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Impact of Alcohol Consumption on Atrial Fibrillation Outcomes Following Pulmonary Vein Isolation

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Abstract

Moderate to heavy alcohol use has been shown to be associated with increased atrial fibrillation (AF) incidence. However, the relationship between alcohol use and AF recurrence after pulmonary vein isolation (PVI) is not well known.We sought to study the impact of different alcohol consumption levels on outcomes after AF ablation.A retrospective analysis was performed of 226 consecutive patients undergoing first time PVI for AF. Clinical data were collected including alcohol intake classified into 3 groups: none-rare (< 1 drink/ week), moderate (1-7 drinks/ week), and heavy (> 7 drinks/ week). Patients were followed for recurrences within the first 3 months (blanking period; early recurrence) and after 3 months up to 1 year (late recurrence) after the ablation. Paroxysmal and persistent AF had early recurrence rates of 29.1% and 32.2%, and late recurrence rates of 30.2% and 44.1%, respectively. The none-rare alcohol group had a higher frequency of diabetes mellitus (p=0.007). Neither moderate or heavy alcohol consumption, in reference to the none-rare group, was significantly predictive of early or late AF recurrence on adjusted multivariate logistic regression analysis (p>0.05).Despite known associations between alcohol and incidence of AF, alcohol consumption is not associated with early or late AF recurrence after PVI in this cohort.

Introduction

Alcohol consumption in moderation has been reported to have beneficial cardiovascular protective effect.[1], [2] Recent evidence continues to emerge on the physiologic and genetic mechanisms through which alcohol may reduce the risk of developing CVD.[3] Nonetheless, alcohol intake has been implicated with an increased incidence of atrial fibrillation.[4] The heart holiday syndrome, in fact, was first described in 1978 by Ettinger et al and linked to binge alcohol drinking behavior preceding AF occurrence.[5] Incidence of AF is also elevated in chronic levels of modest alcohol intake.[6]Abstinence from alcohol remains the optimal management of alcohol related heart disease including atrial fibrillation.[7]

Catheter ablation has become the mainstay of therapy in many symptomatic patients with atrial fibrillation. In addition, long-term control of AF requires modification of risk factors and management of associated comorbidities.[8], [9] Identifying predictors of AF recurrence after catheter ablation could help focus the management of these potential risk factors and better select patients who would likely have favorable outcomes. A recent study has shown that alcohol consumption may be an independent predictor of paroxysmal AF (PAF) recurrence after catheter ablation,[10] but the study was small and did not include persistent AF patients. In this study, we further explore the association of different alcohol consumption levels with early and late recurrence rates of AF (both paroxysmal and persistent) and AF-free survival after pulmonary vein isolation by catheter ablation.

Key Words

alcohol; arrhythmia, atrial fibrillation; catheter ablation; pulmonary vein isolation; recurrence.

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Methods

Study Subjects

This study was approved by the Institutional Review Board at the University of Colorado. In this retrospective observational study, we reviewed the medical records of 226 consecutive patients who underwent first-time PVI for symptomatic, non-valvular AF from January 2011 to April 2014 at the University of Colorado ([Figure 1]). Patient baseline characteristics and clinical data were collected. AF with self-terminated episodes within seven days prior to the catheter ablation procedure was defined as paroxysmal AF (PAF). AF that continued for more than seven days was defined as persistent AF (PsAF). Only patients who had a history taken regarding alcohol use were included in the study. Alcohol consumption habits were classified into three groups: none-rare (<1 drink per week), moderate (1-7 drinks per week), and heavy (>7 drinks per week). One drink was defined as 6 fl. oz. of alcohol. Patient data was de-identified.

Ablation Procedure

All patients underwent pulmonary vein isolation. Entrance and exit block was assessed for all veins. PAF patients underwent PVI alone; some PAF patients had additional cavotricuspid isthmus

(CTI) ablation only if clinically indicated (inducible or history of typical CTI dependent flutter). In persistent AF (PsAF) patients, at the discretion of the operator, patients underwent PVI alone or PVI with additional linear, complex fractionated atrial electrograms (CFAE), and/or non-PV trigger ablation.

