

Challenging Achievement of Bidirectional Block After Linear Ablation Affects the Rhythm Outcome in Patients With Persistent Atrial Fibrillation

Tae-Hoon Kim, MD; Junbeom Park, MD, PhD; Jae-Sun Uhm, MD, PhD; Jong-Youn Kim, MD, PhD; Boyoung Joung, MD, PhD; Moon-Hyoung Lee, MD, PhD; Hui-Nam Pak, MD, PhD

Background—It is not clear whether bidirectional block (BDB) of linear ablations reduces atrial fibrillation (AF) recurrence after radiofrequency catheter ablation. We hypothesized that BDB of linear ablation has prognostic significance after radiofrequency catheter ablation for persistent AF.

Methods and Results—Among 1793 consecutive patients in the Yonsei AF ablation cohort, this observational cohort study included 398 patients with persistent AF (75.6% male; age, 59.8 ± 10.3 years) who underwent catheter ablation with a consistent ablation protocol of the Dallas lesion set: circumferential pulmonary vein isolation; cavotricuspid isthmus ablation (CTI); roof line (RL); posterior-inferior line (PIL); and anterior line (AL). BDB rates of de novo ablation lines were 100% in circumferential pulmonary vein isolation, 100% in CTI, 84.7% in RL, 44.7% in PIL, and 63.6% in AL. During 29.0 ± 18.4 months of follow-up, 31.7% (126/398) of the patients showed clinical recurrence. Left atrial posterior wall (LAPW) isolation (BDBs of RL and PIL) was independently associated with lower clinical AF/atrial tachycardia recurrence (hazard ratio, 0.68; 95% Cl, 0.47–0.98; *P*=0.041; log-rank, *P*=0.017), whereas BDBs of RL or AL were not (log-rank, *P*=0.178 for RL; *P*=0.764 for AL). Among 52 patients who underwent repeat procedures (23.0±16.1 months after de novo procedure), the BDB maintenance rates for CTI, RL, PIL, and AL were 94.2% (49 of 52), 63.5% (33 of 47), 62.1% (18 of 29), and 61.8% (21 of 34), respectively.

Conclusions—Although PIL crosses the esophageal contact area, LAPW isolation is important for better clinical outcome in catheter ablation with a linear ablation strategy for patients with persistent AF. (*J Am Heart Assoc.* 2016;5: e003894 doi: 10.1161/JAHA.116.003894)

Key Words: atrial fibrillation • catheter ablation • linear ablation • posterior wall isolation

G atheter ablation is an established treatment modality for patients with paroxysmal atrial fibrillation (AF),¹ and circumferential pulmonary vein isolation (CPVI) is the cornerstone technique of AF catheter ablation.² However, in persistent AF (PeAF), non-pulmonary-vein (PV) triggers play important roles in the pathophysiology and CPVI alone generally does not achieve a satisfactory clinical outcome.³ Therefore, many additional substrate modification strategies

Correspondence to: Hui-Nam Pak, MD, PhD, 50 Yonseiro, Seodaemun-gu, Seoul, Korea 120-752. E-mail: hnpak@yuhs.ac

Received May 12, 2016; accepted September 9, 2016.

have been proposed for PeAF ablation. One of the most widely used strategies is additional linear ablation in conjunction with CPVI^{4,5}; however, the benefit of additional linear lesions remains controversial. Although many previous studies have demonstrated an incremental benefit of additional linear ablation post-CPVI,4-8 linear ablation can be technically challenging to achieve bidirectional block (BDB), may be proarrhythmic if it is incomplete, and has a risk of complications.9 A recent large, randomized, controlled trial, STAR AF II, showed no incremental benefit of additional linear ablation with a 74% BDB rate of additional linear lesions.¹⁰ Because it is not clear whether completeness of linear ablations influences the clinical outcome of catheter ablation, we hypothesized that BDB of linear ablation has prognostic significance after catheter ablation for persistent AF. The aims of this study were to (1) characterize the rate of achievement of complete BDB for each linear ablation lesion and durability of BDB at repeat procedures, (2) explore predictors for BDB achievement, and (3) investigate the prognostic value of complete BDB of each linear lesion after the procedure among patients with persistent AF who underwent catheter ablation.

From the Yonsei University Health System, Seoul, Korea (T.-H.K., J.-S.U., J.-.Y.K., B.J., M.-H.L., H.-N.P.); Ewha Womans University, Seoul, Korea (J.P.).

Accompanying Tables S1, S2 and Figure S1 are available at http://jaha.ahajournals.org/content/5/10/e003894/DC1/embed/inline-supplementarymaterial-1.pdf

^{© 2016} The Authors. Published on behalf of the American Heart Association, Inc., by Wiley Blackwell. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Methods

Study Population

The study protocol adhered to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board at Yonsei University Health System. All patients provided written informed consent for inclusion in the Yonsei AF Ablation Cohort Database (ClinicalTrials.gov Identifier: NCT02138695). Among 1793 patients with AF who underwent catheter ablation, the study population included 398 patients with PeAF (75.6% male; age, 59.8 ± 10.3 years) who underwent a catheter ablation procedure with a consistent ablation protocol of the Dallas lesion set: CPVI; cavotricuspid isthmus (CTI) ablation; posterior wall box lesion (roof line [RL] and posterior inferior line [PIL]); and anterior line (AL).⁶ Exclusion criteria were as follows: (1) permanent AF refractory to electrical cardioversion; (2) AF with valvular disease >grade 2; (3) any form of cardiomyopathy with uncontrolled heart failure or a left ventricular ejection fraction of <45%; (4) congenital heart disease; (5) history of cardiac surgery; and (6) previous ablation procedure. Before all ablation procedures, the anatomy of the LA and PV was visually defined on three-dimensional (3D) computed tomography (CT) scans (64 Channel, Light Speed Volume CT; Brilliance 63; Philips, Best, The Netherlands). All antiarrhythmic drugs were discontinued for a period of at least 5 half-lives, and amiodarone was stopped at least 4 weeks before the procedure.

