Segmental Ostial Ablation to Isolate the Pulmonary Veins During Atrial Fibrillation
Feasibility and Mechanistic Insights

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Background—The purpose of this study was to determine the feasibility and mechanistic implications of segmental pulmonary vein (PV) ostial ablation during atrial fibrillation (AF).

Methods and Results—Forty consecutive patients underwent PV isolation for AF. Among 125 PVs targeted for isolation, ablation was performed during AF in 70 veins and during sinus rhythm in 55 veins. A decapolar Lasso catheter was positioned near the ostium. During AF, ostial ablation was performed near the Lasso catheter electrodes that recorded a tachycardia with a cycle length shorter than in the adjacent left atrium. During sinus rhythm, ostial ablation was guided by PV potentials. Complete PV isolation was achieved in 70 PVs (100%) ablated during AF and in 53 PVs (96%) ablated during sinus rhythm (P=0.4). The mean durations of radiofrequency energy needed for isolation were 7.4±4.4 and 5.2±3.9 minutes during AF and sinus rhythm, respectively (P<0.01). Before ablation, an immediate recurrence of AF (IRAF), occurred after cardioversion in 18 of 40 patients, and IRAF was consistently abolished by PV isolation. The probability of AF termination during isolation of a PV was directly related to the extent of tachycardia in that vein. As more PVs were isolated, induction of persistent AF by rapid pacing became less likely.

Conclusions—Segmental ostial ablation guided by PV tachycardia during AF is feasible and as efficacious as during sinus rhythm. The responses to cardioversion, ablation, and rapid pacing observed in this study imply that IRAF is triggered by the PVs and that PV tachycardias may play an important role in the perpetuation of AF. (Circulation. 2002;106: 1256-1262.)

Key Words: fibrillation ■ veins ■ catheter ablation

Pulmonary vein (PV) isolation can be achieved by segmental ostial ablation guided by PV potentials recorded during sinus rhythm and/or atrial pacing.1,2 During an ongoing episode of atrial fibrillation (AF), the PVs can be isolated by circumferential ablation.3 However, because PV potentials may be obscured during the chaotic electrical activity of AF, the feasibility of segmental ostial ablation during the arrhythmia has been unclear.

Prior experimental and clinical studies have demonstrated that rapid rhythms arising in the PVs (variably referred to as rapid focal activity,4 repetitive rapid activity,5 intermittent PV tachycardia,6 or paroxysmal cycle length shortening7) are common during AF. The results of these prior studies have suggested that rapid PV rhythms may play an important role in the maintenance of AF1,6,8 or may be a marker of an arrhythmogenic PV that triggers AF during sinus rhythm.7

The present study was designed to test the hypothesis that intermittent bursts of PV tachycardia are an indicator of arrhythmogenic PV muscle fascicles and can be used to guide segmental ostial ablation to isolate the PVs during AF. In addition, to further clarify the mechanistic significance of intermittent PV tachycardia, the responses to cardioversion and rapid pacing were examined before and after PV isolation.

Methods

Patient Characteristics
The subjects of this study were 40 consecutive patients who underwent PV isolation for paroxysmal (37) or persistent (3) AF. There were 32 men and 8 women; mean age was 54±10 years. The clinical characteristics of the patients are described in the Table.

Electrophysiology Study
All patients provided written informed consent. A quadripolar electrode catheter (EP Technologies, Inc) was positioned in the distal coronary sinus. Transseptal catheterization was performed and systemic anticoagulation was achieved to maintain an activated clotting time of 250 to 350 seconds. Venograms of the left superior (LS), left inferior (LI), and right superior (RS) PVs were performed. A deflectable decapolar catheter with a distal ring configuration (Lasso catheter, Biosense Webster) was advanced sequentially into each PV and was used for ostial mapping. A deflectable, quadripolar 7F
Clinical Characteristics of Patients Who Underwent Pulmonary Vein Isolation During Atrial Fibrillation and Sinus Rhythm