Post-ablation Management and Follow up

Patients were followed monthly for the first 3 months and then every 3-6 months thereafter. All asymptomatic patients had 12 lead electrocardiograms at 1, 3, 6 and 12 months after the ablation procedure. Patients with symptoms suggestive of AF recurrence had new 12-lead electrocardiograms and/or ambulatory monitoring. AF recurrence was defined as the presence of evident tachyarrhythmia on 12-lead electrocardiogram or atrial arrhythmia lasting for 30 seconds or more on ambulatory cardiac monitor. AF recurrences were considered separately in the first 3 months (early period or blanking period) and after 3 months (late period) following catheter ablation. AF-free survival time was defined as the number of days from the date of catheter ablation to the first documented AF recurrence in the pertinent follow up period (early or late).

Statistical Analysis

on ECG All data were analyzed using SPSS software version 22.0. Normality of continuous variables was tested using Shapiro-Wilkins test. Continuous variables following Bayesian normal distribution were presented as mean ± SD and analyzed using unpaired t-test of independent samples. Continuous variables not following normal distribution were presented as median (25th to 75th interquartile range) and compared using Mann-Whitney U test. Categorical variables were tested using Fisher's exact test. Univariate logistic regression analysis was performed to test each individual potential variable for the prediction of early or late AF recurrence. Variables that have p<0.2 were entered in a multivariable logistic regression analysis to test the independence of AF recurrence prediction. A Kaplan-Meier estimation with a log-rank test was performed comparing the study groups. All probability values were 2-sided, and a P of <0.05 was considered significant.

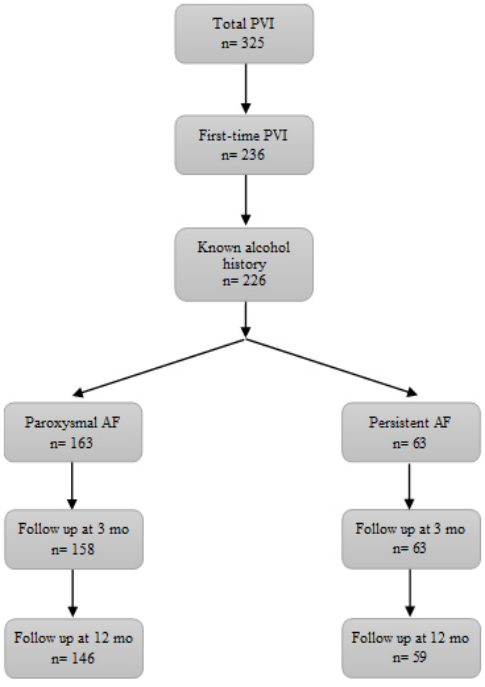

Figure 1: **Schematic diagram of the study population. Patients who underwent PVI for the first time and had documented alcohol consumption levels were included. Patients who were lost to follow up were excluded from subsequent analyses.**

Results

Patient Population and Ablation Procedure

Two hundred twenty six consecutive patients with symptomatic, non-valvular AF underwent their first PVI in the period of January 2011 to April 2014. Baseline characteristics of patients in each group are summarized in [Table 1]. The only significant difference was the higher prevalence of diabetes mellitus in the none-rare alcohol group. For all patients, mean age was 62.1 +/- 9.9 years (range 31-84, median=63 years) and 153 (67.7%) were men. PAF was present in 163 (72.1%) patients. The prevalence of PAF was higher as the level of alcohol consumption increased; however, this was not statistically significant among the alcohol groups. Mean AF history was 4.1 +/- 4.9 years (range 2 months to 46 years). Most patients (56.2%) had one drug failure history while 15.0% had 2 or more drug failures.

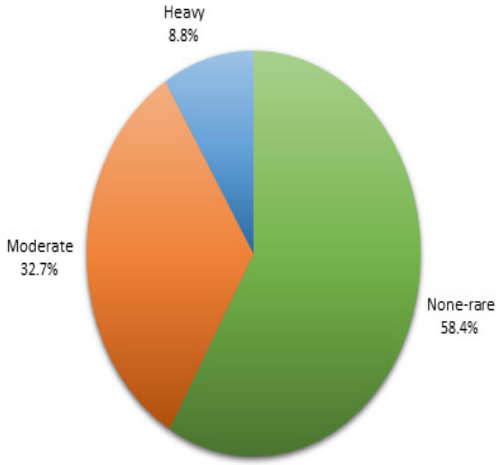

Figure 2: **Distribution of study population (patients undergoing first time PVI) demonstrated by alcohol consumption levels**

All of the patients were undergoing PVI for the first time; however, prior catheter ablation had been performed in 23 patients for atrial flutter (AFL), 1 for AVNRT and 2 for VT. Eleven patients had a history of sick sinus syndrome. Pacemakers were present in 22 patients (20 dual chamber, 1 single chamber, and 1 biventricular pacemaker). An alcohol use survey on admission showed that the majority of patients, 132 (58.4%), had none to rare (<1 drink per week) alcohol use, while 74 (32.7%) and 20 (8.8%) patients reported moderate (1-7 drink per week) and heavy (>1 drink per week) alcohol use, respectively ([Figure 2]).

