Complete Isolation of Left Atrium Surrounding the Pulmonary Veins

New Insights From the Double-Lasso Technique in Paroxysmal Atrial Fibrillation

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Background—Paroxysmal atrial fibrillation (PAF) can be eliminated with continuous circular lesions (CCLs) around the pulmonary veins (PVs), but it is unclear whether all PVs are completely isolated.

Methods and Results—Forty-one patients with symptomatic PAF underwent 3D mapping, and all PV ostia were marked on the 3D map based on venography. Irrigated radiofrequency energy was applied at a distance from the PV ostia guided by 2 Lasso catheters placed within the ipsilateral superior and inferior PVs. The mean radiofrequency duration was 1550 ± 511 seconds for left-sided PVs and 1512 ± 506 seconds for right-sided PVs. After isolation, automatic activity was observed in the right-sided PVs in 87.8% and in the left-sided PVs in 80.5%. During the procedure, a spontaneous or induced PV tachycardia (PVT) with a cycle length of 189 ± 29 ms was observed in 19 patients. During a mean follow-up of 6 months, atrial tachyarrhythmias recurred in 10 patients. Nine patients underwent a repeat procedure. Conduction gaps in the left CCL in 9 patients and in the right CCL in 2 patients were closed during the second procedure. A spontaneous PVT with a cycle length of 212 ± 44 ms was demonstrated in 7 of 9 patients, even though no PVT had been observed in 6 of these 7 patients during the first procedure. No AF recurred in 39 patients after PV isolation during follow-up.

Conclusions—Automatic activity and fast tachycardia within the PVs could reflect an arrhythmogenic substrate in patients with PAF, which could be eliminated by isolating all PVs with CCLs guided by 3D mapping and the double-Lasso technique in the majority of patients. (Circulation. 2004;110:2090-2096.)

Key Words: fibrillation □ ablation □ mapping □ pulmonary vein □ atrium

Previous studies have demonstrated that paroxysmal atrial fibrillation (PAF) could be initiated by spontaneous focal discharges originating from the pulmonary veins (PVs).1,2 This important finding has led to the development of segmental ostial ablation (SOA) to isolate the PVs, electrophysiologically guided by PV spikes,3–6 and continuous circular lesions (CCLs) around PVs, anatomically guided by 3D electroanatomic mapping.7–10 A recent study has shown that CCL is more effective than SOA in patients with PAF.8 No studies have provided definite information as to whether all PV spikes are completely eliminated.7–10 We have previously shown that PV isolation is important to prevent recurrence of atrial fibrillation (AF).9 In the present study, we prospectively investigated the isolation of all PVs by CCLs in the left atrium (LA), electrophysiological findings within the isolated PVs, and the recurrence of atrial tachyarrhythmias after CCLs in patients with PAF.

Methods

Patient Characteristics

This prospective study included 41 consecutive patients (29 males; 63 ± 9 years) with highly symptomatic PAF. AF was first diagnosed 7.6 ± 6.2 years before referral and had been ineffectively treated by a mean of 3.1 ± 1.1 antiarrhythmic drugs, including amiodarone in 26 patients (63.4%). Common-type atrial flutter had been documented in 19 patients (46.3%) and ablated in 7 (17.1%). Five patients had recurrent PAF after SOA. Coronary artery disease had been diagnosed in 5 patients. Dual-chamber pacemakers had been implanted in 3 patients. Primary hypertension had been documented in 23 patients (56.1%). Mean LA diameter was 42.6 ± 5.1 mm.

Electrophysiological Study

All patients provided written informed consent. The ablation procedure was performed under sedation with a continuous infusion of propofol. Two standard catheters were positioned: a 6F (Biosense-Webster, Inc) at the His bundle region via a femoral vein and a 6F catheter in the coronary sinus via the left subclavian vein. Three 8F SL1 sheaths (St. Jude Medical, Inc) were advanced to the LA by a
modified Brockenbrough technique: 2 sheaths over one puncture site and the third sheath via a second puncture site. After transseptal catheterization, intravenous heparin was administered to maintain an activated clotting time of 250 to 300 seconds. Additionally, continuous infusions with heparinized saline were connected to the transseptal sheaths (flow rate of 10 mL/h) to avoid thrombus formation or air embolism.

