Catheter Ablation of Long-Standing Persistent Atrial Fibrillation

5-Year Outcomes of the Hamburg Sequential Ablation Strategy

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Objectives
This study describes the 5-year efficacy of catheter ablation for long-standing persistent atrial fibrillation (LS-AF).

Background
Long-term outcome data after catheter ablation for LS-AF are limited.

Methods
Long-term follow-up of 56 months (range 49 to 67 months) was performed in 202 patients (age 61 ± 9 years) who underwent the sequential ablation strategy for symptomatic LS-AF. Initial ablation strategy was circumferential pulmonary vein isolation (PVI). Additional ablation was performed only in acute PVI nonresponder, if direct current cardioversion failed after PVI.

Results
After the first ablation procedure, sinus rhythm was documented in 41 of 202 (20.3%) patients. After multiple procedures, sinus rhythm was maintained in 91 of 202 (45.0%) patients, including 24 patients receiving antiarrhythmic drugs. In 105 patients, PVI was the sole ablative therapy, 49 (46.7%) of those patients remained in sinus rhythm during follow-up. Patients with a total AF duration of <2 years had a significantly higher ablation success rate than patients whose AF duration was >2 years (76.5% vs. 42.2%, respectively; p = 0.033). Persistent AF duration (hazard ratio: 1.09 [95% confidence interval: 1.04 to 1.13]; p < 0.001) independently predicted arrhythmia recurrences, and acute PVI responders had a reduced risk of relapse (hazard ratio: 0.57 [95% confidence interval: 0.41 to 0.78]; p < 0.001) after the first ablation.

Conclusions
During 5-year follow-up, single- and multiple ablation procedure success was 20% and 45%, respectively, for patients with LS-AF. For patients with a total AF duration of <2 years, the outcomes were favorable.

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Pulmonary vein isolation (PVI) is a well-established treatment option in patients with atrial fibrillation (AF). In long-term follow-up of as long as 5 years, the multiple procedure success rate is approximately 80% in patients with paroxysmal AF (PAF) (1–3). However, recurrences are frequent, and repeat ablation is often required to maintain freedom from AF (1–3). Current guidelines from HRS/EHRA/ECAS state that: 1) ablation strategies that target the PVs and/or PV antrum should form the cornerstone for most AF ablation procedures; and 2) if the PVs are targeted, complete electrical isolation should be the goal (1). However, in patients with long-standing persistent AF (LS-AF), PVI alone may not be sufficient as outcomes after PVI alone are disappointing, with success rates ranging from 36% to 56% at medium term follow-up (2–5). To improve outcomes in patients with LS-AF, various ablation strategies in addition to PVI have been described. The most widely used additional ablation strategy is the ablation of complex fractionated atrial electrograms (CFAE) (6,7). However, numerous gaps in our knowledge remain such as the adjunctive benefit of these techniques and the long-term efficacy of LS-AF ablation in general. Until recently, long-term outcome data of >2 years’ follow-up after catheter ablation for LS-AF have been sparse (8).

We previously evaluated the short-term outcomes of catheter ablation for LS-AF (5). In this study, we present long-term follow-up data from the same cohort. The objectives of this study were to determine: 1) the long-term efficacy of the sequential
Ablation strategy for treatment of LS-AF; 2) the regression of LS-AF toward PAF after ablation; and 3) predictors of recurrence.

Methods

Study population. Two hundred and five patients were consecutively enrolled in the initial study. The study population and methods have been published previously (5). Three patients were lost to follow-up. Long-term follow-up and data analysis were performed for the remaining 202 patients (age 61 ± 9 years). All patients had symptomatic LS-AF refractory to antiarrhythmic drugs (AAD) and underwent radiofrequency current catheter ablation at our institution between November 2003 and July 2007. The LS-AF was defined as continuous AF of >1 year duration (9). Baseline characteristics of the patient population are presented in Table 1. Total AF duration was 99 ± 64 months (median 84 months [range 60 to 120 months]), duration of continuous AF (persistent AF) was 49 ± 44 (median 36 months [range 20 to 60 months]).

