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NEW INSIGHTS IN AF ABLATION

The Electrical Isolation of the Left Atrial Posterior Wall in Catheter Ablation of Persistent Atrial Fibrillation

Jung Myung Lee, MD, PhD,[a] Jaemin Shim, MD, PhD,[b] Junbeom Park, MD, PhD,[c] Hee Tae Yu, MD, PhD,[d] Tae-Hoon Kim, MD,[d] Jin-Kyu Park, MD, PhD,[e] Jae-Sun Uhm, MD, PhD,[d] Jin-Bae Kim, MD, PhD,[a] Boyoung Joung, MD, PhD,[d] Moon-Hyoung Lee, MD, PhD,[d] Young-Hoon Kim, MD, PhD,[b] Hui-Nam Pak, MD, PhD,[d] for the POBI-AF Investigators

ABSTRACT

OBJECTIVES This study explored whether complete electrical isolation of the left atrial (LA) posterior wall improves the rhythm outcome of catheter ablation of persistent atrial fibrillation (AF).

BACKGROUND Although the STAR AF2 (Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial Part II) proved no additional benefit of empirical extra-pulmonary vein (PV) LA ablation, the long-term recurrence rate after circumferential PV isolation (CPVI) alone remains high.

METHODS We randomly assigned 217 patients with persistent AF (83.1% men, age 58.7 ± 10.8 years, 73.3% long-standing persistent AF) to ablation with CPVI alone (CPVI group) or CPVI with a POsterior wall Box Isolation (POBI group). The endpoint of the POBI group was the elimination of the posterior atrial potentials by roof and posterior inferior lines and touch-up focal ablation.

RESULTS After a mean follow-up of 16.2 ± 8.8 months, the clinical recurrence rate did not significantly differ between the 2 groups (23.8% vs. 26.5%; $p = 0.779$) in the CPVI and POBI groups. The recurrence rate for atrial tachycardias (16.0% vs. 11.1%; $p = 0.913$) and cardioversion rates (6.7% vs. 13.7%; $p = 0.093$) to control clinical recurrences also did not significantly differ between the 2 groups. At the final follow-up, sinus rhythm was maintained without antiarrhythmic drug in 50.5% and 55.9% in the CPVI and POBI groups, respectively ($p = 0.522$). No significant difference was found in the major complication rates between the 2 groups, but the total ablation time was significantly longer in the POBI group (4,289 ± 1,837 s vs. 5,365 ± 2,358 s; $p < 0.001$).

CONCLUSIONS In patients with persistent AF, an empirical complete POBI did not improve the rhythm outcome of catheter ablation or influence the type of recurrent atrial arrhythmia. (Comparison of Circumferential Pulmonary Vein Isolation Alone Versus Linear Ablation in Addition to Circumferential Pulmonary Vein Isolation for Catheter Ablation in Persistent Atrial Fibrillation: Prospective Randomized Controlled Trial; NCT02721121).
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From the [a]Kyung Hee University Medical College, Seoul, Republic of Korea; [b]Korea University Cardiovascular Center, Seoul, Republic of Korea; [c]Ewha Womans University, Seoul, Republic of Korea; [d]Yonsei University Health System, Seoul, Republic of Korea; and the [e]Hanyang University, Seoul, Republic of Korea. Supported by grants (HI18C0070 and HI19C0114) from the Korea Health 21 R and D Project, Ministry of Health and Welfare, and a grant (NRF-2017R1A2B4003983) from the Basic Science Research Program run by the National Research Foundation of Korea (NRF). All authors have reported that they have no relationships relevant to the contents of this paper to disclose.
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ABBREVIATIONS AND ACRONYMS

3-D = 3-dimensional
AAD = antiarrhythmic drug
AF = atrial fibrillation
AT = atrial tachycardia
BDB = bidirectional block
CFAE = complex fractionated atrial electrogram
CPVI = circumferential pulmonary vein isolation
CT = computed tomography
E/Em = mitral inflow velocity/mitral annulus tissue velocity
ECG = electrocardiogram
LA = left atrium
POBI = posterior box isolation
PV = pulmonary vein
RF = radiofrequency
RFCA = radiofrequency catheter ablation

Radiofrequency catheter ablation (RFCA) is an effective treatment for atrial fibrillation (AF), especially symptomatic drug-refractory AF (1). The elimination of the triggers of AF through circumferential pulmonary vein isolation (CPVI) has been the most important technique for AF ablation (2). However, RFCA of persistent AF is still challenging, and CPVI alone has generally been accepted as an insufficient modality for the long-term maintenance of sinus rhythm in these populations until recently (3). This might be due to the changes in the mechanism with the progression of AF (4). In the early course of AF, triggers from the pulmonary veins (PVs) are the predominate mechanism. However, in the later stage, change in the underlying atrial substrate with remodeling becomes a more important mechanism in the persistence of AF (5). Thus, an empirical extra-PV ablation for substrate modification strategies has been developed and applied in patients with persistent AF for many years (6,7) and has been found to be beneficial in a couple of trials (8–10). In contrast, the recent randomized STAR AF2 (The Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial Part II) (11) failed to prove the beneficial effect

