Predictors of first-pass isolation in patients with recurrent atrial fibrillation: A retrospective cohort study

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BACKGROUND Pulmonary vein isolation (PVI) is superior to antiarrhythmics for the management of atrial fibrillation, but repeat ablation is often required for durable rhythm control. Factors influencing first-pass isolation (FPI) and whether FPI predicts durable isolation are not well known.

OBJECTIVE The study sought to determine factors associated with FPI and rates of chronic reconnection among those with and without FPI at index PVI in patients undergoing repeat ablation.

METHODS We retrospectively identified 483 patients at our institution who underwent first-time PVI in 2021. Of these, 63 who had repeat ablation between 2021 and 2023 were included in the study. Logistic regression was used for statistical analysis for predictors of FPI during index PVI.

RESULTS The mean age was 65 years, 67% of patients were male, 90% were White, and 73% had persistent atrial fibrillation. At index PVI, FPI was achieved in 58% of left pulmonary veins (PVs), 48% of right PVs, and 25% of posterior wall isolations. Bilateral FPI was achieved in 35% of patients. At redo PVI, the right superior PV (47%) was most frequently reconnected. Lack of PFI of the right PVs at index PVI was associated with a 14-fold risk of chronic reconnection. Elevated left atrial voltage predicted the absence of FPI of the right PVs but not the left PVs.

CONCLUSION Increased left atrial voltage predicts a lack of FPI in the right PVs but not in the left PVs. Lack of FPI of right PVs predicts chronic reconnection.

KEYWORDS Atrial fibrillation; Pulmonary vein isolation; Catheter ablation; Chronic reconnection; First-pass isolation

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Introduction

Pulmonary vein isolation (PVI) is superior to antiarrhythmic therapy for maintaining sinus rhythm in patients with atrial fibrillation (AF).[1–4] PVI is associated with improved quality of life and lower rates of stroke, heart failure hospitalizations, and mortality.[5,6] PVI may also delay the progression of paroxysmal to permanent AF when compared with pharmacological rhythm control strategies.[6,7] While newer technologies have improved procedural safety, efficiency, and efficacy, many patients still require repeat ablation for durable rhythm control.[1,3] Prior studies have shown that acute procedural success improves long-term freedom from AF.[8] First-pass isolation (FPI), which refers to electrical isolation of the pulmonary veins (PVs) upon or before completion of the ablation lesion set, predicted lower rates of recurrence compared with patients without FPI in a small study.[8] However, there is limited data on what factors influence FPI and whether FPI during initial ablation predicts durable PVI and lower rates of chronic reconnection. It is also unknown whether the ability to achieve FPI differs between PVs, and whether the absence of FPI predicts reconnection in left pulmonary veins (LPVs) and right pulmonary veins (RPVs) to the same degree.[5,8–10] This study aimed to identify characteristics associated with FPI and chronic electrical reconnection by examining parameters from the index procedure in patients undergoing repeat ablation.

Methods

Population

We retrospectively identified consecutive patients with a prior diagnosis of atrial fibrillation who underwent first-time PVI at Beth Israel Deaconess Medical Center (BIDMC) between January and December of 2021. Those who had repeat ablation at BIDMC sometime after the index ablation and before July 2023 were included in this study. Clinical and

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KEY FINDINGS

- Elevated left atrial voltage predicts lack of first-pass isolation of the right pulmonary veins.
- First-pass isolation of the left pulmonary veins is not affected by left atrial voltage.
- Lack of first-pass isolation in the right pulmonary veins at index procedure is associated with an increased likelihood of chronic reconnection.

procedural data were extracted from the online medical record. Patient demographics, cardiovascular history including type of atrial arrhythmia prompting repeat ablation and procedural data from both index and redo procedures were included for analysis. The BIDMC Committee on Clinical Investigations approved our investigation as exempt research with internal review board number 2024P000381.

PVI procedural characteristics

Index and redo procedures were performed with radiofrequency (RF). All procedures were performed under general anesthesia with either conventional ventilation; high-frequency, low-tidal-volume ventilation; or high-frequency jet ventilation depending on physician preference. Percutaneous modified Seldinger technique under ultrasound guidance was used for unilateral femoral venous access, using 3 venous sheaths, typically in the right femoral vein. Intravenous heparin was administered intraprocedurally to maintain an activated coagulation time >300 to 350 seconds. Intracardiac echocardiography was used to guide a single transseptal puncture, facilitate catheter positioning, and monitor for intraprocedural complications. Patients had an esophageal temperature probe placed for dynamic temperature monitoring during the procedure. Transesophageal or intracardiac echography was used for assessment of left atrial (LA) appendage clot in the event of missed doses of anticoagulation.

