Left Atrial Posterior Wall Isolation Does Not Improve the Outcome of Circumferential Pulmonary Vein Ablation for Atrial Fibrillation

A Prospective Randomized Study

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Background—Ablation of the pulmonary veins (PVs) for atrial fibrillation treatment is often combined with linear radiofrequency lesions along the left atrium (LA) to improve the success rate. The study was designed to assess the contribution of LA posterior wall isolation to the outcome of circumferential pulmonary vein ablation (CPVA).

Methods and Results—CPVA consisted of continuous radiofrequency lesions encircling both ipsilateral PVs plus an ablation line along the mitral isthmus. Patients were then randomized into 2 groups. In the first group, superior PVs were connected by linear lesions along the LA roof (CPVA-1 group). In the second group, the LA posterior wall was isolated by adding a second line connecting the inferior aspect of the 2 inferior PVs (CPVA-2 group). The study included 120 patients (53±11 years, 77% male, 60% paroxysmal atrial fibrillation, LA of 41.3±5.4 mm, 46% with hypertension, and 22% with structural heart disease). After a single ablation procedure and a mean follow-up of 10±4 months, 24 (40%) patients of the CPVA-1 group had atrial fibrillation recurrences and 3 (5%) had new-onset LA flutter. In the CPVA-2 group, recurrences were due to atrial fibrillation episodes in 23 patients (38%) and LA flutter in 4 (7%). Freedom from arrhythmia recurrences was not statistically different in the CPVA-1 group as compared with the CPVA-2 group (log rank \( P=0.943 \)).

Conclusion—Isolation of the LA posterior wall did not increase the success rate of CPVA. (Circ Arrhythmia Electrophysiol. 2009;2:35-40.)

Key Words: arrhythmia | catheter ablation | atrium

Because the initial description of paroxysmal atrial fibrillation (AF) triggered by pulmonary vein (PV) firing,1 several approaches to catheter ablation have been developed to treat AF. At present, PV isolation is performed in almost all AF ablation procedures.2–4 Deployment of linear lesions along the left atrium (LA) in addition to PV ablation has been shown to improve the success rate.5–7 The most commonly performed procedure involves ablation of the mitral isthmus and connection of the superior contralateral PVs through the LA roof.6,8 Other authors have suggested a lesion set in which the LA posterior wall is also excluded by connecting superior and inferior contralateral PVs along 2 ablation lines.9,10–12 However, there are no data comparing the 2 approaches.

Clinical Perspective see p 40

The aim of this prospective randomized study was to evaluate whether isolation of the LA posterior wall decreased arrhythmia recurrence risk after circumferential pulmonary vein ablation (CPVA).

Methods

The study included 120 consecutive patients undergoing a first catheter ablation for symptomatic, drug-refractory (≥2 antiarrhythmics) AF, classified as paroxysmal, persistent, or long-standing, according to consensus.13 No patient refused to give consent and no patient was lost to follow-up. The study protocol was approved by the hospital’s ethics committee. The authors take responsibility for the integrity of the data. All the authors have read and agreed to the manuscript as written.

All patients underwent transesophageal echocardiography 1 to 5 days before ablation to exclude the presence of intracavitary thrombus. A transthoracic echocardiogram and a gadolinium-enhanced magnetic resonance angiogram were also obtained before the procedure.

After trans-septal access, a bolus of intravenous heparin (5000 IU) was administered, with an additional bolus to maintain an activated clotting time of >250 seconds. The procedure was performed under deep sedation. Ablation was assisted by a 3D map of the LA and its adjacent structures, produced with CARTO (Biosense Webster) or NavX (St Jude Medical) systems. Magnetic resonance angiogram images were integrated into the navigation system to support the LA anatomic reconstruction. Radiofrequency was delivered by a...
thermocouple-equipped 3.5-mm cooled-tip catheter at a target temperature of 48°C and a maximum output of 40 W.

