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THE PRESENT AND FUTURE

REVIEW TOPIC OF THE WEEK

Alcohol and Atrial Fibrillation

A Sobering Review

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ABSTRACT

Alcohol is popular in Western culture, supported by a perception that modest intake is cardioprotective. However, excessive drinking has detrimental implications for cardiovascular disease. Atrial fibrillation (AF) following an alcohol binge or the "holiday heart syndrome" is well characterized. However, more modest levels of alcohol intake on a regular basis may also increase the risk of AF. The pathophysiological mechanisms responsible for the relationship between alcohol and AF may include direct toxicity and alcohol's contribution to obesity, sleep-disordered breathing, and hypertension. We aim to provide a comprehensive review of the epidemiology and pathophysiology by which alcohol may be responsible for AF and determine whether alcohol abstinence is required for patients with AF.
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What is the definition of a problem drinker? Someone who drinks more than his or her doctor. Although spoken in jest, a somewhat arbitrary distinction exists between the quantity of alcohol that is cardioprotective and that which is contributory to heart disease. Atrial fibrillation and/or flutter (AF) are the most common symptomatic arrhythmias worldwide, and the combination of an aging population and lifestyle factors has propelled AF to an "emerging epidemic" of cardiovascular disease. Increasingly, attention has shifted towards modifiable risk factors to prevent AF onset and progression.

The association between excessive drinking and various forms of cardiovascular disease is well established. In particular, significant alcohol consumption is associated with a higher risk of AF, hypertension, left ventricular hypertrophy (LVH), obstructive sleep apnea (OSA), and cardiomyopathy. However, smaller amounts of alcohol may reduce the incidence of coronary disease. Counterbalanced is an acceptance that even moderate levels of habitual consumption are associated with AF.

In this review, we examine published reports pertaining to alcohol and AF, including pathophysiology, the role of binge drinking, habitual consumption at all levels, links between alcohol and other AF risk factors, and prognostic implications.

EPIDEMIOLOGY

Alcohol is ubiquitous in Western countries, with 53% of Americans regularly consuming alcohol and 61 million (44% of drinkers) consuming ≥5 standard drinks on a single occasion (binge drinking) in the last month (1). "Holiday heart syndrome" (HHS) remains a common emergency department presentation, with

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation and/or flutter

CI = confidence interval

HHS = holiday heart syndrome

HR = hazard ratio

HRV = heart rate variability

LVH = left ventricular hypertrophy

OR = odds ratio

PVI = pulmonary vein isolation

RR = relative risk

SDB = sleep-disordered breathing

AF precipitated by alcohol in 35% to 62% of cases (2,3). Three large meta-analyses have demonstrated that moderate habitual consumption, even after correcting for binge drinking, increases the incidence of AF in a dose-dependent manner (4–6), with men and women equally affected. Alcohol consumption has been defined as: light (<7 standard drinks/week); moderate (7 to 21 standard drinks/week); and heavy (>21 standard drinks/week), where 1 standard drink is approximately 12 g of alcohol.

PATHOPHYSIOLOGICAL MECHANISMS OF ALCOHOL-ASSOCIATED AF

Alcohol may act as a trigger for AF (**Figure 1**) and facilitate progressive atrial remodeling with regular long-term consumption (**Figure 2**).

ELECTROPHYSIOLOGICAL EFFECTS OF ALCOHOL. Sustained short-term alcohol consumption may induce electrical atrial remodeling, producing an arrhythmogenic substrate. In rabbits, a 5-day alcohol infusion significantly reduced L-type calcium ($I_{Ca,L}$) and sodium (I_{Na}) current density (7). An up-regulation in protein expression of the acetylcholine-sensitive potassium channel Kir3.1 (I_{KACh}) was seen in rat atria exposed to ethanol and its metabolite acetaldehyde. Increased I_{KACh} activity shortens the action potential by promoting repolarization (8). Similarly, alcohol administration shortened pulmonary vein action potential duration by increasing I_{to} to outward potassium current activity in rabbit pulmonary vein cardiomyocytes, although it did not alter automaticity or triggered activity of these cells (9). In a closed-chest porcine model, Anadon et al. (10) demonstrated that acute intoxication increased AF susceptibility following burst atrial pacing. The direct effect of alcohol shortening the atrial action potential and, as such, atrial wavelength provides the electrophysiological milieu for re-entry and AF.

