Moderate alcohol consumption is associated with atrial electrical and structural changes: Insights from high-density left atrial electroanatomic mapping

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BACKGROUND Regular alcohol intake is an important modifiable risk factor associated with atrial fibrillation (AF) and left atrial (LA) dilation.

OBJECTIVE The purpose of this study was to determine the impact of different degrees of alcohol consumption on atrial remodeling using high-density electroanatomic mapping.

METHODS We enrolled 75 patients before AF ablation to undergo high-density LA mapping (CARTO, Biosense Webster) using a multipolar catheter. The Confidense algorithm was used to create maps during distal coronary sinus pacing at 600 ms. Bipolar voltage and complex atrial activity were assessed, and isochronal activation maps were created to determine global conduction velocity (CV). Patients were classified as lifelong nondrinkers, mild drinkers (2–7 drinks/week), or moderate drinkers (8–21 drinks/week).

RESULTS High-density electroanatomic mapping (mean 1016 ± 445 points per patient) was performed on 25 lifelong nondrinkers, 25 mild drinkers (4.4 ± 2.3 drinks/week), and 25 moderate drinkers (14.0 ± 4.2 drinks/week). Moderate drinkers had significantly lower mean global bipolar voltages (1.53 ± 0.62 mV vs 1.89 ± 0.45 mV; $P = .02$), slower CV (33.5 ± 14.4 cm/s vs 41.7 ± 12.1 cm/s; $P = .04$), and a higher proportion of complex atrial potentials (7.8% ± 4.7% vs 4.5% ± 2.7%; $P = .004$) compared to nondrinkers. Global voltage and CV did not differ significantly in mild drinkers, but there was a significant increase in global complex potentials (6.6% ± 4.6%; $P = .04$) and regional low-voltage zones (<0.5 mV) in the septum and lateral wall ($P < .05$) compared with nondrinkers.

CONCLUSION Regular moderate alcohol consumption, but not mild consumption, is an important modifiable risk factor for AF associated with lower atrial voltage and conduction slowing. These electrical and structural changes may explain the propensity to AF in regular drinkers.

KEYWORDS Alcohol; Atrial fibrillation; Atrial substrate; Conduction velocity; Electroanatomic mapping; Left atrium; Voltage

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Introduction

Excessive alcohol consumption has emerged as a potentially modifiable risk factor for atrial fibrillation (AF).[1] Both binge drinking and habitual alcohol consumption have been implicated in electrical and structural changes involving the left atrium (LA). Acute electrophysiological effects of excessive alcohol include shortening of atrial refractoriness and slowing of intra-atrial conduction.[2] More recently, binge drinking has been found to activate c-Jun N-terminal kinase (JNK), leading to sarcoplasmic reticulum calcium mishandling[3] and causing contractile dysfunction related to oxidative stress, mitochondrial damage, and cardiac steatosis,[4] thereby increasing susceptibility to "holiday heart syndrome."

Observational studies suggest that regular alcohol consumption, even at moderate levels, may increase AF risk. A meta-analysis of 7 studies involving 859,420 patients and 12,554 AF cases demonstrated an 8% increase in incident AF for each additional daily standard drink.[5] Whereas alcoholic cardiomyopathy is well described in the ventricle for those consuming >80 g/d for >10 years,[6] the

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thinner-walled atrium may be more susceptible to toxicity at lower doses. Compared to abstainers, those consuming even 1 drink per day have been reported to have a higher prevalence of atrial "low-voltage zones".[7] There is a dose-related relationship between regular alcohol consumption and LA enlargement, with each additional 10 g associated with a 0.16-mm increase in LA size.[8]

Despite the association between regular alcohol intake and AF, detailed human electrophysiological studies describing the nature of alcohol-related atrial remodeling are lacking. We aimed to determine the impact of regular alcohol consumption on electrical and structural changes in the LA in patients with a history of AF using high-density electroanatomic mapping before AF ablation.

Methods

Patient population

This multicenter cross-sectional study was conducted from March 2016 to May 2018 at 2 hospitals. We recruited 75 patients with paroxysmal or persistent AF willing to consent to high-density LA mapping during initial AF ablation using the CARTO (Biosense Webster, Diamond Bar, CA) 3-dimensional electroanatomic mapping system. The study was approved by Alfred Health and Melbourne Health Human Research Ethics Committees, and all patients provided written informed consent.

Patients self-reported their average alcohol consumption in standard drinks per week (where 1 standard drink ∼ 12 g alcohol) over the preceding 12 months. Those consuming 2–7 drinks/week were considered mild drinkers, and those consuming 8–21 drinks/week were defined as moderate drinkers. We aimed to recruit 25 consecutive patients from each of the 3 drinking categories (none, mild, moderate).

Exclusion criteria included (1) occasional drinkers, defined as >1 consecutive month of nondrinking during the preceding 12 months; (2) binge drinkers, defined as ≥5 standard drinks in a 2-hour sitting > monthly; (3) significant structural heart disease (left ventricular ejection fraction <40% or previous myocardial infarction); (4) permanent AF; (5) alcoholic liver cirrhosis; (6) severe renal impairment; and (7) previous AF ablation.

