Long-Term Results of Catheter Ablation in Paroxysmal Atrial Fibrillation
Lessons From a 5-Year Follow-Up

Feifan Ouyang, MD*; Roland Tilz, MD*; Julian Chun, MD; Boris Schmidt, MD; Erik Wissner, MD; Thomas Zerm, MD; Kars Neven, MD; Bulent Köktürk, MD; Melanie Konstantinidou, MD; Andreas Metzner, MD; Alexander Fuernkranz, MD; Karl-Heinz Kuck, MD

Background—Paroxysmal atrial fibrillation (AF) naturally progresses toward chronic AF at an estimated rate of 15% to 30% over a 1- to 3-year period. Pulmonary vein (PV) isolation is increasingly performed for the treatment of drug-refractory paroxysmal AF. The long-term data on clinical outcome after circumferential PV isolation are limited.

Methods and Results—From 2003 to late 2004, 161 patients (121 men; age, 59.8±9.7 years) with symptomatic paroxysmal AF and normal left ventricular function underwent circumferential PV isolation guided by 3-dimensional mapping and double Lasso technique. Right-sided and left-sided continuous circular lesions encircling the ipsilateral PVs were placed with irrigated radiofrequency energy. The procedure end point was the absence of all PV spikes for at least 30 minutes after PV isolation verified by 2 Lasso catheters placed within the ipsilateral PVs. Sinus rhythm was present in 75 patients (46.6%) after the initial procedure during a median follow-up period of 4.8 years (0.33 to 5.5 years). A second procedure was performed in 66 and a third procedure in 12 patients. Recovered PV isolation conduction was observed in 62 of 66 patients (94.0%) during the second and in 8 of 12 patients (66.7%) during the third procedure. After a median of 1 (1 to 3) procedure, stable sinus rhythm was achieved in 128 of 161 patients (79.5%), whereas clinical improvement occurred in an additional 21 of 161 patients (13.0%) during a median follow-up of 4.6 years (0.33 to 5.5 years). Four patients in stable sinus rhythm died during follow-up. Progression toward chronic AF was observed in 4 patients (2.4%); however, only 2 patients reported symptoms.

Conclusion—In patients with paroxysmal AF and normal left ventricular function, circumferential PV isolation results in stable sinus rhythm in the majority of patients, and low incidence of chronic AF was observed after ablation during up to 5 years of follow-up. (Circulation. 2010;122:2368-2377.)

Key words: ablation ■ arrhythmia ■ catheter ablation ■ electrophysiology ■ fibrillation ■ mapping ■ pulmonary vein

The incidence of atrial fibrillation (AF) increases with age and is the most common sustained arrhythmia.1,2 It is well known that paroxysmal AF (PAF) commonly precedes the development of chronic AF.3–7 Epidemiological studies have shown that PAF naturally progresses toward chronic AF at an estimated rate of 15% to 30% over a 1- to 3-year period.3–7 Recent electrophysiological studies have demonstrated that in the majority of patients with PAF, AF could be initiated by spontaneous focal discharges originating from the pulmonary veins (PVs).8,9 This important finding has led to the development of segmental and circumferential PV isolation (CPVI).10–12 A recent study has demonstrated that CPVI is more effective than segmental PVI in patients with PAF or short-standing persistent AF.13 According to recent international guidelines (Heart Rhythm Society and European Heart Rhythm Association), PVI forms the cornerstone during catheter ablation of PAF, demonstrating a high procedural success rate during a 6- to 20-month follow-up period.10–14 Data on long-term follow-up after CPVI are limited.15–19 In the present study, we prospectively investigated the long-term outcome after radiofrequency catheter ablation of PAF.

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From the II Med. Abteilung, Asklepios Klinik St. Georg, Hamburg, Germany.
*Drs Ouyang and Tilz contributed equally to this article.
Correspondence to Feifan Ouyang, MD, II Med. Abteilung, Allgemeines Krankenhaus St. Georg, Lohmühlenstrasse 5, 20099 Hamburg, Germany.
E-mail Ouyangfeifan@aol.com
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Methods

Patient Characteristics
This study enrolled consecutive symptomatic patients with PAF and normal left ventricular (LV) function undergoing CPVI at our hospital between 2003 and the end of 2004. Transesophageal echocardiography was performed in all patients to rule out left atrial (LA) thrombus before ablation. Anticoagulation treatment with warfarin was stopped 3 days before ablation and replaced by intravenous heparin to maintain a partial thromboplastin time of 2 to 3 times the normal value.

