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The Impact of Alcohol Intake on Atrial Fibrillation

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Abstract

Purpose of Review To evaluate (1) the impact of acute and habitual alcohol consumption on atrial fibrillation (AF) and atrial remodeling and (2) the role of alcohol reduction and/or abstinence in the primary and secondary prevention of AF.

Recent Findings Acute alcohol consumption appears to be a common AF trigger, with animal and human studies demonstrating changes in electrophysiological parameters, autonomic tone, and cellular properties expected to promote AF. Habitual consumption is associated with adverse atrial remodeling, higher risk of incident AF, and AF recurrence. Randomized data suggest that reduction in excessive alcohol consumption may reduce the risk of recurrent AF episodes and AF burden.

Summary Alcohol is an increasingly recognized risk factor for both new onset AF and discrete AF episodes. Excessive consumption should be avoided for primary and secondary prevention of AF.

Keywords Atrial fibrillation · Alcohol · Left atrium · Remodeling · Binge drinking · Lifestyle

Abbreviations

AF	Atrial fibrillation
ERP	Effective refractory period
HR	Hazard ratio
LA	Left atrium
OR	Odds ratio
RR	Relative risk

Introduction

Atrial fibrillation (AF) is an emerging epidemic [1] and alcohol consumption ubiquitous in Western society [2]. The acute onset of arrhythmias following binge drinking was first described in the 1970s and termed "Holiday Heart Syndrome" due to the observed higher incidence of AF episodes after weekends and public holidays. Since then, numerous studies have studied the relationship between alcohol and AF. In this review, we summarize the latest literature pertaining to the acute and chronic effects of alcohol on the atrium (Fig. 1) and the role of alcohol reduction in the primary and secondary prevention of AF.

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Epidemiology

Acute Relationships

Numerous observational studies have established a temporal association between acute alcohol consumption and onset of an AF episode in vulnerable individuals. This was first reported by Ettinger et al. who observed a higher incidence of alcohol-related atrial arrhythmias in binge drinkers following the weekend and in December and January [3]. This was termed the "Holiday Heart Syndrome," and while episodes usually terminated within 24 h, 26% of patients had recurrences over the next 12 months with subsequent binges [4]. In a case control of 100 individuals presenting with acute AF, alcohol intake within 2 days prior to presentation was significantly higher than in matched controls [5]. In patients with paroxysmal AF, alcohol is the most commonly reported trigger—"sometimes" triggering AF in 31% and "always" triggering AF in 4% [6••]. However, the absolute incidence of

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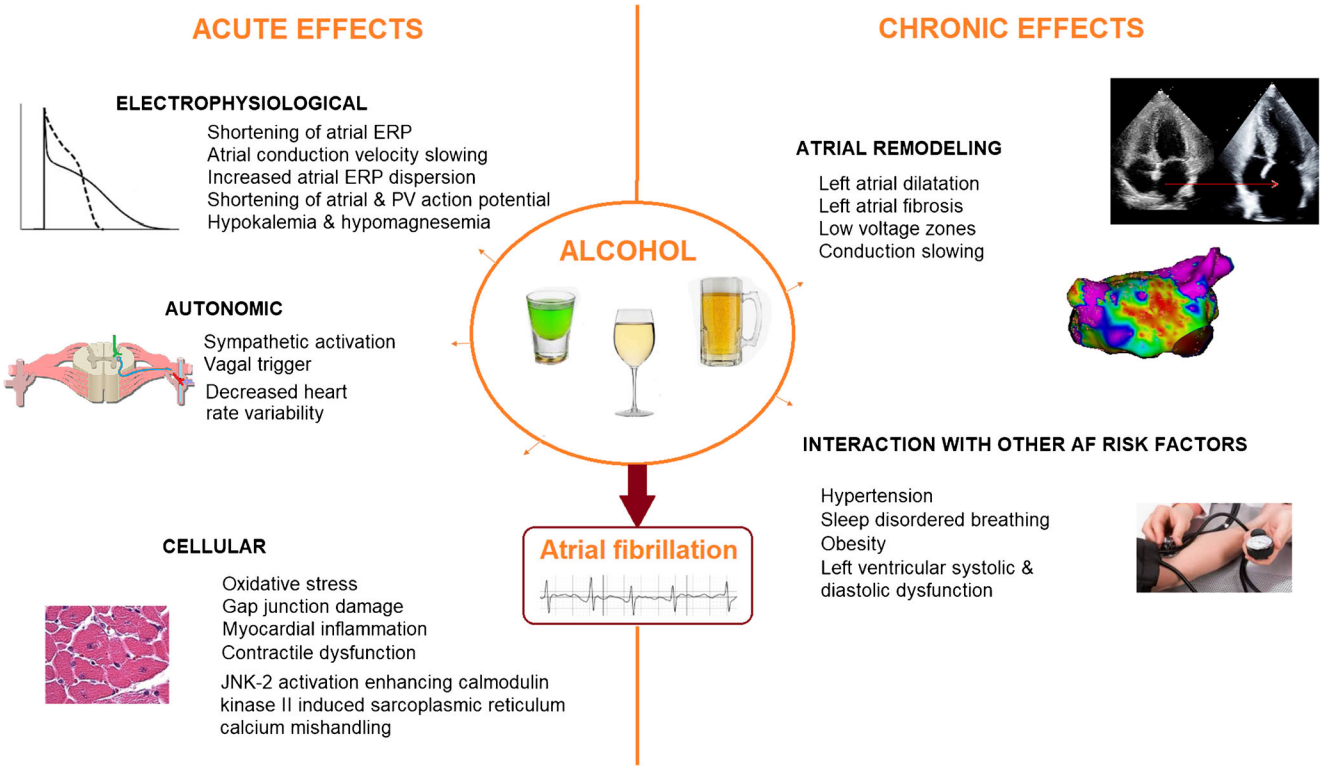

