JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER

VOL. 68, NO. 23, 2016
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2016.08.074

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.
(J Am Coll Cardiol 2016;68:2567–76) © 2016 by the American College of Cardiology Foundation.

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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Manuscript received May 10, 2016; revised manuscript received July 28, 2016, accepted August 31, 2016.

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).