Electrophysiological Findings During Ablation of Persistent Atrial Fibrillation With Electroanatomic Mapping and Double Lasso Catheter Technique

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Background—Pulmonary veins (PVs) can be completely isolated with continuous circular lesions (CCLs) around the ipsilateral PVs. However, electrophysiological findings have not been described in detail during ablation of persistent atrial fibrillation (AF).

Methods and Results—Forty patients with symptomatic persistent AF underwent complete isolation of the right-sided and left-sided ipsilateral PVs guided by 3D mapping and double Lasso technique during AF. Irrigated ablation was initially performed in the right-sided CCLs and subsequently in the left-sided CCLs. After complete isolation of both lateral PVs, stable sinus rhythm was achieved after AF termination in 12 patients; AF persisted and required cardioversion in 18 patients. In the remaining 10 patients, AF changed in 15 of 40 patients to a median of 4 days after the initial ablation. All atrial tachycardias were successfully terminated during the procedure. Atrial tachyarrhythmias recurred in 15 of 40 patients at a median of 35 days after the initial procedure in 14 patients. During the repeat study, recovered PV conduction was found in 13 patients and successfully abolished by focal ablation of the conduction gap of the previous CCLs. After a mean of 8±2 months of follow-up, 38 (95%) of the 40 patients were free of AF.

Conclusions—In patients with persistent AF, CCLs can result in either AF termination or conversion to macroreentrant atrial tachycardia in 55% of the patients. In addition, recovered PV conduction after the initial procedure is a dominant finding in recurrent atrial tachyarrhythmias and can be successfully abolished. (Circulation. 2005;112:3038-3048.)

Key Words: arrhythmia ■ mapping ■ catheter ablation ■ fibrillation ■ tachyarrhythmias

It has been shown that segmental ostial isolation of the pulmonary veins (PVs) in patients with persistent atrial fibrillation (AF) is much less effective than in patients with paroxysmal AF. However, complete PV isolation from the left atrium (LA) with continuous circular lesions (CCLs) around the PVs guided by 3D mapping has been shown to have similar efficacy in patients with paroxysmal and persistent AF. We have recently demonstrated that the PVs can be completely isolated from the LA with CCLs around the ipsilateral PVs guided by 3D electroanatomic mapping and double Lasso technique during coronary sinus (CS) pacing. However, electrophysiological findings during ablation of persistent AF have not been described in detail. In the present study, we prospectively investigated the electrophysiological findings during ablation of persistent AF guided by 3D mapping and double Lasso technique and recurrent atrial tachyarrhythmias after ablation.

Methods

Patient Characteristics

This prospective study included 40 consecutive symptomatic patients (30 males aged 60±9 years [range 38 to 77 years]) with persistent AF that lasted for 7 days to 1 year and required either pharmacological or electrical cardioversion. Persistent AF lasted for 7 days to 1 month in 10 patients, 1 to 3 months in 7 patients, 3 to 6 months in 12 patients, and 6 to 12 months in 11 patients. Thirty-eight patients had previous documentation of paroxysmal AF. All patients had been ineffectively treated with a mean of 3.3±1.1 antiarrhythmic drugs, including amiodarone in 26 patients (65%). Common-type atrial flutter (AFL) had been documented previously in 4 patients and ablated in 1 patient. Primary hypertension had been documented in 25 patients (62.5%). Five patients had recurrent AF after segmental ostial isolation. In 11 patients, structural heart disease was documented: moderate aortic valve stenosis in 1 patient, moderate left ventricular hypertrophy due to primary hypertension in 3 patients, rheumatic mitral stenosis after percutaneous mitral balloon valvuloplasty in 1 patient, and coronary artery disease in 6 patients. The mean LA diameter was 47.4±5.6 mm (range 36 to 66 mm).
Transesophageal echocardiography was performed to rule out LA thrombi in all patients. Anticoagulation treatment with warfarin was stopped on admission and replaced by intravenous heparin to maintain partial thromboplastin time at 2 to 3 times higher than the control value in all patients.