### 3D Electroanatomic Mapping and Irrigated Radiofrequency Ablation

The method of 3D electroanatomic mapping in the LA has been described previously in detail.\(^9,11\) Mapping was performed with a 3.5-mm-tip catheter (ThermoCool Navi-Star, Biosense-Webster) during coronary sinus pacing or sinus rhythm. In case of AF, sinus rhythm was restored by external cardioversion. In 4 patients, AF recurred immediately after DC shock; 50 mg of intravenous flecaïnid was administered, and cardioversion was repeated. After LA reconstruction, each PV ostium was identified by selective venography and tagged on the electroanatomic map. Two decapolar Lasso catheters (Biosense-Webster) were placed within the ipsilateral superior and inferior PVs or within the superior and inferior branches of a common PV during radiofrequency (RF) delivery (Figure 1A).

Irrigated RF energy was delivered as described previously with a target temperature of 45°C, a maximal power limit of 50 W, and an infusion rate of 17 mL/min.\(^{1,6}\) RF ablation sites were tagged on the reconstructed 3D LA. RF energy was applied for \(\geq 30\) seconds until the maximal local electrogram amplitude decreased by \(\geq 70\%\) or double potentials were noted.\(^{10}\) Irrigated RF ablation was performed in the posterior wall more than 1 cm and in the anterior wall more than 5 mm from the angiographically defined PV ostia (Figure 1B).\(^{9,10}\) However, in case of a relatively narrow border between the anterior aspect of the left PVs and the LA appendage, \(\geq 2\) ablation was performed within 5 mm of the ostium of the PVs.

The end point of the CCL was defined as (1) absence of all PV spikes documented with the 2 Lasso catheters within the ipsilateral PVs at least 30 minutes after isolation and (2) no recurrence of the PV spikes within all PVs after intravenous administration of 9 to 12 mg of adenosine during sinus rhythm or coronary sinus pacing. After isolation, induction of PV tachycardia (PVT) within the isolated PVs was performed by programmed stimulation with up to 3 extrastimuli and burst pacing to local refractoriness.

### Postablation Care and Follow-Up

After the procedure, intravenous heparin was administered for 3 days in all patients, followed by warfarin for at least 3 months. All patients were kept on the previously ineffective antiarrhythmic drugs for 1 month after ablation. One day after the procedure, surface ECG, transthoracic echocardiography, and 24-hour Holter recording were performed and repeated after 1, 3, and 6 months by the referring physician or the ablation center. All patients had a telemetry ECG recorder (Philips Telemedizin) to document symptomatic arrhythmias or to transfer an ECG once per week if asymptomatic for 6 months. Transeosophageal echocardiography was performed 3 months after ablation to detect whether an interatrial shunt had occurred.

### Statistical Analysis

All values are expressed as mean±SD.

### Results

#### Irrigated RF Ablation in the LA

By selective PV angiography, a common PV ostium was demonstrated in the left-sided PVs (LCPV) in 13 patients (31.7%), and in the right-sided PVs (RCPV) in 3 patients (7.3%). All PVs were successfully isolated by 2 CCLs without amplitude reduction of the PV spike. In patients without previous SOA, the ipsilateral PV spikes disappeared simultaneously in 32 (88.9%) of 36 patients in the right-sided PVs (Figure 2A) and in 30 (82.4%) of 36 patients in the left-sided PVs at completion of the respective CCL. In the 5 patients with previous SOA, PV spikes were identified in all 4 PVs. During RF delivery, the superior and inferior PV spikes disappeared simultaneously in 1 of 5 patients in the right-sided PVs (Figure 2B) and in 1 of 5 patients in the left-sided PVs at completion of the CCL. After isolation, PV spikes recurred in the right-sided PVs in 8 patients (19.5%) and in the left-sided PVs in 8 patients (19.5%) after intravenous administration of 9 to 12 mg of adenosine (Figure 3A). Furthermore, in 1 patient, intravenous administration of 9 mg of adenosine resulted in transiently reconducted PV spikes and automatic activity from the right superior PV (RSPV), which incidentally initiated a short episode of AF after isolation of the right-sided PVs (Figure 3B). All reconducted spikes were abolished by further RF delivery in the CCLs by the earliest PV spikes on the 2 Lasso catheters. Elimination of the reconducted PV spike was confirmed by a repeat intra-
venous administration of adenosine. Mean RF duration was 1550±511 seconds for left-sided PVs and 1512±506 seconds for right-sided PVs. No vagal reflexes or cough was observed during irrigated RF delivery in any patient. The cavotricuspid isthmus was also successfully ablated during the procedure in 13 patients, including 1 with reconnection over the isthmus.