Electrophysiological Mapping

Intracardiac electrograms were recorded using the Prucka CardioLab Electrophysiology system (General Electric Medical Systems, Inc., Milwaukee, WI), and radiofrequency (RF) catheter ablation (RFCA) was performed in all patients using 3D electroanatomical mapping (NavX, St. Jude Medical, Inc., Minnetonka, MN) merged with 3D spiral CT. Double transseptal punctures were made and multiview pulmonary venograms were obtained. After securing trans-septal access, a circumferential PV-mapping catheter (Lasso; Biosense-Webster Inc., Diamond Bar, CA) was introduced with a long sheath (Schwartz left 1; St. Jude Medical). Systemic anticoagulation was performed with intravenous heparin to maintain an activated clotting time of 350 to 400 seconds during the procedure. For electroanatomical mapping, 3D geometry of both the left atrium (LA) and PV was generated using the NavX system and then merged with 3D spiral CT images.

RFCA

Details of the RFCA technique and strategy used in our center are described in our previous study.¹¹ Briefly, we used an open irrigated-tip catheter (Coolflex; 25–35 W, irrigation rate of 10–15 mL/min; St. Jude Medical) to deliver RF energy for ablation. All patients initially underwent CPVI and CTI ablation. RL, PIL, and AL⁶ were added as the standard lesion set, also known as the "Dallas lesion set" (Figure 1A). To generate the posterior box lesion, linear ablations of RL and PIL were made by connecting both sides of the CPVI at the top and bottom levels, respectively. AL was generated by ablation from the mitral annulus at the 12 o'clock position toward the LA RL.⁶ If atrial tachyarrhythmias could not be terminated by standard lesion set ablation, internal cardioversion and evaluation of BDB state were performed. BDB of RL was confirmed by differential pacing from LA appendage versus LA posterior



Figure 1. A, Catheter Dallas lesion ablation set with electroanatomical activation map acquired during stable right atrial pacing revealing LAPW isolation without AL block. B, The same patient recurred as atrial tachycardia, and the redo mapping (activation map) 32 months after the index procedure shows focal tachycardia originated from LAPW and conducted to the anterior portion of LA through the reconnected RL. AL indicates anterior line; AT, atrial tachycardia; LAPW, left atrial posterior wall; RL, roof line.

wall (LAPW) and successful generation of PIL was considered to be achievement of LAPW isolation, which was defined as no endocardial electrogram in the LAPW with a setting of RL block and no capture of isolated LAPW pacing (Figure 1A). BDB of AL was confirmed by differential pacing from LA appendage versus LA septum.⁶ When BDB of linear ablation lines was not achieved, additional ablations were performed to achieve BDB of these lines. However, if BDB could not be achieved after 3 attempts of linear ablation, those lines were kept unblocked to avoid collateral damage. The operators could opt to perform additional ablations in the superior vena cava or non-PV foci, or conduct complex fractionated electrograms¹² at their discretion. If there were mappable AF triggers or atrial premature beats with isoproterenol infusion (5 μ g/min), we carefully mapped and ablated those non-PV foci as much as possible. All RFCA procedures were conducted according to the above specific protocol by 2 operators with more than 10 years of experience.

Postablation Management and Follow-up

Among 398 patients, 95 (23.9%) maintained antiarrhythmic medication before AF recurrence because of a high chance of recurrence with frequent atrial premature beats or short runs of nonsustained atrial tachycardia (AT). Patients visited the outpatient clinic regularly at 1, 3, 6, and 12 months post-RFCA and then every 6 months thereafter or whenever they experienced symptoms. All patients underwent electrocardiography (ECG) during every visit and 24-hour Holter recording at 3 and 6 months and then every 6 months, in accord with the 2012 HRS/EHRA/ECAS Expert Consensus Statement guidelines.¹³ However, patients reporting symptoms of palpitations underwent Holter monitor or event monitor recordings and were evaluated for the possibility of arrhythmia recurrence. The primary endpoint was the clinical recurrence of atrial tachyarrhythmia as any episode of AF or AT lasting for at least 30 seconds in duration.¹³ Any ECG documentation of AF/AT recurrence after 3 months of the blanking period was diagnosed as clinical recurrence.¹³ However, AF/AT recurrence in the first 3 months after catheter ablation (blanking period) was counted as early recurrence. Early recurrence was neither classified as clinical AF/AT recurrence nor used in all data analyses.

Statistical Analysis

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences, Chicago, IL) software for Windows (version 20.0). Continuous variables were expressed as mean \pm SD and were compared using the Student *t* test. Categorical variables were reported as frequency (percentage) and compared using chi-square test and Fisher's exact test.

Kaplan-Meier analyses with log-rank tests were used to calculate AF recurrence-free survival over time and compare recurrence rates across groups. Logistic regression analyses were used to identify predictors of LAPW isolation, and Cox regression analyses were used to assess independent predictors of AF and/or AT recurrence after RFCA. Age, sex, and all other variables with P value of less than 0.1 in the univariate analyses were selected for the multivariate analyses. Once AF/AT recurrence was documented by ECG after 3 months of blanking period, we considered those patients as clinical recurrence of AT/AF. Therefore, the repeated measurements of ECG or Holter recording after clinical recurrence event were not used in statistical analyses. The duration between catheter ablation and first documentation of AF/AT recurrence after 3 months of blanking period was calculated as month and used in Kaplan-Meier analysis and Coxregression analysis. A P<0.05 (two-sided) was considered to be statistically significant.

