Safety and efficacy outcomes of left atrial posterior wall isolation compared to pulmonary vein isolation and pulmonary vein isolation with linear ablation for the treatment of persistent atrial fibrillation

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Background Pulmonary wall isolation (PWI) is increasingly used as an adjunctive lesion set to compliment pulmonary vein isolation (PVI), especially in patients with persistent atrial fibrillation (AF). The objective was to compare outcomes of catheter ablation in patients with persistent AF undergoing PVI with and without adjunctive PWI.

Methods We performed a retrospective study of 558 patients who underwent de novo and repeat ablation for persistent AF. Subjects were matched using propensity score adjustments. Outcomes were freedom from recurrent atrial arrhythmia and adverse events.

Results Among 558 patients who underwent ablation for persistent AF, 78 (14%) underwent PVI + PWI, 255 (46%) underwent PVI, and 225 (40%) underwent PVI + linear ablation. Stratified logistic regression analysis with propensity matching revealed higher odds of recurrent arrhythmia with PVI + PWI when compared to PVI (odds ratio [OR] 2.25, 95% CI 1.08-4.69, $P = .030$) and when compared to PVI + linear (OR 2.31, 95% CI 1.01-5.28, $P = .048$). Within the PVI + PWI group, 57.7% of subjects were in normal sinus rhythm at 6 months compared to 73.9% and 72.2% in PVI and PVI + linear groups, respectively. Adverse events were rare, with 19 events total identified across all groups.

Conclusions PVI + PWI does not appear to be as effective as PVI or PVI + linear ablation in reducing the recurrence of arrhythmia within 6 months of the index procedure in patients with persistent AF. A prospective, randomized controlled trial comparing these ablation techniques is needed to clarify the role of extensive substrate modification for treatment of persistent AF.

Condensed Abstract PWI is increasingly used as an adjunctive lesion set to compliment PVI in patients with persistent AF. We performed a retrospective study of 558 patients who underwent de novo and repeat ablation for persistent AF to compare the outcomes between PVI with and without adjunctive PWI. We found an increased incidence in recurrence of AF and other atrial arrhythmias at 6 months in the PVI + PWI cohort compared to PVI with or without additional linear ablation. A prospective, randomized controlled trial comparing these ablation techniques is needed to clarify the role of extensive substrate modification for treatment of persistent AF. (Am Heart J 2020;220:89-96.)

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Pulmonary vein isolation (PVI) has been the most commonly used strategy for the catheter ablation of atrial fibrillation (AF) due to the identification of AF triggers found within the pulmonary veins.[1,2] However, there remains a high rate of AF recurrence with PVI alone, most frequently due to pulmonary vein reconnection or to the presence of triggers outside of the pulmonary veins.

Adjunctive techniques apply additional lesions to the left atrial wall to isolate or eliminate additional arrhythmogenic areas.[3-6] Because of the common embryologic origin of the left atrial posterior wall and pulmonary veins

and the frequency of nonpulmonary vein triggers from the posterior wall, one of these strategies involves performing additional ablation to isolate the left atrial posterior wall. This is accomplished by isolating the pulmonary veins and subsequently creating lesions along the left atrial roof to connect the lesion sets superiorly as well as the left atrial floor to connect them inferiorly.

Studies comparing the individual ablative techniques remain sparse with mixed results and are often limited because of small sample sizes.[7-15] Comparisons of the safety of PVI, PVI with adjunctive linear ablation (PVI + linear), or PVI with posterior wall isolation (PVI + PWI) are also limited.[16,17] To better understand the effectiveness and safety of PVI relative to PVI + linear and PVI + PWI, we compared the frequency of recurrent atrial tachycardia, atrial flutter, or atrial fibrillation (AT/AFL/AF) and occurrence of adverse events in patients with persistent AF undergoing AF ablation with each technique.

