Journal of the American College of Cardiology
Vol. 46, No. 6, 2005
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2005.05.069
Published by Elsevier Inc.

Pulmonary Vein Isolation as an End Point for Left Atrial Circumferential Ablation of Atrial Fibrillation

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OBJECTIVES We sought to determine whether elimination of pulmonary vein (PV) arrhythmogenicity is necessary for the efficacy of left atrial circumferential ablation (LACA) for atrial fibrillation (AF).

BACKGROUND The PVs often provide triggers or drivers of AF. It has been shown that LACA is more effective than PV isolation in eliminating paroxysmal AF. However, it is not clear whether complete PV isolation is necessary for the efficacy of LACA.

METHODS In 60 consecutive patients with paroxysmal (n = 39) or chronic (n = 21) AF (mean age 53 ± 12 years), LACA to encircle the left- and right-sided PVs, with additional lines in the posterior left atrium and along the mitral isthmus, was performed under the guidance of an electroanatomic navigation system. The PVs were mapped with a decapolar ring catheter before and after LACA. If PV isolation was incomplete, no attempts at complete isolation were made.

RESULTS After LACA, there was incomplete electrical isolation of one or more PVs in 48 (80%) of the 60 patients. The prevalence of PV tachycardias was 82% before and 8% after LACA ($p < 0.001$). At 11 ± 1 months of follow-up, 10 (83%) of the 12 patients with complete and 39 (81%) of 48 patients with incomplete PV isolation were free from recurrent AF without antiarrhythmic drug therapy ($p = 1.0$). A successful outcome was not related to the number of completely isolated PVs per patient ($p = 0.6$).

CONCLUSIONS Left atrial circumferential ablation modifies the arrhythmogenic substrate within the PVs. Complete electrical isolation of the PVs is not a requirement for a successful outcome after LACA. (J Am Coll Cardiol 2005;46:1060–6) © 2005 by the American College of Cardiology Foundation

Arrhythmogenic foci within the pulmonary veins (PVs) often initiate and/or perpetuate an episode of atrial fibrillation (AF) (1–3), providing the rationale for PV isolation as a method of eliminating AF (4–7). However, the mechanisms of AF are multifactorial (8), and AF also may be driven by mechanisms independent of the PVs. A recent study demonstrated that left atrial circumferential ablation (LACA) to encircle the PVs is more effective than PV isolation in patients with paroxysmal AF (9). The extent to which the efficacy of LACA depends on PV isolation is not well established.

The purpose of this prospective study was to determine the effects of LACA on the arrhythmogenic activity of the PVs and to determine whether the clinical efficacy of LACA depends on PV isolation.

METHODS

Study subjects. The subjects of this study were 60 consecutive patients who underwent LACA for paroxysmal (n = 39) or chronic AF (n = 21). The mean age of the patients was 53 ± 12 years. There were 50 men and 10 women. Atrial fibrillation was first diagnosed 6 ± 6 years before LACA. The patients with paroxysmal AF experienced 12 ± 17 episodes of AF per month. The duration of the most recent episode of AF in patients with chronic AF was 13 ± 9 months. Structural heart disease was present in nine patients (15%), coronary artery disease in five, and hypertensive heart disease in four. The mean left ventricular ejection fraction was 0.55 ± 0.08. The mean left atrial (LA) diameter was 41 ± 5 mm in patients with paroxysmal AF and 47 ± 6 mm in patients with chronic AF ($p < 0.01$). Other demographic and clinical characteristics were similar among patients with paroxysmal and chronic AF.

Electrophysiologic study. All patients provided written, informed consent. All antiarrhythmic medications except amiodarone were discontinued four to five half-lives before the procedure. Vascular access was obtained through a femoral vein. A quadripolar electrode catheter (EP Technologies, San Jose, California) was positioned within the coronary sinus (CS). After trans-septal puncture, heparin was infused to maintain an activated clotting time of 275 to 350 s. A decapolar circular catheter (Lasso, Biosense-Webster, Diamond Bar, California) and a temperature-controlled 8-mm-tip quadripolar catheter (Navistar, Biosense-Webster) were advanced into the LA and used for mapping and ablation.

Bipolar and unipolar electrograms were recorded digitally at a bandpass of 30 to 500 Hz and 0.5 to 200 Hz, respectively (EPMed Systems, West Berlin, New Jersey).

