Although pulmonary vein (PV) isolation is an established end point for patients with paroxysmal atrial fibrillation (AF), the procedural end point for patients with the persistent form of the arrhythmia remains elusive. Circumferential or antral PV isolation yields long-term sinus rhythm in only ≈24% of patients with long-standing persistent AF.1 Interestingly, ostial PV isolation, when compared with the more antral or proximal approach in which much more of the left atrium is included, also eliminated persistent AF in only 20% of patients.2 The latter study was published a decade before the former, which speaks to the lack of progress on this front.

It should come as no surprise that investigators have used a variety of other strategies, as standalone or as an adjunct to PV isolation, in this challenging group of patients. These include targeting complex, fractionated atrial electrograms,3 linear ablation,4–6 and extra-PV triggers. Although there is evidence that complex, fractionated atrial electrogram ablation results in AF slowing7 and, in general, improves outcome in patients with persistent AF,8 the problem lies in identification of electrograms that represent driver as opposed to bystander sites. Linear ablation at the left atrium roof and the mitral isthmus helps improve outcomes by eliminating AF drivers, triggers (eg, the ligament of Marshall),9 and perhaps atrial delubking.

Even if any of these targets are added to PV isolation, AF frequently persists and requires cardioversion at the end of the procedure. Although some patients may do well, the acute outcome is nonetheless unsettling for both the electrophysiologist and the patient. About 9 years ago, Haïssaguerre et al10 published their results with a stepwise ablation approach in patients with persistent AF; the problem lies in identification of electrograms that represent driver as opposed to bystander sites. Linear ablation at the left atrium roof and the mitral isthmus helps improve outcomes by eliminating AF drivers, triggers (eg, the ligament of Marshall); and perhaps atrial delubking.

In this issue of Circulation: Arrhythmia and Electrophysiology, Scherr et al11 extend the earlier findings and present the long-term outcome of patients (N=150; long-standing persistent AF in 97 [65%]) who underwent a stepwise ablation procedure for persistent AF. AF was terminated during ablation in 120 patients (80%), to sinus rhythm in 30 patients (25%), and to atrial tachycardia (AT) in 90 patients (75%). Among the latter, further ablation yielded sinus rhythm in 75 patients (83%), with the remainder requiring cardioversion. After a total of 317 procedures (median, 2) and a median follow-up of almost 5 years after the last ablation procedure, 65% of patients remained in sinus rhythm (assessed by periodic 24-hour Holter monitors and a 7-day Holter monitor at final follow-up) without antiarrhythmic drugs. Arrhythmia-free outcomes were ≈90%, 80%, and 63% at 1, 2, and 5 years, respectively, after the last ablation procedure. Failure to terminate AF, left atrium diameter >5 cm, continuous AF >18 months in duration, and structural heart disease were independently associated with arrhythmia recurrence.

The study by Scherr et al11 is unique and noteworthy for several reasons. First, it confirms the authors’ earlier findings that persistent AF may be terminated during radiofrequency ablation in ≈80% of patients. Further, an inability to terminate AF during ablation was found to be the strongest predictor of arrhythmia recurrence. However, despite the excellent acute and midterm results, long-term freedom from atrial arrhythmias could only be achieved in about two thirds of the patients. These findings are also in line with those of other studies that have documented late attrition among patients who had undergone PV isolation for paroxysmal AF.12

Possible factors that may help explain late recurrences include lack of complete, transmural lesions, incomplete understanding of the arrhythmia mechanisms, and slow drug washout (eg, amiodarone). But the fact that late recurrences are seen in patients in both paroxysmal and persistent AF and have been reported by different yet pioneering institutions may also point to a more universal problem. Recall that the atria of patients with even lone, paroxysmal AF show evidence of structural remodeling, specifically, low-voltage areas, scar, and slow conduction.13 In patients with persistent AF and those with coexisting medical problems, these changes in structure and function are more pronounced.14 Catheter ablation is effective in eliminating triggers and drivers of AF in both paroxysmal and persistent AF, but of course does not undo the structural changes (actually, probably exacerbates atrial uncoupling in persistent AF) that led to AF in the first place. Catheter ablation also does not render the atrium immune to the onslaught of pathophysiologic insults related to comorbidities such as sleep apnea, obesity, hypertension, and diabetes mellitus. It is conceivable that these conditions

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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(Circ Arrhythm Electrophysiol. 2015;8:2-4. DOI: 10.1161/CIRCEP.115.002674.) © 2015 American Heart Association, Inc.

