Although pulmonary vein isolation (PVI) is well accepted to be the cornerstone of ablation for paroxysmal atrial fibrillation (AF), there remains lack of consensus on the optimal ablation strategy in patients with persistent and long-standing persistent AF.1–3 Although an ablation strategy limited primarily to PVI, with or without targeting of documented nonpulmonary vein (PV) triggers, results in lower long-term AF-free survival rates in patients with persistent and long-standing persistent AF than paroxysmal AF, outcomes are not improved with more extensive substrate modification strategies.4,5 It has been shown that ≈50% of patients with persistent and long-standing persistent AF who undergo extensive substrate modification experience persistent organized atrial tachyarrhythmias (OAT) after ablation.4,5 In contrast, patients with persistent and long-standing persistent AF treated with a more targeted ablation strategy (PVI with or without documented non-PV trigger ablation) are more likely to experience arrhythmia recurrences in the form of AF instead of OATs.6 However, when the arrhythmia recurrence in these patients is paroxysmal in nature, this likely suggests a favorable modification of the underlying AF substrate, which becomes less capable of sustaining AF.

The objective of this study, therefore, was to determine the nature of initial arrhythmia recurrence in patients with persistent and long-standing persistent AF undergoing antral pulmonary vein isolation and nonpulmonary vein trigger ablation and correlated recurrence type with long-term ablation efficacy after the last procedure.

**Background**—Transformation from persistent to paroxysmal atrial fibrillation (AF) after ablation suggests modification of the underlying substrate. We examined the nature of initial arrhythmia recurrence in patients with nonparoxysmal AF undergoing antral pulmonary vein isolation and nonpulmonary vein trigger ablation and correlated recurrence type with long-term ablation efficacy after the last procedure.

**Methods and Results**—Three hundred and seventeen consecutive patients with persistent (n=200) and long-standing persistent (n=117) AF undergoing first ablation were included. AF recurrence was defined as early (≤6 weeks after ablation) and paroxysmal (either spontaneous conversion or treated with cardioversion ≤7 days) or late (>6 weeks after ablation) and paroxysmal (either spontaneous conversion or treated with cardioversion ≤7 days) or persistent (lasting >7 days). During median follow-up of 29.8 (interquartile range: 14.8–49.9) months, 221 patients had ≥1 recurrence. Initial recurrence was paroxysmal in 169 patients (76%) and persistent in 52 patients (24%). Patients experiencing paroxysmal (versus persistent) initial recurrence were more likely to achieve long-term freedom off antiarrhythmic drugs (hazard ratio, 2.2; 95% confidence interval, 1.5–3.2; P<0.0001), freedom on/off antiarrhythmic drugs (hazard ratio, 2.5; 95% confidence interval, 1.6–3.8; P<0.0001), and arrhythmia control (hazard ratio, 5.2; 95% confidence interval, 2.9–9.2; P<0.0001) after last ablation.

**Conclusions**—In patients with persistent and long-standing persistent AF, limited ablation targeting pulmonary veins and documented nonpulmonary vein triggers improves the maintenance of sinus rhythm and reverses disease progression. Transformation to paroxysmal AF after initial ablation may be a step toward long-term freedom from recurrent arrhythmia.  

**Key Words:** atrial fibrillation ■ catheter ablation ■ pulmonary vein ■ recurrence

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WHAT IS KNOWN

- Long-term outcomes of catheter ablation for persistent and long-standing persistent AF are worse than for paroxysmal AF.
- Ablation limited to antral PVI and targeting of non-PV triggers has additional effects on the underlying left atrial substrate including attenuation of the distribution of complex fractionated electrograms, modification of the autonomic system (ganglionic plexi), and compartmentalization of the LA.

WHAT THE STUDY ADDS

- This study compares long-term ablation outcomes in patients with nonparoxysmal AF treated with antral PVI and non-PV trigger ablation based on the type of initial recurrence after ablation.
- Among patients with nonparoxysmal AF who experienced at least one recurrence after ablation, the initial recurrence was paroxysmal in nature in 76%; those with initial paroxysmal recurrence type were more likely to achieve long-term freedom off AADs, freedom on/off AADs, and arrhythmia control after last ablation.
- Transformation from nonparoxysmal to paroxysmal AF after catheter ablation may represent a step toward long-term freedom from recurrent arrhythmia.