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This study was supported by the Ellen and Robert Thompson Atrial Fibrillation Research Fund. Dr. Lemola was supported by the Swiss National Science Foundation.

Manuscript received September 21, 2004; revised manuscript received May 8, 2005, accepted May 13, 2005.

Abbreviations and Acronyms

AF	= atrial fibrillation
CS	= coronary sinus
LA	= left atrium/atrial
LACA	= left atrial circumferential ablation
PV	= pulmonary vein
RF	= radiofrequency

Atrial pacing was performed from the CS with a stimulator (EPMed Systems, Clinical Stimulator model EP-3).

Radiofrequency (RF) catheter ablation. Radiofrequency catheter ablation was performed after construction of the LA shell and PVs using an electroanatomic mapping system (CARTO, Biosense-Webster), as previously described (10). Ablation was performed during AF to encircle the left- and right-sided PVs 1 to 2 cm from the PV ostia. When there was a narrow rim of tissue between the left-sided PVs and the LA appendage, ablation was performed at the base of the ostium of the PV. Additional lines were created in the posterior LA between the two encircling lesions and also along the mitral isthmus from the inferior aspect of the left inferior PV to the mitral annulus (Fig. 1). Completeness of conduction block across these lines was not assessed.

Radiofrequency energy was delivered at a maximum power output of 70 W and a target temperature of 55°C for 20 to 40 s at each site. The end point of ablation at each site was an 80% decrease in the local electrogram amplitude or 40 s of energy application, whichever came first. If there was no change in the electrogram amplitude after 40 s of RF energy application, the catheter was moved to a new site. After completion of the encircling lesions, the area within the circles, outside the PVs, was mapped, and in 60% of patients, sites where the local atrial electrogram amplitude was >0.2 mV were found. Individual applications of RF energy were delivered at these sites using the same end points as during creation of the ablation lines. In addition, when AF was still present, sites inside the encircling ablation lines where the cycle length was shorter than the atrial cycle length in the CS also were ablated.

The mean duration of RF energy application was 39 ± 12 min, and the mean procedure and fluoroscopy times were 192 ± 39 and 50 ± 11 min, respectively. None of the patients had an acute complication.

After the ablation procedure, the patients were observed in a monitored hospital bed overnight and anticoagulated with heparin. All patients were anticoagulated with warfarin for three months or longer after the procedure. In patients who were treated with an antiarrhythmic medication before the procedure, treatment with the same drug was continued for eight to 12 weeks after the procedure.

Study protocol. The study protocol was approved by our Institutional Review Board. Before ablation, a decapolar circular mapping catheter (Lasso, Biosense-Webster) was inserted into the LA through the original trans-septal puncture site. Each PV was mapped for the presence of PV potentials during sinus rhythm and during CS pacing. In the patients who presented in sinus rhythm, AF was induced by rapid atrial pacing. Each PV was mapped for the presence of PV tachycardias, defined as rapid electrical activity within a PV with a cycle length shorter than that in the adjacent LA or CS (Fig. 2) (2,3). The ring catheter then was removed from the LA, and LACA was performed during AF.

After LACA, the ring catheter was again inserted into the LA and used to re-map each PV during sinus rhythm, during CS pacing, and during an induced episode of AF. Residual PV potentials were not ablated, and complete isolation of the PVs was not attempted.

Complete PV isolation was defined as the absence of PV potentials at each electrode of the decapolar ring catheter positioned at the ostium of the PVs, as well as complete entrance block into a PV during sinus rhythm and an induced episode of AF. The interval between the CS pacing stimulus and PV potentials recorded at the PV ostium was measured off-line using digital calipers.

Follow-up. All patients were seen in an outpatient clinic two to three months after the procedure and every six months thereafter. The patients were contacted by a nurse practitioner every two months and questioned about symptoms. In addition, patients were asked to contact the nurse practitioner whenever they experienced symptoms. In the event of any symptoms suggestive of AF, the patient was given an event monitor to document the cause of symptoms. No patient was lost to follow-up, and the mean duration of follow-up was 11 ± 1 months. Because recurrences of AF or

