A Combined Therapy Using Encircling Pulmonary Vein Isolation and Supplemental Segmental Ostial Isolation for the Treatment of Atrial Fibrillation


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Electrical isolation of the pulmonary veins (PV) has become a curative treatment for patients with atrial fibrillation (AF). Recently, there have been many reports that circumferential PV isolation (CPI) on the atrial side has a better outcome than segmental ostial PV isolation (SOPI). However, reports on the combination of CPI using electroanatomic mapping and SOPI using a circular mapping catheter have been few. The aim of the present study was to investigate the efficacy and safety of a combined therapy using CPI and supplemental SOPI for the treatment of AF. We performed CPI in 120 patients with drug-refractory AF. In 27 of those patients CPI resulted in a disconnection between the left atrium (LA) and PVs. In the remaining patients, supplemental SOPI completed the LA-PV disconnection. After an average follow-up period of 10.4 months, 81.7%, 90.5% and 71.4% of the patients with paroxysmal, persistent and chronic AF, respectively, have been free of AF. In 14.1% of the patients with paroxysmal AF, a greatly reduced frequency and/or duration of the episodes of AF were observed after the ablation. No fatal complications were encountered. The present results suggest that the combination of CPI and supplemental SOPI is efficient and safe for the treatment of AF.

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Key words: Catheter ablation, Electroanatomic mapping, Lasso catheter, Bepridil, Radiofrequency energy

Introduction

Electrical isolation of pulmonary veins (PVs) has become a curative treatment for patients with drug refractory atrial fibrillation (AF). Initially, isolation of the PVs was performed segmentally at the ostia of
the PVs using a circular mapping catheter.\textsuperscript{1–4)} However, subsequent reports showed that circumferential PV isolation (CPI) on the atrial side had a better outcome as compared with segmental ostial PV isolation (SOPI).\textsuperscript{5–8)} However, reports on the combination of encircling PV isolation using electoranoatomic mapping (CARTO Biosense) and segmental ostial PV isolation using a circular mapping catheter have been sparse.\textsuperscript{9–11)} The present study aimed to investigate the efficacy and safety of a combined therapy using encircling PV isolation and supplemental segmental ostial isolation for the treatment of AF. Although a randomized prospective study is required to determine which is the best of the three methods (CPI, SOPI or CPI + SOPI), the purpose of the present study was to examine the usefulness of supplemental SOPI after CPI.

**Methods**

**Study population**

One hundred and twenty consecutive patients with drug-refractory AF were included in the study. All patients signed an informed consent. “Persistent AF” and “chronic AF” were defined as having AF lasting for 2 weeks to 6 months and >6 months, respectively. The baseline characteristics of these patients are presented in Table 1. Segmental ostial PV isolation was previously performed in seven patients in whom AF recurred.

**Catheter positions**

Under the guidance of fluoroscopy a decapolar catheter (Daig Corp. Minnetonka, MN, USA; or Irvine Biomedical, Irvine, CA, USA) was inserted into the coronary sinus through the left subclavian vein. Access to the left atrial chamber was via a transseptal puncture guided by intra-cardiac echocardiography using a 9-MHz, 9 French intracardiac echography (ICE) catheter (Ultra ICE, Boston Scientific, San Jose, CA, USA) placed in the right atrium. Three sheaths (SL1 \( \times 2 \), Daig Corp. Minnetonka, MN, USA; and Soft Tip, Boston Scientific, San Jose, CA, USA) were introduced into the left atrium through the atrial septum via the right femoral vein (in most cases less than two of the three sheaths were positioned in the left atrium simultaneously). During left atrial mapping and ablation, heparin was administered to achieve a serum activated clotting time >250 seconds.

Two SL1 sheaths were advanced into the left (or right) superior and inferior pulmonary veins and selective pulmonary venography was obtained by injecting contrast medium simultaneously (Figure 1A). Then the 8.5-French Soft Tip sheath was introduced into the pulmonary veins, and through the sheath the 9-MHz ICE catheter was introduced into the pulmonary veins. By pulling back the ICE catheter the junction between the pulmonary vein and left atrium was recognized (Figure 2). Two circular mapping catheters (Lasso 20-pole 15–20 mm, Biosense-Webster, CA, USA) were introduced into the left- and right-sided superior and inferior pulmonary veins through the two SL1 sheaths with the ring electrodes positioned 5 mm inside from the LA-PV junction (Figure 1B). The electrograms from the ostia of the pulmonary veins were recorded with the Lasso catheters using an EP laboratory system (DUO, Bard, MA, USA). A Navistar catheter (F-curve, CARTO, Biosense-Webster, CA, USA) was used to construct a three-dimensional (3-D) shell of the LA including the mitral annulus and four PVs. Under fluoroscopic guidance, the PV ostium was tagged on the 3-D map of the LA (Figure 3A).