**Electrophysiological Study**

All patients provided written informed consent. The ablation procedure was performed with patients taking previously prescribed antiarrhythmic drugs and under sedation with a continuous infusion of propofol. Two standard catheters were positioned: a 6F catheter (Biosense-Webster, Inc) at the His bundle region via a femoral vein and a multipolar electrode 6F catheter in the CS via the left subclavian vein. Placement of 3 RF sheaths (SL1, St. Jude Medical, Inc) in the LA with a modified Brockenbrough technique has been described previously in detail.4,5 After transseptal catheterization, intravenous heparin was administered to maintain an activated clotting time of 250 to 300 seconds. The activated clotting time was monitored every 30 minutes, and the heparin dose was adjusted accordingly. Additionally, continuous infusions of heparinized saline were connected to the transseptal sheaths (flow rate of 10 mL/h) to avoid potential 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.6 Electrical and pharmacological cardioversion were not attempted before complete isolation. Mapping was performed with a 3.5-mm-tip catheter (ThermoCool Navigator, Biosense Webster) during persistent AF. After reconstruction of the LA, each PV ostium identified by selective venography was 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.6,7 PV activation was defined as disorganized spikes with beat-to-beat variation of activation sequences or organized spikes with very similar or identical activation sequence regardless of cycle length (CL) changes.

Irrigated RF energy was delivered as described previously with a target temperature of 45°C, a maximal power of 40 W, and an infusion rate of 1 mL/min.4,3 In all patients, maximal power of 30 W was delivered to the posterior wall to avoid the potential risk of LA-esophageal fistula.4 RF ablation was initially performed to create the right-sided CCLs and subsequently on the left-sided CCLs after complete isolation of the right-sided PVs. These CCLs were performed in the posterior wall ∼1 cm and in the anterior wall ∼5 mm from the angiographically defined PV ostia.

Mapping and ablation of macroreentrant tachycardia (Macro-AT) was performed after complete isolation of the right-sided and left-sided PVs if persistent AF changed to Macro-AT during the initial procedure. Mapping and ablation of the critical isthmus was initially performed when clinical tachycardia presented as Macro-AT during a repeat procedure. Also, conduction gaps in the previous CCLs during the second procedure were identified and ablated. The repeat procedure was usually performed during sinus rhythm (SR) or AF and was guided by 2 Lasso catheters within the ipsilateral PVs. If discrete PV spikes were recorded in the ipsilateral PVs during SR or AF, a 7F mapping catheter (ThermoCool, Biosense Webster) was advanced close to the site with the earliest PV spikes and then withdrawn away from the PV ostia about 1 cm in the posterior wall or 5 mm in the anterior wall. The conduction gaps in the previous CCLs usually presented with low amplitude and fragmented or double atrial potentials.5 An additional conduction gap was considered if PV activation sequence changed after 1 conduction gap was closed.

Electrical cardioversion was performed after complete isolation of the bilateral PVs in case of no AF termination or no change to Macro-AT. The end point of CCLs was defined as absence of all PV spikes documented with the 2 Lasso catheters within the ipsilateral PVs at least 30 minutes after PV isolation during SR.

**Postablation Care and Follow-Up**

Intravenous heparin was administered to all patients for 3 days after the procedure, followed by warfarin for 6 months. All patients were kept on the previously ineffective antiarrhythmic drugs for 3 months after the ablation. One day after the procedure, a surface ECG, a transthoracic echocardiography, and a 24-hour Holter recording were performed and repeated after 1, 3, 6, and 12 months. All patients had a telemetry ECG recorder (Philips Telemedizin) for 6 months to document symptomatic arrhythmias or to transfer an ECG once per week if asymptomatic. Any episode of symptomatic or asymptomatic atrial tachyarrhythmia that lasted more than 30 seconds and was identified on the surface ECG, Holter monitoring, or telemetry ECG recorder was considered a recurrence. In addition, no blanking period during follow-up was used in the present study.

**Statistical Analysis**

All values are expressed as mean±SD. Mann-Whitney U and Wilcoxon tests were used for comparisons. A probability value <0.05 was considered significant.