**Automatic Activity Within the Isolated PVs**

After RF ablation, regular or irregular automatic activity dissociated from the atrial activity was observed in 97.2% of patients (35 of 36 patients) without previous PV isolation. Note change of activation sequence on 2 Lasso catheters and interval prolongation between left and right panels before simultaneous isolation of both LSPV and LIPV (PV spike marked by asterisk). Also, far-field atrial activation from LA appendage (marked by arrow) is shown on catheter from LSPV before and after isolation. B, Tracings are ECG leads I, II, and V1 and intracardiac electrograms recorded from 2 Lasso catheters within RSPV and RIPV, mapping catheter (Mp), catheter inside CS, and catheter at His bundle region (HBE) before RF application (in left panel) and during 6th RF application (middle panel) and 15th application (right panel) in patient with previous SOA. Note that isolation of RSPV (marked by asterisk) and RIPV (marked by arrow) occurs separately during 6th RF and 15th RF applications, respectively.

**Tachycardia Within the PV During the Procedure**

After isolation of both PVs by either the right or left CCL, a PVT with a cycle length (CL) of 188.8±8.5 ms (range 180 to

80.5% (33 of 41). This automatic activity was most frequently observed in the RCPV (100%, 3 of 3), followed by the LCPV (84.6%, 11 of 13), the RSPV (71.1%, 27 of 38), the left superior PV (LSPV; 64.3%, 18 of 28), the right inferior PV (RIPV; 44.7%, 17 of 38), and the left inferior PV (LIPV; 35.7%, 10 of 28). In patients without common PV and previous SOA, automatic activity dissociated between the superior and inferior PVs was noted in right-sided PVs in 16 (48.5%) of 33 patients and in left-sided PVs in 12 (60.0%) of 20 patients, whereas automatic activity within the ipsilateral superior and inferior PVs with a fixed interval between the ipsilateral 2 PVs was noted in 17 (51.5%) of 33 patients in right-sided PVs (Figure 4) and in 8 (40.0%) of 20 patients in left-sided PVs.

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200 ms) occurred spontaneously in the opposite-sided PVs in 4 patients without previous SOA. The tachycardia was located within the LCPV, LSPV, RSPV, and LIPV. In those 4 patients, no PVT was induced after isolation of all PVs.

After successful isolation of the PVs, programmed pacing and burst pacing within the isolated areas were performed only in the 36 patients without previous SOA. Successful capture in at least one of all PVs was achieved in 34 patients. No programmed stimulation was performed in the 5 patients with previous SOA. In 44.1% (15 of 34) of patients, a PVT with a CL of 188.6±32.4 ms (range 120 to 245 ms) was reproducibly induced by programmed stimulation. Also, a PVT in the RSPV (CL 205 ms) was reproducibly initiated by 2 spontaneous automatic PV activities from the RIPV in 1 of those 15 patients (Figure 5). The PVT occurred in the RSPV in 5 patients and in the LCPV in 5, followed by the LSPV in 3, the LIPV in 2, and the RIPV in 2. The PVTs were organized in 12 and disorganized in 5 patients. In 10 of 15 patients with sustained tachycardia, transient entrainment and reproducible termination of the induced tachycardia could be demonstrated within the isolated PVs (Figures 6A through 6C).

