Outcome of Total Pulmonary Vein Isolation in Patients with Persistent Atrial Fibrillation

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Background: Although the efficacy of pulmonary vein (PV) isolation for paroxysmal atrial fibrillation (AF) has been well-established, its effect on persistent AF has not been sufficiently established to date.

Methods and Results: In 68 consecutive patients (mean age, 52 ± 10 years) with paroxysmal (45) and persistent (23) AF, isolation of all four PVs was performed and the subsequent clinical outcome was evaluated. In total, 268/272 PVs (99%) were completely isolated from the left atrium by radiofrequency applications. During a mean follow-up period of 11 months, 84% of patients with paroxysmal AF and 57% of patients with persistent AF were free from symptomatic AF without any antiarrhythmic drug (AAD) therapy (p = 0.04). In the remaining recurrent AF patients, no significant difference between the paroxysmal and persistent AF was observed as long as they took AADs which had been ineffective at baseline (freedom from AF; 98% and 96%, respectively, p = NS). Repeat procedure performed in the 12 recurrent patients (paroxysmal AF 6, persistent AF 6) allowed 11 (92%) of them to become free from AF recurrence without AADs.

Conclusion: Electrical isolation of PV by standard catheter technique is equally and highly effective for both paroxysmal and persistent AF patients, when all four PVs were isolated. (J Arrhythmia 2005; 21: 378–383)

Key words: Atrial fibrillation, Catheter ablation, Pulmonary vein

Introduction
It has been well recognized that pulmonary veins (PVs) play an important role not only in the initiation but also in the maintenance of atrial fibrillation (AF).1–4 Although the efficacy of PV isolation to suppress the occurrence of paroxysmal AF has been already recognized, its effect on persistent AF has not been clarified yet.5–7 We conducted this study to evaluate and compare the effects of total PV isolation on both paroxysmal and persistent AF.

Methods
1) Study Subjects
This study consisted of 68 patients who underwent total PV isolation for paroxysmal (n = 45) or persistent (n = 23) AF and could be observed in a mean follow-up period of 11.8 ± 3.6 (6 to 24). There were 58 men and 10 women, and their mean age was 52 ± 10 years. “Persistent AF” in this study was defined as AF lasting for more than 7 days (a mean of 110 ± 94, 7 to 913), and with either electrical or pharmacological cardioversion required to restore
AF to sinus rhythm (SR). 8)

2) Electrophysiological Study

After written informed consent was obtained for each patient, the electrophysiological study was performed as described previously under approval protocol of the institution. 9) The left atrium (LA) and PVs were explored through either a patent foramen ovale (10 patients) or transeptal catheterization with 2 catheters: 1 for circumferential PV mapping, and the other for ablation. Direct visualization of all 4 PVs was performed using selective venography, which was performed during mid-expiration by hand injection of contrast medium (10–20 ml) in biplane views and displayed during the procedure to show the venous anatomy and the location of the LA-PV junction. PV mapping was performed with a steerable circular catheter of 15, 20 or 25 mm in diameter, selected on the basis of the predetermined measurement of a PV ostial diameter on venography, and equipped with twenty 1-mm electrodes in a loop made of shape-retaining material (Lasso, Biosense Webster) orthogonal to the shaft. PV potentials (PVPs) were defined as described previously and recorded in bipolar mode of 10 bipoles (1 to 2, 3 to 4, ..., up to 19 to 20) through band-pass filters of 30 to 500 Hz and an amplification of 1 to 2 cm/mV on polygraphy (EP Med System, Century Medical).

3) Ablation Procedure

In each case, all four PVs were targeted to be electrically disconnected from the LA, except the PVs with small diameters (less than 12 mm) and without arrhythmogenicity (Figure 1A, B). Radiofrequency (RF) current ablation was performed as proximally as possible at its ostium or antrum.

Figure 1

(A) and (B) Schematic drawing of the electrical PV isolation procedure. A deflectable 20-polar catheter with a distal ring configuration (Lasso catheter, Biosense Webster) was attached at the ostium of pulmonary vein. Radiofrequency (RF) energy was delivered at ostium or antrum of pulmonary vein (PV). Each of the all four PVs was individually isolated from left atrium at its ostium or antrum.

(C) These panels demonstrated each stage leading to PV isolation during coronary sinus pacing. Shown are surface ECG leads I, II, V5 and aVL, and 10 bipolar electrograms recorded by Lasso catheter positioned at the ostium of left superior PV. Asterisk (*) shows the earliest activation or polarity reversal sites on each electrograms at which RF current was applied. Partial disappearance of PV potential (PVP) was observed step by step, and finally the electrical isolation was completed.

