Impact of Atrial Fibrillation Termination Site and Termination Mode in Catheter Ablation on Arrhythmia Recurrence

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Background: Although atrial fibrillation (AF) termination has been reported as a predictor of clinical outcome after persistent AF (PsAF) ablation, the relationship between AF termination site and mode and clinical outcome has not been fully evaluated.

Methods and Results: A total of 135 patients (62±9 years) underwent their first ablation procedure for PsAF (76 longstanding PsAF). With an endpoint of AF termination, the ablation procedure was performed sequentially in the following order: pulmonary vein (PV) antrum isolation, and left atrial and right atrial substrate modification. AF termination was achieved in 69 patients (51%; 24 at the PV antrum, and 45 in the atrium; direct conversion to sinus rhythm in 21, and atrial tachycardia [AT] in 48). With a mean of 1.7±0.7 procedures/patient, 100 patients (74%) were free from atrial tachyarrhythmia (ATa) during a median of 15.0 months of follow-up. During the initial procedure, the AF termination site (atrium vs. PV antrum, hazard ratio [HR], 1.38; 95% confidence interval [CI]: 0.72–3.77; no termination vs. PV antrum, HR, 2.32; 95% CI: 1.26–6.30; P=0.023) and mode (AT vs. sinus rhythm, HR, 1.47; 95% CI: 0.77–4.01; no termination vs. sinus rhythm, HR, 2.38; 95% CI: 1.26–6.46; P=0.017) were independent predictors of ATa recurrence after the last ablation procedure.

Conclusions: The site and mode of AF termination during the index ablation procedure predict ATa recurrence following multiple catheter ablation procedures for PsAF. (Circ J 2014; 78: 78–84)

Key Words: Atrial fibrillation; Catheter ablation; Persistent atrial fibrillation

Catheter ablation is an established therapy for drug-resistant atrial fibrillation (AF), and pulmonary vein antrum isolation (PVAI) has become a widely accepted strategy. Although the ablation strategy for persistent AF (PsAF) and procedural endpoint remain controversial, several reports have shown that AF termination during the procedure leads to a better clinical outcome. The relationship between AF termination site/mode and clinical outcome, however, has not been fully evaluated. The aim of this study was to investigate the clinical impact of AF termination site and termination mode during PsAF ablation on clinical outcome.
the evaluation of the relevant cardiac anatomy before the procedure.

Surface electrocardiogram (ECG) and bipolar intracardiac electrograms were continuously monitored and stored on a computer-based digital recording system (LabSystem PRO; Bard Electrophysiology, Lowell, MA, USA). Bipolar electrograms were filtered from 30 to 500 Hz. A 7-Fr 20-pole or 14-pole 1-site mapping catheter (Irvine Biomedical, Irvin, CA, USA) was inserted through the right jugular vein and positioned in the coronary sinus for pacing, recording and internal cardioversion. The electrophysiological study was performed under mild sedation with pentazocine and hydroxyzine pamoate.

**Catheter Ablation Protocol**

The details of the ablation protocol have been reported previously. After 1 transseptal puncture, 1 long sheath (SL0; AF Division, St. Jude Medical, Minneapolis, MN, USA) was introduced into both superior PV. Pulmonary venography during ventricular pacing and contrast esophagography were done to obtain the relative locations of the PV ostia vis-a-vis the esophagus. A 100-μg/kg body weight of heparin was given following the transseptal puncture, and heparinized saline was additionally infused to maintain the activated clotting time at 300–350 s. Two decapolar circular mapping catheters (Lasso; Biosense Webster, Diamond Bar, CA, USA) were placed in the superior and inferior PV, and the left- and right-sided ipsilateral PV were circumferentially ablated under the guidance of a 3-D mapping system (CARTO3; Biosense Webster). Posteriorly, ablation was performed anatomically in the LA, approximately 1–3 cm from the PV ostia. Anteriorly, ablation was performed on the edge of the left PV guided by early PV potentials. The electrophysiological endpoint of the PVAI was the achievement of bidirectional conduction block between the LA and PV, and the anatomic endpoint was the creation of a complete continuous circumferential lesion around the ipsilateral veins. Radiofrequency (RF) current was delivered point-by-point for 30 s with a 3.5-mm externally irrigated-tip quadrupolar ablation catheter (Thermocool; Biosense Webster) with a power of up to 35 W, target temperature ≤38°C and irrigation rate of 30 ml/min. The power was limited to 20 W on the posterior wall close to the esophagus. The substrate modification, when AF persisted after the PVAI, was performed sequentially using a linear defragmentation approach in both atria. The endpoint of the substrate ablation was the termination of AF and restoration of sinus rhythm by ablation. If AF continued after this step, the patients underwent internal electrical cardioversion. No anti-arrhythmic drugs were given during the procedure. Termination of AF was defined as conversion of AF to sinus rhythm directly or via 1 or more intermediate atrial tachycardias (AT). If AF was converted to an AT, it was mapped and ablated using 3-D activation and entrainment mapping. After restoration of sinus rhythm, a cavotricuspid isthmus line was created with an endpoint of bidirectional conduction block in all patients.

