Patterns of Pulmonary Vein Potential Disappearance During Encircling Ipsilateral Pulmonary Vein Isolation Can Predict Recurrence of Atrial Fibrillation

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Background: The relationship between pulmonary vein (PV) potential (PVP) disappearance patterns during encircling ipsilateral pulmonary vein isolation (EIPVI) of atrial fibrillation (AF), and outcome was examined.

Methods and Results: A total of 352 consecutive AF patients (age, 61±12 years; 269 men, 76.4%; paroxysmal AF, n=239; persistent AF, n=73; and long-standing persistent AF, n=40) who underwent initial AF ablation were studied. After EIPVI with a double Lasso technique, pacing was performed from the PV carina to confirm isolation of the carina. PVP disappearance patterns were classified into 3 types: A, both superior and inferior PVP disappeared simultaneously; B, superior and inferior PVP disappeared separately; and C, additional RF applications were required inside the encircling lesions to eliminate the PVP after creating anatomical encircling lesions. The relationship between these patterns and outcome was examined. Six groups were defined according to the combination of right and left ipsilateral PVP disappearance patterns. The incidence of A-A, A-B, B-B, A-C, B-C, and C-C was 7.1%, 14.2%, 16.2%, 15.3%, 27.3%, and 19.9%, respectively. AF recurrence-free rate at 2 years for these 6 groups was 96%, 81%, 78%, 64%, 64%, and 59%, respectively (P<0.02). The incidence of a carina isolation was 153/154 (99.4%) for type A, 221/259 (85.3%) for type B, and 145/290 (50.0%) for type C.

Conclusions: PVP disappearance pattern during EIPVI was significantly associated with the incidence of residual PV carina conduction and AF recurrence. (Circ J 2014; 78: 601–609)

Key Words: Atrial fibrillation; Carina; Encircling ipsilateral pulmonary vein isolation; Pulmonary vein potential; Recurrence

The pulmonary veins (PVs) have been proven to be a major origin of atrial fibrillation (AF). Isolation of the PV-left atrial (LA) junction can cure AF, and encircling ipsilateral pulmonary vein isolation (EIPVI) with the double Lasso technique is one of the widely used ablation procedures to treat AF. Although it has been recognized that the PV potentials (PVPs) disappear in different ways while the encircling lesions are drawn at the PV-LA junction, the relationship between the patterns of PVP disappearance and AF recurrence remains unknown. This study was undertaken to clarify this relationship.

Methods

Subjects

The subjects for this retrospective cohort study were drawn from 398 consecutive patients who underwent initial catheter ablation of AF refractory to ≥2 class I, III, or IV anti-arrhythmic drugs (AADs) including amiodarone during the period between January 2006 and August 2009. All AADs except for amiodarone were discontinued for at least 5 half-lives prior to the study. Baseline characteristics including age, gender, medical history, medication and echocardiographic findings were recorded. The Institutional Review Board approved the study protocol, and all patients provided written, informed consent for the procedure.
Figure 1. Intracardiac tracings of the different disappearance patterns of the pulmonary vein (PV) potentials (PVPs) during PV isolation. (A) All the PVPs disappeared simultaneously in both the superior and inferior PV during encircling ipsilateral PV isolation (EIPVI) (type A). (B) The inferior and superior PVPs separately disappeared during EIPVI (type B). (C) The right superior PVPs remained after EIPVI and were successfully eliminated by additional radiofrequency (RF) applications delivered inside and contiguous to the encircling lesions toward the earliest site of the PVP recorded from a circular catheter at the PV ostium (type C). Note that both the ablation and circular catheters recorded an artifact caused by contact between those catheters when RF application was added inside the encircling lesions closer to the circular catheter. Arrowheads, PVPs. ABLd(p), distal (proximal) electrode pair of the ablation catheter; CSd(p), distal (proximal) electrode pair of the coronary sinus catheter; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.
Electrophysiological Study
The electrophysiology study and ablation strategy have been previously described in detail. In brief, the procedure was performed under sedation with i.v. thymal in the fasting state. For mapping and pacing, a multi-electrode catheter was placed in the coronary sinus. LA catheterization was performed with a single transseptal puncture technique. i.v. heparin was given to maintain an activated clotting time between 250 and 350s after the atrial transseptal procedure. PV angiograms of both the left and right PVs were obtained in the right anterior oblique 30° and left anterior oblique 60° projections to determine the anatomical relationships of the PV ostia and LA. A 9-Fr intravascular ultrasound catheter (UltraICE™; Boston Scientific, Natick, MA, USA) was introduced into all 4 PV to determine the edge of the PV ostia, and the ostial diameters were measured to determine the appropriate size of the circular mapping catheter to be used.

