Catheter Ablation of Persistent Atrial Fibrillation

RAKESH LATCHAMSETTY, MD and AMAN CHUGH, MD

Division of Cardiovascular Medicine, University of Michigan, Ann Arbor, MI

ABSTRACT. Catheter ablation for symptomatic, drug-resistant atrial fibrillation (AF) has become an important therapeutic option over the past decade. Pulmonary vein isolation (PVI) has been established as the cornerstone for ablation of paroxysmal AF. However, there is a dearth of data regarding the ideal approach for patients with persistent AF. It is generally accepted that PVI alone is insufficient for adequate long-term sinus rhythm maintenance in these patients. Adjunctive ablation such as ablating complex fractionated atrial electrograms, performing linear lesions, or targeting ganglionated plexi have been proposed to improve procedural efficacy. Newer methods focusing on electrogram analysis to target potential AF drivers are also being investigated. In this review, we will examine the evidence base and discuss a practical approach to catheter ablation of persistent AF. In addition to ablative strategy, we will also discuss our patient selection process and periprocedural management.

KEYWORDS. persistent atrial fibrillation, catheter ablation, radiofrequency.

Introduction

Since the recognition of pulmonary vein triggers in patients with paroxysmal atrial fibrillation (AF), catheter ablation has grown to represent an important option in the interventional management of AF. Pulmonary vein isolation (PVI) in patients with paroxysmal AF has shown promising outcomes in comparison to medical management; however, success rates with persistent AF are modest with PVI as the sole strategy. Differences in outcomes are likely related to a more complex atrial substrate in patients with persistent AF and the fact that the mechanisms responsible for maintenance of persistent AF more often reside outside the pulmonary veins (PVs).

In order to overcome this limitation, strategies with varying degrees of complexity, reproducibility, and success have evolved to target non-PV substrates; but overall success rates still trail those for ablation of paroxysmal AF, and repeat procedures are frequently required. However, improvement in outcomes attributable to improved mechanistic understanding as well as technological advancements has been realized and catheter ablation is recognized as a class IIa indication for management of symptomatic, medically refractory persistent AF.

Patient selection

The initial and critical step toward meaningful outcomes with AF ablation is proper patient selection. Reasonable candidates for catheter ablation of persistent AF are those that meet the following criteria.

Inclusion Criteria:

1) Symptomatic AF due to rapid and/or irregular ventricular rates or loss of atrioventricular synchrony
2) Contraindication to or, failure or intolerance of antiarrhythmic drugs

Exclusion criteria:

1) Significant non-cardiac comorbidities that would limit benefit of an ablation procedure or place the patient at high risk of a procedure-related complication
2) Severe left atrium (LA) dilatation >60 mm

While these criteria are not absolute, they can serve as a general guideline for patient selection. Some criteria may
also be challenging to establish. For example, it may be difficult to ascertain whether the patient is symptomatic with respect to AF. A trial of cardioversion with or without the use of an antiarrhythmic medication may be performed. The patient is subsequently asked to contrast his/her quality of life during AF versus sinus rhythm. Many “mildly symptomatic” or “asymptomatic” patients often report significant improvement following conversion to sinus rhythm.

Although catheter ablation is not contraindicated in patients with a severely enlarged LA, these patients should be informed prior to the procedure that the probability of success with ablation may be lower and that the need for a repeat procedure or concomitant antiarrhythmic medication is higher. While most patients have failed at least one antiarrhythmic prior to referral to an AF ablation center, some patients may be offered a procedure without a trial of medical therapy either due to contraindications or concern for long-term side effects, e.g., young patients.

Although increased age is not an absolute contraindication to catheter ablation, comorbidities and underlying functional status should be considered prior to initiating a left atrial ablation strategy. Atroventricular junction ablation with implantation of a pacemaker is a reasonable option in patients whose ventricular rates are difficult to control despite medical therapy. However, pacemaker dependence makes this an unattractive option in younger patients and in those in whom symptoms are attributable to lack of atrioventricular synchrony.