Circ Arrhythm Electrophysiol is available at http://circp.ahajournals.org

DOI: 10.1161/CIRCEP.115.002674
continue to exact a toll on the atrial substrate after a seemingly successful ablation procedure and contribute to arrhythmia recurrence. This hypothesis is supported by results of recent study that showed that aggressive management of these conditions is associated with a better arrhythmia-free survival after catheter ablation.\(^1\)

AF termination in patients with persistent AF is not an easy task. It usually takes 4 to 6 hours\(^16,17\) and is both mentally and physically grueling. The operator’s spirits may be buoyed when AF finally terminates, but this celebration is short lived because now one has to give chase to AT(s). Other limitations include the need for repeat procedures, atrial scarring, and pericarditis/pericardial effusions related to extensive ablation. An obvious question is why go through the trouble if long-term outcomes are modest? Proponents of an AF termination strategy may counter that if such an effort is not expended, the outcomes are likely to be worse. Note that the long-term success rate as reported in this study is the highest among patients undergoing catheter ablation of persistent AF.

Ideally, a large, multicenter, randomized study is required to answer the question whether AF termination is superior to other strategies. Such a study would be difficult to conduct for many reasons. Short of these data, and if one does not wish to pursue AF termination, what is a reasonable approach to patients with persistent AF? As mentioned earlier, simple PV isolation is unlikely to be sufficient in such patients. A recent study using the second-generation cryoballoon reported a 60% success rate after 1 year and a single procedure in patients with persistent AF.\(^16\) However, the majority of patients in the study presented to the laboratory in sinus rhythm. These are select patients whose atria are likely to have undergone less structural and electrical changes compared with patients in the study by Scherr et al,\(^11\) in which the mean duration of continuous AF was \(\approx 13\) months.

After PV isolation, the next step is to map and ablate complex, fractionated atrial electrogram sites, followed by linear ablation at the left atrial roof. The operator may elect to stop at this point because it is likely that the various steps have at least resulted in AF slowing. Alternatively, the right atrium may be targeted next if there is a right-to-left gradient in frequency or complexity. If AF persists or other, admittedly arbitrary end points (procedure, and radiofrequency duration of \(\approx 5\) hours, and 90 minutes, respectively) have been reached, the procedure is concluded. A similar approach is undertaken if the patient presents for a repeat procedure for AF; however, a greater emphasis is placed on arrhythmia termination at that time.

The major difference between the stepwise approach and the protocol outlined here is that AF termination is not mandatory and that it may be pursued at the repeat session. It is also important to note that even if AF does not terminate and yet extensive ablation was performed during the index procedure, the recurrent arrhythmia is often AT, and not AF. This “lenient” strategy is associated with a reasonable midterm success rate of \(\approx 80\%\) without antiarrhythmic drugs.\(^16\) The advantages of an AF termination strategy are that the AT(s) may be eliminated at the first session and that if the patient does present for a repeat procedure, it is usually for AT, an arrhythmia that, as opposed to AF, can be readily mapped.

It should be mentioned, however, that these postablation ATs may themselves be challenging to ablate and may recur despite an excellent acute outcome.\(^19\)

Whichever approach one uses, catheter ablation of persistent AF is typically guided more by intuition than by objective evidence. However, recent reports suggest that we may be getting closer to understanding mechanisms of AF unique to a given patient.\(^20,21\) Such a patient-specific approach may help streamline the ablation procedure, prevent recurrence, and help avoid unnecessary ablation. Until then, this excellent offering by Scherr et al\(^11\) reminds us that an aggressive arrhythmia such as persistent AF calls for an extensive ablation strategy. Whether it is necessary to acutely terminate the arrhythmia during the initial ablation procedure remains unknown.

**Disclosures**

None.

**References**


Catheter Ablation of Persistent Atrial Fibrillation: How Much Is Enough?
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Circ Arrhythm Electrophysiol. 2015;8:2-4
doi: 10.1161/CIRCEP.115.002674

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