Procedures were performed with electroanatomic mapping using the CARTO 3 (Biosense Webster) or EnSite NavX 3D (Abbott) systems. The index procedures of patients performed using the CARTO 3 mapping system were analyzed using CARTONET, a cloud-based storage and analysis system, for LA volume, LA maximum voltage, number and duration of lesions, impedance drop, stability, and ablation index. Cases that used the EnSite NavX system were analyzed for LA maximum voltage, number and duration of lesions, and impedance drop. Ablations were performed using a 3.5-mm irrigated-tip force-sensing ablation catheter. PVs were ablated circumferentially with a wide antral approach. In addition to PVI, additional ablation including posterior wall (PW) isolation with box lesion set or asymmetric en bloc PW isolation, cavotricuspid isthmus (CTI), and additional ablation lines were performed in some cases. These were performed on an individual patient basis at operator discretion. At procedure completion, protamine was usually given to reverse anticoagulation before venous sheaths were removed. Groin hemostasis was achieved with manual compression and preferentially with figure-of-eight sutures.

Table 1 Patient characteristics at index ablation (N = 63)

Age, y	65.4 ± 9.9
Race	
Asian	1 (1.6)
Black/African American	1 (1.6)
White	57 (90.5)
Ethnicity (Hispanic/Latino)	7 (11.1)
Male	42 (66.7)
BMI, kg/m^2	29.8 ± 6.2
Atrial fibrillation subtype	
Paroxysmal	17 (26.9)
Persistent	46 (73)
History of typical atrial flutter	14 (22.2)
Prior cardioversion	49 (77.8)
Prior AAD trial	33 (52.4)
Comorbidities	
Hypertension	33 (52.5)
Diabetes mellitus	5 (7.9)
Cerebrovascular accident/TIA	3 (4.7)
Coronary artery disease	5 (7.94)
Obstructive sleep apnea	18 (28.6)
Congestive heart failure	22 (34.9)
CHA_2DS_2-VASc score	2.1 ± 1.5
LA dimension (4-chamber view)	5.36 ± 1.0
LVEF, %	54.6 ± 9.5

Values are mean ± SD or n (%).

AAD = antiarrhythmic drug; BMI = body mass index; CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65–74 years, sex category; LA, left atrium; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.

Statistical analysis

Categorical variables were represented as frequency and percentage and continuous variables were represented as mean ± SD. Using logistic regression, univariable and multivariable models were developed to determine intraprocedural predictors of FPI at index ablation and chronic reconnection at the time of redo ablation. Percentiles were used to determine the most predictive threshold for maximum voltage. A P value was considered significant if <.05. All statistical tests were performed using Stata version 18.0 (StataCorp).

Results

A total of 483 patients underwent first-time PVI between January and December 2021. Of the 483 patients, 15% (n = 71) underwent repeat ablation between May 2021 and July 2023. Six patients who had initial cryoballoon ablation and 2 patients who had repeat ablation at outside institutions were excluded, leaving 63 patients in the analysis. Baseline patient characteristics at the time of index ablation are shown in Table 1. The mean age was 65 ± 10 years, 67% of patients were male, and 90% were White. At index PVI, 73% (n = 46) of patients had persistent AF and 27% (n = 17) had paroxysmal AF. A history of atrial flutter was present in 22% (n = 14) of patients. Mean LA dimension (4-chamber) was 5.4 ± 1 cm and left ventricular ejection fraction was 55 ±

Table 2 Index ablation procedural characteristics (N = 63)

Index procedure lesion set	
Bilateral WACA only	24 (38.1)
WACA plus PW isolation	36 (57.1)
Bilateral WACAs and additional ablation	3 (4.5)
CTI line	30 (47.6)
First-pass isolation rates	
No PVs	18 (28.6)
Bilateral PVs	22 (34.9)
Left PVs	37 (58.7)
Right PVs	30 (47.6)
PW (n = 36)	9 (25)
Additional lesions by PV region	
Right posterior	12 (19.1)
Right anterior	7 (11.1)
Right anterior and posterior	13 (22.2)
Left posterior	22 (34.9)
Left anterior	2 (3.17)
Left anterior and posterior	2 (3.17)
Complete carina lines	
Right carina line	14 (22.2)
Left carina line	4 (6.35)

Values are n (%).