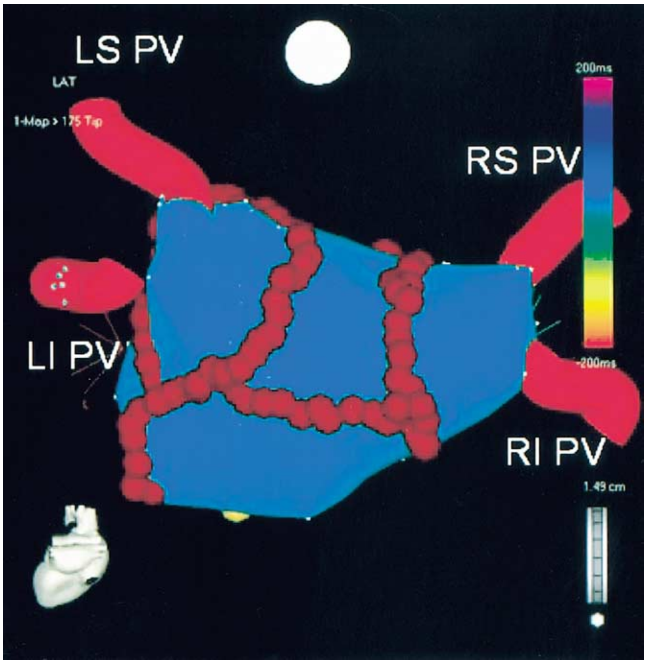

Figure 1. Left atrial (LA) circumferential ablation. Shown is the posteroanterior projection of the LA. Ablation lines encircle the left- and right-sided pulmonary veins (PV), and there are additional ablation lines in the posterior LA and along the mitral isthmus. LI = left inferior; LS = left superior; RI = right inferior; RS = right superior.