Patients were randomized into 2 ablation groups. In both, continuous radiofrequency lesions surrounding each ipsilateral PV antrum were deployed until the local electrogram inside the encircled area disappeared or was dissociated or, when this was not possible, until the bipolar voltage amplitude dropped to <0.15 mV; electric block was confirmed by the inability to conduct to the LA after pacing at several sites within the PV antrum.2,14 PV antrum was defined as the anatomic transition between LA and PV structures and was mainly identified by 3-dimensional reconstruction. Mitral isthmus ablation was also performed in all patients by creating a radiofrequency line from the inferior-lateral aspect of the left PV lesions to the mitral annulus. Then, in the first group (CPVA-1), a radiofrequency line was created connecting contralateral PV-encircling lesions through the LA roof. In the second group (CPVA-2), the LA posterior wall was excluded by adding a second ablation line connecting the inferior aspect of the 2 inferior PVs. In both groups, separated local double potentials or potential disappearance all along the LA roof ablation line was used as the criterion to define electric block.6 In the CPVA-2 group, after completion of the roof line, the infero-posterior line was deployed until the absence or dissociation of local electrogram inside the excluded LA posterior region was observed; isolation was confirmed by the inability to conduct to the remaining atria after pacing at several sites within the surrounded LA posterior region with the ablation catheter, observing the local capture in the proximal bipole of the pacing catheter when possible10 (Figure 1).

Each end point of the ablation procedure was assessed in sinus rhythm, performing electric cardioversion if necessary.

Follow-Up
Patients were followed up at the outpatient clinic at 1, 4, and 7 months after the ablation procedure and every 6 months thereafter if they remained asymptomatic. Routine 48-hour Holter monitoring was performed before each visit. Patients were also asked to come to the emergency department if any symptom suggestive of recurrence occurred between scheduled visits. All patients continued oral anticoagulation to maintain an international normalized ratio between 2.0 and 3.0 for a minimum of 2 months after ablation. All patients received antiarrhythmic medication for a minimum of 1 month after the procedure to decrease early recurrences (flecainide if no structural heart disease was diagnosed or amiodarone if there was evidence of structural heart disease). Ablation was considered successful in those patients with no AF recurrences or LA flutter after a blanking period of 3 months. Minimum follow-up of this series was 6 months.

Statistical Analysis
The primary end point of the study was freedom from arrhythmia recurrence after a single ablation procedure. On the basis of our own experience, at 6-month follow-up, 55% of patients were expected to be free of arrhythmia after a single CPVA-2 procedure. With a sample size of 60 patients per arm, a log-rank test for equality of survival curves will have 80% power and a 2-sided α value of 0.05 to detect an expected 20% reduction in freedom from arrhythmia in the CPVA-1 group. Subjects were included during the first 18 months of the 24-month study, with no loss to follow-up expected.

Randomization was performed according to a computer-generated algorithm in blocks of 20 patients. The ablation group was blinded to patients and to the physicians evaluating the outcome of the procedure.

Data are reported as mean±SD. Comparisons between groups were performed using Student t test or χ2 analysis. Arrhythmia-free survival curves for each group were presented as Kaplan–Meier plots and compared by log-rank test.

Cox method was used to estimate the effect of LA posterior wall isolation after adjusting for baseline variables. The following potential predictors of recurrence were considered: age, sex, type and duration of AF, LA diameter, left ventricular end-diastolic and end-systolic diameters, left ventricular ejection fraction, hypertension, and structural heart disease. Stepwise method with criteria of P<0.05 for inclusion and P≥0.10 for removal was used to select the covariates and report the estimates from the model that included those covariates and the variable isolation (or not) of the LA posterior wall.

A 2-sided probability value ≤0.05 was considered statistically significant. Analyses were performed using SPSS 12.0 (SPSS Inc) and Stata 9 (Stata Corp) statistical packages.

Results
The study included 120 consecutive patients; baseline characteristics are shown in Table 1. No significant baseline differences were observed between the groups. Procedure details are given in Table 2. End points of the procedure were confirmed using previously described criteria in 54 and 55 patients of the CPVA-1 and CPVA-2 groups, respectively (90% versus 92%; P=0.75).