Methods

Study design and cohort formation

We performed a retrospective analysis of the Duke Center for Atrial Fibrillation database, including all patients that underwent AF ablation at Duke University Medical Center between January 1, 2014 and March 15, 2017. Patients who were 18 years of age and older undergoing catheter ablation for persistent AF, with a minimum of 6-month follow-up data and no prior history of surgical ablation or posterior wall ablation, were eligible for inclusion. As per Heart Rhythm Society consensus criteria, *persistent AF* was defined as AF that lasted longer than 7 days but less than 12 months.[1] We included patients undergoing de novo and redo catheter ablation procedures. Patients meeting the inclusion criteria were divided into 3 groups based on the type of ablation performed: PVI, PVI + linear, and PVI + PWI. No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

Catheter ablation procedure

Informed consent was obtained from all patients before the ablation procedure. General anesthesia was provided, and heparin was administered to maintain an activated clotting time between 300 and 400 seconds. Transseptal puncture and ablation were performed under direct visualization using intracardiac echocardiography. Electroanatomical mapping was performed using either CARTO (Biosense-Webster Inc., Diamond Bar, CA) or NavX (St Jude Medical, Inc, Minneapolis, MN). Radiofrequency ablation was performed with irrigated catheters using 0.9% normal saline and a point-by-point technique. Contact force sensing was used in cases performed after Food and Drug Administration approval of the available catheters. PVI was performed using a wide area circumferential technique in all patients, and entrance and exit blocks were documented in all cases using a multipolar mapping catheter. In addition to PVI, patients in the PVI + linear ablation group also received 1 or more of the following additional linear ablations: mitral isthmus line connecting the left inferior pulmonary vein to the mitral valve, left atrial (LA) roof line connecting the left superior pulmonary vein to the right superior pulmonary vein, and cavotricuspid isthmus line connecting the tricuspid valve to the inferior vena cava. Patients in the PVI + PWI group received PVI with additional linear ablation along the LA roof to connect the left superior pulmonary vein to the right superior pulmonary vein and linear ablation along the LA floor to connect the inferior margin of the left inferior pulmonary vein to the right inferior pulmonary vein to obtain block into the posterior wall. Patients in the PVI + PWI group could also receive additional linear ablation. Bidirectional block was confirmed across all linear ablations using differential pacing techniques. Adenosine was administered during testing of block at the discretion of the operator. Antiarrhythmic drugs were continued at the discretion of the provider.

Outcomes and follow-up

The primary outcome was recurrence of arrhythmia at 6 months. For the purpose of this analysis, we defined *recurrent arrhythmia* as AT/AFL/AF on a 12-lead electrocardiogram for $\geq$30 seconds on a continuous monitor or implantable device, or that required cardioversion, as previously documented in the literature.[18] We instituted a 3-month blanking period following the procedure to exclude any procedure-related arrhythmias as recommended by the most recent Heart Rhythm Society consensus document.[1] Secondary outcomes were freedom from AT/AFL/AF at 1 month after ablation, change in Canadian Cardiovascular Society AF symptom severity (CCS) score and New York Heart Association (NYHA) class between baseline and 6 months, and freedom from adverse events.

Patients were seen in person by a provider in the electrophysiology clinic within 8 weeks of the ablation procedure and again 6 months after the procedure, and 12-lead ECG was acquired at these appointments. If the patient complained of AF-related symptoms, additional ECG, Holter, or event monitoring was performed at the discretion of the provider. All available long-term monitoring data (eg, in-hospital telemetry, pacemaker, ICD, or implantable monitor data; Holter and event monitoring data) were manually reviewed by the investigators and included in the end point adjudication. Additional assessment of AF symptom severity was performed by a dedicated AF coordinator nurse (J. F.) immediately prior to the ablation procedure and 1 and 6 months after the procedure by in person or telephone

interview. Periprocedural complications, NYHA class, and CCS score were recorded during each coordinator interview. AF ablation procedures were reviewed by the authors (J. S. S. and B. D. A.) blinded to procedural outcomes to identify the type of ablation performed, confirm that entrance and exit block and/or bidirectional block was achieved acutely with each lesion set, and confirm the indication for the ablation was persistent AF.

Statistical analysis

A power calculation determined that a minimum sample size of 75 patients in the PVI + PWI cohort would achieve 80% power to detect a 20% difference in rate of recurrent AT/AFL/AF with a 2-sided significance level of .05 using a χ^2 test, assuming a rate of recurrence of 40% in the PVI cohort. The safety outcome of this analysis was the occurrence of serious adverse events as a result of the procedure, including major bleeding, pericardial tamponade, transient ischemic attack or stroke, atrioesophageal fistula, phrenic nerve palsy, and death.