Electrophysiological study. After written informed consent, all patients underwent a transesophageal echocardiogram before the procedure. Oral anticoagulation (OAC) therapy was stopped at least 3 days before ablation and replaced with low-molecular-weight heparin. The procedure was performed under deep sedation utilizing midazolam, fentanyl, and a continuous infusion of propofol. Two standard catheters were positioned at the His bundle region and inside the coronary sinus. Two or 3 SL1 sheaths (St. Jude Medical, Minneapolis, Minnesota) were advanced to and inside the coronary sinus. Two or 3 SL1 sheaths (St. Jude Medical, Minneapolis, Minnesota) were advanced to and inside the coronary sinus. Two or 3 SL1 sheaths (St. Jude Medical, Minneapolis, Minnesota) were advanced to and inside the coronary sinus. Two or 3 SL1 sheaths (St. Jude Medical, Minneapolis, Minnesota) were advanced to and inside the coronary sinus.

PVB: non-PV triggers were used at that point. If DC cardioversion was successful, patients were defined as acute PVI responder (Fig. 1). The CFAE ablation was performed, as described before, in an attempt to convert AF to SR or AT (5). Termination was defined as transition directly from AF to SR or by 1 or multiple ATs (8). The CFAEs were analyzed visually and were defined as published by Nademanee et al. (6): 1) fractionated electrograms composed of >1 deflections and/or continuous deflection of a prolonged activation complex; and 2) atrial electrograms with <120 ms CL recorded over a 5-s recording period.

During ablation of CFAEs or LA linear lesions, the Lasso catheter was positioned in the left atrial appendage (LAA) to continuously record LAA activity. Only in the presence of a (macro) AT were linear lesions applied. Electrophysiological evidence of bidirectional block was validated in SR (12). Superior vena cava isolation was attempted only if spontaneous focal-discharge was demonstrated from this location. Patients requiring ablation strategies in addition to PVI were defined as acute PVI nonresponder.

Ablation protocol during repeat procedure. Repeated electrophysiology procedures were undertaken for recurrent atrial tachyarrhythmias (ATa). The initial strategy was an assessment of PV reconduction, followed by closure of all PV conduction gaps and electrical reisolation. Ablation of CFAEs was only performed in a PVI nonresponder if: 1) DC cardioversion failed after repeat PVI; or 2) patients demonstrated no PV reconduction (5). In patients with no PV reconduction presenting in SR, AF was induced by burst stimulation from the LAA before CFAE ablation.

Post-ablation treatment and follow-up. The OAC therapy was started immediately post-procedure, targeting an

### Table 1 Baseline Patient Characteristics (N = 202)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>61 ± 9</td>
</tr>
<tr>
<td>Male</td>
<td>160 (79)</td>
</tr>
<tr>
<td>Total AF duration, months</td>
<td>99 ± 64</td>
</tr>
<tr>
<td>Persistent AF duration, months</td>
<td>49 ± 44</td>
</tr>
<tr>
<td>Patients treated with amiodarone</td>
<td>115 (57)</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>32 (16)</td>
</tr>
<tr>
<td>LA diameter, mm</td>
<td>49 ± 6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>155 (77)</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>60 ± 7</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n (%).

AF = atrial fibrillation; LA = left atrial; LVEF = left ventricular ejection fraction.
international normalized ratio of 2 to 3. Where the LAA was isolated, lifelong OAC therapy was recommended. In all other patients, OAC therapy was continued for at least 3 months. Thereafter, indication for anticoagulation therapy was solely based on the patient’s CHADS₂ (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and prior stroke or transient ischemic attack) score (9). Before discharge, a 24-h Holter recording and echocardiographic evaluation was performed. Discontinuation of AADs was recommended 3 months after ablation. A transthoracic echocardiogram, 12-lead electrocardiogram, and 24-h Holter recording were obtained at our outpatient clinic or by the referring physician 1, 3, and 6 months after ablation and thereafter at 6-month intervals.

