Background—Rapid pulmonary vein (PV) activity has been shown to maintain paroxysmal atrial fibrillation (AF). We evaluated in persistent AF the cycle length (CL) gradient between PVs and the left atrium (LA) in an attempt to identify the subset of patients where PVs play an important role.

Methods and Results—Ninety-seve consecutive patients undergoing first ablation for persistent AF were studied. For each PV, the CL of the fastest activation was assessed over 1 minute (PV\text{fast}) using Lasso recordings. The PV to LA CL gradient was quantified by the ratio of PV\text{fast} to LA appendage (LAA) AF CL. Stepwise ablation terminated AF in 73 patients (75%). In the AF termination group, the PV\text{fast} CL was much shorter than the LAA CL resulting in lower PV\text{fast}/LAA ratios compared with the nontermination group (71±10% versus 92±7%; \(P<0.001\)). Within the termination group, PV\text{fast}/LAA ratios were notably lower if AF terminated after PV isolation or limited adjunctive substrate ablation compared with patients who required moderate or extensive ablation (63±6% versus 75±8%; \(P<0.001\)). PV\text{fast}/LAA ratio <69% predicted AF termination after PV isolation or limited substrate ablation with 74% positive predictive value and 95% negative predictive value. After a mean follow-up of 29±17 months, freedom from arrhythmia recurrence off-antiarrhythmic drugs was achieved in most patients with PV\text{fast}/LAA ratios <69% as opposed to the remaining population (80% versus 43%; \(P<0.001\)).

Conclusions—The PV to LA CL gradient may identify the subset of patients in whom persistent AF is likely to terminate after PV isolation or limited substrate ablation and better long-term outcomes are achieved. (Circ Arrhythm Electrophysiol. 2014;7:473-482.)

Key Words: atrial fibrillation ■ cardiac electrophysiology ■ pulmonary veins

Clinical Perspective on p 482

Previous clinical studies have demonstrated that intermittent rapid rhythms arising in the PVs are commonly observed during sustained episodes of paroxysmal AF. These rapid activities were identified when the cycle length (CL) recorded inside the PV was shorter than the AF CL recorded in the adjacent left atrium (LA)\(^6\) or when a clustering of shorter CL was observed on the plotted frequency histogram of the PV activity.\(^7\) These studies demonstrated that intermittent rapid PV rhythms represent an active phenomenon that may have a critical role in the maintenance of AF by providing a continued refueling of the fibrillatory process.\(^6,7\) Whether the identification of such PV activities can help characterize the contribu- tion of PVs in the maintenance of persistent AF has not been addressed. We hypothesized that a high gradient between the CL of PV activity and the LA AF CL would identify patients where PVs play an important role, whereas the absence of
such a gradient would point toward passive PV activity. We, therefore, aimed to evaluate if this CL gradient would predict (1) procedural AF termination, (2) AF termination with PVI only, and (3) postablation clinical success.

Methods

Study Population
The study population consisted of consecutive patients who underwent first-time catheter ablation for symptomatic drug-refractory persistent AF. AF was defined as persistent (sustained >7 days or lasting <7 days but necessitating cardioversion) or long-lasting persistent (continuous AF of >1 year duration). All patients were in AF spontaneously at the beginning of the procedure and had PV mapping with a circumferential catheter before ablation. To evaluate the contribution of PV activity to the maintenance of AF, only patients in whom isolation of all PV’s was completed before starting substrate-based ablation were included.

All patients provided written informed consent.

Electrophysiological Study
Antiarrhythmic medication was discontinued ≥25 half-lives before ablation, with the exception of amiodarone. Before the procedure, all patients were receiving oral anticoagulation therapy for ≥1 month, and transthoracic echocardiography was performed <48 hours before the procedure to exclude atrial thrombi.

Surface electrocardiograms and bipolar intracardiac electrograms were monitored continuously and stored on a computer-based digital amplifier/recorder system (Labsystem Pro; Bard Electrophysiology, Lowell, MA). Signals were band pass–filtered as follows: ECGs from 0.1 to 50 Hz; PV electrograms from 100 to 250 Hz; other intracardiac electrograms recorded at adjacent sites (Figure 1B). In such cases, the shortest CL of each fascicle was considered for analysis. To derive the maximum difference in CL between PVs and the LA CL, the lowest value of the 4 PVs was considered for analysis for both the mean CL and the CL of the fastest PV activation (PVmean and PVfast, respectively).

