RESEARCH ARTICLE

Redo Procedures in Patients with Paroxysmal Atrial Fibrillation

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Introduction

Radiofrequency catheter ablation can effectively restore and maintain sinus rhythm in patients with paroxysmal atrial fibrillation (PAF) in whom medical therapy has failed.1–2 The cornerstone of catheter ablation procedures for PAF is electrical isolation of all pulmonary veins (PVs) at the PV–left atrial junction.3 However, the efficacy of PV isolation (PVI) procedures is limited by a high rate of AF recurrence; after an initially successful procedure, the rate of freedom from AF at 1 year is only 60–80%.4–6 Recurrent atrial arrhythmias include AF, which can be related to PV reconnection or non-PV triggers, focal or re-entrant atrial tachycardia (AT), and various forms of atrial flutter.

Risk factors for recurrence

Based on epidemiological data, recurrent atrial arrhythmias after ablation are associated with the type and duration of AF, cardiac structural abnormalities, characteristics of the atrial electrical substrate, and other clinical features of the patient (Table 1). However, the role of these risk factors in prospective risk stratification remains untested.

Patients with persistent and permanent AF are more likely to experience recurrence than those with PAF, and the recurrence rate increases with duration of AF prior to ablation.5,9–11 Cardiac structural abnormalities, particularly left atrial enlargement and impaired left ventricular function, are also associated with recurrence.5,9–14

Recommendations for monitoring

Since atrial arrhythmias recur commonly after PVI, it is recommended that patients be seen in follow-up at a minimum of 3 months following the ablation procedure and then every 6 months for at least 2 years.9 Any patient complaining of palpitations during that period should receive an event monitor to screen for recurrent AF/flutter/tachycardia, defined as an episode lasting at least 30–60 s. In addition, any patient in whom warfarin discontinuation is being considered should have continuous electrocardiographic monitoring performed to screen for asymptomatic atrial arrhythmia.
Why does recurrence happen?

AF may recur after ablation as a result of several mechanisms. These include: 1) peri-procedural inflammation; 2) delayed lesion maturation; 3) incomplete PVI; 4) PV reconnection (recovery of conduction in a previously isolated vein); 5) development of triggers in a non-isolated PV; 6) development of triggers ostial to the site of previous PV disconnection; 7) development of non-PV triggers; and 8) development of other ATs as a result of underlying abnormalities, atrial substrate, or lesions created during the original ablation procedure.

At the time of repeat ablation, both PV reconnection and non-PV triggers are observed (Table 2). Approximately 90% of ectopic foci that initiate AF originate from PVs, and in the majority of redo AF ablations, there is evidence of PV connection. Indeed, permanent PVI is challenging to achieve. Badger and colleagues recently used delayed enhancement magnetic resonance imaging (MRI) to demonstrate that after an initially successful AF ablation, complete circumferential scarring of all four PV antra was present in only 7% of patients. New AF triggers are found in a minority of patients (14–18%). Arrhythmias other than AF, particularly right and left atrial flutters, are observed in 20–50% of patients.

When does recurrence happen?

The timing of AF recurrence after ablation has important implications for its management. Recurrent atrial arrhythmias may represent: 1) a delayed therapeutic effect, or 2) treatment failure due to incomplete PVI, recovery of PV conduction, or new arrhythmogenic foci. An arrhythmia that occurs early after ablation may result from periprocedural inflammation or delayed lesion maturation, and may therefore be transient. To guide management, recurrence is often categorized based on its timing after the initial procedure as early (<3 months), late (3–12 months), and very late (>12 months).

Early recurrence (<3 months)

The development of atrial arrhythmias early after PVI increases the risk of long-term treatment failure. However, 30–50% of patients who have early recurrent episodes of AF after PVI experience a successful long-term clinical outcome, as some early atrial arrhythmias, particularly in the first 2 weeks after PVI, are thought to be caused by an inflammatory effect of radiofrequency energy or delayed therapeutic effect as the ablation lesion matures.

Late recurrence (3–12 months)

Atrial arrhythmias that recur late after PVI are less likely to be caused by transient mechanisms such as inflammation or delayed lesion maturation and more likely to represent treatment failure, whether due to PV reconnection or development of a new trigger. Lee and colleagues found that the strongest predictors of late AF recurrence were early AF recurrence and the presence of multiple AF foci during the original ablation procedure.

Very late recurrence (>12 months)

Patients who develop very late AF recurrence after ablation represent an understudied group. Mainigi and colleagues found PV reconnection in the majority of patients with very late recurrence of AF who underwent repeat ablation as well as new triggers (both PV and non-PV).