The acute cardiac effects of alcohol in humans were first described in 14 patients who underwent electrophysiological studies before and after ~5 standard drinks of whiskey. As in animal models, alcohol shortened the effective refractory period, and also slowed intra-atrial conduction (11). In a study of habitual moderate-heavy drinkers, ingestion of ~6 standard drinks of whiskey prolonged the His-ventricular (H-V) interval and shortened sinus node recovery time, with an atrial or ventricular tachyarrhythmia inducible in 71% (12). Interatrial conduction, as determined by signal-averaged sinus P-wave duration, is significantly longer in patients with a history of AF following a binge compared with age-matched controls. However, following 1.5 g/kg ethanol, P-wave duration was prolonged in the control group with no history of AF (13), suggesting that alcohol directly slows interatrial conduction in all. Interatrial electromechanical delay has also been demonstrated acutely on tissue Doppler echocardiography (14).

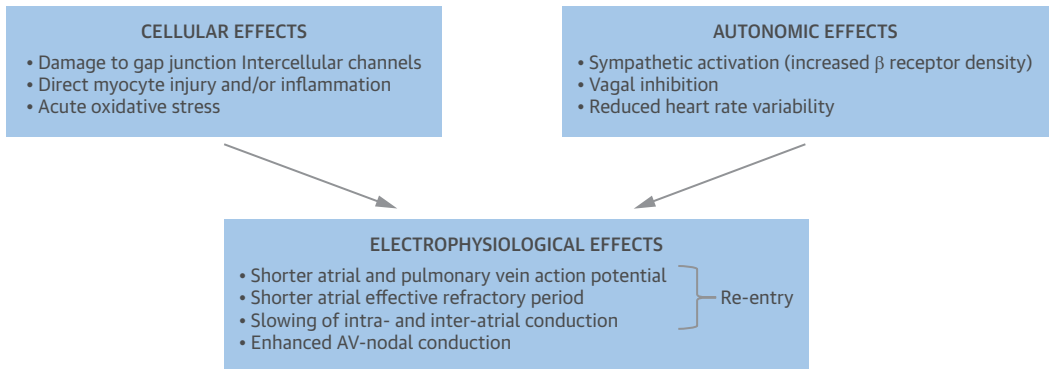
In 48 patients with AF, atrial effective refractory periods were significantly shorter in drinkers compared with nondrinkers (15). Conduction slowing, in combination with shortening of atrial refractoriness, shortens wavelength and facilitates re-entry. To date, electrophysiological changes during the washout or hangover period have not been well characterized. Hypokalemia is also common in chronic heavy drinkers, and is primarily mediated by inappropriate kaliuresis from the coexistent hypomagnesemia present in 30% of heavy drinkers (16). Potassium loss may be exacerbated by vomiting during a binge, and predisposes to AF by increasing excitability, as cellular hyperpolarization lowers the resting membrane potential, which may increase sodium channel recruitment, leading to a faster upstroke.

AUTONOMIC EFFECTS OF ALCOHOL. Alcohol has effects on autonomic modulation, which may contribute to AF. Mäki et al. (17) demonstrated a sympathetic response to 1.25 g/kg alcohol with a 29% increase in blood lymphocyte β-receptor density in patients with previous alcohol-induced AF. However, even lower alcohol doses stimulate the sympathetic nervous system, promoting adrenaline secretion from the adrenal medulla. Perman (18) found significant increases in urinary adrenaline excretion in 43 patients consuming 0.27 g/kg to 0.54 g/kg wine or whiskey, with differences seen even at alcohol concentrations <0.04%.

In patients without prior AF, there is a significant reduction in short-term heart rate variability (HRV) following acute alcohol ingestion (19). Süfke et al. (20) demonstrated a sustained increase in the ratio between low- and high-frequency components of HRV. This "hyperadrenergic state" persists at least 24 h after intoxication, and may explain why some patients present with AF the day after a binge.

Alcohol may affect the parasympathetic system. Quintana et al. (21) reported significantly greater "high frequency HRV" in habitual light-moderate drinkers, consistent with parasympathetic modulation of autonomic tone. Moreover, vagal triggers, such as rest, sleep, and eating, are common provocateurs in alcohol-mediated paroxysmal AF (22).

FIGURE 1 Potential Mechanisms for Acute Alcohol Consumption as a Trigger for AF



Acute alcohol consumption has direct cellular effects on atrial myocytes and influences autonomic function, forming the electrophysiological milieu for onset and maintenance of AF. AF = atrial fibrillation; AV = atrioventricular.