Fig. 1 Relationship between acute and chronic alcohol intake and atrial fibrillation. ERP effective refractory period; JNK c-Jun N-terminal kinase; PV pulmonary vein

arrhythmias following binge drinking in those without prior AF remains low. In 3028 young adults who undertook smartphone-based ECG monitoring after binge drinking during Octoberfest, 26% had sinus tachycardia, 1.3% had premature atrial complexes, and 0.8% developed AF [7]. Therefore, it appears that there are likely as yet undetermined mechanistic interactions between acute alcohol consumption and some underlying propensities (potentially genetic and/or environmental) that render some more versus less prone to alcohol-induced AF.

Chronic Relationships

Large-scale meta-analyses based on numerous population-based cohorts suggest that habitual alcohol consumption increases the risk of incident AF. However, the threshold for "harm" remains the subject of debate, and not every study has unequivocally demonstrated a clear association (Table 1). A 2014 meta-analysis of 7 prospective studies with 12,554 new cases of AF found a linear dose-response relationship starting at 1 standard drink per day (RR 1.08; 95% CI 1.06 to 1.10), increasing by ~8% for each additional daily standard drink (1 standard drink ~ 12 g alcohol). Results were significant even after exclusion of binge drinkers, and wine and spirits appeared to have a stronger association than beer [13]. Therefore, no clear threshold regarding the amount of alcohol consumed as pertains to AF risk has been established, but rather it appears that the risk simply increases as the amount of alcohol consumed increases. A more recent meta-analysis suggested that "moderate" habitual consumption (1–2 drinks per day) was only associated with a heightened risk of AF in males (HR 1.26, 95% CI 1.04–1.54) but not females (HR 1.03, 95% CI 0.86–1.25) while > 2 drinks/day remained significant for both sexes [20].

A large Korean population-based study found that drinking frequency, rather than the amount consumed, carried the greatest risk of new AF. Patients who drank on a daily basis had the highest risk (HR 1.412, 95% CI 1.373–1.453), while a larger amount of alcohol per drinking session did not increase the risk [19]. The potential benefits of mild alcohol consumption on risk of cardiovascular disease, represented by a "U-shaped" curve [21], need to be counterbalanced against the higher risk of AF, and again there are likely individual-level predispositions that influence those relative harms and benefits. Interestingly, in a study comparing "wet" (no alcohol restrictions) and "dry" (alcohol prohibited) counties in Texas, wet counties had a higher prevalence and incidence of AF, but a lower incidence and prevalence of myocardial infarction. Conversion of a county from "dry" to "wet" was associated with a higher AF incidence [22]. However, given evidence that those who "abused" alcohol had a higher risk of myocardial infarction (HR 1.45, 95% CI 1.40–1.51), heart failure (HR 2.34, 95% CI 2.29–2.39), and AF (HR 2.14, 95% CI 2.08–2.19) in a large Californian longitudinal