Results

Baseline Characteristics

Baseline characteristics of overall study population with respect to the presence or absence of clinical AF/AT recurrence are shown in Table 1. There were no differences in baseline characteristics between patients with clinical AF/AT AT recurrence and those without.

Table 2 summarizes the procedural characteristics. In 398 patients with PeAF who achieved 100% CPVI, BDB rates of additional linear ablations were 100% in CTI, 84.7% in RL, 44.7% in PIL (confirmed by LAPW isolation in patients with BDB of RL), and 63.6% in AL. LAPW isolation has a same meaning to achievement of both RL and PIL blocks, and no patient showed PIL block without RL block. There were no differences in the rate of achievement of BDBs for CTI, RL, PIL, and AL between patients with clinical recurrence and those without. Patients with clinical AF/AT recurrence showed longer total procedural time than those without clinical AF/AT recurrence (234.67 \pm 56.21 vs 210.70 \pm 47.86 minutes; *P*<0.001), but no difference in ablation time (6424.69 \pm 1594.93 vs 6345.24 \pm 1217.80 seconds; *P*=0.586).

Predictors of Successful BDB of Additional Lines

Table 3 shows logistic regression analysis of predictors for successful BDB of additional linear ablation lines. There were no significant predictors for BDB achievement of RL and PIL. Older age (odds ratio [OR], 1.03; 95% CI, 1.01–1.05; P=0.016) and greater LA dimension in echocardiography (OR, 1.04; 95% CI, 1.01–1.08; P=0.025) were independently associated with BDB of AL.

	All Subjects (n=398)	Clinical AF/AT Recurrence (-) (n=272)	Clinical AF/AT Recurrence (+) (n=126)	P Value
Age, y	59.81±10.30	59.84±10.83	59.74±9.09	0.928
Male sex, n (%)	301 (75.6)	203 (74.6)	98 (77.8)	0.497
Body mass index, kg/m ²	25.09±2.83	24.97±2.74	25.34±3.00	0.227
Body surface area, m ²	1.82±0.18	1.81±0.18	1.83±0.17	0.224
CHA ₂ DS ₂ -VASc score	2.01±1.73	2.04±1.82	1.93±1.51	0.536
CHF, n (%)	54 (13.6)	41 (15.1)	13 (10.3)	0.197
Hypertension, n (%)	218 (54.8)	147 (54.0)	71 (56.3)	0.667
Diabetes mellitus, n (%)	69 (17.4)	46 (16.9)	23 (18.4)	0.716
Stroke/TIA, n (%)	65 (16.3)	46 (16.9)	19 (15.1)	0.646
Vascular disease, n (%)	67 (16.8)	43 (15.8)	24 (19.0)	0.422
AAD at discharge, n (%)	95 (23.9)	59 (21.7)	36 (28.6)	0.134
TTE				
LA dimension, mm	44.24±5.81	44.13±6.03	44.48±5.34	0.576
LA volume index, mL/m ²	42.20±12.73	42.02±13.65	42.60±10.50	0.682
LV mass index, g/m ²	97.20±24.43	97.26±24.79	97.08±23.73	0.950
LVEF, %	61.17±9.41	61.14±9.89	61.22±8.31	0.935
LVEDD	50.51±4.95	50.48±4.97	50.57±4.91	0.862
E/Em	10.78±4.22	10.95±4.31	10.41±4.00	0.224

Table 1. Clinical and Echocardiographic Parameters According to Clinical AF/AT Recurrence

Values are expressed as n (%) or mean±SD. Any AF/AT recurrence in the first 3 months (blanking period) after catheter ablation was not counted as clinical AF/AT recurrence. AAD indicates antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; CHF, congestive heart failure; E/Em, the ratio of early diastolic mitral inflow velocity (E) to early diastolic mitral annular velocity (Em); LA, left atrium; LV, left ventricle; LVEDD, LV end diastolic dimension; LVEF, LV ejection fraction; LVMI, LV mass index; TIA, transient ischemic attack; TTE, transthoracic echocardiography.

Achievement of BDB for Additional Lines and Clinical Outcome

During 29.0 \pm 18.4 months of follow-up, 126 of 398 patients (31.7%) experienced clinical AF/AT recurrence. Kaplan–Meier analysis according to BDB of RL (log-rank, *P*=0.178; Figure 2A) or AL (log-rank, *P*=0.764; Figure 2C) showed no significant benefit for clinical outcome after catheter ablation.

However, patients with LAPW isolation showed a significantly lower clinical recurrence rate compared with those without LAPW isolation (log-rank, P=0.017; Figure 2B). Patients with a larger number of BDB-achieving linear ablation lines showed no significant benefit compared with those with fewer BDBachieving linear lines (2–3 vs 0–1; log-rank, P=0.073; Figure 2D). In multivariate Cox regression analysis, achievement of LAPW isolation was independently associated with lower clinical recurrence of AF/AT after catheter ablation

Table 2. Procedural Characteristics

	All Subjects (n=398)	Clinical AF/AT Recurrence (-) (n=272)	Clinical AF/AT Recurrence (+) (n=126)	P Value			
Total procedure time, minute	218.31±51.80	210.70±47.86	234.67±56.21	<0.001*			
Ablation time, second	6370.32±1346.72	6345.24±1217.80	6424.69±1594.93	0.586			
Achievement of BDB (%)							
Cavotricuspid isthmus line	398 (100)	272 (100)	126 (100)				
Roof line [†]	337 (84.7)	236 (86.8)	101 (80.2)	0.089			
Posterior-inferior line (LAPW isolation) †	178 (44.7)	130 (47.8)	48 (38.1)	0.070			
Anterior line	253 (63.6)	178 (65.4)	75 (59.5)	0.254			

Values are expressed as n (%) or mean±SD. AF indicates atrial fibrillation; AT, atrial tachycardia; BDB, bidirectional block; LAPW, left atrial posterior wall. *P<0.05.

