Circumferential Pulmonary Vein Ablation With Additional Linear Ablation Results in an Increased Incidence of Left Atrial Flutter Compared With Segmental Pulmonary Vein Isolation as an Initial Approach to Ablation of Paroxysmal Atrial Fibrillation

Navinder Sawhney, MD; Ramtin Anousheh, MD, MPH; Wei Chen, MPH; Gregory K. Feld, MD

Background—There has been growing concern that linear ablation is associated with an increased risk of iatrogenic arrhythmias in patients undergoing ablation for atrial fibrillation (AF). Therefore, we compared circumferential pulmonary vein ablation plus left atrial linear ablation (CPVA/LALA) with segmental pulmonary vein isolation (PVI) in patients with paroxysmal AF.

Methods and Results—Sixty-six consecutive patients with paroxysmal AF were prospectively randomly assigned to receive PVI versus CPVA/LALA (consisting of encircling lesions around the pulmonary veins), a roof line, and a mitral isthmus line with documentation of bidirectional mitral isthmus block. All patients were seen at 1, 3, 6, and every 12 months after ablation, with 14-day continuous ECG monitoring every 6 months. At 16.4 ± 6.3 months after 1 ablation procedure, 19 patients (58%) remained free of atrial arrhythmias after PVI versus 17 patients (51%) after CPVA/LALA (P = 0.62). After PVI, 14 patients had recurrent paroxysmal AF, whereas after CPVA/LALA, 8 patients had recurrent AF, 6 had atypical left atrial flutter (LAFL), and 2 had both AF and LAFL (P = 0.32 between PVI versus CPVA/LALA for AF but P = 0.002 for LAFL). Twenty-eight patients (85%) remained arrhythmia-free after CPVA/LALA versus PVI (91 versus 73 minutes, P = 0.04).

Conclusions—As an initial ablation approach in patients with paroxysmal AF, more LAFL occurred after CPVA/LALA and fluoroscopy times were longer compared with segmental PVI. (Circ Arrhythm Electrophysiol. 2010;3:243-248.)

Key Words: atrial fibrillation ■ pulmonary vein isolation ■ circumferential pulmonary vein ablation ■ linear ablation ■ left atrial flutter

Although circumferential pulmonary vein ablation (CPVA) is commonly preformed as an initial approach to atrial fibrillation (AF) ablation, and randomized trials have shown an improvement in AF ablation success rates with additional left atrial linear ablation (LALA) at the LA roof or mitral isthmus (MI),1,2 there has been a growing concern about the potential proarrhythmic effect of additional ablation,3,4 particularly with regard to the occurrence of atypical left atrial flutter (LAFL).

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Therefore, we conducted a randomized, prospective study comparing the efficacy of segmental pulmonary vein isolation (PVI) versus CPVA/LALA at the LA roof and MI (with documented bidirectional MI block), as an initial approach to ablation in selected patients with paroxysmal AF.

Methods

Patient Population

There were 66 consecutive patients enrolled in this study with symptomatic, medically refractory paroxysmal AF who underwent catheter ablation for the treatment of their AF and agreed to be prospectively randomly assigned with regard to the initial ablation strategy. For the purpose of this study, paroxysmal AF was defined as self-terminating AF of < 48 hours’ duration. Exclusion criteria included a previous ablation procedure, permanent or persistent AF, refusal to provide informed consent, contraindication to anticoagulation, myocardial infarction or cardiac surgery within 3 months of enrollment, and intracardiac thrombus identified on transesophageal echocardiography. In those patients already on warfarin, it was held for 5 days before ablation, and patients were bridged with enoxaparin 1 mg/kg SQ bid up to the night before the ablation procedure. All antiarrhythmic drugs were held for 5 half-lives before ablation. The Human Studies Committee at the University of California, San

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Correspondence to Navinder Sawhney, MD, University of California, San Diego, 4168 Front St, MC 8649, San Diego, CA 92103-8649. E-mail navinsawhney@gmail.com
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of any evidence of PV reconnection during this waiting period. Ablation was repeated as described above in the event to elicit any nonpulmonary vein triggers and confirm persistent PVI.