Electroanatomic mapping protocol

Antiarrhythmic medications were stopped at least 5 half-lives before AF ablation. After induction of general anesthesia, a transesophageal echocardiographic probe was inserted to exclude LA thrombus and guide transseptal puncture. All catheters were inserted via the right femoral vein. Diagnostic catheters included a decapolar coronary sinus (CS) catheter and a quadripolar His-bundle/right ventricular catheter. Double transseptal puncture was performed using a BRK needle via 8F and 8.5F long SL1 sheaths (St Jude Medical, St Paul, MN), and heparin was administered for a target activated clotting time ∼350 seconds.

A steerable circular 20-pole multipolar pulmonary vein mapping catheter (Lasso, Biosense Webster; with 2-5-2 mm electrode spacing) and a contact-force irrigated ablation catheter were then introduced into the LA. Patients presenting in AF underwent external cardioversion to restore sinus rhythm. After a 5-minute waiting period, voltage and activation maps were collected using the Confidense algorithm (CARTO) during stable pacing from the distal coronary sinus (CSd) at 600-ms cycle length. Patients with recurrent AF during the waiting period did not undergo research mapping and proceeded to pulmonary vein isolation. A target of 1000 points evenly distributed across all LA regions with a mapping fill threshold of 10 mm and density acquisition filter of 1 mm^2 was set and assisted with the Confidense software module (Supplemental Figure 1A). Average point density was derived from the final point count and atrial surface area obtained from the CARTO module.

Several measures were undertaken to ensure tissue contact and accurate electrogram annotation during continuous mapping. They included use of the tissue proximity indicator (an impedance-based algorithm), application of an internal point filter to within 5 mm of the chamber surface geometry, and correlation of geometry with the contact force–enabled ablation catheter.

Atrial voltage and conduction analysis

Analysis of each electrogram was performed offline. The LA was divided into anterior, posterior, septal, lateral (including LA appendage), and superior and inferior regions, excluding the pulmonary veins and mitral annulus. Although we collected data using the Confidense algorithm, all acquired points were also manually reviewed. Only points demonstrating characteristics of near-field signals were included. These signals demonstrated at least 2 sharp peaks and were consistent with anatomically adjacent signals in terms of signal quality, electrogram timing, and proximity to the geometric shell. Points not fulfilling these criteria were excluded. Incorrectly collected points including artifact, atrial ectopics, and far-field ventricular electrograms were deleted. Complex fractionated atrial electrograms (CFAEs) were defined as having at least 3 deflections >50-ms duration. Double potentials were defined as having 2 discrete deflections separated by an isoelectric interval. Both of these groupings were considered "complex signals," representing atrial substrate. After manual annotation of each point, maps were exported for further signal processing (MATLAB 9.1, Mathworks, Natick, MA).

Bipolar voltage was defined using the peak-to-peak electrogram voltage. Low voltage was defined as bipolar voltage <0.5 mV. However, to ensure this was not an internal point, it was only annotated if contiguous low-voltage points were collected within a 5-mm radius. Isochronal activation maps were created using the Confidense algorithm during CSd pacing at 600 ms. Local activation time was annotated per the algorithm based on bipolar and unipolar signals using the maximum negative slope (–dV/dT), unipolar signals were compared with simultaneous bipolar activity in order to exclude potential far-field signals. A scar filter of 0.05 mV was set, and these areas were not assigned a local activation time.