**Results**

**Complete Isolation of Right-Sided PVs in Patients With Persistent AF**

Before ablation, PV spikes within the right-sided PVs were disorganized in 55 (70.5%) of 78 PVs and organized in 23 (29.5%) of 78. The disorganized PV spikes were found in a right common PV in 1 (50%) of 2 patients, in the right superior PV (RSPV) in 26 (68.5%) of 38 patients, and in the right inferior PV (RIPV) in 28 (73.7%) of 38 patients (Figure 1A). The organized PV spikes were shown in the right common PV in 1 (50%) of 2 patients, in the RSPV in 12 patients (31.5%), and in RIPV in 10 patients (26.3%). During RF delivery, the disorganized PV activation within the right-sided PVs became organized with the same or similar PV activation sequence and prolonged CL (Figure 1B). The right-sided PV spikes disappeared simultaneously (Figure 1C) in 37 (92.5%) of 40 patients. Mean RF duration was 1626±428 seconds for right-sided CCLs.

During RF delivery on the right-sided CCLs, persistent AF terminated in 1 patient before complete isolation of the PVs and in 1 patient after complete isolation of the PVs. In the patient with AF termination after complete isolation of the right-sided PVs, a PV tachycardia with a similar CL compared with that before ablation remained within the RSPV (Figures 2A and 2B). Attempted focal ablation within the RSPV (20 W) terminated the PV tachycardia after 5 seconds. In the other 5 patients, persistent AF changed to AFL in 3 patients and left Macro-AT in 1 patient before isolation (Figure 3A) and to AFL in 1 patient after isolation. During these tachycardias, 1-to-1 activation from the LA to the right-sided PVs was demonstrated in all 4 patients before the right-sided PV isolation. In 1 patient, intermittent fast PV tachycardia from the RSPV suddenly reinitiated AF via conduction gap on the CCLs (Figure 3B). This episode of AF terminated spontaneously before complete isolation of the right-sided PVs.
Figure 1. A–C. Tracings are ECG leads I, II, and V1 and intracardiac electrograms recorded from 2 Lasso catheters within the RSPV and RIPV, a mapping catheter (Map), a catheter inside the CS, and a catheter at the His bundle region (HBE) in a patient with persistent AF for 4 months. In A, note that the PV spikes recorded within the RSPV and RIPV are disorganized, with beat-to-beat variation of PV activation sequences and CL before the right-sided CCLs. In B, note that the PV spikes within the RSPV and RIPV become organized with a similar beat-to-beat PV activation and a variation of CL from 177 to 317 ms during RF application #20 on the CCLs. In C, note that the slow PV spikes with identical activation sequence (marked by asterisk) suddenly disappear when CCLs are completed during RF application #28.
Complete Isolation of Left-Sided PVs in Patients With Persistent AF

Complete isolation of left-sided PVs was performed during SR, because stable SR was achieved in 3 patients after complete isolation of the right-sided PVs. In 4 patients (left Macro-AT in 1 and AFL in 3) after complete isolation of the right-sided PVs, 1-to-1 conduction into the left-sided PVs was also demonstrated during these tachycardias. Complete isolation of the left-sided PVs was performed during the tachycardias in these 4 patients.

In 33 patients with sustained AF after complete isolation of the right-sided PVs, PV spikes within the left-sided PVs were disorganized in 29 (51.8%) of 56 PVs and organized in 27 (48.2%) of 56 PVs. The disorganized PV spikes were found in a left common PV in 10 (17.2%) of 12 patients, in the left superior PV (LSPV) in 10 (47.6%) of 21 patients, and in the left inferior PV (LIPV) in 9 (12.7%) of 21 patients. Organized PV spikes were found in a left common PV in 2 (16.7%) of 12 patients, in the LSPV in 11 (52.4%) of 21 patients, and in LIPV in 12 (57.1%) of 21 patients. During RF delivery, the disorganized PV activation within the ipsilateral left-sided PVs became organized. The PV spikes were completely isolated in these 33 patients. Mean RF duration was 1795±502 seconds for left-sided CCLs.

During RF delivery on the left-sided CCLs, persistent AF terminated in 7 patients before complete isolation of the left-sided PVs (Figure 4) and in 1 patient after isolation of the left-sided PVs. Additionally, persistent AF changed to left Macro-AT in 5 patients (Figure 5A) and AFL in 2 patients before complete isolation of the left-sided PVs. During these tachycardias, 1-to-1 conduction from the LA to the left-sided PVs was demonstrated in these 8 patients. In 1 patient, AFL degenerated into AF due to intermittent PV tachycardia from the LSPV. This episode of AF terminated spontaneously before complete isolation of the left-sided PVs.