Methods

Study Population and Data Collection

We identified patients with persistent and long-standing persistent AF who underwent ablation at the Hospital of the University of Pennsylvania between April 1, 2008, and December 31, 2012, and retrospectively selected all consecutive, eligible patients of each AF type from our ablation database (Figure 1). Eligible patients included those who had undergone AF ablation for the first time, had completed their initial 30-day transtelephonic monitor (TTM), and had at least 1 year of follow-up after the initial ablation procedure. We used the 2012 HRS/EHRA/ECAS Ablation Consensus Statement and the 2014 AHA/ACC/HRS AF guidelines to categorize persistent AF (continuous AF lasting >7 days) and long-standing persistent AF (uninterrupted AF lasting ≥12 months).

Baseline clinical, demographic, and echocardiographic characteristics previously shown to be associated with ablation success were abstracted from patient charts. All participants provided written informed consent for both the ablation procedure and inclusion in our AF ablation registry. This study was approved by the University of Pennsylvania Health System’s Institutional Review Board.

Ablation Procedure

Our AF ablation approach has been previously described. Briefly, antiarrhythmic drugs (AADs) were discontinued >5 half-lives before ablation in all patients (except amiodarone, which was discontinued >2 weeks before ablation). Catheters were placed in the coronary sinus and posterior right atrium. A bolus of unfractionated heparin was then administered, and heparin infusion was titrated to maintain an activated clotting time >325 seconds for duration of procedure. Two transeptal punctures were performed under intracardiac echocardiographic guidance (Acuson; Siemens, Malvern, PA), through which the ablation and circular mapping catheters were introduced in the left atrium (LA). Wide-area circumferential antral PVI was performed by isolating the ipsilateral left and right veins, after which stimulation was performed and any reproducibly induced non-PV triggers of AF were targeted. In patients with clinical history of typical atrial flutter or in those where typical flutter was induced, cavitricuspid isthmus ablation was performed to achieve bidirectional block. Atypical flutters and other OATs were only targeted if they were reproducibly induced and documented to have occurred spontaneously before the ablation procedure. The ablation strategy in these cases was guided by activation and entrainment mapping using standard techniques. Acute procedural success was defined as persistent PVI (both entrance and exit block) at least 20 minutes after ablation.

Postablation Follow-Up

After the ablation procedures, all patients were discharged on an AAD and either warfarin or a non–vitamin-K oral anticoagulant. All patients were also taught to do twice daily pulse checks to assess for asymptomatic arrhythmia recurrence. Additionally, each patient was sent home with a TTM device (Lifewatch, Rosemont, IL; CardioNet, Malvern, PA; or Medcomp Inc, Melbourne, FL) for continuous monitoring for 30 days postablation. After AF ablation, patients were seen for routine follow-up in the outpatient clinic at the Hospital of University of Pennsylvania around 6 weeks, 6 months, and 1 year. Beyond this period, yearly clinic visits were advised but not mandated. Routine practice at our institution is to perform a 30-day TTM around the 6-month and 1-year follow-up appointments; additional TTMs are prescribed if the patients report symptoms suggestive of arrhythmia recurrences. In the absence of documented arrhythmia recurrence, AADs were typically discontinued between 3 and 6 months postablation.

Early Versus Late Recurrences of Atrial Arrhythmias

We define early recurrence of atrial arrhythmia (ERAA) as any AF or OAT lasting >30 seconds occurring within the first 6 weeks after the index ablation (blanking period). As we have previously reported, we chose 6 weeks as the censor period to delineate ERAA because that was when patients routinely return for their first postablation follow-up. We define any arrhythmia events beyond the first clinic visit (at 6 weeks) as late recurrence, and these were typically diagnosed either on routine or symptom-driven electrocardiograms, Holter monitoring, or TTM. At each follow-up visit, patients with pacemakers or implantable cardioverter defibrillators had their devices interrogated for atrial high-rate episodes and those with episodes lasting ≥30 seconds in duration were considered to have sustained arrhythmia recurrence.

