Background: The incidence and clinical implication of dissociated pulmonary vein (PV) electrical activities after circumferential antrum PV ablation for paroxysmal atrial fibrillation (AF) remains unclear.

Methods and Results: A total of 196 patients with symptomatic paroxysmal AF who underwent circumferential antrum PV ablation were prospectively studied. Dissociated PV electrical activities were observed in 101 patients (Group 1), but absent in the remaining 95 patients (Group 2). There were no significant differences in the baseline clinical characteristics between them, except that Group 2 had a higher prevalence of hypertension (30 vs. 44%, P=0.04). After 21.8±7.9 months of follow-up, 148 had no recurrence of AF after the initial procedure. AF recurrence rate was significantly higher in Group 2 than in Group 1 (P=0.023). Relapse of PV conduction was the major cause of AF recurrence in both groups (16/16 vs. 19/23, P=0.08), and the overall procedural success rate after the redo ablation procedure was similar in the 2 groups (90 vs. 86%, P=0.44). However, the total number of patients with non-PV foci was significantly higher in Group 2 than in Group 1 (12/95 vs. 2/101, P<0.01).

Conclusions: Dissociated PV electrical activities might identify a subgroup of patients with relatively higher initial procedural success with circumferential PV antrum ablation. (Circ J 2011; 75: 73–79)

Key Words: Catheter ablation; Paroxysmal atrial fibrillation; Pulmonary vein isolation

Catheter ablation to disconnect the pulmonary veins (PV) electrically from the left atrium (LA) has been shown to be an effective treatment for atrial fibrillation (AF), especially in those patients with paroxysmal AF. Indeed, documentation of PV isolation has been recommended as one of the procedural endpoint for catheter ablation of AF. Among different techniques, segmental PV ostial ablation and circumferential PV antrum ablation are the major ablation strategies used in clinical practice. During these ablation procedures, dissociated PV electrical activities are frequently observed after achieving PV electrical isolation. Nevertheless, the incidence and characteristics of the dissociated PV electrical activities varied with the patient population as well as the ablation techniques. Weerasooriya et al demonstrated that dissociated PV electrical activities were observed in 23% of patients with paroxysmal AF, and in 12% of the PV after segmental PV ostial ablation. However, Ouyang et al reported that dissociated PV electrical activities occurred in up to 97% of patients with paroxysmal AF following circumferential PV antrum isolation (PVAI). However, the clinical implication of the presence of dissociated PV electrical activities after PVAI remains unclear. The purpose of this study was to investigate the relationship between the occurrence of dissociated PV electrical activities after PVAI and the long-term clinical outcome in patients with paroxysmal AF.
Methods

Patient Population
From March 2006 to June 2008, 196 consecutive patients (135 men, mean age 56±11 years) with symptomatic paroxysmal AF, which could not be controlled by 3±1 antiarrhythmic drugs, were included in this prospective study. Their mean duration of AF was 64.8±70.6 months. Among them, 72 patients (37%) had hypertension, and 4 patients (2%) had coronary artery disease. Patients with persistent AF, previous AF ablation, significant structural heart diseases, including heart failure, cardiomyopathy and valvular heart diseases, and other significant co-morbidities were excluded. Their mean left ventricular ejection fraction and LA diameter were 65.0±4.9% and 36.0±4.7 mm, respectively. The study protocol was approved by the local Institutional Review Board, and all patients provided written informed consent.