Table 1 Key studies examining habitual alcohol intake and risk of incident AF

Study	AF cases/ participants	Follow-up	Study design	Summary of key findings
Krahn et al. [8] 1995	299/ 3983	44 years	Prospective cohort	"Alcoholism" was associated with higher risk of new AF (RR 2.07; 95% CI 1.38–3.10)
Wilhelmsen et al. [9] 2001	754/ 7495	25.2 years	Population-based cohort	"Alcohol abuse" associated with higher risk of AF hospitalization (OR 1.21; 95% CI 1.02–1.42)
Frost et al. [10] 2004	556/ 47,949	5.7 years	Prospective cohort	Increased risk of AF in men with increasing consumption, with adjusted HRs in quintiles 2, 3, 4, and 5 of 1.04, 1.44, 1.25, and 1.46, respectively (p for trend = 0.04). Trend not statistically significant for women
Mukamal et al. [11] 2005	1071/ 16,415	16.3 years	Prospective cohort	Heavier consumption in men (35+ SDs/week) increased the risk of incident AF (HR 1.45; 95% CI 1.02–2.04)
Conen et al. [12] 2008	653/ 34,715	12.4 years	Prospective cohort	Alcohol consumption ≥ 14 SDs/week in women increased incident AF risk (HR 1.49; 95% CI 1.05–2.11)
Larsson et al. [13] 2014	6019/ 68,848	12 years	Prospective cohort	Dose-dependent increase in AF risk (RR 1.12, 1.18, 1.43 for 7–14 SDs/week, 15–21 SDs/week, > 21 SDs/week, respectively, compared with < 1 SD/week). Wine and spirits increased AF risk, but not beer
McManus et al. [14] 2016	1088/5220	6.0 years	Prospective cohort	Each 10 g/day of alcohol associated with a 5% higher risk of new AF (HR 1.05; 95% CI, 1.01–1.09) and 24% (95% CI, 8–75) of this association explained by left atrial dilatation
Gemes et al. [15] 2017	1697/47002	8 years	Population-based cohort	Overall higher risk of AF in those drinking > 7 SDs/week compared with abstainers (HR 1.38; 95%.CI 1.06–1.80), although "non-risky" drinking (< 1 SD/day in women, < 2 SD/day in men) did not demonstrate an association with AF
Dixit et al. [16] 2017	1631/15222	19.7 years	Prospective cohort	Each decade abstinent associated with a 20% (95% CI 11–28%) lower risk of new AF; every additional decade of previous consumption associated with a 13% (95% CI 3–25%) increase in AF risk
Bazal et al. [17] 2019	241/6527	4.4 years	Prospective observational study	Mediterranean drinking pattern (10–30 g/d in men & 5–15 g/day in women, red wine preferred) did not increase AF risk compared with non-drinkers (HR: 0.96; 95% CI: 0.67–1.37)
Johansson et al. [18] 2020	5320/ 109,230	1,484,547 person-years	Population-based cohort	Alcohol consumption was associated with higher risk of AF in men (HR 1.21; 95% CI 1.09–1.34 for > 5 SDs/week compared with < 1 SD/week; p = 0.001 for trend), but not women (p = 0.09 for trend)
Kim et al. [19] 2020	195,829/ 9,776,956	79,960,860 person-years	Population-based cohort	Daily drinkers had the highest risk of incident AF (HR 1.41; 95% CI 1.37–1.45) compared with those drinking twice/week; however, amount of intake per drinking session did not increase risk of incident AF

AF atrial fibrillation; *CI* confidence interval; *HR* hazard ratio; *OR* odds ratio; *RCT* randomized controlled trial; *RR* relative risk; *SD* standard drink (1 SD ~ 12 g alcohol)

healthcare database [23], "more" is not "better," with consistent evidence of harmful effects on all cardiovascular outcomes when alcohol is consumed in excess.