Classification of Initial Recurrence Type After Ablation

We classified the nature of the first arrhythmia recurrence after index ablation in each patient as either paroxysmal or persistent and also as either AF or OAT. The first arrhythmia recurrence was considered to be paroxysmal in nature if the patient converted spontaneously or with electric cardioversion within 7 days of AF onset. Of note, for patients experiencing sustained arrhythmia recurrence after AF ablation, our practice is to perform cardioversion at the earliest opportunity (typically <48–72 hours) after arrhythmia onset is recognized. All arrhythmia recurrences lasting >7 days were classified as being persistent in nature.
Outcomes of Interest

The primary outcomes of interest included freedom from arrhythmia off AADs, freedom from arrhythmia on or off AADs, and arrhythmia control after last ablation. Freedom from arrhythmia off AADs was defined as the absence of any atrial arrhythmia recurrence (AF or OAT lasting >30 seconds) off all AADs at the last follow-up, whereas freedom from arrhythmia on or off AADs was defined as freedom from AF/OAT either on or off previously ineffective AADs. Arrhythmia control was defined as ≥56 episodes of documented sustained AF/OAT per year, which self-terminated within 24 hours or required no more than one cardioversion per year, on or off AADs.14 We chose to include arrhythmia control as an end point because evaluating AF recurrence as a binary outcome can underestimate the positive impact of ablation in patients with persistent AF who have only rare recurrences or dramatically reduced AF burden after ablation. Outcomes were assessed at each follow-up visit, and failures were recorded time to event since last ablation.

Statistical Analysis

Clinical and demographic characteristics at the time of ablation were aggregated for comparison between AF types using χ² tests for categorical variables and t tests for continuous variables. Results are presented as percentages for categorical measures and mean (SD) for continuous measures. χ² and ANOVA tests were then used to evaluate clinical and demographic predictors of type of arrhythmia recurrence after last ablation (persistent recurrence, paroxysmal recurrence, or no recurrence). Proportional hazards models were used to examine predictors of freedom from arrhythmia off AADs, freedom from arrhythmia on or off AADs, and arrhythmia control after last ablation. The proportional hazards assumption was examined for each predictor before analysis. Multivariable models of long-term outcomes after last ablation was then assembled using univariate predictors with a P value <0.05. Results are presented as hazards ratios indicating the risk of loss of freedom or loss of arrhythmia control associated with each predictor. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC), and a P value <0.05 was considered statistically significant. Bonferroni correction was used to adjust for multiple pairwise comparisons of baseline differences between groups and for predictors of type of arrhythmia recurrence.

Results

Three hundred and seventeen patients participated in the study. These included 200 consecutive patients with persistent and 117 consecutive patients with long-standing persistent AF. Mean age of the entire cohort was 61.2±9.5 years, and 83% were men.

Baseline characteristics among patients with persistent and long-standing persistent AF are reported in Table 1. There were no significant differences in age, sex, or clinical comorbidities among patients with persistent versus long-standing persistent AF. Although those with persistent AF had a smaller mean LA diameter (4.6±0.7 versus 4.8±0.7 cm; P=0.03), this did not reach significance after adjusting for multiple pairwise comparisons. At the index ablation procedure, in addition to PVI, non-PV triggers were identified and targeted for ablation in 36 patients (11%), and a cavotricuspid isthmus line was performed for clinical or inducible typical atrial flutter in 67 patients (21%). Also, lines in the LA (mitral isthmus or roof line) were performed in 26 patients (8%) for clinical or inducible left-sided macroreentrant arrhythmias.

Incidence and Clinical Characteristics of Recurrence After Ablation

A total of 167 patients (53%) had at least one ERAA episode with the initial episode being persistent in nature in 37 patients (22%) and paroxysmal in 130 patients (78%). ERAA type was AF in 151 patients (90%) and OAT in 16 patients (10%). During a median follow-up of 29.8 (14.8–49.9) months from the index ablation (including ERAA episodes within the 6-week blanking period), 221 patients (70%) had at least one arrhythmia recurrence. Of these, 52 arrhythmia recurrences (24%) were persistent and 169 arrhythmia recurrences (76%) were paroxysmal. Of the 169 patients whose first recurrence type was paroxysmal in nature, at the last follow-up (allowing for multiple ablation procedures), 17 (10%) had reverted to persistent AF; whereas 68 (40%) remained as paroxysmal AF, and 84 (50%) were free of any arrhythmia recurrence since their last