**Recurrent Atrial Tachyarrhythmias After CCL**

After a median of 178±30 days of follow-up, atrial tachyarrhythmias recurred in 9 patients without previous SOA and in 1 patient with previous SOA at a median of 4 days (range 1 to 42 days) after the ablation. Thirty-one (75.6%) of 41 patients were free of PAF without antiarrhythmic drugs 4 weeks after the procedure. A repeat ablation was performed at a median of 8 days (range 2 to 90 days) after the initial procedure in 9 patients who experienced highly symptomatic atrial tachyarrhythmias unresponsive to antiarrhythmic drugs. One patient refused a repeat procedure. During the repeat procedures, conduction gaps in the previous CCL were found in the left-sided CCL in 9 patients and in the right-sided CCL in 2 patients using 2 Lasso catheters within the ipsilateral PVs. During the second procedure, a PVT with a CL of 212±44 (160 to 265 ms) was demonstrated in 7 patients. The tachycardias originated within the LCPV in 2 patients (Figure 7A), the LSPV in 2 patients, and the LIPV in 3 patients. The PVTs activated the LA via the conduction gaps. No spontaneous or induced PVT had been observed during the first procedure in 6 of those 7 patients. All conduction gaps were successfully closed by irrigated RF applications during the second procedure (Figure 7B). Subsequently, automatic activity was observed within the isolated PVs in 8 patients without previous SOA. One of these patients had shown no automatic activity in the first procedure.

After the second procedure, 8 of the 9 patients were free of PAF during a median of 131±12 days of follow-up. In summary, 39 (95.1%) of the 41 patients were free of PAF after ablation, including 9 patients after the second procedure. Additionally, no asymptomatic AF but atrial extrasystoles were recorded by telemetry ECG in 10 patients with sinus rhythm during follow-up.

**Complications**

Noninfectious pericarditis occurred after the first procedure in 2 patients. RF duration for both patients was not different from the remaining patients. The pericarditis subsided 7 and 9 days after ablation, respectively. A narrowing in the superior branch of the RIPV (30%) was observed due to a dislodgement of the mapping catheter during RF in 1 patient. The patient was asymptomatic and demonstrated no evidence of progressive narrowing on MRI 3 months after the ablation. The procedure time was 246±39 minutes, with a fluoroscopy time of 25.8±10.3 minutes. No interatrial shunt was observed on transesophageal echocardiography 3 months after the ablation procedure.
Discussion

The present study describes isolation of the PVs by irrigated RF to create CCLs in the LA, conduction gaps in the CCL in recurrent PAF after CCL, and electrophysiological findings within the isolated areas based on the 2-Lasso technique.

**PV Isolation by CCLs in the LA**

PV isolation, which has become the cornerstone for catheter ablation of PAF, consists of SOA and CCL. A recent randomized study has shown that CCL is more effective in preventing PAF recurrence than SOA. This may be due to the elimination of triggered activity and/or mother waves near the PV ostium that drive AF, the isolation of relatively large areas that are not available for perpetuating AF, and vagal denervation by CCL. In most studies using CCL, amplitude reduction within the ablation area was the only end point studied. In the present study, no line between the ipsilateral PVs was deployed, which predisposes to breakthrough conduction of both veins in case of a single gap in CCL. Complete CCLs were critical for successful ablation in the present study. With 2 Lasso catheters within the ipsilateral PVs, PV isolation occurred simultaneously in 88.9% of right-sided PVs and 82.4% of left-sided PVs in the 36 patients without previous SOA. The ipsilateral PVs were separately isolated in 80% of right-sided PVs and 80% of left-sided PVs in all 5 patients with previous SOA. This phenomenon may be explained by the fact that in patients with prior SOA, each vein is likely to have separate conduction gaps to the LA, which are closed sequentially by an advancing CCL. PV isolation provides an electrophysiological end point for CCL. The simultaneous use of 2 Lasso catheters gives insights into the electrical interactions of the ipsilateral PVs and helps identify conduction gaps in the CCL after intravenous administration of adenosine and in recurrent arrhythmias after CCL.