Vagal activation shortens atrial refractoriness and may give rise to single or multiple dominant rotors, resulting in waves of excitation and fibrillatory conduction; whereas sympathetic activation increases intracellular calcium and spontaneous release from the sarcoplasmic reticulum (23). Moreover, AF itself may be triggered by simultaneous discharge of both sympathetic and parasympathetic limbs (24). Patterson et al. (25) demonstrated that concurrent infusion of noradrenaline and acetylcholine caused early afterdepolarization and triggered activity, promoting arrhythmogenesis.

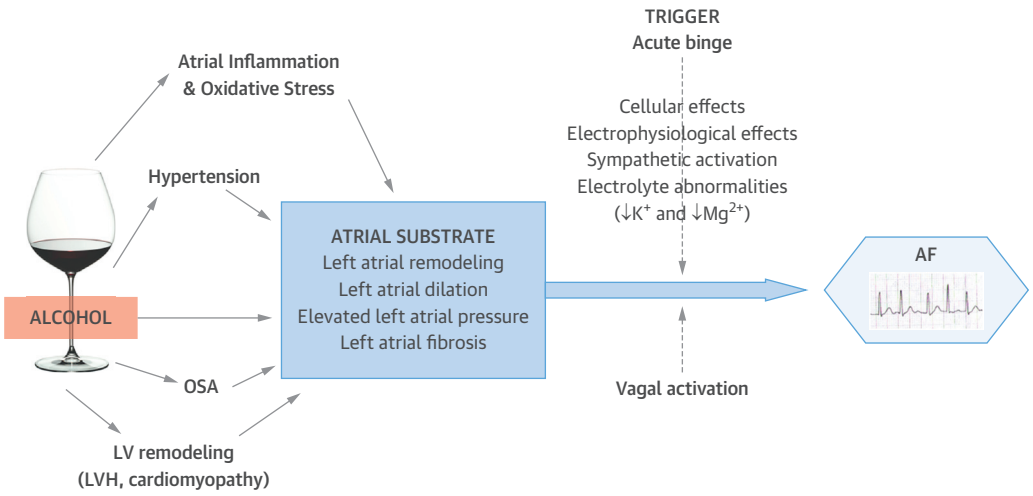
ATRIAL STRUCTURAL EFFECTS OF ALCOHOL. Alcohol has direct effects on atrial excitation-contraction coupling and may cause tissue fibrosis. Rats consuming alcohol for 2 months had a reduction in myofilament calcium sensitivity and an attenuated response to inotropes (26). Ultrastructural changes in "alcoholic animals" drinking for >1 year included localized dilation and cystic changes in intercalated discs critical to cell-cell impulse propagation (27). In patients with paroxysmal AF undergoing pulmonary vein isolation (PVI), daily drinking was an independent multivariate predictor of discrete atrial fibrosis, the hallmark of structural remodeling in AF. The probability of regional low voltage increased by 10% for every standard drink consumed (28).

Although light-moderate consumption of ≤14 standard drinks/week did not alter the prognosis in 6,797 patients with severe systolic dysfunction (29), heavier drinking may cause cardiomyopathy. Alcohol and its metabolite, acetaldehyde, have direct cardiotoxic effects. Alcohol may impair excitation-contraction coupling, inhibit calcium release from the sarcoplasmic reticulum, and cause oxidative stress, protein damage, and lipid peroxidation (30). Myocarditis with a lymphocytic infiltrate and focal necrosis is present in 30% of patients with alcoholic cardiomyopathy (31). In otherwise healthy binge drinkers, cardiac magnetic resonance imaging demonstrates transient increases in ventricular T2-signal intensity representative of myocardial edema, and global relative enhancement consistent with hyperemia, with associated troponin elevations suggestive of acute inflammation (32). Whether similar changes occur in the atria following binge drinking is yet to be determined.

ALCOHOL AND BINGE DRINKING: "HOLIDAY HEART SYNDROME"

Ettinger et al. (33) first coined the term "holiday heart syndrome" (HHS) in 24 patients hospitalized with AF following a weekend binge. Although many of these were regular drinkers, subsequent studies showed that HHS also occurred in infrequent and nondrinkers after a binge (34). Interestingly, although many patients develop AF at the time of intoxication, others may present 12 to 36 h later (35). In fact, a "hangover" may be merely a manifestation of mild alcohol withdrawal, characterized by sympathetic hyperactivity, with a 17% heart rate increase observed in healthy non-alcoholics 12 h post-binge (36). Alcohol also has a diuretic effect, elevating antidiuretic hormone and aldosterone, potentially causing electrolyte disturbances that further contribute to a proarrhythmic state. Acetaldehyde, a potent cardiac toxin and alcohol metabolite, also has effects that may persist into the hangover period (37).

