Segmental Pulmonary Vein Isolation for Paroxysmal Atrial Fibrillation Improves Quality of Life and Clinical Outcomes

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The purpose of this study was to clarify the change in the quality of life (QOL) and clinical outcomes following segmental pulmonary vein (PV) isolation for paroxysmal atrial fibrillation (AF) in 50 patients with drug-refractory, paroxysmal AF. The left superior, left inferior, and right superior PVs were targeted for isolation in all patients, and the right inferior PV was isolated in 4 patients. AF recurred in 22 of 50 patients, and these patients were treated with class I or class III antiarrhythmic drugs that had been ineffective before the ablation procedure. The symptom severity and frequency was scored and the QOL was assessed using the Short-Form-36 questionnaire (SF-36) before the PV isolation and at the end of the follow-up period (6.0±3.0 months). PV isolation resulted in a reduction in the symptom severity (p<0.001) and symptom frequency (p<0.001) scores as compared with the pre-ablation values. Ninety percent of the patients had a >90% reduction in the frequency of symptomatic episodes of AF after the ablation procedure. The mean SF-36 physical and mental component summary scores also significantly improved after PV isolation as compared with the pre-ablation values (both for p<0.001). With a segmental isolation approach that targets at least 3 PVs, satisfactory improvement in the symptoms and QOL can be achieved in patients with drug-refractory, paroxysmal AF.  

**Key Words:** Atrial fibrillation; Catheter ablation; Pulmonary vein; Quality of life

Segmental isolation of the pulmonary veins (PVs) can effectively eliminate atrial fibrillation (AF)1–4 and has become a widely used therapeutic method that is guided by the PV potentials recorded near the ostia of the PVs.1–3 However, little is known about the change in the quality of life (QOL) and clinical outcomes following the segmental PV isolation for paroxysmal AF, so the purpose of this study was to clarify them.

**Methods**

*Study Population*

The subjects in this study consisted of 50 patients with drug-refractory, paroxysmal AF who underwent segmental ostial ablation to isolate the PVs. There were 34 men and 16 women (mean age, 58±7 years). The mean duration of symptomatic AF was 6.5±6.8 years, and mean number of symptomatic episodes was 16±10 per month. A mean of 3.1±1.1 antiarrhythmic drugs had been ineffective in preventing recurrences of AF before the ablation procedure (Table 1). Three patients had coronary artery disease, 4 had valvular heart disease, 2 had primary cardiomyopathy, 2 had hypertensive heart disease, and the remaining 41 patients did not have any structural heart disease. In 12 patients, a linear ablation at the cavo-tricuspid isthmus was also performed for typical atrial flutter. Echocardiography demonstrated a mean left ventricular ejection fraction (LVEF) of 0.65±0.09 (range, 0.52–0.82), and mean left atrial diameter of 40±7 mm (range, 29–56 mm).

**Electrophysiology Study and Radiofrequency Catheter Ablation**

Segmental isolation of the PVs was performed as previously described.3,4 After informed consent was obtained, right femoral venous access was obtained and an octapolar electrode catheter was positioned in the coronary sinus. After transseptal catheterization, a 7Fr decapolar ring catheter with 1 mm inter-electrode spacing of paired electrodes at intervals of 4.5 or 6.0 mm (Lasso™, Biosense Webster, Inc, Diamond Bar, CA, USA) and a 7Fr quadripolar ablation catheter with a 4 mm distal electrode, embedded thermistor, 2–5–2 mm inter-electrode spacing, and a deflectable tip (Biosense Webster) were inserted into the left atrium.

In all cases, mapping and catheter ablation were performed during sinus rhythm or atrial pacing. Segmental isolation of the left superior, right superior and left inferior PVs was attempted in each of the 50 patients. Segmental isolation of the right inferior PVs was also attempted in 4 patients. Pulmonary venous angiograms were performed to identify the location of the ostia of the PVs. The Lasso™ catheter was positioned inside the PV, within 5 mm of the ostium. For optimal separation of the PV potentials from the atrial electrograms, mapping and ablation in the left superior and inferior PVs were performed during distal coronary sinus pacing at a cycle length of 600 ms. Target sites for ablation patients, a linear ablation at the cavo-tricuspid isthmus was also performed for typical atrial flutter. Echocardiography demonstrated a mean left ventricular ejection fraction (LVEF) of 0.65±0.09 (range, 0.52–0.82), and mean left atrial diameter of 40±7 mm (range, 29–56 mm).
were selected by identifying the PV potentials on high-speed recordings (150 mm/s) that had an equivalent or earlier activation relative to the adjacent Lasso™ catheter recording sites. The ablation catheter was always positioned in close proximity and on the ostial side of the Lasso™ catheter.

