Obstructive Sleep Apnea as a Predictor of Inducible Atrial Flutter During Pulmonary Vein Isolation in Patients With Atrial Fibrillation: Clinical Significance and Follow-Up Outcomes

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Abstract

Background: Atrial fibrillation (AF) and atrial flutter (AFL) often co-exist in patients and may lead to severe symptoms and complications. Despite their coexistence, prophylactic cavotricuspid isthmus (CTI) ablation has failed to reduce the incidence of recurrent AF or new on-set AFL. In contrast, the presence of inducible AFL during pulmonary vein isolation (PVI) has been shown to be predictive of symptomatic AFL during follow-up. However, the potential role of obstructive sleep apnea (OSA) as a predictor of inducible AFL during PVI in patients with AF remains unclear. Therefore, this study aimed to examine the potential role of OSA as a predictor of inducible AFL during PVI in patients with AF and reexamine the clinical significance of inducible AFL during PVI in terms of recurrent AFL or AF during follow-up.

Methods: We conducted a single-center, non-randomized retrospective study on patients who underwent PVI between October 2013 and December 2020. A total of 192 patients were included in the study after screening 257 patients for exclusion criteria, which included a previous history of AFL or previous PVI or Maze procedure. All patients underwent a transesophageal echocardiogram (TEE) prior to their ablation to rule out a left atrial appendage thrombus. The PVI was performed using both fluoroscopic and electroanatomic mapping derived from intracardiac echocardiography. After the confirmation of PVI, additional electrophysiology (EP) testing was performed. AFL was classified as typical or atypical based on the origin and activation pattern. Descriptive and frequency statistics were performed to describe the demographic and clinical characteristics of the sample, and Chi-square and Fisher's exact tests were used to compare independent groups on categorical outcomes. Logistic regression analysis was performed to adjust for confounding variables. The study was approved by the Institutional Review Board, and informed consent was waived given the retrospective nature of the study.

Results: Of the 192 patients included in the study, 52% (n = 100) had inducible AFL after PVI, with 43% (n = 82) having typical right AFL. Bivariate analysis showed statistically significant differences between the groups for OSA (P = 0.04) and persistent AF (P = 0.047) when examining the outcome of any inducible AFL. Similarly, only OSA (P = 0.04) and persistent AF (P = 0.043) were significant when examining the outcome of typical right AFL. Multivariate analysis showed that only OSA was significantly associated with any inducible AFL after controlling for other variables (adjusted odds ratio (AOR) = 1.92, 95% confidence interval (CI): 1.003 - 3.69, P = 0.049). Of the 100 patients with inducible AFL, 89 underwent additional ablation for AFL prior to completion of their procedure. At 1 year, the rates of recurrence for AF, AFL, and either AF or AFL were 31%, 10%, and 38%, respectively. There was no significant difference in the rates of recurrence of AF, AFL, or either AF/AFL at 1 year when accounting for the presence of inducible AFL or the efficacy of additional AFL ablation.

Conclusions: In conclusion, our study found a high incidence of inducible AFL during PVI, particularly among patients with OSA. However, the clinical significance of inducible AFL in relation to the recurrence rates of AF or AFL at 1-year post-PVI remains unclear. Our findings suggest that successful ablation of inducible AFL during PVI may not provide clinical benefit in reducing AF or AFL recurrence. To establish the clinical significance of inducible AFL during PVI in various patient populations, further prospective studies with larger sample sizes and longer follow-up periods are necessary.

Keywords: Pulmonary vein isolation; Inducible atrial flutter; Atrial fibrillation ablation; Repeat catheter ablation; Pulmonary vein reconnection; Atrial flutter

Introduction

Atrial fibrillation (AF) and atrial flutter (AFL) often coexist in

patients, and it is not uncommon for a person with AF to also experience episodes of AFL. In fact, studies have shown that the presence of AF may increase the likelihood of developing AFL, and *vice versa* [1, 2]. One study conducted by the Euro Heart Survey found that approximately 25% of patients with AF also had AFL [1]. Another registry study of 407 consecutive patients found that AF and AFL were present together in about 15% of cases [2].