Electrophysiology Study
All patients provided written informed consent. The ablation procedure was performed under sedation with continuous infusion of propofol. Two standard catheters were positioned as follows: a 6F catheter (Biosense-Webster Inc, Diamond Bar, Calif) at the His bundle region via a femoral vein and a multipolar electrode 6F catheter into the coronary sinus via the left or right subclavian vein. Placement of three 8F sheaths (SL1, St. Jude Medical Inc, St. Paul, Minn) in the LA using the modified Brockenbrough technique was performed as previously described in detail. After transseptal access, intravenous heparin was administered, targeting an activated clotting time of 250 to 300 seconds, and monitored every 30 minutes throughout the procedure with adjustment to the heparin dosage according to the activated clotting time. Additionally, the transseptal sheaths were continuously flushed with heparinized saline to avoid thrombus formation or air embolism.

Three-Dimensional Electroanatomic Mapping and Irrigated Radiofrequency Ablation
The method of 3-dimensional electroanatomic mapping of the LA has previously been described in detail. Mapping was performed with a 3.5-mm-tip catheter (ThermoCool Navi-Star, Biosense Webster). After reconstruction of the LA, each PV ostium was identified by selective venography and tagged on the 3-dimensional electroanatomic map. Two decapolar circular mapping catheters (Lasso, Biosense-Webster Inc) were placed inside the ipsilateral superior and inferior PVs or within the superior and inferior branches of a common PV to verify PV1 during radiofrequency current ablation. Irrigated radiofrequency current energy was delivered as previously described, targeting a maximum temperature of 43°C, a maximal power of 40 W, and an infusion rate of 17 to 25 mL/min. Along the posterior wall, the maximal power was limited to 30 W. Septal and lateral continuous circular lesions (CCLs) around the ipsilateral PVs were deployed = 1 cm posterior and = 5 mm anterior from the angiographically defined PV ostia. The end point was defined as the absence of any PV spike recorded on 2 Lasso catheters placed within the ipsilateral superior and inferior PVs at least 30 minutes after PV isolation and the absence of recurrent PV spikes after intravenous administration of 9 to 12 mg adenosine during SR. In patients without recovered PV conduction, the procedural end point was defined as the absence of PV spikes recorded on 2 Lasso catheters placed within the ipsilateral superior and inferior PVs at least 30 minutes after PV1 and the absence of recurrent PV spikes after intravenous administration of 9 to 12 mg adenosine during SR. In patients without recovered PV conduction, the initial mapping and ablation strategy targeted non-PV triggers. If non-PV triggers were absent, ablation of complex fractionated atrial electrograms was performed during either spontaneous or induced AF with intravenous orciprenalin if necessary.

Ablation Protocol During Repeat Procedures
Two decapolar Lasso catheters were positioned inside the ipsilateral superior and inferior PVs or within the superior and inferior branches of a common PV to assess recovered PV conduction and to facilitate localization of conduction gaps along previously placed CCLs after selective PV angiography. The location of conduction gaps along previously deployed CCLs was arbitrarily defined as the roof, anterosuperior, anteroinferior, inferior, posteroinferior, and posterosuperior region. Irrigated radiofrequency energy was delivered as previously described during the initial procedure. In the presence of clinical documentation of atrial tachycardia (AT), mapping and ablation was the initial procedural step. To achieve electric PV1, all PVs were assessed for recovered conduction after AT termination. Conduction gaps were closed with irrigated radiofrequency ablation.

In patients with recovered PV conduction, the procedural end point was defined as the absence of PV spikes recorded on 2 Lasso catheters placed within the ipsilateral superior and inferior PVs at least 30 minutes after PV1 and the absence of recurrent PV spikes after intravenous administration of 9 to 12 mg adenosine during SR. In patients without recovered PV conduction, the initial mapping and ablation strategy targeted non-PV triggers. If non-PV triggers were absent, ablation of complex fractionated atrial electrograms was performed during either spontaneous or induced AF with intravenous orciprenalin if necessary.

