Resumption of Electrical Conduction in Previously Isolated Pulmonary Veins
Rationale for a Different Strategy?

Kumaraswamy Nanthakumar, MD; Vance J. Plumb, MD; Andrew E. Epstein, MD; George D. Veenhuyzen, MD; Dale Link, RN; G. Neal Kay, MD

**Background**—Atrial fibrillation (AF) may recur after pulmonary vein isolation (PVI) as the result of either recurrent PV conduction or non-PV foci. This study characterized the electrophysiological findings of patients with recurrent AF after initially successful PVI and the clinical outcome after a repeat procedure.

**Methods and Results**—Among 185 patients undergoing PVI, 52 reported no significant improvement in their clinical course. We analyzed PV conduction in 51 PVs (15 patients) at repeat PVI. All PVs were isolated with either RF (30 W, 50°C, 60 seconds) or cryoablation (−80°C for 5 minutes). At repeat study, 42 of the previously isolated 51 PVs had return of conduction. All patients had recurrent conduction in ≥2 PVs, with only 1 non-PV focus identified. The mean number of RF applications required to re-isolate the PVs was fewer at the repeat compared with the initial procedure (10±6 versus 4±2, *P*<0.005). Over a period of 15±6 months, all but 1 patient was clinically improved by the second procedure.

**Conclusions**—In patients with recurrent AF after PVI, return of PV conduction can be expected. Repeat PVI provides significant clinical benefit for these patients. These results suggest that if permanent PV isolation is the ablation strategy, different techniques may be required to improve long-term efficacy. (Circulation. 2004;109:1226-1229.)

**Key Words:** mapping • catheter ablation • arrhythmia

The techniques used for catheter ablation of atrial fibrillation (AF) by targeting triggering foci in the pulmonary veins (PV) have evolved from initial ablation of PV foci to empiric isolation of all PVs. An anatomic approach targeting the substrate for AF maintenance, by ablating the left atrium surrounding the PVs, was concurrently developed, which in a randomized trial has proven to have a lower recurrence risk than PV isolation (PVI). Recurrent AF after PVI could be related to failure to maintain conduction block from the PVs or the presence of non-PV triggering foci. If recurrent PV conduction is responsible for relapses, repeat isolation may be appropriate. In this report, we characterize PV conduction at repeat electrophysiological study in patients with recurrent AF after initially successful PVI and the outcome of a repeat procedure.

**Methods**

This study was approved by the Institutional Review Board for Research Involving Human Subjects at the University of Alabama at Birmingham and included patients with recurrent AF who underwent repeat electrophysiological study after PVI at the University of Alabama at Birmingham.

**Initial Procedure**

The electrophysiological studies were performed during intravenous sedation. Double transseptal catheterization was performed, and heparin was administered to maintain the activated clotting time >250 seconds. PV mapping was done with either a circular mapping catheter (Lasso, Webster Biosense), or a 31-mm basket catheter (Constellation, Boston Scientific). When the basket catheter was used, tirofiban was also infused. Mapping catheters were positioned in the high right atrium, superior vena cava, coronary sinus, and the PVs. Segmental isolation of all 4 PVs was performed at the initial procedure with RF (n=12) (30 W, 55°C, 60 seconds) or cryoablation (n=3) (−80°C for 5 minutes) with complete elimination or dissociation of PV potentials as the end point. The ablation was performed just outside the ostium of the pulmonary veins (determined by venography and recording of left atrial and PV electrograms). The end point was complete PVI and noninducibility of AF during isoproterenol infusion (2 to 4 µg/min) and rapid atrial pacing (cycle lengths as short as 180 ms). All patients were followed by telephone contact and in the clinic (6 weeks after ablation and every 3 months thereafter or as symptoms dictated) with serial electrocardiograms and questioned for symptoms suggestive of recurrent AF. Patients were classified as deriving no significant clinical benefit if they required AV nodal ablation, institution of amiodarone, or continued to have AF despite previously ineffective antiarrhythmic drugs.

**Repeat Procedure**

Patients with symptomatic recurrence were offered repeat electrophysiological study and ablation. All PVs were assessed for return of conduction. Repeat PVI was performed with the use of RF energy delivered to the PV ostium for 60 seconds, at 30 W, with a target temperature of 55°C. Isoproterenol was infused, and rapid atrial...
pacing was performed to a cycle length of 180 ms to assess ablation efficacy.