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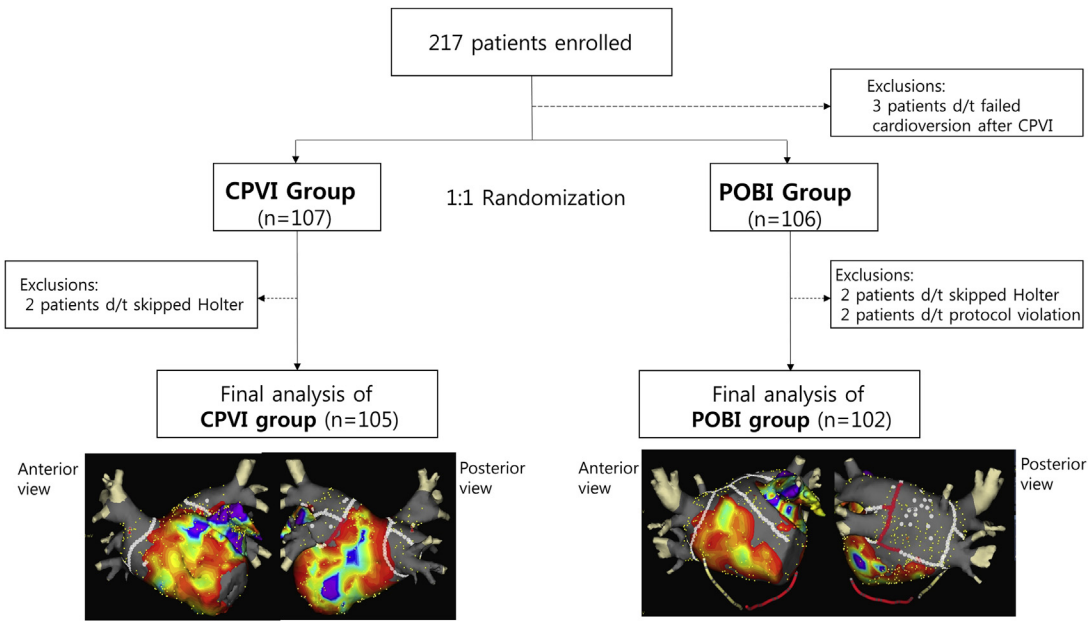
of empirical extra-PV left atrial (LA) ablation as compared with the CPVI. This may be due to the fact that the persistent AF category includes a wide spectrum of AF progression, the achievement of complete bi-directional block of multiple ablation lines is difficult, and reconnections of the CPVI and linear ablation are relatively common. Therefore, a more focused and effective ablation strategy without extensive cardiac tissue damage is required. The role of the LA posterior wall has been suggested to be involved in the initiation and maintenance mechanism of AF (12,13), and an additional Posterior wall box Isolation (POBI) was found to improve the AF-free survival in patients with persistent AF in our previous study and others (14,15). Hence, we hypothesized that additional complete electrical POBI improves the rhythm outcome of persistent AF ablation as compared with CPVI alone. To achieve a complete POBI with minimal risk of collateral damage to the posterior mediastinal structures, we conducted a focal ablation of the remnant atrial potentials on the LA posterior wall after a roof line and posterior inferior line ablation and confirmed the electrical isolation by acquiring a contact voltage map and exit block.

METHODS

STUDY POPULATION AND RANDOMIZATION. The study protocol adhered to the Declaration of Helsinki and was approved by the institutional review board. Proper written informed consent was obtained from all patients.

The study population included patients with persistent AF who underwent RFCA for symptomatic and drug-refractory non-valvular AF at 5 tertiary hospitals in Korea. Exclusion criteria were as follows: 1) AF with rheumatic valvular disease; 2) significant structural heart disease other than left ventricular hypertrophy; 3) LA diameter of ≥60 mm; and 4) history of AF ablation or cardiac surgery. Before all ablation procedures, the absence of any LA thrombi was confirmed using transesophageal echocardiography or computed tomography (CT), and the anatomy of the LA and PVs was visually defined using three-dimensional (3-D) CT scans (64-channel, Light Speed Volume CT, Philips, Brilliance 63, Amsterdam, the Netherlands). All antiarrhythmic drugs (AADs) were discontinued for at least 5 half-lives. This study was performed with an open-labeled prospective multicenter randomized protocol. Randomization was performed by core laboratory clinical research coordinators (Yonsei University), and informed consent was acquired by physicians in each participating institution. Both the patients and doctors were blinded to the initial allocation, and the rhythm outcome was registered by the research coordinators based on the Holter and electrocardiogram (ECG) documentation. This protocol was registered in the institutional review boards of each hospital and with clinicaltrials.gov (NCT02721121). The patients were prospectively and randomly assigned to 2 groups based on the method of RFCA: the CPVI alone and CPVI plus a complete POBI (with or without an anterior line) groups. **Figure 1** shows the flow chart of the patients who met the inclusion/exclusion criteria for the study population. Of the 217 enrolled patients, 3 were excluded because of an unsuccessful internal cardioversion after the CPVI, and 107 and 106 were assigned to the CPVI and POBI groups, respectively. After a successful catheter ablation procedure, 2 patients each in the CPVI and POBI groups dropped out due to skipping the protocol-based rhythm follow-up schedule, and 2 patients who did not undergo LA voltage mapping were also excluded in the POBI group due to protocol violations. Therefore, 105 and

FIGURE 1 Flow Chart of the Patients Who Met the Inclusion/Exclusion Criteria



Ablation lesions and voltage map after catheter ablation in the CPVI-alone and posterior box isolation groups. CPVI = circumferential pulmonary vein isolation; POBI = posterior box isolation.