EIPVI Technique
When the baseline heart rhythm was AF, sinus rhythm was restored by external cardioversion. An LA reconstruction was achieved with a 3-D electroanatomic mapping system (CARTO™; Biosense-Webster, Diamond Bar, CA, USA) and a 4-mm tip non-irrigated ablation catheter (Navi-Star™; Biosense-Webster) during coronary sinus pacing or sinus rhythm. The ostia of the 4 PV were tagged on the 3-D electroanatomic map with the guidance of a PV angiogram and intracardiac echocardiogram. PVI was performed with an EIPVI technique guided by PV mapping with a double Lasso technique and CARTO system as previously reported. Two 20-electrode bipolar-type circular catheters (Lasso™; Biosense-Webster) were placed at the ostia of the ipsilateral PV or superior and inferior branches of PV with a common ostium to record the PVPVs. The ipsilateral PVs were encircled as a single unit, and encircling isolation lines were created with contiguous coalescent radiofrequency (RF) lesions using a dragging technique. RF current was applied at sites >1 cm in the posterior wall and >5 mm in the anterior wall, away from the PV ostia. In the case of a relatively narrow border between the anterior aspect of the left PV and the LA appendage, ablation was performed within 5 mm from the PV ostia. RF energy was delivered with a target temperature of 55°C and maximum power setting of 30 W for 30–60 s. When the PVPVs did not disappear despite a completely continuous circle lesion on the CARTO image, RF applications were added inside and contiguously to the encircling RF lesions using a dragging technique. RF current was applied at sites >5 mm from the LA appendage, ablation was performed within 5 mm from the PV ostia. Lasso catheters were used to achieve bidirectional conduction block in all cases after successful EIPVI.

The patterns of PVP disappearance during PVI were classified into 3 types: type A, all the PVPVs disappeared simultaneously in both the superior and inferior PVs (Figure 1A); type B, the superior and inferior PVPVs disappeared separately (Figure 1B); and type C, additional RF applications were required inside the encircling lesions to eliminate the PVPs after the achievement of anatomical encircling lesions (Figure 1C). According to a combination of the PVP disappearance patterns for the left and right ipsilateral PVs, 6 groups were defined as follows: A-A, A-B, B-B, A-C, B-C, and C-C.

Follow-up
Clinical follow-up was performed at 2 weeks, 1 month and every month thereafter, using 12-lead electrocardiogram (ECG). A 24-h Holter recording was performed at 1, 3, 6, and 12 months. All patients who reported symptoms were given an event monitor to document the cause of the symptoms. AADs were continued for the first 3 months after the procedure as a blanking period in all the patients. AADs were then discontinued in patients with paroxysmal AF, but continued in those with persistent and long-standing persistent AF. Successful ablation was defined as the absence of any AF or other sustained atrial tachycardias lasting for ≥30 s that were documented on ECG after the blanking period.

Statistical Analysis
The data are expressed as mean±SD for continuous variables, and frequencies and percentages for categorical variables. Statistical significance was evaluated using Chi-squared analysis or Fisher exact test for categorical variables and unpaired t-test or Wilcoxon analysis for continuous variables. Kruskal-Wallis analysis was used to compare the continuous variables among 3 groups. AF recurrence-free rates were calculated using the Kaplan-Meier actuarial survival method, and log-rank statistics were used for comparisons between groups. P<0.05 was considered statistically significant.

<table>
<thead>
<tr>
<th>Table 1. Patient Characteristics</th>
<th>Total n=352</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>60±11</td>
</tr>
<tr>
<td>Male</td>
<td>269 (76.4)</td>
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<tr>
<td>Symptomatic AF</td>
<td>297 (84.4)</td>
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<tr>
<td>Paroxysmal AF</td>
<td>239 (67.9)</td>
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<tr>
<td>Persistent AF</td>
<td>73 (20.7)</td>
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<tr>
<td>Long-standing persistent AF</td>
<td>40 (11.4)</td>
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<tr>
<td>BMI</td>
<td>24.0±3.6</td>
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<tr>
<td>Duration of AF history (years)</td>
<td>4.3±4.4</td>
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<tr>
<td>Structural heart disease</td>
<td>80 (22.7)</td>
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<tr>
<td>Hypertension</td>
<td>166 (47.2)</td>
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<tr>
<td>Diabetes</td>
<td>43 (12.2)</td>
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<tr>
<td>Echocardiography</td>
<td></td>
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<tr>
<td>LVD (mm)</td>
<td>47.3±5.1</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>39.1±6.2</td>
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<tr>
<td>LVEF (%)</td>
<td>61.0±8.3</td>
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</tbody>
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Data given as n (%) or mean±SD. AF, atrial fibrillation; BMI, body mass index; LAD, left atrial dimension; LVD, left ventricular dimension; LVEF, left ventricular ejection fraction.
Results