One of the motivating factors for patients undergoing catheter ablation of AF is to be able to discontinue anticoagulation. However, patients should be counseled that, in general, catheter ablation of AF is indicated for symptomatic improvement. During the initial consultation, in addition to discussing the procedural details, success and complication rates, it is also important to review the pathophysiology of AF with the patient. We discuss the fact that since substrate abnormalities (particularly in patients with persistent AF) are documented throughout the atria, extensive mapping and ablation of both atria may be required. We also discuss the importance of optimizing treatment of coexisting conditions such as hypertension, sleep apnea, obesity, and heart failure, even after a successful ablation procedure. As a result, patients and referring physicians may have a better insight into the complexities of AF management.

Preprocedural management

Patients selected for catheter ablation at our institution are anticoagulated prior to the procedure with either warfarin or one of the novel anticoagulants. Given the data supporting fewer thromboembolic events without an increase in bleeding complications with uninterrupted warfarin, the majority of patients on warfarin are maintained at therapeutic levels throughout the peri procedural period. Patients on dabigatran are asked to hold their dose for 36 h prior to the procedure. All patients with persistent AF undergo a transesophageal echocardiogram to verify the absence of a LA thrombus, irrespective of anticoagulation status. The use of a computed tomography (CT) scan or magnetic resonance imaging (MRI) may be performed prior to the procedure if one suspects variant PV or LA anatomy. Preprocedure imaging has not been associated with improved procedural efficacy or clinical outcomes and is not obtained routinely. In some cases, however, preprocedure imaging can provide potentially valuable information in patients in whom linear ablation will be performed. If a patient has undergone a prior ablation procedure or arrhythmia surgery, it is important to review the procedural/operative findings as they may influence one’s approach during the upcoming procedure.

Preablative preparation and access

Anesthesia

There are several sedation options available during catheter ablation of AF. Medications that are familiar to most cardiologists (e.g., morphine, diazepam) can be administered by a cardiac nurse for patients suitable for moderate sedation. Patients requiring deep sedation may receive continuous infusion of propofol and other medications that require the expertise of a specialist in anesthesia. Alternatively, patients may undergo the procedure under general anesthesia. There are advantages and disadvantages to each of these approaches. The moderate sedation approach is likely associated with a lower cost and may not require the expertise of an anesthesiologist but the patients may not tolerate relatively long procedures. Catheter stability is better with the use of general anesthesia, especially if JET ventilation is used; however, such procedures performed under general anesthesia are also associated with a higher prevalence of esophageal injury. General anesthesia is associated with higher cost, and probably associated with a higher risk of hypotension, and may also be problematic in assessing proximity of the ablation catheter to the phrenic nerve if paralytics are also used. We prefer deep sedation with intravenous propofol as long as the patient is able to maintain his/her airway. The majority of patients can be sedated adequately even during long procedures with this approach.

Venous and left atrial access

Vascular access is usually obtained with three sheaths introduced into a femoral vein. Two of these are long 8.5 French sheaths intended for LA access. A third sheath is utilized for coronary sinus (CS) cannulation. A single or double transseptal puncture is performed with the use of intracardiac echocardiography. A Cook (Cook Medical, Bloomington, IN) or BRK (St. Jude, Inc., Minneapolis, MN) needle is most often used for the transseptal puncture. A J-tip SafeSept guidewire (Pressure Products, Inc., San Pedro, CA) is sometimes used to
facilitate puncture, particularly in patients with smaller atria. For a thick or fibrous septum, most often encountered in patients who have undergone prior transseptal catheterization, LA access may be gained using radiofrequency (RF) energy applied at the tip of the needle (Baylis Medical Inc., Montreal, Canada).

**Intraprocedural anticoagulation**

Following transseptal puncture and verification of hemodynamic stability, anticoagulation is given via boluses and continuous infusion of intravenous heparin to maintain an activated clotting time (ACT) at 300–350 s. Patients already anticoagulated with warfarin will have a baseline ACT measured prior to heparin administration and require less heparin than patients who are not taking therapeutic doses of warfarin."16