Follow-Up
All patients were monitored in hospital for 3 to 5 days postprocedure. Antiarrhythmic drugs (AADs) were discontinued 3 months after the index procedure in the absence of a continued indication. Patients were re-evaluated at 1, 3, 6, 9, and 12 months, and in the absence of AF or symptoms, followed up with their referring physician. At each visit, ambulatory 24- to 48-hour monitoring was performed to detect asymptomatic arrhythmias. One year from the last procedure, patients were seen every 6 months by their referring cardiologist. All patients underwent 24-hour Holter monitoring within the last 3 months of follow-up. In the event of arrhythmia recurrence, patients were offered a trial of drug therapy and then additional ablation. As for the index procedure, the sequential stepwise ablation was performed with the end point of AF termination.

Clinical Outcome
Success after first procedure was defined as maintenance of sinus rhythm (absence of symptomatic and asymptomatic AF or AT) during follow-up after the index ablation, with a postprocedural blanking period of 3 months. Success after the last procedure was defined as maintenance of sinus rhythm after the last ablation with or without AADs with a postprocedural blanking period of 3 months.

Statistical Analysis
Continuous variables are presented as arithmetic mean±SD or median with interquartile range where indicated. Categorical variables are expressed as absolute numbers and percentages. Categorical variables were compared with the χ² test or the Fisher exact test, and continuous variables with the unpaired Student t test or the Mann–Whitney test, as appropriate. One-way ANOVA test was used to compare values between groups categorized according to the extent of substrate-based ablation needed to terminate AF. Diagnostic performance of predictors...
of AF termination was evaluated by receiver-operator characteristic analysis. The optimal cutpoint was chosen as the combination with the highest sensitivity and specificity. To analyze independent predictive factors of AF termination during ablation, and independent factors of clinical success, univariate factors presenting a $P$ value $<0.1$ were analyzed using logistic regression (multivariate analysis). Candidate covariates for adjustment were age, duration of continuous AF, LA dimensions, structural heart disease, ejection fraction, hypertension, and amiodarone use. Cumulative event rates (recurrence of arrhythmia) were calculated according to the Kaplan–Meier method, and the log-rank test was used to detect significant differences between groups. All tests were 2-tailed, and statistical significance was assumed for $P$ values $<0.05$. Statistical analysis was performed using the software SPSS, 17.0 (SPSS, Inc, Chicago, IL).

## Results

A total of 97 consecutive patients were studied. The baseline characteristics of the patient population are presented in Table 1. The mean age was $58\pm11$ years and 81% were men.

### Table. Clinical Characteristics of the Study Population

<table>
<thead>
<tr>
<th></th>
<th>Total (n=97)</th>
<th>AF Termination Group (n=73)</th>
<th>AF Nontermination Group (n=24)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>58±11</td>
<td>56±10</td>
<td>64±9</td>
<td>0.001</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>81</td>
<td>85</td>
<td>71</td>
<td>0.123</td>
</tr>
<tr>
<td>History of AF, mo</td>
<td>74±63</td>
<td>75±66</td>
<td>70±51</td>
<td>0.726</td>
</tr>
<tr>
<td>Duration of continuous AF, mo</td>
<td>19±21</td>
<td>16±17</td>
<td>28±28</td>
<td>0.025</td>
</tr>
<tr>
<td>Long-lasting persistent AF, %</td>
<td>58</td>
<td>53</td>
<td>71</td>
<td>0.134</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>56±14</td>
<td>56±13</td>
<td>53±15</td>
<td>0.363</td>
</tr>
<tr>
<td>LV dysfunction (LVEF &lt;50%), %</td>
<td>26</td>
<td>25</td>
<td>29</td>
<td>0.661</td>
</tr>
<tr>
<td>LA diameter, mm</td>
<td>46±7</td>
<td>46±7</td>
<td>48±7</td>
<td>0.128</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>41</td>
<td>37</td>
<td>54</td>
<td>0.138</td>
</tr>
<tr>
<td>Structural heart disease, %</td>
<td>40</td>
<td>37</td>
<td>50</td>
<td>0.259</td>
</tr>
<tr>
<td>Number of failed AAD</td>
<td>1.9±0.9</td>
<td>2.0±0.9</td>
<td>1.9±1.2</td>
<td>0.755</td>
</tr>
<tr>
<td>Administration of amiodarone, %</td>
<td>45</td>
<td>41</td>
<td>58</td>
<td>0.141</td>
</tr>
</tbody>
</table>

AAD indicates antiarrhythmic drugs; AF, atrial fibrillation; LA, left atrial; and LVEF, left ventricular ejection fraction.
The mean duration of continuous AF was 19±21 months (median, 12 months; interquartile range, 6–24 months).