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>CPVA-1 Group</th>
<th>CPVA-2 Group</th>
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<tbody>
<tr>
<td>Patients</td>
<td>60</td>
<td>60</td>
<td></td>
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<tr>
<td>Type of AF</td>
<td></td>
<td></td>
<td>0.75</td>
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<tr>
<td>Paroxysmal</td>
<td>37 (62)</td>
<td>35 (58)</td>
<td></td>
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<tr>
<td>Persistent</td>
<td>11 (18)</td>
<td>13 (22)</td>
<td></td>
</tr>
<tr>
<td>Long-standing</td>
<td>12 (20)</td>
<td>12 (20)</td>
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<tr>
<td>Age, years</td>
<td>52.5±10.9</td>
<td>52.9±10.8</td>
<td>0.83</td>
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<tr>
<td>Male sex</td>
<td>44 (73)</td>
<td>48 (80)</td>
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<tr>
<td>Duration of AF, months</td>
<td>60.8±55.7</td>
<td>67.1±48.2</td>
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<tr>
<td>LA diameter, mm</td>
<td>41.1±5.0</td>
<td>41.6±5.9</td>
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<tr>
<td>LV end-diastolic diameter, mm</td>
<td>52.7±4.1</td>
<td>52.5±5.4</td>
<td>0.80</td>
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<tr>
<td>LV end-systolic diameter, mm</td>
<td>32.8±4.8</td>
<td>34.4±7.1</td>
<td>0.25</td>
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<tr>
<td>LV ejection fraction, %</td>
<td>59.8±9.8</td>
<td>59.5±10.1</td>
<td>0.88</td>
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<tr>
<td>Hypertension</td>
<td>26 (43)</td>
<td>29 (48)</td>
<td>0.58</td>
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<tr>
<td>Structural heart disease</td>
<td>13 (22)</td>
<td>13 (22)</td>
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</table>

Data are presented as n (%) or mean±SD.
After a mean follow-up of 9.8±4.3 months, 33 patients (55%) in both groups had no arrhythmia recurrences after a single ablation procedure (log-rank test \( P=0.943 \)). The success rate was higher in paroxysmal AF than in persistent/long-standing AF, but no statistical differences were observed in arrhythmia recurrences between those with or without LA posterior wall isolation (Figure 2). Among patients with no recurrences, 28 CPVA-1 and 27 CPVA-2 patients (47% and 45%, respectively) were not treated with antiarrhythmics (log-rank test \( P=0.908 \)), and 5 CPVA-1 and 6 CPVA-2 patients were taking 1 antiarrhythmic drug: in 3 and 4 patients, respectively, the antiarrhythmic was not withdrawn during the blanking period due to early recurrences, but they had no arrhythmias after the 3-month blanking period, and 2 patients of each group took flecainide due to symptomatic premature atrial beats, but they had no sustained episodes.

In the CPVA-1 group, recurrences were due to AF episodes in 24 patients (40%) and to LA flutter in 3 (5%). In the CPVA-2 group, 23 patients (38%) had AF recurrences, and 4 (7%) had new-onset LA flutter.

Cox regression indicated that the baseline LA diameter was the only covariate significantly associated with arrhythmia recurrence (hazard ratio, 1.078 [95% CI, 1.011 to 1.148]; \( P=0.021 \)). The adjusted hazard ratio obtained for the variable isolation of the LA posterior wall was consistent with the log rank test result (hazard ratio, 0.893 [95% CI, 0.581 to 1.549]; \( P=0.722 \)).

**Complications**

There were no differences between the groups in the number of procedural complications (Table 2). Two CPVA-1 patients and 1 CPVA-2 patient experienced a transient cerebrovascular ischemia, which was resolved under heparin with normal computed tomography scanning. One patient in each group showed transient inferior myocardial ischemia, probably related to catheter manipulation during trans-septal catheterization because of air embolism; the ischemia was re-

<table>
<thead>
<tr>
<th>Table 2. Procedural Details</th>
<th>CPVA-1 Group</th>
<th>CPVA-2 Group</th>
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<tr>
<td>Patients</td>
<td>60</td>
<td>60</td>
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<td>Procedural time, minutes</td>
<td>114.3±23.4</td>
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<td>23.2±7.8</td>
<td>22.6±8.3</td>
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<tr>
<td>Radiofrequency time, minutes</td>
<td>39.2±7.7</td>
<td>42.5±9.2</td>
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<tr>
<td>Complications</td>
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<td></td>
<td>0.65</td>
</tr>
<tr>
<td>Transient cerebrovascular ischemia</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Transient inferior myocardial ischemia</td>
<td>1</td>
<td>1</td>
<td></td>
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</tbody>
</table>

Data are presented as n (%) or mean±SD.