**Esophagus**

Atrial-esophageal fistula is a rare but devastating complication. It is imperative to account for the esophagus during ablation of the posterior LA to prevent this potentially life-threatening complication. We typically employ one of two strategies to identify the esophagus prior to initiation of ablation: 1) barium swallow, which can be performed by administering barium paste (E-Z-EM, Inc., Lake Success, NY), or 2) a radiopaque probe inserted orally into the esophagus (Figure 1). In either case, the course of the esophagus can be followed on fluoroscopy and/or tagged on the three-dimensional (3D) map. The former is used in patients undergoing the procedure with moderate sedation and appears to be safe with respect to the risk of aspiration, and the latter with deeper sedation. When RF ablation is necessary at a location near the esophagus, it is best to deliver short-duration, low-power lesions, which likely help reduce the risk of esophageal injury. Some electrophysiology laboratories utilize an esophageal temperature probe but esophageal injury has still been documented in patients in whom such an approach was used.19

**Mapping and ablation of persistent atrial fibrillation**

After transseptal catheterization, LA geometry is created using a multipolar catheter (Lasso, Biosense Webster, Diamond Bar, CA), and 3D mapping system (CARTO 3, Biosense Webster, or EnSite NavX, St. Jude Medical, St. Paul, MN). Although this step may take a few minutes, accurate recapitulation of the LA geometry helps streamline the ablation procedure. It also helps reduce exposure to ionizing radiation. Prior to ablation, the global AF cycle length is measured in both appendages. This information may be prognostically important and also gives the operator real-time feedback as to the impact of ablation on the atrial substrate.21

The first step is to perform antral PVI using an irrigated-tip ablation catheter (Thermocool, Biosense Webster). The distinction between antral and ostial isolation of the PVs is more than a semantic one. A more proximal approach during antral ablation has been shown to be superior to an ostial approach in eliminating the contribution of the PV/posterior LA in patients with AF.22 The antral approach also targets additional drivers that may be located within the antra and reduces the risk of PV stenosis. We use 25 watts of irrigated RF during antral PVI. Prior to application of RF energy application around the anterior aspect of the right superior PV, it is important to perform high outpacing to rule out proximity to the right phrenic nerve.

**Substrate mapping and ablation**

After PVI, the operator again measures the AF cycle length by placing a catheter in the left atrial appendage (LAA). Usually there is little impact on the AF cycle length after PVI. This supports the observation that PVI as a sole approach is inadequate in patients with persistent AF. The next step is to map and ablate complex, fractionated atrial electrograms (CFAEs). There is much controversy regarding the definition and the incremental impact of CFAE ablation. However, a meta-analysis suggested that CFAE ablation probably is associated with improved outcomes in patients with persistent AF. CFAEs were originally defined as either 1) atrial electrograms that have fractionated electrograms composed of two deflections or more, and/or perturbation of the baseline with continuous deflection of a prolonged activation complex, or 2) atrial electrograms with a very short cycle length (<120 ms)

However, there is much subjectivity in this definition. Also, there is poor anatomic correlation between sites with complex electrograms and short cycle lengths. While it is straightforward to identify sites with a cycle length <120 ms if the electrograms are discrete, the problem is that such sites are relatively infrequent outside the pulmonary vein/posterior LA region. After PV isolation, sites with short cycle lengths in this region would have already been ablated during the PV portion of the procedure. It is also quite challenging to adjudicate local activation rates when the signals are complex. While signal processing (i.e., dominant frequency, DF) is helpful in determining the local activation rate, it is not practically feasible with currently available technology to obtain this information real-time during an ablation procedure. Whether substrate ablation guided by DF mapping is superior to visual identification of CFAEs is also unknown.

The above limitations are further compounded when one considers the multiple possible mechanisms responsible for generating complex electrograms. A prior study showed that the majority of CFAEs are inscribed because of far-field activation, especially in areas with overlapping myocardium such as the septum and the inferior LA–CS complex (Figure 2). More recent studies have also confirmed the functional nature of CFAE sites. Thus, it is clear that not all CFAEs represent driver sites.
It is also follows then that we are ablating too much atrial tissue because of our inability to prospectively distinguish driver from bystander sites.

Nonetheless, given the fact that CFAE ablation has been shown to slow or terminate AF and to improve outcomes in patients with persistent AF, it is reasonable to pursue electrogram-guided ablation after PV isolation. The “high-yield” areas, i.e., sites where ablation tends to increase the AF cycle length or terminate AF, include the base of the LAA, the inferior LA–CS complex, and the anterior LA. After CFAE ablation in the LA, the appendage cycle lengths are again compared. At this point there is often an increase in the AF cycle length. However, in some patients it may be difficult to demonstrate prolongation in the AF cycle length despite extensive ablation.