Statistical Analysis
Comparison of continuous variables was made by paired 2-tailed t-tests.

Results
Between January 2001 and February 2003, 185 patients were treated with PVI. Among these, 52 reported no significant clinical benefit. We analyzed 51 previously isolated PVs from 15 patients (mean age, 52±9 years) who had repeat PVI. All had failed a class 1 or 3 antiarrhythmic drug (amiodarone, 64%; class 1A, 57%; class 1C, 57%; sotalol, 57%). If the 15 patients, AF was paroxysmal in 14 and permanent in 1. The interval between the initial and repeat procedures was 107±100 days.

In patients with AF recurrence, 42 of the 51 previously isolated PVs exhibited return of electrical conduction (Table). All patients had return of conduction in ≥2 PVs. Fewer RF applications were required to isolate the PVs at the repeat compared with the initial procedure (10±6 versus 4±2, P=0.01). Only 1 patient had an extra-PV focus that was ablated within the vein of Marshall and also had recurrent conduction in 2 previously isolated PVs. Figure 1A illustrates PV potentials in one of the patients at initial study during AF. Figure 1B illustrates absence of PV potentials in the same left superior pulmonary vein (LSPV) after 10 RF applications around its entire circumference. The patient had recurrence of AF 4 months later and underwent repeat ablation with recurrent conduction

Findings at Initial and Repeat Ablation

<table>
<thead>
<tr>
<th></th>
<th>Initial Ablation (n=51)</th>
<th>Repeat Ablation (n=51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of PV isolated/patient</td>
<td>3.5±0.7</td>
<td>3.3±0.6</td>
</tr>
<tr>
<td>No. of lesions/vein</td>
<td>8.8±5.7</td>
<td>5.6±5.1</td>
</tr>
<tr>
<td>Mean No. of lesions/LSPV</td>
<td>11.4±6.0</td>
<td>5.1±4.0</td>
</tr>
<tr>
<td>Mean No. of lesions/LIPV</td>
<td>7.8±5.4</td>
<td>4.1±4.2</td>
</tr>
<tr>
<td>Mean No. of lesions/RSPV</td>
<td>8.0±5.0</td>
<td>7.0±6.1</td>
</tr>
<tr>
<td>Mean No. of lesions/RIPV</td>
<td>7.4±6.6</td>
<td>6.8±6.4</td>
</tr>
<tr>
<td>Non-PV focus</td>
<td>3 of 15 patients</td>
<td>1 of 15 patients</td>
</tr>
<tr>
<td>Linear lesion</td>
<td>1 of 15 patients</td>
<td>3 of 15 patients</td>
</tr>
<tr>
<td>Flutter ablation</td>
<td>5 of 15 patients</td>
<td>5 of 15 patients</td>
</tr>
</tbody>
</table>

LSVP indicates left superior pulmonary vein; LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; and RIPV, right inferior pulmonary vein.

Figure 1.
A, Pre–initial PVI LSPV. Intracardiac recordings are from a 64-pole basket catheter positioned in the LSPV. Intracardiac electrograms reveal presence of PV potentials. B, Post–initial PVI LSPV. Intracardiac recordings are from a 64-pole basket catheter in the same LSPV after ablation.
in this PV (Figure 2A). Repeat isolation required 4 RF applications to 30% of the PV circumference (Figure 2B). The only complication in this series was an asymptomatic 50% PV stenosis that remained isolated at repeat study. Among the other patients without clinical benefit after a first PVI, 13 are awaiting repeat ablation, amiodarone was started in 21, and 3 underwent AV nodal ablation.

Over a period of 15 ± 2 months, 1 patient had development of permanent AF after the second PVI procedure. All other patients were clinically improved (6 on antiarrhythmic medication). There were no procedural complications from repeat ablation, and no patient had signs or symptoms of PV stenosis.

Discussion

Patients with recurrent AF after initially successful PVI had return of conduction in most PVs at repeat electrophysiologic study. Repeat PVI required fewer RF lesions to achieve successful PVI than at initial procedure and was associated with clinical improvement.