Furthermore, the coexistence of AF and AFL may be associated with more severe symptoms and complications. For example, a nationwide cohort study in Taiwan found that patients with both AF and AFL had a significantly higher risk of adverse outcomes, such as stroke and heart failure, compared to patients with either AF or AFL alone [3]. These findings are consistent with other studies that have suggested a link between the coexistence of AF and AFL and increased morbidity and mortality [1, 2].

Despite the coexistence of AF and AFL, several studies have shown that prophylactic cavotricuspid isthmus (CTI) ablation failed to reduce the incidence of recurrent AF or new onset AFL and did not increase AF-free survival time [4-6]. For instance, the randomized control trial by Pontoppidan et al showed that prophylactic CTI ablation failed to reduce the incidence of recurrent AF or new onset AFL [4]. A second randomized control trial by Kim et al showed similar results with no evidence of reduced incidence of recurrent AF or new onset AFL [5]. A cohort study with a large number of patients by Mesquita et al also showed that prophylactic CTI ablation failed to increase AF-free survival time [6].

On the contrary, the presence of inducible flutter during pulmonary vein isolation (PVI) has been shown to be predictive of symptomatic AFL during follow-up. To date, only one study has investigated the clinical significance of inducible AFL during PVI in patients with AF. In this study, a history of AFL was found to be the only variable associated with inducibility of AFL during PVI. Notably, this study did not examine the potential role of obstructive sleep apnea (OSA) as a predictor. The same study found that AFL occurs in at least one-third of patients with AF and may be observed in two-thirds of patients undergoing PVI for AF. Additionally, typical AFL was observed in about 80% of these episodes. The occurrence of typical AFL during a PVI procedure was predictive of symptomatic AFL during follow-up after PVI. These findings suggested that it may be appropriate to ablate the CTI whenever typical AFL is observed in the course of a catheter ablation procedure aimed at the elimination of AF [7].

Given the known relationship between OSA and atrial arrhythmias, the aim of this study was twofold. First, we sought to examine the potential role of OSA as a predictor of inducible AFL during PVI in patients with AF. Second, we sought to reexamine whether the presence of inducible AFL during PVI had clinical significance in terms of recurrent AFL or AF during follow-up.

Materials and Methods

Study design

This was a single-center non-randomized retrospective study

performed on patients requiring PVI between October 2013 and December 2020. A total of 257 that underwent PVI were initially screened for our exclusionary criteria, which included a previous history of AFL, or history of previous PVI or Maze procedures.

Study population

The study included patients between October 2013 and December 2020 that required PVI as clinically indicated by the presence of persistent or treatment resistant paroxysmal AF. A total of 257 that underwent PVI were initially screened for our exclusionary criteria, which included a previous history of AFL or previous PVI or Maze procedure. A total remaining cohort of 192 patients were included in the study. All procedures were conducted with informed consent. All patients underwent a transesophageal echocardiogram (TEE) prior to their ablation to rule out a left atrial appendage thrombus. All patients underwent PVI through a femoral vein approach using both fluoroscopic and electroanatomic mapping derived from intracardiac echocardiography. Following confirmation of PVI, patients underwent additional electrophysiology (EP) testing using a deflectable decapolar electrophysiological catheter that was positioned in the coronary sinus. Decremental pacing was performed until the atrioventricular (AV) node effective refractory period (ERP) was reached, after which burst atrial pacing with atrial extra stimuli was deployed in attempts to induce atrial dysrhythmias (Fig. 1). The procedures were conducted using standard EP laboratory equipment and techniques.

AFL was classified as "typical" if it was determined to be arising from the right atrium and involving macro reentry through the CTI, as evidenced by the presence of a counterclockwise or clockwise activation on electromagnetic mapping. When electroanatomic mapping was not used, the presence of a right to left concentric activation pattern on the coronary sinus catheter was used to infer the origin of the AFL in the right atrium. AFL was considered "atypical" if it was found to be arising from the left atrium, or if the AFL was nonsustained, or if it did not exhibit the typical activation pattern that would suggest involvement of the CTI.