Even though there is no prospective method that helps the operator distinguish between active and passive CFAE sites, a few practical rules may be helpful. A prior study showed that ablation of continuous electrograms (Figure 3) was shown to be associated with prolongation of the AF cycle length and AF termination. A more recent, randomized study showed that such areas of high-grade fractionation are more likely to slow AF than other CFAE sites. Also, identification of “electrogram offset” between the distal and proximal bipoles of the mapping catheter can be quite helpful. RF energy application at these sites also seems to have a positive effect on the fibrillatory process.

At this point, the contributions of the PVs and CFAEs have been addressed, and the operator has a choice to perform transthoracic cardioversion or additional ablation to further modify the LA substrate and/or to terminate AF. It should be noted that in the absence of large, randomized trials comparing various ablation strategies, the ideal endpoint for catheter ablation of persistent AF is unknown. This problem is magnified by the widely differing approaches among experienced investigators and varying results even when similar strategies are utilized.

If the decision is made to restore sinus rhythm by transthoracic cardioversion, programmed atrial stimulation with isoproterenol infusion may be considered.
Inducible organized arrhythmias, which may be a trigger/driver of AF, should be mapped and ablated.

**Linear ablation**

If the desired procedural endpoint includes AF termination, linear ablation at the LA roof and/or mitral isthmus is frequently required, particularly in patients with longstanding AF. Specifically, the combination of PVI and CFAE ablation only terminates persistent AF in approximately one-half of the patients. Linear ablation increases this number to approximately 80%. The mechanisms by which linear ablation slows or terminates AF in humans is unknown. Experimental studies suggest that roof ablation may disrupt re-entrant circuits at the superior left atrium. The benefits of mitral isthmus ablation may in part be due to elimination of the ligament of Marshall, which may be eliminated endocardially or epicardially in the CS venous system. It is also possible that linear ablation results in compartmentalization of the left atrium, which may help prevent perpetuation of AF.

If linear ablation is performed, it is critical to demonstrate bidirectional conduction block across the isthmus because incomplete lesions may be associated with arrhythmia recurrence. Mitral isthmus ablation is commenced from the lateral mitral annulus and carried out to the ostia of the left PVs. Typically high power (35 watts of irrigated RF) is required at the endocardial mitral isthmus. Although some laboratories use higher power (up to 50 watts), higher power settings seem to be associated with higher prevalence of perforation and tamponade. After just endocardial ablation, conduction block across the mitral isthmus can only be demonstrated in about one-third of the patients. In the remaining two-thirds, epicardial energy delivery is required within the CS. The presence of the circumflex artery (or one of its branches) at the mitral isthmus in part helps explain why epicardial energy delivery is required. The arterial blood flow probably prevents adequate heating due to convective heat loss. Other factors include the presence of endocardial pouches and the ligament of Marshall, which may be responsible for epicardial conduction across the mitral isthmus. The ablation catheter is carefully advanced to the distal CS to the level of the endocardial line as visualized on the 3D mapping system. One is unlikely to achieve conduction block without reaching this level. If the ablation catheter cannot be advanced to this level and the mitral isthmus ablation is being performed for perimital flutter, then the operator should choose an anterior approach (from the anterior annulus to the right-sided PVs). If the diagnostic catheter cannot be advanced to the desired position in the distal CS at the beginning of the procedure, it is likely best to avoid empiric mitral isthmus ablation since obtaining linear block would be

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**Figure 2:** Complex fractionated electrogram due to far-field activation. This electrogram was recorded from the left atrial septum in a patient undergoing catheter ablation of long-standing persistent atrial fibrillation. The fractionated electrogram denoted by the oval at first glance appears to be a reasonable target for ablation. However, closer inspection reveals that the electrogram is generated by two sources, one near-field (L, LA) and one far-field (R, RA). A lack of constant interval (blue brackets) between the two is further evidence that the electrogram is not entirely due to local activation. Ablation of this site is unlikely to slow or terminate AF.
challenging. The inability to ensure the completeness of the line may be met with proarrhythmia.