102 patients in the CPVI and POBI groups, respectively, were finally included for the data analysis.

ECHOCARDIOGRAPHIC EVALUATION. All patients underwent transthoracic echocardiography (Sonos 5500, Philips Medical System, Andover, Massachusetts, or Vivid 7, GE Vingmed Ultrasound, Horten, Norway) before undergoing RFCA. The chamber size, transmitral Doppler flow velocity, ratio of the early diastolic peak mitral inflow velocity, and early diastolic mitral annular velocity (E/Em) were acquired following the American Society of Echocardiography guidelines. Transesophageal echocardiography was performed to exclude any intracardiac thrombi by the physician's discretion.

ELECTROPHYSIOLOGICAL MAPPING AND RFCA. The intracardiac electrograms were recorded using the Prucka CardioLa Electrophysiology system (General Electric Medical Systems, Inc., Milwaukee, Wisconsin), and RFCA was performed in all patients using a 3-D electroanatomical mapping system (NavX, St Jude Medical, Inc., Minnetonka, Minnesota, or Carto system, Biosense Webster, Diamond Bar, California) merged with 3-D spiral CT. Double transseptal punctures were performed and multiview pulmonary venograms were obtained.

TABLE 1 Baseline Clinical Characteristics

	Total (N = 207)	CPVI (n = 105)	POBI (n = 102)	p Value
Age, yrs	58.7 ± 10.8	58.6 ± 11.0	58.9 ± 10.5	0.866
Male	172 (83.1)	84 (80.0)	88 (86.3)	0.308
AF duration, months	38.5 ± 38.8	33.1 ± 31.4	44.0 ± 44.6	0.044
Long-standing PeAF	151 (73.3)	72 (69.2)	79 (77.5)	0.240
Comorbidities				
Heart failure	47 (22.7)	24 (22.9)	23 (22.5)	1.0
Hypertension	97 (46.9)	53 (50.5)	44 (43.1)	0.358
Diabetes mellitus	21 (10.1)	18 (17.1)	13 (12.7)	0.489
Stroke	23 (11.1)	13 (12.4)	10 (9.8)	0.712
TIA	3 (1.4)	1 (1.0)	2 (2.0)	0.966
Vascular disease	13 (6.3)	6 (5.7)	7 (6.9)	0.942
CHA_2DS_2-VASc score	1.72 ± 1.45	1.9 ± 1.6	1.6 ± 1.3	0.139
Echocardiographic parameters				
LA dimension, mm	44.8 ± 6	44.5 ± 6.7	45.0 ± 5.3	0.560
LA volume index, ml/m^2	43.7 ± 12.8	43.3 ± 12.2	44.2 ± 13.4	0.644
LV ejection fraction, %	59.0 ± 9.2	58.8 ± 9.5	59.2 ± 9.0	0.751
E/Em	10.1 ± 4.3	10.6 ± 5.0	9.6 ± 3.4	0.098
LVEDD, mm	50.2 ± 5.3	50.6 ± 5.5	49.9 ± 4.7	0.352
LVMI, g/m^2	93 ± 22.5	93.8 ± 24.6	92.2 ± 20.2	0.605

Values are mean ± SD or n (%).

AF = atrial fibrillation; CPVI = circumferential pulmonary vein isolation; E/Em = mitral inflow velocity/mitral annulus tissue velocity; LA = left atrium; LV = left ventricle; LVEDD = left ventricular end-diastolic diameter; LVMI = left ventricular mass index; PeAF = persistent atrial fibrillation; POBI = posterior box isolation; TIA = transient ischemia attack.

TABLE 2 Procedure-Related Characteristics

	Total (N = 207)	CPVI (n = 105)	POBI (n = 102)	p Value
Procedure time, min	216.6 ± 71.4	206.8 ± 77.7	226.7 ± 63.1	0.044
Ablation time, s	4,819 ± 2,172	4,289 ± 1,837	5,365 ± 2,358	<0.001
Fluoroscopy time, min	36.5 ± 17.4	35.0 ± 18.2	38.0 ± 16.6	0.224
Ablation targets				
CPVI	207 (100.0)	105 (100.0)	102 (100.0)	
POBI	102 (49.3)	0 (0.0)	102 (100.0)	
Anterior line (BDB/attempted)	59/85	0/0	59/85 (69.4*)	
Extra PV triggers				
LA	5 (2.4)	3 (2.9)†	2 (2.0)‡	1.000
RA	3 (1.4)	0 (0.0)	3 (2.9)§	0.118
Complications‖	13 (6.3)	7 (6.6)	6 (5.9)	0.439
Major complications	7 (3.4)	6 (5.7)	1 (1.0)	0.134
Tamponade	4 (1.9)	4 (3.8)	0 (0.0)	0.137
Sinus node dysfunction¶	2 (1.0)	1 (0.9)	1 (1.0)	1.0
Atrioesophageal fistula	1 (0.5)	1 (1.0)	0 (0.0)	1.0
Minor complications				
Pericarditis	3 (1.4)	1 (1.0)	2 (2.0)	0.618
Pseudoaneurysm	2 (1.0)	0 (0.0)	2 (2.0)	0.242