[†]BDB of lines in 2 patients was not confirmed and was counted as no achievement of bidirectional block.

Table 3. Logistic Regression Analysis of Clinical Variables Predictive of Bidirectional Block

	Univariate Analysis		Multivariate Analysis			
	OR (95% CI)	P Value	OR (95% CI)	P Value		
Roof line						
Male	0.73 (0.37–1.43)	0.354	1.18 (0.48–2.57)	0.795		
Age	1.04 (1.01–1.06)	0.008	1.03 (1.00–1.06)	0.053		
Body mass index, kg/m ²	0.94 (0.85–1.03)	0.174				
Body surface area, m ²	0.21 (0.05–0.96)	0.044	0.40 (0.06–2.92)	0.369		
Hypertension	1.30 (0.76–2.25)	0.341				
Diabetes mellitus	1.71 (0.74–3.93)	0.209				
LA dimension, mm	1.01 (0.96–1.06)	0.784				
Ablation time, second	1.00 (1.00–1.00)	0.889				
Procedure time, minute	1.00 (0.99–1.00)	0.066	1.00 (0.99–1.00)	0.113		
Posterior-inferior line		-				
Male	0.62 (0.39–0.99)	0.044	0.75 (0.42–1.33)	0.321		
Age	1.01 (0.99–1.03)	0.580	1.00 (0.98–1.03)	0.782		
Body mass index, kg/m ²	0.96 (0.90–1.03)	0.276				
Body surface area, m ²	0.29 (0.09–0.89)	0.030	0.67 (0.14–3.17)	0.618		
Hypertension	1.11 (075–1.65)	0.612				
Diabetes mellitus	1.08 (0.64–1.82)	0.777				
LA dimension, mm	0.96 (0.93–1.00)	0.026	0.97 (0.93–1.01)	0.095		
Ablation time, minute	0.99 (0.98–1.00)	0.035	0.99 (0.98–1.00)	0.135		
Procedure time, minute	1.00 (0.99–1.00)	0.126				
Anterior line						
Male	0.77 (0.47–1.25)	0.293	0.81 (0.49–1.34)	0.407		
Age	1.03 (1.01–1.05)	0.007	1.03 (1.01–1.05)	0.016*		
Body mass index, kg/m ²	0.98 (0.92–1.06)	0.669				
Body surface area, m ²	0.48 (0.15–1.51)	0.209				
Hypertension	1.38 (0.92–2.09)	0.121				
Diabetes mellitus	1.17 (0.68–2.02)	0.577				
LA dimension, mm	1.05 (1.01–1.08)	0.016	1.04 (1.01–1.08)	0.025*		
Ablation time, minute	1.00 (0.99–1.01)	0.885				
Procedure time, minute	1.00 (0.99–1.00)	0.306				

LA indicates left atrium: OR. odds ratio.

*P<0.05 in multivariate analysis.

(hazard ratio [HR], 0.68; 95% Cl, 0.47–0.98; *P*=0.041; Table 4).

Maintenance of Bidirectional Blocks of Additional Lines in Redo Procedures

Among 126 patients with AF recurrence, 52 (41.3%) underwent repeat procedures at 23.02 ± 16.05 months after the de novo procedure. Achievement rates of LAPW isolation and BDB for linear lines at de novo procedure, redo mapping, and

postrepeat ablation are presented in Figure 3, respectively. BDB rates for CTI, RL, LAPW, and AL were 100%, 90.4%, 55.8%, and 65.4% at the de novo procedure, and 94.2%, 63.5%, 34.6%, and 40.4% at the redo mapping, respectively; thus, the BDB maintenance rates for CTI, RL, PIL, and AL were 94.2% (49 of 52), 63.5% (33 of 47), 62.1% (18 of 29), and 61.8% (21 of 34), respectively. After redo procedures, BDB was finally achieved in 100% for CTI, 94.2% for RL, 65.4% for PIL, and 76.9% for AL (Figure 3A). Among patients who achieved LAPW isolation at the de novo procedure (n=29),



Figure 2. A, Kaplan–Meier analysis of AF/AT recurrence-free rate according to bidirectional block achievement of roof line, (B) posteriorinferior line (LAPW isolation), (C) anterior line, and (D) the number of lines with bidirectional block among roof line, posterior-inferior line, and anterior line (0–1 vs 2–3). AF indicates atrial fibrillation; AT, atrial tachycardia; BDB, bidirectional block; LAPW, left atrial posterior wall.

achievement rates of BDB for linear lines are presented in Figure 3B.

Discussion

The main finding of the current study was that patients who achieved LAPW isolation in AF catheter ablation with a linear ablation strategy showed better clinical outcomes than those without LAPW isolation. BDBs of RL or AL did not affect AF/AT recurrence. At the de novo procedure, the overall BDB rate for linear ablations was 64.3%, and 74.2% of previously confirmed BDBs were maintained at the repeat procedure 23.0 ± 16.1 months after the de novo procedure. The LAPW isolation rate was 44.7% and was maintained in 62.1% at the repeat procedure.