CTI = cavotricuspid isthmus; PV = pulmonary vein; PW = posterior wall; WACA = wide anterior circumferential ablation.

Table 3 Procedural characteristics at index and redo ablations

Variable	Index (n = 63)	Redo (n = 63)
Time to procedure, mo	59.1 ± 65.5	13.7 ± 7.1
Reason for procedure		
AF	69 (100)	33 (52.4)
Typical AFL	—	1 (1.6)
Atypical AFL	—	13 (20.6)
Combination of AF and AFL	—	15 (23.8)
Other arrhythmia	—	1 (1.5)
Ventilation		
High-frequency jet	39 (61.9)	60 (95.2)
High frequency, low tidal volume	2 (3.17)	2 (3.2)
Conventional	22 (34.9)	1 (1.6)
Mapping catheters		
PentaRay	54 (88.5)	27 (42.9)
Octaray	—	31 (49.21)
HD grid	3 (4.9)	4 (6.35)
Other	4 (6.56)	1 (1.59)
Ablation catheters		
SMARTTOUCH SF	56 (88.9)	58 (92.1)
TactiCath	7 (11.1)	5 (7.9)
Ablation duration, min	33.4 ± 9.9	13.2 ± 6.7
Number of lesions	143.7 ± 37.8	48.7 ± 24.3
Fluoroless (yes)	23 (40.4)	48 (77.4)
Fluoroscopy time, min	6.15 ± 3.76	7.83 ± 6.37

Values are mean ± SD or n (%).

AF = atrial fibrillation; AFL = atrial flutter.

9%. The mean time from AF diagnosis to index PVI was 59 ± 66 months, with 78% (n = 49) of patients having had a prior cardioversion and 52% (n = 33) having trialed an antiarrhythmic before the procedure.

Index ablation

At the index procedure, PVI was performed in 38% (n = 24) of patients, PVI and PW isolation in 57% (n = 36) of patients, and PVI and additional ablation other than PW isolation (eg, roof line only) in 5% (n = 3) of patients (Table 2). Forty-seven percent of patients had a concurrent CTI ablation. FPI was achieved in 59% (n = 37) of left pulmonary veins (LPVs), 48% (n = 30) of right pulmonary veins (RPVs), and 25% (n = 9) of PW isolations. FPI of the PVs was achieved bilaterally in 35% (n = 22) of patients. Absence of FPI in any PV was present in 29% (n = 18) of patients. There were no patients in whom FPI of the PW but not the PVs was achieved. In cases in which FPI of the RPVs was not achieved, additional lesions were delivered anteriorly in 11% (n = 7), posteriorly in 19% (n = 12), and both anteriorly and posteriorly in 22% (n = 13) of patients. For the LPVs, additional lesions were delivered anteriorly in 3% (n = 2), posteriorly in 35% (n = 22), and both anteriorly and posteriorly in 3% (n = 2) of patients. In addition to focal touch-up lesions, a complete carina line was performed in the RPVs in 22% (n = 14) and in the LPVs in 6% (n = 4) of patients.

Redo ablation

The mean time from index PVI to redo ablation was 14 ± 7.1 months. The arrhythmia prompting repeat ablation was recurrent AF alone in 33 (52%) patients, typical atrial flutter in 1 (2%), atypical atrial flutter in 13 (21%), or a combination of all 3 arrythmias in 15 (24%). Table 3 contrasts procedural characteristics of the index compared with the repeat ablation. Repeat ablation was performed using high-frequency jet ventilation in 95% (n = 60) of cases and 76% (n = 48) cases were fluoroless, compared with 62% (n = 39) and 40% (n = 23), respectively, at index ablation. The mean redo RF ablation time was 13.2 ± 7 minutes and the total number of lesions was 49 ± 24, compared with 33 ± 10 minutes and 144 ± 38 lesions at index procedure, respectively.