During RF energy delivery in the CS, low power is delivered (20 watts) as the catheter is slowly withdrawn. If CS ablation is performed during sinus rhythm, isthmus conduction is assessed real-time during pacing from the LAA or the coronary sinus (Figure 4). The operator observes for an acute change in the CS activation sequence (distal-to-proximal to proximal-to-distal) during LAA pacing. Differential pacing from the other side of the line, that is, the CS bipoles, helps rule out slow conduction. Mitral isthmus block can be achieved in about 85% of patients, but it may be challenging in some patients, owing to CS anatomy, in addition to the factors noted above. It is also worth noting that mitral isthmus ablation is associated with a high prevalence of arterial injury to the branches of the circumflex artery. Although most patients with arterial injury remain asymptomatic, nonetheless, the operator should carefully weigh the risks and benefits prior to embarking on prophylactic mitral isthmus ablation.

Linear ablation at the LA roof probably has more of an impact on the fibrillatory process than at the mitral isthmus. It is also technically easier to perform linear ablation at the roof than at the mitral isthmus. The operator advances the ablation catheter into the left superior PV. The long sheath should then be advanced proximal to the proximal bipole. The catheter–sheath unit is then rotated clockwise and the progress of the catheter across the roof is monitored on the 3D map. The catheter is maneuvered toward the ostium of the right superior PV and the process is repeated until the electrograms across the line have been abolished. Owing to the thinness of the roof myocardium and the fact that ample sheath support is associated with excellent contact force, only 25 watts (or 30 watts if the line is relatively anterior) are required. Not uncommonly the catheter may skip at the mid-roof and dislodge into the right superior PV, leaving a potential gap. The catheter is then manipulated out of the right superior PV and is then directed superiorly at the potential gap.

Figure 3: After pulmonary vein isolation, ablation of complex, fractionated electrograms (CFAEs) was performed in this patient with longstanding persistent atrial fibrillation. Shown are two representative electrograms recorded from the inferior left atrium (LA) and the base of the LA appendage. Note, the nearly continuous electrical activity as shown in the ovals (see Figure 6).
Dynamic conduction across the LA roof can also be assessed during LAA pacing or even sinus rhythm. Linear block is heralded by the presence of widely split double potentials across the roof. The second potential is inscribed due to ascending, activation of the posterior LA after creation of conduction block at the roof. In the absence of conduction block at the roof, the posterior LA is activated in a descending fashion, during sinus rhythm or LAA pacing. After creation of linear block, the wavefront during sinus rhythm or LAA pacing, blocks at the roof, and the posterior LA is activated in an ascending fashion (Figure 5). Although linear block at the roof can be demonstrated in about 95% of patients, it may be difficult to rule out the presence of slow conduction. Akin to the mitral isthmus, atrial arteries LA may impede the creation of roof block in patients with persistent AF.

**Atrial tachycardias**

When AF termination is observed during ablation, conversion is most commonly preceded by cycle length prolongation and then conversion to an atrial tachycardia (AT) as opposed to sinus rhythm (Figures 6–10). The ATs may coexist during AF and can serve as drivers that are only manifest after elimination of higher frequency drivers. The possible mechanisms include focal discharge, and small or large (macro-re-entrant) re-entrant circuits. In the context of an already lengthy procedure to terminate AF, detailed activation mapping is probably an inefficient way to delineate the mechanism of the tachycardia. Limited activation mapping along with strategic entrainment mapping can usually provide the diagnosis within a few minutes. Often there may be more than one intervening AT before sinus rhythms is finally restored. All the PVs and linear lesions are then checked for complete isolation and linear block, respectively. Additional ablation may be required to effect these endpoints. During an initial, lengthy stepwise ablation procedure for AF, we do not perform an aggressive induction protocol with isoproterenol infusion.

**Right atrial ablation**

If a patient with persistent AF remains in AF after a stepwise ablation approach (consisting of PV isolation, LA–CS CFAEs, and linear LA ablation) during the initial procedure, it is probably reasonable to perform trans-thoracic cardioversion at this point. Although patients in whom AF can be terminated with RF seem do to very well, studies have also shown that patients in whom AF termination was or was not a procedural endpoint still fared well. Thus, in the absence of robust data from randomized trials, it is not clear if AF termination is mandatory for a favorable outcome.