Table 1: Risk factors for atrial fibrillation (AF) recurrence

<table>
<thead>
<tr>
<th>Patient-related</th>
<th>Cardiac structural changes</th>
<th>Clinical features</th>
<th>Genetic factors</th>
<th>Biomarkers</th>
<th>Electrical substrate</th>
<th>Medications</th>
<th>High-normal thyroid function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>AF duration and type (paroxysmal versus persistent and permanent)</td>
<td>Left atrial size, left ventricular function, hypertrophic cardiomyopathy</td>
<td>Hypertension, obstructive sleep apnea, increased body mass index</td>
<td>Single nucleotide polymorphisms in chromosome 4q25</td>
<td>C-reactive protein, natriuretic peptides, white blood cell count, fibrinogen</td>
<td>P-wave dispersion, triggering pulmonary vein</td>
<td>Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers</td>
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Table 2: Frequency of arrhythmia type at repeat ablation procedure

<table>
<thead>
<tr>
<th>Type of recurrent arrhythmia</th>
<th>Frequency (%)*</th>
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</thead>
<tbody>
<tr>
<td>Reconnected pulmonary vein</td>
<td>&gt;95</td>
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<tr>
<td>Pulmonary vein trigger</td>
<td>54–77</td>
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<tr>
<td>Development of new trigger</td>
<td>14–18</td>
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<tr>
<td>Stable, regular arrhythmia other than atrial fibrillation</td>
<td>18.7–50</td>
</tr>
<tr>
<td>Left atrial flutter</td>
<td>6.7</td>
</tr>
<tr>
<td>Typical right atrial flutter</td>
<td>6.7</td>
</tr>
</tbody>
</table>

*At repeat ablation

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Implications for management
Since not all early recurrent atrial arrhythmias persist, it seems that a repeat ablation should generally be delayed for at least 2–3 months following the initial procedure, as long as the patient’s symptoms can be controlled with medical therapy and direct current cardioversion (DCCV). In a minority of patients, AF that recurs after PVI can be controlled with a previously ineffective antiarrhythmic drug. Beyond 3 months, a repeat ablation procedure is reasonable to undertake.

A practical approach to the redo procedure
One suggested approach to redo procedures in PAF is shown in Figure 1. The first step is to assess for PV reconnection and reisolate the veins if necessary. Repeat PVI (without linear ablation) provides effective treatment for many instances of recurrent AF in patients in whom an initial PVI procedure failed. Once isolation of the PVs is confirmed, non-PV triggers should be sought, using atrial pacing and isoproterenol infusion to provoke AF and direct current cardioversion if necessary to restore normal sinus rhythm. Radiofrequency energy may then be directed at the site of the earliest activity during the initiation of AF or toward isolation of a venous structure, such as the superior vena cava (SVC), that is found to be active.

Clinical atrial flutters after PVI should be targeted systematically. A cavotricuspid isthmus ablation is reasonable if typical atrial flutter has been documented clinically or during electrophysiological study. Empiric linear lesions should be approached with caution.

Complete linear lesions may be difficult to achieve in the left atrium (LA), particularly in regions such as the mitral annulus. Since incomplete lesions lead to recurrent tachycardia, we suggest that linear lesions be directed toward ablation of clinical tachycardia and that block across the line be confirmed.

Establishing PVI and locating AF triggers
Most PVI procedures fail due to electrical reconnection of the PVs. Indeed at the time of redo AF ablation procedures, >95% of patients have PV reconnection. Recovery of conduction into a previously isolated PV does not necessarily imply that the vein is arrhythmogenic, but reconnected PVs have been demonstrated to contain AF triggers in the majority of cases. Thus, establishment of PVI is an essential step in the redo AF procedure.

AF triggers inside and outside the PVs can be provoked using atrial pacing, isoproterenol infusion, and DCCV if necessary. The origin of APCs that initiate AF can be determined by morphology on the surface electrocardiogram, the intracardiac activation sequence, and mapping of the earliest recorded local activation. The goal of this part of the procedure is to identify sites where atrial premature depolarizations that initiate AF demonstrate earliest bipolar activity or a local unipolar QS pattern. An example of this approach is demonstrated in Figure 2.

A number of non-PV sites, particularly those that share an embryologic relationship to the sinus venosus, have been implicated in the initiation and maintenance of AF (Figure 3). The most common are the SVC, coronary sinus (CS), ligament of Marshall (LOM), crista terminalis (CT), and LA posterior wall.