<table>
<thead>
<tr>
<th></th>
<th>AF (n=32)</th>
<th>Sinus Rhythm (n=8)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55±10</td>
<td>48±8</td>
<td>0.1</td>
</tr>
<tr>
<td>Male/female</td>
<td>26/6</td>
<td>6/2</td>
<td>0.6</td>
</tr>
<tr>
<td>Paroxysmal/persistent AF</td>
<td>30/2</td>
<td>7/1</td>
<td>0.5</td>
</tr>
<tr>
<td>Duration of AF, y</td>
<td>8±2</td>
<td>7±5</td>
<td>0.7</td>
</tr>
<tr>
<td>Frequency of symptoms, episodes per mo</td>
<td>18±15</td>
<td>25±8</td>
<td>0.4</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.54±0.03</td>
<td>0.56±0.02</td>
<td>0.3</td>
</tr>
<tr>
<td>Left atrial diameter, mm</td>
<td>41.2±3.4</td>
<td>42.0±4.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>7 (22%)</td>
<td>0</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Continuous variables expressed as mean±SD.

The catheter with 2–5–2-mm interelectrode spacing and a 4-mm distal electrode with an embedded thermistor (EP Technologies, Inc) was used for mapping and radiofrequency energy delivery. Bipolar and unipolar electrograms were filtered at bandpass settings of 30 to 500 Hz and 0.5 to 200 Hz, respectively, and were recorded digitally (EPMed Systems, Inc).

Study Protocol

Among the 40 patients, 11 patients were in AF on presentation to the electrophysiology laboratory. In the other patients, AF was induced by rapid atrial pacing. The PVs were sequentially mapped with the Lasso catheter during AF to assess the presence of intermittent PV tachycardia, defined as a PV rhythm that intermittently had a cycle length that was shorter than the AF cycle length recorded in the adjacent left atrium.6

After at least 3 minutes of recordings from each of the PVs during AF, transmural cardioversion was performed. Sinus rhythm was restored in all patients, but AF recurred within 60 seconds after cardioversion (immediate recurrence of AF, IRAF) in 18 patients (45%). PV isolation was performed during AF in these 18 patients. Among the 22 patients who did not have IRAF, AF was induced by pacing in 14 patients who were randomly selected. In the remaining 8 patients, PV isolation was performed during sinus rhythm or atrial pacing. There were no significant differences in the clinical characteristics of patients who had PV isolation performed during AF or sinus rhythm (Table).

The Lasso catheter was positioned inside a PV, within 5 mm of the ostium. When a PV was isolated during sinus rhythm or atrial pacing, ostial sites with the earliest bipolar activation and/or the most rapid unipolar intrinsic deflection were targeted for ablation.1,2,9 When a PV was isolated during AF, ostial sites at which an intermittent PV tachycardia was recorded were targeted for ablation (Figure 1). When intermittent PV tachycardia was recorded by several electrodes, an attempt was made to target the ostial site corresponding to the most rapid intrinsic deflection of the unipolar electrogram. In 2 of 70 PVs that were isolated during AF, no PV tachycardia was observed; in these 2 veins, ostial sites that displayed a high-frequency bipolar PV potential and/or rapid unipolar intrinsic deflection during AF were targeted for ablation (Figure 2).

The ablation catheter was maneuvered to a position adjacent to the target electrode of the Lasso catheter and then withdrawn to the edge of the ostium. Radiofrequency energy was delivered at the PV ostium with a target temperature of 52°C and a maximum power output of 30 to 35 W for 30 to 45 seconds (EP Technologies, Inc). The end point of ablation was complete entrance block into the PV ostium (Figure 3) and the elimination of all ostial PV potentials during sinus rhythm and atrial pacing (Figure 4).

If AF still was present after isolation of a PV, transthoracic cardioversion was performed. If IRAF occurred, other PVs were isolated during AF. If AF terminated during ablation (Figure 5A), then PV potentials were assessed during sinus rhythm and atrial pacing. If there was evidence of residual conduction over a PV fascicle (Figure 5B), radiofrequency energy was delivered at these ostial sites during sinus rhythm or atrial pacing (Figure 5C). If there was no IRAF, atrial pacing was performed at cycle lengths of 200 to 180 ms to determine whether AF was still inducible. To confirm noninducibility, induction was attempted 5 times. AF that terminated spontaneously within 5 minutes of induction was considered nonsustained. If the induced AF was nonsustained, the remaining PVs were isolated during sinus rhythm. If AF was persistent, then an additional PV was isolated during AF. Transthoracic cardioversion and rapid atrial pacing to determine whether persistent AF still was inducible were performed after isolation of each PV.