Table 1. Association Between Baseline Characteristics and Initial AF Type at Time of Ablation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Persistent (n=200)</th>
<th>LSP (n=117)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, n (%)</td>
<td>162 (81)</td>
<td>166 (83)</td>
<td>0.60</td>
</tr>
<tr>
<td>Age, y, mean (SD)</td>
<td>61.4 (9.9)</td>
<td>60.9 (0.8)</td>
<td>0.62</td>
</tr>
<tr>
<td>Body mass index, kg/m², mean (SD)</td>
<td>31.5 (6.4)</td>
<td>32.0 (6.5)</td>
<td>0.58</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>130 (65)</td>
<td>127 (63.5)</td>
<td>0.75</td>
</tr>
<tr>
<td>Congestive heart failure, n (%)</td>
<td>62 (31)</td>
<td>53 (26.5)</td>
<td>0.32</td>
</tr>
<tr>
<td>Obstructive sleep apnea, n (%)</td>
<td>46 (23)</td>
<td>55 (27.5)</td>
<td>0.30</td>
</tr>
<tr>
<td>Left ventricular EF, %, mean (SD)</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td>0.29</td>
</tr>
<tr>
<td>Left atrial diameter (cm), mean (SD)</td>
<td>4.6 (0.7)</td>
<td>4.8 (0.7)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; EF, ejection fraction; IQR, interquartile range; and LSP, long-standing persistent.

* A P value of 0.005 was used for all comparisons to adjust for multiple pairwise comparisons.
ablation. Including all events, arrhythmia initially recurred as AF in 195 patients (62%) and OAT in 26 patients (8%). In the paroxysmal recurrence group, 108 patients (64%) spontaneously converted, whereas 61 patients (36%) were electrically cardioverted within 7 days of onset. Patients experiencing persistent-type recurrence after index ablation had longer duration of uninterrupted AF preablation compared with those with paroxysmal-type recurrence or no arrhythmia recurrences (24.1±54.2 versus 11.8±18.9 and 10.2±10.0 months; P<0.001).

Assessment of Long-Term Outcomes

During a median follow-up of 29.8 months (interquartile range: 14.8–49.9 months) from the index ablation, 75 patients (24%) from the original cohort underwent 90 repeat ablations (1 repeat procedure in 64, 2 repeat procedures in 9, and 4 repeat procedures in 2). After repeat ablation(s), during a median follow-up of 23.2 months (interquartile range: 12.1–41.1 months) since the last procedure, 177 patients (56%) experienced freedom from AADs, 203 patients (64%) experienced freedom on or off AADs, whereas 265 patients (84%) achieved arrhythmia control (208 [78%] of whom were off AADs). The occurrence of freedom from arrhythmia (both off AADs and on/off AADs) and arrhythmia control were comparable among patients with persistent and long-standing persistent AF.

Baseline clinical and demographic predictors associated with long-term freedom from arrhythmia off AADs after last ablation include male sex (58% versus 41%; P=0.014), congestive heart failure (46% versus 60%; P=0.009), and LA diameter (4.57±0.65 versus 4.79±0.76 cm; P=0.006). Long-term freedom from arrhythmias either on or off AADs was associated with smaller LA diameter (4.60±0.66 versus 4.79±0.76 cm; P=0.01). Arrhythmia control either on or off AADs after last ablation was associated with shorter duration of AF before index ablation (16.6±27.8 versus 11.6±26.2 months; P=0.04), younger age (60±9 versus 63±10 years; P<0.01), and smaller LA diameter (4.6±0.7 versus 4.8±0.8 cm; P=0.01).