Right atrium
AF triggers from the SVC are found in up to 20% of patients undergoing a repeat procedure after PVI. SVC isolation is logical in patients presenting for redo procedures with SVC triggers and can be performed with a very low risk of SVC stenosis and damage to the sinus node. However, in order to avoid diaphragmatic paralysis, high-output pacing should be performed along the lateral aspect of the SVC to identify the course of the phrenic nerve prior to ablation. In a small group of patients, a persistent left SVC was demonstrated to be arrhythmogenic in patients presenting with AF recurrence after PVI, through connections from the CS and the LA. Electrical isolation of the left SVC may be appropriate in such patients. The CT is another well-described right atrial AF focus.

Left atrium
AF may originate in the LOM, a neuromuscular bundle that travels from the CS to the region between the left atrial appendage (LAA) and left superior PV, or in the CS itself; these venous structures contain myocardial
connections to the atria as well as autonomic input. Provocation of ectopic activity originating in the LOM often requires infusion of isoproterenol and may be difficult to distinguish from PV or left posterior free wall ectopy, given the variable insertion site in the LA. Ectopic foci that initiate AF have also been found to originate in the posterior free wall of the LA. If present, ablation may be directed at the site of the earliest activation, or linear or box-shaped ablation lesion set may be placed about the ectopic focus, with the top and bottom of the box connecting the superior and inferior veins, respectively. Hocini and colleagues found that patients with PAF, a roof line joining the superior PVs with complete linear block, slowed the fibrillatory cycle length, increased the rate of termination and non-inducibility of AF, and improved clinical outcomes compared with PVI alone.

Several other non-PV trigger sites are under investigation. Recently, Di Biase and colleagues reported the LAA as a site of AF initiation in a substantial minority of patients undergoing redo AF ablation (paroxysmal and non-paroxysmal). LAA isolation was achieved successfully in most patients, albeit with a 1.8% incidence of cardiac tamponade, likely due to the thin-walled nature of the LAA. A few small clinical trials have explored the efficacy and safety of ablation of ganglionated plexi in the LA in AF. However, further research is required before this approach is incorporated into the treatment of patients with AF.

Post-PVI atrial tachycardia/atrial flutter

AT that develops after AF ablation is a common and challenging clinical scenario. Spontaneous post-PVI AT may have a different prognostic significance than AT that is induced at electrophysiological study but not observed clinically. Hocini and colleagues found that only 3 of 10 patients who had atrial flutters induced by pacing (9 peri-mitral and 1 caused by local reentry in the anterior LA wall) after PVI developed clinical flutter in 15 months of follow-up.
Post-PVI AT can be characterized by entrainment and/or activation mapping. Entrainment has the advantages of distinguishing LA from right atrium reentry, establishing the relationship of individual pacing sites to the reentry circuit, and facilitating the localization of focal automatic tachycardias, as the post-pacing interval decreases with proximity to the focus. Disadvantages are that entrainment requires a stable tachycardia, which nonetheless may accelerate or terminate during pacing, and that pacing may be required from many areas. A point-by-point activation map also requires a stable tachycardia, which nonetheless may accelerate or terminate during pacing, and that pacing may be required from many areas. A point-by-point activation map also requires a stable tachycardia and acquisition of a large number of points. Efficiency is improved with multi-electrode activation mapping, which reduces the time required to generate an accurate map that defines the substrate (including scar and isthmuses of conduction) and allows the use of entrainment at selected sites. Entrainment and activation mapping may be combined to identify the optimal ablation site for post-PVI atrial flutters. An example of this approach, which potentially allows less ablation with better results, is demonstrated in Figure 4.

Patel and colleagues demonstrated the utility of a multi-electrode mapping catheter used in combination with an electro-anatomic mapping system in post-PVI AT. In this study, the approach to AT ablation consisted of four steps: 1) rapid multi-electrode mapping of the chamber during tachycardia (less than 15 min per tachycardia); 2) analysis of atrial activation patterns to identify wave fronts of electric propagation; 3) targeted entrainment at putative channels; and 4) catheter ablation at these “isthmuses.” In 17 consecutive patients (mean age, 62 years; mean left ventricular ejection fraction, 61%; mean 2.3 discrete tachycardias per patient), 90% of ATs were terminated with this approach.