If AF termination is the procedural endpoint after a stepwise approach in the LA has failed to eliminate AF, the right atrium (RA) may be playing a role. The cycle lengths of the two appendages are again compared. If there is a clear gradient from right to left, then the RA is targeted for further ablation (Figures 11–13). If the two cycle lengths are similar and yet the mapping reveals high-grade fractionation in the RA and the LA remains defragmented, it is probably reasonable to target the RA. Another hint that the RA may be the driver is if an

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**Figure 4:** Demonstration of linear block at the mitral isthmus during radiofrequency ablation in the distal coronary sinus (CS) and pacing from the left atrial appendage (LAA). Note the sudden change in the CS activation sequence from distal-to-proximal to proximal-to-distal. Further, note the appearance of a double potential (dashed arrows) and significant increase in the conduction delay, also compatible with conduction block.
episode of immediate recurrence of AF occurs after transthoracic cardioversion, and the activation clearly points to a RA origin.

The RA is targeted in the form of CFAEs. The high-yield areas include the base of the RA appendage (Figure 14), atrial myocardium around the free-wall aspect of the tricuspid annulus, and the posterior RA. There is almost always entrance block into the superior vena cava (SVC), ruling it out as a driver in most patients with longstanding, persistent AF. Hence, SVC isolation alone is unlikely to have a meaningful impact in slowing or terminating AF. Although linear lesions in the RA are a part of the classic cut-and-sew Maze procedures, analogous lines connecting the venae cavae at the free wall and septal aspects are rarely performed during a catheter-based procedure. There is a concern of phrenic nerve and sinus nodal injury with the former. With the latter, there is probably a risk of interatrial conduction delay related to injury to Bachmann’s bundle. Although AF may occasionally terminate during CFAE ablation at the cavotricuspid isthmus, it is unclear if linear ablation at this site has antifibrillatory effects. Patients with longer AF duration and large RA volume are more likely to require RA ablation for AF termination.49

Other methods
While not routinely performed in our laboratory, several other methods have been suggested as alternative or additional ablation strategies. Ablation of sites harboring ganglionated plexi (GP) has been used as a potential adjunct to PVI during ablation of persistent AF. This technique involves ablation focused at sites of autonomic innervation primarily in the LA, but may include areas in the RA. These sites are either identified with the use of high-frequency stimulation or targeted based on their expected anatomic locations. While ablation solely targeting sites of GP seems to be inferior to PVI alone,50

Figure 5: Demonstration of conduction block at the LA roof during sinus rhythm (posterior-anterior view with cranial angulation). After LA breakthrough at Bachmann’s bundle (red area), the wavefront blocks at the LA roof. As a result the posterior LA is activated in an ascending fashion. LAA: left atrial appendage; PV: pulmonary vein; LC: left common; RS: right superior; RI: right inferior.
GP ablation as an adjunct to PVI may result in improved sinus rhythm maintenance. Whether this is a superior method to CFAE ablation is not established as no large head-to-head trials have been conducted. Furthermore, there is likely significant overlap in areas targeted during PVI and GP ablation.

Real time spectral or DF mapping has also been suggested as a potential tool to identify ablation targets. Off-line analysis has suggested that sites at which ablation terminated AF had high DF and elimination of left-to-right atrial frequency gradients predicts improved sinus rhythm maintenance. An overall decrease in global DF of 11% was also shown to be associated with a favorable outcome. Use of real-time frequency mapping to guide ablation does face some technical and conceptual obstacles. Rapid acquisition and analysis of high-resolution atrial electrograms throughout the left and/or right atria can be challenging. Furthermore, opponents of this method counter that spatiotemporal instability of real-time frequency mapping undermine its ability to identify local rotors or sources of AF. A recent study using computational methods to identify and ablate focal sources of AF has shown promising results with both rapid conversion of persistent AF during ablation as well as excellent long-term sinus rhythm maintenance. These results will need to be further evaluated in large-scale multicenter trials.