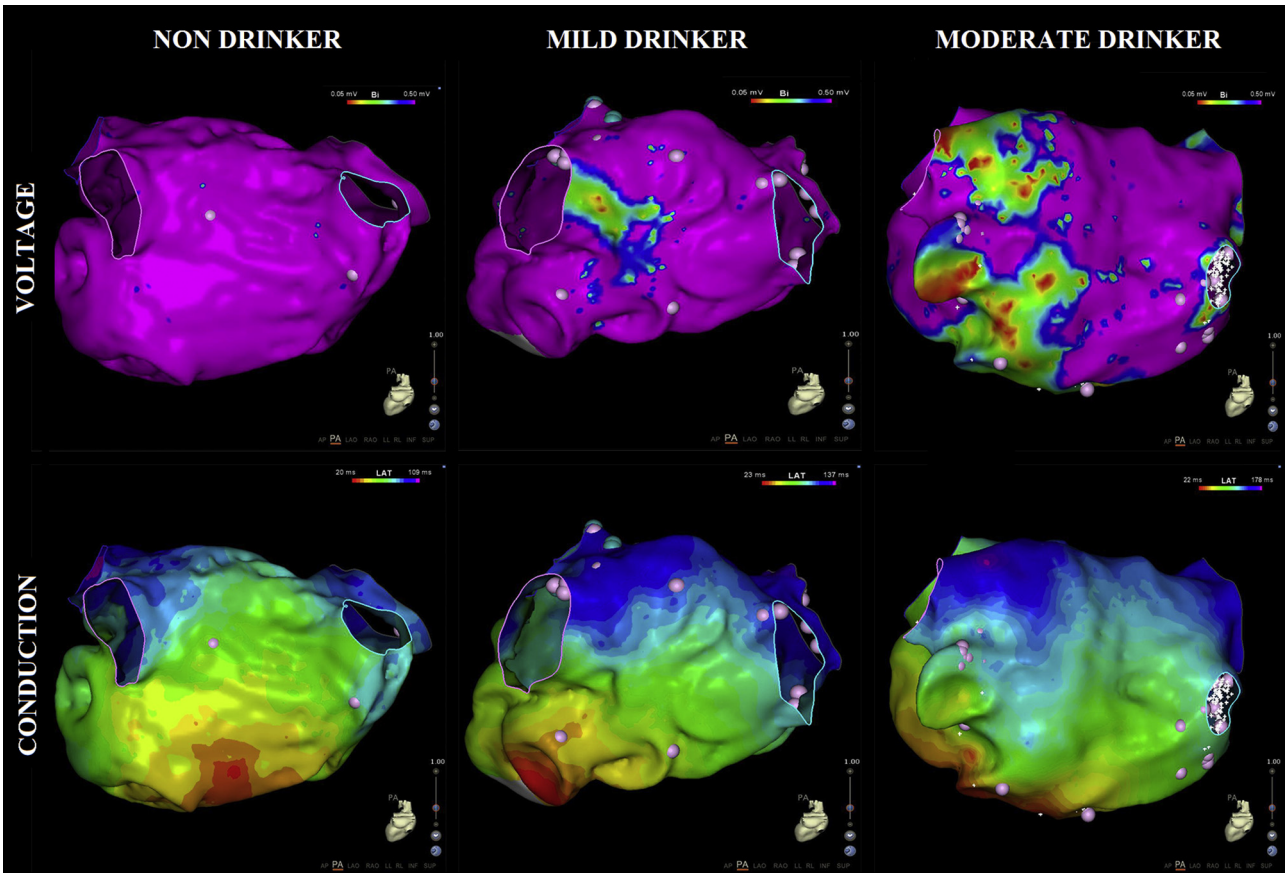

Figure 1 Representative high-density voltage (**top**) and propagation maps (**bottom**) of the posterior left atrium for nondrinkers, mild drinkers, and moderate drinkers.

Mean regional conduction velocity (CV) was calculated by MATLAB using the polynomial surface method. In brief, this method assigns a fitting "window" per region, with a minimum of 20 points required. Each region is assigned subsets of coordinates in space (x, y, z) and activation time. These are fitted to a smooth polynomial surface in 3-dimensional space, using a standard least squares algorithm (Supplemental Figure 1B), which provides robustness against outliers. The gradient is then calculated from the fit and used to calculate velocity components, with final velocities at each point calculated from the weighted average of velocity components from every fit including that point.[9–12] Mean regional CVs from the 6 regions were derived from the average of velocities at each point in the region. Global CV was taken as the average of the 6 mean regional CVs. Investigators were blinded to drinking status during electrogram analysis.

Follow-up

Follow-up after AF ablation included 12-lead electrocardiography at onset of symptoms and during outpatient review at 3 months post discharge and every 6 months thereafter. Holter monitoring was performed at 6 and 12 months or for symptoms. Recurrent AF was defined as any atrial tachyarrhythmia lasting ≥30 seconds.

Statistical analysis

Continuous data are summarized as mean ± SD or median, where appropriate. The Shapiro–Wilk test was performed to confirm normal distribution of data, and the Student *t* test was performed for comparisons of 2 variables, with analysis of variance test used for 3 variables. The Mann–Whitney *U* test was used for continuous variables when normal distribution was not present. Clinical characteristics expressed as categorical variables were compared using the χ^2 or Fisher exact test. Multiple linear regression was performed to identify multivariate predictors of low voltage, CV, and complex signals, with each of these used as a continuous dependent variable. Clinical parameters with univariate $P < .15$ were included in multivariate analysis. Logistic regression was used to identify electrophysiological predictors of postablation recurrence. The Statistical Package for the Social Sciences for Windows version 23 (IBM Corp, Armonk, NY) was used to perform data analysis. $P < .05$ were considered significant.

Results

Patient characteristics

Before AF ablation, 75 patients (69% male; mean age 58.7 ± 9.1 years; median CHA_2DS_2-VASc score 1) underwent high-density LA mapping during CS pacing. There were 25 lifelong nondrinkers, 25 mild drinkers (4.4 ± 2.3

drinks/week), and 25 moderate drinkers (14.0 ± 4.2 drinks/week). Representative voltage and propagation maps for the 3 groups are shown in Figure 1.

Baseline characteristics for all 3 groups are listed in Table 1. The 3 groups had a similar profile with respect to age, gender, AF phenotype, and medical comorbidities. Moderate drinkers had significantly larger LA size than nondrinkers (28.0 ± 4.7 cm^2 vs 22.7 ± 3.8 cm^2; P = .008).

Electroanatomic mapping

Mean global LA voltage, global CV, and % complex potentials are shown in Figures 2, 3A, and 3B, respectively. Mean mapping time was 15 ± 5 minutes, with 1016 ± 445 points collected per patient after filtering and manual annotation. There was no significant difference in the number of points between groups (P = .71) or in point density between groups (average point density for nondrinkers 7.2 points/cm^2 vs mild drinkers 8.1 points/cm^2 vs moderate drinkers 5.9 points/cm^2; P = .46).