Recurrence was defined as episodes of AF or AT lasting >30 s as documented by 12-lead electrocardiogram or Holter monitoring. This study did not adhere to a pre-defined blanking period. Clinical success was defined as freedom from recurrence during the entire follow-up period. Regression of persistent AF was defined as change from LS-AF to PAF or maintenance of SR on AAD after arrhythmia recurrence.

**Statistical analysis.** Categorical variables are expressed as absolute and relative frequencies. Continuous variables are expressed as mean ± SD or median and interquartile range as appropriate. Group mean differences were examined by the Student’s t test for independent samples. Differences in categorical variables between groups were compared by the chi-square test of significance. Event-free survival were estimated by the method of Kaplan-Meier and compared by the log-rank test. Predictors of arrhythmia recurrence were performed using Cox proportional hazards regression models.
The following variables were used as exploratory variables in univariate and multiple survival prediction models: age, sex, total AF duration, persistent AF duration, amiodarone, structural heart disease, coronary artery disease, LA diameter, hypertension, left ventricular ejection fraction, CHADS2 score, procedure duration, fluoroscopy duration, termination, complications, and PVI as the sole ablation strategy. Variables that were univariately associated with survival (p < 0.2) were considered for a multiple survival prediction model.

The multivariate prediction models for time to recurrence after the index procedure and after the final ablation procedure were performed by stepwise regression based on likelihood ratios. For each variable, hazard ratio (HR), 95% confidence interval (CI), and Wald test p values of the final model are displayed. A HR of <1 indicates a reduced likelihood of relapse for increasing values of the variable. A 2-tailed probability value of < 0.05 was deemed significant. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agreed to the manuscript as written.

Results

Clinical outcomes after a single procedure. During a median follow-up of 56 months (range 49 to 67 months), SR was maintained in 41 of 202 (20.3%) patients (Figs. 2 and 3). Recurrent arrhythmia after the index procedure was persistent AF in 103 of 202 (51.0%) patients, PAF in 27 of 202 (13.4%) patients, and AT in 31 of 202 (15.3%) patients (Fig. 2). Regression of AF occurred in 36 of 202 (17.8%) patients (16 patients maintained SR after the reinitiation of AADs, and 20 patients regressed to PAF). Arrhythmia recurred within the first year after ablation in 13 of 202 (64.4%) patients. Thirty-one (15.3%) patients had recurrences after 12 months including 10 (5.0%) patients with recurrences >3 years after ablation.

Clinical outcomes after the last procedure. During a median follow-up of 50 months (range 36 to 61 months), 91 of 202 (45.0%) patients remained in SR, including 24 patients taking AADs (amiodarone in 2 patients). Regression of AF was noted in 47 (23.3%) patients (36 patients maintained SR after reinitiation of AADs, and 11 patients changed to PAF). Recurrent arrhythmia was persistent AF in 65 (58.6%) patients, AT in 19 (17.1%), and PAF in 27 (24.3%).

Summary of ablation procedures. Procedural details are summarized in Table 2. A total of 383 procedures were performed in 202 patients (median 2, range 1 to 5). PVI was performed in all 202 patients and was the sole ablative strategy in 105 (52.0%) patients by the final procedure. Recovered PV conduction was found in 97 of 126 (77.0%) patients at the first, 12 of 42 (28.6%) at the second, and no (0%) patient at the third or fourth redo procedures. Three patients at the first redo procedure and 1 patient at the second redo procedure presented in SR without PV reconnection, therefore requiring AF induction before CFAE ablation.

Isolation of LAA occurred in 10 of 97 (10.3%) patients undergoing PVI and additional ablation (acute PVI nonresponder): this affected no patient during the first, 4 patients during the second, 3 during the third, and 3 at the fourth procedure.