**Procedural Termination of AF**

AF was terminated by catheter ablation in 73 of 97 patients (75%), whereas in the remaining 24 patients (25%), AF could not be terminated and required electric cardioversion. Baseline LAA CL was comparable between the termination and nontermination group (156±29 versus 161±24, respectively; \(P=0.34\)).

**PV Activity of CL and Procedural Termination of AF**

At baseline, the lowest mean CL of the 4 PVs (PV\text{mean}) did not significantly differ between patients with AF termination compared with patients without termination (157±27 versus 166±34 ms; \(P=0.186\); Figure 2A). On the contrary, the fastest recorded PV CL (PV\text{fast}) was significantly shorter in patients with AF termination compared with those in whom AF could not be terminated (114±23 versus 143±31 ms; \(P<0.001\)). There was, however, a notable overlap of values between the 2 groups (Figure 2B). Nonetheless, fast PV activities were rarely observed in patients in whom AF could not be terminated by ablation. A cut-off value, PV\text{fast} ≤110 ms, predicted AF termination with 95% positive predictive value (sensitivity 53%, specificity 92%, negative predictive value 39%). The fastest PV CL was recorded in the left superior PV in 39% of patients, the left inferior PV in 24%, the right superior PV in 21%, and the right inferior PV in 15%. Figure 3 displays an example of the baseline LAA and PV recordings from a 45-year-old man with continuous AF duration of 8 months.

**PV to LA CL Gradient and Procedural AF Termination**

The gradient between the fastest PV activity and the LA AF CL (PV\text{fast}/LAA ratio) showed a limited overlap of values between the AF termination and the nontermination group (Figure 3C). In the nontermination group, the PV\text{fast} CLs were similar to the LAA CLs resulting in a mean PV\text{fast}/LAA ratio of 92±7%.

On the contrary, the PV\text{fast} CLs were much shorter than the LAA CLs and resulted in a significantly lower PV\text{fast}/LAA ratio (ie, higher gradient) of 71±10% (\(P<0.001\)) in the AF termination group. The receiver-operator characteristic curve analysis of the PV\text{fast}/LAA ratio yielded an optimal cut-off value ≤85% to predict AF termination with an area under the curve of 0.968 (95% confidence interval [CI], 0.922–1.000; \(P<0.001\); Figure 4A). PV\text{fast}/LAA ratio ≤85% provided a 96% positive predictive value, 91% negative predictive value, 97% sensitivity, and 88% specificity for AF termination.

**Predictors of Procedural AF Termination**

The preprocedural clinical variables were compared in patients in whom AF terminated by catheter ablation versus those in whom AF could not be terminated. AF termination was associated with a younger age (56±10 versus 64±9 years; \(P=0.001\)), a shorter duration of continuous AF (16±17 versus 28±28 months; \(P=0.025\)), and a nonsignificant trend toward smaller LA dimensions (46±7 versus 48±7 mm; \(P=0.13\)). Using a stepwise logistical regression technique incorporating preablation clinical and procedural variables, only the PV\text{fast}/LAA ratio independently predicted AF termination (adjusted odds ratio [OR], 0.691; 95% CI, 0.580–0.823; \(P<0.001\)).

**PV to LA CL Gradient: Ablation Time to AF Termination and Mode of Termination**

AF terminated during PVI in 11 patients (11%), whereas in the remaining 62 patients (64%), AF terminated during the electrogram-guided or linear ablation steps. In the latter group, the additional (after PVI) procedural and ablation times were 64±3 minutes (median, 54; interquartile range, 30–90) and 34±21 minutes (median, 30; interquartile range, 19–45), respectively.