Statistical analysis

A priori sample size calculation was performed for the purpose of collecting a large enough sample to have adequate statistical power. The researchers hypothesized a proportion of OSA in the "any inducible AFL" group of 60% and a proportion of 40% for OSA in the control group. Using a two-tailed hypothesis, the aforementioned proportions for 60% versus 40%, an alpha value of 0.05, and beta value of 0.20 (1-beta = 0.80; 80%), and equal allocation to treatment arms (1:1), a total of 97 participants would be needed in each treatment arm for a total sample size of 192.

Descriptive and frequency statistics were performed to describe the demographic and clinical characteristics of the sample. Chi-square and Fisher's exact tests were performed to compare
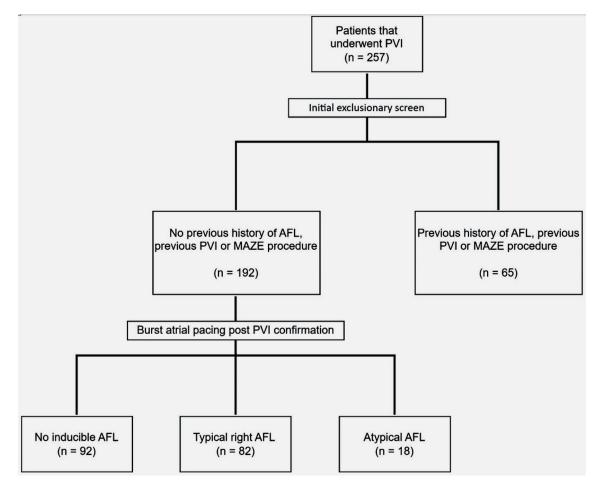
Figure 1. Flow diagram illustrating patient selection. AFL: atrial flutter; PVI: pulmonary vein isolation; Maze: Cox maze procedure.

independent groups on categorical outcomes. Frequencies and percentages were reported and interpreted for the analyses of categorical outcomes. The statistical assumption of normality was assessed using Shapiro-Wilk test and when the assumption was violated, non-parametric Mann-Whitney U tests were used to compare the groups on continuous outcomes. Medians and interquartile ranges were reported for the comparisons of continuous outcomes. Logistic regression analysis was performed to adjust for confounding, demographic, and clinical variables when predicting for a binary, categorical outcome. Adjusted odds ratios (AOR) with 95% confidence interval (95% CI) were reported for the logistic regression analyses. Statistical significance was assumed at an alpha value of 0.05 and all analyses were performed using SPSS version 29 (Armonk, NY: IBM Corp.). Additional statistical and graphical analysis were performed using Graph-Pad Prism version 9.5.1 (Boston, MA: Dotmatics LLC.).

Ethical considerations

The study was approved by the Institutional Review Board (IRB) at the University of Tennessee Graduate School of Medicine, Knoxville, TN with IRB number 4326. Informed consent was waived by the IRB, given the retrospective nature of the

study. The study was conducted in compliance with the institution's ethical standards and the revised Declaration of Helsinki.

Results

Baseline characteristics

A total of 192 patients were included in the study after exclusion of patients with history of PVI, Maze, AFL, or CTI ablation (n = 65). The median age was 66 (interquartile range (IQR): 49 - 71) and the median body mass index (BMI) was 32 (IQR: 28 - 37). Of the 192 patients, 37% of the patients were female and 53% had persistent AF. Table 1 shows the baseline patient demographics. Table 2 shows the baseline background medical therapy.