Atrial voltage

Moderate drinkers had significantly lower mean global bipolar voltages (1.53 ± 0.62 mV) compared with nondrinkers (1.89 ± 0.45 mV; P = .02) (Figure 2). However, mean global bipolar voltages did not significantly differ between mild drinkers (1.77 ± 0.51mV; P = .41) and nondrinkers. There was a significantly greater proportion of low-voltage electrograms in moderate drinkers (30.6% ± 24.3%; P = .02) but not mild drinkers (23.2% ± 15.1%; P = .12) compared with nondrinkers (18.0% ± 6.9%). Scar (% points with bipolar voltage <0.1 mV) was more prevalent in moderate drinkers (3.2% ± 4.9%) compared with mild drinkers (2.4% ± 2.2%) and nondrinkers (1.6% ± 1.8%), although this was nonsignificant (P = .23).

Regional differences in mean voltage and % low-voltage regions are shown in Figures 4A and 4B, respectively. Of note, mild drinkers had significantly lower mean voltages in the septal region compared with nondrinkers (1.3 ± 0.4 mV vs 1.6 ± 0.6 mV; P = .03), whereas there were no significant differences in other regions. Mild drinkers also had significantly more areas of low voltage in the septal (20.7% ± 13.5% vs 31.5% ± 17.3%; P = .02) and lateral regions (38.4% ± 27.7% vs 24.8% ± 17.2%; P = .046) compared to lifelong nondrinkers.

Univariate and multivariate clinical predictors of low global voltage are listed in Table 2. In addition to age and gender, moderate alcohol consumption (8–21 drinks/week), but not mild consumption, was a significant multivariate predictor of atrial low voltage (P = .04). Overall, women had lower mean global voltage (1.56 ± 0.27 mV vs 1.80 ± 0.62 mV; P = .04) and no significant difference in CV compared to men (34.9 ± 11.9 cm/s vs 41.1 ± 13.8 cm/s; P = .10).

Atrial conduction

Moderate drinkers had significantly slower CV (33.5 ± 14.4 cm/s vs 41.7 ± 12.1 cm/s; P = .04) and a higher proportion of complex potentials (7.8% ± 4.7% vs 4.5% ± 2.7%; P = .004) compared to nondrinkers (Figures 3A and 3B, respectively). These % complex potentials encompassed CFAEs (moderate drinkers 5.7% ± 3.2% vs nondrinkers 3.6% ± 2.4%; P = .02) and double potentials

Table 1 Baseline characteristics

Parameter	Nondrinkers (n = 25)	Mild drinkers (n = 25)	Moderate drinkers (n = 25)	*P* value
Age (y)	57 ± 9	58 ± 10	62 ± 7	.29
Female gender	7 (28)	10 (40)	6 (24)	.58
Hypertension	7 (28)	7 (28)	9 (36)	.65
Diabetes mellitus	1 (4)	1 (4)	1 (4)	1
Dyslipidemia	9 (36)	6 (24)	5 (20)	.36
TIA/stroke	2 (8)	0 (0)	2 (8)	.36
CHA_2DS_2-VASc score	1.0 ± 1.2	1.0 ± 0.9	1.2 ± 1.2	.87
Paroxysmal AF	12 (48)	14 (56)	11 (44)	.70
Cardioversion to SR before mapping	7 (28)	5 (20)	7 (28)	.64
Time since AF diagnosis (months)	57 ± 54	54 ± 48	72 ± 66	.56
Ethnicity (Anglo-Saxon)	22 (88)	24 (96)	23 (92)	.59
Weight (kg)	88 ± 14	89 ± 12	92 ± 14	.61
Body mass index (kg/m^2)	29 ± 4	29 ± 3	30 ± 7	.59
Antiarrhythmic therapy	19 (76)	17 (68)	15 (60)	.19
Flecainide	9 (36)	6 (24)	4 (16)	
Sotalol	7 (28)	9 (36)	9 (36)	
Amiodarone	3 (12)	2 (8)	2 (8)	
Alcohol intake (standard drinks/week)	0	4.4 ± 2.3	14.0 ± 4.2	<.001
Echocardiographic parameters				
LVEF (%)	56 ± 3	58 ± 5	57 ± 5	.45
LVEDD (mm)	50 ± 5	51 ± 5	50 ± 4	.90
LA area (cm^2)	22.7 ± 3.8	24.7 ± 4.9	28.0 ± 4.7	.008

Values are given as mean ± SD or n (%) unless otherwise indicated.

AF = atrial fibrillation; LA = left atrium; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; SR = sinus rhythm; TIA = transient ischemic attack.

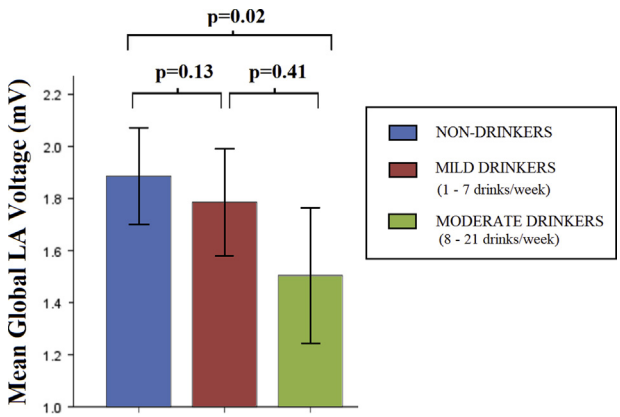

Figure 2 Mean global left atrial (LA) voltage by alcohol consumption category.