Baseline Characteristics and Clinical Outcome
Among 398 patients, 28 (7.0%) and 4 (1.0%) were excluded because of absence of PVPs in some of the 4 PVs before ablation, and unsuccessful PVI, respectively. Fourteen patients (3.5%) were dropped from follow-up at <3 months. The remaining 352 patients (88.4%) were enrolled for further study. The baseline characteristics of the study patients are listed in Table 1. The mean age was 61±12 years and a male predominance (269/352; 76.4%) was noted. Paroxysmal, persistent, and long-standing persistent AF accounted for 239 (67.9%), 73 (20.7%), and 40 (11.4%) of the patients, respectively; 221/239 (92.5%) with paroxysmal, 57/73 (78.1%) with persistent, and 19/40 (47.5%) with long-standing persistent AF had symptoms including palpitations, breathlessness, easy fatigability, and chest discomfort. Eighty patients (22.7%) had structural heart disease including congenital heart disease, valvular disease, ischemic heart disease, cardiomyopathy, or unknown ventricular dysfunction. During a mean follow-up of 19±13 months (range, 3–53 months) after the procedure, 253 patients remained free of AF (175/239, 73.2% with paroxysmal AF; 50/73, 68.5% with persistent AF; and 28/40, 70.0% with long-standing persistent AF). The AF recurrence-free rate was similar among the patients with paroxysmal AF (without AADs), persistent AF (with AADs), and long-standing persistent AF (with AADs; P=0.83).

PVP Disappearance Patterns
The results of the PVP disappearance patterns in 704 ipsilateral PV of 352 patients are shown in Figure 2A. Type A, B, and C patterns occurred in 155/704 (22.0%), 259/704 (36.8%), and 290/704 (41.2%), respectively. The incidence of a type A pattern was significantly lower than the other patterns (P<0.001).
This difference is likely to be due to the significantly lower incidence of a type A disappearance pattern in the right PV. In terms of a combination of the PVP disappearance patterns for the left and right ipsilateral PVs, an A-A pattern occurred in only 25 patients (7.1%). In 219 patients (62.5%), a type C pattern occurred in at least one of the left or right ipsilateral PV (Figure 2B). Among 290 ipsilateral PVs with a type C disappearance pattern, RF applications were added at 433 locations: 201 locations, at a mean of 6.5±3.6 mm inside the encircling line, in 133 left-sided PVs; and 232 locations, at a mean of 7.5±4.2 mm inside the encircling line, in 157 right-sided PVs. There was no significant relationship between PV ostial diameter and PVP disappearance pattern.

Figure 3. Atrial fibrillation (AF) recurrence-free rate according to the combined pulmonary vein (PV) potential disappearance patterns of the right and left ipsilateral PVs.

**PVP Disappearance Pattern and AF Recurrence After EIPVI**

AF recurrence-free rate significantly differed with combination of PVP disappearance patterns for the left and right ipsilateral PVs (Figure 3; P=0.02). The AF recurrence-free rate at 2 years of follow-up was 96%, 81%, 78%, 64%, 64%, and 59%, for combinations A-A, A-B, B-B, A-C, B-C, and C-C, respectively.

**Incidence of PV Carina Isolation and PVP Disappearance Pattern**

When the incidence of PV carina isolation was compared among the types of PVP disappearance pattern, PV carina isolation was achieved in 99% of the ipsilateral PVs with type A; in 85% of those with type B; and in 50% of those with type C (Figure 4A). The incidence of PV carina isolation with types A and B was similar between the left and right ipsilateral PVs, whereas that with type C was significantly greater in the left ipsilateral PVs than the right ipsilateral PVs (Figure 4B). The achievement of PV carina isolation was associated with outcome of catheter ablation (Figure 5). AF recurrence-free rate was significantly higher in patients with PV carina isolation on both sides than in any other patients. The AF recurrence-free rate tended to be higher in patients with PV carina isolation on 1 side than in those without PV carina isolation on either side.

**Clinical Characteristics and PVP Disappearance Pattern**

When 3 representative combinations of the PVP disappearance patterns (A-A, B-B and C-C) were selected, the AF recurrence-free rate was significantly lower in A-A and B-B than C-C (P=0.002 and 0.02, respectively). The AF recurrence-free rate was lower in pattern A-A than B-B despite the lack of statistical significance (P=0.07). The LA dimension and body mass index were significantly larger in pattern C-C than A-A and B-B (A-A vs. B-B vs. C-C, 37±5 mm vs. 38±6 mm vs. 42±7 mm, P=0.001; A-A vs. B-B vs. C-C, 24.0±3.0 kg/m² vs. 22.7±3.0 kg/m² vs. 24.9±3.2 kg/m², P=0.001; respectively; Table 2). The incidence of structural heart disease tended to be higher in pattern C-C than A-A and B-B (A-A vs. B-B vs. C-C, 3 [12.0%] vs. 12 [21.1%] vs. 23 [32.9%], P=0.08).