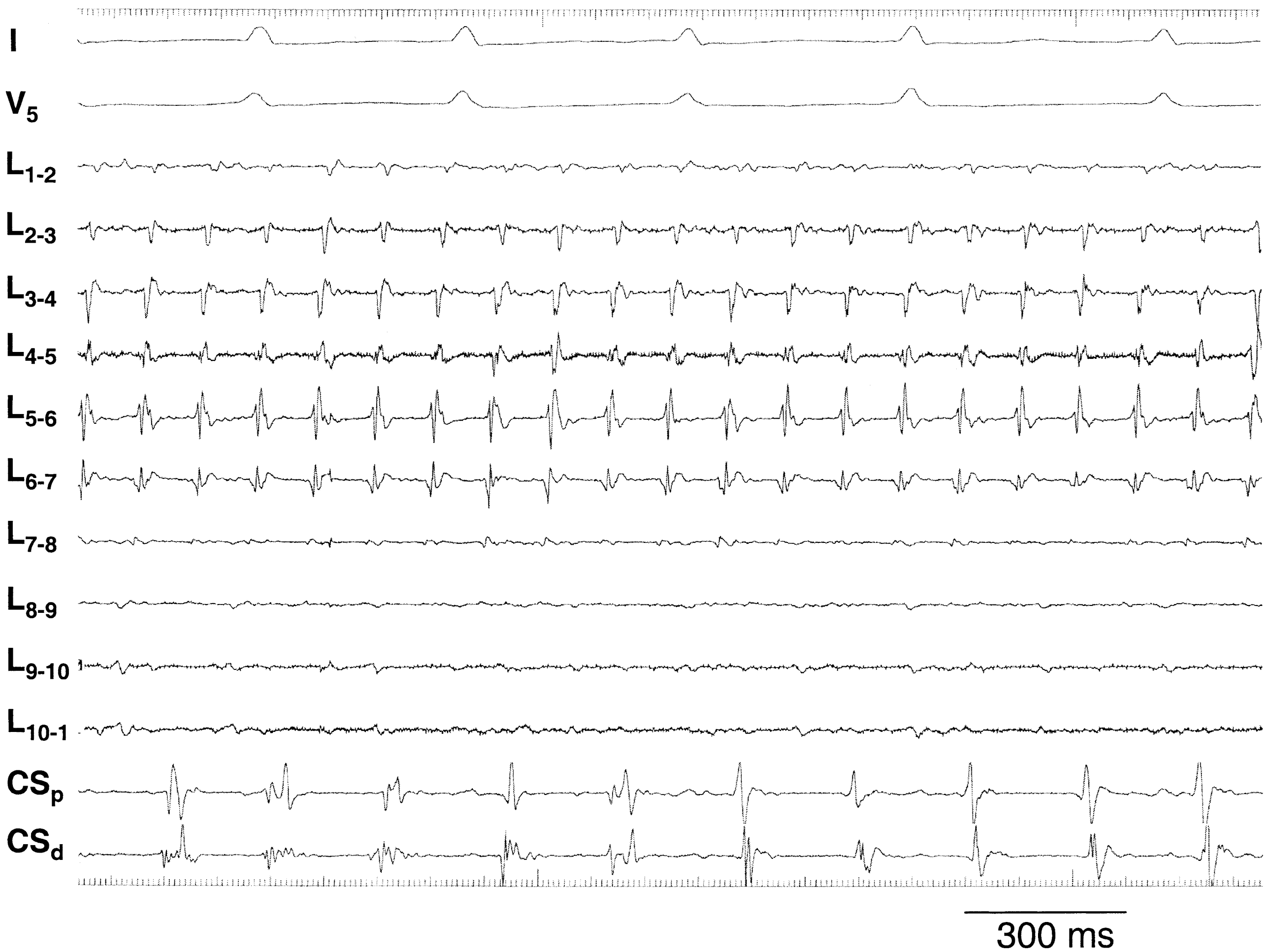

Figure 2. An example of a pulmonary vein (PV) tachycardia. Shown are electrocardiographic leads I and V_5, bipolar electrograms recorded with a decapolar ring catheter positioned at the ostium of a left superior PV (L_{1-2}, . . ., L_{10-1}), and electrograms recorded within the coronary sinus (CS_d, CS_p). The mean cycle length of the PV tachycardia was 110 ms, and the cycle length within the CS was 245 ms.

atrial flutter within the first weeks after ablation may be transient (11), a blanking period of six weeks was applied.

Statistical analysis. Continuous variables are expressed as the mean value ± SD and were compared by the Student *t* test. The change in stimulus-to-PV potential intervals was analyzed with the paired *t* test. Categorical variables were compared by chi-square analysis or with the Fisher exact test when n was <5. Freedom from recurrent AF was determined by Kaplan-Meier analysis with the log-rank test. A $p < 0.05$ indicated statistical significance.

RESULTS

Pulmonary vein potentials before and after LACA. Before LACA, PV potentials were recorded in 213 (94%) of the 226 PVs. The PV potentials were present in one or more PVs in all 60 patients (100%). After LACA, there were PV potentials indicative of one or more functioning PV fascicles in 37 (63%) of the 59 left superior PVs, 31 (58%) of the 53 left inferior PVs, 33 (56%) of the 59 right superior PVs, and 15 (32%) of the 47 right inferior PVs. Overall, there was incomplete electrical isolation of one or more PVs in 48 (80%) of the 60 patients after LACA (Fig. 3).

The mean of the shortest interval between the stimulus and PV potentials recorded at the PV ostium during pacing from the CS increased by 41 ± 40% (from 83 ± 22 ms to 117 ± 38 ms; $p < 0.01$) (Fig. 4).

Pulmonary vein tachycardias before and after LACA. Among the 60 patients, PV tachycardias were recorded in one or more PVs in 49 (82%) before and in five patients (8%) after LACA ($p < 0.001$).

The PV tachycardias had a mean cycle length of 149 ± 38 ms before LACA and 157 ± 41ms after LACA ($p = 0.4$). The simultaneous cycle length at the adjacent LA or CS was 200 ± 37 ms before LACA and 336 ± 270 ms after LACA, respectively ($p < 0.01$).

Number of completely isolated PVs and freedom from recurrent AF. At a mean follow-up of 11 ± 1 months, 39 (81%) of 48 patients with incomplete PV isolation and 10 (83%) of 12 patients with complete PV isolation were in sinus rhythm in the absence of antiarrhythmic drug therapy and had no further episodes of symptomatic AF ($p = 1.0$,

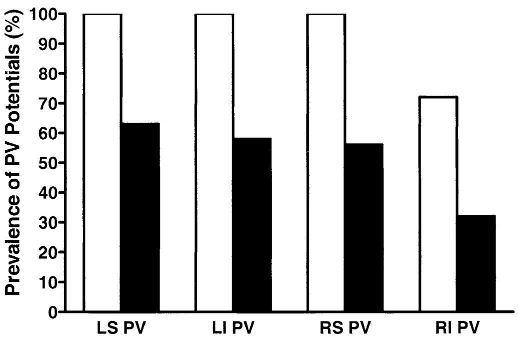

Figure 3. Prevalence of pulmonary vein (PV) potentials before **(open bars)** and after **(solid bars)** left atrial circumferential ablation. Other abbreviations as in Figure 1.