Linear Lesion Generation With Catheter Ablation

Linear lesion generation was initially suggested and attempted in the surgical treatment of AF, and Cox et al

demonstrated the feasibility of curing AF by biatrial linear lesion generation, with a success rate of 93%.¹⁴ Linear ablation in catheter ablation is derived from the concept underlying surgical treatment of AF and modifies atrial substrates and compartmentalizes the atrium into smaller regions to reduce the critical mass of atrial tissue.¹⁵ However, complete conduction block with transmural lesion generation remains challenging with catheter ablation, and durability of conduction block is also an important issue for long-term successful AF ablation. Even in AF surgery, transmurality of the lesions is reported to be achievable in only up to 75% of cases.¹⁶ Although Rostock et al reported conduction recovery in 90% of cases for mitral isthmus line and 79% for RL at the repeat procedure,¹⁷ there are a lack of data on the initial achievement and durability of BDB rate of linear ablation lesions. In this study, the overall de novo BDB rate for linear ablations, including RL, PIL, and AL, was 64.3%, and only 74.2% of previously confirmed BDBs were maintained at repeat procedure. Although we used a consistent ablation protocol in this study, the patients in whom BDB can be

	Univariate Analysis		Multivariate Analysis		
Total Population	HR (95% CI)	P Value	HR (95% CI)	P Value	
Male	1.18 (0.77–1.79)	0.452	1.27 (0.68–2.38)	0.461	
Age	1.00 (0.99–1.02)	0.663	1.01 (0.99–1.03)	0.505	
Body mass index, kg/m ²	1.08 (1.01–1.15)	0.025*	1.10 (0.99–1.21)	0.082	
Body surface area, m ²	2.18 (0.77–6.14)	0.141	0.68 (0.09–5.45)	0.721	
Hypertension	1.05 (0.74–1.50)	0.782			
Diabetes mellitus	1.15 (0.73–1.81)	0.548			
LA dimension, mm	1.01 (0.98–1.04)	0.626	0.99 (0.96–1.02)	0.517	
Achievement of BDB					
Roof line	0.74 (0.47–1.15)	0.184			
Posterior-inferior line (LAPW isolation)	0.65 (0.45–0.93)	0.019*	0.68 (0.47–0.98)	0.041*	
Anterior line	0.95 (0.66–1.36)	0.766			

Table 4. Univariate and	Multivariate Cox	Regression	Analyses of	of Clinical AF	=/AT	Recurrence After	Catheter Ablation
		0			,		

Any AF/AT recurrence in the first 3 months (blanking period) after catheter ablation was not counted as clinical AF/AT recurrence. AF indicates atrial fibrillation; AT, atrial tachycardia; BDB, bidirectional block; HR, hazard ratio; LA, left atrium; LAPW, left atrial posterior wall. * P<0.05.

achieved might be somewhat different from others. Recently, Kim et al reported a lower reconnection of previously isolated PV potential in women than in men on the second procedure.¹⁸ It is possible that genetic or intrinsic sex difference results in a thinner LA myocardial layer in women than in men.¹⁹ Therefore, BDB achievement after linear ablation can be affected by myocardial wall thickness, lesion length, or extent of low-voltage scar tissue. In this study, we found a higher BDB rate of the PIL in females and a smaller LA dimension on univariate logistic regression analyses. On the other hand, old age and a larger LA dimension were independently associated with BDB of the AL, suggesting that LA with advanced remodeling and fibrosis also contributes to the achievement of BDB.

Clinical Implication of LA Posterior Wall Isolation

In this study, we demonstrated that achievement of LAPW isolation by additional linear ablations of RL and PIL was associated with a better clinical outcome. Although Tamborero et al²⁰ reported no beneficial effect of LAPW isolation with linear ablations of RL and PIL, their study group consisted of 60% paroxysmal AF cases. Like PVs, LAPW embryologically originates from the cells of the primordial PV^{21} and thus might contribute to the initiation of AF with triggered activity²² and also have a role in perpetuation of AF.^{23,24} LAPW myocytes are known to have higher arrhythmogenic potential than other parts of the LA because of larger intracellular Ca²⁺ transients, more sarcoplasmic reticulum calcium content, and less protein expression of the Na-Ca exchanger,²⁵ as shown in a representative example of recurred AT in Figure 1B. In this

patient, LAPW isolation was achieved at de novo procedure, but recurred focal AT originated from LAPW conducted through the reconnected RL. Moreover, LA size is an important determinant of AF perpetuation, and therefore LA mass reduction by LAPW isolation might modify the AF substrate and have a beneficial effect on the clinical outcome of catheter ablation—the so-called critical mass hypothesis.²⁶

Various Additional Linear Ablation Strategies

The standard lesion set of additional linear ablation post-CPVI has not yet been clearly defined. Although the most commonly added linear lesions are the mitral isthmus and RL,^{4,5} some researchers also suggested a lesion set in which LAPW is isolated by performing RL and PIL.^{7,27} Furthermore, the surgical ablation lesion set reported by Edgerton et al, which is known as the Dallas lesion set, can be generated successfully with the catheter ablation technique.^{6,28} In this study, we performed Dallas lesion set additional linear ablation with RL and PIL for LAPW isolation in nearly 400 patients with more than 2 years of follow-up. Our results indicated that although BDB of PIL and consequent LAPW isolation is difficult to achieve compared to RL or AL, it seems to be worth the effort.