Ablation of Macro-AT After Complete PV Isolation

During AF ablation, AF changed to AFL with a CL of 279.7±41.5 ms (range 230 to 340 ms) in 6 patients (including 2 patients with reinitiated AF). Among these 6 patients, only 3 had previously documented AFL and had not been ablated. After complete isolation of the bilateral PVs, irrigated RF delivery in the cavitricuspid isthmus resulted in bidirectional conduction block over the cavitricuspid isthmus in all 6 patients.

In 6 patients who developed a left Macro-AT with a CL of 280.0±27.7 ms (range 230 to 325 ms) during AF ablation (5 patients during left CCLs and 1 patient during right CCLs), mapping demonstrated a critical isthmus between the left CCLs and the lateral mitral annulus (MA) in 4 patients (Figure 5B), between the CCLs on the posterior wall in 1 patient, and within the LA anterior wall not related to the...
CCLs in 1 patient. All tachycardias were terminated successfully with irrigated RF energy. In 2 patients with left Macro-AT around the MA, RF delivery in the critical isthmus resulted in conversion to a different tachycardia, which was confirmed as common-type AFL by entrainment mapping and successfully ablated (Figure 5C). After tachycardia termination, all isthmuses of the left Macro-AT were successfully blocked except the isthmus between the left CCLs and MA in 2 patients. In these 2 patients without block of the tachycardia isthmus, no RF energy was delivered inside the CS.

Arrhythmias After Complete Isolation of Both-Sided PVs and Electrical Cardioversion

The outcome of persistent AF after complete isolation of bilateral PVs is shown in Figure 6. Stable SR after AF termination was achieved in 12 patients (group I), stable Macro-AT (group II; left Macro-AT in 6 or AFL in 4 patients) in 10 patients, and persistent AF in 18 patients (group III). In all patients from group I and group II, all PVs were successfully isolated during SR or during Macro-AT.

In the 18 patients from group III, the fibrillatory CL recorded from the CS was 170.4 ms before ablation and 190.1 ms after complete isolation of bilateral PVs. In these 18 patients, stable SR was achieved with a single cardioversion of 200 to 360 J in 17 patients and with 2 cardioversions in 1 patient. No recovered PV spikes after cardioversion were demonstrated during stable SR in 18 patients. In 1 patient after a successful cardioversion, frequent atrial extrasystoles from the right-sided PVs activated the atria without PV spikes during SR (Figure 7A), suggestive of unidirectional block. Pacing within the right-sided PVs confirmed 1-to-1 conduction with the same P-wave morphology and a long interval from the stimulus artifact to the onset of the P wave (Figure 7B). The conduction gap in the roof was closed by a few RF applications, and success was confirmed by pacing within the right-sided PVs after ablation (Figure 7C).
Clinical Outcome After Initial CCLs

Atrial tachyarrhythmias recurred in 15 patients at a median of 4 days (range 1 to 42 days) after the initial ablation, including 4 (33.3%) of 12 patients from group I, 4 (40%) of 10 patients from group II, and 7 (38.9%) of 18 patients from group III. A repeat ablation was performed at a median of 35 days (range 3 to 155 days) after the initial procedure in 14 patients.

Among these 14 patients, 7 experienced highly symptomatic atrial tachycardia (AT; repetitive AT with variable CL in 3, persistent AT with stable CL in 4), 4 had only paroxysmal AF, and 3 patients with persistent AF required electrical cardioversion. All arrhythmias were unresponsive to antiarrhythmic drugs.

In the 3 patients with repetitive AT, mapping demonstrated that a tachycardia from the LSPV activated the atria via a conduction gap in 1 patient. Pacing within the PV with recovered conduction demonstrated very similar P-wave morphology in the other 2 patients with SR during the procedure. The recovered PV conduction was found in the right-sided PVs in 1 and in the left-sided PVs in the other 2 patients. A few RF applications on the conduction gap resulted in tachycardia termination in 1 patient and complete isolation of recovered PVs in these 3 patients.