(2.1% ± 2.5% vs 0.9% ± 0.9%; $P = .05$). The proportion of complex potentials was significantly greater in mild drinkers (6.6% ± 4.6%) compared with nondrinkers (4.5% ± 2.7%; $P = .047$). There was no significant difference in mean CV between mild drinkers and nondrinkers.

Regional analysis of CV and % complex potentials is shown in Figures 5A and 5B, respectively. Moderate alcohol consumption was associated with reductions in regional tissue voltage, which reached statistical significance in the anterior (30.8 ± 18.5 cm/s vs 45.6 ± 25.2 cm/s; $P = .04$) and superior regions (33.6 ± 21.0 cm/s vs 55.1 ± 25.1 cm/s; $P = .003$) compared to nondrinkers. The anterior region was also the most common site for observed differences in complex potentials (moderate drinkers 7.8 ± 9.2 vs nondrinkers 2.7 ± 3.5; $P = .01$), particularly CFAE (6.4 ± 7.4 vs 2.4 ± 3.2; $P = .03$). Regional differences in % CFAEs and % double potentials are shown in Supplemental Figure 2.

A modest positive correlation was observed between mean bipolar voltage and CV in 5 of 6 regions: anterior (r = 0.44; $P < .001$), posterior (r = 0.43; $P < .001$), superior (r = 0.43; $P < .001$), inferior (r = 0.38; $P = .001$), septal (r = 0.35; $P = .004$), and lateral (r = 0.07; $P = .55$). Analyses for independent predictors of atrial conduction abnormalities are given in Table 3. Significant univariate predictors of conduction slowing were female gender ($P = .05$), moderate alcohol consumption ($P = .01$), and antiarrhythmic therapy ($P = .04$); however, only moderate alcohol consumption ($P = .01$) and female gender ($P = .03$) were multivariate predictors. Univariate predictors of complex signals (CFAE and double potentials) were persistent AF ($P = .01$), AF duration ($P = .05$), and moderate alcohol consumption ($P = .04$), but only AF duration was a significant multivariate predictor ($P = .02$). Mild alcohol consumption did not predict low voltage, conduction slowing, or presence complex signals on univariate or multivariate analysis ($P > .05$).

Follow-up

After 18.7 ± 5.4 months of follow-up from initial AF ablation, 28 of 75 patients (37%) developed recurrent AF, and 9 of 75 (12%) underwent repeat ablation. Logistic regression was performed to determine univariate electrophysiological predictors of recurrence after AF ablation. Lower mean global voltage (odds ratio [OR] 0.30; 95% confidence interval [CI] 0.11–0.83), higher proportion of low-voltage (<0.5 mV) electrograms (OR 1.05; 95% CI 1.01–1.10), and % complex potentials (OR 1.16; 95% CI 1.03–1.31) were all significant predictors of outcome. Mean global CV (OR 0.98; 95% CI 0.95–1.02), % double potentials (OR 1.22; 95% CI 0.97–1.54), and % CFAE (OR 1.15; 95% 0.99–1.35) did not reach significance.

Discussion

This cross-sectional study of patients with a history of AF and relatively low prevalence of other comorbidities reports the electrical and structural changes in the atrium associated with long-term alcohol consumption. The key findings are as follows.

1. Regular moderate drinkers (average ~14 drinks/week) had significantly lower global atrial voltage, proportion of low voltage, and slower CVs.

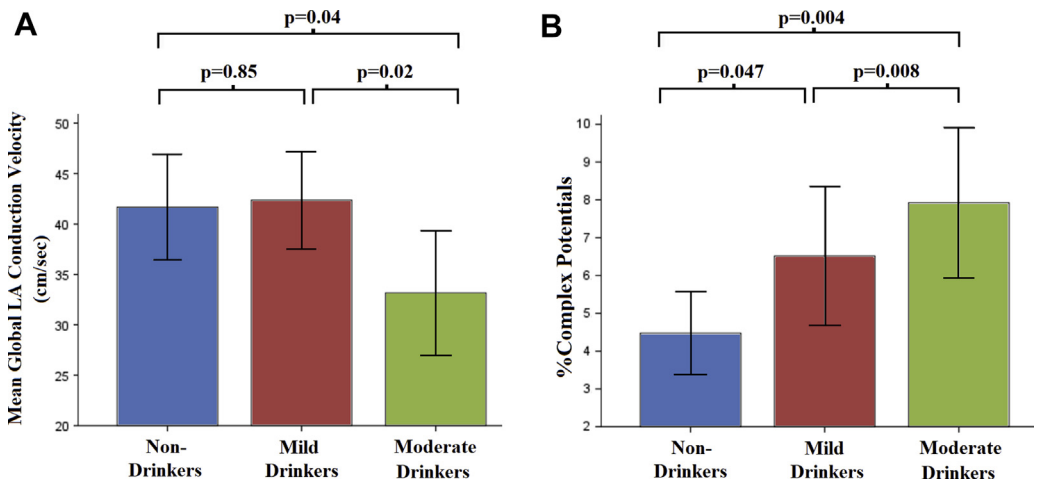

Figure 3 **A:** Mean global left atrial (LA) conduction velocity. **B:** Global % complex potentials by alcohol consumption category.