Table 4 demonstrates findings at repeat ablation. Reconnection of at least 1 PV was present in 63% (n = 40) of patients. The RPVs were found to be reconnected in 54% of patients and the LPVs in 32% of patients. The right superior PV was most frequently reconnected (48%), followed by the right inferior PV (44%), the left superior PV (30%), and finally the left inferior PV (22%). The PW was reconnected in 64% (n = 23) of patients. At redo, 16% had repeat ablation of CTI and 10% had other repeat ablation performed. The LPVs were reisolated anteriorly in 15% (n = 3), posteriorly in 40% (n = 3), and both anteriorly and posteriorly in 45% (n = 9) of cases. The RPVs were reisolated anteriorly in 25% (n = 8), posteriorly in 28% (n = 9), and both anteriorly and posteriorly in 47% (n = 15) of cases. In addition to reisolation of reconnected areas, patients underwent new lesion sets with 25% (n = 16) undergoing PW isolation, 33% (n = 21) undergoing CTI ablation, and 49% (n = 31) undergoing additional ablation lines.

Predictors of FPI

Of the 63 patients included in this analysis, 55 (87%) had the index PVI performed using CARTO 3 and 8 (13%) using the

Table 4 Redo ablation characteristics (N = 63)

Chronic reconnection	
Chronic reconnection in at least 1 PV	40 (63.4)
Left PVs	20 (31.75)
Left superior PV	19 (30.2)
Left lower PV	14 (22.2)
Left common PV	1 (1.6)
Right PVs	34 (53.9)
Right superior PV	30 (47.6)
Right lower PV	28 (44.4)
Right middle PV	1 (1.6)
Posterior wall (n = 36)	23 (63.8)
Reisolation lesion set	
Reisolation left PVs (n = 20)	20 (31.75)
Anterior	3 (15)
Posterior	8 (40)
Both	9 (45)
Reisolation right PVs (n =33)	35 (50.7)
Anterior	8 (25)
Posterior	9 (28.12)
Both	15 (46.88)
Reisolation posterior wall (n =36)	21 (58.3)
Repeat CTI line	10 (15.87)
Repeat additional ablation	6 (9.52)
New lesion set	
Posterior wall lesion set	16 (25.4)
CTI line	21 (33.3)
Additional ablation lines	31 (49.21)

Values are n (%).
CTI = cavotricuspid isthmus; PV = pulmonary vein.

EnSite NavX electroanatomic mapping system. Two cases were excluded from this subanalysis because the procedural files were corrupted and could not be retrieved for review. The ablation data and maps from the index PVI of 61 patients were analyzed to determine predictors of FPI of the PVs at index ablation. Maximum voltage was obtained during coronary sinus pacing using high-density electroanatomic maps that included the body of the LA and PV ostia but excluded the LA appendage. The median and mean voltage was 8.72 mV and 9.53 ± 4.4 mV, respectively, and the absolute voltage range was 2.37 to 23.78 mV (Table 5). For the LPVs, the mean number of RF lesions delivered was 43 ± 15 and the mean RF duration was 13 ± 5 minutes. For the RPVs, the mean number of delivered lesions was 57 ± 19 and the mean ablation duration was 16 ± 5 minutes. The impedance drop was similar between LPVs (10.1 ± 3.1 Ω) and RPVs (9.9 ± 2.7 Ω). After adjusting for demographic and clinical characteristics (age, sex, hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, and obstructive sleep apnea), each 1-mV increase in LA voltage increased the likelihood of not obtaining FPI in the RPVs by 24% (odds ratio [OR] 1.24, 95% confidence interval [CI] 1.04–1.47, $P = .014$), and after a threshold of 8.83 mV, this likelihood increased 5-fold (OR 5.22, 95% CI 1.5–18.06, $P = .009$) (Table 6) on multivariable analysis. Hypertension was associated with lack of FPI of the LPVs on univariable analysis, and was borderline significant on multivariable analysis (OR 3.54, 95% CI 1.08–11.64, $P = .037$). For the LPVs, neither voltage, ablation duration nor any adjusted clinical characteristics were associated with lack of FPI on multivariable analysis (Supplemental Table 1).

Table 5 Index lesion procedural characteristics (n = 61)

Left atrial maximum voltage, mV	9.53 ± 4.41
Left pulmonary veins	
Number of ablation lesions	42.7 ± 14.6
Duration ablation, min	12.6 ± 4.5
Impedance drop, Ω	10.1 ± 3.1
Right pulmonary veins	
Number of ablation lesions	56.9 ± 18.8
Duration ablation, min	15.9 ± 5.4
Impedance drop, Ω	9.9 ± 2.7

Values are mean ± SD.