Value are mean ± SD or n (%). *Percentage was calculated among those who had undergone an anterior line ablation. †Trigger locations were left atrial septum (1), posterior wall (1), and distal coronary sinus (1). ‡Trigger locations were left atrial septum (1), and mitral annulus (1). §Trigger locations were crista terminalis (2) and tricuspid annulus (1). ‖Complications: pericarditis, pseudoaneurysm, pericardial effusion, cardiac tamponade, sinus node dysfunction, atrioesophageal fistula. ¶All sinus node dysfunction recovered within 24 h after the procedure.

BDB = bidirectional block; PV = pulmonary vein; RA = right atrium; other abbreviations as in Table 1.

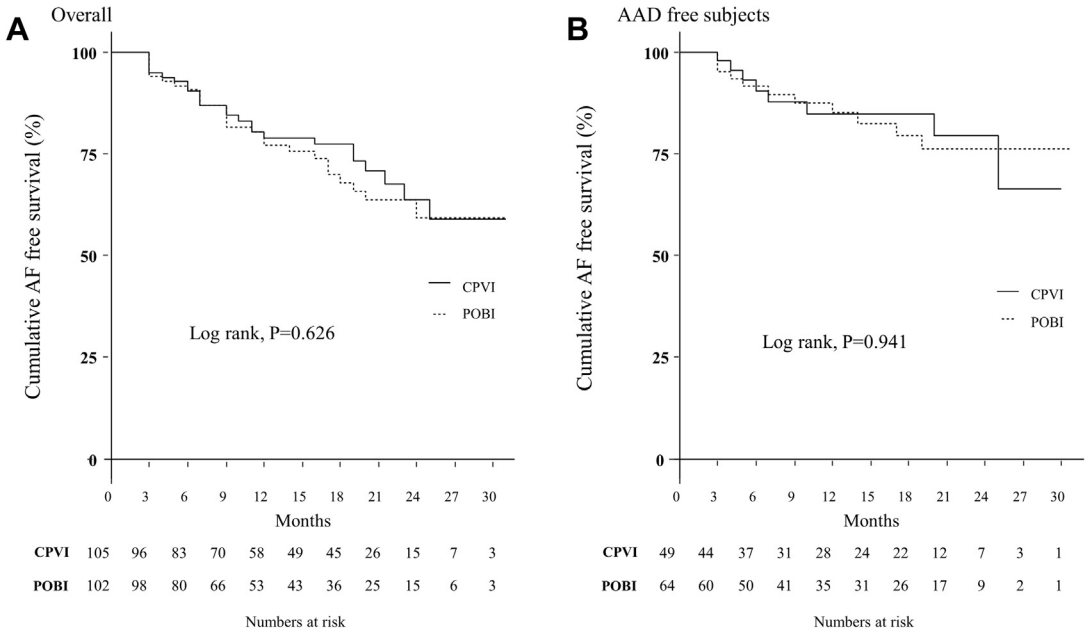
The details of the RFCA technique and strategy have been described in our previous studies (16). Briefly, for the CPVI ablation, continuous circumferential lesions were created at the level of the LA antrum encircling the right and left PVs guided by the electroanatomical mapping system using an open-irrigated, 3.5-mm tip deflectable catheter (SmartTouch, Biosense Webster, Inc., Coolflex, St. Jude Medical, Inc.; 30 to 35 W; 45°C). We performed a CPVI and cavotricuspid isthmus ablation in all patients. The CPVI was verified during an isoproterenol infusion after a 30-min waiting time. For the POBI group, the linear ablations along the roof and posterior inferior wall were performed by connecting both sides of the CPVI at the top and bottom levels, respectively. We defined the POBI as: 1) successful bidirectional block of the roof line; 2) voltage abatement of <0.1 mV in the LA posterior wall; and 3) entrance and exit block. Although the achievement of a bidirectional block of the posterior inferior line was not mandatory, we could eliminate remnant potential in LA posterior wall (Online Figure 1A) by touch-up ablations and confirm POBI by voltage map and entrance and exit blocks (Online Figure 1B). We achieved those criteria in all patients in the POBI group. The achievement of bidirectional block of the posterior inferior line was not mandatory due to the risk of esophageal injury. Instead, we conducted a voltage map-guided point ablation for any remnant atrial potentials on the LA posterior wall to achieve a complete POBI, and confirmed the electrical exit block of POBI by 10 mA pacing. An additional anterior linear ablation was performed in the POBI group (mostly in patients with long-standing persistent AF) based on the physician's discretion by ablation from the mitral annulus at the 12 o'clock position toward the LA roof line (10).

