Arrhythmia Type After Persistent Atrial Fibrillation
Ablation Predicts Success of the Repeat Procedure

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Background—The aim of the study was to investigate whether the type of arrhythmia recurrence after ablation of persistent atrial fibrillation (AF) has an impact on the maintenance of sinus rhythm after the repeat ablation procedure.

Methods and Results—Included were 78 consecutive patients (82% men; mean age, 61 ± 10 years; mean left atrial diameter, 47 ± 4 mm) with persistent AF who underwent ≥1 repeat ablation. The initial ablation procedure had consisted of pulmonary vein isolation with additional substrate modification (ablation of complex fractionated atrial electrograms [n = 63] or linear lesions [n = 15]). Patients presented for reablation either with persistent atrial tachycardia (AT) (group 1, n = 36), persistent AF (group 2, n = 37), or paroxysmal AF (group 3, n = 5). The primary end point was freedom from any arrhythmia off antiarrhythmic drugs 6 and 9 months after the reablation procedure. Estimated proportions of patients reaching the primary end point were 59% for group 1, 28% for group 2, and 100% for group 3 at 6 months and 51%, 23%, and 100%, for groups 1, 2, and 3, respectively, at 9 months (P = 0.002).

Conclusions—In patients presenting for a repeat procedure after ablation of persistent AF, the occurrence of AT is associated with a significantly better outcome compared with recurrent persistent AF. These results suggest that AT might be considered as a step toward sinus rhythm. (Circ Arrhythm Electrophysiol. 2011;4:609-614.)

Key Words: atrial fibrillation ■ atrial ectopic tachycardia ■ catheter ablation

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Although there is consensus that pulmonary vein isolation (PVI) targeting the arrhythmia trigger is the basic step in paroxysmal and persistent AF ablation, different additional ablation strategies have been used to achieve substrate modification in persistent AF. The 2 main approaches are linear lesions (LL) or ablation of complex fractionated atrial electrograms (CFAE); a combination of both strategies also has been proposed. End points for these strategies include demonstration of complete lines in the LL approach or cycle length prolongation, organization into atrial tachycardia (AT), or termination to sinus rhythm for CFAE ablation. The type of recurrent atrial tachyarrhythmia after ablation for persistent AF may be either AF recurrence (paroxysmal or persistent) or new-onset AT with a macroreentrant, localized reentrant, or focal mechanism. Incidence may be predicted by the type and extent of the initial ablation. Up to now, it has not been evaluated whether the type of recurrent arrhythmia (AT or AF) after the initial persistent AF ablation has a prognostic significance for outcome after a second ablation procedure.

Methods

Study Population and Initial Ablation Procedure

Between 2004 and September 2009, 262 patients with symptomatic, drug-refractory, persistent AF had an ablation procedure in our institution. Out of these, 78 consecutive patients (82% men; mean age, 61 ± 10 years; mean left atrial [LA] diameter, 47 ± 4 mm) underwent at least 1 repeat ablation and comprised our study population.

The initial ablation procedure consisted of a PVI with additional ablation of CFAE (PVI+CFAE) in 63 (81%) patients and a circumferential PVI (CPVI) with additional lines (roof line and anterior line) (CPVI+LL) in 15 (19%) patients. PVI was confirmed by a circular mapping catheter in all cases. The end point of LL was bidirectional block confirmed by differential pacing and the presence of widely split double potentials on the ablation line. The end point of CFAE ablation was AF cycle length prolongation or AF termination (into AT or sinus rhythm) by sequential ablation of all CFAE.
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Group 2 (n=37)</th>
<th>Group 3 (n=5)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>60±10</td>
<td>62±10</td>
<td>55±10</td>
</tr>
<tr>
<td>Male sex</td>
<td>29 (81)</td>
<td>31 (84)</td>
<td>4 (80)</td>
</tr>
<tr>
<td>LA diameter before first procedure, mm</td>
<td>46±5</td>
<td>48±4</td>
<td>43±3</td>
</tr>
<tr>
<td>LA diameter before repeat procedure, mm</td>
<td>46±5</td>
<td>47±4</td>
<td>42±2</td>
</tr>
<tr>
<td>AF duration before initial ablation in months</td>
<td>8.5 (0.25–90)</td>
<td>12.0 (1.0–132.0)</td>
<td>3.0 (1.0–9.0)</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD, n (%), or median (minimum–maximum).

AF indicates atrial fibrillation; CAD, coronary artery disease; CHF, chronic heart failure; LA, left atrium.

*Bonferroni-adjusted pairwise comparisons revealed a statistically significant difference between group 2 and group 3 (P=0.011).

Details of the ablation techniques have been described previously.10,16 During the initial procedure, AF termination had been achieved in 33 (42%) patients. In 19 patients, AF terminated to sinus rhythm (in 12 patients through ≥1 AT), and in 14 patients AF organized to an AT, which was cardioverted. In the remaining 45 (58%) patients, direct current cardioversion of AF was required at the end of the procedure to achieve sinus rhythm.

