohol, Ettinger et al documented the close temporal relationship between acute

Corresponding Address : David Conen MD MPH, Department of Medicine, University Hospital, Petersgraben 4, 4031 Basel, Switzerland.

alcoholic excesses and occurrence of AF.¹¹ Because most of the documented alcoholic excesses occurred on a week-end or public holiday, the authors called this phenomenon the holiday heart syndrome, a term that is still used clinically today to describe this phenomenon. In subsequent studies, similar AF episodes during and shortly after excessive alcohol intake have also been observed in individuals who did not usually consume alcohol and who had apparently healthy hearts,¹² suggesting that alcohol may have a direct arrhythmic effect. Still another study suggested that acute alcohol intoxication was particularly important in individuals aged <65 years.¹³ Interestingly, the direct arrhythmic effect of alcohol has also been shown in experimental porcine models.¹⁴ Anadon et al. designed an endocardial atrial stimulation protocol which they applied to nine pigs at three different timepoints: at baseline, i.e. without ethanol infusion, after the first ethanol infusion (ethanol blood level 100-200 mg/dL) and after the second ethanol infusion (ethanol blood level 250-300 mg/dL). They showed that acute alcohol administration increased the inducibility of AF, mainly at high blood alcohol levels.¹⁴

Regular Alcohol Consumption and Atrial Fibrillation

Several prospective cohort studies have assessed the effects of regular alcohol consumption on the risk of incident AF,¹⁵⁻²¹ as shown in Table 1. In these studies, alcohol consumption is usually measured in drinks per day, one alcoholic drink usually corresponding to 10-15 grams of pure alcohol, depending on alcohol type. For example in the Copenhagen City Heart Study, a population-based cohort study from Denmark, moderate alcohol consumption was not associated with incident AF in both men and women. However, there was a significant increased risk of incident AF among men consuming at least 35 alcoholic drinks per week, even after multivariable adjustment for potential confounders (hazard ratio 1.45, 95% confidence interval 1.02-2.04).¹⁹ Similar findings were obtained in the Danish Diet, Cancer, and Health Study, another population based cohort study from Denmark, where the multivariable adjusted hazard ratio among men for consuming a similar amount of alcohol was 1.46 (95% confidence interval 1.05-2.04).¹⁷ In

the Framingham Heart Study, the consumption of 36 grams of alcohol per day was associated with a significant 34% increased risk of incident AF (95% confidence interval 1%-78%).¹⁶ Gender-specific analyses did not provide significant results, possibly due to the relatively small number of AF cases in this analysis. One study among elderly individuals did not find a significant relationship between alcohol consumption and risk of AF, again suggesting that the effect of alcohol on AF occurrence may be stronger in younger individuals.¹⁸ In all these prospective studies, few women consumed elevated amounts of alcohol, and it remained uncertain, whether and what amount of alcohol consumption per day conferred an increased risk of developing AF. We therefore assessed the relationship between regular alcohol intake and new-onset AF in the Women's Health Study, a large prospective cohort of initially healthy women free of cardiovascular disease and cancer at baseline.¹⁵ In this study, we found that consuming up to two alcoholic drinks per day was not associated with an increased risk of incident AF compared with nondrinking women. As in earlier studies, consuming higher amounts of alcohol was uncommon in the Women's Health study. Nevertheless, we showed that consuming at least two alcoholic beverages per day on a regular basis was associated with a relative risk for incident AF of 1.60 (95% confidence interval 1.13-2.25) after multivariable adjustment. Updating alcohol consumption over time provided similar results (hazard ratio 1.49, 96% confidence interval 1.05-2.11). Based on these findings, we estimated that approximately two percent of all incident AF cases could be attributed to the consumption of at least two alcoholic drinks per day, suggesting a modest impact of increased alcohol consumption on the overall AF burden.¹⁵