The following complications occurred in 18 (4.7%) of 383 procedures: ischemic stroke (n = 2), transient ischemic attack (n = 1), femoral hematoma requiring blood transfusion (n = 11) and vascular surgery (n = 3 of 11), pneumothorax (n = 1), aspiration pneumonia (n = 1), transient pulmonary edema (n = 1), and cardiac tamponade (n = 1).

Cerebrovascular events occurred during follow-up as follows: cerebral hemorrhage (n = 1), stroke (n = 9), and transient ischemic attack (n = 4) including 3 periprocedural
events as stated above. Thromboembolic events occurred in 2 patients without ATa recurrence and in 1 patient with his first ATa episode after ablation. The latter 3 patients had CHADS2 scores of 1, 2, and 3, respectively, and were not receiving OAC therapy at the time of the event.

Five deaths occurred during follow-up due to myocardial infarction (n = 1), leukemia (n = 1), non-Hodgkin’s lymphoma (n = 1), gallbladder cancer (n = 1), and unknown cause (n = 1).

**PVI as the sole ablative strategy.** At the first procedure, 165 of 202 (81.7%) patients were acute PVI responders (Tables 2, 3), and therefore received PVI as the sole ablation strategy. Arrhythmia recurrence occurred in 132 of 165 (80.0%) patients. By the last procedure, PVI was the sole ablation strategy in 105 of 202 (52.0%) patients (acute PVI responder).

In the overall population, PVI alone was able to establish long-term SR in 24.3% (49 of 202) of the patients and in 46.7% (49 of 105) of acute PVI responders. Regression of AF was noted in another 27 of 105 (25.7%) acute PVI responders (SR after readministration of AADs in 21 and change to PAF in 6 patients).

The only significant difference between patients who maintained SR after PVI alone and the remaining patients was the mean duration of persistent AF (35.2 ± 22.5 months vs. 53.5 ± 48.5 months; p = 0.045).

Acute PVI responders at the first procedure had a significantly lower risk for arrhythmia recurrence (HR: 0.54 [95% CI: 0.39 to 0.74]; p < 0.001) than acute PVI nonresponders. Patients undergoing PVI plus additional ablation had a nonsignificantly higher risk for procedural complications compared to patients undergoing PVI alone.

### Figure 3 Single and Multiple Procedure Outcomes
Kaplan-Meier event-free survival curve after the first procedure (blue line) and after the last procedure (red line). Plus sign (+) indicates censored. Numbers at bottom indicate patients at risk. ATa = atrial tachyarrhythmia.

### Table 2 Summary of Ablation Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>PVI Only Until This Procedure</th>
<th>CFAE</th>
<th>LA Line</th>
<th>SVC/AES</th>
</tr>
</thead>
<tbody>
<tr>
<td>First procedure (n = 202)</td>
<td>165 (165)</td>
<td>29 (29)</td>
<td>12 (12)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Second procedure (n = 126)</td>
<td>0 (60)</td>
<td>15 (21)</td>
<td>24 (26)</td>
<td>13 (0)</td>
</tr>
<tr>
<td>Third procedure (n = 42)</td>
<td>0 (5)</td>
<td>15 (20)</td>
<td>21 (26)</td>
<td>1 (0)</td>
</tr>
<tr>
<td>Fourth procedure (n = 11)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>3 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Fifth procedure (n = 2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Ablation summary (last procedure)</td>
<td>105</td>
<td>60</td>
<td>60</td>
<td>21</td>
</tr>
</tbody>
</table>

**Bold values** indicate patients in whom this ablation strategy was performed for the first time. Values in parentheses indicate patients in whom this ablation strategy was performed either for the first time or in whom it was repeated.

AES = atrial extrasystoles; CFAE = complex fractionated atrial electrogram; LA = left atrial; PVI = pulmonary vein isolation; SVC = superior caval vein.
alone (6.7% vs. 11.3%; p = 0.244). Additionally, a 10% incidence of LAA isolation was noted in the latter group.