Postablation Care and Follow-Up
Intravenous heparin was administered for 3 days after the procedure, followed by warfarin therapy for at least 6 months. Previously ineffective antiarrhythmic drugs (AADs) were continued for 3 months after the ablation. One day after the procedure, a 12-lead surface ECG, a transthoracic echocardiogram, and a 24-hour Holter monitor were performed and repeated after 1, 3, 6, and 12 months. Clinical follow-up was regularly carried out every 6 months at the outpatient clinic performing a 12-lead surface ECG and 24-hour Holter monitor. Recurrence was defined as symptomatic and/or asymptomatic episodes of atrial tachyarrhythmias (ATa) lasting >30 seconds and identified on 12-lead surface ECG or Holter monitoring. Clinical follow-up was completed in March 2009. This study did not adhere to a predefined blanking period. Clinical success was defined as freedom from ATa recurrence off AAD before the last follow-up and clinical improvement defined as either >90% reduction of symptomatic ATa before the last follow-up and off AAD or >90% reduction of symptomatic ATa while taking previously ineffective AAD.

Statistical Analysis
All values are expressed as mean±SD or median (minimum and maximum values) as appropriate. The Mann-Whitney U and Wilcoxon tests were used for comparisons. Survival curves were generated with the Kaplan-Meier technique.

Results
Between 2003 and the end of 2004, 171 consecutive symptomatic patients with PAF and normal LV function underwent CPVI at our hospital. Ten patients living outside Germany were excluded from the study because complete follow-up at our facility could not be guaranteed. Therefore, this study included 161 patients (121 male; age, 59.8±9.7 years; Table 1). Among the 161 patients, the CHADS2 score was 0 in 48 patients (29.8%), 1 in 86 patients (53.4%), 2 in 19 patients (11.8%), 3 in 7 patients (4.3%), and 5 in 1 patient (0.6%).

Clinical Outcome After the Initial Ablation Procedure
Among 161 patients, all PVs were completely isolated during the first procedure. During a median follow-up period of 4.8 years (0.33 to 5.5 years), 86 patients (53.4%) demonstrated recurrent ATa. Time of ATa recurrence was within the first month in 36 patients (41.9%), 1 to 3 months in 7 patients (8.1%), 3 to 6 months in 7 patients (8.1%), 6 to 12 months in 12 patients (14.0%), 12 to 24 months in 14 patients (16.3%), 24 to 36 months in 2 patients (2.3%), 36 to 48 months in 4 patients (4.7%), 48 to 60 months in 3 patients (3.6%), and >60 months in 1 patient (1.2%). The distribution of ATa is shown in Figure 1.

After the first procedure, only 1 patient progressed toward chronic AF. Clinical improvement was observed in an additional 15 patients (9.3%) who did not require a
repeat procedure, whereas a repeat procedure was refused by 4 patients demonstrating lack of clinical improvement (Figure 2).

Electrophysiological Findings and Follow-Up After the Second Ablation Procedure

In 66 patients, a repeat procedure was performed at a median of 120 days (2 to 1771 days) after the initial procedure. The second procedure was performed within the first month in 21 patients (31.8%), between 1 and 3 months in 8 patients (12.1%), and after 3 months in 37 patients (56.1%). During the second procedure, mapping demonstrated a macro-AT with its critical isthmus between the mitral annulus and the left-sided PVs in 9 patients, a macro-AT with its critical isthmus between both CCLs in 2 patients, and a macro-AT within the right atrial free wall in 1 patient. Conduction block at the critical isthmus terminated all macro-ATs except in 1 patient with the critical isthmus between the mitral annulus and the left-sided PVs. Recovered PV conduction during SR was found in 62 of 66 patients (94%); conduction gaps were located along the right-sided PVs in 40 patients (61%) and the left-sided PVs in 51 patients (77%). All conduction gaps were successfully closed with a minimal number of irrigated radiofrequency current applications. After CPVI, frequent atrial extrasystoles were identified and ablated at the superior crista terminalis in 1 patient and within the superior vena cava in 2 patients.

In 1 of 4 patients without recovered PV conduction, mapping and ablation was successfully performed, targeting a focal AT originating from the roof of the LA. In 2 patients with documented early AT recurrence before the ablation procedure, programmed stimulation during intravenous isoproterenol infusion failed to initiate an AT. Thus, no ablation was performed in these 2 patients. Ablation of complex fractionated atrial electrograms was performed in only 1 patient.