(D) Electrograms demonstrated PV isolation during ongoing atrial fibrillation (AF). Circumferential PVP disappeared all at once during the fifth RF application at the antrum of the vein.
regardless of the ongoing rhythm (SR or AF). In cases with SR, the segment(s) of the PV ostial perimeter identical to the earliest activation site with the electrogram polarity reversal were preferentially targeted (Figure 1C). On the other hand, in patients who underwent PV isolation under ongoing AF, PV ostial segments demonstrating the electrogram polarity reversal or the earliest activation during a transient or sustained organization of PVP activation were preferentially targeted (Figure 1D).

RF energy was delivered between the distal electrode (8-mm tip) of the thermocouple-equipped ablation catheter and the electric plate positioned on the body surface (target: 50°C) with a power limit of 30 to 35 W for 60 to 90 seconds at each site. The end point was the establishment of the bidirectional block between the LA and PV. After the elimination of PV muscle conduction distal to the ablation site(s) was indicated either by abolition or dissociation of distal PVPs, absence of conduction from PV to the LA was also confirmed by pacing inside the PV with the mapping catheter or the Lasso catheter. If necessary, additional RF ablation was performed targeting the remaining foci.

4) Definition of Procedure Outcome

In this study, “success” of the procedure was defined as maintenance of SR without antiarrhythmic drug (AAD) therapy during a whole follow-up period, whereas the outcome was designed “effective” when AF was suppressed under AAD treatment but not without AAD. Finally, “unsuccessful procedure” was defined as recurrence of AF even under AAD treatment.

5) Patient Follow-up

After the procedure, all patients were given a periodical follow-up (once a month) in an outpatient clinic and recurrence of AF was evaluated by symptoms, ECG recordings and 24-hour ambulatory monitorings (1, 3, 6, 9, and 12 months after the procedure). When sustained AF recurred after the early unstable period (usually within one week after the procedure), AAD, which had been previously non-effective, was re-started either temporarily or continuously. A repeat ablation session was recommended for patients whose procedures were judged as unsuccessful at three months after the initial procedure.

6) Statistical Analysis

All values are expressed as mean ± SD. Statistical analysis was done using Student’s t-test (unpaired) or chi-square analysis. Differences with $p < 0.05$ was considered statistically significant.

Results

1) Patient Characteristics

As shown in Table 1, there were no significant differences in age, gender, history of AF and number of administered drugs between paroxysmal and persistent AF patients. However, the dimension of the LA was significantly larger and the ejection fraction was significantly lower in patients with persistent AF compared to those with paroxysmal AF ($p < 0.05$).

2) Procedural Indices and Complications

There were no significant differences between the paroxysmal and persistent AF patients in procedure number, procedure time, the number of isolated PVs, coexisting ratio of atrial flutter and the number of extra PV foci. One patient with paroxysmal AF had cardiac tamponade during the procedure, which was relieved only by percutaneous puncture and drainage. In another patient also with paroxysmal AF, asymptomatic stenosis of the left inferior PV (50–75%) was detected by computerized tomography scan 3 months after the ablation procedure (Table 2).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline characteristics of both patient groups.</th>
<th>Table 2</th>
<th>Results of ablation procedure.</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Paroxysmal AF</td>
<td>Persistent AF</td>
<td>Procedure number</td>
</tr>
<tr>
<td>Age (y/o)</td>
<td>52.2 ± 9.8</td>
<td>50.0 ± 10.3</td>
<td>1.2 ± 0.4</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>36/9</td>
<td>22/1</td>
<td>4.9 ± 1.1</td>
</tr>
<tr>
<td>History (y)</td>
<td>4.0 ± 4.1</td>
<td>5.6 ± 3.8</td>
<td>3.9 ± 0.5</td>
</tr>
<tr>
<td>Drugs</td>
<td>3.4 ± 1.2</td>
<td>3.6 ± 1.2</td>
<td>26/46</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>36.5 ± 4.2</td>
<td>39.5 ± 6.0</td>
<td>3 (SVC 1)</td>
</tr>
<tr>
<td>EF (%)</td>
<td>66.4 ± 7.9</td>
<td>62.3 ± 5.8</td>
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AF indicates atrial fibrillation; PV, pulmonary vein; AFL, atrial flutter; SVC, superior vena cava.
3) Efficacy of Total Isolation on Paroxysmal and Persistent AF

In a mean follow-up period of 12 months, 84% (38/45) and 57% (13/23) of patients with paroxysmal and persistent AF, were free from AF without any AAD treatment, respectively ($p < 0.05$) (success of procedure, **Figure 2A**). As for the remaining recurrent patients, most of them could maintain the SR as long as they took AADs which had been ineffective at baseline. In total, there was no significant difference between patients with paroxysmal and persistent AF in the ratio of maintaining SR either with or without AADs (98% vs 96% in the former and the latter, respectively) (**Figure 2B**).