Prognostic Implications of Initial Recurrence Type

Persistent initial recurrence type versus paroxysmal type after initial ablation was significantly associated with lack of arrhythmia freedom off AADs during follow-up (Figure 2). After controlling for characteristics found to be significant in the univariable analysis (Table 2), persistent initial recurrence continued to predict lack of freedom off AADs after last ablation (hazard ratio [HR], 2.19; 95% confidence interval [CI],

### Table 2. Risk of Failing to Achieve Long-Term Freedom off AADs After Last Ablation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable, HR (95% CI)</th>
<th>Multivariable, HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of AF before index ablation, mo</td>
<td>1.0 (0.99–1.01)</td>
<td>...</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.60 (0.40–0.90)</td>
<td>0.67 (0.44–1.01)</td>
</tr>
<tr>
<td>Age, y</td>
<td>1.02 (0.99–1.04)</td>
<td>...</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>1.01 (0.99–1.04)</td>
<td>...</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.25 (0.87–1.81)</td>
<td>...</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.59 (1.13–2.26)</td>
<td>1.80 (1.26–2.57)</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>1.16 (0.80–1.68)</td>
<td>...</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>0.99 (0.98–1.01)</td>
<td>...</td>
</tr>
<tr>
<td>Left atrial diameter, cm</td>
<td>1.42 (1.11–1.82)</td>
<td>1.33 (1.05–1.69)</td>
</tr>
<tr>
<td>Persistent vs paroxysmal AF</td>
<td>2.17 (1.49–3.16)</td>
<td>2.19 (1.49–3.21)</td>
</tr>
</tbody>
</table>

AAD indicates antiarrhythmic drug; AF, atrial fibrillation; CI, confidence interval; and HR, hazard ratio.
There is lack of consensus on the optimal ablation strategy for patients with nonparoxysmal AF. Although not proven, it is widely accepted that substrate abnormalities (instead of triggers) underlie nonparoxysmal forms of AF. Thus, many operators have adopted extensive ablation strategies for this patient population. These include empirical linear lesion sets and complex fractionated electrogram ablation. We acknowledge the modest (56%) long-term rates of complete freedom from AF off AADs that was achieved in our study. It can be argued that more extensive ablation approaches may be required to achieve better outcomes for these patients as has been shown in some nonrandomized studies that report higher rates of long-term ablation success using more extensive ablation strategies.15–17 However, in all of these studies, >1 ablation attempt was required to achieve better outcomes. Furthermore, the positive results of these nonrandomized studies have never been reproduced by prospective randomized controlled trials that have consistently failed to demonstrate the benefit of more extensive ablation strategies over PVI in this patient population.2,3

Our study shows that a limited ablation strategy of PVI and ablation of only documented non-PV triggers can favorably alter the arrhythmia behavior in >75% of patients with nonparoxysmal AF. This suggests that PVI and trigger-focused ablation is adequate to modify the underlying substrate in patients with nonparoxysmal AF and provides further evidence that excessive ablation may not be necessary.

Implications of Transformation From Nonparoxysmal to Paroxysmal Atrial Fibrillation

In our study, those patients whose AF nature transformed from nonparoxysmal to paroxysmal after initial ablation had significantly better long-term outcomes after ≥1 ablation attempts, suggesting that the transformation to paroxysmal AF may indicate favorable remodeling of the underlying substrate responsible for the maintenance of AF in addition to eliminating triggers. It is interesting that among patients whose first

### Table 3. Risk of Failing to Achieve Long-Term Freedom Either on or off AADs After Last Ablation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable, HR (95% CI)</th>
<th>Multivariable, HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of AF before index ablation, mo</td>
<td>1.00 (0.99–1.01)</td>
<td>...</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.91 (0.56–1.49)</td>
<td>...</td>
</tr>
<tr>
<td>Age, y</td>
<td>1.02 (1.00–1.05)</td>
<td>...</td>
</tr>
<tr>
<td>Body mass index, kg/m^2</td>
<td>1.02 (0.99–1.05)</td>
<td>...</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.23 (0.82–1.84)</td>
<td>...</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.44 (0.97–2.13)</td>
<td>...</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>1.31 (0.87–1.97)</td>
<td>...</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>0.99 (0.98–1.01)</td>
<td>...</td>
</tr>
<tr>
<td>Left atrial diameter, cm</td>
<td>1.42 (1.08–1.86)</td>
<td>1.24 (0.95–1.60)</td>
</tr>
<tr>
<td>Persistent vs paroxysmal AF recurrence after index ablation</td>
<td>2.59 (1.71–3.90)</td>
<td>2.46 (1.63–3.72)</td>
</tr>
</tbody>
</table>

AAD indicates antiarrhythmic drug; AF, atrial fibrillation; CI, confidence interval; and HR, hazard ratio.