**Predictors of arrhythmia recurrence.** After a single procedure, univariate predictors of recurrence were persistent AF duration, total AF duration, and PVI as the sole ablative strategy. For each additional year of persistent AF, the risk of arrhythmia recurrence increased by 10.0% (HR: 1.10 [95% CI: 1.05 to 1.14]; p < 0.001). For each additional year of total AF duration, the risk for arrhythmia recurrence increased by 4.9% (HR: 1.05 [95% CI: 1.01 to 1.07]; p = 0.002). PVI performed alone was associated with a significantly reduced risk of relapse. In multivariate analyses, persistent AF duration (HR: 1.09 [95% CI: 1.04 to 1.13]; p < 0.001) and PVI as the sole ablative strategy (HR: 0.57 [95% CI: 0.41 to 0.78]; p < 0.001) independently predicted arrhythmia recurrences.

Univariate predictors of arrhythmia recurrence after the last ablation procedure were persistent AF duration (HR: 1.07 [95% CI: 1.04 to 1.13]; p < 0.001) and total AF duration (HR: 1.06 [95% CI: 1.02 to 1.10]; p < 0.001). In multivariate analyses, only total AF duration (HR: 1.06 [95% CI: 1.02 to 1.10]; p < 0.001) predicted arrhythmia recurrence. Interestingly, when considering overall procedures, PVI alone was no longer a significant parameter of maintenance of long-term SR.

Patients with a total AF duration of <2 years had a significantly higher success rate compared to other patients (76.5% vs. 42.2% in SR; p = 0.033) (Fig. 4). Patients with a total AF duration of >2 years were almost 3 times more likely to relapse after the last ablation (HR: 2.81 [95% CI: 1.04 to 7.63]; p = 0.042).

**Discussion**

In this study, we found that: 1) circumferential PVI alone was sufficient to restore SR in 24% of patients with LS-AF; 2) 5-year outcomes of LS-AF ablation remain mediocre with a 45% multiple-procedure success rate; 3) AF regression is a common phenomenon found in 23% of patients; and 4) persistent AF duration independently predicted arrhythmia recurrences whereas acute PVI responders had a reduced risk of relapse after the first ablation.

**Pulmonary vein isolation in LS-AF.** PVI is an effective therapy for PAF patients, with success rates ranging from 57% to 80% at up to 5 years of follow-up (13–16). For patients with LS-AF, there is conflicting evidence about the long-term efficacy of PVI as the first-line ablative strategy (17,18). In this study, using the sequential approach, PVI was the first-line therapy for all patients. Additional ablative strategies, for example, CFAEs, were only applied in PVI nonresponders—if DC cardioversion failed after PVI or at repeat ablation procedures when patients demonstrated no PV reconnection.

In patients with LS-AF, observed >5 years after ablation, PVI alone was sufficient to restore and maintain SR in 24% of patients. Regression of AF was noted in another 13% of those patients, resulting in clinical improvement. This finding suggests that the PVs and the antrum are important substrates in patients with LS-AF. Interestingly, after the first procedure, PVI alone was associated with a 46% relative risk reduction in arrhythmia recurrence compared to acute PVI nonresponders. Thus, successful DC cardioversion after PVI may identify patients who have a less diseased LA.

For the majority of patients, repeat ablation and additional ablative strategies are required to maintain SR in 45% of patients. Interestingly, success rates were similar between patients undergoing PVI alone and PVI nonresponder undergoing additional ablation strategies.

**Procedural success** was 37.6% after 1 or 2 procedures as compared to 45% after as many as 5 procedures. More than 2 procedures were performed in 42 of 202 (22.3%) patients. Although the patient number is not large enough to draw a definite conclusion, these data indicate that the success rate beyond the second procedure is reasonable. Importantly, in patients undergoing >1 redo procedure, ablation strategies in addition to PVI are required in the majority of patients, and the incidence of ATs as the clinical arrhythmia increases. The ATs are usually clinically worse tolerated but more amenable to ablation than AF. The relatively high incidence of redo procedures of LA linear lesions in this study indicates the difficulty of obtaining durable complete lines.