In the AF termination group, the PV\text{fast}/LAA ratio was compared between patients in whom AF terminated during PVI (PVI term) versus those who required adjunctive substrate-based ablation to terminate AF. The extent of substrate-based ablation was further categorized according to the quartiles of ablation time needed to terminate AF after completion of PVI. Limited or extensive substrate-based ablation was defined as the lowest and highest quartiles, whereas moderate ablation was defined as the interquartile range of ablation time. In patients with AF termination during PVI, the PV\text{fast} CLs were much shorter than the LA AF CL with a mean PV\text{fast}/LAA ratio of 63±6% (Figure 5). A similar PV to LA CL gradient was found in the group of patients with AF termination after limited substrate ablation (PV\text{fast}/LAA ratio, 63±6%; \(P=0.995\)). In both groups, the PV\text{fast}/LAA ratios were notably lower compared with that in the patients where moderate or extensive substrate ablation was required. The mean PV\text{fast}/LAA ratio was 74±8% in patients with AF termination after moderate substrate ablation (\(P=0.001\) versus PVI term and \(P<0.001\) versus limited substrate ablation) and 79±7% in those with AF termination after extensive substrate ablation (\(P=0.001\) versus each of PVI term and limited substrate ablation). The receiver-operator characteristic curve analysis to discriminate patients with AF termination after PVI or limited substrate ablation from those who required more substantial ablation yielded an optimal cut-off value <69% with an area under the curve of 0.921 (95% CI, 0.867–0.975; \(P<0.001\); Figure 4B). A PV\text{fast}/LAA ratio <69% provided a 74% positive predictive value, 95% negative predictive value, 88% sensitivity, and 89% specificity for AF termination after PVI or limited additional substrate ablation.

The PV to LA CL gradient was also evaluated with respect to the mode of AF termination. AF terminated after an intermediate step of AT in 52 patients (71%) and directly into sinus rhythm in the remaining 21 (29%). Termination into sinus rhythm was associated with significantly lower PV\text{fast}/LAA ratios when compared with termination into an AT (66±10% versus 73±9%; \(P=0.005\)).

**Predictors of AF Termination After PVI or Limited Substrate Ablation**

The preprocedural clinical variables were compared between patients in whom AF terminated after PVI or limited additional...
substrate ablation and those who required more than limited substrate ablation to terminate AF. AF termination with no or limited substrate ablation was associated with younger age (53±9 versus 60±11 years; P=0.014), shorter duration of continuous AF (10±8 versus 22±23 months; P=0.016), and lower prevalence of structural heart disease (19% versus 48%; P=0.014). In the multivariate analysis incorporating preablation clinical and procedural variables, both the PVfast/LAA ratio (adjusted OR, 0.772; 95% CI, 0.688–0.866; P<0.001) and the presence of structural heart disease (adjusted OR, 0.071; 95% CI, 0.012–0.438; P=0.004) independently predicted termination of AF with PVI only or limited additional substrate ablation.

Follow-Up and Clinical Outcome
Two patients were lost to follow-up after the initial procedure. After a mean follow-up of 36±18 months, freedom from atrial arrhythmia was achieved in 34 patients (36%) after a single ablation procedure with or without AADs. Among the patients who presented with recurrent arrhythmia, 38% were in persistent AF, 12% in paroxysmal AF, and the remaining 50% were in AT (persistent or paroxysmal). Recurrence in persistent AF was more often observed in the nontermination group compared with the termination group (52% versus 18%; P=0.001).

A repeat ablation procedure was performed in 41 out of 61 patients with arrhythmia recurrence. Ten patients underwent >2 procedures. After 1.6±0.7 procedures and a mean follow-up of 29±17 months from the last procedure, the overall success rate was 71% (including 21% on AADs; n=20). Long-term clinical success was higher in patients with AF termination during the index procedure (81%; 28% taking AADs) compared with the nontermination group (39%; P<0.001; 44% taking AADs).

PV Activity to LA CL Gradient and Long-Term Clinical Outcome
In patients with a PVfast/LAA ratio >85%, freedom from atrial arrhythmias after the last procedure was achieved only in 41%
of cases (44% taking AADs) against 80% (29% taking AADs) in patients with a ratio ≤85% (P<0.001).