POST-ABLATION VOLTAGE MAP AND THE ABLATION ENDPOINT. After the CPVI and/or linear ablation, we acquired a LA voltage map during high right atrial pacing at 500 ms to prevent any rate-dependent activation changes. In patients with sustaining AF or atrial tachycardia (AT) after the protocol-based ablation lesion set, we restored sinus rhythm using internal cardioversion. We obtained the peak-to-peak amplitude of the contact bipolar electrograms from 350 to 500 points on the LA endocardium. In the POBI group, we repeated the LA posterior wall voltage map until the elimination of any remnant atrial potentials (bipolar voltage ≥0.2 mV) on the entire LA posterior wall. Figure 1 shows the typical ablation lesions and voltage map after catheter ablation for the CPVI alone and POBI groups. After completion of the protocol-based ablation, the procedure ended when no immediate recurrence of AF was observed within 10 min after cardioversion with an isoproterenol infusion (5 μg/min). If further AF triggers or frequent unifocal atrial premature beats were observed under the isoproterenol effect, the extra-PV foci were ablated as much as possible.

POST-ABLATION MANAGEMENT AND FOLLOW-UP. The patients visited the outpatient clinic regularly at 1, 3, 6, and 12 months and then every 6 months thereafter or whenever symptoms occurred after the RFCA. All patients underwent ECG during each visit and 24-h Holter recording at 3 and 6 months and every 6 months, based on the 2017 HRS/EHRA/ECAS/APHRS/SOLACE Expert Consensus Statement guidelines (17). Holter monitoring or event monitor recordings were obtained when patients reported palpitations suggestive of arrhythmia recurrence. AF recurrence was defined as any episode of AF or AT of at least 30 s in duration. Any ECG documentation of an AF recurrence within a 3-month blanking period was diagnosed as an early recurrence, and an AF recurrence at more than 3 months after the procedure was diagnosed as a clinical recurrence.

DATA ANALYSIS. We estimated the sample size based on the pilot data of participating institutions and previous reports (14,15). To calculate proper

FIGURE 2 Kaplan-Meier Analysis of the AF Recurrence-Free Survival Rate



Kaplan-Meier analysis of the AF recurrence-free survival rate in the overall subjects **(A)** and AAD-free subjects **(B)** based on 1 of 2 ablation strategies. AF = atrial fibrillation; AAD = anti-arrhythmic drug; other abbreviations as in Figure 1.

sample size, we used R software version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria) with "pwr" package (parameters: p1 = 0.38, p2 = 0.20, power = 80%, alpha = 0.05). Continuous variables were summarized as the mean ± SD and were compared using Student's *t*-tests. Categorical variables were summarized as a proportion of the group total and were compared using chi-squared tests or Fisher exact tests, where appropriate. All outcome analyses were performed on patients who underwent RFCA and were followed for longer than the initial 3-month blanking period. A Kaplan-Meier analysis with a log-rank test was used to calculate the AF recurrence-free survival over time and to compare the recurrence rates across the groups. A 2-sided $p < 0.05$ was considered to indicate statistical significance. The statistical analyses were performed using R software version 3.5.2.

RESULTS

PATIENT CHARACTERISTICS. The baseline clinical characteristics of the CPVI alone (n = 105) and complete POBI groups (n = 102) are summarized in Table 1. The mean age was 58.7 ± 10.8 years, and 172 patients (83.1%) were men. The mean CHA_2DS_2-VASc