**Ablation**

Radiofrequency (RF) energy was delivered with a temperature-controlled, 4 mm-tip, deflectable catheter (Navistar, Biosense-Webster, CA, USA) with a target temperature of 55\degree C and maximum output of

<table>
<thead>
<tr>
<th>Table 1 Baseline characteristics.</th>
<th>N = 120</th>
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<tbody>
<tr>
<td>Male/female</td>
<td>96/24</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.8 ± 11.0</td>
</tr>
<tr>
<td>Type of AF</td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>71</td>
</tr>
<tr>
<td>Persistent</td>
<td>21</td>
</tr>
<tr>
<td>Chronic</td>
<td>28</td>
</tr>
<tr>
<td>Previous segmental PV ablation</td>
<td>7</td>
</tr>
<tr>
<td>Failed antiarrhythmic drugs</td>
<td>2.7 ± 1.1</td>
</tr>
<tr>
<td>Underlying heart disease</td>
<td></td>
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<tr>
<td>Lone AF</td>
<td>69</td>
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<tr>
<td>Hypertensive heart disease</td>
<td>15</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>7</td>
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<tr>
<td>Sick sinus syndrome</td>
<td>7</td>
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<tr>
<td>Chronic renal failure on regular hemodialysis</td>
<td>7</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>6</td>
</tr>
<tr>
<td>Oschemic heart disease</td>
<td>5</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
</tr>
<tr>
<td>Left atrial size (mm)</td>
<td>37.1 ± 8.2</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>60.0 ± 11.8</td>
</tr>
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LVEF: left ventricular ejection fraction
Figure 1  Selective pulmonary venography of the left PVs and right superior pulmonary vein (RSPV), and the position of the Lasso catheters in the pulmonary veins (right anterior oblique view 30°).
A, Selective pulmonary venogram (PVram). A left superior and inferior PVram was obtained by injecting contrast medium simultaneously via two SL-1 sheaths. A right inferior PVram was not performed because of the difficulty in inserting the SL-1 sheath. B, Position of the Lasso catheters in the pulmonary veins.

Figure 2  Intravascular echocardiogram of the pulmonary vein (RSPV). By pulling back the ICE catheter from inside the PV to the LA, the PV-LA junction was clearly recognized. A fluoroscopic view of the ICE position at the junction point was stored and served as a reference when the PV ostia were tagged on the 3-D map.
30 W. PV isolation was performed during pacing from the electrodes in the coronary sinus for the left-sided PVs and during sinus rhythm for the right-sided PVs. Since most patients complained of back pain during the RF delivery to the posterior wall of the LA, 7.5 mg of pentazocine was administered intravenously before the energy delivery. The ablation catheter was moved from one point to another to create linear encircling RF lesions around the left- and right-sided PVs \(< 2\) cm from the PV ostia (Figure 3B). For the anterior aspect of the left PVs, an encircling line was created along the PV-LA junction, which consisted of the prominent ridge between the PV and left atrial appendage. The RF energy was delivered for at least 20 seconds at each position. If high-frequency potentials were still recorded with the circular catheters in the PVs even after the completion of a circumferential line (the completion of the line was defined graphically on the CARTO map), segmental ostial ablation was added, guided by ostial PV potentials.

The endpoint of the procedure was the elimination of the PV potentials. PV disconnection was confirmed by the loss of atrial capture during pacing from the distal bipole of the ablation catheter advanced into the pulmonary veins.

In 69 patients conduction block at the cavo-tricuspid isthmus was also created by the application of RF energy using an 8 mm-tip ablation catheter (EPT-5770TN4, Boston Scientific, San Jose, CA, USA) through an 8F-sheath (RAMP, Daig Corp. Minnetonka, MN, USA) after the PV isolation. No difference in the type of AF or inducibility of atrial flutter after the PV isolation was observed between the groups with and without cavo-tricuspid isthmus ablation (CTIA).

At the end of the procedure, an intra-vascular echogram of the PVs was obtained to evaluate whether the ablation caused stenosis of the PVs.