Continuous variables were expressed as mean ± SD when normally distributed or median and interquartile range otherwise. Categorical variables are presented as absolute numbers and percentages and compared using likelihood ratio χ^2 tests. The independent-samples *t* test or Wilcoxon tests were used to compare continuous variables. Baseline patient characteristics were compared between the treatment groups including PVI, PVI + linear, and PVI + PWI. To control for confounders when comparing freedom from recurrent AT/AFL/AF, subjects in the PVI and PVI + linear groups were matched to the PVI + PWI group using propensity score analysis. The following variables were used for propensity score analysis: age, gender, race, date of procedure, CHA2DS2-VASc score, presence of mitral valve disease, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea, baseline antiarrhythmic drug, baseline CCS score, baseline heart failure, and baseline NYHA score. Individual factors already included within the CHA2DS2-VASc score, such as hypertension and history of cerebrovascular accident (CVA), were not included in the propensity analysis avoid collinearity. Within the propensity score matched groups, baseline patient characteristics were compared using r^2 for continuous data and Cramer Φ for categorical data with cutoffs of 0.01 and 0.10, respectively. The primary outcome of recurrence of AT/AFL/AF was evaluated using stratified logistic regression, with strata formed by the matched subject pairs, in three 2-way comparisons among the groups. Unadjusted and adjusted sensitivity analyses were performed after excluding all patients with prior AT/AFL/AF ablation. The proportions of type of arrhythmia that recurred within each group (paroxysmal AF, persistent AF, or AT/AFL) and the secondary outcome of adverse effects were presented descriptively as rates due to the small number of events.

The protocol was reviewed and approved by the Duke University institutional review board. SAS (Cary, NC) version 9.4 was used for all of the statistical analyses.

Results

Baseline characteristics

A total of 723 medical records were identified and reviewed for potential inclusion in the study cohort. A total of 149 patients were excluded because of ablations performed for alternative indications, and 16 subjects were excluded for inadequate follow-up. Two of the 16 subjects excluded for inadequate follow-up died prior to the 6-month follow-up mark: 1 from respiratory failure approximately 2 months after the procedure and the other from unknown causes not documented in medical record review. Among the 558 patients who underwent ablation for persistent AF between January 1, 2015, and March 15, 2017, 78 (14%) underwent PVI + PWI, 255 (46%) patients underwent PVI, and 225 (40%) underwent PVI + linear ablation. Successful PWI was achieved in 77/78 subjects (99%). One subject with attempted PWI had successful block across the roof line but unsuccessful block across the floor line. This patient was excluded from further analyses. Propensity score analysis matched 56, 56, and 203 patient pairs in the PVI + PWI versus PVI, PVI + PWI versus PVI + linear, and PVI versus PVI + linear comparisons, respectively.

The baseline characteristics of the total population are shown in Table I. There were differences in the frequency of heart failure, use of prior antiarrhythmic drug therapy, left atrial diameter, ablation time, use of contact force measuring ablation catheters, history of prior AF ablation, and the severity of HF symptoms between groups. The baseline characteristics of patients included in the propensity score matched study populations are shown in Table II. Overall, patient characteristics were similar across the matched treatment groups. There was a trend toward higher rates of prior AT/AFL/AF ablation in the PVI + PWI group compared to PVI alone (21% vs 9%), but this difference was not statistically significant ($P = .06$). Rates of prior AF ablation were comparable between the PVI + PWI and PVI + linear groups (27% vs 26%, $P = .977$).

Freedom from recurrent AT/AF

None of the subjects had a repeat ablation within the 6-month follow-up period. One-month interviews were completed on 474/558 patients. Recurrent AT/AFL/AF was documented at the 1-month follow-up in 83/202 patients undergoing PVI (41%), 88/202 patients undergoing PVI + linear ablation (44%), and 24/70 patients undergoing PVI + PWI (34%) ($P = .39$ for difference between groups). As prespecified in the analysis plan, follow-up was complete in 558/558 patients at the 6-month interval. Recurrent AT/AFL/AF was documented