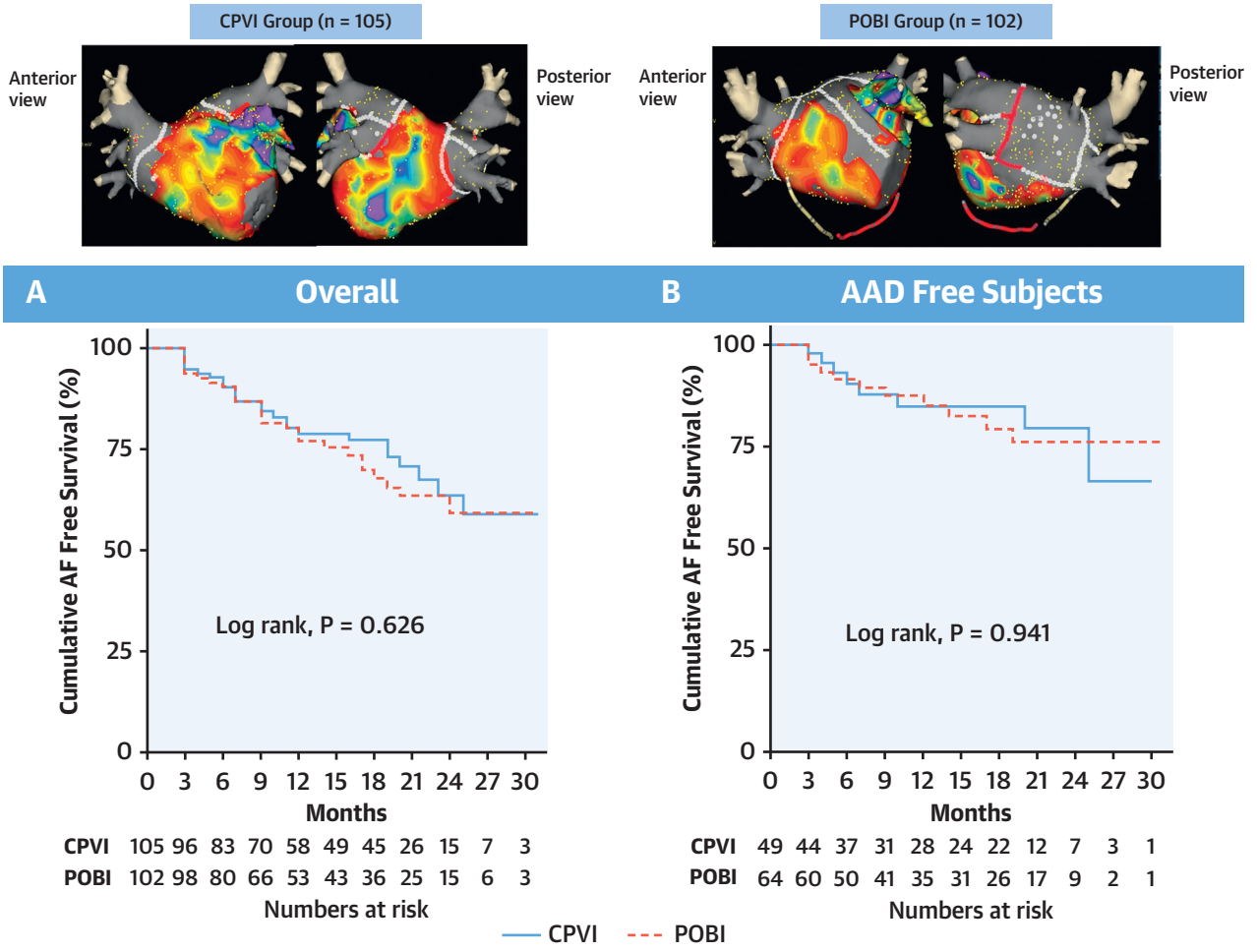
TABLE 3 Clinical Rhythm Outcomes

	Total (N = 207)	CPVI (n = 105)	POBI (n = 102)	p Value
Post-ABL medication				
ACEI or ARB	71 (34.3)	41 (39.0)	30 (29.4)	0.189
Beta blocker	81 (39.1)	45 (43.7)	36 (36.0)	0.329
Statin	68 (32.9)	37 (34.9)	31 (31.0)	0.552
AAD use				
AADs at discharge	90 (43.5)	54 (52.4)	36 (36.0)	0.027
AADs after 3 months	97 (46.9)	54 (51.4)	43 (42.2)	0.231
AADs at clinical recurrence	33/52 (63.5)	15/25 (60.0)	18/27 (66.7)	0.618
AADs at final follow-up	86 (41.5)	48 (45.7)	38 (37.3)	0.217
Clinical recurrence	52 (25.1)	25 (23.8)	27 (26.5)	0.779
Recurrence type AF	45 (86.5)	21 (84.0)	24 (88.9)	0.913
Recurrence type AT	7 (13.5)	4 (16.0)	3 (11.1)	0.913
Cardioversion	21 (10.1)	7 (6.7)	14 (13.7)	0.093
Single procedure success, off AAD	110 (53.1)	53 (50.5)	57 (55.9)	0.522
Repeat AF ablation	13 (6.3)	3 (2.9)	10 (9.8)	0.076
PV reconnection cases				0.733
No PV reconnection	2	0 (0.0)	2 (20.0)	
≥1 PV reconnections	11	3 (100.0)	8 (80.0)	
POBI reconnection		NA	5 (50.0)	NA
Anterior line reconnection		NA	4 (66.7)*	NA

Values are n (%). *6 patients underwent complete anterior line block at the first RFCA.

AAD = antiarrhythmic drug; ABL = ablation; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; AT = atrial tachycardia; NA = not applicable; POBI = posterior box isolation; RFCA = radiofrequency catheter ablation; SR = sinus rhythm; other abbreviations as in Tables 1 and 2.

CENTRAL ILLUSTRATION **Single Procedure AT/AF Freedom Between CPVI-Alone Group and POBI Group**



Lee, J.M. et al. J Am Coll Cardiol EP. 2019;5(11):1253-61.

Single procedure AT/AF freedom with **(A)** and without antiarrhythmic drugs between CPVI-alone group and POBI group **(B)**. AAD = antiarrhythmic drug; AF = atrial fibrillation; AT = atrial tachycardia; CPVI = circumferential pulmonary vein isolation; POBI = posterior box isolation.

(Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65 to 74 years, Sex category) score was 1.7 ± 1.5. Of the 207 study participants, 47 (22.7%) had a history of heart failure, and 97 (46.9%) had hypertension. No significant difference was found in the comorbidities between the groups (p = NS). The 2 ablation groups were well balanced with regard to the baseline demographics and echocardiographic parameters. However, the duration of AF (time from the first diagnosis of AF) in the patients assigned to the POBI group was longer than that in those in the CPVI group (33.1 ± 31.4 months vs. 44.0 ± 44.6 months; p = 0.044).