**Adjunctive pharmacotherapy**

In 32 (45%), 15 (71%) and all patients with paroxysmal, persistent and chronic AF, respectively, the antiarrhythmic drugs prescribed before the ablation were continued after the ablation. After 3 to 6 months the drugs were discontinued if there were no recurrences of AF. The adjunctive antiarrhythmic drugs were as follows. Class I drugs in 28 patients (disopyramide 6, cibenzoline 3, aprindine 9 and pilsicainide 10), Class II in 12 (carvedilol 9, atenolol 2 and bisoprolol 1), Class III in 4 (amiodarone 4), and Class IV in 35 (bepridil 34, and verapamil 1).

**Follow-up**

Outpatient follow-up occurred every month for 12 months and every 6 months thereafter. All patients were administered warfarin to achieve an INR between 1.5 and 2.5, for at least a month after the ablation procedure. In the patients with paroxysmal AF, the determination of whether the outcome of the ablation was successful or not was determined by the symptoms and ECG recordings, including the ambulatory ECG. “Success” was defined as a patient
having no episodes of symptomatic AF, and “improvement” as the duration and/or frequency of the symptomatic AF episodes decreasing substantially as compared with that before the ablation. In the patients with persistent or chronic AF, maintenance of sinus rhythm was confirmed by recording the ECG. The mean follow-up period was 10.4 ± 6.0 months.

**Results**

**Ablation procedure**

In 27 out of 120 patients, completion of the encircling lesions resulted in the loss of the PV potentials in all the pulmonary veins. **Figure 4** shows that creating an encircling line around the left- and right-sided PVs was associated with a simultaneous disappearance of the PV potentials in the ipsilateral superior and inferior PVs, indicating PV disconnection. In the rest of the patients, however, the PV potentials persisted in the recordings from the Lasso catheters except that the proportion of males was larger in the combined therapy group (male/female, CPI: 17/10 vs. CPI + SOPI: 79/14).

**Figure 4** LA-PV disconnection by encircling pulmonary vein isolation.

A, The tracings are the surface leads II and V1, and the intracardiac electrograms recorded from a catheter inside the coronary sinus (Cs), ablation catheter (ABL) and 2 Lasso catheters positioned in the left superior pulmonary vein (LSPV) and left inferior pulmonary vein (LIPV) during pacing from the distal Cs electrode pair. Completion of an encircling line around the left-sided PVs resulted in the simultaneous disappearance of the PV potentials (white arrows) in the LSPV and LIPV (red arrow), indicating conduction block between the left atrium and PVs during pacing from the distal Cs electrode pair. B, Pacing from a Lasso catheter within the LSPV captured the spike-potentials (white arrows) recorded from the Lasso catheters in the LS- and LIPV but not the atrial electrograms (A) recorded from the Cs catheter. C, Pacing from the Lasso catheter within the LIPV captured the spike-potentials (white arrows) recorded from the Lasso catheters in the LS- and LIPV but not the atrial electrograms (A) recorded from the Cs catheter. D, The tracings are those of the surface leads II and V1, and intracardiac electrograms recorded from a catheter inside the Cs, ablation catheter (ABL) and 2 Lasso catheters positioned in the RSPV and RIPV during pacing from an electrode pair in the right atrium in the same patients shown in panels A–C. Completion of an encircling line around the right-sided PVs also eliminated the PV potentials (white arrows) in the RSPV and RIPV simultaneously (red arrow).
The total procedure and fluoroscopy times were 242 ± 72 and 121 ± 42 minutes, respectively.

Outcome
The outcome of the ablation was evaluated >1 month after the ablation. Since several patients had episodes of paroxysmal AF during the one month just after the ablation and no recurrence thereafter, recurrence of AF in that period was censored. The outcome of the ablation is shown in Table 2. In all, 81.7%, 90.5% and 71.4% of the patients with paroxysmal, persistent and chronic AF, respectively, were free of AF. Fourteen percent of the patients with paroxysmal AF had a greatly reduced frequency and/or duration of the episodes of AF as compared to those before the ablation (defined as “improvement”). There was no difference in the outcome between the groups with CPI only and those with CPI + SOPI (success/improvement/no improvement, CPI: 81.5/7.4/11.1 vs. CPI + SOPI: 80.6/8.6/10.8%) or between those with and without cavo-tricuspid isthmus ablation (success/improvement/no improvement, CTIA (+) 84.1/8.7/7.2 vs. CTIA (−) 76.5/7.8/15.7%).

Table 2 Outcome of combined ablation therapy for treating AF.