**Method for Segmental PVI**

Each pulmonary vein (PV) was mapped using the Lasso catheter placed at the ostium using fluoroscopic, 3D mapping (ESI NavX, St Jude Medical, Inc, St Paul, Minn) and intracardiac ultrasound guidance, to record PV potentials (during distal coronary sinus pacing for the left PVs and during sinus rhythm for the right PVs). PVI was performed by sequential application of radiofrequency energy at sites proximal to the Lasso catheter (Figure 1), where the earliest bipolar PV potentials were recorded, until all PV potentials were eliminated. Radiofrequency energy was delivered in a temperature-controlled manner (EPT-1000 or Maestro, Boston Scientific, Inc, Natick, Mass, or Navistar, Biosense-Webster, Inc, Diamond Bar, Calif) and a circular 20-pole Lasso catheter (Biosense Webster, Inc, Diamond Bar, Calif) were placed for mapping the PVs. Before transseptal puncture, unfractionated heparin (10 000 to 15 000 U) was administered as a bolus followed by a continuous intravenous infusion to maintain an activated clotting time >350 seconds throughout the procedure, as measured every 15 minutes.

**Method for CPVA +LALA**

A 3D geometry of the LA was either constructed using an electroanatomic mapping system (CARTO, Biosense Webster Inc, Diamond Bar, Calif or ESI NavX, St Jude Medical), or a 3D CT image of the LA and PVs was imported and registered in the mapping system before ablation (CartoMerge, Biosense Webster, Inc, or Fusion, St Jude, Inc, software). Radiofrequency energy was applied at a maximum power of 50 W and maximum temperature of 55°C for up to 30 seconds at each location (EPT-1000 or Maestro, Boston Scientific, Inc, Natick, Mass, or Stockert 70 RF, Biosense-Webster, Inc, radiofrequency generators, respectively) to encircle the left and right PVs at least 10 mm proximal to the PV ostia. Radiofrequency energy was applied at each location around the PVs until the maximum local electrogram amplitude was <0.5 mV. Linear ablation was then performed at the LA roof connecting the two encircling lesions until maximum local electrogram amplitude was <0.5 mV along the entire line, and at the MI, from the mitral valve annulus up to the left encircling lesion (Figure 2). After ablation, pacing from the left atrial appendage and the proximal coronary sinus was performed to document bidirectional MI block. If block was not achieved, ablation was performed within the coronary sinus with an 8-mm tip catheter at a maximum power of 50 W and maximum temperature of 55°C, with the catheter tip deflected toward the atrium, as the catheter was gradually withdrawn from the distal to proximal coronary sinus, until bidirectional MI block was achieved. The Lasso catheter was then placed in all 4 PVs to confirm PVI. If PVI was not complete, ablation was performed around the antrum along the CPVA lines or at the carina between the PVs until all PV potentials were eliminated. Isoproterenol was infused intravenously at 20 μg/min to elicit any nonpulmonary vein triggers and confirm persistent PVI. Persistent PVI was also confirmed 30 minutes after initial documentation of PVI. Ablation was repeated as described above in the event of any evidence of PV reconnection during this waiting period.

**Monitoring During Ablation**

Esophageal position and temperature were monitored during all left atrial ablations using a nasogastric tube containing a temperature probe continually repositioned in the esophagus at the level of the ablation catheter to avoid any temperature rise above 38°C. Pacing was performed through the ablation catheter at all locations before
ablation in the anterior right PVs at 10 mA output and 10 ms pulse duration to ensure lack of phrenic nerve capture.

Postablation Care
After ablation, patients were hospitalized overnight and administered enoxaparin 1 mg/kg SQ every 12 hours starting approximately 6 hours after sheaths were pulled and hemostasis achieved. Patients were discharged on the antiarrhythmic drug regimen they had been on before ablation (most commonly a class IC drug) and were maintained on this medication for up to 90 days at the discretion of their physician, after which it was discontinued.

Follow-Up
After discharge, all patients were seen in the University of California, San Diego, outpatient arrhythmia clinic at 1, 3, 6, 12, and 24 months after ablation and at 12-month intervals thereafter. Before the 6- and 12-month follow-up visits, patients underwent 14-day continuous mobile outpatient telemetry monitoring to evaluate for recurrence of symptomatic or asymptomatic atrial arrhythmias. In addition, additional event monitors were provided to any patient reporting symptoms suggesting recurrent arrhythmia. No patients were lost to follow-up. Because atrial arrhythmias that occur early after an ablation procedure may be transient, atrial arrhythmias that occurred within the first 3 months were excluded from the analysis as recommended by the HRS consensus guidelines. Repeat ablation was performed if the patient had recurrent symptomatic atrial arrhythmias after antiarrhythmic medications after the 90-day blanking period after their initial ablation.

Repeat Ablation in the Segmental PVI Group
In those presenting with recurrent paroxysmal AF, segmental PVI was repeated in a manner identical to that of the first procedure, but only in PVs that had reconnected. When repeat PVI was completed, isoproterenol was infused in a dose of 20 μg/min and if ectopic atrial beats arising from nonpulmonary vein foci were induced, these were also ablated. After left atrial ablation, the CTI was mapped to confirm persistence of bidirectional block. If conduction across the CTI had recurred, repeat ablation was performed until bidirectional block was achieved.