**Clinical Outcome and Recurrent Atrial Tachyarrhythmias After CCL in Patients With PAF**

Previous studies have demonstrated that PAF can recur after CCL in 12% to 30% of patients. In the present study, the recurrence rate after the first procedure could have been lower than 24.4% if early repeat procedures had not been performed. PV spikes have been demonstrated in almost all patients with recurrent PAF after SOA, but it is not known whether there are reconducted PV spikes in recurrent PAF after CCL. In the present study, 9 patients demonstrated a reconducted PV spike during the repeat procedure. In addition, a fast PVT to the LA was demonstrated in 7 patients. More importantly, no AF recurred after all conduction gaps were closed in the previous CCL during the second procedure in 8 patients. These data are consistent with a recent surgical study that showed that recurrent PAF was due to an incomplete circular lesion and could be cured by closing the gap in the previous CCL in 1 patient. These data strongly support the hypothesis that it is necessary to isolate all PVs to prevent recurrence. Of course, this hypothesis can only be proven when all patients, including asymptomatic patients, undergo a control study.

**Arrhythmogenic Substrates Within Isolated PVs in Patients With PAF**

Spontaneous automatic activity within isolated PVs has been reported in 5% to 33.6% of PVs in patients undergoing SOA. In the present study using 2 Lasso catheters within the ipsilateral PVs, automatic activity dissociated from atrial
activity after PV isolation was demonstrated in right-sided PVs in 87.8% and in left-sided PVs in 80.5%. Automatic activity occurred during the second procedure in 1 patient in whom it had not been recorded in the first procedure. The high incidence of automatic activity within the PVs in this study is due to more myocardium with a potential for automatic activity within the isolated area and prolonged simultaneous recording from the ipsilateral PVs after complete CCL. The automatic activity may explain the spontaneous recurrence of PAF and PVT when the CCLs are not completed.

A spontaneous or induced PVT has been reported in ≈5% to 10% patients after SOA. In the present study, PVT with a CL of 188.6 ± 32.4 ms could be reproducibly induced within the isolated PVs in 15 of 36 patients without previous SOA. Also, in patients who had not undergone SOA, spontaneous PVT with a short CL occurred in 4 patients during the first procedure and in 7 patients during the second procedure before complete isolation of all PVs. The sustained PVT could be reproducibly terminated and transiently entrained by burst pacing from the same PV. These data strongly suggest that reentry is responsible for fast PVT, which is consistent with previous clinical and experimental studies. The high incidence of PVT in the present study indicates that the periosteal myocardium is susceptible to the development of reentrant tachycardia. Several facts suggest that the PVs and PV ostia may be a privileged site for reentrant tachycardia. Abrupt changes in fiber orientation near the PV ostia result in marked conduction delay during premature and rapid stimulation. In addition, myocardial fibers within the PVs exhibit an abbreviated refractoriness and decremental conduction properties, both of which findings favor the occurrence of reentry. On the basis of the present study and previous studies, we hypothesize that in the majority of patients with PAF, a fast PVT initiated by automatic activity from the PVs acts as the mother circuit, which subsequently breaks into multiple reentry circuits due to very short CL and inhomogeneous conduction around the PV ostia. This hypothesis provides a rationale for CCL to isolate the PVs from the LA. It also underlines the importance of the PV-LA junction not only in the initiation but also in the perpetuation of PAF.

**Study Limitations**
This study has several limitations. First, the presence of 3 catheters in the LA could theoretically increase the risk of complications; however, this was not observed in patients in the present study. Second, the methods used in the present study have a higher cost. However, this was a prospective study, which will help improve our understanding of the role of the PVs and the PV-LA junction in the initiation and perpetuation of PAF. Further investigation will be required to determine whether such an approach will have practical implications.

**Conclusions**
On the basis of the 2-Lasso technique in patients with PAF undergoing CCLs around the PVs, automatic activity was observed in the majority of patients after isolation. In addition, a fast spontaneous or induced PVT was observed in 25 of 36 patients without previous SOA during the first and second procedures. This automatic activity and PVT could provide an arrhythmogenic substrate for PAF, which could be eliminated in the majority of patients by isolating all PVs.
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