In those with a history of AF, habitual alcohol consumption appeared to increase the risk of AF progression. In a UK registry of 418 paroxysmal AF patients followed for 2.7 years, moderate-to-high alcohol consumption (> 21 drinks/week) was associated with progression to persistent AF (OR 3.0, 95% CI 1.1–8.0) [24]. Higher recurrence rates in regular drinkers following catheter ablation of AF have also been observed: in a study of 1361 consecutive paroxysmal AF patients undergoing ablation, alcohol consumption (88 ± 137 g/week, 46% of all patients) was associated with a higher AF recurrence rate after initial ablation (41.9% vs 34.1%; p = 0.003) [25]. Consumption frequency (HR 1.07 per 1 day/week increase, CI 1.00–1.15) most strongly predicted recurrence risk [25]. In a smaller study of 122 consecutive patients with paroxysmal AF undergoing ablation, abstainers had the highest success rates (81.3%), followed by moderate (1–7 drinks/week in women, 1–14 drinks per week in men) drinkers (69.2%), and then heavy drinkers (35.1%; log-rank p < 0.001), with alcohol being a multivariate predictor of recurrence (HR 1.58; 95% CI, 1.09–2.30) [26]. In 40 patients with persistent AF undergoing ablation, consumption > 30 g/week was associated with a higher risk of arrhythmia recurrence [27].

Potential Interactions

Alcohol is causally linked with other AF risk factors, including hypertension, sleep apnea, and left ventricular dysfunction. In a case control, daily drinkers had a significantly higher

risk of developing hypertension (OR 1.75, 95% CI 1.13–2.72) [28], and a meta-analysis of 36 trials found significant reductions in blood pressure in those consuming 2+ drinks/day who reduced their alcohol intake [29]. Obstructive sleep apnea is an increasingly recognized AF risk factor, and in an observational study, the sedative effects of excessive alcohol (0.5 g/kg) resulted in a higher mean apnea/hypopnea index than alcohol-free nights (9.7 ± 2.1 vs 7.1 ± 1.9; $p = 0.017$) [30]. Interestingly, even independent of obstructive sleep apnea, alcohol may lead to insomnia and general sleep disturbance, and evidence is now emerging that such sleep disturbances, even independent of obstructive sleep apnea, may predict AF [31–33]. Heavy alcohol consumption (≥ 80 g/day) over several years may lead to left ventricular systolic dysfunction [34] while moderate consumption (≥ 20 g/day) is associated with left ventricular diastolic dysfunction [35]. Hospitalized patients with alcoholic cardiomyopathy have a high incidence of comorbid AF, reported in 31.5% of admissions [36].

Alcohol and AF Mechanisms

Acute Relationships

Several animal studies have provided insights into alcohol's acute effects on atrial electrophysiology. In a study of rats utilizing atrial optical mapping, acute alcohol perfusion decreased atrial conduction velocities and shortened right atrial action potential and effective refractory period (ERP) with increased dispersion of refractoriness in a dose-dependent fashion [37•]. Yan et al. recently reported enhanced activation of c-Jun N-terminal kinase (JNK) signaling in both rabbits and Langendorff-perfused human atrial preparations following binge alcohol exposure. This resulted in activation of calmodulin kinase II, a "proarrhythmic" molecule that resulted in sarcoplasmic reticulum calcium mishandling with aberrant calcium waves and greater AF inducibility [38•]. Other animal studies have reported acute changes in ion channel activity following alcohol infusion, including reduced density of atrial L-type calcium ($I_{Ca,L}$) and sodium (I_{Na}) currents [39], potassium channel Kir3.1 (I_{KACh}) upregulation resulting action potential shortening [40], and increased pulmonary vein I_{to} outward potassium current activity in pulmonary vein cardiomyocytes [41].

Acute alcohol consumption may predispose to AF in humans by altering atrial electrical properties, direct cardiac toxicity, or via changes in autonomic tone. In 14 patients undergoing electrophysiological study pre- and post-intoxication with whiskey, alcohol shortened atrial effective refractory period and slowed intra-atrial conduction [42]. P wave prolongation representing interatrial conduction slowing was demonstrated following a binge in patients with a history of AF and non-AF controls [43], with interatrial electromechanical delay seen on tissue Doppler echocardiography in another study [44].

Perturbations in autonomic nervous system activity induced by binge drinking may predispose to AF. Several observational studies have shown evidence of sympathetic activation. Key findings within the first 24 h following intoxication include increased urinary adrenaline excretion (even at alcohol concentrations below 0.04%) [45], 29% increase in lymphocyte β-receptor density [46], increased low frequency/high frequency ratio on frequency domain analyses [46, 47], and reduced heart rate variability—particularly the SDNN (standard deviation of NN intervals) [48]. Acetaldehyde, a key alcohol metabolite, may also selectively inhibit vagal tone and activate the sympathetic nervous system [19]. However, in some patients, alcohol may induce AF through parasympathetic activation. In a study of 133 paroxysmal AF patients, those with alcohol-triggered AF were more likely to report other vagal triggers (OR 10.32, 95% CI 1.1–101; $p = 0.045$) [49].