Electrophysiological Procedures
All the antiarrhythmic drugs were discontinued for at least 5 half-lives and Amiodarone for 2 months before the procedure. Transesophageal echocardiography was performed in all patients to exclude the presence of intracardiac thrombi. Electrophysiological study was performed after overnight fasting and mild sedated state with administration of intravenous fentanyl. A 6F decapolar catheter (Diag, St. Jude Medical, Inc) was positioned in the coronary sinus via the left subclavian vein and a 6F quadripolar catheter (Diag, St. Jude Medical, Inc) was positioned in the right ventricle via a femoral vein. Two 8F 65 cm long sheath (SL1, St. Jude Medical, Inc) were advanced to the LA through standard transseptal puncture. After transseptal puncture, intravenous heparin was administered to maintain an activated clotting time of 250 to 300 s. A deflectable decapolar circular catheter (Lasso catheter, Biosense Webster or A-focus catheter, IBI, St. Jude Medical, Inc) was advanced through the sheath for PV mapping, and a deflectable quadriipolar open irrigated catheter (Navi-star, Biosense Webster or IBI, St. Jude Medical, Inc) was inserted into the LA for mapping and ablation. Intracardial electrograms were recorded using a digital electrophysiological recording system (Prucka CardioLab, General Electric Health Care System Inc, Milwaukee, WI, USA) and were filtered from 30 to 300Hz.

3-Dimensional (D) Electroanatomical Mapping and Catheter Ablation
Circumferential PV antrum ablation procedure was guided by 3-D electroanatomical mapping using CARTO (Biosense Webster) or EnSite-NavX (St.Jude Medical, Inc) system. Before the ablation procedure, detailed 3-D geometry of the LA was created by obtaining contact bipolar electrogram (100–150 points) during sinus rhythm or AF. Furthermore, the anatomical locations of the PV ostium were tagged on the 3-D electroanatomical maps according to the selective PV angiogram. Circumferential ablation surrounding the 2 ipsilateral PV at the antrum was then performed similar to that described previously8 (Figure 1), but using a single circular catheter. Catheter ablation was performed using irrigated radiofrequency energy (Stockert generator, Biosense Webster Inc; Diamond Bar, CA, USA) delivered with a maximal temperature of 45°C and a maximal power of 35 W using an infusion rate of 17 ml/min. During the ablation procedure, the circular mapping catheter was positioned in the ipsilateral upper PV for recording of the PV electrical activities. After initial ablation procedure with documented electrical isolation of upper PV, the circular mapping was then positioned to the lower PV to confirm the presence of PV isolation. The procedural endpoint was electrical isolation of all PV with the disappearance or dissociation of the PV potentials from the LA.

After acute successful circumferential ablation to isolate both left and right PV, programmed electrical stimulation was performed to exclude other supraventricular tachycardias as well as non-PV triggers for AF. Those patients with inducible supraventricular tachycardias or non-PV foci for AF underwent further catheter ablation for these arrhythmias.

Finally, the circular mapping catheter and the ablation catheter was then positioned to the left upper and lower PV, respectively to record any re-connection or dissociation of PV potentials from the LA for 5 min. Similarly, the right-
Dissociated PV Activities and Ablation Outcomes

Patients with reconnection of PV to LA received further catheter ablation to achieve complete PV isolation. The occurrence of dissociated PV electrical activities was defined as the presence of at least 2 consecutive PV potentials without any propagation to the LA. Pacing within the veins at high output using ablation catheter was performed in those PV without dissociated electrical activities to make sure the bi-directional conduction block was achieved between LA and the PV (Figure 2). Patients were then classified into 2 groups according to the presence of dissociated PV activities. Patients with reconnection of PV to LA received further catheter ablation to achieve complete PV isolation.

Figure 2. Pacing inside the pulmonary veins (PV) demonstrating the exit conduction block from the PV to the left atrium (LA). Tracings from top to bottom are surface lead I, aVF and V1, and electrogram recording from His recording (HIS), coronary sinus (CS) from proximal to distal, 10 continuous bipolar recordings of the circular catheter (Lasso), and the ablation catheter (ABL). Pacing was performed at cycle length of 400 ms inside the right inferior PV using the ablation catheter and the circular catheter was placed inside the right superior PV. Notice that the PV sleeve muscle was captured while the LA was in sinus rhythm without capturing.