**Repeat Procedure**

In patients with recurrence of atrial tachyarrhythmia (ATa), the PVAI was evaluated first. In the presence of conduction recovery, re-isolation of the PV was performed. In patients in whom the baseline rhythm was sinus rhythm, the previous lesion set was evaluated and completed. Then, AT was induced by programmed stimulation if the type of recurrence was AT. Induction testing was not performed if the type of recurrence was AF. Patients in whom the baseline rhythm was PsAF underwent repeat stepwise ablation with the same strategy as in the initial procedure. If stable AT was present, its mechanism was deduced using 3-D activation and entrainment mapping.

**Follow-up**

Patients underwent continuous ECG monitoring as inpatients for 3 days following the procedure. The first outpatient clinic visit was 3 weeks after the ablation procedure. The follow-up visits consisted of a clinical interview, ECG, and 24-h Holter monitoring every 3 months at the cardiology clinic. Anti-arrhythmic drugs were prescribed during the first 3 months for a blanking period. If any symptoms suggestive of an arrhythmia occurred between the scheduled visits, the patients were asked to come to the emergency department, and a 12-lead ECG or 24-h Holter monitoring, and/or 1-month-event recording were performed in order to define the cause of the symptoms. For the detection of any asymptomatic events, we used an external loop recorder (Spider Flash, Sorin, France), which enabled the automatic detection of ATs for 14 consecutive days. Recurrent AF was defined according to the patient’s symptoms, and/or if an episode of AF lasting >30 s was documented on ECG. Repeat procedure was strongly recommended for the patients with documented recurrent ATa.

**Statistical Analysis**

Continuous data are expressed as mean ± SD for normally distributed variables or as the median (interquartile range [IQR]; 25th–75th percentiles) for non-normally distributed variables, and were compared using Student’s t-test or Mann-Whitney U-test, respectively. Multivariate Cox method was used to determine the predictors of recurrent ATa. Variables with P<0.05 on univariate analysis were included in the multivariate Cox regression model. Categorical variables were compared using the chi-squared test. P<0.05 indicated statistical significance. Kaplan-Meier analysis was used to determine the percentage of patients free from ATa. The difference in ATa-free survival was evaluated using log-rank test. The following patient and procedural variables were evaluated in association with arrhythmia freedom after the last ablation procedure: age, sex,
Figure 1. Distribution of atrial fibrillation termination site in the initial and second procedures. AW, anterior wall; CS, coronary sinus; CT, crista terminalis; FO, fossa ovalis; IVC, inferior vena cava; LA, left atrium; LAA, left atrial appendage; LA, left atrial anterior wall; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; MA, mitral annulus; PW, posterior wall; RAA, right atrial appendage; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; SVC, superior vena cava.

Figure 2. Mechanisms of the mappable atrial tachycardia (AT) in the initial and second procedures. CTI, cavotricuspid isthmus-dependent AT; LA, roof, left atrium roof-dependent AT; localized/focal, localized AT/focal AT; macro, macroreentrant AT; MI, mitral isthmus-dependent AT. All other acronyms as in Figure 1.
AF Termination Site/Mode and Arrhythmia Recurrence

Conduction was found in 60 patients (76%); conduction gaps were located along the right-sided PV lesions in 43 patients and the left-sided PV lesions in 44 patients. Among the 23 patients in whom the baseline rhythm was AF, AF converted to AT during the RF applications at the PV antrum and atrium in 2 (9%) and 7 (30%), respectively (Figure 1). Direct conversion to sinus rhythm was not observed in any patients, and the remaining 14 (61%) required electrical cardioversion to restore sinus rhythm after a sequential substrate modification. The correlation between the results of the initial ablation procedure and the baseline rhythm in the second procedure is shown in Table 2. Termination mode correlated with baseline rhythm in the second procedure. AF was terminated again during PVAI in 2 patients in whom AF was terminated during the PVAI in the initial procedure. Among the patients in whom sinus rhythm was directly restored in the initial procedure, only 1 had AT (localized AT in the LA appendage). The mechanism of the mappable AT is shown in Figure 2. In 12 patients (9%), a third procedure was performed at a median of 12 months after the initial procedure. Recovered PV conduction was found in 2 patients. In 2 (2%), a fourth procedure was performed at a median of 22.5 months after the initial procedure. No recovered PV conduction was found. At a median follow-up of 15 months (IQR, 11–19 months) and after a mean of 1.7 ± 0.7 procedures per patient, 100 patients (74%; including 15% receiving an anti-arrhythmic drug) were free from ATa.