Table I. Baseline characteristics of total population by ablation strategy

	N missing	PVI n = 255	PVI + linear n = 225	PVI + PWI n = 78	*P* value
Age, y, median (25th-75th)	0	67 (59-73)	68 (61-73)	66 (56-74)	.45
HTN, n (%)	0	171 (67)	144 (64)	46 (59)	.44
DM, n (%)	0	46 (18)	43 (19)	20 (26)	.36
Mitral valve disease, n (%)	0	15 (6)	18 (8)	12 (15)	.06
Male gender, n (%)	0	171 (67)	164 (73)	53 (68)	.36
Prior MI, n (%)	0	33 (13)	36 (16)	10 (13)	.48
HF, n (%)	0	77 (30)	99 (44)	36 (46)	<.01
NYHA class, n (%)	10				<.01
I		56 (22)	38 (17)	8 (10)	
II		145 (57)	151 (67)	31 (39)	
III		51 (20)	34 (15)	38 (49)	
IV		3 (1)	2 (1)	1 (1)	
COPD, n (%)	0	28 (11)	27 (12)	11 (14)	.76
Prior CVA/TIA, n (%)	0	20 (8)	20 (9)	6 (8)	.87
CHADS-VASC, mean (SD)	0	2.6 (1.6)	2.7 (1.7)	2.7 (1.9)	.68
Prior antiarrhythmic drug, n (%)	0	163 (64)	167 (74)	36 (46)	<.01
CCS, mean (SD)	12	2.8 (0.9)	2.9 (0.8)	2.8 (0.9)	.14
LA diameter, cm, mean (SD)	228	4.2 (0.7)	4.2 (0.8)	4.6 (0.7)	.02
LV ejection fraction, %, mean (SD)	21	53 (10)	52 (10)	50 (11)	.11
Ablation time, s, mean (SD)	78	52 (28)	63 (30)	53 (21)	<.01
Contact force catheter, n (%)	11	156 (61)	101 (45)	66 (85)	<.01
Prior AT/AFL/AF ablation, n (%)	0	34 (13)	55 (24)	16 (21)	.01
Long-term monitoring, n (%)	0	74 (29)	68 (30)	22 (29)	.93

Legend: y = years, HTN = hypertension, DM = diabetes mellitus, MI = myocardial infarction, HF = heart failure, TIA = transient ischemic attack, LV = left ventricle, s = seconds, min = minutes.

at the 6-month follow-up in 59/255 patients undergoing PVI (23%), 59/166 patients undergoing PVI + linear ablation (26%), and 33/78 patients undergoing PVI + PWI (42%) (P = .004 for difference between groups). In the propensity matched cohorts, there were no differences in the frequency of antiarrhythmic drug use at 6-month follow-up (54% in PVI + linear vs 41% in PVI + PWI, P = .18; 38% in PVI vs 39% in PVI + PWI, P = .85; and 39% in PVI and 46% in PVI + linear, P = .19). The propensity matched adjusted analysis of recurrent AT/AFL/AF at 6 months revealed an odds ratio (OR) of 2.25 for PVI + PWI compared to PVI (95% CI 1.08-4.69, P = .030), 2.31 for patients undergoing PVI + PWI compared to PVI + linear (95% CI 1.01-5.28, P = .048), and 1.1 for PVI compared to PVI + linear (95% CI 0.70-1.76, P = .66). The risk of recurrence of AT/AFL/AF at 6 months by each comparison group is shown in Figure 1.

Sensitivity analyses

A total of 105 patients had prior AT/AFL/AF ablation and were excluded from the sensitivity analyses. A total of 453 patients underwent de novo ablation, 221 patients had PVI, 170 patients had PVI + linear ablation, and 62 patients had PVI + PWI. Recurrent AT/AFL/AF was documented at the 6-month follow-up in 44/221 patients undergoing de novo PVI (20%), 40/170 patients undergoing de novo PVI + linear ablation (24%), and 24/62 patients undergoing de novo PVI + PWI ablation (39%) (P = .01 for difference between groups). After adjustment for age, gender, race, date of procedure, CHA2DS2-VASc score, presence of mitral valve disease, COPD, obstructive sleep apnea, baseline antiarrhythmic drug, baseline CCS score, baseline heart failure, and baseline NYHA score, we found that PVI + PWI remained associated with likelihood of AT/AFL/AF at 6-month follow-up (P = .038) with an OR of 2.5 (95% CI 1.2-5.1) for PVI + PWI compared to PVI alone and an OR of 1.3 (95% CI 0.8-2.2) for PVI + PWI compared to PVI + linear ablation.