COMPARISON OF THE PROCEDURAL CHARACTERISTICS. The procedural results and clinical outcomes are summarized in Table 2. The total procedure time (206.8 ± 77.7 min vs. 226.7 ± 63.1 min; p = 0.044) and radiofrequency (RF) energy delivery time (4,289 ± 1,837 s vs. 5,365 ± 2,358 s; p < 0.001) were significantly longer in the POBI group. A posterior wall isolation was achieved in all patients assigned to the POBI group. An anterior line was added in 83.3% of the POBI group, and bidirectional block of the anterior line was achieved in 69.4%. There was no cross-over to the other ablation strategy. No statistical difference was found in the complication rates between the 2 groups (Table 2). Although the major complication rate did not

significantly differ between the 2 groups, 1 patient had an atrioesophageal fistula in the CPVI alone group. That patient died because of a major stroke and septic shock 3 months after the AF ablation, and the family members refused surgical treatment.

PRIMARY OUTCOME. During the 16.2 ± 8.8 month follow-up, neither the early recurrence rate within 3 months of the RFCA (40.0% vs. 45.1%; p = 0.548) nor the clinical recurrence rate (23.8% vs. 26.5%; p = 0.779) significantly differed between the CPVI alone and POBI groups. The Kaplan-Meier analysis showed no significant difference in the overall AF recurrence (log-rank; p = 0.626) or AAD-free AF recurrence (log-rank; p = 0.941) (**Figure 2**) between the 2 groups. Although the AAD prescription rate in the CPVI group was higher than that in the POBI group at discharge (p = 0.027), it did not differ after a 3-month blanking period (p = 0.231) or at the time of the clinical recurrence (p = 0.618) (**Table 3**). Finally, the freedom from any documented AF without AADs was 50.5% and 55.9% in the CPVI alone and POBI groups, respectively (p = 0.522). The presence of bidirectional block of the anterior line in the POBI group did not affect the clinical recurrence rate (23.7% [14 of 59] with complete block vs. 23.1% [6 of 26] with incomplete block; p = 0.948) (Online Table 1).

SECONDARY OUTCOME. Of 52 patients with clinical recurrences, 45 and 7 had AF and AT, respectively, at the time of the recurrence. Among the patients with a clinical recurrence, the proportion of AT (16.0% [4 of 25] vs. 11.1% [3 of 27]; p = 0.913) and that requiring cardioversion (28.0% [7 of 25] vs. 51.9% [14 of 27]; p = 0.142) did not significantly differ between the CPVI alone and POBI groups. Overall, 6.7% (7 of 105) and 13.7% (14 of 102) of the CPVI and POBI groups underwent cardioversion to control AAD-resistant recurring atrial arrhythmias. Finally, sinus rhythm was maintained without AAD in 50.5% and 55.9% in the CPVI and POBI groups, respectively (p = 0.522), with a single procedure (**Table 3**).

Repeat ablation procedures were performed in 13 patients (2.9% in the CPVI group vs. 9.8% in the POBI group; p = 0.076), and reconnected PV potentials were found in 100% (3 of 3) and 80% (8 of 10) in the CPVI and POBI groups, respectively. In 10 patients in the POBI group who underwent repeat procedures, we found the reappearance of atrial potentials at the POBI site in 50% and reconnections of a previously blocked LA anterior line in 66.7% (4 of 6) (**Table 3**).

DISCUSSION

MAIN FINDINGS. In this prospective multicenter randomized study, we evaluated the role of a complete POBI in addition to the CPVI for RF ablation in patients with persistent AF. We found no reduction in the AF recurrence with the additional POBI despite a longer procedure time, and the 1-year recurrence rate was substantial regardless of any additional extra-PV ablation after the CPVI (**Central Illustration**). Therefore, a routine empirical extra-PV LA ablation is not justified with the current technology, and more sophisticated mapping techniques for non-PV foci and long-lasting CPVI ablation methods are required.

RHYTHM OUTCOME OF THE PERSISTENT AF ABLATION. Why is it really difficult to obtain a good rhythm outcome after persistent AF ablation? This question is answered by considering not only the nature of the disease, but also the individual characteristics of the patient and the ablation technique. Because AF is a progressive degenerative disease, the persistent AF category includes AF with varying degrees of atrial remodeling (18). Therefore, obtaining consistent good results is difficult with a single empirical ablation lesion set. In the presence of significant atrial remodeling, extra-PV triggers are known to play an important role in the AF induction and maintenance (5), and an empirical extra-PV LA ablation, such as a linear ablation or complex fractionated atrial electrogram (CFAE)-guided ablation, has been performed in patients with persistent AF (6,7). Haissaguerre et al. (19) proposed a rational linear ablation protocol called the stepwise approach, and its clinical utility for an empirical linear ablation has been demonstrated in several non-randomized clinical studies (8–10). However, Verma et al. (11) reversed this dogma by showing that an empirical extra-PV ablation has no additional benefit over the CPVI in a multicenter prospective randomized trial. After the STAR AF2 report, the frequency of an empirical extra-PV ablation significantly decreased, but no difference was found in the rhythm outcome in our cohort study (20). Current guidelines also do not recommend a routine empirical extra-PV ablation in patients with persistent AF (17).