Isolation of the LAA has also been suggested in patients presenting for repeat ablation where the LAA has been identified as a potential driver. Appendage isolation in these patients has been shown to decrease AF recurrence. In most cases, however, drivers around the LA appendage can likely be eliminated during CFAE ablation, without complete electrical disconnection. LA appendage isolation may also be quite challenging unless there is already atrial uncoupling present. The non-contractile LA appendage may also be source of thromboembolism, despite sinus rhythm.

A practical approach
Although there is much debate regarding the ablation strategy and the procedural endpoint in patients with persistent AF, it is generally agreed that a more extensive approach is more likely to eliminate AF. On the flip side, such a strategy is also likely to result in atrial tachycardia that frequently requires a repeat ablation procedure, not to mention atrial uncoupling. If the goal of the procedure is AF elimination, as opposed to AF “control,” PV isolation as the sole strategy is unlikely to be effective. Admittedly, it is difficult to strike a balance between too much and not enough ablation in patients with persistent AF. In our laboratory, the current strategy in patients undergoing catheter ablation for persistent AF is PV isolation followed by CFAE ablation. If AF terminates to
Figure 7: (Continued from Figure 6) The first atrial tachycardia spontaneously gave way to another mitral isthmus dependent flutter, as shown by a post-pacing interval that approximates the tachycardia cycle length. The atrial electrogram (arrow) is coincident with the ventricular electrogram at the annulus. Endocardial ablation from the lateral mitral annulus to the left-sided pulmonary veins had no appreciable effect on the tachycardia (see Figure 8).

Figure 8: (Continued from Figure 7.) Because endocardial ablation failed to terminate perimital atrial flutter, epicardial ablation was performed in the distal coronary sinus. The tachycardia terminates to another tachycardia as evidenced by the change in p-wave morphology (arrows) and prolongation of the cycle length (see Figure 9).
Figure 9: (Continued from Figure 8) Termination of a small re-entrant circuit at the posterior base of the LA appendage (LAA), finally resulting in sinus rhythm (see Figure 10).

Figure 10: The lesion set required to terminate longstanding persistent AF shown in Figures 6–9. PV: pulmonary vein; LS: left superior; LI: left inferior; RS: right superior; RI: right inferior; AP: anterior-posterior; PA: posterior-anterior.
AT, then the AT is mapped and ablated until sinus rhythm is achieved. In younger patients and in those with little structural heart disease, a strategy of PV isolation and CFAE ablation is reasonable for the initial procedure. In most such cases, AF does not terminate and transthoracic cardioversion is performed. In those with longlasting persistent arrhythmia, i.e., continuous AF lasting >12 months, or in those with extensive structural involvement, linear ablation at the LA roof is performed (Figure 15). If AF terminates, then the AT is mapped and ablated. If AF persists after PV/CFAE/linear ablation at the roof, transthoracic cardioversion is performed. In patients presenting for a repeat procedure for AF, the PVs are reisolated, and LA defragmentation is verified or performed as needed. If there is an obvious gradient from RA to LA, then the RA is targeted with the endpoint of defragmentation.

Outcomes
While conversion to sinus rhythm during ablation of persistent AF has been associated with excellent...
Figure 12: (Continued from Figure 11.) Local slowing and organization (arrow) of atrial fibrillation during radiofrequency ablation at the base of the right atrium appendage (see Figure 13).

Figure 13: (Continued from Figure 12.) Termination of AF to sinus rhythm (arrow) during radiofrequency ablation within the proximal coronary sinus. AF was no longer inducible with isoproterenol infusion.
outcomes, it is not clear that a strategy of ablation until termination of AF is necessary. Using similar stepwise ablation protocols, results have varied for termination of persistent AF during ablation from 48% to 85% despite similar long-term outcomes (Table 1). This implies either that AF termination is not necessary for good long-term outcomes or that, if all drivers/sources were not eliminated at the first session during which AF was not terminated, they can be addressed during a session, since at least half of patients to undergo repeat procedures. In other words, the cumulative effect of multiple ablation procedures may be equivalent to AF termination during the first session. At a follow-up of 1–2 years, approximately 85% of patients were reported to be arrhythmia-free without antiarrhythmic medications. Despite extensive, and frequently repeat ablation procedures, atrial function and transport appear to be preserved in the majority of patients. Concerns do exist, however, with the potential for unintended electrical and mechanical consequences such as LAA isolation and development of left atrial diastolic dysfunction ("stiff left atrial syndrome").