Type of recurrent arrhythmia according to ablation strategy

Secondary analysis of the primary outcome was performed to identify the types of arrhythmia that recurred at 6 months within each group. Within the PVI + PWI group, 57.7% of the subjects were in normal sinus rhythm (NSR) at 6 months, 10.3% were in paroxysmal AF, 25.6% were in persistent AF, and 6.4% were in AT or atrial flutter. Within the PVI group, 73.9% of the subjects were in NSR at 6 months, 10.2% were in paroxysmal AF, 14.4% were in persistent AF, and 1.5% were in AT or atrial flutter. Within the PVI + linear group, 72.2% of the subjects were in NSR at 6 months, 13.2% were in paroxysmal AF, 13.7% were in persistent AF, and 0.9% were in AT or atrial flutter. Figure 2 demonstrates the proportions of rhythm types across all 3 groups at 6-month follow-up.

Table II. Baseline characteristics of propensity score matched populations by ablation strategy

	PVI n = 203	PVI + linear n = 203	PVI n = 56	PVI + PWI n = 56	PVI + linear n = 56	PVI + PWI n = 56
Age, y, median (25th-75th)	67 (60-73)	68 (61-73)	70 (60-75)	68 (61-74)	69 (63-74)	68 (62-76)
HTN, n (%)	69 (34)	75 (37)	33 (59)	31 (55)	36 (64)	33 (59)
DM, n (%)	36 (18)	41 (20)	13 (23)	13 (23)	15 (27)	14 (25)
Mitral valve disease, n (%)	16 (8)	18 (9)	6 (11)	6 (11)	8 (14)	9 (16)
Male gender, n (%)	142 (70)	146 (72)	37 (66)	36 (64)	39 (70)	38 (68)
Prior MI, n (%)	28 (14)	35 (17)	8 (14)	8 (14)	8 (14)	9 (16)
HF, n (%)	75 (37)	81 (40)	22 (39)	21 (38)	28 (50)	27 (48)
NYHA class, n (%)						
I	37 (18)	35 (17)	7 (12)	6 (11)	5 (9)	7 (12)
II	132 (65)	134 (66)	27 (48)	24 (43)	27 (48)	23 (41)
III	32 (16)	34 (17)	21 (38)	25 (44)	24 (43)	25 (45)
IV	2 (1)	0 (0)	1 (2)	1 (2)	0 (0)	1 (2)
COPD, n (%)	22 (11)	24 (12)	7 (13)	6 (11)	9 (16)	8 (14)
Prior CVA/TIA, n (%)	14 (7)	18 (9)	3 (5)	5 (9)	4 (7)	5 (9)
CHA2DS2-Vasc, median (25th-75th)	2 (1-4)	3 (1-4)	3 (2-4)	3 (1-4)	3 (2-4)	3 (1-4)
Prior antiarrhythmic drug, n (%)	138 (68)	148 (73)	29 (52)	28 (50)	32 (57)	31 (55)
CCS, n (%)						
0	4 (2)	4 (2)	1 (2)	1 (2)	1 (2)	1 (2)
1	10 (5)	10 (5)	4 (7)	5 (9)	6 (11)	5 (9)
2	30 (15)	26 (13)	9 (16)	9 (16)	7 (12)	8 (14)
3	124 (61)	126 (62)	30 (54)	28 (50)	27 (48)	27 (48)
4	35 (17)	37 (18)	12 (21)	13 (23)	15 (27)	15 (27)
LA diameter, cm, mean (SD)	4.2 (0.7)	4.2 (0.8)	4.3 (0.7)	4.6 (0.6)	4.2 (1)	4.6 (0.6)
LV ejection fraction, %, mean (SD)	52 (11)	52 (10)	52 (11)	50 (11)	52 (10)	50 (11)
Ablation time, min, mean (SD)	51 (29)	63 (31)	46 (18)	53 (22)	59 (26)	52 (21)
Contact force ablation catheter, n (%)	110 (54)	104 (51)	49 (87)	44 (79)	48 (86)	44 (79)
Prior AT/AFL/AF ablation, n (%)	33 (16)	46 (23)	5 (9)	12 (21)	14 (26)	15 (27)
Long-term monitoring, n (%)	59 (29)	61 (30)	16 (29)	19 (34)	16 (29)	19 (34)

Legend: y = years, HTN = hypertension, DM = diabetes mellitus, MI = myocardial infarction, HF = heart failure, TIA = transient ischemic attack, LV = left ventricle, s = seconds, min = minutes.