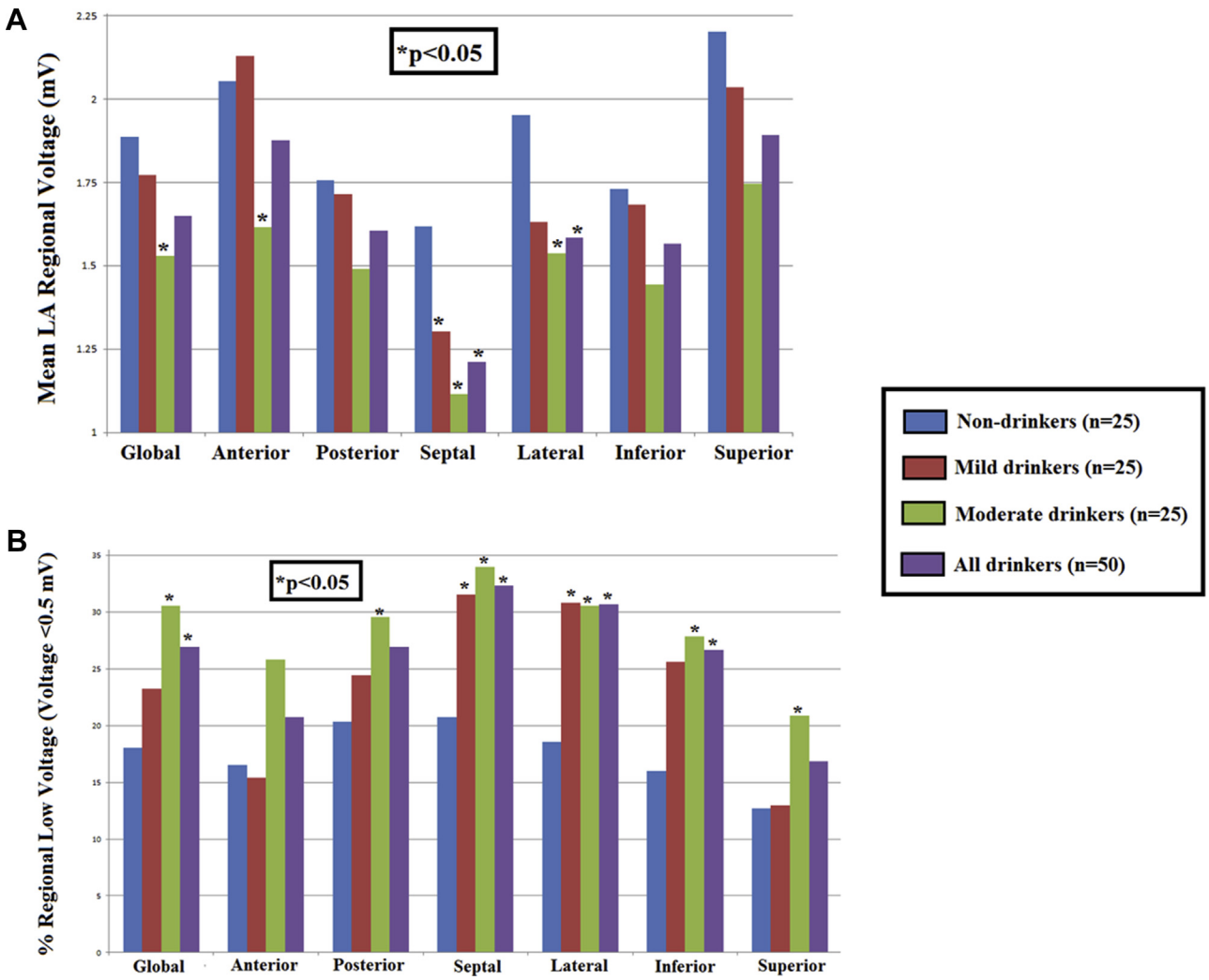

Figure 4 **A:** Regional mean voltage distribution. **B**: Regional % low-voltage regions by alcohol consumption category. *P <.05 for comparisons with non-drinkers.

2. Moderate alcohol consumption, together with older age and female gender, was a stronger multivariate predictor of lower voltage than other AF risk factors, such as obesity and hypertension.
3. Milder drinkers (≤7 drinks/week) did not demonstrate significant differences in global voltage and CVs compared with nondrinkers, suggesting a safe threshold for alcohol consumption.

Table 2 Multivariate predictors of low global voltage

		Multivariate analysis			
Parameter	Univariate *P* value	Standardized β coefficient	95% CI for β	*t*	*P* value
Age	.001	−0.348	(−0.037, −0.008)	−3.059	.003
Gender	.02	−0.251	(−0.522, −0.030)	−2.247	.03
Moderate ETOH*	.02	−0.230	(−0.526, −0.001)	−2.013	.04
AF duration	.07	−0.168	(−0.004, 0.001)	−1.507	.14
Hypertension	.14	−0.034	(−0.287, 0.212)	−0.303	.76
AF type	.23	—			
Mild ETOH*	.51	—			
Body mass index	.90	—			
Dyslipidemia	.91	—			
AAD therapy	.95	—			
Diabetes	.98	—			

AAD = antiarrhythmic drug; AF = atrial fibrillation; CI = confidence interval; ETOH = alcohol.
*Compared with all other groups.