Fisher exact test). Both in patients with paroxysmal and chronic AF, a successful outcome was independent of the number of PVs that were electrically isolated ($p = 0.6$) (Fig. 5).

Pulmonary vein isolation and LA flutter. Among the 60 patients, 10 (17%) developed LA flutter after LACA. There were residual PV potentials in 7 (70%) of the 10 patients with LA flutter and in 41 (82%) of the 50 patients without LA flutter ($p = 0.4$, Fisher exact test). Four patients in whom LA flutter persisted beyond three months underwent successful ablation of the atrial flutter. The successful ablation site was the mitral isthmus in two patients, the LA roof in one patient, and a gap in the ablation line encircling the right pulmonary veins in one patient.

Complications. There were no complications in any of the patients who participated in this study.

DISCUSSION

Main findings. With the techniques used in this study, LACA for AF usually was associated with incomplete PV isolation. Although PV potentials were still present in at least one PV in 80% of patients, there usually was a conduction delay between the LA and PVs, and the prevalence of PV tachycardias was markedly reduced after LACA. Most importantly, a successful outcome after LACA was found to be independent of the number of PVs that were electrically isolated, and freedom from symptomatic AF during follow-up was just as likely when none of the PVs were completely isolated as when all four PVs were

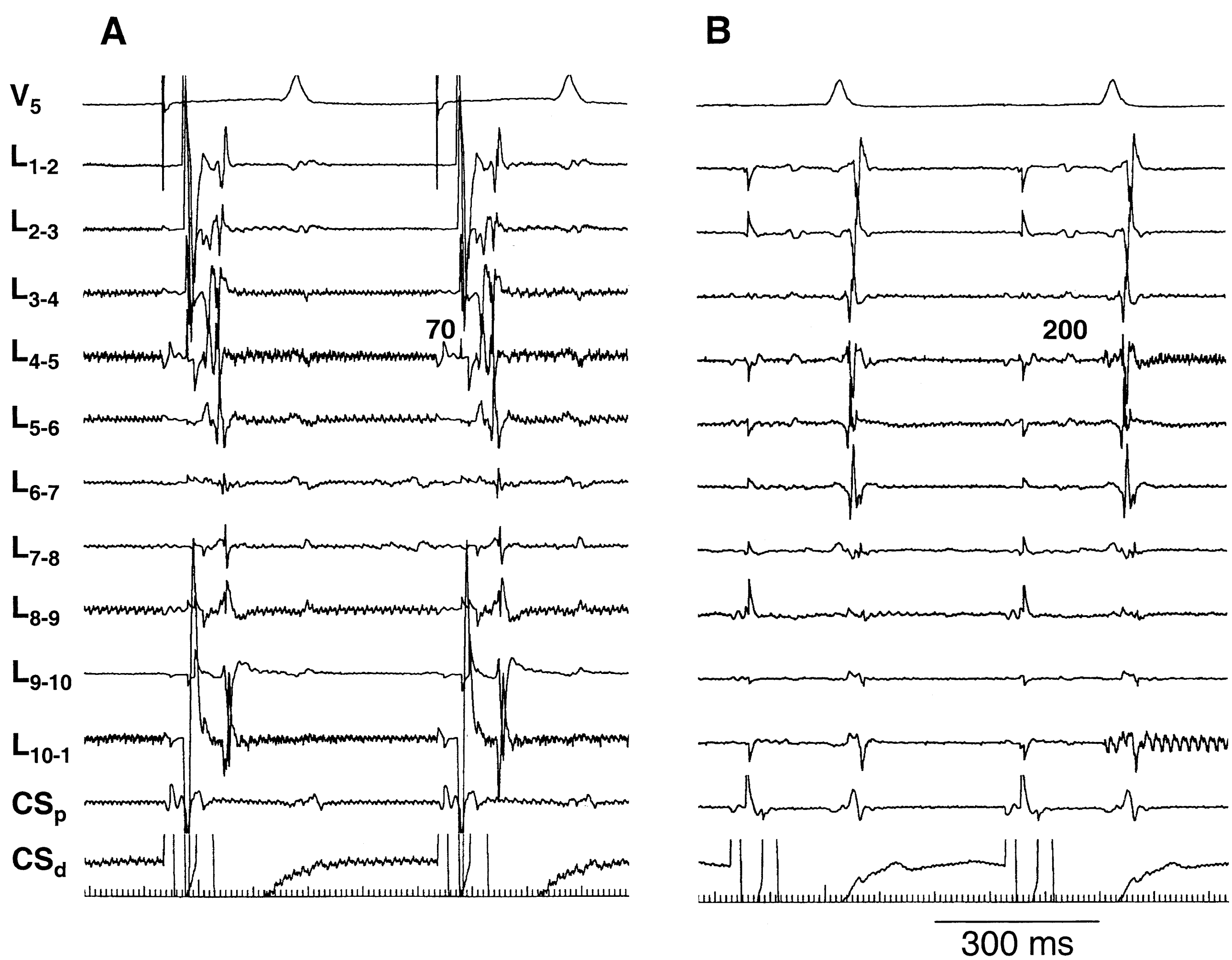

Figure 4. Effect of left atrial circumferential ablation (LACA) on activation of pulmonary vein (PV) potentials during coronary sinus (CS) pacing. Shown is the shortest stimulus-to-PV potential interval recorded in the same left superior PV before (70 ms) **(A)** and after LACA (200 ms) **(B)**.

JACC Vol. 46, No. 6, 2005
September 20, 2005:1060–6

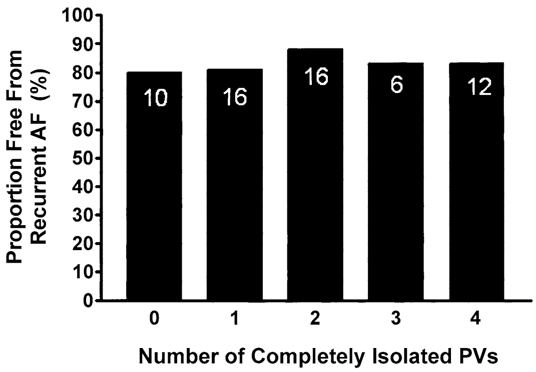

Figure 5. Freedom from recurrent atrial fibrillation (AF) and number of completely isolated pulmonary veins (PVs). The probability of freedom from recurrent AF after left atrial circumferential ablation was unrelated to the number of isolated PVs. The number of patients is shown within each bar.