FIGURE 2 Habitual Alcohol Consumption and AF: Pathophysiology



Habitual alcohol consumption predisposes to AF by direct effects on left atrial substrate and interaction with other AF risk factors, including hypertension, obstructive sleep apnea and left ventricular dysfunction. AF = atrial fibrillation; HRV = heart rate variability; K^+ = potassium; LV = left ventricle; LVH = left ventricular hypertrophy; Mg^{2+} = magnesium; OSA = obstructive sleep apnea.

Although AF usually terminates within 24 h in HHS, 26% of patients have recurrences at 1 year with subsequent binges (38). Liang et al. (39) found that binge drinking (>5 standard drinks) in addition to habitual moderate consumption of ≤21 standard drinks/week was associated with a similar risk of AF as habitual heavy drinking.

Although HHS is often considered benign, heavy binge drinking has been linked with sudden cardiac death, particularly in patients with pre-existing structural heart disease. In 309 sudden cardiac death patients with 2.8 risk factors for coronary disease, the relative risk of dying within 2 h of drinking was 3.00 (95% confidence interval [CI]: 1.61 to 5.68) (40). In this vulnerable group, alcohol may precipitate ventricular tachycardia by QTc prolongation. Rossinen et al. (41) demonstrated QTc prolongation (13 ms to 25 ms; $p < 0.05$) following 0.72 g/kg alcohol in patients with stable coronary disease, with similar findings unrelated to autonomic changes in healthy controls.

A meta-analysis of 29,457 participants in 23 studies demonstrated the complex physiological interplay of alcohol at different time points after consumption. Moderate consumption was associated with an immediately higher cardiovascular risk that was attenuated after 24 h, and became protective against ischemic stroke within 1 week. The investigators speculate that an increase in plasminogen activator inhibitor activity is responsible for events in the first 1 h to 3 h, with improvements in endothelial function, flow-mediated vasodilation, and fibrinolytic factors seen by 12 h to 24 h (42).

HABITUAL ALCOHOL CONSUMPTION AS A RISK FACTOR FOR AF

Although heavy habitual alcohol consumption and binge drinking are closely associated with AF, the relationship between light-moderate habitual consumption and dose-dependent risk of AF has emerged in 3 large meta-analyses.

Larsson et al. (4) reported a 12-year follow-up of 859,420 patients together with a meta-analysis of 7 prospective studies, including 12,554 AF cases. After excluding binge drinkers and adjusting for other AF risk factors, all 7 studies reported a positive association between alcohol and AF. For each extra alcoholic drink per day, AF incidence increased 8%. The relative risks (RRs) were: 1.08 for 7 standard drinks/week (95% CI: 1.06 to 1.10); 1.17 for 14 standard drinks/week; 1.26 for 21 standard drinks/week; 1.36 for 28 standard drinks/week; and 1.47 for 35 standard drinks/week. Of those consuming >14 standard drinks/week, only wine (RR: 1.35; 95% CI: 1.08 to 1.68) and liquor (RR: 1.46; 95% CI: 1.18 to 1.81) were associated with AF, but not beer (RR: 1.03). This may be related to the higher alcohol concentration of wine and liquor, and differences in consumption behavior between drinkers of different beverages.

Kodama et al. (5) reported similar findings in an earlier meta-analysis of 14 retrospective and prospective studies, encompassing both case controls and cohort studies. The pooled estimate of RR for the highest category of alcohol consumption compared with the lowest category was 1.51 (95% CI: 1.31 to 1.74), with an 8% increase in AF risk for each 6 standard drinks/week consumed (5). Samokhvalov et al. (6) found a slightly higher threshold for AF risk, but also demonstrated a dose-response curve. The risk of AF was increased by 17% in women consuming >14 standard drinks/week and by 25% in men consuming >21 standard drinks/week (6).