Figure 3. Ectopic beat inside the right pulmonary vein (PV) triggered atrial fibrillation (AF) before isolation (Left) and the AF persisted after PV were completely isolated (Right). Tracings from top to bottom are the same as in Figure 2. Paper speed = 50 mm/s.
Figure 4. Representative tracings of the dissociated PV activities recorded by the circular catheter from the PV after circumferential PV antrum isolation. Tracings from top to bottom are from high right atrium (HRA), right ventricular apex (RVA), other abbreviations are as in Figure 2. (A) Spontaneous repetitive firing and the isolated automaticity inside from the right PV was recorded after circumferential PV antrum isolation. ABL was placed in the LA. (B) Ongoing tachycardia with the cycle length of 323ms inside the right PV was dissociated from the sinus rhythm in the atria after circumferential PV antrum isolation (part of the circular catheter was out of the isolation line) (C) Slow autonomic PV activities (indicated by black arrow) recorded by the circular catheter from the right PV after circumferential PV antrum isolation. (D) Dissociated couplet activities from the right PV after circumferential PV antrum isolation.
Dissociated PV Activities and Ablation Outcomes

(Section 1) or absence (Group 2) of dissociated PV electrical activities after ablation (Figures 3, 4).

**Postablation Follow-up**

All patients were treated with previously ineffective anti-arrhythmic agents for 3 months and were followed-up in the outpatient clinic after the procedure. Surface electrocardiogram (ECG) and 24-h Holter recording were performed at Day 3, and then at 1, 3, and 6 months after the procedure. Furthermore, ECG was also performed anytime if the patients experienced palpitation.

Patients who had documented recurrence of AF after discontinuation of anti-arrhythmic drugs underwent a repeated ablation procedure. During the second procedure, PV investigation was performed first and re-isolation was done if LA-PV relapse occurred. Programmed electrical stimulation with isoproterenol infusion was given to increase the heart rate by 30% of the baseline beats. If atrial tachycardias or other superaventricular tachycardias were induced, further ablation for these arrhythmias should be done.

**Statistical Analysis**

Continuous variables are expressed as mean±SD. Group differences for continuous data were then examined by the Mann–Whitney 2-sample test. Categorical variables were compared with the Chi-squared test, and chi-square test for trend. The cumulative risk of recurrence of AF within each group was estimated by means of the Kaplan–Meier method. P<0.05 was considered statistically significant.

**Results**

Acute successful circumferential PV antrum isolation was achieved in all patients. In this study, dissociated PV electrical activities were observed in 101 patients (51.5%, Group 1), and 95 patients had no dissociated PV electrical activities (48.5%, Group 2). There were no significant differences in the baseline clinical characteristics between the 2 groups, except that Group 2 patients had a higher prevalence of hypertension (Table). Furthermore, there was also no significant difference in the prevalence of co-existing other supraventricular tachycardias.

### Table. Clinical Characteristics of the Study Population

<table>
<thead>
<tr>
<th></th>
<th>With dissociated pulmonary veins activities (n=101)</th>
<th>Without dissociated pulmonary veins activities (n=95)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>54.8±2.3</td>
<td>56.6±11.6</td>
<td>0.31</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>68 (67)</td>
<td>67 (71)</td>
<td>0.63</td>
</tr>
<tr>
<td>Duration of atrial fibrillation, months</td>
<td>68.3±65.1</td>
<td>73.5±64.6</td>
<td>0.61</td>
</tr>
<tr>
<td>Left atrial dimension, mm</td>
<td>36.5±4.4</td>
<td>36.4±5.0</td>
<td>0.82</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>65.2±4.8</td>
<td>64.5±4.9</td>
<td>0.87</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>30 (30)</td>
<td>42 (44)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Coronary artery disease, n (%)</td>
<td>2 (2)</td>
<td>2 (2)</td>
<td>0.95</td>
</tr>
<tr>
<td>Non-pulmonary veins foci, n (%)</td>
<td>2 (2)</td>
<td>6 (6)</td>
<td>0.12</td>
</tr>
<tr>
<td>Co-existing supraventricular tachycardia, n (%)</td>
<td>12 (12)</td>
<td>15 (16)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

**Figure 5.** Dissociated upper and lower PV activities recorded from the circular catheter and the ablation catheter. The solid arrows indicate the isolated dissociated activities recorded by the ABL in the left inferior PV, and the dashed arrows indicate the much slower activity recorded by the circular catheter in the left superior PV. All the abbreviations are as in Figures 1 and 2.
tricular tachycardia or non-PV foci between Group 1 and Group 2 patients (Table).