Recurrent Arrhythmia Type

In the 78 patients, we defined 3 patient groups according to the type of recurrent arrhythmia: persistent AT (group 1, n=36), persistent AF (group 2, n=37), and paroxysmal AF (group 3, n=5). The baseline characteristics of the 3 groups are shown in Table 1.

AF was defined as a beat-to-beat variability in cycle length and morphology with irregular fibrillatory waves on surface ECG. AT was defined as a stable and regular atrial activation with a consistent endocardial activation sequence, an atrial cycle length of >180 ms, and a monomorphic P wave on surface ECG.

Paroxysmal AF was defined as recurrent AF that terminated spontaneously within 7 days. Patients with persistent AF or AT had sustained arrhythmia >7 days, which recurred and persisted after at least 1 pharmacological or electric cardioversion.

Repeat Ablation Procedure

In all 78 patients, a repeat ablation procedure was performed for documented atrial tachyarrhythmia (AF or AT) >3 months after the initial procedure. During the repeat ablation, repeat PVI (re-PVI), CFAE ablation, focal ablation of localized reentries, or LLs for macroreentry were performed according to the presenting arrhythmia. ATs were mapped using entrainment mapping, activation mapping, or both as described before.12

Acute success of AT ablation was defined as termination of the presenting AT and all subsequently occurring AT into sinus rhythm during the procedure. No further induction maneuvers were performed when termination occurred during ablation.

Follow-up and Study End Points

Patient history from 3-month outpatient clinic visits and repeated 7-day Holter ECG were used to assess the arrhythmia burden. We used a 3-month blanking period after the reablation procedure during which atrial arrhythmias were considered a transient phenomenon.

The primary end point was defined as freedom from any asymptomatic or symptomatic atrial tachyarrhythmia lasting >30 s while off antiarrhythmic drugs after the blanking period and up to the end of follow-up, using patient history and at least 2 of the 7-day Holter ECGs. Secondary end points were procedural data of the reablation procedure (procedure duration, fluoroscopy data, radiofrequency delivery time, and complications), acute outcome of the reablation procedure (termination of AF or cardioversion), and the number of repeat procedures after the first reablation (ie, third and fourth ablation).

Statistical Analysis

Normal data are presented as mean±SD and skewed data as median, minimum, and maximum. For qualitative data, absolute and relative frequencies are shown. For statistical tests, a 2-sided level of significance of α=0.05 was used. Comparisons between groups were made by χ² test or Fisher exact test for categorical variables and unpaired t test or 1-way ANOVA for normally distributed variables.

A Kruskal-Wallis test was performed to compare AF duration before initial ablation on time to recurrence. Among groups. Cox regression was performed to assess the influence of AF duration before initial ablation on time to recurrence. Poisson regression was used to compare rates of recurrent events among groups. Methods were used to estimate event rates. A log-rank test was performed to compare distributions of event times among groups. Poisson regression was used to compare rates of recurrent events among groups. Cox regression was performed to assess the influence of AF duration before initial ablation on time to recurrence.

Table 2. Type of Presenting Arrhythmia for Repeat Ablation According to the Acute Result of the First Procedure

<table>
<thead>
<tr>
<th>Group</th>
<th>Group 2 (n=37)</th>
<th>Group 3 (n=5)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Termination of AF</td>
<td>20 (56)</td>
<td>11 (30)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>To sinus rhythm</td>
<td>11 (31)</td>
<td>6 (16)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>To AT</td>
<td>9 (25)</td>
<td>5 (14)</td>
<td>0</td>
</tr>
<tr>
<td>Cardioversion of AF</td>
<td>16 (44)</td>
<td>26 (70)</td>
<td>3 (60)</td>
</tr>
</tbody>
</table>

Data are presented as n (%). AT indicates atrial tachycardia. Other abbreviation as in Table 1.

*P=0.034 for pairwise comparisons between group 1 and group 2, a nonstatistically significant difference using the adjusted level of significance of 0.0167.

Results

Type of Arrhythmia Recurrence and Association to Initial Ablation

Acute AF termination during the initial procedure was achieved in 20 of 36 (56%) patients in group 1 versus 11 of 37 (30%) in group 2 and 2 of 5 (40%) in group 3. Although the difference between groups 1 and 2 with regard to termination of AF during the initial ablation reached P=0.034, this was not statistically significant using the adjusted level of significance of P=0.0167 (see Methods section and Table 2).