To minimize the probability of recurrent AF, the LS, LI, and RS PVs were targeted for ablation in all patients.8 The right inferior (RI) PV was isolated in 7 patients in whom an intermittent PV tachycardia was observed in that vein.

After isolation of all targeted PVs, isoproterenol was infused at a rate of 4 to 8 μg/min to confirm complete isolation of the PVs and to determine whether there were any arrhythmogenic foci inducible by sympathetic activation.

Follow-Up

After the ablation procedure, all patients were observed in a monitored bed for 24 hours. Heparin was administered intravenously...
for 24 hours, followed by warfarin for 1 to 3 months after the procedure. Low-molecular-weight heparin was administered for 4 days after discharge.

The patients were seen in an outpatient clinic 4 weeks after the procedure and every 3 to 4 months thereafter. All patients who reported symptoms were given an event monitor to document the cause of symptoms. No patients were lost to follow-up. Computerized tomography was performed before and 3 to 4 months after the ablation procedure to assess the PVs for stenosis.

**Statistical Analysis**

Continuous variables are expressed as mean±1 SD. Continuous variables were compared by Student’s t test. Categorical variables were compared by χ² analysis or with the Fisher exact test. A P<0.05 indicated statistical significance.

**Results**

**Intermittent Pulmonary Vein Tachycardia**

Intermittent bursts of PV tachycardia were recorded in 68 of 70 PVs in which ostial ablation was performed during AF. The intermittent bursts of PV tachycardia occurred 3.9±4.2 times/min and had a mean duration of 648±503 ms. The mean cycle length of the PV tachycardias was 107±29 ms; the simultaneous cycle length in the adjacent left atrium was 177±30 ms (P<0.01).

**Efficacy of PV Isolation**

Complete electrical isolation was achieved in 70 of the 70 PVs (100%) isolated during AF and in 53 of the 55 PVs (96%) isolated during sinus rhythm or atrial pacing (P=0.4). The mean duration of applications of radiofrequency energy needed to achieve complete electrical isolation was 7.4±4.4 minutes per vein when ablation was performed during AF, compared with 5.2±3.9 minutes when ablation was performed during sinus rhythm or atrial pacing (P<0.01). Among the PVs in which isolation was started in AF, 12±20% of the total radiofrequency energy was applied in the setting of sinus rhythm, either after spontaneous or transthoracic cardioversion.

**Figure 2.** Use of unipolar recordings to identify ostial ablation sites during AF. Bipolar electrograms revealed PV potentials during AF (A). Unipolar recordings demonstrated that the earliest, steepest, and largest intrinsic deflection was recorded at electrode 8; this site was targeted for ablation (B). Catheter positions and abbreviations as in Figure 1.

**Figure 3.** An end point of ablation. Before isolation, there was PV tachycardia (asterisk) with exit block to the left atrium (A). After PV isolation (B), ablation catheter was moved to the right superior PV, but the Lasso catheter was left in the left superior PV. Absence of electrograms within the LS PV during AF indicates complete isolation (B). Catheter positions and abbreviations as in Figure 1.
Procedure Duration and Duration of Fluoroscopy
The mean procedure duration for isolation of a PV was 26.7±16.5 minutes per vein when ablation was performed during AF and 25.7±20.3 minutes when isolation was performed during sinus rhythm or atrial pacing (P=0.8). There was no significant difference in the duration of fluoroscopy per vein when isolation was performed during AF, 9.6±7.7 minutes, and during sinus rhythm or atrial pacing, 8.9±7.2 minutes (P=0.6).

Percent Circumference of PV Ostium Ablated for Complete Isolation
The percent of the circumference of the PV ostium ablated to achieve complete electrical isolation was 48±17% when RF energy was delivered during AF and 45±22% when RF energy was delivered during sinus rhythm or atrial pacing (P=0.4).