Ablation Strategies for LA Posterior Wall Isolation

Although several researchers recently suggested the beneficial effect of LAPW isolation on clinical outcome of PeAF catheter ablation,^{29,30} the results are inconsistent²⁰ and the studies used different ablation strategies for LAPW isolation. Whereas



Figure 3. A, Bidirectional block rates of additional lines in de novo procedure, redo mapping, and postredo procedure in a total of 52 patients who underwent the redo procedure and (B) 29 who achieved LAPW isolation at the de novo procedure. AL indicates anterior line; CTI, cavotricuspid isthmus; LAPW, left atrial posterior wall; RL, roof line.

our group and others performed additional linear ablation with RL and PIL for LAPW isolation,^{20,29} Bai et al conducted LAPW isolation with extensive ablation of the entire LAPW and reported an additional benefit over CPVI alone in the PeAF ablation procedure.³⁰ Furthermore, they verified CPVI and LAPW isolation by performing a repeat procedure regardless of arrhythmia recurrence, and therefore assessed the true impact of LAPW isolation on clinical outcome.

If complete, LAPW with linear lesions seems to have a critical mass reduction effect with LA compartmentalization and fewer ablation lesions with less myocardial injury. However, BDB of PIL is hard to achieve and there are safety concerns over collateral damage, including esophagus injury. Although there were no differences in the major complication rates and ablation-related complication rates between patients with LAPW isolation and those without (Table S1), there was a case of atrioesophageal fistula in each group. The overall incidence of atrioesophageal fistula was 0.098% (2 of 2047) in the Yonsei AF Ablation cohort. Therefore, further studies comparing the safety and complications related to these procedures are warranted. Moreover, incomplete BDB with gap formation might be rather proarrhythmic. However, there were no differences in the recurrence types of tachycardia (AF/AT; Table S2) or AT recurrence rates (Figure S1) between patients with BDB and those without in this study, and an extensive LAPW ablation strategy could result in more myocardial injury and, consequently, might exhibit arrhythmogenicity.^{31,32} Further prospective, randomized studies with different ablation strategies for LAPW isolation as endpoints are warranted.

Study Limitations

This study was an observational cohort study from a single center. Although we confirmed BDB of all linear lesions, some lesions might have conduction recovery, which may have affected the clinical outcome. Whether complete LAPW isolation has a significant beneficial effect on clinical outcome or incomplete BDB has a proarrhythmic effect remain to be elucidated.

Conclusion

Although BDB of PIL is hard to achieve while avoiding the esophageal contact area, LAPW isolation is important for a better clinical outcome in catheter ablation with additional linear ablation strategy for patients with PeAF.

Sources of Funding

This work was supported by a grant (A085136) from the Korea Health 21 R&D Project, Ministry of Health and Welfare.

Disclosures

None.

References

 January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW; American College of Cardiology/American Heart Association Task Force on Practice G. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol.* 2014;64:e1–e76.

- Pappone C, Augello G, Sala S, Gugliotta F, Vicedomini G, Gulletta S, Paglino G, Mazzone P, Sora N, Greiss I, Santagostino A, LiVolsi L, Pappone N, Radinovic A, Manguso F, Santinelli V. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF Study. J Am Coll Cardiol. 2006;48:2340–2347.
- Tilz RR, Rillig A, Thum AM, Arya A, Wohlmuth P, Metzner A, Mathew S, Yoshiga Y, Wissner E, Kuck KH, Ouyang F. Catheter ablation of long-standing persistent atrial fibrillation: 5-year outcomes of the Hamburg Sequential Ablation Strategy. J Am Coll Cardiol. 2012;60:1921–1929.
- Willems S, Klemm H, Rostock T, Brandstrup B, Ventura R, Steven D, Risius T, Lutomsky B, Meinertz T. Substrate modification combined with pulmonary vein isolation improves outcome of catheter ablation in patients with persistent atrial fibrillation: a prospective randomized comparison. *Eur Heart J.* 2006;27:2871–2878.
- Fassini G, Riva S, Chiodelli R, Trevisi N, Berti M, Carbucicchio C, Maccabelli G, Giraldi F, Bella PD. Left mitral isthmus ablation associated with PV isolation: long-term results of a prospective randomized study. *J Cardiovasc Electrophysiol*. 2005;16:1150–1156.
- Pak HN, Oh YS, Lim HE, Kim YH, Hwang C. Comparison of voltage map-guided left atrial anterior wall ablation versus left lateral mitral isthmus ablation in patients with persistent atrial fibrillation. *Heart Rhythm*. 2011;8:199–206.
- Pappone C, Manguso F, Vicedomini G, Gugliotta F, Santinelli O, Ferro A, Gulletta S, Sala S, Sora N, Paglino G, Augello G, Agricola E, Zangrillo A, Alfieri O, Santinelli V. Prevention of iatrogenic atrial tachycardia after ablation of atrial fibrillation: a prospective randomized study comparing circumferential pulmonary vein ablation with a modified approach. *Circulation*. 2004;110:3036–3042.
- Jais P, Hocini M, Hsu LF, Sanders P, Scavee C, Weerasooriya R, Macle L, Raybaud F, Garrigue S, Shah DC, Le Metayer P, Clementy J, Haissaguerre M. Technique and results of linear ablation at the mitral isthmus. *Circulation*. 2004;110:2996–3002.
- Sawhney N, Anousheh R, Chen W, Feld GK. Circumferential pulmonary vein ablation with additional linear ablation results in an increased incidence of left atrial flutter compared with segmental pulmonary vein isolation as an initial approach to ablation of paroxysmal atrial fibrillation. *Circ Arrhythm Electrophysiol.* 2010;3:243–248.
- Verma A, Jiang CY, Betts TR, Chen J, Deisenhofer I, Mantovan R, Macle L, Morillo CA, Haverkamp W, Weerasooriya R, Albenque JP, Nardi S, Menardi E, Novak P, Sanders P; Investigators SAI. Approaches to catheter ablation for persistent atrial fibrillation. *N Engl J Med*. 2015;372:1812–1822.
- Mun HS, Joung B, Shim J, Hwang HJ, Kim JY, Lee MH, Pak HN. Does additional linear ablation after circumferential pulmonary vein isolation improve clinical outcome in patients with paroxysmal atrial fibrillation? Prospective randomised study *Heart*. 2012;98:480–484.
- Verma A, Mantovan R, Macle L, De Martino G, Chen J, Morillo CA, Novak P, Calzolari V, Guerra PG, Nair G, Torrecilla EG, Khaykin Y. Substrate and trigger ablation for reduction of atrial fibrillation (STAR AF): a randomized, multicentre, international trial. *Eur Heart J.* 2010;31:1344–1356.
- 13. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ Jr, Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim YH, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao HM, Wilber D. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace*. 2012;14:528–606.
- Cox JL, Schuessler RB, Lappas DG, Boineau JP. An 8 1/2-year clinical experience with surgery for atrial fibrillation. *Ann Surg.* 1996;224:267–273; discussion 273-265.
- Henry WL, Morganroth J, Pearlman AS, Clark CE, Redwood DR, Itscoitz SB, Epstein SE. Relation between echocardiographically determined left atrial size and atrial fibrillation. *Circulation*. 1976;53:273–279.