**What to do when there is no PV reconnection, non-PV triggers, or flutters**

Rarely, a patient presenting for redo AF ablation demonstrates no PV reconnection, non-PV triggers, or inducible atrial flutter. In this situation, empiric linear ablation has been explored. However, empiric linear ablation lesions should be approached with caution and, in our opinion, should be reserved for patients in whom atrial flutter is demonstrated. Complete lesions, across which block is demonstrated, can be difficult to achieve in the LA, particularly in regions such as the mitral annulus. Since incomplete lesions frequently lead to AF recurrence or gap-related AT, creation of complete lesions is crucial to reduce the risk of pro-arrhythmia.

**Mitral isthmus line**

A number of studies have evaluated the efficacy of performing linear ablations in addition to PVI. A strategy...
Figure 4: (a) An activation map performed during spontaneous post-pulmonary vein isolation atrial flutter (tachycardia cycle length = 205 ms) demonstrates an isthmus of conduction at the roof, with diastolic activity shown on the ablation catheter. (b) Entrainment at this “roof gap” is performed with the post-pacing interval equal to the tachycardia cycle length. (c) The first ablative lesion delivered at this site resulted in tachycardia termination.
of linear mitral isthmus ablation (lateral mitral annulus to the left inferior PV) has also been evaluated in combination with PVI isolation. In 100 patients with PAF undergoing PVI and cavo-tricuspid isthmus ablation, a linear mitral isthmus line was created, and bidirectional block was confirmed by demonstrating double potentials along the ablation line during CS pacing, differential pacing techniques, and an activation detour by pacing either side of the line.\textsuperscript{21} After endocardial and epicardial mitral isthmus ablation, block was achieved in 92\% of patients; these patients were significantly more likely to be arrhythmia-free without antiarrhythmic drugs at 1 year after the last procedure than those who did not receive mitral isthmus ablation (87\% versus 69\%, \textit{p}=0.002).\textsuperscript{19}

**Posterior line and posterior wall box lesions**

Box isolation was designed to avoid placement of vertical lesions along the esophageal aspect of the posterior LA. Complete isolation of the posterior LA including all PVs is created through continuous lesions at the anterior portions of the ipsilateral PVs, followed by linear ablation of LA roof and bottom, and is associated with a high clinical success rate.\textsuperscript{46}

**Anterior line**

In 24 patients who had failed PVI, a line of ablation transecting the anterior LA was performed in addition to repeat PVI and cavo-tricuspid isthmus ablation. A line joining the superior PVs anteriorly was connected to the anterior mitral annulus. Complete linear block was demonstrated by double potentials along the line, differential pacing techniques, and an activation detour. However, despite repeated ablation, complete block was achieved in only 58\% of patients. Only a third of patients in whom complete block could not be achieved remained arrhythmia-free without antiarrhythmics. This demonstrated that completion of a linear transection of the anterior LA is difficult and is associated with only modest long-term arrhythmia suppression.\textsuperscript{18}

**Recurrence after multiple procedures**

Even after multiple redo procedures, PV reconnection still occurs, demonstrating the difficulty of achieving permanent PVI.\textsuperscript{47} Indeed, the electrophysiological characteristics of patients undergoing first and multiple redo procedures are similar. That is, PV reconnection is present in the majority (two-thirds) of patients, and non-PV triggers (such as the SVC and CT) in the remaining third. In these patients, repeat PVI plus left atrial linear ablations effectively eliminated the AF, a reasonable success rate at 1–2 years.\textsuperscript{48} However, before undertaking a multiple-redo procedure, the patient’s cumulative fluoroscopic dose should be assessed.

**Conclusions**

Atrial arrhythmias recur in a third of PAF patients after initially successful PVI and should be meticulously monitored for. Arrhythmias that persist for more than 3 months after the initial ablation may reasonably prompt a redo procedure. Confirmation of PVI is an essential component of the redo procedure. Non-PV triggers, automatic foci that give rise to premature atrial beats and bursts of AF, should be sought, with isoproterenol infusion, atrial pacing, and DCCV if necessary. Common locations include the SVC, CS, LOM, CT, and LA posterior wall. Finally, post-PVI atrial flutters should be ablated systematically, assuring the completeness of any ablation lines that are created in order to minimize the risk of future pro-arrhythmia.

**References**


3. Calkins H, Brugada J, Packer DL, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation developed in partnership with the European Heart Rhythm Association (EHRA) and the European Cardiac Arrhythmia Society (ECAS); in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). Endorsed and approved by the governing bodies of the American College of Cardiology, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, and the Heart Rhythm Society. \textit{Europace} 2007; 9:335–379.