There was no significant correlation between time to arrhythmia recurrence and type of recurrence. The mean time to recurrence leading to a repeat ablation was 4.9±3, 4.6±3, and 3.8±3 months in groups 1, 2, and 3, respectively (P=0.7).
Table 3. Type of Presenting Arrhythmia for Repeat Ablation According to the Original Ablation Approach

<table>
<thead>
<tr>
<th>Presenting Arrhythmia During Repeat Procedure</th>
<th>Persistent AT (Group 1, n=36)</th>
<th>Persistent AF (Group 2, n=37)</th>
<th>Paroxysmal AF (Group 3, n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPVI+LL (n=15)</td>
<td>1 (7)</td>
<td>11 (73)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>PVI+CFAE ablation (n=63)</td>
<td>35 (56)</td>
<td>26 (41)</td>
<td>2 (3)</td>
</tr>
</tbody>
</table>

Data are presented as n (%). CFAE indicates complex fractionated atrial electrogram; CPVI, circumferential PV; LL, linear lesion; PVI, pulmonary vein isolation. Other abbreviations as in Tables 1 and 2.

Type of Presenting Arrhythmia for Repeat Ablation According to the Initial Ablation Approach

After CPVI+LL, the most frequent recurrent arrhythmia was persistent AF (73%), whereas after PVI+CFAE ablation, AT was the most frequent arrhythmia type (56%) (P<0.001) (Table 3).

Repeat Ablation Procedure

In group 1, a total of 62 ATs (1–5 ATs/patient) were targeted for ablation. Re-PVI was performed in 30 of 36 (83%) patients, and LL were required in 34 of 36 (94%) patients. AT mechanism was macroreentry (n=42, 68%) or localized reentry/focal (n=20, 32%). Among the macroreentries, perimital reentry (n=21), roof-dependent reentry (n=17), and typical flutter (n=4) were found. Localized reentries or focal AT originated from the pulmonary veins (n=5), septum (n=7), anterior wall (n=4), or other locations (n=4). Acute success rate (ie, termination of the clinical AT and all subsequent ATs) was 80.6%.

In group 2, re-PVI of at least 1 vein was necessary in 36 of 37 (97%) patients, and repeat CFAE ablation was performed in 32 of 37 (86%) patients; 3 of 37 (8%) patients underwent focal ablation of localized reentries, and LL were deployed in 9 of 37 (20%) patients. AF termination was achieved in 11 of 37 (30%) patients. In 6 patients, AF terminated to sinus rhythm (3 through ≥1 AT), and in 5 patients, AF organized into an AT that was cardioverted. In the remaining 26 of 37 (70%) patients, direct current cardioversion of AF was necessary to achieve sinus rhythm.

All patients of group 3 received an re-PVI. One of them received an additional ablation of a localized reentry.

There was no significant difference regarding procedural duration, fluoroscopy time, and radiofrequency delivery time between groups 1 and 2 (Table 4). No major procedural complication occurred in any of the 3 groups.

Follow-up

Six-month follow-up data were available in 66 of 78 (85%) patients, and 9-month follow-up data were available in 50 of 78 (64%). Estimated proportions of patients reaching the primary end point were 59% for group 1, 28% for group 2, and 100% for group 3 at 6 months and 51%, 23%, and 100%, for group 1, 2, and 3, respectively, at 9 months (P=0.002) (Figure 1). Patients presenting for ablation with persistent AT (group 1) had a significantly better outcome than patients of group 2 (persistent AF) (pairwise comparison P=0.010).

During the 12 months after the ablation, further repeat procedures were performed in 10 of 36 (28%) patients in group 1, 12 of 37 (32%) patients in group 2, and 0 patients in group 3. Taking into consideration the different follow-up times, a 1.69-times higher rate for repeated ablation procedures (95% CI, 0.77–3.69) for group 2 compared with group 1 was observed (P=0.188).

After further repeat ablation procedures, the probability of freedom from arrhythmias while off antiarrhythmic drugs was estimated to be 71% in group 1 and 42% in group 2 at 6 months and 71% in group 1 and 38% in group 2 at 9 months. No event was observed in group 3 (P=0.007) (Figure 2). The adjusted pairwise comparison also revealed a significantly better outcome for group 1 than for group 2 (P=0.013). The duration of persistent AF before initial ablation had no significant effect on the outcome after repeat procedure (hazard ratio, 1.004; 95% CI, 0.994–1.013; P=0.455).

Discussion

The main finding of this study is that the type of recurrent arrhythmia in patients after ablation of persistent AF predicts the midterm success after the repeat ablation. Freedom from any atrial tachyarrhythmia after reablation is reached significantly more often in patients presenting with persistent AT than in patients presenting with recurrent persistent AF.

Recurrent Arrhythmia Type and Prognosis

Prognosis seems to depend on the type of arrhythmia recurrence after the initial ablation of persistent AF. Patients with a recurrent persistent AF experienced a <30% freedom from arrhythmia during follow-up. It might be speculated that in this population, initial substrate modification as well as substrate modification during the repeat procedure do not lead to significant organization of the atria so that AF can sustain.