In the 4 patients with persistent AT, mapping demonstrated AFL with CL of 240 ms in 1 patient and left Macro-AT with CL of 255±17.8 ms (range 230 to 270 ms) in the other 3 patients. The critical isthmus of these left Macro-ATs was between the 2 CCLs on the posterior wall in 1 patient and between the left CCLs and the lateral MA in 2 patients, including 1 patient without conduction block during the initial procedure. During these 4 Macro-ATs, recovered PV conduction with 1-to-1 conduction was demonstrated in the right-sided PVs in 3 patients and in the left-sided PVs in 3 patients. In 1 patient, PV activation in the left-sided PVs occurred sporadically or with 4-to-1 conduction (Figures 8A and 8B). Irrigated endocardial RF delivery resulted in tachycardia termination in 4 patients and conduction block over tachycardia isthmus in 2 patients (1 with AFL, 1 with left Macro-AT with isthmus between the CCLs). In 1 patient with an isthmus between the left CCLs and MA, the tachycardia isthmus was successfully blocked by delivering RF energy within the CS. In the other patient, conduction block could not be achieved owing to a very small CS. After Macro-AT termination, recovered PV conduction during SR was demonstrated in the right-sided PV in 3 patients and in the left-sided PVs in 4 patients (Figure 8C). All recovered PV conduction was successfully ablating by closing the conduction gaps in the previous CCLs (Figure 8C).

In 7 patients with recurrent AF, recovered PV conduction was observed in 6 patients and was found in the right-sided PVs in 5 and in the left-sided PV in 4 patients. All conduction gaps were successfully closed by irrigated RF delivery in the conduction gap of the previous CCLs during the second procedure. In 1 patient without recovered PV conduction (group III), frequent atrial extrasystoles/salvos with a short coupling interval originated from the inferolateral MA and were abolished by 6 RF applications. In addition, infrequent atrial extrasystoles with a long coupling interval with an origin from the superior vena cava were found during the procedure. Empirical isolation of the superior vena cava was performed in spite of lack of AF initiation.

Surface ECG and 24-hour Holter recordings were completed in all 40 patients 3 months after ablation, in 33 patients 6 months after ablation, and in 6 patients 12 months after ablation. After a mean of 243±58 days (range 148 to 375 days) of follow-up, only asymptomatic short episodes of AT were documented on the Holter ECG after the second procedure in the patient who had mitral valvuloplasty. In summary, 38 (95%) of the 40 patients were free of atrial tachyarrhythmias without antiarrhythmic drugs after ablation, including 14 patients who had a second procedure.

Procedure-Related Complications

Vagal reflexes were observed during irrigated RF delivery in 1 (2.5%) of 40 patients during the initial procedure. No complication occurred during the initial and repeat proce-
Figure 5. A and B, Tracings are ECG leads I and II and intracardiac electrograms recorded from 2 Lasso catheters within the LSPV and LIPV, a mapping catheter (Map), a catheter inside the CS, and a catheter at the His bundle region (His) during left-sided CCLs in a patient with persistent AF for 8 months. In A, note after conversion from AF to Macro-AT with a CL of 280 ms (1) activation within the LSPV with 1-to-1 conduction from the LA and (2) activation within the LIPV with 2-to-1 or 4-to-1 conduction from the LA. In B, note concealed entrainment from mapping catheter (Map) in the left isthmus between the left CCLs and the lateral MA after complete isolation of left-sided PVs. In C, tracings are ECG leads I, II, III, AVR, and AVF and intracardiac electrograms recorded from a mapping catheter (Map) within the CS and a catheter inside the CS after failed tachycardia termination by endocardial ablation with 10 applications. Note that during the first application within the CS, the tachycardia CL prolongs suddenly to 440 ms with a different activation sequence from Map to the CS, which indicates a different AT.
mental ostial isolation approach. Simultaneous isolation of ipsilateral PVs in patients with persistent AF. This finding was consistent with the previous studies that used the segmental ostial isolation approach. Complete PV isolation during persistent AF and the clinical outcome after complete PV isolation in patients with persistent AF.