Many of the individual studies were underpowered to demonstrate a relationship between alcohol and AF, particularly in the primary prevention population, where the incidence of AF was relatively low. Therefore, the conclusions regarding the relationship between low-moderate levels of alcohol intake and AF are largely drawn from the meta-analyses. There are important limitations when interpreting large population-based observational studies. Firstly, all studies (**Table 1**) determine the quantity of alcohol by self-reporting, rather than by objective blood or urine samples. This may have underestimated the AF risk due to under-reporting of alcohol consumption. Second, AF episodes may be asymptomatic, with the majority of studies largely relying on symptomatic episodes and presentation for electrocardiograms (ECGs), rather than dedicated monitoring. For instance, the Framingham (43) and Copenhagen City Heart (44) studies only performed routine ECGs every 2 to 4 and 5 to 10 years, respectively, with AF largely determined from hospital admissions, rather than routine monitoring or primary practice. Third, "AF events" often excluded atrial flutter. In studies (28,45,46) (**Table 1**) investigating patients with prior AF, the follow-up was generally shorter and the risk of AF recurrence consistently higher with light-moderate habitual consumption.

On the basis of the current review, we did not find a safe level of daily alcohol intake in patients with a history of AF; however, this recommendation is on the basis of observational and nonrandomized studies.

Heavy habitual consumption is a well-established risk factor for AF, and may be a more important risk factor than hypertension or obesity. In a cohort of 8,602 subjects, the HR of developing AF was 2.68 for heavy drinkers (≥40 standard drinks/week), compared with 1.72 for obesity and 1.02 for hypertension (47). In a longitudinal study of 26,163 earthquake survivors, drinking >25 standard drinks/week was the strongest predictor of AF, with a hazard ratio (HR) of 3.8, compared with HRs of 1.9 for obesity and 1.08 for hypertension (48).

ALCOHOL AND OTHER AF RISK FACTORS: AN INTERMEDIARY OR A CONFOUNDING VARIABLE?

Although there is little doubt that alcohol is independently associated with AF, its interaction with other AF risk factors, particularly in habitual drinkers, may be understated. In particular, hypertension, obesity, OSA, and cardiomyopathy may be caused or exacerbated by alcohol.

Alcohol may be responsible for 16% of hypertensive disease (49), with the incidence of hypertension increased by 40% if consuming >14 standard drinks/week. In a meta-analysis of 15 randomized trials, alcohol reduction significantly lowered systolic and diastolic blood pressures in a dose-dependent fashion (50). Hypertension may be present in up to two-thirds of AF patients (51), and AF is often preceded by LVH and atrial hypertrophy (52). In those with LVH, AF incidence is reduced by 40% if a systolic blood pressure <130 mm Hg is achieved (53).

Obesity is a powerful determinant of left atrial (LA) size and a well-recognized modifiable AF risk factor (54). Despite alcohol's relatively high energy content, it has not been consistently shown to cause weight gain or metabolic syndrome in light-moderate drinkers (55). Moderate consumption (7 to 21 standard drinks/week) may even reduce new-onset diabetes by 30% (56). However, several observational studies indicate that drinking >21 standard drinks/week and binge drinking can increase body mass index, waist circumference, and waist-to-hip ratio (57). Recently published studies have focused on the benefits of structured weight reduction and exercise in reducing AF symptoms, beneficial cardiac remodeling, and sinus rhythm maintenance following PVI (54). The impact of the recommended intake of <3 standard drinks/week was not specifically addressed.

Sleep-disordered breathing (SDB), encompassing OSA, is an established AF risk factor linked with alcohol. An Apnea Hypopnea Index >5 increases the risk of incident AF by 55% over 12 years (58). SDB predisposes to AF in multiple ways, including hypercapneic hypoxia, increased oxidative stress, and inflammation causing LA remodeling. AF episodes may be triggered by sympathetic hyperactivity and acute hypertension during apneic episodes, and large negative intrathoracic pressure swings causing LA stretch (59). Scanlan et al. (60) showed that even modest alcohol consumption (0.5g/kg) before sleep increased the Apnea Hypopnea Index. Mechanisms