COMPARISON WITH THE STAR AF2. Compared with STAR AF2, this study focused on the mechanistic role of the LA posterior wall and the difficulty in achieving a complete POBI. Embryologically, the LA posterior wall is derived from the primitive PVs, which play an important role in maintaining AF (13) with a complex fiber orientation at the venoatrial junctions merging with the septopulmonary bundle (21). Although Kim et al. (22) reported a better rhythm outcome after a complete POBI during the de novo ablation procedure in patients with persistent AF, the complete POBI rate was 56%, and it decreased to 35% during the repeat

procedure. The main reason for the difficulty in achieving a complete POBI is because the posterior inferior line is attached to the esophagus. To overcome this, the present study achieved a complete POBI by a focal ablation of the remnant atrial potentials after a linear ablation and confirmed the complete isolation by a voltage map and exit block at high-output pacing. Compared with the STAR AF2, the patient population in terms of age, AF duration, and LA size, the bidirectional block rate of the linear ablation (74% vs. 69% of anterior line) and AAD maintenance rate (47% vs. 44%) were similar between the 2 studies. In this study, we found that an empirically conducted complete POBI did not show any additional benefit in the rhythm outcome of the persistent AF ablation, which was consistent with the STAR AF2. Therefore, it is time to re-evaluate whether linear lesion set, which was proposed by Cox in 1987 (23), is mandatory for AF rhythm control.

HOW TO IMPROVE THE PERSISTENT AF ABLATION OUTCOME? In contrast to the 1-year AF-free survival rate of the STAR AF2 of 50% to 60%, it was approximately 80% in this study. The recurrence rate of AT in the POBI group was not higher than that in the CPVI alone group. This might have been due to the endurance of the ablation with a moderately increased RF power (20) or complete electrical isolation of the LA posterior wall. Isoproterenol provocation and additional ablation of non-PV foci may also improve the outcome (24). Another convincing difference is that the STAR AF2 used a stricter rhythm monitoring protocol by using a trans-telephonic monitor. Although we followed the practice guidelines (17), rhythm monitoring by using Holter monitoring may overestimate the success rate compared with continuous monitoring by an implantable loop recorder. To improve the persistent AF ablation outcome, early intervention might be better during the early persistent AF stage (17). A long-lasting CPVI is essential to guarantee a better rhythm outcome, and we expect a better long-term outcome after a high-power short duration CPVI (25) or cryoballoon ablation (26). Detection and ablation of non-PV foci play an important role in improving the clinical outcome (24), but the current mapping technology has limitations regarding trigger mapping; hence, the proper concomitant use of AADs is also important. A personalized approach based on precision medicine, such as a simulation-guided ablation integrated by an image-based anatomy and individualized low-voltage area based on a tailored ablation strategy, may improve the ablation outcome in patients with persistent AF (27–29). Therefore, a strategy that targets patient-specific traits and a focused but long-lasting electrical isolation is needed rather than sticking to the universal ablation lesion set in patients with persistent AF.

STUDY LIMITATIONS. First, we did not include a strategy combining a CFAE ablation. A previous study suggested that a combined ablation strategy for CPVI, CFAE, and linear lesions may be the most effective method to prevent recurrent atrial arrhythmias (9). However, a meta-analysis showed that CFAE ablation did not improve the clinical outcome after RFCA of persistent AF (30). Second, we did not use any maneuvers, such as adenosine provocation, to test the durability of the PV isolation. However, we used an isoproterenol challenge and 30-min waiting time to detect any PV reconnections. Third, the current study included a relatively small number of patients; hence, the findings from this study cannot be generalized to all patients with persistent AF. Complete bidirectional block of the anterior line could not be achieved in approximately 30% of patients in the POBI group, and it may have affected the results of the RFCA. Nevertheless, the clinical recurrence rate did not significantly differ in the patients who had a complete bidirectional block of the anterior line was achieved (Online Table 1). Despite the conflicting data, monitoring of the esophageal temperature might be useful. One patient in the CPVI only group who did not underwent esophageal temperature monitoring died of atrioesophageal fistula.

CONCLUSIONS

In patients with persistent AF, an empirical POBI did not improve the rhythm outcome of the catheter ablation or influence the type of recurrent atrial arrhythmia. Therefore, a routine empirical extra-PV LA ablation is not justified with the current technology, and a more sophisticated mapping technique for non-PV foci and long-lasting CPVI ablation methods are required.

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ADDRESS FOR CORRESPONDENCE: Dr. Hui-Nam Pak, Yonsei University Health System, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea. E-mail: hnpak@yuhs.ac.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In patients with persistent AF, PV isolation alone has shown a considerable recurrence rate. Additional LA ablation beyond PV has not been proven beneficial. However, some investigators suggested than the additional ablation for the posterior wall may improve the outcome of catheter ablation.

TRANSLATIONAL OUTLOOK: Addition of posterior wall ablation achieving no remnant electrical potential on posterior wall by point-by-point ablation was technically feasible. However, routine addition of posterior wall ablation did not improve the rhythm outcome. More sophisticated technique such as a tailored ablation strategy by individual electrical characteristics of substrate and more effective ablation methods are needed.

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KEY WORDS catheter ablation, linear ablation, persistent atrial fibrillation, recurrence

APPENDIX For a supplemental figure and table, please see the online version of this paper.