### Table 4. Risk of Failing to Achieve Long-Term Arrhythmia Control Either on or off AADs After Last Ablation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable, HR (95% CI)</th>
<th>Multivariable, HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of AF before index ablation, mo</td>
<td>1.01 (1.00–1.01)</td>
<td>1.00 (0.99–1.01)</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.04 (0.49–2.21)</td>
<td>...</td>
</tr>
<tr>
<td>Age, y</td>
<td>1.05 (1.02–1.09)</td>
<td>1.05 (1.01–1.09)</td>
</tr>
<tr>
<td>Body mass index, kg/m^2</td>
<td>1.02 (0.98–1.06)</td>
<td>...</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.13 (0.63–2.04)</td>
<td>...</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.09 (0.60–2.0)</td>
<td>...</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>1.33 (0.74–2.41)</td>
<td>...</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>1.01 (0.99–1.04)</td>
<td>...</td>
</tr>
<tr>
<td>Left atrial diameter, cm</td>
<td>1.57 (1.11–2.23)</td>
<td>1.23 (0.91–1.67)</td>
</tr>
<tr>
<td>Persistent vs paroxysmal AF recurrence after index ablation</td>
<td>5.86 (3.35–10.23)</td>
<td>5.15 (2.90–9.17)</td>
</tr>
</tbody>
</table>

AAD indicates antiarrhythmic drug; AF, atrial fibrillation; CI, confidence interval; and HR, hazard ratio.

### Discussion

In patients with persistent and long-standing persistent AF undergoing an ablation strategy focused on PVI and targeting of documented non-PV triggers, initial arrhythmia recurrences in the majority of patients were as paroxysmal AF, and patients experiencing paroxysmal-type recurrences had better long-term arrhythmia outcomes compared with those whose initial recurrence was persistent type. Our observations suggest that a limited initial ablation approach can favorably modify the underlying mechanisms responsible for arrhythmia maintenance in patients with persistent and long-standing persistent AF.
recurrence was paroxysmal in nature, long-term outcomes were similar between patients whose arrhythmia converted spontaneously versus those requiring cardioversion within 7 days of arrhythmia onset. Our findings would suggest that even in patients whose recurrence might have become persistent without cardioversion, early termination of arrhythmia may modify underlying AF mechanisms favorably to support sinus rhythm maintenance in the long term. Consistent with our findings, Baman et al. have shown that early cardioversion for recurrent AF is associated with improved long-term ablation success.

In patients with nonparoxysmal forms of AF, transformation to paroxysmal AF after ablation may have several important consequences. Change to paroxysmal AF decreases total AF burden that allows for LA remodeling. Lo et al. examined electrophysiological findings in patients with nonparoxysmal AF undergoing ablation with a stepwise approach and found that overall LA bipolar voltage increased, total area of low voltage (<0.5 mV) decreased, and total LA volume decreased in patients whose arrhythmia recurrence had been transformed to paroxysmal AF compared with those who recurred as persistent AF. Although in the current study, we did not assess and compare bipolar voltage abnormalities during the initial and repeat ablation procedures, we have previously shown that after PVI, patients who remain arrhythmia free experience favorable atrial and even ventricular remodeling.

It remains unclear as to what may be the mechanism underlying favorable LA remodeling in our study population. Because the end point of our strategy is PVI and ablation of non-PV AF triggers, it can be argued that decreasing the number of AF triggers transformed the nature of AF from persistent to paroxysmal. Consistent with this hypothesis, in patients experiencing AF recurrence that underwent repeat ablation, isolating the reconnected veins alone in the majority was sufficient to achieve long-term arrhythmia control. However, because we perform antral PVI, it is possible that this may result in substrate modification. We have previously shown that antral PVI can attenuate the distribution of complex fractionated electrograms both in PV and non-PV regions. Other investigators have demonstrated alteration of spectral characteristics of AF and attenuation of LA dominant frequency distributions after PVI. Furthermore, the wide circumferential lesion set used during antral PVI may have modified ganglionic plexi. In addition, a wide circumferential antral approach can compartmentalize the LA, thus potentially reducing the critical tissue mass required for the maintenance of persistent and meandering rotors.