Radiofrequency ablation was performed using a maximum power of 30 W and a maximum electrode-tissue interface temperature of 52–55°C.3,4 The applications of energy were 60–90 s in duration. The end-point for ablation was the elimination of the PV potentials at all Lasso™ catheter recording sites. Therapy with antiarrhythmic drugs was discontinued at least 48 h before the procedure. Narrowing of the PVs was examined by computed tomography scanning 2–6 months after the ablation procedure.

Assessment of Symptom Frequency and Severity
Symptom severity and frequency were scored by a previously established questionnaire,6,7 which each patient was asked to complete before and after the PV isolation. Patients were asked if they had any episodes of their rhythm problem since their ablation. Symptom frequency was scored as: 1 = never; 2 = infrequent; 3 = sometimes; and 4 = very frequent.6,7 Symptom severity was scored as: 1 = none; 2 = mild; 3 = moderate; 4 = severe; and 5 = very severe.6,7 The questionnaire after the PV isolation was given at the end of the follow-up period.

Assessment of the Health-Related QOL (HRQOL)
Patients completed the Short Form-36 (SF-36), a 36-item self-administered questionnaire, before and after the PV isolation (6.0±3.0 months). It measured the multidimensional properties of the HRQOL on a scale ranging from 0 to 100, with lower scores representing a lower health state and evaluated their health favorably. This widely used questionnaire has been validated and is a reliable tool for measuring HRQOL.

Table 1 Antiarrhythmic Drugs Used Before and After Segmental Isolation of Pulmonary Veins

<table>
<thead>
<tr>
<th>Drug</th>
<th>Before PV isolation</th>
<th>After PV isolation</th>
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<tbody>
<tr>
<td></td>
<td>n (% use in 50 patients)</td>
<td>n (% use in 22 patients)</td>
</tr>
<tr>
<td>Aprindine</td>
<td>6 (12%)</td>
<td>0</td>
</tr>
<tr>
<td>Cibenzoline</td>
<td>23 (46%)</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>23 (46%)</td>
<td>3 (14%)</td>
</tr>
<tr>
<td>Flecainide</td>
<td>16 (32%)</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>Pilsicainide</td>
<td>19 (38%)</td>
<td>3 (14%)</td>
</tr>
<tr>
<td>Procanthidine</td>
<td>1 (2%)</td>
<td>0</td>
</tr>
<tr>
<td>Propafenone</td>
<td>11 (22%)</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>Pimelol</td>
<td>19 (38%)</td>
<td>5 (23%)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>9 (18%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Sotalol</td>
<td>2 (4%)</td>
<td>0</td>
</tr>
<tr>
<td>β-blocker</td>
<td>13 (26%)</td>
<td>0</td>
</tr>
<tr>
<td>Verapamil</td>
<td>11 (22%)</td>
<td>0</td>
</tr>
<tr>
<td>Digitalis</td>
<td>10 (20%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Fig. 1. Change in the symptom severity and symptom frequency scores before and after segmental pulmonary vein isolation.

Recurrence of AF After PV Isolation
By 6.0±3.0 months of follow-up, AF had recurred in 22 of the 50 patients (44%) with paroxysmal AF and in all those it recurred within 10 days of the procedure. These patients were treated with a class I or class III antiarrhythmic drug (Table 1). To avoid the effect of the use of new antiarrhythmic drugs on the QOL and the possibility of their side effects, an antiarrhythmic drug that had previously social functioning (SF), role-emotional (RE) and mental health (MH), and computed 2 component scales (physical (PCS) and mental (MCS)). The 8 health concepts were measured on a scale of 0–100. The concepts of PF, RP, BP, SF, and RE defined the health status as the absence of limitations or disabilities. The GH, VT, and MH were bipolar in nature and measured a wider range of negative and positive health states. For these scales, a score in the mid range was earned when patients reported no limitation or disability, and a score of 100 was earned only when patients reported a positive health state and evaluated their health favorably. This widely used questionnaire has been validated and is a reliable tool for measuring HRQOL.

Statistical Analysis
Continuous variables were expressed as mean±1 standard deviation and were compared using the Student’s t test or non-parametric sign test, as appropriate. A p-value <0.05 was considered statistically significant.

Results
 PV Isolation
Electrical isolation was achieved in 48 of the 50 left superior (96%), 48 of the 50 right superior (96%), 49 of the 50 left inferior (98%) and 4 of the 4 right inferior PVs in which isolation was attempted (100%). There were no significant differences in the efficacy of the isolation procedure among the 4 PVs. All of the targeted PVs were completely isolated in 46 of the 50 patients (92%).