With regard to the subgroup of patients with PV\textsubscript{fast}/LAA ratio <69%, the arrhythmia-free survival after the last procedure with or without AADs was superior when compared with the remaining population (84% versus 64%; P=0.049). A ratio <69% provided additional outcome stratification over an 85% cut-off as, among the patients without arrhythmia recurrence, only 8% were on AADs compared with 44% in the subgroup with a 69% to 85% PV\textsubscript{fast}/LAA ratio (P=0.002). Therefore, even among the patients with a more favorable outcome (ie, with PV\textsubscript{fast}/LAA ratio ≤85%), a higher clinical success rate off-AADs was observed in patients with a ratio <69% compared with those with a 69% to 85% ratio (80% versus 55%);

**Figure 3.** Baseline tracings of the LAA and 4 PVs from a 45-year-old man with continuous AF for 8 months. **Left.** The fastest recorded PV activities observed over a 1-min observation window are illustrated for each vein. Far-field LAA activity is apparent in the left superior PV (asterisks). Rapid PV activities are observed in all 4 PVs, the fastest being recorded in the left inferior PV (PV\textsubscript{fast}, 82 ms). Of note, these fast activities occur as intermittent bursts that are separated by slow PV rhythm (slower than the LAA AF CL). The mean PV CLs (averaged on 100 beats) are lowest in the right superior PV (PV\textsubscript{mean}, 154 ms). Although no gradient of CL is observed between the PV\textsubscript{mean} and the LAA CL, the PV\textsubscript{fast} CL is much lower than the LAA CL (PV\textsubscript{fast}/LAA ratio, 57%). The high PV to LAA CL gradient alternating with periods of slow PV rhythm (gradient inversion) both suggested intermittent active PV firing. **Right.** Catheter ablation terminated AF after PV isolation, during the second min of radiofrequency application for adjunctive substrate-based ablation. AF indicates atrial fibrillation; CL, cycle length; LAA, left atrial appendage; and PV, pulmonary vein.

**Figure 4.** Procedural outcome according to the PV\textsubscript{fast} to left atrial AF CL gradient. Receiver-operating characteristic curve analysis of the PV\textsubscript{fast}/LAA ratio to predict (A) AF termination during stepwise ablation and (B) AF termination with only PV isolation or limited substrate-based ablation (first quartile of ablation time). Arrows show optimal cut-off point for sensitivity and specificity. AF indicates atrial fibrillation; CI, confidence interval; CL, cycle length; LAA, left atrial appendage; and PV, pulmonary vein.
Also, among the patients with arrhythmia recurrence, paroxysmal forms of AF were more often observed in the subgroup with PV_{fast}/LAA ratio <69% than in the rest of the study population (25% versus 6%; \(P=0.032\); Figure 6). Figure 7 displays Kaplan–Meier arrhythmia-free survival curves stratified according to PV_{fast}/LAA cut-off values.

**Predictors of Success After the Last Ablation Procedure**

In comparison with the patients with recurrent arrhythmias, patients who remained in stable sinus rhythm after the last procedure were younger (56±10 versus 63±9 years; \(P=0.002\)), had lower LA dimension (45±6 versus 50±7 mm; \(P=0.003\)).
and a trend toward shorter duration of continuous AF (16±17 versus 26±28 months; \( P = 0.056 \)). In the multivariate analysis incorporating preablation clinical and procedural variables, both the PV\textsubscript{fast}/LAA ratio (adjusted OR, 0.939; 95% CI, 0.899–0.981; \( P = 0.004 \)) and the LA dimension (adjusted OR, 0.905; 95% CI, 0.840–0.974; \( P = 0.008 \)) independently predicted long-term freedom from recurrent arrhythmia.

Discussion

Main Findings

The present study evaluated whether the analysis of the PV activity in relation to the atrial AF CL could help stratify the procedural and long-term outcome of patients undergoing persistent AF ablation. The major findings of this study are: (1) the occurrence of intermittent rapid activity within the PVs, but not their mean CL, helps characterize the contribution of PVs to the maintenance of persistent AF; (2) a high CL gradient between the fastest recorded PV activity and the AF CL (PV\textsubscript{fast}/LAA ratio <69%) identifies patients in whom AF is likely to terminate after PVI or limited additional substrate ablation; (3) the absence of substantial gradient between the fastest PV activity and the AF CL (PV\textsubscript{fast}/LAA ratio >85%) identifies patients in whom AF is unlikely to terminate by ablation and the long-term success is limited.