Preoperative TEE

All patients received a TEE the day of their procedure to exclude left atrial appendage thrombus. The median ejection fraction (EF) was 55%. Table 3 shows the baseline echocar-

Table 1. Baseline Characteristics of the Patients

Characteristics	All patients (n =192)
Age (years)	66 (49 -71)
Sex	
Male	122 (63.5%)
Female	70 (36.5%)
BMI	32 (28 - 37)
Medical history	
OSA	92 (47.9%)
COPD	12 (6.3%)
Asthma	10 (5.2%)
Hypertension	153 (79.7%)
Hyperlipidemia	132 (68.8%)
Diabetes mellitus	50 (26%)
Coronary artery disease	58 (30.2%)
Failed previous antiarrhythmic	86 (44.8%)
Procedural indication	
Paroxysmal AF	90 (46.9%)
Persistent AF	102 (53.1%)

Data for continuous variables (Age and BMI) are expressed as median and range. Data for categorical variables is expressed as mean ± standard deviation or proportion (percentages). AF: atrial fibrillation; BMI: body mass index; COPD: chronic obstructive pulmonary disease; OSA: obstructive sleep apnea.

diogram parameters.

AFL induction

After completion of the PVI, patients underwent rapid atrial pacing in attempts to induce AFL. AFL was induced in 52% of the patients (n = 100). Typical right AFL occurred in 43% of patients (n = 82). Figure 2 shows the incidence of inducible AFL. AFL ablation was performed on 89 of the 100 patients with inducible AFL after completion of the PVI.

Bivariate analysis

Bivariate analysis was performed on the patients' baseline demographics and preop TEE findings to determine risk factors for inducible AFL at the time of PVI. Categorial variables were examined via Chi-square analysis for the outcomes of any inducible AFL, typical right AFL, and atypical AFL. When comparing the "any inducible AFL" groups, statistically significant differences between the groups were detected for OSA, P = 0.04, and persistent AF, P = 0.047. All other comparisons (gender, chronic obstructive pulmonary disease (COPD), asthma, hypertension, hyperlipidemia, diabetes, coronary artery disease and failure of at least one antiarrhythmic) yielded nonsignificant results. Similarly, for the comparison of "typical right AFL", only OSA, P = 0.04, and persistent AF, P = 0.043, yielded statistically signifi-

cant differences. Finally, for the comparison of "atypical AFL", only female gender, P = 0.002, yielded a statistically significant difference. Table 4 shows all the descriptive statistics associated with the analyses on the categorical variables.

Due to the violation of normality for all continuous parameters of interest, non-parametric between-subjects statistical tests were performed on the current data. When comparing the "any inducible AFL" groups, statistically significant differences between the groups were detected for BMI, P = 0.015, and for left atrial size, P = 0.03. All other comparisons (age, EF, right atrial size, tricuspid regurgitation (TR) severity, and mitral regurgitation (MR) severity) yielded nonsignificant results. Similarly, for the comparison of "typical right AFL" groups, only BMI, P = 0.015, and left atrial size, P = 0.02, yielded statistically significant differences. Finally, for the comparison of "atypical AFL" groups, there were no significant differences detected. Table 5 shows all the descriptive statistics associated with the analyses on the continuous variables.

Multivariate analysis

The variables of gender, AF type, BMI, OSA, failure of at least one antiarrhythmic, left atrial size, right atrial size, TR severity, and MR severity were entered into a logistic regression model predicting for the binary outcome, "any inducible AFL." Only OSA was significantly associated with the outcome, AOR = 1.92, 95% CI: 1.003 - 3.69, P = 0.049, when controlling for all the other variables. The findings for the other independent parameters are presented in Table 6.

Ablation of inducible AFL at the time of PVI

Out of the 100 patients that had inducible AFL at the time of PVI, 89 patients went on to have an additional ablation for AFL prior to completion of their procedure. Of the 11 patients that did not undergo an additional AFL ablation, nine had atypical AFL.

Recurrence of AF/AFL at 1 year

At 1 year, we observed the following rates of recurrence: 31% for AF, 10% for AFL, and 38% for either AF or AFL. Recurrence during the follow-up period was defined as either an ECG or outpatient monitor showing AF or AFL, or hospitalization for documented AF or AFL. There was no significant difference in the rates of recurrence of AF, AFL, or either AF/AFL at 1 year when accounting for the presence of inducible AFL, inducible AFL that was ablated and inducible AFL that was not ablated (Table 7).