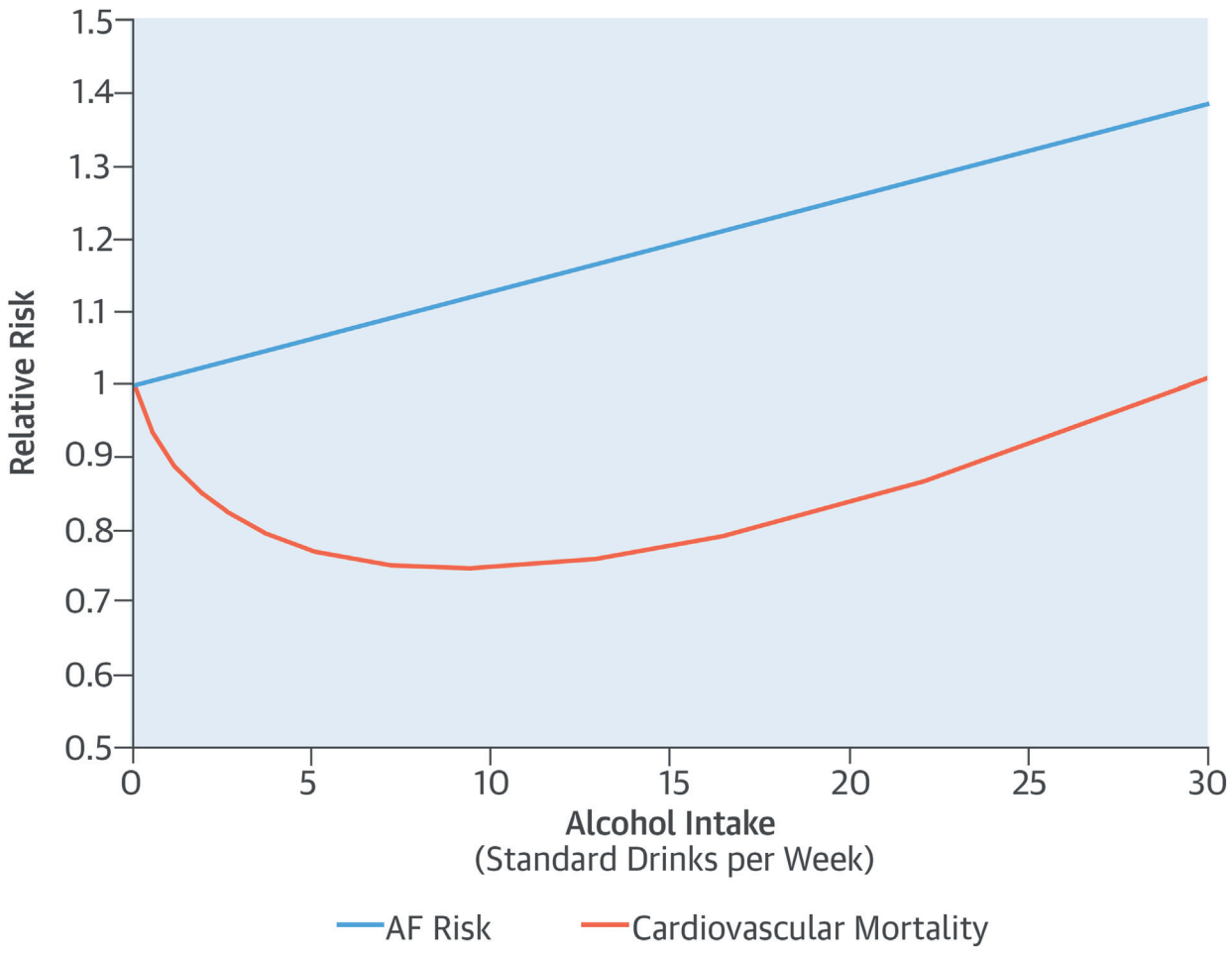
TABLE 1 Major Studies Examining the Impact of Alcohol Consumption on AF and AFL*