Repeat Ablation in the CPVA+LALA Group
In those presenting with recurrent paroxysmal AF, CPVA+LALA was repeated in a manner identical to that of the first procedure, with documentation of PVI, reduction of electrogram amplitude to <0.5 mV along the entire length of each line, and documentation of bidirectional MI block. In patients who had LAFI, a combination of 3D electroanatomic activation mapping and pacing entrainment was used to define a critical isthmus to be ablated in the reentrant circuit to eliminate all spontaneous or pacing induced macroreentrant atrial flutters. LAFI was diagnosed by demonstrating the majority of the tachycardia cycle length within the LA during 3D activation mapping and pacing entrainment identifying a critical isthmus with a pacing interval within 20 ms of the tachycardia cycle length. Catheter ablation of all spontaneous or pacing-induced LAFI was attempted until there was restoration of sinus rhythm, and LAFI could no longer be induced by rapid atrial pacing at pacing cycle lengths down to 2:1 atrial capture.

Statistical Analysis
All continuous variables are reported as mean±1 SD and were compared using the Student 𝑡 test. Categorical variables were compared by 𝛥2 or Fisher exact method, as appropriate. Survival curves and event rate were calculated according to the Kaplan–Meier method, and a log-rank test was performed to compare curves. A 2-tailed probability value <0.05 was considered to be statistically significant. Statistical analysis was performed using SAS software version 9.1 (SAS Inc).

Table. Clinical Characteristics of Patients

<table>
<thead>
<tr>
<th></th>
<th>PVI (n=33)</th>
<th>Linear (n=33)</th>
<th>𝑃  Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>23/10 (70/30)</td>
<td>25/8 (76/24)</td>
<td>0.58</td>
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<tr>
<td>Age, y</td>
<td>55.2±11.7</td>
<td>58.6±9.6</td>
<td>0.20</td>
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<tr>
<td>Hypertension</td>
<td>15 (45)</td>
<td>22 (67)</td>
<td>0.08</td>
</tr>
<tr>
<td>Duration of AF, y</td>
<td>5.2±5</td>
<td>6.0±5.7</td>
<td>0.54</td>
</tr>
<tr>
<td>Left atrial size, mm</td>
<td>3.6±0.3</td>
<td>3.7±0.4</td>
<td>0.47</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>61.8±5.8</td>
<td>61.1±4.3</td>
<td>0.60</td>
</tr>
<tr>
<td>Fluoroscopy time, min</td>
<td>73±21</td>
<td>91±21</td>
<td>0.04</td>
</tr>
<tr>
<td>β-blocker therapy</td>
<td>10 (30)</td>
<td>14 (42)</td>
<td>0.3</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>3 (9)</td>
<td>5 (15)</td>
<td>0.45</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>1 (3)</td>
<td>0</td>
<td>0.31</td>
</tr>
<tr>
<td>Antiarrhythmic (class I or class III)</td>
<td>32 (97)</td>
<td>33 (100)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages.

Results

Clinical Characteristics of the Patients Enrolled
The study population consisted of 66 patients with paroxysmal AF who were prospectively randomly assigned to undergo either segmental PVI (n=33) or CPVA+LALA (n=33), as described in the methods section above. The mean age was 58±11 years, mean duration of AF was 5.6±5.3 years, mean ejection fraction was 61±5% and mean left atrial size was 3.6±0.4 mm. Forty-eight patients were male, and 37 had a diagnosis of hypertension. The clinical characteristics of the patients were not significantly different between the 2 groups (Table).

Follow-Up
All patients were seen in the University of California, San Diego, outpatient arrhythmia clinic at 1, 3, 6, 12, and 24 months after ablation and at 12-month intervals thereafter. Before the 6-, 12-, and 24-month follow-up visits, all patients underwent 14-day continuous mobile outpatient telemetry monitoring to evaluate for recurrence of symptomatic or asymptomatic atrial arrhythmias. No patients were lost to follow-up. Twelve patients were followed up to 12 months, 44 patients were followed between 12 to 24 months, and 10 patients were followed more than 24 months. There was no significant difference between 2 groups in the length of the follow-up (𝑃=0.44).

Procedural Results
In the segmental PVI group, all PVs were isolated in all patients. In the CPVA+LALA group, PVI was achieved in all patients and bidirectional MI block was achieved in 30 of 33 patients (91%). In 97% (n=29) of patients in whom MI block was achieved, ablation was required within the coronary sinus to achieve bidirectional block. In 3 patients, bidirectional MI block could not be achieved.