Markers and Role of PV Activity in Persistent AF

There has been an accumulating body of evidence demonstrating that PVs play an important role in a subset of patients with persistent AF. Our group previously showed that the PVs were the dominant triggers reinitiating chronic AF after cardioversion (94%), and their ablation resulted in sinus rhythm maintenance in a significant proportion of patients. More recently, Inoue et al\(^5\) observed reproducible immediate recurrences of AF after cardioversion in 27% of 263 patients with persistent AF. The triggers reinitiating AF originated mostly from the PVs (81%). The role of the reinitiating triggers in the persistence of AF was demonstrated by the strong influence of their successful elimination on clinical outcome. These findings support the hypothesis that PV activity may be elevated enough to trigger repetitive paroxysmal AF episodes before the preceding one terminates leading to persistent AF. The role of PV is further supported by the evidence that a substantial proportion of patients can achieve stable long-term sinus rhythm off-AAD after PVI only even in longstanding persistent AF.\(^{11,12}\) The challenge however remains to identify during ongoing AF that subgroup of patients with persistent AF where PVs play a major role. Previous studies including mostly patients with paroxysmal AF have shown that intermittent rapid PV activities during sustained AF were recorded from the same PVs that exhibited arrhythmogenic foci that triggered AF during sinus rhythm.\(^7\) The likelihood of inducing persistent AF by rapid pacing was markedly diminished after the elimination of the intermittent bursts of PV tachycardia. Moreover, the probability of AF termination during isolation of a PV was directly related to the extent of tachycardia recorded in that vein.\(^6,8\) These observations suggest that the PVs are not only a source of the triggers that initiate AF but may also have a role in the maintenance of AF. This has been further corroborated by the observation that isolation of each PV in patients with sustained paroxysmal AF episodes was associated with a gradual slowing of the fibrillatory process that culminated in the termination of AF.\(^{13}\) Intermittent bursts of PV tachycardia may maintain AF in the same way as intermittent bursts of rapid pacing do prevent the tendency toward spontaneous conversion of experimental pacing induced AF.\(^{14}\)
AF. We could demonstrate that the recording of a significant CL gradient between PV activity and the LA AF CL allowed to discriminate patients whose AF was likely to terminate with PVI only or limited additional substrate ablation. Moreover, long-term freedom from arrhythmia recurrence was achieved in most of these patients as opposed to the rest of the study population. Also, both termination of AF directly to sinus rhythm and recurrences in paroxysmal AF were more often observed. Both findings further suggest a trigger-dependent mechanism of AF persistence as opposed to one based on advanced changes in the substrate.

On the contrary, the absence of a significant gradient between the fastest PV and the AF CL pointed toward passive PV activity. Indeed, we observed that procedural AF termination could not be achieved in most of these patients or required extensive substrate modification. A passive role of PVs was further suggested by the limited long-term success rate achieved despite PVI. In these patients, the mechanism underlying AF persistence was likely attributable to advanced atrial substrate changes.

Role of PV in Patients With AF Termination After Limited Additional Substrate Ablation

It is usually considered that termination of AF after limited additional defragmentation is a direct effect of the early identification of critical AF targets located outside the PVs. However, these patients could be specifically discriminated from the rest of the study population based on the identification of rapid PV rhythms in the same way as those with AF termination during PVI. Therefore, our findings reinforce the major role of PVs in these patients although limited substrate-based modification could still be required to achieve AF termination.

It has been shown experimentally that the longer AF has been present for, the longer artificially induced AF paroxysms last.14 Therefore, one can reasonably assume that in persistent forms of AF, a certain period of latency is likely before AF terminates once critical targets have been ablated. This may also explain why AF failed to terminate during PVI in some of the patients with a high PV to LA CL gradient. Consistent with the latency assumption is the observation that sinus rhythm restoration occurred well after the cessation of radiofrequency application rather than during ongoing ablation in more than one third of the study population (37%). These considerations raise the question whether adjunctive substrate-based ablation was indeed warranted to achieve similar long-term outcome in patients demonstrating high PV to LA CL gradients.