Two recent meta-analyses summarized the current evidence on the relationship between regular alcohol consumption and new onset AF,^{22,23} and both found a significant positive relationship between alcohol intake and incident AF. For example, Kodama et al found an overall summary relative risk for AF of 1.51 (95% confidence interval 1.31-1.74) comparing the highest with the lowest alcohol exposure category in each individual study.²² Both meta-analyses found that a linear model adequately described the association between alcohol consumption and AF occur-

Table 1 | Prospective Studies on Alcohol Consumption and Incident Atrial Fibrillation

Author, Year, Country, Study	Partici- pants (% wom- en)	Age (mean or range)	Follow Up in yrs	AF Cases	Method of AF Detection	Cate- gory of Alcohol Intake	Reference Group	Adjustments	Relative Risk (95% CI)
Conen et al. ¹⁵ , 2008, USA, Women's Health Study	34'715 (100)	53	12.4	653	Report of partic- ipants, confirmed medical record review	≥2 drinks / day	No drink- ing	Age, SBP, BMI, smoking, exer- cise, race/ethnic- ity, education, RTA, history of hypertension, di- abetes, hypercho- lesterolemia	1.60 (1.13 -2.25)
Djousse et al. ¹⁶ , 2004, USA, Fram- ingham Study	5'727 (49)	45.7	--*	1'055	Verifica- tion by ECG	>36g/day	No drink- ing	Age, SBP, history of myocardial infarction, CHF, LVH, VHD, edu- cation	1.34 (1.01 – 1.78)
Frost et al. ¹⁷ , 2004, Denmark, Danish Diet, Cancer and Health Study	47'949 (53)	56	5.7	556	Diagnose in The Danish National Registry	1st quin- tile	5th quin- tile	Age, body height, BMI smoking, SBP, treatment of hy- pertension, total serum cholester- ol, education	
	men 22'528			374		mean 68.7 g/day	mean 4.1 g/day		1.46 (1.05 – 2.04)
	women 25'421			182		mean 38.8 g/day	mean 1.1 g/day		1.14 (0.70 – 1.85)
Mukamal et al. ¹⁸ , 2007, USA, The Cardiovas- cular Health Study	5'609 (58)	72.7	9.1	1'232	Verifi- cation by ECG, medical reports, registry	≥14 drinks/ week	No drink- ing	Age, sex, race, income, height, waist circumfer- ence, physical activity, use of psychoactive medication, dia- betes, hyperten- sion, CHD, CHF, total cholesterol level	1.09 (0.88 – 1.37)
Mukamal et al. ¹⁹ , 2005, Denmark, The Copen- hagen City Heart Study	16'415 (53.8)			1'071	Verifi- cation by ECG, medical reports, registry			Age, smoking, education, cohabitation, family history of CVD, diabetes, income, physical activity, BMI, FEV1, height	
	men 7'588	51	16.3	548		≥35 drinks/ week	< 1/ week		1.45 (1.02 – 2.04)
	women 8'827	52	18.8	523		≥21 drinks/ week	< 1/ week		1.04 (0.64 – 1.70)

Ruigómez et al. ²⁰ , 2002, UK, General Practice Research Database	6'035 (53)	40-89	--*	1'035	Questionnaire with validation	>42 units / week	No drinking	Age, sex, cardiovascular morbidity	2.4 (1.4 – 4.1)
Krahn et al. (21), 1995, Canada, The Manitoba Follow-Up Study	3'983 (0)	31	38.7*	299	ECG or medical reports	Reported alcohol abuse	No reported alcohol abuse	Age	2.07 (1.38 – 3.10)

* nested case-control study

SBP – Systolic Blood Pressure; BMI – Body Mass Index; RTA – randomized treatment assignment; CHF – Congestive Heart Failure; LVH – left ventricular hypertrophy; VHD – valvular heart disease; CHD – Coronary Heart Disease; CVD – Cardiovascular Diseases; FEV1 – Forced expiratory volume in 1 second

rence, and that the risk of AF increased by a significant 8% for every unit of alcohol consumed per day.^{22,23} However, the absence of a potential threshold effect for the effect of alcohol in incident AF (as described above) in these meta-analyses has to be interpreted with some caution mainly for two reasons. First, individual patient data were not available in both meta-analysis, limiting the possibilities to precisely model an exact dose-response relationship between alcohol consumption and AF occurrence. Second, in both systematic reviews the main analyses combined men and women although the available evidence suggests that men and women may have different susceptibilities towards alcohol,²⁴ as described above.