Recurrence of AF After PV Isolation
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been given to the patient before the PV isolation was randomly chosen, and it was continued during the follow-up period. The remaining 28 patients were not given any antiarrhythmic drugs. No patients had persistent AF at the end of follow-up period.

**Symptom Severity and Frequency**

The mean symptom severity and frequency scores before and after PV isolation are shown in Fig. 1. There was a significant reduction in both the symptom severity and symptom frequency scores (both for p<0.001). Forty-five patients (90%) markedly improved with a ≥90% reduction in the frequency of symptomatic episodes of AF in the absence of antiarrhythmic drug therapy or during treatment with an antiarrhythmic drug that had been ineffective before the ablation procedure.

**HRQOL**

Before the PV isolation, the scores of all the concepts on the SF-36 were less than 50. However, the scores of all 8 concepts increased after the PV isolation, and 7 concepts (RP, BP, GH, VT, SF, RE, and MH) significantly improved after the PV isolation as compared with those before (Figs. 2, 3). Both the PCS score and MCS score were also significantly higher after the PV isolation than before (both for p<0.001; Fig. 4).

The subgroup analysis of the patients treated with or without antiarrhythmic drugs after the PV isolation is shown in Table 2. In both groups, the scores of all 8 concepts and the 2 component scales increased after the PV isolation. However, there was no significant difference in any of the scores before or after the PV isolation between the 2 groups. Further, no significant difference in the change in each score before and after PV isolation was observed between the 2 groups.

**Complications**

No potential complications occurred during the isolation procedure or during the follow-up period. In 13 patients, 25–50% narrowing of the left superior, right superior, or left inferior PVs was detected by a computed tomography scan at 2–6 months after the ablation procedure. These patients were all asymptomatic.

**Discussion**

**Major Findings**

The results of this study demonstrate that segmental ostial ablation to isolate the PVs resulted in a significant reduction in the symptom frequency and symptom severity and an improvement in the QOL of patients with drug-refractory paroxysmal AF. Although the incidence of the recurrence of AF was relatively high, antiarrhythmic drugs were effective in reducing the symptom frequency and severity.

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**Table 2** Effect of Antiarrhythmic Drug Use on the SF-36 Scales Before and After Segmental Isolation of the Pulmonary Veins

<table>
<thead>
<tr>
<th></th>
<th>Physical component</th>
<th></th>
<th>Mental component</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>PF</td>
<td>RP</td>
<td>BP</td>
<td>GH</td>
</tr>
<tr>
<td>No antiarrhythmic drugs after PV isolation (n=28)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>47±13</td>
<td>42±14</td>
<td>48±11</td>
<td>44±9</td>
</tr>
<tr>
<td>After</td>
<td>50±10</td>
<td>49±10</td>
<td>53±8</td>
<td>48±10*</td>
</tr>
<tr>
<td>Δ</td>
<td>3±17</td>
<td>7±16</td>
<td>5±12</td>
<td>5±11</td>
</tr>
<tr>
<td>Antiarrhythmic drugs after PV isolation (n=22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>45±17</td>
<td>38±15</td>
<td>47±10</td>
<td>39±10</td>
</tr>
<tr>
<td>After</td>
<td>49±11</td>
<td>45±13</td>
<td>50±9</td>
<td>44±9*</td>
</tr>
<tr>
<td>Δ</td>
<td>4±11</td>
<td>6±15</td>
<td>3±8</td>
<td>5±8</td>
</tr>
</tbody>
</table>

Values are mean±SD. Twenty-two patients with recurrence of atrial fibrillation after the pulmonary vein (PV) isolation were treated with an antiarrhythmic drug. Δ, the change in the score between that obtained before and after the PV isolation. *p<0.05 vs before PV isolation. BP, bodily pain; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical functioning; RE, role-emotional; RP, role-physical; SF, social functioning; VT, vitality.
symptom severity in most of those cases. More than a 90% reduction in the frequency of symptomatic episodes of AF during treatment with antiarrhythmic drugs that had been ineffective before the ablation procedure was observed in 17 of 22 patients (78%).

Each score for the concepts on the SF-36 before the PV isolation was less than 50, indicating that symptomatic and frequent attacks of AF can cause a worsening of the HRQOL in patients with drug-refractory paroxysmal AF. However, all of those improved up to a score of around or above 50 after the PV isolation, indicating that the elimination or reduction in the AF attacks, with or without antiarrhythmic drugs, following the ablation procedure can improve the HRQOL in most patients with paroxysmal AF.