Alcohol is an established cause of cardiomyopathy and binge drinking may cause myocardial injury and inflammation, as evidenced by troponin rises, increased ventricular T2-signal intensity (myocardial edema) and global relative enhancement (hyperemeia) seen on cardiac MRI following a heavy binge [50]. Mechanisms include oxidative stress, mitochondrial dysfunction, abnormal fatty acid metabolism [51], and apoptosis [52]. While these studies primarily examined the ventricle, the thinner-walled atrium may also be equally or more vulnerable to such "injury." Alcohol excess also may cause electrolyte disturbances that predispose to AF, including hypokalemia from its acute diuretic properties (exacerbated by vomiting) and hypomagnesemia seen in 30% of heavy drinkers [53].

Chronic Relationships

Electrical and cellular changes after prolonged alcohol exposure have been reported in animal studies. Observations include reduced myofilament calcium sensitivity in rats consuming 2 months of alcohol [54], atrial conduction slowing, increased dispersion of refractoriness, reduced right atrial ERP, and increased mRNA expression of KCNQ1 and connexin-40 following 6 months of alcohol [37•] and cystic changes in intercalated discs after 12 months [55]. In humans, habitual alcohol consumption has been associated with increased risk of adverse atrial remodeling and incident AF. In the Framingham cohort study with 1088 cases of incident AF over median 6 years follow-up, each 10-g increase in daily alcohol consumption was associated with a 0.16-mm (95% CI 0.10–0.21) increase in LA dimension, with ~ 24% of the incident AF risk estimated to be explained by this LA enlargement [14]. For 601 participants with stable coronary disease with

serial echocardiograms over 5 years, each standard deviation increase in AUDIT-C score (used to measure alcohol consumption) was associated with a 24% increase in indexed LA volume [56]. In a study of 3946 asymptomatic individuals undergoing echocardiographic strain assessment, reduced left atrial strain was observed even in those consuming > 1 drink/week, while recent abstainers had strain measurements in between nondrinkers and current drinkers [57]. In a cross-sectional study of 160 AF patients undergoing cardiac MRIs in sinus rhythm, regular alcohol consumption (15.8 ± 6.9 standard drinks/week) was associated with reduced left atrial mechanical function compared with lifelong non-drinkers (left atrial emptying fraction 40 ± 14% vs. 52 ± 15%; $p < 0.001$) [58].

Excessive alcohol consumption may also cause adverse atrial electrical remodeling. In paroxysmal AF patients undergoing ablation, daily alcohol consumption was an independent predictor of low-voltage zones, with the probability of regional low voltage rising by 10% for every additional drink consumed [26]. In a study of 75 AF patients undergoing high-density electroanatomical mapping of the LA in sinus rhythm, "moderate" drinkers (14.0 ± 4.2 drinks/week) had lower mean global bipolar voltages (1.53 ± 0.62 mV vs 1.89 ± 0.45 mV; $P = .02$), and conduction slowing (33.5 ± 14.4 cm/s vs 41.7 ± 12.1 cm/s; $P = .04$) compared with lifelong non-drinkers, while mild drinkers (4.4 ± 2.3 drinks/week) did not have evidence of adverse electrical remodeling [59]. In an observational study of 195 patients undergoing electrophysiology study, atrial flutter patients younger than 60 years of age were more likely to be daily drinkers (OR 17, 95% CI 1.6–92), with right atrial effective refractory period becoming progressively shorter with higher alcohol intake [60]. Adverse electrical and mechanical atrial remodeling may explain the heightened propensity for ischemic stroke associated with alcohol excess in the AF population. In a retrospective study of 25,252 low-risk AF patients followed for 5 years, previous alcohol-related hospitalization was associated with a doubling in risk of subsequent ischemic stroke [61]. It should be noted that anticoagulation in heavy drinkers with AF has been associated with higher bleeding risk (HR 2.37; 95% CI 1.24–4.53) in large scale registries, highlighting the challenges in managing this patient population.