isolated. These results demonstrate that when LACA is performed during AF with the end points used in this study, complete electrical isolation of the PVs is not necessary for a successful outcome.

PV isolation and freedom from recurrent AF. Previous studies have demonstrated that recurrent AF after PV isolation is associated with recurrent conduction through previously isolated PVs (12,13). However, in the present study, many patients remained free of recurrent AF despite the presence of incomplete PV isolation immediately after LACA. Therefore, whereas the efficacy of PV isolation depends on complete and lasting PV disconnection from the LA, the efficacy of LACA does not. This highlights the fact that LACA eliminates AF by mechanisms other than complete PV isolation. In addition, by targeting sites within the encircling lesions where relatively rapid cycle lengths were observed during AF, the profibrillatory effects of PV tachycardias may have been eliminated, despite the fact that complete PV isolation was not achieved.

In a randomized study, LACA was found to be more effective than PV isolation by segmental ostial ablation in patients with paroxysmal AF (10). It is likely that the incremental efficacy of LACA is attributable to mechanisms of action that are independent of the PVs. These mechanisms of action may include LA compartmentalization (14), elimination of anchor points for rotors (14–16), and autonomic denervation (17). None of these mechanisms of action require complete PV isolation. Furthermore, a reduction in the prevalence or elimination of PV tachycardias does not require complete PV isolation. Therefore, the end points of voltage abatement and elimination of residual sites displaying relatively rapid cycle lengths used in the present study appear to be adequate for achieving an acceptable clinical outcome.

A previous study demonstrated an excellent success rate when intraoperative RF ablation was performed using a lesion set that did not isolate the PVs (18). Furthermore, other investigators have demonstrated that recurrent AF often is eliminated after RF ablation that targets fractionated electrograms (19), with no attempts to isolate the PVs or create lines of block. The results of these studies validate the conclusion that PV isolation is not necessarily required to eliminate AF.