AF symptom severity

CCS score data were available at baseline and 6-month follow up in 177/255 patients who received PVI, 171/225 patients who received PVI + linear ablation, and 70/78 patients who received PVI + PWI. The mean change in CCS score was −2.3 (SD 1.2) among patients who received PVI, −2.3 (SD 1.2) among patients who received PVI + linear ablation, and −2 (SD 1.4) among patients who received PVI + PWI (P = .09 for difference). NYHA classification was available at baseline and 6-month follow-up in 179/255 patients who received PVI, 173/225 patients who received PVI + linear ablation, and 70 patients who received PVI + PWI. The mean change in NYHA class was −0.9 (0.8) among those who received PVI, −0.8 (0.7) among those who received PVI + linear ablation, and −0.9 (1) among those who received PVI + PWI (P = .5 for difference). Among the propensity score matched patients, change in CCS and NYHA classification is shown in Table III. There were no significant differences in the change in symptom severity between ablation strategies.

Safety outcomes

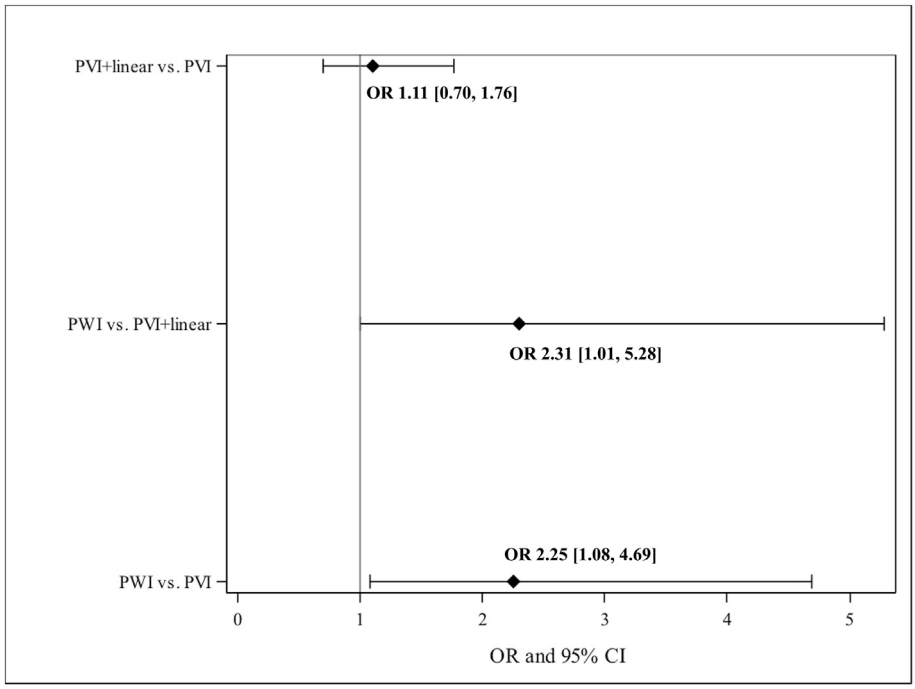
For the secondary outcome of adverse events, a total number of 19 adverse events were identified across all 3 groups. Within the PVI + PWI group, 3.8% of the subjects had an adverse event compared to 3.9% in the PVI and 2.7% in the PVI + linear groups (Table IV). Differences in complication rates were not calculated because of the small number of events across all groups.

Discussion

Our retrospective analysis suggests that PVI + PWI is associated with an increased recurrence of AT/AFL/AF at 6 months compared to PVI alone and PVI + linear ablation in patients with persistent AF. Patients undergoing PVI + PWI experienced increases in both organized AT/AFL and persistent AF compared to patients undergoing PVI or PVI + linear ablation.

The PVI + PWI technique may be associated with higher frequency of recurrent AF symptoms in our population for a variety of reasons. Although isolation of the posterior wall was confirmed at the time of the procedure, it is possible that subsequent reconnection may have occurred. Indeed, reconnection across ablation lesions is the most frequent cause of recurrent AF after PVI.[19,20] Even when achieving durable PWI with a hybrid endocardial-epicardial ablation procedure, Kumar et al demonstrated no significant reduction in the rates of

Figure 1



Forest plot of risk of recurrence of arrhythmia at follow-up. Plotted ORs for the risk of recurrence of AT/AFL/AF at 6-month follow-up for each ablation type group.