The Role of Alcohol Reduction

The impact of lifestyle interventions on secondary AF prevention has been increasingly studied in recent years, and Table 2 summarizes key studies examining alcohol intake in the AF population. Abed et al. randomized 150 AF patients to a weight reduction program and intensive risk factor management that included

Table 2 Key studies examining habitual alcohol intake in the AF population

Study	AF patients	Follow-up	Study design	Summary of key findings
Ruigomez et al. [24] 2005	525	2.7 years	Prospective observational	Regular alcohol consumption > 14 SDs/week was associated an increased risk in progression from paroxysmal to persistent AF phenotype (OR 3.0, 95% CI 1.1–8.0)
Planas et al. [62] 2006	115	2.5 years	Prospective observational	Light-moderate alcohol consumption (< 23 SDs/week in men, < 12 SDs/week in women) predicted AF recurrence (50% vs 24%; $p = 0.01$)
Marcus et al. [60] 2008	132	N/A	Case control	AF and atrial flutter patients were more likely to be daily drinkers (27% vs 14%;$p = 0.001$), although after multivariate adjustment, only atrial flutter patients ≤ 60 years were more likely to be daily drinkers (OR 17; 95% CI 1.6–192)
Qiao et al. [26] 2015	122	21 months	Prospective observational	Alcohol consumption following AF ablation associated with higher recurrence rates (64.9% women > 7 SDs/week and men > 14 SDs/week; 30.8% for women 1–7 SDs /week and men 1–14 SDs/week; 18.7% abstainers; log-rank $p < 0.001$)
Takigawa et al. [25] 2016	1361	53 months	Retrospective cohort	Intake frequency associated with AF recurrence after ablation (HR 1.07 per 1 day/week increase, 95% CI 1.00–1.15, $p = 0.04$). Alcohol consumption associated with success rates after initial ablation, but not repeat ablation
Barham et al. [63] 2016	226	12 months	Retrospective cohort	In multivariate analysis, neither moderate (1–7 SDs/week) nor heavy (> 7 SDs/week) alcohol consumption predicted AF recurrence following ablation
Voskoboinik et al. [64••] 2020	140	6 months	Randomized controlled trial	Regular drinkers (> 10 SDs/week) with prior AF assigned to abstinence reduced their intake from 16.8 ± 7.7 to 2.1 ± 3.7 SDs/week and had longer AF-free survival (HR 0.55; 95% CI 0.36–0.84; $p = 0.005$) than controls ($n = 70$). The abstinence group also had lower AF burden (0.5%, IQR 0.0–3.0% vs 1.2%, IQR 0.0–10.3%; $p = 0.01$) and lost weight (mean − 3.7 kg; 95% CI − 4.8 to − 2.5).

AF atrial fibrillation; *CI* confidence interval; *HR* hazard ratio; *OR* odds ratio; *SD* standard drink (1 SD ~ 12 g alcohol)

alcohol reduction to < 30 g/week, and found a reduction in number and duration of AF episodes [65]. Similar interventions in an observational study of 281 patients undergoing AF ablation found improved arrhythmia-free survival with those undergoing risk factor modification [66]. However, less than a third of the patients in these studies consumed > 30 g/week. In the first randomized study of 140 AF patients who were regular drinkers (> 10 standard drinks or 120 g/week), significant reduction in alcohol consumption over a 6-month period (from 16.8 ± 7.7 to 2.1 ± 3.7 in the "abstinence" group) resulted in lower AF burden (0.5% [interquartile range, 0.0 to 3.0] vs. 1.2% [0.0 to 10.3]; $P = 0.01$) and longer freedom from AF recurrence (HR 0.55; 95% confidence interval, 0.36 to 0.84; $P = 0.005$) compared with controls who were allowed to continue their usual level of consumption [64••]. The benefits of alcohol abstinence in the primary prevention setting were reported by Dixit et al. from the ARIC cohort study comprising 15,222 participants with 1631 cases of incident AF over 19.7 years follow-up [16]. Every decade abstinent from alcohol portended a 20% lower rate of new AF, while each decade of previous alcohol consumption carried a 13% higher AF risk [67].

Conclusions

Alcohol is a well-established trigger of acute AF episodes, and excessive consumption is associated with increased risk of incident AF and adverse left atrial remodeling. Mechanisms are multifactorial and defining the exact threshold for harm requires further investigation. Future research is required to identify individual-level propensities that may enhance or diminish alcohol-related effects, underlying mechanisms that may reveal novel targets for prevention and therapeutics relevant to all AF in general, and optimal approaches to effectively change behavior to help patients reduce their alcohol consumption. Reduction in excessive alcohol consumption is likely beneficial for both the primary and secondary prevention of AF.

Compliance with Ethical Standards

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Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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