Termination of AF During RF Energy Application
AF terminated in 18 of 30 patients (60%) during or within 15 seconds after delivery of radiofrequency energy at ostial sites that displayed an intermittent PV tachycardia (Figure 5). Bursts of intermittent PV tachycardia were more frequent (6.7±4.3 versus 3.0±3.6 episodes/min, P=0.02) and had a longer duration (5.300±558 versus 1.009±160 ms/episode, P<0.01) in the PVs in which isolation was associated with termination of AF than in the PVs in which AF persisted after isolation.

Prevention of IRAF
Before ablation, 18 patients had IRAF after cardioversion of atrial fibrillation. IRAF no longer occurred after isolation of 1 PV in 13 patients, 2 PVs in 4 patients, and 3 PVs in the remaining patient.

Number of PVs Isolated and Inducibility of AF
Among the 25 patients in whom AF was induced by burst atrial pacing after isolation of each PV, persistent AF still was inducible in 12 (48%) after isolation of 1 PV, in 6 (12%) after isolation of 2 PVs, in 3 (9%) after isolation of 3 PVs, and in 2 (8%) after isolation of 4 PVs (P=0.003). The mean duration of nonsustained AF after pulmonary vein isolation was 0.19±0.32 minutes.

Clinical Outcomes
Each of the patients who underwent isolation of all PVs during sinus rhythm and 26 of the 32 patients (81%) who had at least 1 PV isolated during AF were free from recurrent episodes of AF without any antiarrhythmic therapy (P=0.3).

There were no instances of PV stenosis or other complications among the 40 patients in this study.

Discussion
Main Findings
The results of this study demonstrate that segmental ostial ablation to isolate the PVs can be performed during AF when guided by intermittent bursts of PV tachycardia. The results of ablation during AF were similar to when ablation was guided by PV potentials in the setting of sinus rhythm, with acute success rates of 96% to 100% with the 2 approaches. Approximately 50% of the ostial circumference was ablated to achieve electrical isolation during both AF and sinus rhythm, indicating that the segmental approach to ostial ablation is just as feasible during AF as during sinus rhythm. The only procedural end point that differed between the two approaches was the amount of radiofrequency energy needed for isolation, which was a mean of 2.2 minutes per vein longer when ablation was performed during AF.

One of the observations in this study was that postcardioversion IRAF was consistently abolished by PV isolation, implying that IRAF often is initiated by depolarizations originating in the PVs. Another observation was that persistent AF often converted to sinus rhythm during isolation of the PVs and that this phenomenon was associated with the amount of tachycardia originating in that vein. This, along with the observation that persistent AF became inducible less often as more PVs were isolated, demonstrates that the PVs...
are not only a source of the triggers that initiate AF but also may play an important role in the maintenance of AF.

Segmental Ostial Ablation During AF
In this study, intermittent PV tachycardia was used to identify the ostial locations of arrhythmogenic PV muscle fascicles. The percent of the ostial circumference that was ablated to achieve electrical isolation was similar among the PVs that were isolated during AF or during sinus rhythm, confirming that intermittent PV tachycardia recorded near the ostia reflect the presence of an underlying muscle fascicle near the ostial recording sites.

More minutes of radiofrequency energy were necessary to completely isolate the PVs during AF. There are at least 2 possible explanations for this. First, because PV muscle fascicles may be broad enough to allow a PV tachycardia to be recorded by several electrodes of the Lasso catheter, localization of the successful ablation sites was not as precise as during sinus rhythm. Second, when ablation is performed in the setting of sinus rhythm, the position of the ablation catheter relative to the target electrode of the Lasso catheter can be confirmed by comparing the morphologies of the unipolar electrograms recorded by the ablation and Lasso catheters. This was difficult during AF, making it more likely that radiofrequency energy was delivered to ineffective sites.

Immediate Recurrences of Atrial Fibrillation
IRAF has been observed after cardioversion in up to 40% of patients who undergo catheter ablation of AF. Episodes of IRAF have been used to localize the arrhythmogenic foci that trigger AF. In the present study, no attempt was made to localize the source of the premature depolarizations that triggered episodes of IRAF. Nevertheless, episodes of IRAF were consistently abolished by PV isolation. This observation
provides strong evidence that IRAF often is initiated by depolarizations that originate in the PVs.