The reasons for failure of PVI include non-PV triggers and/or failure to achieve lasting PV conduction block. The present study shows that patients with recurrent AF after PVI usually have return of conduction in multiple PVs. The salutary effects of repeat PVI suggest that the resumption of left atrial (LA)-PV conduction may serve as important marker of the arrhythmogenic milieu that predisposes to AF and support repeat ablation after an initially successful procedure.

Recurrent PV Conduction in Patients With Recurrent AF

In the study by Oral et al., the anatomic wide-area circumferential ablation approach was compared with segmental PVI. Recurrent AF was more common with the segmental ostial ablation (32%) than after wide area circumferential left atrial ablation (10%). The amount of ablative energy was much higher with the circumferential LA ablation technique. Concordant with our findings, at repeat mapping after PVI in 7 patients, all had at least 1 PV with recurrent PV conduction. Recently, Cappato et al. also demonstrated that PV conduc-

Figure 2. A. Pre–repeat PVI LSPV. Top 3 tracings are surface ECG leads I, AVL, and V1, with bipolar electrograms from the His bundle region and coronary sinus. Ablation catheter is positioned at the ostium of the LSPV of the same patient as in the Figure. Circular mapping catheter is positioned in the LSPV. Electrograms from the circular catheter demonstrate both PV and LA potential, indicating return of conduction in the previously isolated vein. B, Post-repeat PVI LSPV. Electrograms from circular catheters in the same LSPV after repeat ablation reveal absence PV potentials and presence of LA potentials.
tion commonly recurs after PVI (80% of ablated PV ostia showed some recurrent conduction). However, clinical success after the first procedure was reported in 32% of patients despite the presence of recurrent PV conduction. This suggests that isolation may not be an absolute requirement for a successful procedure. Interestingly, greater conduction delay between the LA and the PV was observed for patients who became asymptomatic as compared with those who remained symptomatic after ablation. This suggests that though acute PVI may not be a good predictor of long-term elimination of AF, the greater the delay in PV conduction, the better the clinical outcome. It logically follows that permanent isolation would improve the results of this procedure.

Gerstenfeld et al\(^6\) reported recurrent conduction in 61% of PVs (34 patients) after PVI with 82% of patient having at least 1 PV with recurrent conduction. Importantly, this group only isolated those PVs with identifiable triggers, making it difficult to interpret the cause of recurrent AF in this population.

**Why Does the Wide Area Circumferential Ablation Technique Appear to Have a Lower Recurrence Rate?**

The wide area circumferential approach may provide a lower risk of recurrent AF than segmental PVI.\(^4\) However, it is unlikely that these strategies target the same physiological and anatomic substrates. Stabile et al\(^7\) demonstrated the wide area circumferential approach rarely produces PVI, suggesting that conduction block is not essential for long-term success. However, that study did not investigate whether or not the wide area circumferential approach resulted in delay in LA-PV conduction. The wide area circumferential approach uses greater RF energy (60 W for 42 minutes) than the segmental approach (30 W for 18 minutes),\(^4\) with a similar risk of complications.

Why is the wide area circumferential approach associated with a lower risk of recurrent AF? First, this technique targets a larger amount of myocardium rather than only the first few millimeters of the PV ostia. This strategy may directly ablate arrhythmogenic foci even when permanent PVI is not achieved. In addition, the PVs have a shorter refractory period than the LA, and there is often conduction delay or block of premature beats originating in the PV at the PV-left atrial junction. Circumferential ablation in the left atrium may increase this probability. The greater energy delivery should result in greater reduction in viable tissue in the zone of anisotropy.\(^8\) The segmental PVI technique has limited power delivery because of concern for the risk of PV stenosis, a factor than may predispose to recurrent PV conduction.\(^9\) It is important to point out that although acute PVI does not ensure lasting PVI and is a poor predictor of outcome, it has not been shown that AF can recur with lasting PVI of all PVs. Thus, it may be that it is the execution and not the strategy that is faulty when AF recurs after this procedure.

**Conclusions**

Successful PVI with previously standard target settings for RF energy or cryoablation often does not ensure lasting PVI. In patients with recurrence of AF after PVI, return of conduction can be expected in a significant number of previously isolated PVs. Repeat PVI may significantly benefit these patients. These results suggest that alternative strategies may be required to reduce the risk of recurrent AF.

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**References**

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