Complication rates in this study were in keeping with previous publications (9). In PVI nonresponders, more extensive ablation and more procedures were required. That

### Table 3

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Acute PVI Responder (n = 105)</th>
<th>Acute PVI Nonresponder (n = 97)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>61 ± 9</td>
<td>62 ± 9</td>
<td>0.103</td>
</tr>
<tr>
<td>Male</td>
<td>83 (79)</td>
<td>77 (79)</td>
<td>0.953</td>
</tr>
<tr>
<td>Total AF duration, months</td>
<td>95 ± 56</td>
<td>105 ± 72</td>
<td>0.260</td>
</tr>
<tr>
<td>Total AF duration &lt; 2 yrs</td>
<td>8 (8)</td>
<td>9 (9)</td>
<td>0.671</td>
</tr>
<tr>
<td>Persistent AF duration, months</td>
<td>44 ± 33</td>
<td>55 ± 53</td>
<td>0.077</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>55 (52)</td>
<td>60 (62)</td>
<td>0.174</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>17 (16)</td>
<td>15 (15)</td>
<td>0.888</td>
</tr>
<tr>
<td>LA diameter, mm</td>
<td>48 ± 5</td>
<td>50 ± 6</td>
<td>0.023</td>
</tr>
<tr>
<td>Hypertension</td>
<td>80 (76)</td>
<td>75 (77)</td>
<td>0.850</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>60 ± 6</td>
<td>60 ± 7</td>
<td>0.834</td>
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<tr>
<td>CHADS2 score</td>
<td>1 ± 1</td>
<td>1 ± 1</td>
<td>0.572</td>
</tr>
<tr>
<td>Number of procedures</td>
<td>1.5 ± 0.6</td>
<td>2.4 ± 2.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Procedure duration, min</td>
<td>223 ± 66</td>
<td>238 ± 64</td>
<td>0.107</td>
</tr>
<tr>
<td>Fluoroscopy duration, min</td>
<td>30 ± 14</td>
<td>31 ± 11</td>
<td>0.380</td>
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<tr>
<td>Complications</td>
<td>7 (7)</td>
<td>11 (11)</td>
<td>0.244</td>
</tr>
<tr>
<td>LAA isolation</td>
<td>0 (0)</td>
<td>10 (10)</td>
<td>0.001</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>49 (47)</td>
<td>42 (43)</td>
<td>0.631</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n (%).

CHADS2 = congestive heart failure, hypertension, age >75 years, diabetes mellitus, and prior stroke or transient ischemic attack; LAA = left atrial appendage; other abbreviations as in Tables 1 and 2.
may have resulted in an increased complication rate per patient, although it did not reach statistical significance.

**Comparison with previous studies.** Our study evaluated a sequential approach to AF ablation while reserving additional ablative strategies for PVI nonresponders. That makes this study unique and comparison with other studies difficult. In all other studies, either PVI or additional ablative strategies were performed, and DC cardioversion after PVI was not attempted.

A recently published systematic review of the literature evaluated the impact of ablation strategies on the outcomes of LS-AF ablation (17). A total of 32 studies, including 4 randomized controlled trials, were analyzed. The meta-analysis found that with respect to single-procedure and drug-free success: 1) PVI is a superior approach compared to PV ablation alone; 2) CFAE ablation alone is an inferior strategy compared to PV ablation plus linear ablation at the roof and mitral isthmus; and 3) CFAE ablation may or may not provide incremental benefit when added to PVI (17). The researchers concluded that, because of variation in success within and between techniques, the optimal ablation technique for LS-AF remains unclear.