First Author, Year (Ref. #)	Cases/Participants	% Male	Age (yrs)	Follow-Up (yrs)	Study Design	AF/AFL Ascertainment	Key Findings
Rich et al., 1985 (35)	58/116	76	18–70	N/A	Case control	Medical records	AF patients were more likely to be heavy drinkers (>32 standard drinks/week) than controls (OR: 3.70; 95% CI: 1.70-8.05). Alcohol withdrawal was more common in those with alcohol-related AF.
Koskinen et al., 1987 (72)	100/200	82	21–64	N/A	Case control	ECG	AF patients were significantly more likely to have consumed alcohol within 2 days of AF onset than controls, with the highest mean daily alcohol intake in "lone AF" patients.
Cohen et al., 1988 (73)	28/3,966	–	–	3–9	Retrospective cohort	Medical records	Heavy drinkers (42+ standard drinks/week) had a higher risk of developing AF (RR: 2.3) and AFL (RR: 3.0) than those consuming <7 standard drinks/week ($p < 0.05$ for both).
Krahn et al., 1995 (74)	299/3,983	100	18–62	44	Population-based prospective cohort	ECG, medical report	"Alcoholism" (quantity unspecified) increased the risk of developing AF (RR: 2.07; 95% CI: 1.38–3.10).
Wilhelmsen et al., 2001 (75)	754/7,495	100	47–55	25.2	Population-based prospective cohort	Registry	"Alcohol abuse" (quantity specified) increased the risk of future AF hospitalization (OR: 1.21; 95% CI 1.02-1.42).
Ruigómez et al., 2002 (76)	1,035/6,035	47	40–89	N/A	Nested case control	ECG, Holter, echocardiogram	Heavy alcohol consumption increased risk of developing chronic AF (adjusted RR: 2.4; 95% CI: 1.4-4.1 for those consuming >28 standard drinks/week).
Djoussé et al., 2004 (43)	1,055/4,672	52	28–62	>50	Population-based prospective cohort	ECG, medical records	Moderate alcohol intake <21 standard drinks/week did not increase risk of AF/AFL, but heavier intake >21 standard drinks/week increased risk by 34% (multivariate-adjusted RR: 1.34; 95% CI: 1.01–1.78).
Frost et al., 2004 (77)	556/4,7949	47	50–64	5.7	Hospital-based prospective cohort	Registry	Increased risk of AF and AFL (HR: 1.44; 95% CI: 1.04-2.01) in men with moderate (~12 standard drinks/week) consumption.
Mukamal et al., 2005 (44)	1,071/16,415	46	26–75	16.3	Population-based prospective cohort	ECG, registry, medical records	No increased AF/AFL risk with moderate consumption in men and women, heavy consumption in men (35+ standard drinks/week) increased AF/AFL risk (HR: 1.45; 95% CI: 1.02–2.04).
Ruigómez et al., 2005 (45)	70/418	49	40–89	2.7	Prospective observational	ECG, medical records	In patients with paroxysmal AF, alcohol consumption >14 standard drinks/week increased risk of progression to "chronic AF" 3-fold.
Planas et al., 2006 (46)	32/115	64	59 ± 14	2.5	Prospective observational	ECG	In patients with prior AF, light-moderate alcohol consumption (<23 standard drinks/week in men, <12 standard drinks/week in women) significantly predicted AF recurrence (50% vs. 24%; $p = 0.01$).
Mukamal et al., 2007 (78)	1,232/5,609	50	65+	9.1	Population-based prospective cohort	ECG, registry, medical records	Habitual alcohol consumption (at all levels) in adults >65 years of age did not increase risk of AF or death.
Conen et al., 2008 (79)	653/3,4715	0	49–60	12.4	Population-based prospective cohort	ECG, medical records	Compared with nondrinkers, consumption ≥14 standard drinks/week in women increased AF risk (HR: 1.49; 95% CI: 1.05-2.11).
Marcus et al., 2008 (15)	74/260	75	59 ± 12	N/A	Case control	Medical records	AF/AFL patients were more likely to be daily drinkers (27% vs. 14%).
Liang et al., 2012 (46)	2,093/30,433	70	55+	4.7	Review of 2 antihypertensive RCTs	ECG, questionnaire	Light-moderate drinking (1-14 standard drinks/week for women; 1-21 standard drinks/week for men) associated with increase in AF risk in patients with cardiovascular disease (HR: 1.14; 95% CI: 1.04-1.26).
Larsson et al., 2014 (4)	6,019/68,848	62	45–83	12	Population-based prospective cohort	Registry	Dose-dependent increase in risk of AF/AFL (RR 1.12, 1.18, 1.43 for 7-14 standard drinks/week, 15-21 standard drinks/week, >21 standard drinks/week, respectively). Only wine and liquor (not beer) increased risk.
Qiao et al., 2015 (28)	40/122	74	55 ± 9	1.8	Prospective observational	ECG, 3-monthly, 7-day Holter	Alcohol intake post-PVI predicted recurrent AF (recurrence rate 64.9% women >7 standard drinks/week and men >14 standard drinks/week; 30.8% for women 1-7 standard drinks /week and men 1-14 standard drinks/week; 18.7% abstainers).

*1 standard drink ~ 12 g alcohol.

AF = atrial fibrillation; AFL = atrial flutter; CI = confidence interval; ECG = electrocardiography; HR = hazard ratio; N/A = not available; OR = odds ratio; PVI = pulmonary vein isolation; RCT = randomized controlled trial; RR = relative risk.

CENTRAL ILLUSTRATION **Habitual Alcohol Consumption: Long-Term Risk of Atrial Fibrillation and Cardiovascular Mortality**



Voskoboinik, A. et al. J Am Coll Cardiol. 2016;68(23):2567–76.