- Deneke T, Khargi K, Muller KM, Lemke B, Mugge A, Laczkovics A, Becker AE, Grewe PH. Histopathology of intraoperatively induced linear radiofrequency ablation lesions in patients with chronic atrial fibrillation. *Eur Heart J.* 2005;26:1797–1803.
- Rostock T, O'Neill MD, Sanders P, Rotter M, Jais P, Hocini M, Takahashi Y, Sacher F, Jonsson A, Hsu LF, Clementy J, Haissaguerre M. Characterization of conduction recovery across left atrial linear lesions in patients with paroxysmal and persistent atrial fibrillation. *J Cardiovasc Electrophysiol*. 2006;17:1106–1111.
- Kim TH, Park J, Uhm JS, Joung B, Lee MH, Pak HN. Pulmonary vein reconnection predicts good clinical outcome after second catheter ablation for atrial fibrillation. *Europace*. 2016 pii: euw128. [Epub ahead of print].
- Tsai WC, Chen YC, Lin YK, Chen SA, Chen YJ. Sex differences in the electrophysiological characteristics of pulmonary veins and left atrium and their clinical implication in atrial fibrillation. *Circ Arrhythm Electrophysiol.* 2011;4:550–559.
- Tamborero D, Mont L, Berruezo A, Matiello M, Benito B, Sitges M, Vidal B, de Caralt TM, Perea RJ, Vatasescu R, Brugada J. Left atrial posterior wall isolation does not improve the outcome of circumferential pulmonary vein ablation for atrial fibrillation: a prospective randomized study. *Circ Arrhythm Electrophysiol*. 2009;2:35–40.
- Ho SY, Cabrera JA, Sanchez-Quintana D. Left atrial anatomy revisited. Circ Arrhythm Electrophysiol. 2012;5:220–228.
- 22. Lin WS, Tai CT, Hsieh MH, Tsai CF, Lin YK, Tsao HM, Huang JL, Yu WC, Yang SP, Ding YA, Chang MS, Chen SA. Catheter ablation of paroxysmal atrial fibrillation initiated by non-pulmonary vein ectopy. *Circulation*. 2003;107:3176–3183.
- Sanders P, Berenfeld O, Hocini M, Jais P, Vaidyanathan R, Hsu LF, Garrigue S, Takahashi Y, Rotter M, Sacher F, Scavee C, Ploutz-Snyder R, Jalife J, Haissaguerre M. Spectral analysis identifies sites of high-frequency activity maintaining atrial fibrillation in humans. *Circulation*. 2005;112:789–797.
- Huang JL, Tai CT, Lin YJ, Ting CT, Chen YT, Chang MS, Lin FY, Lai WT, Chen SA. The mechanisms of an increased dominant frequency in the left atrial posterior wall during atrial fibrillation in acute atrial dilatation. *J Cardiovasc Electrophysiol.* 2006;17:178–188.
- Suenari K, Chen YC, Kao YH, Cheng CC, Lin YK, Chen YJ, Chen SA. Discrepant electrophysiological characteristics and calcium homeostasis of left atrial anterior and posterior myocytes. *Basic Res Cardiol.* 2011;106:65–74.
- Zou R, Kneller J, Leon LJ, Nattel S. Substrate size as a determinant of fibrillatory activity maintenance in a mathematical model of canine atrium. *Am J Physiol Heart Circ Physiol*. 2005;289:H1002–H1012.
- Sanders P, Hocini M, Jais P, Sacher F, Hsu LF, Takahashi Y, Rotter M, Rostock T, Nalliah CJ, Clementy J, Haissaguerre M. Complete isolation of the pulmonary veins and posterior left atrium in chronic atrial fibrillation. Long-term clinical outcome. *Eur Heart J.* 2007;28:1862–1871.
- Edgerton JR, Jackman WM, Mahoney C, Mack MJ. Totally thorascopic surgical ablation of persistent AF and long-standing persistent atrial fibrillation using the "Dallas" lesion set. *Heart Rhythm.* 2009;6:S64–S70.
- 29. Kim JS, Shin SY, Na JO, Choi CU, Kim SH, Kim JW, Kim EJ, Rha SW, Park CG, Seo HS, Oh DJ, Hwang C, Lim HE. Does isolation of the left atrial posterior wall improve clinical outcomes after radiofrequency catheter ablation for persistent atrial fibrillation? A prospective randomized clinical trial. *Int J Cardiol.* 2015;181:277–283.
- 30. Bai R, Di Biase L, Mohanty P, Trivedi C, Dello Russo A, Themistoclakis S, Casella M, Santarelli P, Fassini G, Santangeli P, Mohanty S, Rossillo A, Pelargonio G, Horton R, Sanchez J, Gallinghouse J, Burkhardt JD, Ma CS, Tondo C, Natale A. Proven isolation of the pulmonary vein antrum with or without left atrial posterior wall isolation in patients with persistent atrial fibrillation. *Heart Rhythm.* 2016;13:132–140.
- Lim HE, Choi CU, Na JO, Choi JI, Kim SH, Kim JW, Kim EJ, Han SW, Park SW, Rha SW, Park CG, Seo HS, Oh DJ, Hwang C, Kim YH. Effects of iatrogenic myocardial injury on coronary microvascular function in patients undergoing radiofrequency catheter ablation of atrial fibrillation. *Circ Arrhythm Electrophysiol.* 2013;6:318–326.
- Shim J, Joung B, Park JH, Uhm JS, Lee MH, Pak HN. Long duration of radiofrequency energy delivery is an independent predictor of clinical recurrence after catheter ablation of atrial fibrillation: over 500 cases experience. Int J Cardiol. 2013;167:2667–2672.