A recent meta-analysis evaluated the efficacy of PVI versus PVI plus CFAE ablation after a single procedure without AADs (18); a total of 660 patients enrolled in 7 controlled trials were analyzed. The investigators found that CFAE ablation in addition to PVI increases the rate of SR maintenance in nonparoxysmal AF after a single procedure (relative risk: 1.35 [95% CI: 1.04 to 1.75]; p = 0.022), but does not provide additional clinical benefit in PAF patients. However, direct comparison of studies evaluating LS-AF ablation is difficult, not only because of the different ablative approaches but also because of heterogeneous patient populations. For example, in several studies, patients with a continuous AF duration of <12 months were included and terms like “nonparoxysmal AF” or “chronic AF” used (17).

Despite the relatively conservative ablation strategy used in this study, the single-procedure outcomes concur with prior reports utilizing a more aggressive ablation protocol (19), and at first procedure, PVI as the sole ablative strategy was associated with a lower risk for arrhythmia recurrence. Termination of AF at the first procedure as well as at the last procedure did not influence outcomes. In this study, AF termination was only attempted in acute PVI nonresponders; these patients may, therefore, represent a subgroup of patients with a more diseased LA, and thus explain why, in contrast to other studies, AF termination did not influence outcomes.

A recent study demonstrated that the LAA can be trigger site of AF, and that LAA isolation may improve clinical outcomes (20). However, the clinical impact and long-term thromboembolic risk after LAA isolation is uncertain, and it is important to balance the risks and benefits of additional ablation as they may increase the incidence of potential complications and adverse events such as LAA isolation and the occurrence of iatrogenic AT (2,19,21).
Finally, PV reconduction is found in approximately 75% of patients after the initial procedure (22). Since the PVs are an important trigger and substrate in some patients with LS-AF, achieving durable lesions may improve outcomes. As long as durable isolation of the PVs cannot be established with a single procedure, the final conclusion about the value of PVI will remain uncertain.

There is still conflicting evidence about the efficacy of additional ablation strategies used with PVI in patients with LS-AF. CFAE ablation may improve outcomes but also increases the risk of adverse events. To avoid overtreatment of as many as a quarter of patients who can be successfully treated with PVI only, we believe that PVI as the first-line treatment is a reasonable approach, with further ablation reserved for PVI nonresponder.

**Time to arrhythmia recurrence.** In the majority of patients arrhythmias recurred within the first year; however, late recurrences (>12 months) were noted in 15.3% of patients. These results raise the question as to whether cure for a heterogeneous and complex condition such as LS-AF is feasible, or whether AF recurrence is only a matter of time.

Three patients in whom OAC therapy was discontinued because of apparently stable SR sustained thromboembolic events. Although there is some evidence that OAC therapy may be discontinued after AF ablation in patients at moderate thromboembolic risk, data are sparse and nonrandomized (23). Therefore, the indication for lifelong anticoagulation after ablation should be exclusively based upon the CHA₂DS₂-VASc score (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and prior stroke/transient ischemic attack/thromboembolism, vascular disease, age 65 to 74, sex category female).

**Study limitations.** Because of AF regression and symptom improvement in a significant number of patients, some patients with recurrence did not undergo repeat ablation. A higher rate of reablation may have resulted in improved outcomes. Follow-up assessment of AF recurrence consisted of 24-h Holter monitoring. As implantable loop recorders or 7-day Holter monitoring were not used before ablation, the longest continuous AF duration may have been overestimated, particularly in patients in whom infrequent Holter monitoring was performed. The overall success may, therefore, have been overestimated. This study is descriptive and nonrandomized; its results require confirmation in larger randomized controlled trials. During this study, AF procedures were restricted to patients with a body mass index <35 kg/m². Unfortunately, therefore, we were unable to evaluate the clinical impact of body mass index.

**Conclusions**

In patients with LS-AF, single procedure success is poor during 5-year follow-up. Repeat ablation and additional ablation strategies are often required to maintain SR in 45%.

For patients with a total AF duration of <2 years, the outcome appears to be favorable.

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**REFERENCES**


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