In Group 1 patients, dissociated PV electrical activities were observed in 48 (48%) patients on the left side PV, and 67 (66%) on the right side. Eighty-six patients presented with low-frequent PV electrical activities (cycle length >1,200 ms), and 15 manifested high-frequent PV activities (cycle length <500 ms, including fibrillation, tachycardia and repetitive couplet). Furthermore, simultaneous dissociated PV electrical activities from ipsilateral upper and lower PV was observed in 5 (5%) patients on the left side and 3 (3%) on the right (Figure 5).

After a mean follow-up of 22.8±7.9 (range 20–47) months, 148 (76%) had no recurrence of AF after the initial ablation procedure. AF recurrence was observed in 18% and 32% of Group 1 patients and Group 2 patients, respectively. As shown in Figure 6, the AF recurrence rate was significantly higher in the Group 2 patients than in the Group 1 patients (hazard ratio 1.90, 95% confidence interval 1.10–3.56, P=0.023).

In Group 1, 16/18 (89%) patients had a repeated ablation procedure for recurrence of atrial arrhythmias after termination of antiarrhythmic agents. Among them, 8 (74%) patients had relapse of PV-LA connection in the left PV and 11 (69%) in the right PV, 1 patient (6%) had typical atrial flutter, and 4 patients (25%) had atrial macrore-entrant tachycardias. No new non-PV foci were found after isoproterenol infusion in the second procedure. After the second ablation procedure, 8 (50%) had no further recurrence of atrial arrhythmias.

In Group 2, 23/30 (76%) patients had a repeated ablation procedure for recurrence of atrial arrhythmias after termination of antiarrhythmic agents. Among them, 17 (74%) patients had relapse of PV-LA connection in the left PV and 14 (61%) in the right PV, 1 patient (4%) had recurrence of atrioventricular re-entrant tachycardia, 6 patients (26%) had atrial macrore-entrant tachycardias, and 6 patients (26%) had new non-PV foci after isoproterenol infusion which were originated from the superior vena cava (n=5) and left posterior wall (n=1). After the second ablation procedure, 17 (74%) had no further recurrence of atrial arrhythmias.

Overall, the procedural success rate after the redo ablation procedure was similar between Group 1 and Group 2 patients (90% vs. 86%, P=0.44). However, the total number of patients with non-PV foci was significantly lower in Group 1 patients than in Group 2 (2/101 vs. 12/95, P<0.01).

Complications

Major complications included pericardial tamponade in 6 patients and hemothorax in 1 patient requiring drainage insertion. Furthermore, pseudo-aneurysm was observed in 4 patients.

Discussion

In this study, dissociated PV electrical activities were observed in up to 52% of patients after PVAI for paroxysmal AF. The presence of dissociated PV electrical activities after PVAI procedure was associated with a higher initial procedural success rate. However, those patients without dissociated PV electrical activities after circumferential PV antrum ablation procedure were more likely to have hypertension and had a higher incidence of non-PV trigger foci for their AF. Nevertheless, relapse of PV-LA connection remained to be the major cause of AF recurrence in both groups of patients.