Importance of Sampling Time During PV Activity Evaluation

Studies performing spectral analysis and frequency mapping during AF have demonstrated the ability to localize the sites of rapid and periodic activity closely linked to the sources that maintain AF.15-18 These studies consistently demonstrated that these dominant frequency sources of activity often emanated from the PV region in paroxysmal AF.15,19-21 On the contrary, in patients with persistent AF, the PVs were less likely to harbor sites of high frequency. However, these studies were based on recordings of a few seconds or averaged in sliding windows over 20 to 30 seconds. The assumed temporal stability of the AF activity underlying this methodology is challenged by our findings. Our data indicate that the occurrence of intermittent rapid activity within the PVs, but not their average CL, could help characterize their contribution to AF persistence. The assessment of the fastest recorded PV activity over a 1-minute observation window allowed to detect these episodic burst phenomena that would have otherwise been missed with shorter or averaged recording intervals. The periodicity of these rapid repetitive activities may be as low as 1 per minute and they may occur in temporal clusters of less than 5 seconds.7,8 It is plausible that longer recording intervals may be required in remodeling atria with persistent AF where less frequent rapid PV activity may suffice to sustain AF as opposed to paroxysmal AF episodes where more constant refueling of the fibrillatory process is required.

Study Limitations

This study primarily makes a novel observation and infers a causal link between intermittent rapid PV activities and AF maintenance based on the ablation outcome. However, the assumption that these rapid PV activities actually represented an active phenomenon was not systematically demonstrated by the simultaneous recording of a slower AF CL in the adjacent LA. It is possible that these rapid rhythms were sometimes caused by fractionation of wavefronts entering the PV from the LA instead of by paroxysmal burst of tachycardia generated within the vein.

Moreover, although a relationship between rapid PV rhythms and ablation outcome was demonstrated, their role has not been established by this observational study. Whether these repetitive activities act as triggers of AF or contribute to sustain episodes triggered outside PVs remains to be determined.

Conclusions

An attentive monitoring of the PV activity in relation to the atrial AF CL may discriminate patients in whom AF is likely to terminate after PVI or limited substrate ablation from those in whom AF is unlikely to terminate by ablation and long-term success is limited. By providing the tool to identify the subset of patients where PVs still play an important role in AF persistence, these findings may be a step toward more tailored ablation strategies.

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Disclosures

None.

References

Pulmonary vein (PV) triggers play a major role in the initiation of atrial fibrillation (AF), and PV isolation is the cornerstone of catheter ablation for paroxysmal AF. The success of this approach is limited in nonparoxysmal forms of AF, and adjunctive ablation strategies have been developed to target the alterations in the underlying substrate that may perpetuate AF. Nonetheless, the mechanisms underlying AF persistence are not uniform, and a trigger-based mechanism may be operative in a subset of patients. Identifying these patients remains a challenge. Intermittent rapid rhythms arising in the PVs are commonly observed during sustained episodes of paroxysmal AF. These rapid activities represent an active phenomenon that may have a critical role in the maintenance of AF by providing continued refueling of the fibrillatory process. We therefore evaluated persistent AF to identify the cycle length gradient between PVs and the left atrium in an attempt to identify patients where PVs play an important role. Our study demonstrates that an attentive monitoring of the PV activity in relation to the atrial AF CL may discriminate patients in whom AF is likely to terminate after PV isolation or limited substrate ablation from those in whom AF is unlikely to terminate by ablation and long-term success is limited. By providing the tool to identify the subset of patients in whom the PVs still play an important role in AF persistence, these findings may be a step toward more tailored ablation strategies.

**CLINICAL PERSPECTIVE**

Pulmonary vein (PV) triggers play a major role in the initiation of atrial fibrillation (AF), and PV isolation is the cornerstone of catheter ablation for paroxysmal AF. The success of this approach is limited in nonparoxysmal forms of AF, and adjunctive ablation strategies have been developed to target the alterations in the underlying substrate that may perpetuate AF. Nonetheless, the mechanisms underlying AF persistence are not uniform, and a trigger-based mechanism may be operative in a subset of patients. Identifying these patients remains a challenge. Intermittent rapid rhythms arising in the PVs are commonly observed during sustained episodes of paroxysmal AF. These rapid activities represent an active phenomenon that may have a critical role in the maintenance of AF by providing continued refueling of the fibrillatory process. We therefore evaluated persistent AF to identify the cycle length gradient between PVs and the left atrium in an attempt to identify patients where PVs play an important role. Our study demonstrates that an attentive monitoring of the PV activity in relation to the atrial AF CL may discriminate patients in whom AF is likely to terminate after PV isolation or limited substrate ablation from those in whom AF is unlikely to terminate by ablation and long-term success is limited. By providing the tool to identify the subset of patients in whom the PVs still play an important role in AF persistence, these findings may be a step toward more tailored ablation strategies.
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