Predictors of chronic reconnection

After adjusting for clinical and demographic characteristics, on multivariable analysis we found a borderline difference in the rate of chronic reconnection of the LPVs (OR 4.36, 95% CI 1.09–17.32, $P = .036$) based on whether FPI was obtained at index PVI (Figure 1). However, absence of FPI of the RPVs at index PVI significantly increased the likelihood of chronic reconnection of the RPVs (OR 13.56, 95% CI 3.45–53.31, $P < .001$). Specifically, for the right superior PV, the likelihood of chronic reconnection was increased 7-fold (6.84, 95% CI 2.01–23.27, $P = .002$) and 5-fold for the right inferior PVs (OR 4.83 95% CI 1.44–16.19, $P = .011$). Our study did not find any difference in the rates of chronic reconnection between males and females.

Discussion

Chronic reconnection of the PVs has been proposed as the primary mechanism of recurrent AF after catheter ablation.[10–12] Early studies reported PV reconnection rates as high as 80% to 90% in patients undergoing redo ablation.[9,12] Use of force-sensing catheters, higher power, and stability metrics have increased acute ablation success rates and long-term outcomes.[6,10] Studies evaluating modern ablation approaches have shown rates of PV FPI up to 80% and chronic reconnection of 15% at redo procedures, as well as longer periods of freedom from arrhythmia following initial ablation.[5,13,14]

FPI has been proposed as an indication of lesion quality and associated with increased likelihood of durable PVI.[5,15] Multiple patient and procedural characteristics can affect FPI, including PV morphology, esophageal and phrenic nerve location, LA voltage, and RF lesion quality.[8,10,16] In clinical practice, rates of FPI are often lower for the RPVs than the LPVs, likely due to epicardial fibers that decrease the likelihood of transmural lesions.[10] Higher rates of both acute and chronic reconnection in the RPVs have been found with RF and cryoballoon ablation.[10,11,17,18]

Predictors of FPI

The rates of FPI in our study are lower than those commonly reported with current technologies, likely due

Table 6 Predictors of lack of first-pass isolation

	Univariable			Multivariable		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
Right pulmonary veins						
Per 1-mV increase in voltage	1.23	1.06–1.42	.006*	1.23	1.04–1.47	.014*
Per voltage above 8.83 mV†	4.9	1.65–14.49	.004*	5.22	1.5–18.06	.009*
Ablation duration	1.12	1.01–1.24	.035*	1.13	1.01–1.29	.042*
Obstructive sleep apnea	3.56	1.08–11.68	.036*	3.56	0.89–14.1	.071
Left pulmonary veins						
Hypertension	2.92	1.01–8.42	.047*	3.54	1.08–11.64	.037*

CI = confidence interval; OR = odds ratio.
*Indicates statistical significance.
†Above 8.83 mV, that represents the median LA voltage.

to the use of low-power settings that are no longer used. However, despite the incorporation of higher-power settings and new algorithms to facilitate better lesion quality, FPI can be elusive, even when target values are achieved using contemporary power settings.[19] In addition, early data suggest that even with nearly universal rates of FPI using pulsed field ablation, long-term durability of PVI is not guaranteed.[20] In our study, LA voltage was relatively normally distributed among cases, with a median voltage of 8.83 mV. We found that each 1-mv increase in LA voltage, as well as absolute voltage above 8.83 mV, was associated with significantly lower rates of FPI in the RPVs but not in the LPVs.

This differential effect of voltage on FPI may be related to underlying anatomic differences in the LA musculature surrounding the LPVs and RPVs. Bipolar voltage is influenced by multiple factors including fiber orientation and relationship of fiber orientation to the wavefront of activation. Muscle fiber orientation surrounding the RPVs is complex and distinct from the LPVs.[10] The LA bipolar voltage in our study reflected global values and was not segmented by anatomic area. In addition, the muscle fiber orientation around the RPVs may result in increased epicardial connections that making FPI challenging.[10,16] Rosso and colleagues[16] found that empiric carina ablation resulted in improved rates of FPI of the RPVs, perhaps due to elimination of some of these epicardial connections.