<table>
<thead>
<tr>
<th>Improvement</th>
<th>Success</th>
<th>No improvement</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>Paroxysmal</td>
<td>14.1% (8.5%)</td>
<td>(56.3%)</td>
<td>4.2% (0%)</td>
</tr>
<tr>
<td>Persistent</td>
<td>90.5%</td>
<td>2 (0)</td>
<td>21 (7)</td>
</tr>
<tr>
<td>Chronic</td>
<td>71.4%</td>
<td>8 (0)</td>
<td>28 (5)</td>
</tr>
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</table>

*: free of antiarrhythmic drugs
One patient in whom electrical cardioversion was performed 1 week after the ablation was included.
Twenty-two patients with persistent or chronic AF, in whom sinus rhythm was maintained after the ablation, were taking bepridil, and 4 of those patients were receiving aprindine in addition to the bepridil. One patient with chronic AF in whom AF recurred 1 week after the ablation procedure underwent electrical cardioversion and maintained sinus rhythm thereafter.

**Repeat ablation procedures**

A repeat ablation was performed in 3 patients. In 2 patients recovered connections between the LA and all four PVs were found. These PV potentials were delayed markedly and eliminated by segmental ostial ablation without any further recurrence of AF. In the other patient, a left atrial flutter was treated with linear ablation between the mitral annulus and right superior PV in a second session.

**Complications**

Five patients developed atrial tachycardia. In two patients, the impulse of the tachycardia propagated around the mitral valve. The tachycardia was treated successfully with a linear ablation between the mitral annulus and right superior PV in one patient in the second session and between the mitral annulus and a scar near the left superior PV in the other patient at the end of the first session. Two of the other three patients underwent electrical cardioversion. These three patients were prescribed an antiarrhythmic therapy for 3 months and the medications were discontinued thereafter without any recurrence of the atrial tachycardia. The difference was not statistically significant.

Two patients had cardiac tamponade during the ablation that needed pericardial drainage. No PV stenosis > 25% was observed.

**Discussion**

**Main findings**

In this study, the combination of extensive encircling isolation and segmental ostial isolation in patients with paroxysmal, persistent and chronic AF resulted in a comparable outcome to that of the previous reports where encircling PV isolation was performed to eliminate AF.\(^5\)\(^-\)\(^11\) Although there were several complications in the present study, no fatal complications, such as a perforation of the esophagus, were observed. These findings suggest that the combination of encircling PV isolation and supplemental segmental ostial ablation is efficient, feasible and safe for the treatment of patients with drug refractory AF.

**Segmental vs. circumferential PV isolation**

Many reports have shown that segmental ostial PV isolation is useful in curing paroxysmal AF.\(^1\)\(^-\)\(^4\) Recently, however, anatomical circumferential PV isolation has been shown to be more effective in preventing AF recurrence.\(^5\)\(^-\)\(^11\) Oral et al. directly compared the efficacy of segmental ostial isolation and circumferential isolation of the PVs.\(^6\) In their report the AF free survival rate was higher and the number of repeated sessions was smaller for the circumferential PV isolation as compared to the segmental ostial PV isolation. The advantage of the circumferential PV isolation over the segmental PV isolation was attributed to several effects: (1) elimination of the extra PV foci near the PV ostia, (2) abolition of anchor points for rotors or mother waves that drive AF, (3) reduction of the left atrial myocardium that provides the area available for circulating wavelets during AF, and (4) vagal denervation of the atria.\(^5\)\(^-\)\(^10\)

Most recurrences of AF after PV isolation are due to recovery of the conduction between the left atrium and pulmonary veins.\(^10\) Using basket catheters to record potentials at the PV ostia, Yamada et al. reported that reconnection of the LA and PV occurs at the edge of previously ablated segments in patients with AF recurrence after segmental ostial PV isolation.\(^12\) When the muscle strands connecting the LA and PV are burned segmentally, the edges of the ablated segments may become electrically inert giving the false presumption that permanent conduction block is achieved. After some period of hibernation the muscle fibers may recover to conduct impulses, thus triggering or perpetuating AF. Continuous circular PV isolation would preclude this “edge effect.” This may provide another explanation for the better outcome of circumferential PV isolation than segmental ostial isolation in preventing AF recurrence.

In the present study PV isolation was achieved in as much as 23% of the patients (27 out of 120 patients) with CPI only. Additional RF applications to the PV ostia (SOPI) were often required to complete the PV isolation. In the SOPI performed after CPI, the number of ablation sites was limited to one or two. During the CPI most of the atrial muscle strands connecting the left atrium and PVs would have been ablated. The residual PV potentials after the CPI indicated a gap in the circumferential line, suggesting that some connecting muscle strands were not ablated. SOPI would have dis-
ruptured this residual atrium-PV connection at a more ostial side.