Of those presenting for AF ablation, 63 (27.9%) patients had PsAF. PVI was performed using radiofrequency ablation in most patients, except in 9 patients where cryoballoon ablation was used. Additional linear, CFAE and non-PV trigger ablation was performed, in 54.9%, 8.4%, and 10.2% of patients, respectively.

Characteristics of Patients by Alcohol Consumption Levels

Increased alcohol consumption levels are positively correlated with older age, male sex, higher rate of PAF, greater left atrial volume

index (LAVi) and further need of additional linear, CFAE and non-PV trigger ablation ([Table 1]).

Follow up and Outcomes

In the blanking period (0-3 months), 5 PAF patients were lost to follow up. In the following 3-12 month follow up period, an additional 12 PAF patients and 4 PsAF patients were lost to follow up. Early and late recurrence rates were 29.1% and 32.2% in the PAF group, and 30.2% and 44.1% in the PsAF group, respectively. For PAF patients, early recurrence rates were 30.7%, 29.1% and 29.4% (p=1.000) and late recurrence rates were 34.6%, 33.3% and 25.0% (p=0.846) in the none-rare, moderate and heavy alcohol groups, respectively ([Figure 3A]). In PsAF patients, early recurrence rates were 33.3%, 27.8% and 0.0% (p=0.640) and late recurrence rates were 42.9%, 47.1% and 0.0% (p=0.398) in the none-rare, moderate and heavy alcohol groups, respectively ([Figure 3B]). Among those patients who had an early recurrence, 68.4% developed late recurrences. The presence of early recurrence was independently predictive of late recurrence after catheter ablation based on multivariable logistic regression models adjusting for linear ablation, AF type, and DM (OR 7.797, 95% CI 3.815-15.937, p<0.001).

On univariate logistic regression analysis, none of the alcohol groups showed any significant association with early or late AF recurrence ([Table 2]). Among the baseline characteristics, only age and the absence of diabetes mellitus were significantly associated with higher early and late AF recurrence rates, respectively [age (OR 1.032, 95% CI 1.000-1.065, p=0.050) and absence of DM (OR 0.300, 95% CI 0.110-0.818, p=0.019)].

With multivariable regression models, after adjusting for potential confounding covariates, none of the alcohol levels were independently predictive of early or late AF recurrence ([Figure 4]). Paroxysmal AF and the absence of DM were the only two parameters that remained independently predictive of late AF recurrence [PAF (OR 0.410, 95% CI 0.205-0.820, p=0.012) and absence of DM (OR 0.242, 95% CI 0.085-0.688, p=0.008)].

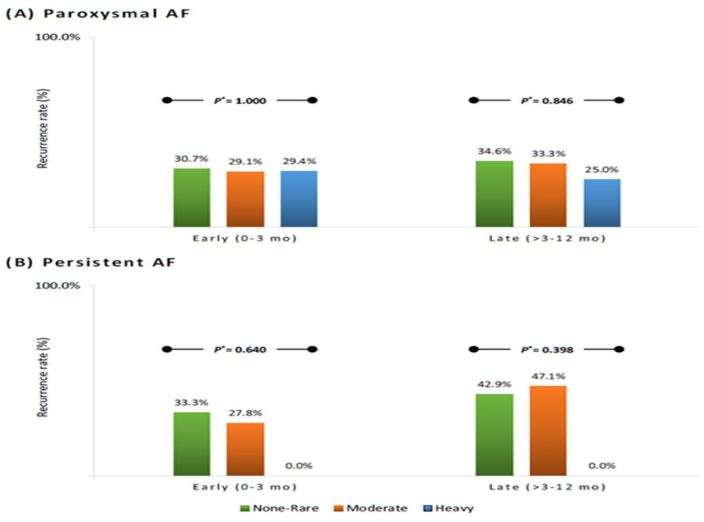

Figure 3: Recurrence rates of PAF (A) and PsAF (B) after catheter ablation in the none-rare, moderate and heavy alcohol consumption groups in the early and late follow up periods. *P value for statistical difference among the three groups of alcohol consumption.