It has been well documented that the arrhythmogenic foci from the PV play an important role in pathogenesis of paroxysmal AF. Previous experimental studies have shown the presence of ectopic pacemaker activities within the PV. These spontaneous trigger activities might originate from the PV antrum or inside the PV and are responsible for the dissociated PV electrical activities observed after circumferential PV antrum ablation. The incidence of dissociated PV electrical activities observed in the present study is higher than those reported by Weerasooriya et al., but lower than those reported by Ouyang et al. The differences in the definition, study population and ablation approaches in our study from others might account for this. In the current study, those patients with dissociated PV electrical activities after ablation reflected the trigger activity either more active or more distal and might represent a subgroup of patients in whom the PV triggers were the predominant mechanism of their AF. As a result, initial circumferential PV antrum ablation could achieve a higher procedural success rate in those patients. However, those patients without dissociated PV electrical activities after ablation were from a heterogeneous population with a higher prevalence of hypertension as well as higher incidence of non-PV triggers. Consistent with our findings, Weerasooriya et al. had reported that structural heart diseases frequently co-existed in their patients without dissociated PV electrical activities after ablation. Similarly, Berruezo et al. found in their study that hypertension is an independent pre-procedural predictors of AF recurrence after circumferential PV ablation to treat AF. They suggested that AF patients with hypertension might have more diseased atria. The diseased atria is a good substrate to maintain AF or prone to be initiated by trigger foci. These findings suggest that the presence of mechanisms other than PV foci are more likely to contribute to AF in those with structural heart diseases. In those patients without dissociated PV electrical activities, they might have higher AF recurrence after circumferential PV antrum ablation alone, and required additional ablation for non-PV foci.

PV electrical activities are heterogeneous, they vary with time and differ from patient to patient. This diversity can sometimes be found in different veins. Therefore, the actual performance of the PV activity during the ablation procedure might not really reflect its true behavior. In patients without proven ‘culprit PV’, you might not clearly exclude the role
of PV triggering in the genesis of paroxysmal AF. Because of this, empirical isolation of all the PV is necessary. However, patients with proven ‘culprit PV’ might not present PV firing after isolation because of some of the PV foci locate at the PV antrum area and are eliminated during ablation. In our study, we did not aim to expose the ‘culprit PV’ and to improve the success rate, but to observe the baseline prevalence of the dissociated PV activities post PVAI and their long term clinical implication. We found that those patients with dissociated PV activities post PVAI had a better long term success rate after a single procedure than those without, suggesting the predominant triggering role in these patients. Although the direct evidence was lacking, the trend was clear.

Over the years, doctors have been trying to select some clinical factors to predict the long term success of AF ablation. In our prospective study, patients with or without dissociated PV activities might predict different long term outcome of paroxysmal AF patients who underwent PVAI, but further studies are needed.

**Clinical Implications**

The baseline dissociated PV electrical activities after ablation reflect the trigger activity either more active or more distal. This might identify a subgroup of patients with more PV trigger activities and PV antrum isolation can achieve relatively higher single procedural success rate. Isoproterenol infusion and more aggressive stimulation protocol should be done after isolation to identify more non-PV triggers and other complicated superaventricular tachycardias, especially for those patients without dissociated PV activities.

**Study Limitations**

There would be an influence on the classification of each group because of the short observation period. Dissociated PV activity sometimes is capricious requiring a longer recording time, so its incidence might be underestimated. Furthermore, provocative maneuvers such as rapid pacing inside the veins and administration of isoproterenol or adenosine were not used in the study to increase the possibility of observing dissociated PV activities or revealing the non-PV trigger foci in the initial procedure. However, in our study we only observed the baseline dissociated PV activity in the specific period of time, and the clinical implication is very clear.

Identifying the triggering veins before isolation and observing their consequent PV activities after isolation will provide direct evidence to support the main finding of this study, but this ‘culprit vein’ can not always be found during the procedure and that is why the empirical circumferential isolation was done for almost all of the patients.

Catheter ablation of other complicated superaventricular tachycardias would affect the result, but the distribution of these tachyarrhythmias in our study was balanced with both groups and therefore the influence is slight.

If the follow-up was based on 7-day Holter monitoring or the event recorder, the result might be better.

**Conclusions**

The results of this study showed that the baseline occurrence of dissociated PV electrical activities after ablation might identify a subgroup of patients with PV foci as dominant mechanism of their AF and had a higher clinical success after circumferential PV antrum ablation.

**Acknowledgement**

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**References**