Results

Ablation Procedure and Clinical Outcome

PVAI with bidirectional conduction block of the cavitricuspid isthmus was successfully achieved in all patients. In 69 of 135 patients (51%), AF was terminated by catheter ablation alone, while cardioversion was required in the remaining 66 patients. Overall, AF was terminated at the PV antrum in 24 (35%) and in the atrium in 45 patients (LA, n=35; right atrium [RA], n=10; 65%; Figure 1). AF converted to AT in 48 patients (70%), and to sinus rhythm in 21 (30%). Among 24 patients with AF termination during the PVAI, AF converted to AT and sinus rhythm directly in 12 patients each. A total of 39 AT were mappable (Figure 2).

In 79 patients (59%), a second procedure was performed at a median of 4 months (IQR, 3–7 months) after the initial procedure. The baseline rhythm was AF, AT or sinus rhythm in 23 (29%), 21 (27%) and 35 (44%), respectively. Recovered PV

<table>
<thead>
<tr>
<th>Baseline rhythm in the second procedure</th>
<th>AF</th>
<th>AT</th>
<th>Sinus rhythm</th>
</tr>
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<tbody>
<tr>
<td>Termination at the PV antrum</td>
<td>2</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Termination at the atrium</td>
<td>1</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td>Conversion to sinus rhythm</td>
<td>0</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Conversion to AT</td>
<td>3</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>No AF termination</td>
<td>20</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

AT, atrial tachycardia; PV, pulmonary vein. Other abbreviation as in Table 1.

Figure 3. (A) Significant difference in number of patients free of atrial tachyarrhythmia (ATa; log-rank test, P=0.013) after the last ablation procedure with regard to atrial fibrillation (AF) termination site (Kaplan-Meier analysis). (B) Significant difference in number of patients free of ATa (log-rank test, P=0.018) after the last ablation procedure with regard to AF termination mode (Kaplan-Meier analysis). AT, atrial tachycardia.
Termination Site and ATa Recurrence

After the last procedure was significantly lower in patients in whom AF terminated during PV antrum ablation vs. during an atrial substrate modification (Figure 3A; log-rank, P=0.04), but this difference was not observed after the index procedure. Also, there was no significant difference in ATa recurrence after the last procedure between the patients with AF termination during LA vs. RA ablation (log-rank, P=0.43).

On multivariate Cox regression analysis, AF termination site in the initial procedure (atrium vs. PV antrum: hazard ratio [HR], 1.38; 95% confidence interval [CI]: 0.72–3.77; no termination vs. PV antrum: HR, 2.32; 95% CI: 1.26–6.30; P=0.023) was a significant predictor of ATa recurrence. No other clinical or echocardiographic parameters were significant predictors of ATa recurrence.

On Kaplan-Meier analysis, the estimated probability of arrhythmia-free survival at 1 year and 2 years of follow-up after the last procedure was 75.9% and 64.3%, respectively.

In total, 228 procedures (median, 2; IQR, 1–2) were performed in 135 patients. In the present study there were 11 major complications (5%). Cardiac tamponade and pericarditis were observed in 3 patients and in 1 patient, respectively. The tamponade was managed successfully by percutaneous pericardiocentesis. Three patients experienced transient gastric hypomotility. Three patients developed transient right phrenic paresis. One patient experienced congestive heart failure requiring a prolongation of hospitalization.

### Table 3. Predictors of ATa Recurrence After Last Ablation Procedure

<table>
<thead>
<tr>
<th></th>
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<th>Multivariate</th>
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<tr>
<td></td>
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<td>P-value</td>
<td>95% CI</td>
<td>HR</td>
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<tr>
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<td>0.96–1.03</td>
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<td>0.87</td>
<td>0.59–1.50</td>
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<td>Structural heart disease (0)</td>
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<td>0.99</td>
<td>0.60–2.03</td>
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<tr>
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<td>0.82</td>
<td>0.15</td>
<td>0.62–1.07</td>
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</tbody>
</table>

ATa, atrial tachyarrhythmia; CI, confidence interval; HR, hazard ratio; PsAF, persistent AF. Other abbreviations as in Tables 1,2.

### Figure 4. During the second ablation procedure, pulmonary vein (PV) reconnection was significantly more prevalent for patients in whom atrial fibrillation terminated around the PV antrum than elsewhere or nowhere in the atrium in the initial procedure (100% vs. 70% vs. 70%; P=0.01).
an independent predictor of ATa recurrence after the last ablation procedure (Table 3).