Figure 2. Accumulated arrhythmia recurrence survival after a single ablation procedure in (A) whole series, (B) subgroup of paroxysmal AF patients, and (C) subgroup of persistent or long-standing AF patients. Solid and dotted lines represent CPVA-1 and CPVA-2 groups, respectively.
solved with sublingual N-methyl-N'-nitro-N-nitrosoguanidine within a few minutes, without consequences.

In addition, 1 CPVA-1 and 2 CPVA-2 patients had post-procedural pericarditis that required nonsteroidal antiinflammatory treatment. Magnetic resonance angiogram performed before and 4 months after ablation in all patients of this series did not reveal any severe (>70%) PV stenosis; one patient of the CPVA-2 group showed a left superior PV narrowing of 55%.

**Second Ablation Procedures**
The ablation procedure was repeated in 25 (20.8%) patients. Overall, after a mean of 1.2 ± 0.4 ablation procedures; 67.7% of the patients of this series remained arrhythmia-free.

In 4 patients, the ablation was repeated due to new-onset LA flutter. In all 4 cases, an activation map produced by the navigation system plus entrainment maneuvers showed that the reentry was established between gaps of the previous right- or left-sided encircling lesions.

In the remaining 21 patients, the second procedure was performed due to AF recurrences. The previous ablation set was evaluated and radiofrequency was delivered in sites showing conduction gaps. Recurrent electric conduction in a mean of 3.1 ± 0.9 PV per patient was found in 17 of the 21 patients (84%), whereas all PV remained isolated in 4 patients. Conduction across the LA roof line and electric activity within the LA posterior wall was observed in 69% and 67% of the CPVA-1 and CPVA-2 patients, respectively. In 1 CPVA-2 patient, extensive fibrosis was observed along both atria, without electric activity in the previously isolated areas; no further ablation was performed and it was decided to leave the patient in permanent AF.

**Discussion**
The main finding of this study is that electric isolation of the LA posterior wall did not increase the success of CPVA. Deployment of linear lesions along the LA roof, mitral isthmus or both locations has been shown to improve the outcome of PV ablation. Moreover, some authors advocate a lesion set in which the LA posterior wall is also excluded by connecting the superior and inferior contralateral PVs through both ablation lines. However, the number and location of linear lesions that will obtain the best results has not been well established. Several surgical methods were originally used to treat AF with a predefined set of linear lesions, based on the multiple wavelet hypothesis and the idea that sustained AF requires a critical amount of contiguous atrial tissue. At present, the main mechanism leading to AF is not clearly defined. PV firing has been considered as a main trigger of paroxysmal AF, and larger LA regions may act as the AF substrate in more persistent AF. In all 4 patients, an activation map produced by the navigation system plus entrainment maneuvers showed that the reentry was established between gaps of the previous right- or left-sided encircling lesions.

The role of the LA posterior wall in triggering and driving fibrillation has been suggested by both human and animal studies. However, in the present series, exclusion of the LA posterior wall had no effect on the incidence of AF recurrences after CPVA. It should be noted that a larger area of posterior venous-atrial tissue was excluded when PV encirclement was performed in this study as compared with procedures in which PVs are ablated at their ostia. A recent study suggested that large PV ablation circles increase the success rate of the procedure. It is thus possible that the AF substrate of the LA posterior wall is mainly located within the lesions around the PV antrum and no further ablation is required.