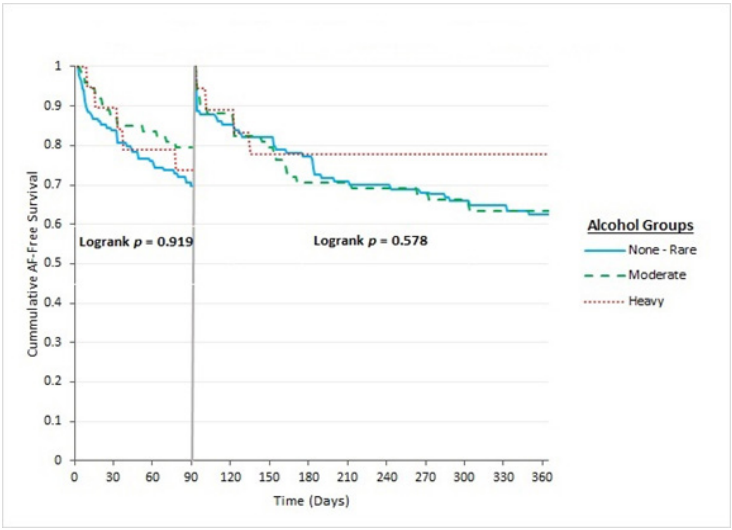

Figure 4: Kaplan-Meier curve demonstrating time to first AF recurrence in early and late follow up periods after catheter ablation according to alcohol consumption groups

Discussion

In this study, we hypothesized that different alcohol consumption levels will have different effects on outcomes after PVI ablation for AF. However, the main finding of our study was that alcohol consumption was not associated with a higher likelihood of early or late AF recurrence in the first year after pulmonary vein isolation by catheter ablation. To the best of our knowledge, this is the first study exploring the impact of alcohol consumption on early and late catheter ablation outcomes of both paroxysmal and persistent atrial fibrillation.

Cutoffs for the 3 levels of alcohol consumption were chosen to better define terms such as none, rare, moderate and heavy that are used in the literature to describe alcohol consumption behavior. Moderate drinking was defined by National Institute on Alcohol Abuse and Alcoholism (NIAAA) as the following: for women, low-risk drinking is no more than 3 drinks on any single day and no more than 7 drinks per week. For men, it is defined as no more than 4 drinks on any single day and no more than 14 drinks per week. Applying this definition to our study would have required further data collection, which is not feasible in a retrospective study. Therefore, we defined moderate drinking, for both men and women, as 1-7 drinks per week to reflect a weekly habit of drinking but not more than daily.

Our main findings are in contrast to a recently published prospective study that shows a significantly lower success rate after catheter ablation in patients with alcohol use, when compared to the abstainer group, and a possible detrimental dose-dependent effect of alcohol consumption on catheter ablation outcomes of PAF.[10] In their 122-patient study, Qiao et al had a predominantly male population, and the authors used the definition of the NIAAA for daily alcohol consumption levels in their study. This is an important distinction since those patients with rare alcohol use, who would have been classified in the none-rare group according to our definition, were actually included under the moderate alcohol group. Despite this, the size of their moderate alcohol group was smaller (10.6% vs. 32.7%), compared to our study. In addition, the size of their heavy alcohol group was larger (32.0% vs. 8.8%).