The ablation strategy used in our cohort at index PVI was primarily low power and long duration. Though these power settings are no longer used, our findings reflect real-world data and remain applicable to current practice for 2 reasons. First, the rate of redo ablation was 15%, which is consistent with published clinical experience in studies using more contemporary power settings over a similar follow-up period.[20,21] Second, despite improved ablation technology with pulsed field ablation resulting in nearly universal FPI, early data suggest that the durable PVI is not guaranteed and that these higher rates of FPI

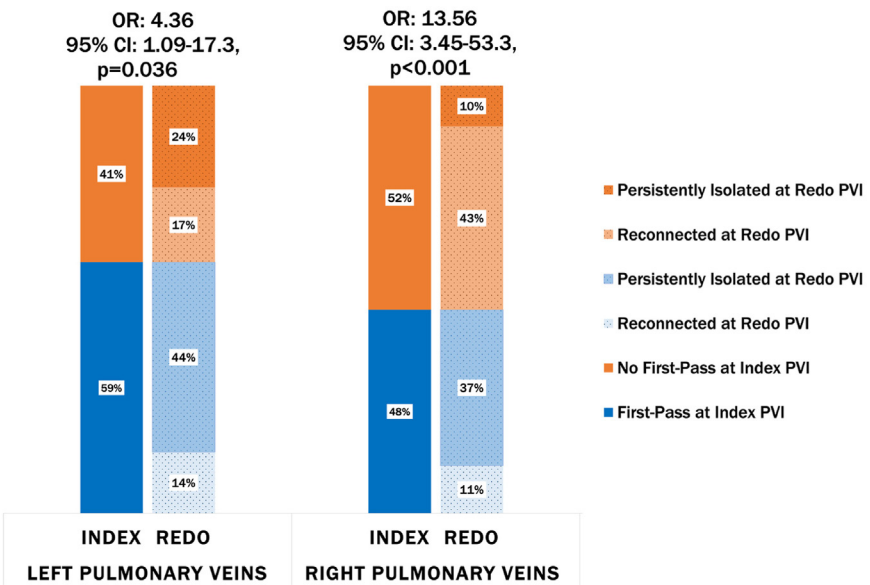

Figure 1 Predictors of chronic reconnection. Rates of first-pass isolation at the index ablation based on anatomical region and the respective rates of chronic reconnection at redo ablation. CI = confidence interval; OR = odds ratio; PVI = pulmonary vein isolation.

have not significantly changed long-term arrhythmia outcomes.[20,22] Though the mean and median voltage were considerably higher than the current clinical standard of 0.05 to 0.5 mV applied to the atrium, accounting for absolute bipolar voltage may be useful for providers when considering an ablation lesion set and strategy.

Differential importance of FPI on LPVs vs RPVs

In our study, we found that lack of FPI had differential effects on the likelihood of reconnection of the RPVs and LPVs. Failure to achieve FPI of the RPVs strongly predicted chronic reconnection at repeat ablation. In contrast, lack of FPI of the LPVs did not strongly predict chronic reconnection. That is, if electrical isolation of the LPVs was achieved during the index procedure, first-pass or not, there was a significant likelihood of chronic isolation at repeat ablation. Prior studies have found that touch-up lesions may be insufficient to prevent chronic gap formation after initial healing, supporting the idea that lack of FPI can lead to greater rates of arrhythmia recurrence warranting repeat procedures.[5,10] We did not find this to be the case for the LPVs; the need for supplemental ablation in the LPVs at index PVI was not associated with chronic reconnection. As discussed previously, a low-power, long-duration ablation strategy was frequently utilized in this cohort at index PVI, a practice that has changed significantly over the past 4 years.[19] Nevertheless, even with this approach, the lack of FPI did not result in increased likelihood of chronic reconnection of the LPVs. This has direct clinical implications and suggests that the need for additional ablation to achieve acute PVI of the LPVs does not confer an increased risk of reconnection in the future. Thus, a high-power short-duration ablation strategy may be beneficial overall, but particularly helpful to achieving better arrhythmia control if it increases the likelihood of achieving FPI of the RPVs.

Our study adds to the current body of knowledge by identifying increased voltage as a predictor of lack of FPI. To our knowledge, this is the first study to demonstrate differential effects of FPI of the LPVs compared with the RPVs on rates of chronic reconnection, and to document voltage as a differential predictor of FPI in the RPVs but not in the LPVs.

Study limitations

Our study is limited by being a single-center, retrospective analysis that limits detailed data availability. There is a potential selection bias in that only patients who underwent repeat ablation at our institution were included.

Conclusion

Increased LA voltage predicted lack of FPI of the RPVs at index ablation. FPI of the LPVs was not affected by LA voltage. Lack of FPI of RPVs was associated with an increased likelihood of chronic reconnection at redo procedure.

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Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hroo.2024.08.008.

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