Clinical Outcome After the Index Ablation
After a mean of 16.4±6.3 months, after 1 procedure, 19 (58%) patients in the segmental PVI group were free of atrial arrhythmias off all antiarrhythmic therapy, as compared with 17 (52%) patients in the CPVA+LALA group (𝑃=0.62).
After 1.3±0.5 ablation procedures in the segmental PVI group, 28 patients (85%) remained free of atrial arrhythmias at the end of the follow-up period, off all antiarrhythmic therapy. After 1.4±0.6 ablation procedures in the CPVA+LALA group, 28 patients (85%) remained free of atrial arrhythmias at the end of the follow-up period off all antiarrhythmic medications. There was no statistically significant difference in the efficacy of segmental PVI versus CPVA+LALA in preventing recurrent atrial arrhythmias overall.

**Patterns of Atrial Arrhythmia Recurrence During Follow-Up**

After 1 ablation procedure, there was recurrence of paroxysmal AF in 14 patients in the segmental PVI group versus 8 patients in the CPVA+LALA group (P=0.32 between groups for recurrence of paroxysmal AF). In the CPVA+LALA group, 2 patients had both recurrence of paroxysmal AF and development of LAFL and 6 patients had no recurrence of AF but developed LAFL (P=0.002 between groups for development of LAFL). The mean time to recurrence for AF or LAFL was similar (9.1±4.9 months versus 9.8±4.9 (P=0.18).

**Occurrences of Left Atrial Flutter During Follow-Up**

During 16.3±6.3 months of follow-up, LAFL only occurred in the CPVA+LALA group (Figure 4). Of 8 patients with LAFL, 2 were controlled with antiarrhythmic medication (one with amiodarone and the other with sotalol) and 6 underwent repeat ablation. In the 6 patients undergoing repeat ablation, 9 LAFLs were identified. Four were MI-dependent, 3 originated from the ridge between the LA appendage and left upper PV (ridge-dependent), and 2 originated from the LA roof (roof-dependent). All LAFLs were successfully ablated, with no inducible arrhythmia at the end of the ablation procedure. One patient had a second recurrence of LAFL and underwent a third ablation that was successful.

**Fluoroscopy Times and Mean Duration of Radiofrequency Application**

Fluoroscopy time was significantly shorter in the segmental PVI group versus the CPVA+LALA group (73 versus 91 minutes, P=0.04). The CPVA+LALA group had more radiofrequency applications and a longer mean duration of radiofrequency application time than the PVI group (91±24 versus 71±26 radiofrequency applications, 45±12 versus 35±13 minutes, P=0.002).

**Complications**

There were 3 complications, including a femoral hematoma in 1 patient that required no intervention, a femoral pseudoaneurysm in 1 patient that was treated medically and resolved, and a pericardial effusion with tamponade in 1 patient seen immediately after transseptal catheterization that required pericardiocentesis, which was successful. There were no cases of symptomatic PV stenosis, although no attempt was made to identify asymptomatic PV stenosis. There were no cases of stroke, phrenic nerve injury, or atrioesophageal fistula. During mitral isthmus ablation using an 8-mm tip catheter with temperature limited to 55°C and a maximum power of 50 W, no cases of CS perforation or left circumflex coronary artery injury were noted, although neither postablation stress testing or angiography was routinely performed. There was no significant difference in complications between the 2 groups.

**Discussion**

This randomized, prospective trial of catheter ablation of paroxysmal AF comparing segmental PVI versus CPVA+LALA at
the LA roof and MI showed that significantly more patients had LAFL in the CPVA+LALA group.

After segmental PVI, LAFL has been reported to occur rarely (in 1% to 2% of patients),6–8 and there were no cases of LAFL in the segmental PVI group in this study. In contrast, when PVI is achieved by CPVA+LALA, LAFL is relatively common, occurring in 10% to 30% of patients during follow-up.3,4,6 The majority of the arrhythmias that occur after CPVA+LALA are due to gaps in the prior ablation lines,4 and one way to potentially avoid these arrhythmias would be to limit the amount of linear ablation performed. Creating linear lesions during ablation may result in complex geometries that promote conduction block and facilitate reentry,4 and in this study, all of the iatrogenic LAFLs were macroreentrant. In patients with paroxysmal AF and structurally normal hearts, the LAFLs that may develop after extensive linear ablation may negate any benefit with regard to reduction in recurrence rates of AF.