Whatever endpoint is ultimately chosen, it is important to consider patient and clinical factors, including procedure or RF duration, fluoroscopy exposure, number of prior ablations, and clinical status of the patient.

Complications

In patients undergoing a catheter ablation for AF at our institution, serious complications occur in about 1.6% of cases (with an additional 1.9% access site vascular

Figure 14: Biatrial electroanatomic map showing where radiofrequency ablation was required to terminate AF. This man had previously undergone a left atrial procedure for persistent AF and now presented for catheter ablation of atrial tachycardia. After elimination of reentrant atrial tachycardia from the left atrium (LA), he had spontaneous AF with isoproterenol infusion. Frequency mapping showed a right-to-left gradient prompting mapping and ablation in the right atrium (RA) to terminate AF. Note the RA is larger than the LA. SVC: superior vena cava; RAA: RA appendage; IVC: inferior vena cava.
complications). Pericardial tamponade occurs in about 1.2% and thromboembolic events in about 0.2% of patients. Patients undergoing a procedure on therapeutic oral anticoagulation do not have any increase in adverse events. With our current approach of identifying the esophagus and avoiding high-power or prolonged RF application on the posterior LA, esophageal injury has been avoided over the last 8 years. Adaptation of antral PV isolation over an ostial approach has also reduced occurrence of PV stenosis to <0.1%.

**Figure 15:** A proposed schema for catheter ablation of longstanding, persistent atrial fibrillation (AF). The blue arrow refers to possible right atrial (RA) ablation and/or additional linear ablation at the mitral isthmus (MI) if AF termination is the procedural endpoint. Alternatively, RA ablation may be performed at a repeat session, if needed. LS Ps AF, longstanding, persistent atrial fibrillation, defined as continuous, uninterrupted AF for at least 1 year. PVI: pulmonary vein isolation; SR: sinus rhythm; CV: cardioversion; CFAE: complex fractionated atrial electrograms; Roof: linear ablation at left atrial roof; with confirmation of conduction block; AT: atrial tachycardia resulting after AF termination that should be mapped and ablated; RFA: radiofrequency ablation.

**Postprocedure management**

For patients undergoing the procedure on the therapeutic level of warfarin, anticoagulation with warfarin is maintained and use of further heparin products can be avoided. For patients with interrupted warfarin or in whom the international normalized ratio is subtherapeutic, warfarin is resumed the night of the procedure and heparin infusion begun 6 h following hemostasis. On discharge, low molecular weight heparin (0.5 mg/kg...
AF: atrial fibrillation; CPVA: circumferential pulmonary vein ablation; CFAE: complex: fractionated atrial electrograms; PVI: pulmonary vein isolation; FIRM: focal impulse and rotor modulation; AAD: antiarrhythmic drugs. Outcome is reported after the final procedure and follow up is reported as the interval from the last procedure.

Patients are discharged the morning following the ablation and seen in clinic for follow up at 3 months and 6 months after the procedure. They are encouraged to call with any change in their clinical status and in particular with any complaints of chest discomfort, dyspnea, dysphagia or odynophagia, fevers or chills, or access-site issues. Patients with early (within the first 3 months) recurrence of AF are recommended to undergo transthoracic cardioversion. The long-term arrhythmia status is assessed in the absence of antiarrhythmic therapy with a 30-day auto-trigger monitor. Anticoagulation is continued in all patients for a minimum of 3 months. Long-term anticoagulation is guided by the patient’s risk for thromboembolism as per the consensus statement.7

Future directions

The above description represents one protocol utilized for the ablation of persistent AF and we fully recognize the existence of multiple other strategies incorporating various other technologies. With pharmacologic and technological advances constantly presenting new alternatives to management, we will need to continue to adapt our protocols to incorporate these changes. Among the innovations being tested are multi-electrode ablation catheters, improvements in current mapping systems, and automated electrogram analysis. Mostly, however, we look forward to an improved understanding of the mechanisms of persistent atrial fibrillation and the identification of optimal targets of ablation beyond the pulmonary veins. Only with such knowledge can we really hope to obtain an optimal and efficient ablation strategy and fully realize the benefits of the available technology.

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References

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