Discussion

In our study the incidence of inducible AFL was 52%, with 82% of those patients experiencing typical inducible AFL and

Table 2. Patient Home Medications and Antiarrhythmic Therapy

Drugs	All patients (n = 192)	Any inducible atrial flutter (n = 100)	P value	Typical right atrial flutter (n = 82)	P value	Atypical atrial flutter (n = 18)	P value
Home medications							
Beta blocker	103 (53.6%)	63 (63%)	0.01*	52 (63.4%)	0.01*	11 (61.1%)	0.20
Non-DHP CCB	50 (26.0%)	21 (21%)	0.10	16 (19.5%)	0.07	5 (27.8%)	0.75
ACEI	49 (25.5%)	30 (30%)	0.19	27 (32.9%)	0.10	3 (16.7%)	0.76
ARBs	36 (18.8%)	15 (15%)	0.17	13 (15.9%)	0.25	2 (11.1%)	0.26
Sacubitril/valsartan	7 (3.6%)	3 (3%)	0.62	3 (3.7%)	1.0	0 (0%)	1.0
SGLT2-I	3 (1.6%)	0 (0%)	0.11	0 (0%)	0.25	0 (0%)	1.0
Spironolactone	19 (9.9%)	12 (12%)	0.31	12 (14.6%)	0.14	0 (0%)	0.60
Thiazide	19 (9.9%)	11 (11%)	0.58	10 (12.2%)	0.43	1 (5.6%)	1.0
Digoxin	2 (1.0%)	1 (1%)	1.0	1 (1.2%)	1.0	0 (0%)	1.0
Loop diuretic	39 (20.3%)	26 (26%)	0.07	23 (28%)	0.04*	3 (16.7%)	1.0
Statin	101 (52.6%)	56 (56%)	0.41	47 (57.3%)	0.33	9 (50%)	1.0
Aspirin	46 (24%)	22 (22%)	0.41	18 (21.9%)	0.43	4 (22.2%)	0.78
DOAC	162 (84.4%)	86 (86%)	0.66	72 (87.8%)	0.44	14 (77.8%)	0.54
Warfarin	13 (6.8%)	9 (9%)	0.26	5 (6.1%)	0.74	4 (22.2%)	0.02*
Current antiarrhythmic therapy							
Amiodarone	105 (54.7%)	59 (59%)	0.53	51 (62.2%)	0.32	8 (44.4%)	0.42
Dronedarone	8 (4.2%)	2 (2%)	0.21	1 (1.2%)	0.19	1 (5.6%)	0.24
Sotalol	6 (3.1%)	3 (3%)	0.75	3 (3.7%)	0.74	0 (0%)	0.71
Dofetilide	5 (2.6%)	1 (1%)	0.34	1 (1.2%)	0.44	0 (0%)	0.60
Flecainide	24 (12.5%)	12 (12%)	0.95	8 (9.8%)	0.79	4 (22.2%)	0.47
Propafenone	2 (1.0%)	2 (2%)	0.09	2 (2.4%)	0.11	0 (0%)	0.59
Previous/failed antiarrhythmic therapy							
Amiodarone	20 (10.4%)	10 (10%)	0.53	6 (7.3%)	0.32	4 (22.2%)	0.42
Dronedarone	21 (10.9%)	13 (13%)	0.21	9 (10.9%)	0.19	4 (22.2%)	0.24
Sotalol	20 (10.4%)	12 (12%)	0.75	10 (12.2%)	0.74	2 (11.1%)	0.71
Dofetilide	6 (3.1%)	3 (3%)	0.34	2 (2.4%)	0.44	1 (5.6%)	0.60
Flecainide	35 (18.2%)	19 (19%)	0.95	15 (18.3%)	0.79	4 (22.2%)	0.47
Propafenone	6 (3.1%)	1 (1%)	0.09	1 (1.2%)	0.11	0 (0%)	0.59

Data are expressed as mean ± standard deviation or proportion (percentages). *P < 0.05 indicates the difference between the two groups is statistically significant. ACEI: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor blockers; SGLT2-I: sodium-glucose cotransporter-2 inhibitors; DOAC: direct oral anticoagulants; non-DHP CCB: non-dihydro-pyridine calcium channel blockers.