AF/AT recurrence with PVI + PWI compared to PVI,[15] suggesting that this is not the only mechanism for recurrence of arrhythmia. Patients undergoing PVI + PWI experienced a nonsignificant trend toward fewer recurrences at the 1-month follow-up compared to PVI or PVI + linear ablation and then went on to experience higher risk between 1 and 6 months. This pattern suggests that the mechanism driving increased risk of AT/AFL/AF after PVI + PWI took some time to develop after ablation.

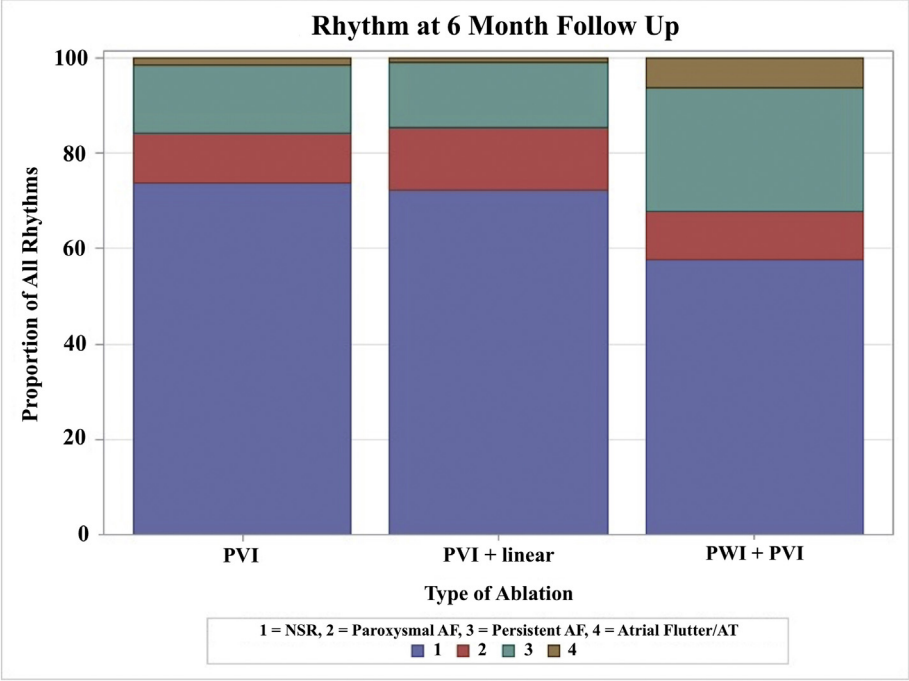
Isolating a larger area of the atrium may create substrate for a macroreentrant pathway leading to atrial flutter, and preventing recurrence of AF may allow maintenance of stable focal AT. This may explain the higher rates of AT/AFL with PVI + PWI. In a recent study by Yokokawa et al comparing different ablation methods for PVI + PWI, the authors also noted an increased incidence of AT after PVI + PWI.[21] Future studies combining PVI + PWI and ablation of the cavotricuspid isthmus and/or mitral isthmus are needed to see if suppression of AF using PWI and AT/AFL using additional linear ablation is needed. Alternative methods for achieving PWI that do not use linear ablation such as posterior wall homogenization may not create substrate for macroreentrant tachycardia and may provide different outcomes. Use of alternative methods of energy delivery such as short-duration high-energy radiofrequency or alternative energy sources such as cryotherapy, ultrasound energy, or laser therapy may also provide different results and should be further evaluated as well.

In our cohort, PVI and PVI + linear ablation have comparable rates of recurrence of AT/AFL/AF at 6 months. However, PVI + linear ablation does appear to have a lower proportion of AT/AFL compared to PVI. This is consistent with the idea that additional linear ablations disrupt macroreentrant pathways that may form as the result of PVI, as suggested by several studies.[4-6] There were no statistically significant differences in the number of adverse events across all groups, although the study was not adequately powered to evaluate this secondary outcome.

Our results are not consistent with what has previously been found in the literature, with a few smaller studies demonstrating lower rates of AF recurrence with PVI + PWI.[11,15] These studies evaluated patients with lower CHA2DS2-VASc scores and lower rates of comorbidities, which may make them more favorable candidates for extensive ablation sets with better outcomes.