Table 1: Patient baseline characteristics by alcohol groups

Parameter	None – Rare (n=132)	Moderate (n=74)	Heavy (n=20)	P value
Age, years	61.3 ± 10.7	62.7 ± 9.0	64.3 ± 6.9	0.361
BMI, kg/m2	30.0 ± 6.0	28.8 ± 6.6	28.0 ± 4.9	0.219
Paroxysmal AF, n (%)	89 (67.4%)	56 (75.7%)	17 (90.0%)	0.081
History of EPS or ablation not for AF, n (%)	18 (15.8%)	15 (21.7%)	2 (12.5%)	0.574
AF history duration, years	4.07 ± 4.06	3.99 ± 6.52	4.98 ± 3.74	0.775
HTN, n (%)	79 (59.8%)	35 (47.3%)	12 (60.0%)	0.222
DM, n (%)	28 (21.2%)	4 (5.4%)	3 (15.0%)	0.007
CAD, n (%)	28 (21.2%)	10 (13.5%)	4 (20.0%)	0.397
$CHADS_2$ score	1.4 ± 1.3	1.0 ± 1.0	1.3 ± 0.9	0.060
Number of failed AADs	1.2 ± 0.8	1.1 ± 0.8	1.4 ± 0.9	0.376
Ablation of additional linear ablation, n (%)	71 (53.8%)	40 (54.1%)	13 (65.0%)	0.693
Ablation of additional CFAE, n (%)	11 (8.3%)	6 (8.1%)	2 (10.0%)	0.874
Ablation of additional non-PV trigger, n (%)	10 (7.6%)	9 (12.2%)	4 (20.0%)	0.152
LAVi, ml/m2	31.9 ± 13.3	33.0 ± 18.7	38.7 ± 15.0	0.302
LVEF ≥ 50%, n (%)	98 (89.9%)	64 (94.1%)	15 (93.8%)	0.724
LVEF 41 – 49%, n (%)	6 (5.5%)	3 (4.4%)	1 (6.3%)	0.894
LVEF 36 – 40%, n (%)	1 (0.9%)	1 (1.5%)	0 (0.0%)	1.000
LVEF ≤ 35%, n (%)	4 (3.7%)	0 (0.0%)	0 (0.0%)	0.392
Early AF recurrence, n (%)	39 (30.2%)	21 (28.8%)	5 (26.3%)	0.974
Late AF recurrence, n (%)	44 (37.0%)	25 (36.8%)	4 (22.2%)	0.500

BMI: body mass index; EP: electrophysiology study; AF: atrial fibrillation; HTN: hypertension; DM: diabetes mellitus; CAD: coronary artery disease; $CHADS_2$ score: congestive heart failure, hypertension, age, DM, stroke/transient ischemic attack score for the thromboembolic risk assessment; AADs: antiarrhythmic drugs; CFAE: ablation of complex fractionated atrial electrograms; PV: pulmonary vein; LAVi: left atrial volume index; LVEF: left ventricular ejection fraction

Alcohol Consumption and Risk of Atrial Fibrillation

There is a considerable volume of evidence today to support the observations linking alcohol consumption patterns and levels to cardiovascular effects, including higher incidence of atrial fibrillation. Alcohol-induced cardiac dysrhythmias are supported by several studies demonstrating various electrophysiologic alterations of the cardiac substrate. Since its description in 1978, the "holiday heart" has shed light on the association of alcohol and cardiac dysrhythmias, specifically atrial fibrillation.[5] Although the pathogenesis of (acute) alcohol-induced dysrhythmias remains poorly delineated, direct and indirect effects on heart rhythm disturbances are implicated.[11]-[16]

Chronic alcohol drinking, especially, has been associated with increased risk of AF even with a lack of alcoholic cardiomyopathy.[17], [18] Several pathologic mechanisms and electrophysiologic changes of the underlying cardiac substrate have been described.[19]-[25] Furthermore, chronic alcohol can be associated with other traditional risk factors, such as hypertension, and promote atrial fibrosis and subsequently AF.[26]

Conflicting Evidence Regarding Alcohol Consumption and Atrial Fibrillation

Several studies have shown a deleterious relationship between the increased daily amount of consumed alcohol and the incidence of AF.[27]-[29] Although there is a significant amount of research showing the relationship of binge alcohol drinking and holiday heart syndrome, the relationship for a full range of alcohol consumption with the risk of AF is less certain.[30],[31] A large number of studies have reported that ethanol intake, of various amounts, was not associated with occurrences of AF.[11], [17], [32] In addition, a recent analysis from the Framingham study did not observe a link between alcohol consumption and AF.[33]

The prevalence of moderate-heavy alcohol drinking in this study population is high (41.6%). The lack of association that we have found between alcohol consumption groups and AF recurrence after ablation adds further understanding to this complex relationship between alcohol consumption and incidence of AF. Nevertheless, the influence of alcohol on cardiovascular health, and specifically AF, remains an area of active debate and research.

Catheter Ablation of Atrial Fibrillation in Alcohol Consuming Patients

With increasing advanced therapies for AF, namely catheter ablation, assessing ablation success rates after these procedures is critical for patients, institutions and physicians. Though the outcomes of these procedures are becoming more promising, the success rates are still below what medical providers and patients hope them to be. Several factors can influence procedural success rates including, but not limited to, patient selection, operator-dependent and procedure-related factors, current technology, ablation lesion durability and the underlying AF pathophysiology. As several risk factors have been linked to the incidence of atrial fibrillation, risk factor modification

Table 2: Univariate logistic regression analysis of early and late AF recurrence by patient characteristics