After the second procedure, recurrent ATa was seen in 22 of 66 patients (33.3%) during a median follow-up period of 4.1 years (0.7 to 5.3 years). ATa recurred within the first month in 2 patients, between 1 to 3 months in 8 patients, between 3 to 6 months in 2 patients, between 6 and 12 months in 2 patients, between 12 to 24 months in 3 patients, between 24 to 36 months in 3 patients, and between 36 to 48 months in 2 patients (Figure 3). Among the 22 patients, PAF progressed toward chronic AF in 3 patients. Clinical improvement was observed in 6 patients. One patient refused a third ablation procedure. In the remaining 12 patients with ATa recurrence, a third ablation was performed. Clinical outcome after the second procedure is shown in Figure 4.

Electrophysiological Findings and Follow-Up After the Third Ablation Procedure

A third ablation procedure was performed in 12 patients at a median of 255 days (89 to 733 days) after the second procedure. In 8 patients, recovered PV conduction was found. Conduction gaps were located along the right CCLs in 4 patients and along the left CCLs in the other 4 patients.

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Table 1. Patient Baseline Characteristics Before Ablation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>59.8 ± 9.7</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>121/40</td>
</tr>
<tr>
<td>Left atrial dimension, mm</td>
<td>42.6 ± 4.7</td>
</tr>
<tr>
<td>Patients with &lt; 40 mm, n (%)</td>
<td>41 (25.5)</td>
</tr>
<tr>
<td>Patients with 40–50 mm, n (%)</td>
<td>114 (70.8)</td>
</tr>
<tr>
<td>Patients with &gt; 50 mm, n (%)</td>
<td>6 (3.7)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>108 (67.0)</td>
</tr>
<tr>
<td>Structural heart disease, n (%)</td>
<td>32 (19.9)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>19 (11.8)</td>
</tr>
<tr>
<td>Severe LV hypertrophy</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>DDD pacemaker</td>
<td>12 (7.5)</td>
</tr>
<tr>
<td>ICD implantation</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>8 (5.0)</td>
</tr>
<tr>
<td>AADs before ablation, n</td>
<td>2.1 ± 1.0</td>
</tr>
<tr>
<td>Amiodarone, n (%)</td>
<td>90 (55.9)</td>
</tr>
<tr>
<td>Embolic events before ablation, n (%)</td>
<td>9 (5.6)</td>
</tr>
</tbody>
</table>

ICD indicates implantable cardioverter-defibrillator.

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![Figure 1](https://example.com/image1.png)  
**Figure 1.** Time to first episode of ATa in 161 patients (Pts) after the initial CPVI. FU indicates follow-up.
(Table 2). In 2 patients without recovery of PV conduction 4 (patient 11) and 10 (patient 12) days after the first procedure, late recovered PV conduction was found during the third procedure along the right-sided PVs in patient 12 and the left-sided PVs in patient 11 (Figure 5). In 5 patients, the recovered conduction gap was at a different location during the third procedure compared with the second procedure performed 3 to 70 days after the first procedure. After complete PVI was confirmed, frequent atrial extrasystoles from the superior vena cava were successfully ablated in 1 patient. In 4 patients without recovered PV conduction noted during the third procedure, macro-ATs were identified and successfully ablated with electrophysiological evidence of conduction block. The site of critical isthmus was identified between the right and left CCLs in 2 patients and between the mitral annulus and left-sided PVs in 1 patient. In that patient, attempts to block the left isthmus during the second procedure were unsuccessful. One patient demonstrated common-type atrial flutter.

After the third ablation procedure, 9 patients were free of ATa during a median follow-up of 4.1 years (2.5 to 4.4 years). In 3 patients (patients 1, 6, and 8 in Table 2), PAF recurred after the third procedure.

Summary of Ablation Procedures and Clinical Outcome Analysis
A total of 239 procedures (a median of 1 [1 to 3]) were performed in 161 patients. Procedure duration was 228±58 minutes with a mean fluoroscopy time of 29.1±11.9 minutes. PVI was performed in all 161 patients during the first procedure, in 50 patients during the second procedure, and in 8 patients during the third procedure. In 145 of 161 patients (88.9%), only CPVI was performed. In 14 of 161 patients (8.7%), additional linear lesions were placed for the treatment of macro-ATs. In 1 of 161 patients (0.6%), additional ablation of complex fractionated atrial electrograms was performed. Although initiation of AF from the superior vena cava could not be confirmed after PVI, additional isolation of the superior vena cava was performed in 3 of 161 patients (1.8%). Clinical outcome after the initial procedure and the first and second repeat procedures is summarized in Figure 6.