**Discussion**

In this study, AF recurrence was associated with PVP disappearance pattern. The outcome of AF ablation was the best when all PVPs disappeared simultaneously in both the superior and inferior PV (A-A), followed by when the superior and inferior PVPs disappeared separately (B-B), and the worst when additional RF applications were required inside the encircling lesions to eliminate the PVPs (C-C). Complete isolation of the PV carina was almost always achieved (99%) when both the superior and inferior PVPs disappeared simultaneously on the isolation line; very highly achieved (85%) when the superior and inferior PVPs disappeared separately on the isolation line; and achieved in half of the procedures when
associated with the PV carina isolation. The possible mechanism underlying the association between PVP disappearance patterns and PV carina isolation is shown in Figure 6. When the PVP disappeared simultaneously in both the superior and inferior PVs (type A), the carina was isolated in all except for one of the left PVs. In such a setting, the musculature extending from the LA to the PV carina, which forms a connection between the musculature extending from the LA to both the superior and inferior PVs, should have been electrically disconnected from the LA by the same circumferential and trans-

Figure 4. Pulmonary vein (PV) carina isolation according to PV potential (PVP) disappearance pattern: (A) overall; (B) right vs. left ipsilateral PVs.
PVP Disappearance Patterns Predict AF Recurrence

In 15% of the PV with a type B PVP disappearance pattern. In this setting, a continuous and transmural circumferential lesion was achieved in the musculature extending from the LA to the superior and inferior PVs, but not in that extending to the PV carina (Figure 6B-b).

When additional RF applications inside the encircling line were required to isolate the PVs (type C), the encircling isolation line was not continuous or transmural. In all of these PVs, additional RF applications near the PV ostium successfully isolated the PVs, but PV carina isolation was observed in half of these PVs. In PVs without a carina isolation, additional RF
Figure 6. Schematic illustrations of the presumable mechanisms underlying the relationship between pulmonary vein (PV) potential (PVP) disappearance pattern and isolation of the PV carina. Yellow areas, musculature extending from the left atrium to the PV and PV carina; red line, the encircling lesions at the left atrial antrum. X, sites of additional radiofrequency applications inside the encircling lesions. Solid and dotted lines, lesions that are continuous and transmural, and those that are not, respectively.
applications electrically disconnected only the musculature extending from the LA to the PVs, and did not affect the musculature extending from the LA to the PV carina because of separation between these 2 musculatures (Figure 6C-a). In contrast, in PVs with carina isolation, additional RF applications electrically disconnected the musculature extending from the LA to both PVs and the carina (Figure 6C-b). These additional RF applications were often required around the PV carina. This was probably because it was difficult to create continuous and transmural lesions around the PV carina due to the thicker layers of atrial myocardial fibers oriented in circumferential, longitudinal, and oblique directions.\(^{13,15-17}\)

**Atrial Size and PVP Disappearance Pattern**

Several studies have identified larger LA as one of the risk factors for AF recurrence after PVI.\(^{18-21}\) One possible mechanism to explain this finding is the presence of more non-PV AF foci in a larger LA where fibrosis and remodeling are more prominent. This study may suggest another possible mechanism. The present study showed that the LA dimension was much larger in the patients who required additional RF applications inside the encircling lesions to isolate the ipsilateral PVs (type C) than in those with successful isolation of the ipsilateral PVs (type A or B). This suggests that the complete electrical isolation of the LA antrum including the PV carina was less likely to be achieved in a larger LA, resulting in a higher rate of AF recurrence for C-C compared to A-A or B-B. The present findings are consistent with the Lin et al.'s report that identified a similar mechanism in which wider area PVI lines were associated with a higher incidence of conduction gaps and epicardial breakthroughs into the carina by examining the distance between the antral isolation line and PV ostium.\(^{22}\)

**Clinical Implications**

The present study suggests that AF recurrence rate after EIPVI might increase when the PVP do not disappear simultaneously in the superior and inferior PVs, likely because the PV carina is not isolated. Therefore, pacing from the PV carina will be required to confirm isolation of the PV carina when such an electrophysiological finding is obtained during EIPVI.

**Study Limitations**

First, this study was subject to the limitations inherent in a retrospective design. Second, an irrigated ablation catheter was not used in this study because it was not available in Japan during the studied period. An irrigated ablation catheter might have improved the ablation outcome.

**Conclusions**

The PVP disappearance pattern during EIPVI had a significant association with AF recurrence, probably because it had a significant association with the isolation of the PV carina, which could affect long-term outcome after EIPVI.

**References**