Role of PVs in Maintenance of AF

Although prior animal and clinical studies have proposed that the rapid rhythms that originate in PVs play an important role in the maintenance of AF, a limitation of those studies was that the response of AF to PV isolation was not evaluated. In the present study, AF often terminated during an ostial application of radiofrequency energy. This observation provides additional evidence that the electrical activity that arises in the PVs plays a role in the maintenance of AF.

In 1950, Prinzmetal et al. proposed that rapid firing in the atrium induced by aconitine could create AF. Probably by a similar mechanism, AF can be made persistent by repeated bursts of rapid atrial pacing. It is possible that intermittent bursts of PV tachycardia serve to perpetuate AF in the same fashion as aconitine-induced rapid firing or bursts of rapid atrial pacing. This would explain why persistent AF often was not inducible by atrial pacing after PV isolation. The importance of the PVs in perpetuating AF may also explain why intraoperative PV isolation sometimes eliminates chronic AF.

It may be argued that termination of AF in the course of PV isolation was a random event that was not directly related to ostial ablation. However, two observations provide strong evidence that termination of AF was a direct effect of PV isolation. First, termination of AF was associated with the amount of intermittent tachycardia recorded within the PV that was undergoing ostial ablation. Second, AF always terminated during or shortly after an effective ostial application of radiofrequency energy. Had termination of AF been a random event, there should have been no relation to the amount of PV tachycardia or to the timing of the energy applications.

In 40% of patients in this study, AF persisted despite successful isolation of the PVs. Furthermore, intraoperative PV isolation by itself does not always eliminate AF. These observations are consistent with perpetuation of AF being a multifactorial process, dependent in some patients on factors other than the PVs.

Previous Studies

In a recent clinical study conducted in 10 patients by O’Donnell et al., paroxysmal cycle length shortening was observed within some PVs during AF and was found to correlate with the presence of arrhythmogenic foci that triggered AF. Therefore, it is likely that a successful clinical outcome in some patients in this study (particularly the patients in whom AF persisted after PV isolation) was attributable to elimination of triggers for AF.

In another prior study, intermittent tachycardias associated with paroxysmal cycle length shortening were recorded during AF in ≈90% of PVs. In the present study, this phenomenon was noted in 97% of pulmonary veins that were isolated during AF. These observations, in conjunction with the results of O’Donnell, et al., suggest that almost all PVs are capable of generating the premature depolarizations that trigger AF, strengthening the case for isolation of as many PVs as possible during the ablation procedure.

The mechanistic significance of paroxysmal cycle length shortening has been questioned. For example, it is possible that paroxysmal cycle length shortening is caused by fractionation of a wave front that enters the PV from the left atrium instead of by a burst of tachycardia generated within the vein. However, intermittent PV tachycardias may be observed within a PV even after complete electrical disconnection of the PV from the left atrium. This observation, along with the results of the present and prior experimental, clinical, and surgical studies, provides strong evidence that paroxysmal cycle length shortening within the PVs is not a passive phenomenon but an important contributor to the maintenance of AF.

Limitations

A majority of patients in this study had paroxysmal AF, and none had severe underlying structural heart disease. Therefore, the findings of this study may not apply to patients with chronic AF or markedly dilated atria.

Implications

Although segmental ostial ablation to isolate the PVs is accomplished most efficiently during sinus rhythm, maintenance of sinus rhythm during an ablation procedure may not be readily achievable, particularly in patients who have had chronic AF. This study demonstrates that segmental ostial ablation is feasible during AF. An advantage of this approach is that it obviates the need for the administration of antiarrhythmic drugs and for multiple electrical cardioversions in patients with IRAF after cardioversion.

The consistent abolition of IRAF by PV isolation among the patients in this study suggests that IRAF is often triggered by arrhythmias arising in the PVs. An implication of this observation is that the occurrence of IRAF after elective cardioversion may predict a high probability of a clinical response to PV isolation.

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