Aspiration pneumonia occurred and was successfully managed in 1 of 161 patients (0.6%). A sterile pericardial effusion developed within 2 days after ablation in 2 of 161 patients (1.2%) but did not require pericardiocentesis. No cardiac tamponade, symptomatic PV stenosis, procedure-related transient ischemic attack or stroke, or atrioesophageal fistula occurred.

After a median follow-up period of 4.8 years (range, 0.33 to 5.5 years), stable SR was present in 75 of 161 patients (46.6%) after the first procedure. After a median of 1 (1 to 3) procedure, stable SR was achieved in 128 patients (79.5%) during a median follow-up period of 4.6 years (range, 0.33 to 5.5 years), whereas recurrent ATas were clinically controlled in an additional 21 of 161 patients (13.0%). With the Kaplan-Meier analysis, the
estimated probability to maintain SR at 5 years of follow-up after a single procedure was 45.3% (Figure 7A) and increased to 78.1% after a median of 1 (1 to 3) procedure (Figure 7B).

Progression toward chronic AF after CPVI was observed in 4 patients. Chronic AF developed after the first procedure in 1 and after the second procedure in 3 patients (Table 3). AF was sustained over 2 to 6 months, as documented by regular 12-lead surface ECG and 24-hour Holter monitoring in 3 patients and by dual-chamber implantable cardioverter-defibrillator interrogation in 1 patient. Persistent AF recurred shortly after external cardioversion in 2 patients. Two patients in chronic AF were asymptomatic. Detailed information on age and LA size is shown in Table 3.

Of 161 patients after the last ablation procedure, 29 (18.1%) were treated with AADs and 22 (13.6%) with warfarin. In comparison, among 128 patients in SR and free from ATa, 19 (14.8%) were treated with AADs (flecainide in 12, sotalol in 5 and amiodarone in 2), and 9 (7.0%) were anticoagulated with warfarin.

Cerebral hemorrhage occurred in an 83-year-old man with stable SR 20 months after ablation on warfarin therapy without regular international normalized ratio monitoring and an international normalized ratio of >4.5. In addition, 2 patients suffered from a transient ischemic attack 20 and 31 months after the ablation procedure while taking daily aspirin. One patient was in stable SR; the second patient was in recurrent AF at the time of the transient ischemic attack. A total of 4 deaths occurred during the follow-up period: An 81-year-old woman died of sudden cardiac death 52 months after ablation; a 51-year-old man committed suicide 51 months after ablation; a 62-year-old woman of pneumonia 4 months after the initial ablation; and a 71-year-old man died during an accident 10 months after the ablation procedure. Twelve-lead surface ECG and 24-hour Holter recordings showed stable SR in all 4 patients.

**Table 2. Distribution of Conduction Gaps During the Second and Third Ablation Procedures**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y/Sex</th>
<th>Time From First to Second Procedure, d</th>
<th>Time From First to Third Procedure, d</th>
<th>Conduction Gaps at the R-CCLs</th>
<th>Conduction Gaps at the L-CCL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>63/F</td>
<td>151</td>
<td>352</td>
<td>Posterosuperior</td>
<td>Anterosuperior</td>
</tr>
<tr>
<td>2</td>
<td>46/M</td>
<td>70</td>
<td>718</td>
<td>Anterosuperior</td>
<td>Anterosuperior</td>
</tr>
<tr>
<td>3</td>
<td>78/F</td>
<td>6</td>
<td>289</td>
<td>Posterosuperior</td>
<td>Inferior</td>
</tr>
<tr>
<td>4</td>
<td>62/F</td>
<td>5</td>
<td>738</td>
<td>Inferior</td>
<td>Inferior</td>
</tr>
<tr>
<td>5</td>
<td>41/F</td>
<td>119</td>
<td>208</td>
<td>Anteroinferior</td>
<td>Anteroinferior</td>
</tr>
<tr>
<td>6*</td>
<td>65/M</td>
<td>184</td>
<td>222</td>
<td>Anteroinferior</td>
<td>Posterosuperior</td>
</tr>
<tr>
<td>7</td>
<td>63/M</td>
<td>48</td>
<td>221</td>
<td>Posterosuperior</td>
<td>Posterosuperior</td>
</tr>
<tr>
<td>8*</td>
<td>67/M</td>
<td>91</td>
<td>317</td>
<td>Posterosuperior</td>
<td>Posteroinferior</td>
</tr>
<tr>
<td>9</td>
<td>67/F</td>
<td>3</td>
<td>644</td>
<td>Anteroinferior</td>
<td>Anterosuperior</td>
</tr>
<tr>
<td>10</td>
<td>41/F</td>
<td>5</td>
<td>497</td>
<td>Anterosuperior</td>
<td>Inferior</td>
</tr>
<tr>
<td>11</td>
<td>63/F</td>
<td>4</td>
<td>865</td>
<td>Posteroinferior</td>
<td>Inferior</td>
</tr>
<tr>
<td>12</td>
<td>46/M</td>
<td>10</td>
<td>728</td>
<td>Posteroinferior</td>
<td>Inferior</td>
</tr>
</tbody>
</table>