ORIGINAL RESEARCH

SUPPLEMENTAL MATERIAL

Follow-up data	LAPW isolation (+) (n = 178)	LAPW isolation (-) (n = 220)	p value
AAD at discharge	35 (19.7%)	60 (27.3%)	0.077
AAD after blanking period	46 (25.8%)	48 (21.8%)	0.347
Procedural characteristics	LAPW isolation(+) (n=178)	LAPW isolation(-) (n=220)	p value
Complications	*10 (5.6%)	† 6 (2.7%)	0.144
Major complications	3 (1.7%)	3 (1.3%)	0.794
‡Ablation-related complications	7 (3.9%)	5 (2.3%)	0.336

Table S1. Anti-arrhythmic drug maintenance and procedure complications according to the achievement of left atrial posterior wall isolation.

AAD = antiarrhythmic drug

AAD after blanking period = AAD use before the clinical recurrence or AAD use at last follow-up.

CFAE = complex fractionated atrial electrogram, CPVI = circumferential pulmonary vein isolation, LAPW = left atrial posterior wall.

*tamponade 2 (1 required open heart surgery), atrio-esophageal (AE) fistula 1, sinus node dysfunction 4, groin complication 3.

†tamponade 2, pleural effusion 1, AE fistula 1, sinus node dysfunction 1, groin complication 1.

‡groin complications excluded.

All sinus node dysfunction did not require pacemaker implantation.

De novo procedure (n=398)	BDB (+)	BDB (-)	p value
Roof line			
Proportion of patients, %	84.7% (337)	15.3% (61)	
Clinical AF/AT recurrence, %	30.0% (101/337)	41.0% (25/61)	0.089
Proportion of AT recurrence, %	48.5% (49/101)	48.0% (12/25)	0.963
Posterior-inferior line			
Proportion of patients, %	44.7% (178)	55.3% (220)	
Clinical AF/AT recurrence, %	27.0% (48/178)	35.5% (78/220)	0.070
Proportion of AT recurrence, %	50.0% (24/48)	47.4% (37/78)	0.780
Anterior line			
Proportion of patients, %	63.6% (253)	36.4% (145)	
Clinical AF/AT recurrence, %	29.6% (75/253)	35.2% (51/145)	0.254
Proportion of AT recurrence, %	46.7% (35/75)	51.0% (26/51)	0.634
Redo mapping (n=52)	BDB (+)	BDB (-)	p value
Roof line			
Proportion of patients, %	63.5% (33)	36.5% (19)	
Proportion of AT recurrence, %	42.4% (14/33)	47.4% (9/19)	0.730
Inducible macro-reentrant AT during	15.2% (5/33)	21.1% (4/19)	0.592
Posterior-inferior line			
Proportion of patients, %	34.6% (18)	65.4% (34)	
Proportion of AT recurrence, %	50.0% (9/18)	41.2% (14/34)	0.542
Inducible macro-reentrant AT during mapping	16.7% (3/18)	17.6% (6/34)	0.929
Anterior line			
Proportion of patients, %	40.4% (21)	59.6% (31)	
Proportion of AT recurrence, %	42.9% (9/21)	45.2% (14/31)	0.870
Inducible macro-reentrant AT during mapping	14.3% (3/21)	19.4% (6/31)	0.635

Table S2. Incidence and mode of recurrences depending on the status of BDB of linear lesions at de novo procedure and redo mapping.

BDB = bidirectional block.

Figure S1. Kaplan-Meier analysis of AT (not AF) recurrence-free rate according to BDB achievement of roof line (**A**), posterior-inferior line (LAPW isolation; **B**), anterior line (**C**), and the number of linear lesions with BDB (0-1 vs. 2-3; **D**). BDB = bidirectional block.