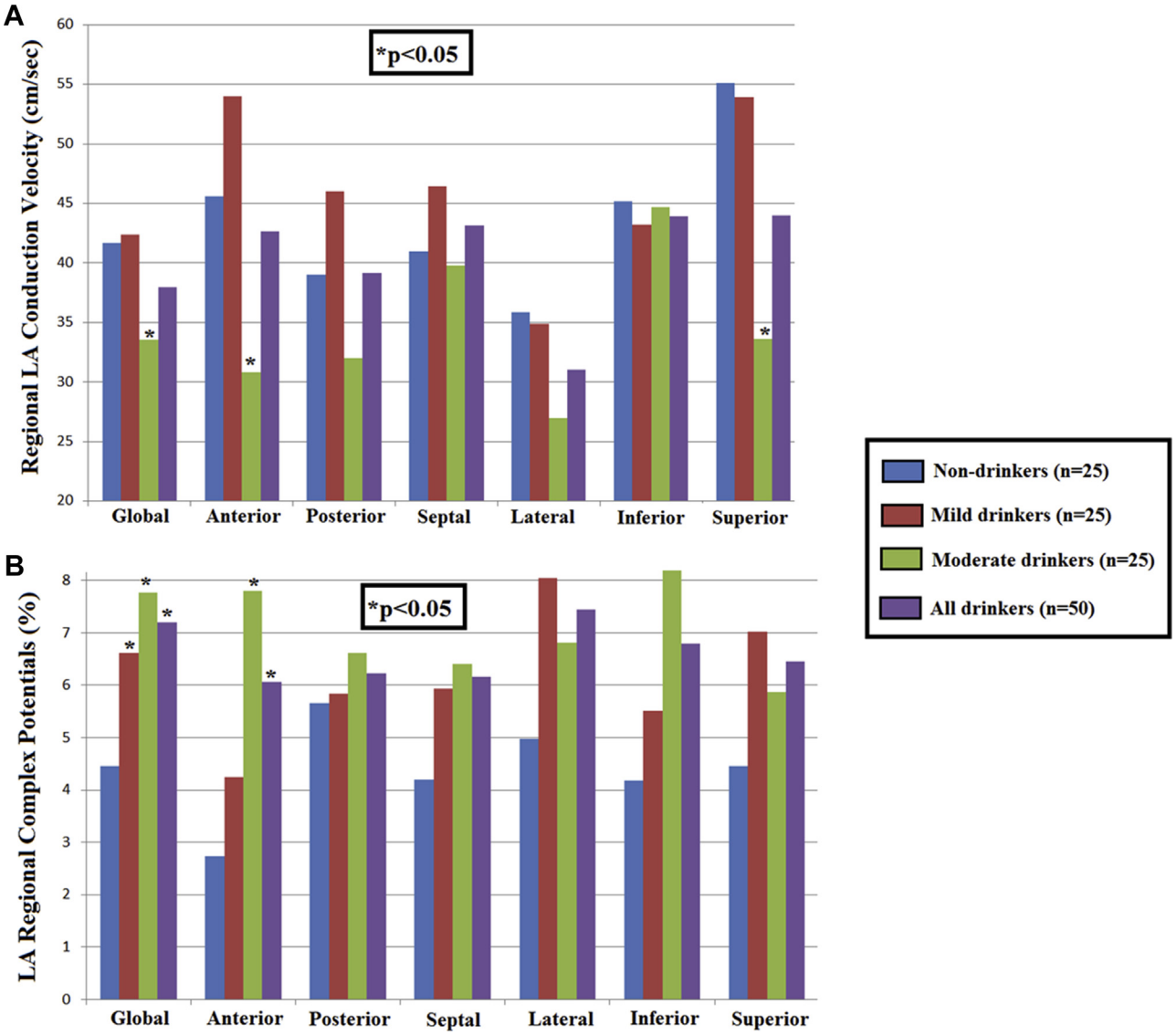

Figure 5 **A:** Regional mean conduction velocity distribution. **B:** Regional % complex potentials by alcohol consumption category. *P <.05 for comparisons with nondrinkers.

Alcohol and AF

Attention to lifestyle has emerged as an important aspect of AF management. Whereas many studies have focused on weight loss,[13] fewer data exist on the impact of regular alcohol consumption, which is ubiquitous in Western culture. Although binge drinking is a well-recognized AF precipitant,[14] habitual consumption even at low to moderate levels may represent an important modifiable risk factor. The majority of middle-aged American adults diagnosed with AF for the first time consume alcohol at mild to moderate levels.[15] In fact, meta-analyses report as few as 1 drink per day is associated with heightened AF risk.[5,16] The mechanisms by which alcohol consumption causes myocardial injury include alterations in sodium and calcium current densities,[17] oxidative stress,[18] apoptosis,[19] inflammation, mitochondrial dysfunction, accelerated protein degradation, and abnormal fatty acid metabolism.[20]

Although it is well described that self-reported consumption underestimates true intake,[21] the present study supports this "relatively low" cutoff as the threshold for potential alcohol-related atrial toxicity. Significant electrophysiological and structural changes in atrial substrate were demonstrated in patients consuming 8–21 drinks/week. Atrial remodeling was not significantly different for most indices in those consuming 1–7 drinks/week compared to nondrinkers, which may support a potentially *safe* threshold for alcohol consumption in the AF population, although this is speculative.