4) Repeat Ablation Procedure

In this study, repeat ablation sessions were performed in 6 of 45 patients (13%) with paroxysmal AF and 6 of 23 patients (26%) with persistent AF at $5.2 \pm 2.6$ months after the initial procedure, for patients who could not maintain SR even under AAD treatment (unsuccessful procedure). During the second procedure, recovery of conduction between PV and LA was observed in at least 3 PVs in each of these patients (mean $3.3 \pm 0.6$ PVs). Complete isolation of all re-conducted PVs was successfully achieved in these patients, so that 6 of 6 patients (100%) with paroxysmal AF and 5 of 6 patients (83%) with persistent AF ($P = \text{NS}$), in total 92% (11/12), became free from AF without AAD. On the other hand, in 6 patients (50%) extra-PV foci were also considered to be culprit lesions responsible for recurrence which were successfully eliminated.

**Discussion**

This study demonstrated that electrical isolation of all four PVs by RF ablation was equally and highly effective for maintaining SR in both paroxysmal and persistent AF patients. Although “success” (no recurrence of AF without AAD) could be achieved with significantly higher probability in patients with paroxysmal AF than persistent AF (84% vs 57%) in the initial session, SR could be maintained under AAD administration in the majority of patients regardless of the type of AF (98% vs 96% in paroxysmal and persistent, respectively).

Recently Oral et al.7 had reported that PV isolation was significantly less effective in persistent AF compared to paroxysmal AF either with or without drugs (83% vs 29% in paroxysmal and persistent AF, respectively). Although their definition of “persistent AF” differed, in our study the mean duration of lasting AF was 110 days and in almost all patients with persistent AF the duration was more than 30 days. The discrepancies between our study and theirs may be caused by the difference in the method of procedure. In their study, at least three PVs were targeted for isolation and isolation of all four PVs was achieved in only 28% of the patients. Furthermore, 84% of all targeted PVs were successfully isolated from the LA. On the other hand, in our study population all four PVs were targeted and 98% of all the targeted PVs were electrically isolated from the LA. It has been demonstrated that the PV acts not only as the origin of atrial premature contraction but also as the substrate for maintaining AF with the specific electrophysiological features distinct from those of the LA.3,4,11 In patients with persistent AF, reduction of the arrhythmogenic substrate by total PV isolation would be desirable to terminate AF and maintain SR.

In this study, a significantly larger number of
patients with persistent AF required AAD to maintain SR compared to paroxysmal AF and the dimension of the LA was also significantly larger in patients with persistent AF (Table 1, 36.5 vs 39.5 mm ($p = 0.02$)). It might be suggested that more advanced degenerative change of LA myocardium in patients with persistent AF$^{12,13}$ is related to the lower “success” rate of complete AF elimination and the greater need for AADs compared to paroxysmal AF.

**Repeat Procedures**

Recurrence of AF after electrical PV isolation continues to be a major limitation of the PV isolation procedure and it has been reported that the recovery of conduction between PV and LA is the most common cause of recurrence.$^{14-16}$ In fact, at least 3 PVs re-connected to LA in patients who underwent a repeat ablation in our study, and most of them became free from AF after re-isolation of these PVs, regardless of the type of AF. Recently, several studies reported advantages of linear RF energy applications in the LA to maintain SR in addition to PV isolation, especially in persistent cases.$^{17,18}$ On the other hand, a recent report by Callans et al.$^{15}$ suggested that perfecting PV isolation by repeat sessions could increase the success rate without making linear lesions and Verma et al.$^{19}$ also described a high success rate for suppressing AF by PV antrum isolation without LA linear ablation. Although the necessity of LA linear ablation to suppress AF remains to be determined, it should be recognized again that total and perfect PV isolation is one of the essential prerequisites for suppressing AF regardless of its type, before making extensive LA lesions.

**Study Limitations**

One limitation of this study is that the clinical outcome of PV isolation procedure was judged partly based on symptoms of patients which might result in missing asymptomatic episodes of AF recurrence.$^{20}$ However, we believe that periodical and frequent contact with the patients including 24-hour ambulatory monitorings could minimize this possibility.

**Conclusion**

Ostial PV isolation by catheter technique is equally and highly effective in patients with paroxysmal and persistent AF, when all four PVs are isolated. However, significantly more patients with persistent AF required AAD than paroxysmal AF to be free from AF. The efficacy of PV isolation can be enhanced by targeting all four PVs at their ostium with circumferential bidirectional block as the endpoint.

**References**