Type of Alcoholic Beverage and Risk of Atrial Fibrillation

It is relatively unclear whether the risk of AF occurrence is influenced by the type of alcoholic beverage consumed. One of the few studies that assessed whether the type of alcoholic beverage consumed influences the risk of developing AF found no difference across beverage type, although the power for these stratified analyses was not optimal.¹⁹ Another study among elderly individuals also showed that type of alcoholic beverage did not influence the relationship between alcohol consumption and AF occurrence.¹⁸ Although more studies are needed, these preliminary results are similar to findings for incident myocardial infarction, where large prospective studies have shown that the type of alcoholic beverage did not alter the relationship between alcohol consumption and occurrence of the disease.²⁵ Even less information is available on whether the

type of alcoholic beverage influences the risk of arrhythmia occurrence in patients with paroxysmal AF. One small study of 100 patients with paroxysmal AF seeking medical assistance found that 34% of patients indicated alcohol consumption as a triggering event for the arrhythmia.²⁶ In the same study, red wine and spirits were more likely to trigger an AF episode than white wine, but these findings certainly need confirmation from large independent studies.

Mechanistic Aspects

Few data are available on factors mediating the relationship between elevated alcohol intake and risk of incident AF. We previously showed that the occurrence of intercurrent cardiovascular events did not attenuate the effect estimates for elevated alcohol consumption.¹⁵ On the other hand, it has been shown that intake of excessive amounts of alcohol may lead to alcoholic cardiomyopathy and congestive heart failure.^{27, 28} Given the close relationship between congestive heart failure and AF occurrence,^{3, 29} the increased risk of AF associated with excessive alcohol intake may be mediated through a toxic effect of alcohol on the myocardium and subsequent development of congestive heart failure. On the other hand, more moderate levels of alcohol intake have been associated with a reduced risk of congestive heart failure in several populations,^{30, 31} which did not translate into a corresponding reduction in risk of new-onset AF.

The hyperadrenergic state of drinking and withdrawal is another possible mechanism by which elevated alcohol intake may increase the risk of new-onset AF.³²⁻³⁴ Alcohol may directly promote the release of adrenaline and noradrenaline by the

adrenal medulla.³² In further studies, Denison et al. found evidence for an elevated adrenergic activity after episodes of heavy drinking³³ and Mäki et al. detected an increased density of β -adrenoceptor receptors in lymphocytes as a surrogate of adrenergic stimulation after alcohol intake in AF patients compared with controls.³⁴

Other potential mechanisms that may explain the increased risk of AF among individuals with elevated alcohol intake include alterations in oxidative stress³⁵ and electrolyte imbalances.³⁴ However, it has to be emphasized that much more studies are needed to get direct insights into the mechanisms by which an excessive consumption of alcoholic beverages leads to an increased risk of AF.

Conclusions

Acute alcohol excesses have been associated with an increased occurrence of atrial arrhythmias, mainly AF. On the other hand, the intake of small to moderate amounts of alcohol on a regular basis is not associated with an increased risk of developing AF in both men and women. However, men consuming at least four and women consuming at least two alcoholic beverages per day have a 50 to 60% increased risk of developing AF independent of other known AF risk factors. The proportion of AF cases attributable to excessive alcohol consumption seems to be small. While the detrimental effects of excessive alcohol consumption are well known, this review of the literature suggests that on a population level, alcohol consumption is not a major contributor to the growing AF burden.

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