**Termination of Persistent AF During CCLs**

It has been demonstrated that AF can be terminated by CCLs in paroxysmal AF and in chronic AF. A recent study demonstrated that in 95% of the patients, AF could be terminated by ablation of complex fractionated atrial electrograms guided by 3D mapping in paroxysmal and chronic AF. In the present study, AF termination occurred in 30% of these patients. AF termination occurred before isolation of the bilateral PVs in 11 patients and after complete isolation of the bilateral PVs in 1 patient. AF termination may be explained by the fact that CCLs on the posterior wall eliminate a number of random reentries and subsequently result in inability of AF to perpetuate itself in these patients. Interestingly, in the 12 patients with AF termination, atrial tachyarrhythmias after the initial procedure recurred owing to recovered PV conduction in 4 patients. Importantly, no atrial tachyarrhythmias occurred after the repeat procedure when the conduction gaps in the previous CCLs were closed. These data strongly support the idea that permanent PV isolation and not AF termination should be the end point of CCLs. Additionally, complete isolation of the right-sided PVs resulted in stable SR and continuous PV tachycardia with similar CL within the RSPV in 1 patient, which suggested a focal source responsible for the initiation and maintenance of persistent AF. This information is similar to a previous finding that focal source is responsible for paroxysmal AF.

**Macro-AT During and After the Procedure**

Macro-AT can coexist with AF or occur after CCLs in 4% to 20% patients. In the present study, persistent AF changed to left Macro-AT in 9 patients and AFL in 7 patients during the initial and a repeat procedures. In 2 of these 6 patients with conversion to AFL during ablation, intermittent PV tachycardia activated the LA via conduction gaps and degenerated into AF. This phenomenon may help explain the clinical observation that AFL can degenerate into AF in some patients. In patients with left Macro-AT, mapping demonstrated that 5 of 6 left Macro-ATs were associated with the previous CCLs during the initial procedure. Also, recurrent Macro-AT was associated with previous CCLs in 3 and AFL in 1 patient during the repeat procedure. In the present study, the majority of Macro-AT was AFL, left Macro-AT with an isthmus between the lateral MA and the left CCLs, or left Macro-AT with an isthmus between 2 CCLs on the posterior wall. This information may support the conclusion of a previous study that reported that CCLs with additional ablation lines on the posterior wall and the MA can be associated with a lower risk of developing left Macro-AT.

An interesting finding in the present study was that Macro-AT with a short CL presented with 1-to-1 passive activation into the PVs via conduction gaps in 12 patients during the initial procedure and in 4 patients during the repeat procedure. During the repeat procedure, recovered PV conduction was successfully eliminated by closing the gap in the previous CCLs in all 4 patients. All tachycardia isthmuses were blocked except the isthmus between the left CCLs and the MA in 2 patients in the present series. Importantly, no left Macro-AT recurred during the follow-up after complete isolation of the bilateral PVs. On the basis of these data, we hypothesize that recurrent Macro-AT after the initial procedure may be initiated by...
Figure 7. A–C, Tracings A through C are ECG leads I, II, and V, and intracardiac electrograms recorded from 2 Lasso catheters within the RSPV and RIPV, a mapping catheter (Map), a catheter inside the CS, and a catheter at the His bundle region (His) in persistent AF for 2 months after isolation of the bilateral PVs and successful cardioversion to SR with 200 J. In A, note the absence of PV spikes during SR after electrical cardioversion and bigeminal atrial extrasystoles (AES) with a fixed interval from PV activity within RSPV to the peak of P wave in lead II, which suggests a unidirectional conduction block over the CCLs. In B, note that pacing at the inferior aspect of the RIPV with a CL of 700 ms resulted in atrial capture with a fixed interval from stimulus artifact to the atrial activation recorded from the CS and an identical morphology of P wave to the spontaneous AES. In C, note that pacing at the inferior aspect of the RIPV with a CL of 800 ms resulted in PV capture with dissociated atrial activation after closing a potential gap in the roof of the right-side CCLs.
intermittent PV tachycardia via conduction gap. This hypothesis provides an explanation why permanent PV isolation can prevent Macro-AT. Also, this hypothesis supports a previous randomized study that concluded that PV isolation alone can prevent recurrence of both AF and AFL in patients with both arrhythmias.¹⁶


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