The mitral isthmus line in particular has been implicated in the development of postablation atrial flutters,9 and in this study 4 of 9 LAFLs were MI dependent, despite achieving and documenting bidirectional MI block in 91% of patients. This observation has been noted in a recent retrospective analysis as well,9 where it has been shown that the incidence of perimital atrial flutter is higher in patients in whom MI ablation was performed during AF ablation, than in those who had not had MI ablation performed. These data suggest that MI ablation is a facilitating factor for the development of perimital flutter and if MI ablation can be avoided, it would be prudent to do so, especially in a patient population with paroxysmal AF and structurally normal hearts. In this study, 2 LAFLs were also noted to arise from a gap in the roof line, and 3 were found to have a critical isthmus involving the ridge between the LA appendage and the left upper pulmonary vein, which was ablated during circumferential ablation of the left pulmonary veins in the CPVA+LALA group. The anatomic and histological evaluation of the ridge between the orifices of the left upper PV and the LA appendage has revealed variable width and thickness.10,11 Like the MI, it is likely that the complex anatomy in this region, along with difficulty stabilizing the catheter along this ridge during radiofrequency catheter ablation, may explain why macroreentrant atrial tachycardias may arise from this region from gaps that arise after ablation, despite initial documentation of PVI.12

Our results differ from those published by Oral et al,13 who reported better success rates with CPVA+LALA at the MI and posterior LA as compared with segmental PVI. A major difference between our study and that published by Oral et al is that we observed a 24% incidence of LAFL when using a similar CPVA+LALA approach, which is significantly higher than the 2.5% incidence reported in that study. It is possible that the incidence of LAFL was underappreciated in the study by Oral et al because continuous cardiac monitoring was not routinely used during follow-up in that study, and the follow-up duration was significantly shorter (164±100 days). Other more recently published studies have reported a similar incidence of LAFL compared with that seen in this prospective study.3

Our findings are consistent with those described in another randomized study comparing these 2 approaches by Karch et al.6 They found no superiority of CPVA over segmental PVI and reported an 18% incidence of LAFL with the CPVA approach with additional linear ablation at the MI.

**Conclusions**

In patients with structurally normal hearts and symptomatic paroxysmal AF, CPVA+LALA is associated with a greater incidence of LAFL as compared with segmental PVI, sug-
gesting that linear ablation should be avoided as an initial approach to ablation in this population of patients.

Limitations

A limitation of this study is the small number of patients enrolled. However, after an interim analysis revealed a significantly greater risk of LAFL in the CPVA/LALA group, we did not think that it was ethically appropriate to continue to randomly assign patients to that arm of the study, especially in light of similar results previously published by Karch et al. Another limitation of this study is that although we did confirm block across the MI line, we did not routinely assess for conduction block across the LA roof line; however, only 2 of the LAFLs observed in this study were found to be due to a gap at the LA roof line. Because all patients in the CPVA+LALA group received linear ablation at the LA roof and MI, it is not clear what the incidence of LAFL would have been if CPVA was preformed alone, without additional linear ablation. Last, we used an 8-mm tip catheter in a temperature controlled manner and not an irrigated-tip catheter as is currently used in many other electrophysiology labs. However, it is not clear that an irrigated-tip catheter produces superior results to an 8-mm catheter or greater safety.14

Disclosures

None.

References


CLINICAL PERSPECTIVE

There has been growing concern that linear ablation is associated with an increased risk of iatrogenic arrhythmias in patients undergoing ablation for atrial fibrillation (AF). Therefore, we compared circumferential pulmonary vein ablation (CPVA) plus left atrial linear ablation (LALA), consisting of encircling lesions around the pulmonary veins, a roof line, and a mitral isthmus line with documentation of bidirectional mitral isthmus block, with segmental pulmonary vein isolation in patients with paroxysmal AF. Sixty-six patients were enrolled in this randomized prospective trial, which demonstrated that as an initial ablation approach, more atypical left atrial flutters occurred after CPVA + LALA compared with segmental pulmonary vein isolation (8 atypical left atrial flutters in the CPVA + LALA group versus 0 in the pulmonary vein isolation group). Overall, there was no significant difference with regard to freedom from all arrhythmias (AF and left atrial flutters) between the 2 groups. At 16.4±3.6 months after 1 ablation procedure, 19 patients (58%) remained free of atrial arrhythmias after pulmonary vein isolation versus 17 patients (51%) after circumferential pulmonary vein ablation plus left atrial linear ablation (P=0.62). The data suggest that additional linear ablation should not be performed as an initial ablation approach in patients with paroxysmal AF because there is no added benefit and an increased risk of iatrogenic arrhythmias.
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