During the second ablation procedure, PV reconnections occurred significantly more often in patients in whom AF terminated around the PV antrum than elsewhere or nowhere in the atrium at initial procedure (100% vs. 70% vs. 70%, P=0.01; Figure 4).

Termination Mode and ATa Recurrence

The patients with direct restoration of sinus rhythm from AF in the initial procedure had a significantly lower ATa recurrence rate after the last procedure than those in whom AF converted to AT (Figure 3B). The difference, however, was not significant when comparison was done at the initial procedure. On multivariate Cox regression analysis, mode of AF termination in the initial procedure (AT vs. sinus rhythm: HR, 1.47; 95% CI: 0.77–4.01; no termination vs. sinus rhythm: HR, 2.38; 95% CI: 1.26–6.46; P=0.017) was an independent predictor of ATa recurrence after the last ablation procedure (Table 3). There was a significant difference in the rate of direct conversion to sinus rhythm between the patients with different termination sites (PV antrum vs. atrium, P=0.01).

Discussion

This study analyzed the impact of AF termination site and mode on arrhythmia recurrence after catheter ablation of PsAF. First, it was found that AF termination site was an independent predictor of arrhythmia recurrence after multiple AF ablation procedures. AF termination during PV antrum ablation in the initial procedure predicted a better clinical outcome. Second, AF termination mode was an independent predictor of clinical outcome after multiple AF ablation procedures. Direct conversion to sinus rhythm during the initial AF ablation procedure predicted a better clinical outcome.

AF Termination During Catheter Ablation

PsAF is a complex arrhythmia and several catheter ablation strategies have been proposed.7–13,16,23–25 PVAI is the first step and substrate modification the second in the vast majority of strategies. Regardless of the different ablation strategies, it has been reported that AF termination results in better clinical outcome in patients with PsAF, which was also observed in the present study. This is reasonable because termination of AF can be interpreted as complete suppression of all AF-initiating and -perpetuating mechanisms active at the time of the ablation procedure. Whether the AF termination site and termination mode affect arrhythmia recurrence, however, has not been fully evaluated.

AF Termination Site and ATa Recurrence

The present study showed that AF termination during PV antral ablation was associated with a better clinical outcome than termination during atrial substrate modification after multiple procedures but not after the initial procedure. Interestingly, all patients who underwent a second procedure among those with AF termination during PVAI had PV reconnections, which was a significantly higher prevalence than in the other patients. Moreover, a reconnection of both sides of the PV was more frequently observed in patients with AF termination during PVAI. These results suggest that reconnection of the PV is strongly associated with the mechanism of recurrence in these patients, and highlights the importance of durable PVAI for the cure of AF.

AF Termination Mode and ATa Recurrence

The present study showed that direct restoration of sinus rhythm was more commonly observed during PVAI than during atrial substrate modification, which suggests that the AF substrate is more complex in the latter patient group. Clinical outcome is better in the patients with direct restoration of sinus rhythm than in those with AF conversion into AT, but the result was similar after the initial procedure because of the high rate of early recurrence in the former group.

A potential mechanism of AF conversion into AT, other than being iatrogenic because of RF-induced slow conduction or incomplete/recovered lesions,26 may be the organization of AF by a diminution of the substrate necessary for and capable of fibrillatory conduction. Also, these organized arrhythmic sources may underlie and drive AF.

AF Termination and ATa Recurrence

Prior studies have shown that AF termination and the duration of AF are predictors of ATa recurrence after PsAF ablation. In this study, both AF duration and AF termination were significant univariate predictors, but AF duration was not a significant predictor on multivariate analysis. In contrast, both the AF termination site and termination mode had a significant impact on arrhythmia recurrence. Presumably they correlate with the amount of substrate better than the other clinical parameters.

In this study, AF terminated most commonly during PV antral ablation. Although prior reports have shown that the success rate after PV isolation is limited, this study found that the PV antrum was an important substrate for the perpetuation of PsAF. Creating durable PVAI lesions is, therefore, important for improving clinical outcome.

Study Limitations

The patients’ own willingness to undergo repeat procedure may have influenced the clinical outcome after the last ablation procedure, but all prior published papers have the same limitation. It is difficult to determine the precise duration of incessant AF. The clinical symptoms and intermittent electrogram recordings are not completely reliable in the majority of PsAF, especially in the vast majority of longstanding PsAF. It is possible that different waiting times resulted in the different PV reconnection rates in the second procedure in each group. Finally, the mechanism of recurrent ATAs was not always clarified at the repeat procedure because the ablation strategy depended on the baseline rhythm and it was sinus rhythm in the majority of patients.

Conclusions

The site and mode of AF termination during the index ablation procedure predict ATa recurrence following multiple catheter ablation procedures for PsAF.

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Disclosures

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References