Table 3. Transesophageal Echocardiogram Prior to PVI

Characteristics	All patients (n = 192)
Ejection fraction (%)	55 (25 - 75)
Left atrial dilation	
Mild	43 (22.4%)
Moderate	19 (9.8%)
Severe	0 (0%)
Right atrial dilation	
Mild	17 (8.9%)
Moderate	4 (2.1%)
Severe	0 (0%)
Mitral regurgitation	
Mild	150 (78.1%)
Moderate	20 (10.4%)
Severe	0 (0%)
Tricuspid regurgitation	
Mild	125 (65.1%)
Moderate	3 (1.6%)
Severe	1 (0.52%)

Data for ejection fraction are expressed as median (range). Data for categorical variables are expressed as mean ± standard deviation or proportion (percentages). PVI: pulmonary vein isolation.

Figure 2. Primary outcome inducible atrial flutter.

18% experiencing atypical inducible AFL. These findings are consistent with those reported in the 2004 retrospective study that evaluated the clinical significance of inducible AFL during PVI, where the incidence of inducible AFL was approximately 65%, with 79% of those patients experiencing typical inducible AFL and 21% experiencing atypical inducible AFL [7]. There are a few potential reasons why the incidence of inducible AFL is high during PVI procedures. One possible explanation is that the electrical isolation of the pulmonary veins can create a pro-arrhythmic substrate that is conducive to the development of AFL. This may occur due to alterations in atrial conduction patterns, changes in refractory periods, or other factors that increase the likelihood of reentrant circuits forming in the atria.

Our study found that OSA, BMI, left atrial size, and persistent AF were significant risk factors for inducible AFL on bivariate analysis. However, on multivariate analysis, only OSA remained a significant risk factor. This finding is consistent with several studies that have reported an association between OSA and AFL. For instance, a study by Gupta et al in 2008 found that patients with OSA had a higher incidence of AFL compared to those without OSA (12.6% vs. 1.2%, P < 0.001). The authors suggested that OSA-induced changes in cardiac autonomic tone and atrial remodeling may contribute to the increased risk of AFL in OSA patients [8].

Similarly, Fein et al (2013) reported an increased incidence of AFL in OSA patients compared to those without OSA (23% vs. 12%, P = 0.03). The authors hypothesized that OSA-related hypoxemia and sympathetic activation may contribute to atrial remodeling and th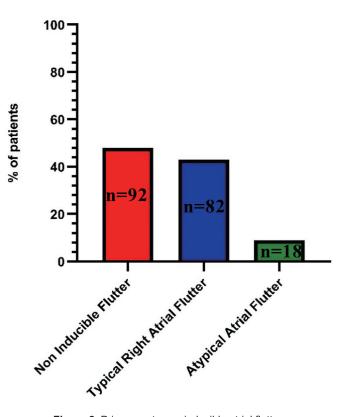e development of AFL [9]. A more recent study by Lee et al (2019) investigated the association between OSA and AFL in patients who underwent catheter ablation for AF. The authors found that OSA was an independent predictor of AFL recurrence after ablation, with OSA patients having a higher risk of recurrence compared to those without OSA (hazard ratio: 2.02, 95% CI: 1.18 - 3.45, P = 0.01). The authors suggested that OSA-related hypoxemia and sympathetic activation may contribute to atrial remodeling and the development of AFL [10].