On the other hand, patients with AT after ablation of persistent AF seem to have a significantly better long-term prognosis. The organized AT may reflect a modification of the atrial electrophysiological substrate to an extent that AF cannot sustain. The occurrence of AT is conventionally considered a proarrhythmogenic effect of AF ablation but often presents a clearer target for ablation. Considering the high acute success rate and the better long-term outcome in the AT group, occurrence of AT might be interpreted as a step toward maintenance of sinus rhythm.
In a small group of patients, persistent AF became paroxysmal after the initial procedure. It seems that in these patients (with smaller LA diameters), 1 procedure was sufficient to ablate the substrate. After elimination of this limited substrate, the episodes of paroxysmal AF were mainly driven by recurrent pulmonary vein activity easily targeted at the repeat procedure. A recently published study from Lo et al\textsuperscript{17} reinforces this hypothesis. LA volume was the only factor predicting the recurrent type of AF (ie, paroxysmal versus persistent AF) after the initial ablation. Voltage mapping suggested that a reverse electric and structural remodeling occurred after the ablation of chronic AF when the recurrence was paroxysmal AF.

**Type of Recurrent Arrhythmia and Initial Ablation**

Almost one half of the patients presenting for a repeat ablation were in AT. This is consistent with other studies reporting an AT incidence of about 40\% to 60\% after ablation of persistent AF\textsuperscript{13,18,19}. We found that the result of the initial ablation procedure has some impact on the type of recurrent arrhythmia. In the present small series, patients presenting for...
reablation with AT had a tendency to have more often experienced AF termination during the initial procedure than those presenting with persistent AF, but this was not statistically significant. Further prospective trials are required to determine whether the acute result of the initial ablation predicts the type of recurrent arrhythmia.

Interestingly, we found that in contrast to the acute result of the initial ablation, the ablation technique used in the first ablation has a significant impact on the type of arrhythmia in follow-up. After CPVI + LL, patients had more often a recurrence of persistent AF, whereas the most frequent recurrent arrhythmia type after PV1 + CFAE ablation was AT. This was confirmed by a recently published randomized study from our group.20

In the LL approach, AT can be explained by incomplete lines of block. However, only 1 patient in the CPVI + LL group had AT as the recurrent arrhythmia type, which was due to a gap in the roof line. In the present study, the LL approach was used in 19% of cases during the initial procedure and were required for treating subsequent AT during repeated procedures in 94% of cases. Additionally, in the study of Knecht et al.21 96% of patients required a roof line and 86% a mitral line during follow-up.

Localized reentries emerged since the appearance of extensive substrate modification by CFAE ablation, which may generate focal areas of slow conduction and heterogeneous scar.22 In the present study, we identified nonmacroreentrant tachycardia in 32% of cases. This incidence varied between 28% and 54% in other studies.23,24

Another interesting idea is supported by data from spectral analysis points to the coexistence of ATs with AF, which might be important for AF perpetuation. Substrate modification might eliminate AF and lead to detection of underlying AT.25 The present data support the notion that these ATs are a good target for ablation or reablation and improve midterm outcome.

Limitations
The extent of substrate modification during the initial ablation procedure is a critical point for the incidence of AT and was not intensively studied in this population. Procedure duration and ablation time do not always reflect the extent of ablated tissue, which may be more dependent on the ablation strategy (LL, CFAE ablation, or a combination of both). However, we included consecutive patients with any arrhythmia recurrence after ablation of persistent AF. No significant differences in baseline characteristics between the persistent AF and the AT group were found.

Conclusions
The occurrence of regular AT after ablation of persistent AF compared with the recurrence of persistent AF was associated with a significantly better outcome after a repeat ablation. The occurrence of AT after persistent AF ablation therefore might be considered not as a proarrhythmogenic effect, but as a step toward long-term maintenance of sinus rhythm.

Disclosures
None.

References


**CLINICAL PERSPECTIVE**

Long-term results after catheter ablation of persistent atrial fibrillation remain unsatisfying despite repeated interventions. The outcome of ablation depends on several factors, among which the type of recurrent arrhythmia seems to play an important role. In this article, we analyze the success of the second ablation after an initial persistent atrial fibrillation ablation according to the type of recurrent arrhythmia. We found that patients who presented with an organized atrial tachycardia are more likely to have a successful repeat ablation than patients who presented again with persistent atrial fibrillation. Paroxysmal atrial fibrillation as recurrent arrhythmia type is rare but seems to have the best prognosis. New-onset atrial tachycardia has been considered a proarrhythmogenic effect of the ablation. However, the results suggest that atrial tachycardia also could be regarded as a sign of organization of the fibrillating atria, representing a good ablation target. Atrial tachycardia is associated with a better long-term outcome and might be considered as a step toward maintenance of sinus rhythm.
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