Impact of Segmental PV Isolation on the Patient’s Symptoms and QOL

Segmental isolation of PVs is performed in widespread in patients with AF1–4 and has been considered more effective for paroxysmal AF than for persistent (>1) month) or chronic AF.\textsuperscript{3} Recently, Oral et al demonstrated that 83% of patients with paroxysmal AF were either free of symptomatic AF or had significant improvement with a segmental isolation approach that targeted at least 3 PVs.\textsuperscript{3} Significant improvement of the symptom frequency and severity was also obtained after the ablation procedure, and no potential complications occurred during the procedure or follow-up period in the present study. Furthermore, the HRQOL assessed by the SF-36, which is a widely used generic assessment tool,\textsuperscript{8–14} significantly improved after the ablation procedure. Therefore, this treatment is an effective and acceptable strategy for treating paroxysmal AF.

Efficacy of Antiarrhythmic Drugs After PV Isolation

We found that antiarrhythmic drugs were effective in most patients in whom AF recurred after the ablation procedure, and the frequency of symptomatic AF episodes was reduced by up to 10% in 18 (81%) of those subjects. Other studies have also demonstrated that treatment with antiarrhythmic drugs that had been ineffective before the ablation procedure became effective in most patients after the ablation procedure.\textsuperscript{3,15,16} A recurrence of AF after PV isolation may be caused either by failure to have permanently isolated the PV, or by the presence of critical foci outside of the PVs. In the present study we did not perform a second procedure in the patients with recurrence of AF, and therefore we could not identify the mechanism of the recurrent AF. However, judging from the effect of the drugs after ablation procedure, recovery of conduction through inadequately ablated muscle fascicles in the muscle sleeves surrounding the PVs may be the most common reason, and antiarrhythmic drugs might have an effect on the conduction through the surviving muscle fascicles.

Another possible cause of the recurrent AF is that new foci triggering AF may appear after the PV isolation. A recent study demonstrated that AF was initiated by ectopic beats from non-PV areas in 68 (28%) of 240 patients with paroxysmal AF.\textsuperscript{17} Haissaguerre et al reported that a total of 30 new ectopic beats originated from previously untargeted PVs, PV ostia proximal to the previous ablation site, or atrial tissue found during repeat ablation procedures in 29 patients with recurrent AF.\textsuperscript{1} Therefore, the antiarrhythmic drugs might have had an effect on the genesis of the new foci in the patients with recurrent AF in this study.

Previous Studies

As mentioned, several studies have reported the effectiveness of segmental PV ablation for AF, based mainly on the results of symptom improvement after PV isolation.\textsuperscript{1} However, no prior studies have examined the change in the HRQOL before and after this treatment.

Several recent studies have reported the QOL of patients with AF\textsuperscript{4,18,19} but the present results may be difficult to compare with those studies, which used other therapies for drug-resistant AF, such as implantable cardioverter defibrillators.\textsuperscript{19} because of the use of different QOL instruments and the lack of a comparison with the general population. One study reported the effect of the Maze operation on the QOL in patients with drug-refractory AF;\textsuperscript{18} the majority of whom (80%) had lone AF and 63% had paroxysmal AF. In that study of Swedish patients, the QOL of the patients with AF was significantly lower than that of the general Swedish population, but it significantly improved at 6 months after the Maze operation, and the QOL measurements obtained at both 6 months and 1 year after operation reached the levels of the general population. Those results are similar to the present study and the data may indicate that the QOL of patients with AF is lower than that of the general population, even if the AF was paroxysmal or the patient does not have structural heart disease, and that, in most patients with drug-resistant paroxysmal AF, curative therapy for AF may improve the QOL to the levels of the age-matched general population.

Study Limitations

Our sample size was relatively small, which might obscure the effectiveness of segmental PV isolation. However, significant differences in the symptom severity and frequency and HRQOL were drawn before and after the PV isolation, which implies that our findings are somewhat robust.

The second limitation is that the clinical efficacy of PV isolation was based on the symptoms reported by the patients. Ambulatory Holter monitoring was not routinely performed in patients who reported having no symptoms during the follow-up. Therefore, asymptomatic episodes of AF might have been missed. However, because all of the patients in this study had symptomatic AF before the ablation, the absence of symptomatic AF after the ablation procedure was considered an acceptable clinical endpoint.

Third, the majority of the patients in this study did not have severe underlying structural heart disease. Therefore, the findings of this study may not apply to patients with chronic AF or markedly dilated atria.

Finally, the follow-up period after the ablation procedure was relatively short, and future studies may be needed to clarify the long-term effect of this treatment on the patient symptoms and QOL.

Conclusions

With a segmental isolation approach that targets at least 3 PVs, a satisfactory improvement in the symptoms and QOL can be achieved in patients with drug-refractory paroxysmal AF.

Acknowledgments

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References