Parameter	0 – 3 month			3- 12 month		
	OR*	95% CI	P value	OR*	95% CI	P value
Age	1.032	1.000–1.065	0.050	1.019	0.989–1.050	0.223
Sex (female)	0.889	0.477–1.658	0.711	1.319	0.718–2.422	0.372
BMI	1.036	0.990–1.085	0.129	1.020	0.973–1.069	0.418
AF type (PAF vs. PsAF)	0.951	0.502–1.801	0.878	0.603	0.324–1.120	0.109
AF history duration	1.030	0.969–1.094	0.344	1.032	0.957–1.114	0.414
HTN (presence vs. absence)	1.010	0.565–1.808	0.972	0.851	0.480–1.510	0.581
DM (presence vs. absence)	0.842	0.370–1.919	0.683	0.300	0.110–0.818	0.019
CAD (presence vs. absence)	0.544	0.236–1.255	0.153	1.027	0.485–2.173	0.945
CHADS2 score	1.062	0.840–1.343	0.617	0.965	0.782–1.267	0.969
Number of failed AADs	1.036	0.717–1.497	0.849	1.006	0.699–1.447	0.976
Alcohol use	71 (53.8%) 11 (8.3%) 10 (7.6%)		40 (54.1%) 6 (8.1%) 9 (12.2%)	13 (65.0%) 2 (10.0%) 4 (20.0%)		0.693 0.874 0.152
Additional (presence): Linear ablation CFAE ablation Non-PV trigger	 0.818 2.346 1.319	 0.458–1.461 0.906–6.078 0.530–3.283	 0.497 0.079 0.551	 0.679 1.682 1.127	 0.382–1.205 0.620–4.566 0.444–2.859	 0.186 0.307 0.802
LAVi	0.983	0.955–1.011	0.224	1.004	0.980–1.029	0.723
LVEF ≥ 50%, n (%) LVEF 41 – 49%, n (%) LVEF 36 – 40%, n (%) LVEF ≤ 35%, n (%)	1.883 0.575 – 0.767	0.515–6.881 0.118–2.801 –... 0.078–7.547	0.339 0.494 – 0.820	1.196 1.115 – 0.836	0.390–3.664 0.302–4.108 – 0.074–9.415	0.754 0.870 – 0.885
Early AF recurrence (presence)				7.265	3.691–14.299	<0.001

BMI: body mass index; PAF: paroxysmal AF; PsAF: persistent AF; EP: electrophysiology; AF: 379 atrial fibrillation; HTN: hypertension; DM: diabetes mellitus; CAD: coronary artery disease; 380 $CHADS_2$ score: congestive heart failure, HTN, age, DM, stroke/transient ischemic attack score 381 for the thromboembolic risk assessment; AADs: antiarrhythmic drugs; CFAE: ablation of 382 complex fractionated atrial electrograms; PV: pulmonary vein; LAVi: left atrial volume index; 383 LVEF: left ventricular ejection fraction. *OR refers to odds ratio of recurrence of AF versus 384 remaining in sinus rhythm after catheter ablation.

was shown to significantly help manage AF and reduce its recurrence, with or without catheter ablation. Risk reduction after catheter ablation may potentially boost the chances of AF-free survival and greatly reduce the costs associated with recurrences after these procedures. However, from our study, it does not appear that alcohol consumption is a major risk factor after ablation that can be altered to reduce recurrences.

Limitations

This is an observational retrospective study that investigates the relationship of alcohol consumption behavior reported at the time of the ablation procedure with early and late recurrence following the ablation procedure. Alcohol consumption in the follow up period was not tracked. Hence, we are assuming that the patients' alcohol consumption patterns remain the same in the follow up period after their ablation. The number of patients in the heavy alcohol group is relatively smaller, and thus the sample size may not have sufficient power to detect differences. Under reporting or recall biases during the alcohol use survey are also possible and are limitations of survey and retrospective studies. In addition, some patients may have a subtype of atrial fibrillation that is more alcohol sensitive. However, the retrospective nature of this study was not able to better define this population in our cohort and may be an area of further research in terms of their outcomes and response to ablation.

Conclusions

Alcohol use is common among patients undergoing catheter ablation of AF. Contrary to known associations of alcohol consumption and incidence of AF, different levels of alcohol consumption were not associated with significantly different rates of AF recurrence after catheter ablation in our cohort of patients undergoing pulmonary vein isolation. Further research is needed to study the effects of alcohol consumption, if any, on outcomes following catheter ablation for atrial fibrillation.

Disclosure

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