**Adjunctive drug therapy**

Although the outcome of the present study was comparable to that of the previous reports where the PVs were isolated circumferentially, 66.7% and 82.1% of patients with persistent and chronic AF, respectively, were taking antiarrhythmic drugs. Fujiki et al. reported a high pharmacological conversion rate by bepridil, a unique Ca-antagonist that also blocks potassium channels and prolongs the action potentials of the heart muscle, in patients with persistent AF. They also reported that a combined therapy with aprindine and bepridil improved the success rate of the pharmacological cardioversion. In the present study 22 patients with persistent or chronic AF, in whom sinus rhythm was maintained after the ablation, were taking bepridil, and 4 of those patients were receiving aprindine in addition to the bepridil. Maintaining sinus rhythm in those patients may have benefited from those drugs. Nevertheless, considering that the patients in the present study were selected for ablation because of drug-resistant AF with a failure of pharmacological or repeated electrical cardioversions, the usefulness of the ablation therapy is worth mentioning.

**RF energy**

In most of the reports on encircling isolation, an 8 mm-tip catheter or irrigation catheter was utilized and the target energy was set at \( > 50 \text{ watts} \), \(^{5-10}\) because a greater energy was required to complete the continuous lesions on the atrial side around the PVs as compared to segmental ostial isolation. It was reported that even the deployment of an 8 mm-tip catheter and a high energy setting was often insufficient to create complete circumferential block lines around the PVs.\(^{11,14}\) Although the complication rate is acceptably low in the anatomical circumferential isolation of PVs, several devastating inadvertent consequences such as perforation of the esophagus have been reported.\(^{15,16}\) This may result from the higher energy settings needed to pursue complete isolation of the PVs. Pappone et al. suggested that lower power and temperature settings for the RF energy applications along the posterior wall may prevent further cases of fistula formations.\(^{16}\) Thus, complete isolation of the PVs and a lower target energy delivery for safety are creating a dilemma for circumferential PV isolation. In the present study the ablation energy was limited to \(< 30 \text{ W} \) and \(55 ^\circ \text{C} \), which are settings that may reduce the risk of an esophageal perforation. The lower target energy and use of a 4 mm-tip ablation catheter in the present study may account for the low success rate of the PV isolation (disappearance of the PV potentials) when the PV isolation was performed by an encircling procedure only on the atrial side.\(^{13}\) However, supplemental segmental applications of RF energy at the PV ostia eliminated the PV potentials achieving a good outcome in preventing the recurrence of AF. The combination of an encircling PV isolation with lower energy and temperature settings and supplemental segmental ostial isolation may provide a safe and efficient solution for the treatment of atrial fibrillation.

**Atrial tachycardia**

It has been reported that an organized left atrial tachycardia occurs as a proarrhythmic complication of extensive left atrial ablation after PV isolation.\(^{6,17-19}\) It was inferred that this was due to the formation of an isthmus delineated by block lines of conduction created by linear RF lesions.\(^{17-19}\) On the other hand, other reports have shown that most of the atrial tachycardias after PV isolation are focal tachycardias which originate from the reconnected segments of prior isolated PVs.\(^{10,20}\) In two patients in the present study, the atrial tachycardia observed after the ablation was a left atrial flutter which was treated by linear ablation in the left atrium. In the remaining three patients, no treatment was needed after the initial 3 months of follow-up. Recurrence of AF and irregular atrial tachycardias were not included in the post-ablation atrial tachycardias in the present study. The present results and other reports show that atrial tachycardia associated with circumferential PV isolation can be treated successfully with ablation therapy or resolves without treatment.

**Limitations**

The evaluation of the outcome of the ablation therapy in the present study depended mostly on the symptoms in the patients with paroxysmal AF. This may have resulted in an overestimation of the AF-free patients after the ablation in this group. However, considering that the patients with paroxysmal AF in the present study were highly symptomatic before the ablation, it seems reasonable to assume that the "symptom-free" patients could be regarded as surrogates for "AF-free patients" to some extent. The mean duration of the follow-up was ten months. Further studies will be needed to determine the long-term efficacy and safety of this combined therapy.
References


Tsuboi N

Combined therapy using encircling and segmental PV isolation

Circulation 2005; 111: 127–135