There are several limitations to our study. First, this was a retrospective analysis and subjects were not randomly allocated to treatment assignment. Although we attempted to control for differences between groups using propensity scoring, we may not have controlled

Figure 2



Proportions of rhythm type at 6-month follow-up by lesion group. A visual depiction of the varying proportions of rhythm type at 6-month follow-up for each lesion group (central illustration).

Table III. Change in AF symptom severity in propensity score matched populations by ablation strategy.

	PVI n = 203	PVI + linear n = 203	*P* value	PVI n = 56	PVI + PWI n = 56	*P* value	PVI + linear n = 56	PVI + PWI n = 56	*P* value
CCS data available at baseline and 6-m follow-up (%)	140 (69)	156 (77)		45 (80)	50 (89)		42 (75)	50 (89)	
Change in CCS from baseline to 6-m follow-up, mean (SD)	−2.4 (1.1)	−2.3 (1.1)	.36	−2.3 (1.1)	−1.9 (1.4)	.16	−2.3 (1.2)	−2.0 (1.4)	.34
NYHA data available at baseline and 6 m (%)	142 (70)	158 (78)		45 (80)	51 (91)		42 (75)	51 (91)	
Change in NYHA class from baseline to 6-m follow-up, mean (SD)	−0.9 (0.7)	−0.8 (0.7)	.37	−1.1 (0.7)	−0.8 (1)	.11	−1.1 (0.7)	−0.8 (1)	.13

Legend: m = month

for all variables important to the outcome of catheter ablation for persistent AF. Second, despite the fact that this is the largest sample size of catheter ablation for PVI + PWI studied to date, we failed to reach the desired sample size of 75 PVI + PWI subjects after propensity score matching. Despite this, our finding that PVI + PWI was inferior to both PVI and PVI + linear ablation did reach significance. Third, follow-up was relatively short at 6 months. This was due to the recent development of the PVI + PWI technique. However, prior studies evaluating these ablation techniques found that recurrence rates are relatively stable after 6 months with most recurrences occurring between 3 and 6 months.[11,15] Fourth, the ablation lesion in the PVI + linear and PVI + PWI groups was heterogeneous in some cases including ablation of the cavotricuspid isthmus, mitral isthmus, or additional substrate modification. The limited sample size precluded subgroup analysis of these lesions sets, and the impact of the variety of linear ablation combinations may have affected the outcomes of interest. Long-term ECG monitoring was performed in approximately one third of the cohort, so episodes of asymptomatic AT/AFL/AF may be underreported. Finally, this study was not adequately powered to evaluate the secondary outcome of adverse events, although the total number of identified adverse events was low across all groups.

Table IV. Adverse events of total population by ablation strategy

	PVI n = 255	PVI + linear n = 225	PVI + PWI n = 78
Groin hematoma, AE fistula, pseudoaneurysm, retroperitoneal bleed, n (%)	4 (2)	3 (1)	3 (4)
TIA/stroke, n (%)	2 (1)	2 (1)	0 (0)
Phrenic nerve palsy, n (%)	1 (0)	0 (0)	0 (0)
Pericarditis, n (%)	2 (1)	1 (0)	0 (0)
HF, n (%)	1 (0)	0 (0)	0 (0)

Legend: AE = atrioesophageal

In conclusion, PWI using adjunctive linear radiofrequency ablation in addition to PVI does not appear to be as effective as PVI alone or PVI + linear ablation in reducing the recurrence of AT/AFL/AF within 6 months of the index procedure in patients with persistent AF. A prospective, randomized controlled trial comparing these ablation techniques is needed to clarify the role of extensive substrate modification for treatment of persistent AF.

Perspectives

Clinical competency in medical knowledge. After adjusting for differences in baseline characteristics, patients receiving PVI + PWI had higher rates of recurrent AT/AFL/AF PVI within 6 months of the index procedure compared to patients receiving PVI alone or PVI + linear ablation. Patients receiving PVI + PWI more frequently experienced AT and AFL compared to PVI with or without additional linear ablation.

Translational outlook. A prospective, randomized controlled trial comparing these ablation techniques is needed to clarify the role of extensive substrate modification for treatment of persistent AF.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2019.11.010.

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