Additionally, we investigated the recurrence rates of AF and AFL at 1-year post-PVI and found that the overall rates of recurrence of AF, AFL, or a combination of both (AF/AFL) were 31%, 10%, and 38%, respectively. However, the presence of inducible AFL during PVI did not significantly affect the recurrence rates of AF, AFL, or AF/AFL at 1-year post-PVI. This differs from the study by Scharf et al [7], which showed that inducible AFL during PVI was predictive of symptomatic AFL during follow-up. However, our study excluded patients with a history of AFL, which likely explains this difference. Furthermore, there was no significant difference in the recurrence rates of AF or AFL when comparing patients who had inducible AFL that was successfully ablated during PVI to those who did not have inducible AFL.

Therefore, our study suggests that the presence of inducible AFL at the time of PVI may not significantly impact the recurrence rates of AF, AFL, or a combination of both at 1-year post-PVI. Additionally, our findings suggest that ablating inducible AFL during PVI may not provide a clinical benefit in

Table 4. Bivariate Analysis for Outcomes "Any, Typical, and Atypical Atrial Flutter"

Variable	Any inducible atrial flutter	P value	Typical right atrial flutter	P value	Atypical atrial flutter	P value
Female	39 (56%)	0.45	26 (46%)	0.78	13 (30%)	0.002*
Persistent AF	60 (59%)	0.047*	50 (54%)	0.043*	10 (19%)	0.44
OSA	55 (60%)	0.04*	46 (55%)	0.04*	9 (20%)	0.44
COPD	6 (50%)	0.88	5 (46%)	0.91	1 (14%)	0.88
Asthma	5 (50%)	0.89	4 (44%)	0.87	1 (17%)	1.0
Hypertension	84 (55%)	0.12	69 (50%)	0.14	15 (18%)	0.45
Hyperlipidemia	71 (54%)	0.48	60 (50%)	0.33	11 (15%)	0.67
Diabetes mellitus	29 (58%)	0.33	24 (53%)	0.33	5 (19%)	0.65
Coronary artery disease	26 (45%)	0.19	21 (40%)	0.19	5 (14%)	0.57
Failed previous antiarrhythmic	46 (55%)	0.56	36 (49%)	0.78	10 (21%)	0.28

Data are expressed as mean ± standard deviation or proportion (percentages). *P < 0.05 indicates the difference between the two groups is statistically significant. AF: atrial fibrillation; COPD: chronic obstructive pulmonary disease; OSA: obstructive sleep apnea.

Table 5. Bivariate Analysis for Outcomes "Any, Typical, and Atypical Atrial Flutter"

Outcome	Variable	Outcome - yes	Outcome - no	P value
Any inducible atrial flutter				
	Age	66.0 (61.5 - 72.5)	65.0 (58.5 - 71.0)	0.28
	BMI	33.3 (29.6 - 38.1)	31.4 (28.2 - 34.5)	0.02*
	EF	55.0 (50.0 - 55.0)	55.0 (50.0 - 55.0)	0.97
	Left atrial size	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.5)	0.03*
	Right atrial size	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.33
	TR severity	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	0.47
	MR severity	1.0 (1.0 - 1.0)	1.0 (1.0 - 1.0)	0.54
Typical right atrial flutter				
	Age	66.0 (62.0 - 70.0)	65.0 (58.5 - 71.0)	0.48
	BMI	33.3 (29.8 - 38.1)	31.4 (28.2 - 34.5)	0.02*
	EF	55.0 (50.0 - 55.0)	55.0 (50.0 - 55.0)	0.54
	Left atrial size	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.5)	0.02*
	Right atrial size	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.22
	TR severity	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	0.42
	MR severity	1.0 (1.0 - 1.0)	1.0 (1.0 - 1.0)	0.63
Atypical atrial flutter				
	Age	70.0 (61.0 - 73.0)	65.0 (58.5 - 71.0)	0.14
	BMI	32.9 (28.0 - 36.6)	31.4 (28.2 - 34.5)	0.30
	EF	55.0 (50.0 - 55.0)	55.0 (50.0 - 55.0)	0.05
	Left atrial size	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.5)	0.42
	Right atrial size	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.70
	TR severity	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	0.95
	MR severity	1.0 (1.0 - 1.0)	1.0 (1.0 - 1.0)	0.53

Data are expressed as median (interquartile range). *P < 0.05 indicates the difference between the two groups is statistically significant. BMI: body mass index; EF: ejection fraction; MR: mitral regurgitation; TR: tricuspid regurgitation.