Mean±SD 58.0±64.8 483.3±242.5

R-CCL indicates CCLs around the ipsilateral septal pulmonary veins; L-CCL, CCLs around the ipsilateral lateral pulmonary veins.

**Discussion**

The present study of 161 patients with normal LV function undergoing CPVI for the treatment of PAF found that during a median follow-up period of 4.6 years after the last procedure, (1) there is a steady rate of ATa recurrence; (2) dormant conduction gaps may be present during the blanking period unmasking at a later time as confirmed during repeat procedures; (3) an excellent outcome can be achieved with SR maintenance after CPVI.
achieved, with 79.5% of patients demonstrating freedom from ATa and 13.0% of patients with clinical improvement after a median of 1 (1 to 3) procedure; and (4) there is a very low incidence of chronic AF.

Rate of Recurrence During Long-Term Follow-Up

In previous studies, early recurrence of AF was common, with an estimated rate of 35% to 50% during the first 2 to 3 months after ablation.21,22 The incidence of very late recurrence (>12 months) after AF ablation is ~5% to 10%.22 In the majority of patients, AF recurs as a result of recovered PV conduction regardless of whether a segmental or CPVI approach was used. In a study by Pappone et al15 using a pure anatomic approach, the incidence of “late” recurrence was 3% among 589 patients. Using a clear, predefined electrophysiological end point, our study demonstrated the highest rate of recurrence during the first 3 months, followed by a steady rate of recurrence throughout the 5-year follow-up period. After a single ablation procedure, the rate of very late recurrence after 1 year was 14.9%, a result comparable to results of 2 earlier studies.16–18 Another important finding is that recovered PV conduction was present in 94% of patients demonstrating ATa recurrence after the first procedure. This is in line with earlier studies demonstrating that recovered PV conduction is the dominant factor for recurrence after segmental or CPVI.10–20 Further information is needed and may be available after an additional 3 to 5 years of follow-up to confirm whether the natural process of atrial fibrosis in the aging heart is involved in the recurrence of AF. Atrial fibrosis can result in an increase of inhomogeneous dispersion of conduction within the atria, favoring perpetuation of AF.1,2

Dormant Conduction During the Blanking Period

Published data10–20 indicate that a repeat catheter ablation procedure is indicated in 20% to 40% of patients as a result of recurrent ATa. Because early recurrence of AF and/or AT during the initial 3 months after AF ablation may resolve spontaneously in 15% of patients, there is consensus that a repeat procedure should be withheld during that period.16 On the other hand, it is also known that some patients will develop highly symptomatic ATa that cannot be effectively controlled with AADs or slowed with rate-controlling medications and are best managed with a repeated ablation procedure during the blanking period. In the majority of patients with recurrent AF after CPVI, recovered PV conduction is present.10–20 In the present study, recovered PV conduction after the initial procedure was noted in 94% of patients. In 29 of 66 patients (43.9%) with drug-refractory ATa, a repeat procedure was performed within 3 months after the initial procedure. In 7 of 8 patients with recovery of PV conduction identified during the third procedure, the site of conduction gap was
different from that noted during the second procedure. It is important to note that in 6 of 8 patients, the second ablation procedure was performed within 10 days after the initial procedure, strongly suggesting that local edema and inflammation induced by radiofrequency lesion formation may have resulted in transient CPVI. Conduction gaps along previously placed CCLs may unmask once lesion maturation is complete after the blanking period. The underlying mechanism may be analogous to the concept of latent reconduction in dormant accessory pathways. On the basis of our findings, we strongly discourage early repeat catheter ablation during the 3-month blanking period unless drug-refractory ATa occurs immediately after the initial procedure. Using this strategy will minimize the likelihood of missing dormant conduction gaps, ultimately resulting in improved clinical outcome after a second procedure.