Estimated long-term risk of developing atrial fibrillation (AF) and cardiovascular mortality in the general population with no prior history of AF on the basis of alcohol consumption in large meta-analyses. AF risk (**blue line**; average follow-up 12 years) as shown has been adapted with permission from Larsson et al. (4). Cardiovascular mortality (**orange line**; average follow-up 11 ± 6 years) as shown has been adapted with permission from Ronksley et al. (69).

include oropharyngeal muscle hypotonia, depressed arousal mechanisms, sleep fragmentation, and reduced hemoglobin affinity for oxygen (61). Epidemiological studies have confirmed the association between alcohol and SDB in a dose-dependent manner. Peppard et al. (62) reported a 25% increased risk of SDB for each standard drink/day increment. Tanigawa et al. (63) demonstrated that moderate-heavy consumption (0.5 to 1 g/kg/day) is associated with SDB, with the mean oxygen desaturation index correlating with alcohol intake.

Although lighter alcohol intake may reduce the risk of heart failure, habitual heavy drinkers may experience the deleterious cardiotoxic effects of alcohol and develop an alcoholic cardiomyopathy. This may progress from unexplained LVH (64) to overt systolic heart failure, particularly if consuming >7 standard drinks/day for 5 years (65). Even if systolic function is normal, one-third of heavy drinkers have echocardiographic evidence of diastolic dysfunction, with deterioration of diastolic parameters correlating with degree of alcohol consumption (66). Elevated LA pressures associated with left ventricular diastolic and/or systolic dysfunction may predispose to AF by stretch-mediated mechanisms.

ALCOHOL AND AF: PROGNOSTIC IMPLICATIONS

Those who continue to consume alcohol have higher rates of progression from paroxysmal to persistent AF, more AF recurrences following PVI, and potentially higher rates of adverse outcomes, such as thromboembolism.

In a cohort of paroxysmal AF patients, 70 of 418 (17%) progressed to persistent AF over 2.7 years. Moderate-heavy alcohol consumption (>14 standard drinks/week) was the strongest risk factor for progression (odds ratio [OR]: 3.0; 95% CI: 1.1 to 8.0) (45). Alcohol was also 1 of the strongest predictors of recurrent AF (RR: 2.3; 95% CI: 1.2 to 4.4) in patients with a first episode of "idiopathic" AF (46). In 122 consecutive patients undergoing PVI, 1-year arrhythmia-free survival was 81% in abstainers, 69% in light-moderate drinkers (1 to 14 standard drinks/week in men, 1 to 7 standard drinks/week in women), and 35% in "heavy" drinkers (28).

A longitudinal cohort study of 3,107 AF patients reported a significantly higher risk of thromboembolism or death (HR: 1.33; 95% CI: 1.08 to 1.63) in male heavy drinkers (>27 standard drinks/week). Thromboembolism was significantly higher in women consuming >20 standard drinks/week (HR: 2.78; 95% CI: 1.02 to 7.60), even after adjusting for anticoagulation and CHA_2DS_2-VASc score (67). These findings contradict a previous observational study of 2,012 patients with AF, whereby moderate consumption (≥14 standard drinks/week) reduced stroke risk (RR: 0.4; p = 0.04) (68). The relationship between alcohol and thrombogenesis in the AF population remains poorly understood.

Nevertheless, the long-term cardiovascular benefits of light-moderate alcohol consumption are represented by a U-shaped curve derived from a meta-analysis (**Central Illustration**) (69). More than 100 nonrandomized studies have demonstrated that light-moderate intake (especially 7 standard drinks/week for women and 14 standard drinks/week for men) may decrease the risk of new-onset coronary artery disease, angina, myocardial infarction, and cardiovascular mortality (70) in nearly one-third of drinkers. The pooled RR for long-term cardiovascular mortality in drinkers was 0.75 (95% CI: 0.68 to 0.81) compared with nondrinkers. Proposed mechanisms include improved lipid profile (increased high-density lipoprotein, apolipoprotein A-I), and reduced platelet aggregation and inflammation (decreased interleukin-5, fibrinogen) (71). However, these studies predominantly included healthy adults, and should not be extended to those with a history of AF or structural heart disease.

CONCLUSIONS

Alcohol is an important risk factor for AF through direct effects on the atrial substrate, and by contributing to hypertension, obesity, and SDB. Habitual drinking at moderate levels, as well as binge drinking, predisposes to AF, with an increase in AF recurrence in those who continue to drink. Although a small amount of alcohol is considered cardioprotective, these benefits do not extend to AF.

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