Alcohol and atrial substrate

The presence of low voltage with the electrophysiological sequelae of conduction slowing and fractionation has been shown to correlate with histologic fibrosis[22] and late gadolinium enhancement on cardiac magnetic resonance imaging.[23]

Table 3 Multivariate predictors of atrial conduction abnormalities

Parameter	Univariate *P* value	Multivariate analysis			
		Standardized β coefficient	95% CI for β	*t*	*P* value
Conduction velocity					
Gender	.05	−0.290	(−14.237,−1.203)	−2.377	.02
Moderate ETOH*	.01	−0.281	(−15.571,−0.054)	−2.021	.04
AF duration	.09	−0.174	(−0.094,0.015)	−0.174	.16
AAD therapy	.04	0.134	(−2.904,9.710)	1.083	.28
Mild ETOH*	.14	0.113	(−4.219,10.240)	0.836	.41
Age	.39	—			
Dyslipidemia	.41	—			
Body mass index	.70	—			
Hypertension	.77	—			
AF type	.94	—			
Diabetes	.95	—			
Percent complex signals					
AF duration	.05	0.341	(0.002, 0.026)	2.385	.02
AF type	.01	−0.260	(−2.543, 0.146)	−1.802	.08
Hypertension	.06	0.100	(−0.880, 1.842)	0.715	.48
Moderate ETOH*	.04	0.020	(−1.448, 1.663)	0.139	.89
Body mass index	.11	—			
Dyslipidemia	.18	—			
Gender	.35	—			
AAD therapy	.43	—			
Mild ETOH*	.62				
Diabetes	.64	—			
Age	.98	—			

Abbreviations as in Table 2.
*Compared with all other groups.

These findings have important implications for prognosis. Verma et al[24] demonstrated a significant increase in recurrent AF after catheter ablation in patients with preexistent LA scarring. In 122 patients undergoing ablation for paroxysmal AF, lifelong nondrinkers had the highest success rates (81%), followed by "moderate" drinkers consuming 1–14 drinks/week for men and 1–7 drinks/week for women (69%), then heavy drinkers (35%).[7] Our findings provide insights into the pathophysiological mechanism responsible for this clinical observation. Excessive alcohol consumption may also be an underappreciated factor resulting in AF progression. In a large cohort study, moderate to heavy alcohol consumption portended a 3-fold higher risk for progression from paroxysmal to persistent AF, whereas more "traditional" risk factors such obesity, hypertension, and diabetes did not reach significance.[25] Regular alcohol consumption is associated with an increase in atrial size independent of AF burden. Our group recently reported progressive impairment in LA mechanical function on cardiac magnetic resonance imaging with increasing alcohol intake,[26] supporting the results of earlier echocardiographic studies.[8] Subtle abnormalities in echocardiographic LA strain have been reported with as few as 1–6 drinks/week.[27]

The presence of LA fibrosis is independently associated with heightened risk of stroke and transient ischemic attack.[28] Recent cohort studies have highlighted the association between excessive alcohol intake and risk of stroke in the AF population.[29] In the present study, lower atrial voltages and conduction slowing demonstrated in moderate drinkers may result in atrial myopathy and impaired LA appendage emptying velocities, which may in part explain this clinical observation.[30]

Study limitations

One of the major limitations of our CV calculation methodology is that it assumes that wavefront propagation is restricted to the endocardial surface and does not include epicardial mapping. We assume that the tissue between mapped points is both structurally and electrically homogeneous. In particular, we have not taken into account the effects of transmural conduction or the effects of structural and functional heterogeneities that exist in a 3-dimensional atrial substrate in the calculation of CVs. Although pacing from the CS enabled a stable and reproducible reference, we acknowledge that wavefront propagation in regions furthest away from the pacing site are less uniform than regions in closer proximity, such as the posterior wall.

Because of the observational study design, there is the possibility for confounding due to unmeasured factors, such as sleep disordered breathing and medication compliance. The relatively small sample size may be underpowered to detect more subtle differences in atrial substrate and ablation outcomes between nondrinkers and mild drinkers. The categorization of alcohol consumption into mild vs moderate was determined by patient reporting and may be unreliable, although the observed biological dose–response effect was

consistent. The findings in the present study are confined to patients with a history of AF undergoing ablation and does not necessarily address the relationship between alcohol consumption and incident AF in the general population. Although the present study demonstrates an association between increasing amounts of alcohol consumption and atrial substrate, further studies are needed to determine the impact of abstinence from alcohol on AF burden and whether reverse remodeling occurs.

Conclusion

Regular moderate alcohol consumption, but not mild consumption, is associated with lower atrial voltage and conduction slowing. These electrical and structural changes may in part explain the propensity to AF in regular drinkers and may represent an important modifiable risk factor for AF.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2018.10.041.

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