**Clinical Outcome After CPVI**

Procedural success is commonly defined as lack of recurrence during the follow-up period. A recent meta-analysis of 31 studies including 2800 patients found that the single-procedure success rate of catheter ablation of all types of AF off AADs was 57% (50% to 64%). An analysis of 34 studies enrolling a total of 3481 patients shows that the success rate off AADs increased to 71% (65% to 77%) after multiple procedures. However, examining data from 6 pioneering centers with greater experience in AF ablation, we find the success rate off AADs to be 80.5% (71% to 88%) in 1039 patients followed up for a period of 6 months to 2.4 years. Performing a second procedure increased the likelihood of success off AADs by an additional 5% to 15% during a relatively short follow-up period. As of now, data are limited on clinical outcome during long-term follow-up. A study evaluating long-term single-procedure success rate in 589 patients undergoing a purely anatomic circumferential PV ablation approach was reported by Pappone et al. The AF-free event rate at the 1-, 2-, and 3-year follow-up was 84%, 79%, and 78%, respectively. In contrast, a study by Cheema et al using the same ablative approach reported a single-procedure long-term success rate of 40%, with an additional 7% of patients demonstrating clinical improvement during a follow-up period of 26 months. This result is comparable to published success rates of 34% after segmental PV, with an additional 6% of patients demonstrating clinical improvement. A similar outcome was reported in a multicenter study. Finally, a recent 3-year follow-up study demonstrated a 29% single-procedure success rate off AADs. After a repeat procedure, the success rate increased to 62% off AADs.

In the present study, the single-procedure success rate was 46.6%, with an additional 9.3% of patients demonstrating clinical improvement. In theory, the single-procedure success rate could be improved if a second procedure is performed after 3 months because a significant number of patients with early ATa recurrence demonstrate quiescence after the blanking period. The success rate after 1.5 procedures increased to 79.5%, and an additional 13.0% of patients experienced clinical improvement. It is important to note that no additional ablation apart from CPVI was performed in 88.9% of patients. The high success rate in our study may be explained by the facts that (1) only patients with PAF and normal LV function were included, a patient population represented in the majority of previously published studies on catheter ablation of AF; (2) CPVI was verified by 2 Lasso catheters positioned within each ipsilateral PV; and (3)
CPVI was performed remote from the angiographically defined PV ostia. Our methodology will invariably isolate a larger area of atrial tissue that is responsible for a high incidence of automaticity and inducible fast PV tachycardias.\(^{12}\) This in turn will result in a low rate of AT\(a\) after completion of CPVI,\(^{2,5}\) possibly because of elimination of triggered activity and/or mother waves within and near the PV ostia. Additionally, 14.8% of patients (19 of 128) with stable SR were reluctant to discontinue AADs during the follow-up period. The use of AADs may also improve clinical success in some patients. Our success rate is lower than that reported in a multicenter study\(^{19}\) including 728 patients with PAF followed up for 57±17 months that reported an overall freedom from atrial arrhythmias of 77.6% after a single procedure and 92.4% after a repeat procedure. The difference may be due to use of higher power with a maximum of 70 W and a relatively younger patient population with a lower rate of primary hypertension. However, Bhargava et al\(^{19}\) did not provide information about progression toward chronic AF after ablation.