The first AF recurrence type was analyzed in this study rather than ultimate AF recurrence type because in patients with persistent or long-standing persistent AF, the atria may need time to remodel after ablation (electrically, anatomically, and mechanically). Thus, any PV or non-PV triggers initiating paroxysmal recurrences after ablation may be more likely to become persistent in the presence of adversely primed atria, which have not been given ample time to readapt to sinus rhythm after ablation. These patients may represent a subgroup in whom early intervention with repeat ablation (even within the blanking period) might maximize the potential for favorable LA remodeling and maintenance of sinus rhythm. In our study, only 24% of patients underwent >1 ablation procedure and 11 patients (3.5%) underwent >2 ablation procedures. The modest rate of long-term freedom off AADs after ablation in our study may be because of the small proportion of patients who chose to undergo repeat ablation. Although we did not assess for AF burden or quality of life after ablation, one possible explanation for the low rates of repeat ablation was that after the initial procedure, the majority of patients were satisfied with the achievement of arrhythmia control. The low rates of occurrence of OAT postablation (which tend to be more symptomatic than AF) may be an additional reason for the lower frequency of repeat ablation in our series. Among those patients who underwent repeat ablation, ≥1 PVs had reconnected in the majority, and isolating the reconnected PVs resulted in long-term freedom from arrhythmias. This observation would suggest that in patients with persistent and long-standing persistent AF, after initial wide-area antral PVI, the nature of AF frequently changes to paroxysmal, and these recurrences are largely mediated by PV reconnection.

Limitations
We acknowledge that this is a retrospective, single-center, observational study. Importantly, to maximize long-term follow-up, we selected patients who underwent ablation from 2008 to 2012, and there was nonuniform use of JET ventilation and steerable sheath technology. Because we have not routinely assessed for symptom or arrhythmia burden systematically postablation, we are unable to quantify the relationship between symptoms with transformation of persistent to paroxysmal AF. Some patients from our study cohort preferred to continue their follow-up beyond 1 year after the ablation with their referring cardiologists. In these patients we had to rely on outcome data beyond 1 year post ablation though office visit notes from the referring physicians. We did, however, attempt to validate long-term outcomes in these patients by regular telephone follow-up by our research coordinators. Because guidelines do not specify a duration cutoff for cardioversion to delineate paroxysmal versus persistent arrhythmia recurrences after ablation, we chose to include patients who underwent cardioversion within 7 days as paroxysmal. However, it is possible that recurrences that were treated with cardioversion may have otherwise become persistent. Although we included several commonly accepted risk factors for recurrence after AF ablation in our analysis, we acknowledge that there may have been additional risk factors (ie, alcohol use, cardiorespiratory fitness, hyperthyroidism, epicardial fat, etc) that were not included in our analysis. The incidence of OAT after limited ablation is low, and we were unable to assess the predictive value of intraprocedural conversion to sinus rhythm on long-term ablation success, and we want to acknowledge that our findings may not be applicable to patients who have undergone AF ablation using more extensive ablation approaches. We also recognize the lower rate of repeat ablation in our study, which may be a reflection of patient preference and referring or operating physician bias.

Conclusions
In the majority of patients with persistent and long-standing persistent AF, an ablation strategy focused on achieving
lasting PVI and targeting of documented non-PV triggers is adequate to modify the underlying AF substrate and transform the nature of arrhythmia recurrence. After initial ablation, arrhythmia recurrences in the majority of patients are paroxysmal AF, and these result primarily from reconnection across one or more previously isolated veins. Isolating reconnected PVs can result in long-term freedom from further arrhythmia recurrences. Our findings suggest that triggers may play an important role in the majority of nonparoxysmal forms of human AF.

Disclosures

None.

References


Pulmonary Vein Antral Isolation and Nonpulmonary Vein Trigger Ablation Are Sufficient to Achieve Favorable Long-Term Outcomes Including Transformation to Paroxysmal Arrhythmias in Patients With Persistent and Long-Standing Persistent Atrial Fibrillation

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