Our results also showed no difference between the CPVA-1 and CPVA-2 groups in terms of the risk of LA flutter. The incidence of new-onset LA flutter has been described after AF ablation procedures, in which gaps along large lesions may create an ideal substrate for reentrant circuits. Pappone et al demonstrated that mitral isthmus ablation plus the addition of 2 posterior linear lesions reduced the risk of developing this arrhythmia after CPVA. In the present study, the deployment of 2 ablation lines connecting left and right sided PVs showed no benefit in preventing LA flutter, compared to creating a single roof line. In all procedures performed to treat LA flutter after the index ablation, a re-entrant circuit through gaps in the prior PV-encircling lesions was observed, in accordance with other series. It is known that the continuity of linear lesions around ipsilateral PVs is difficult to achieve, especially at the PV septal aspect and the region between the LA appendage and the left superior PV.

To our knowledge, this is the first study to demonstrate that the performance of LA posterior wall isolation does not improve the outcome of CPVA. Although the total time of radiofrequency delivery did not increase significantly when the ablation line was added along the LA posterior-inferior wall, there is a major potential risk of lesion to the esophagus, because it is virtually in contact with this region. Moreover, isolation of the posterior LA region could theoretically impair atrial function. Therefore, according to the results of this study, we conclude that the electric exclusion of the LA posterior wall is not necessary when performing CPVA as a predefined lesion set to treat AF.

**Study Limitations**
The study was planned to detect an absolute reduction of 20% in the proportion of freedom from arrhythmia. However, the same number of patients was arrhythmia free in both groups, and consequently, the result from the formal comparison is far from the 5% significance level and the adjusted hazard ratio for arrhythmia recurrence was close to 1. Therefore, the lack of statistical significance may not be attributable to low statistical power.

The effect of LA posterior wall isolation was evaluated as part of a predefined lesion set performed in all patients. Therefore, the study cannot exclude that the isolation of the LA posterior wall may have some effect in individual AF cases. Recently, individualized approaches for AF ablation have been proposed, but the criteria to preselect the ablation method in each patient or the end point for a tailored procedure are still under investigation.

Mitrail isthmus ablation was performed anatomically without demonstrating electric block. This may theoretically create a proarhythmic substrate because of the effect of incomplete linear lesions, although no peri-mitral re-entry
was observed in any patient submitted to a second procedure. Additionally, PV isolation was not assessed by circular catheter mapping, as originally described by Haissaguerre et al. In any case, ablation technique was the same in both groups except for the performance of the infero-posterior ablation line, and probably did not affect the conclusions of the study.

Because no additional catheter was placed at the LA, the achievement of local capture during pacing maneuvers was often difficult to demonstrate because it was assessed by the proximal pair recording of the ablation catheter\(^1\) (while pacing through the distal). However, in these cases, the absence of local electromgram or dissociation from the remaining atria should be a reasonable surrogate marker of the LA posterior wall isolation.\(^5\)

Finally, with the available follow-up limited to routine 48 hour-Holter monitoring and ECG recording when symptoms occurred between scheduled visits, arrhythmia recurrences may have escaped detection in asymptomatic patients. However, this was a pragmatic approach that obtained a reasonable follow-up in light of other published studies.\(^5,7,10,12,32.40–42\); moreover, this limitation should have occurred equally in both ablation groups and therefore would not affect the conclusions of the study.

Conclusion
Isolation of the LA posterior wall did not offer additional benefit over a single roof line lesion with respect to the risk of arrhythmia recurrence after CPVA.

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Disclosures
None.

References
Since the initial description of extensive atrial lesions performed by surgical procedures, there has been a continuous search for the appropriate amount of ablation to cure atrial fibrillation. In addition to the ablation of pulmonary veins, isolation of the left atrial (LA) posterior wall has been used in several surgical and catheter-based approaches, because it has been suggested that this region may play an important role in triggering and maintaining atrial fibrillation. However, isolation of the LA posterior wall could theoretically impair atrial function and may increase the potential risk of esophageal damage. The present study was designed to analyze whether isolation of the LA posterior wall increased the efficacy of circumferential pulmonary vein ablation as compared with the creation of a single LA roof ablation line. Our results showed that isolation of the LA posterior wall did not decrease the probability of atrial fibrillation nor atrial flutter recurrences. Therefore, atrial fibrillation ablation should not systematically include isolation of the LA posterior wall.
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