**Low Incidence of Chronic AF**

Paroxysmal AF commonly precedes and progresses toward chronic AF at an estimated rate of 15% to 30% over a 1- to 3-year period.\(^{3,7,26–28}\) A study from Trieste, Italy, found that during a 10-year follow-up period, 34% of patients with PAF progressed toward chronic AF.\(^{6}\) Furthermore, a study evaluating Japanese patients reported a rate of progression of PAF toward chronic AF of 77% (5.5% of patients per year) during a 14-year follow-up.\(^{26}\) Compared with PAF, chronic AF is known to increase the incidence of death, heart failure, and stroke.\(^{28}\) Recent studies demonstrated the limited short-term success rate of PVI in

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**Table 3. Time to Progression Toward Chronic AF**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y/ Sex</th>
<th>SHD</th>
<th>LA Diameter, mm</th>
<th>PAF Duration, mo</th>
<th>Time to Progression, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>80/M</td>
<td>CABG</td>
<td>55</td>
<td>96</td>
<td>355 After first procedure</td>
</tr>
<tr>
<td>2</td>
<td>57/F</td>
<td>ICD implantation</td>
<td>49</td>
<td>48</td>
<td>210 After second procedure</td>
</tr>
<tr>
<td>3*</td>
<td>68/F</td>
<td>No</td>
<td>42</td>
<td>84</td>
<td>1049 After second procedure</td>
</tr>
<tr>
<td>4</td>
<td>61/F</td>
<td>No</td>
<td>39</td>
<td>60</td>
<td>77 After second procedure</td>
</tr>
</tbody>
</table>

*CABG indicates coronary artery bypass graft; ICD, implantable cardioverter-defibrillator; SHD, Structural heart disease.*
patients with persistent or longstanding persistent AF compared with PAF, with many patients in need of additional substrate modification. \(^{18,20,21,23}\) In our study, only 4 of 161 patients (2.4\%) developed chronic AF over a 5-year follow-up period after CPVI. Two patients reported symptoms caused by chronic AF, whereas regular 12-lead surface ECG and 24-Holter monitor checkups led to a diagnosis in the remaining 2 asymptomatic patients. On the other hand, chronic AF was observed in 4 of 33 patients (12.1\%) with recurrent ATa after a median of 1 (1 to 3) procedure. A randomized study is needed to answer the question of whether CPVI can prevent or delay the progression toward chronic AF in patients with PAF. Furthermore, other factors known to cause atrial structural remodeling (age and underlying heart disease) are involved in AF progression. Proper control of these factors is also of major importance.

**Conclusions**

In the majority of patients with PAF and normal LV function, CPVI can restore stable SR. After successful CPVI, AF may recur at a steady rate during long-term follow-up. The dominant factor for recurrent ATa after CPVI is recovery of PV/LA conduction. Conduction gaps are successfully eliminated by segmental radiofrequency applications along previously placed CCLs. A repeat procedure should be withheld during the initial 3 months after ablation unless the patient is severely symptomatic because dormant conduction gaps may not unmask during the blanking period. Chronic AF after CPVI was observed in a small number of patients during up to 5 years of follow-up.

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**Disclosures**

None.

**References**


Paroxysmal atrial fibrillation (AF) progresses toward chronic AF at an estimated rate of 15% to 30% over a 1- to 3-year period. Compared with paroxysmal AF, chronic AF is known to increase the incidence of death and heart failure and to have less success by catheter ablation. In the present study, we prospectively investigated the long-term outcome after circumferential pulmonary vein isolation in patients with paroxysmal AF. Our data demonstrated the highest rate of recurrence during the first 3 months, followed by a steady rate of recurrence throughout the 5-year follow-up period. The single-procedure success rate was 46.6%, with an additional 9.3% of patients demonstrating clinical improvement. The success rate after a median of 1 procedure (1 to 3) increased to 79.5%, whereas an additional 13.0% of patients experienced clinical improvement. Recovered pulmonary vein conduction was observed in 94.0% of patients during the second and in 66.7% of patients during the third procedure. In 7 of 8 patients with recovery of pulmonary vein conduction identified during the third procedure, the site of conduction gap was different from that noted during the second procedure, which was performed within 10 days after the initial procedure. Only 4 of 161 patients (2.4%) developed chronic AF over an ≈5-year follow-up period. Our study demonstrated that stable sinus rhythm can be achieved by circumferential pulmonary vein isolation with a median of 1 (1 to 3) procedure in the majority of patients with paroxysmal AF. Repeated procedures should be postponed to unmask all potential conduction gaps 3 months after the initial procedure unless refractory arrhythmias occur during the blanking period. A low incidence of chronic AF after ablation was observed during ≈5 years of follow-up, which may suggest early intervention to prevent or delay the progression toward chronic AF.

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