Table 6. Multivariate Analysis for Outcome of "Any Inducible Atrial Flutter"

Parameter	AOR (95% CI)	P value
Constant	0.75 (-)	0.59
Gender (female)	0.63 (0.33 - 1.21)	0.17
Type of atrial fibrillation (persistent)	1.62 (0.88 - 2.96)	0.12
BMI	1.22 (0.63 - 2.36)	0.55
OSA	1.92 (1.03 - 3.69)	0.049*
Failed at least one antiarrhythmic	0.97 (0.53 - 1.79)	0.92
Left atrial size	1.68 (0.96 - 2.95)	0.07
Right atrial size	1.14 (0.45 - 2.90)	0.78
TR severity	1.22 (0.66 - 2.26)	0.53
MR severity	0.68 (0.35 - 1.34)	0.26

Values are expressed as AOR (95% CI). *P < 0.05, statistically significant finding. AOR: adjusted odds ratio; CI: confidence interval; BMI: body mass index; MR: mitral regurgitation; OSA: obstructive sleep apnea; TR: tricuspid regurgitation.

Table 7. Recurrence of Atrial Fibrillation and Atrial Flutter at 1 Year

Group	Atrial fibrillation	P value	Atrial flutter	P value	Either	P value
Inducible (n = 100)	30 (30%)	0.7	14 (14%)	0.09	40 (40%)	0.46
Inducible + ablated (n = 89)	27 (30%)	0.8	12 (13%)	0.20	36 (40%)	0.43
Inducible + not ablated (n = 11)	3 (27%)	1	2 (18%)	0.32	4 (36%)	1

Data are expressed as mean ± standard deviation or proportion (percentages). *P < 0.05 indicates the difference between the two groups is statistically significant.

terms of reducing the recurrence of AF or AFL during follow-up. However, it is important to note that our study was retrospective and had a 1-year follow-up period, which may limit the generalizability of our findings. Future prospective studies with longer follow-up periods and larger sample sizes are needed to confirm these findings and determine the clinical significance of inducible AFL during PVI in patients with different clinical characteristics.

Conclusions

In conclusion, the incidence of inducible AFL during PVI is high, with patients with OSA being at increased risk. However, the clinical significance of inducible AFL remains unclear, as our study found that it may not significantly affect the recurrence rates of AF or AFL at 1-year post-PVI. Furthermore, the successful ablation of inducible AFL during PVI may not provide clinical benefit in reducing the recurrence of AF or AFL. Therefore, more prospective studies with larger sample sizes and longer follow-up periods are needed to determine the clinical significance of inducible AFL during PVI in different patient populations.

Limitations

There are several limitations to our study that should be acknowledged. Firstly, our study design was retrospective, which may have introduced selection bias and limited the scope of our analysis. Secondly, although OSA was a central focus of our paper, we were not able to characterize OSA based on severity or treatment due to limited information in our dataset. This may have influenced our findings related to the association between OSA and AF/AFL. Lastly, we may have missed asymptomatic episodes of AF or AFL during follow-up, which could have affected our estimates of recurrence rates.

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Financial Disclosure

None to disclose.

Conflict of Interest

The authors report no financial relationships regarding the content herein.

Informed Consent

Study was exempt given the retrospective nature.

Author Contributions

Raj Baljepally: writing - review and editing, supervision. John Taylor: writing - original draft, methodology, conceptualization, formal analysis, writing - review and editing. Sohiub N. Assaf: writing - original draft, methodology, conceptualization, formal analysis, writing - review and editing. Abdallah N. Assaf: methodology, conception, and data acquisition. Eric Heidel: statistical analysis. William Mahlow: methodology, conception, supervision. All authors have participated in this work, reviewed it, and agreed with the content of the article.

Data Availability

The data supporting these findings of this study are available from the corresponding author upon reasonable request.

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