PV potentials and PV tachycardias. After LACA, although residual PV potentials were usually present, the prevalence of PV tachycardias was markedly reduced. Therefore, although PV isolation was not complete, the arrhythmogenic potential of the PVs was attenuated. Because PV tachycardias are one of the factors that perpetuate an episode of AF (2,3), the reduction in PV tachycardias by LACA most likely contributed to the successful elimination of recurrent AF.

Atrial pacing in the CS demonstrated a conduction delay between the LA and PVs. A previous study demonstrated that there is a dynamic interplay between the LA and PVs, and that the occurrence of PV tachycardias usually requires input from the LA (2,20). Therefore, partial block of impulses from the LA into the PVs may have been one of the reasons that PV tachycardias were much less prevalent after LACA. In addition, previous studies have shown that complete PV isolation is achievable with noncontiguous RF energy applications at the boundary of the PV antrum and LA (6). The RF lesions that were delivered 1 to 2 cm away from the ostia or at sites of relatively short cycle lengths during AF in the present study may have ablated some of the arrhythmogenic fibers of the PV muscle sleeves.

These effects of LACA may result in modification of the arrhythmogenic activity within the PVs. Furthermore, although complete conduction block across the encircling lesions may not be achieved, decremental conduction can occur, particularly at shorter cycle lengths, and may impede the conduction of PV tachycardias to the LA.

LA flutter. In a previous study, it was suggested that LA flutters can be prevented by complete ablation of all recovered fascicles during a repeat ablation procedure after LA antrum-PV disconnection (21). In this study, LA flutter occurred during follow-up in 17% of patients who underwent LACA, and the occurrence of LA flutter was not related to whether or not there was complete PV isolation. Previous studies have demonstrated that LA flutters after LACA are usually macro–re-entrant and not related to arrhythmogenic activity emanating from the PVs (22,23).

Previous studies. In a previous study, ~80% of patients who underwent PV isolation using a purely anatomic approach were free of recurrent AF during a mean follow-up of 16 months, regardless of whether PV isolation was complete or not (24). In that study, ablation was performed at the ostium of the PVs rather than within the LA, and an 8-mm-tip catheter was used to look for PV potentials. Complete PV isolation was defined as the inability to capture the LA during pacing within a PV. In contrast, in the present study, the extent of PV isolation after LACA was assessed with a decapolar ring catheter, which is more likely to accurately detect residual PV potentials than a standard 8-mm tip catheter.

In a recent study, circumferential PV isolation was not found to be superior to PV isolation by segmental ostial ablation (25). No data on the relationship between the completeness of PV isolation and clinical outcomes were presented.

Study limitations. A limitation of this study is that freedom from AF during follow-up was based on patient-reported symptoms, and asymptomatic episodes of AF may not have been detected. However, a previous study demonstrated that asymptomatic recurrences of AF are rare in patients with symptomatic paroxysmal AF who undergo catheter ablation (26).

It is possible that PVs that were only partially isolated immediately after LACA became completely isolated during follow-up because of post-ablation lesion maturation and progressive fibrosis. Because follow-up electrophysiologic procedures were not routinely performed, this possibility cannot be ruled out.

Conclusions. If ablation is performed during sinus rhythm and the only end point is PV isolation, the best outcomes are achieved if there is complete isolation of all PVs (3,27). Furthermore, it is clear that if wide area circumferential ablation is performed during sinus rhythm, complete PV isolation is also the most desirable end point (28,29). However, when wide area circumferential ablation is performed during AF using end points of voltage abatement inside the encircling lesions and elimination of sites displaying relatively short cycle lengths, complete PV isolation is not required for a successful outcome.

As long as PV stenosis is avoided, there are no deleterious effects of complete PV isolation. Nevertheless, because complete isolation requires additional time and RF energy delivery, it is useful to know that complete elimination of PV potentials may not be necessary to achieve a successful outcome with the type of wide area circumferential ablation technique used in the present study.

After this study was completed, esophageal injury resulting in atrioesophageal fistula formation was recognized as a potential hazard of LACA (30,31). Because of this, the techniques used in this study were modified, with elimination of the posterior wall ablation line, addition of an LA roof line, reduction in the power and duration of RF energy applications on the posterior wall, and real-time visualization of the esophagus with the use of barium paste (32). Further studies are needed to establish the ablation technique with the best balance of efficacy and safety.

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