How To Follow Atrial Fibrillation Ablation Patients?

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Abstract
Catheter ablation is an established treatment option for symptomatic atrial fibrillation (AF), with circumferential pulmonary vein isolation being considered the cornerstone of the procedure. However, this is a complex intervention with potential major complications and with common arrhythmia recurrences. There is consensus among experts that all patients should be seen in follow-up regularly after AF ablation. To date there are limited data regarding the best methodology for routine clinical follow-up of this population. This review summarizes a contemporary insight into management of late complications following AF ablation, post-procedural anticoagulation and arrhythmia monitoring strategies, in order to prevent thromboembolic events, detect and treat arrhythmia recurrences, and discuss the use of upstream therapies after AF ablation.

Introduction
Catheter ablation is a standard treatment for patients with drug-refractory symptomatic atrial fibrillation (AF), commonly performed throughout the world, that may provide long-term benefits regarding arrhythmia recurrence, complications and quality of life. The success of the procedure and the expanding training programs in this field have contributed to an increasing number of ablations performed worldwide. However, this is a complex intervention with potential major complications and with risk of arrhythmia recurrences. Therefore, there is consensus among experts that all patients should be seen in follow-up regularly after the ablation procedure. The best methodology for routine clinical care in order to recognize potential complications and optimize outcome results has not been fully elucidated yet. Nevertheless, a clinical follow-up protocol should include identification and management of late complications, a post-procedural anticoagulation strategy, arrhythmia monitoring in order to detect and treat arrhythmia recurrences and control of associated comorbidities contributing to the risk of AF recurrence (figure 1).

What can we expect after AF ablation? Recovery from catheter ablation is usually quick (1-2 days). After removing the catheters, the patient lies flat for up to 6 hours to prevent bleeding from the puncture sites. Telemetry and blood pressure monitoring is recommended and the health team must be aware of symptoms, delayed complications and patient comorbidities. Common issues influencing the clinical outcome are the risk of thromboembolic events, early recurrence of atrial tachyarrhythmias and control of frequently associated comorbidities, like hypertension, diabetes, sleep apnea, or anxiety.

Late complications following AF ablation are inconsistently reported in retrospective surveys and include stroke, pericardial effusion and cardiac tamponade, iatrogenic atrial tachycardias, pulmonary vein (PV) stenosis, death (stroke, tamponade, atri-oesophageal fistula), arteriovenous fistula and hematoma resulting from vascular access, and phrenic nerve injury. A recent single-centre cohort analysis reported late complications in 4% of the patients submitted to AF ablation. Hopefully, improved ablation techniques and operator experience may contribute to the declining of complications rates.

The incidence of PV stenosis has varied substantially, depending on the ablative technique used and the method of assessment. Recent reports suggest that 1% to 10% of patients undergoing ablation develop PV stenosis. In the recent years, the incidence has fallen with improvements in the mapping and ablation techniques. Nevertheless, this problem continues to be reported and it accounts for approximately 30% of major complications.

From a clinical point of view, some patients with mild (<50%) or moderate stenosis (50-70%) are asymptomatic. Symptoms caused by PV stenosis depend on the severity and the number of the affected veins and range from persistent cough, to chest pain, hemoptyis, and severe exertional dyspnea.

There is general agreement that patients with symptomatic severe PV stenosis should be treated with PV angioplasty with or without stenting. Treatment with catheter angioplasty can improve and, in some cases, completely relieve PV stenosis following AF ablation. It has been shown that stent angioplasty is superior to balloon dilation in treating this complication. However, even with stent implantation, restenosis may occur in 30% to 50% of patients. Also, prompt referral for intervention and use of larger stents seem to be associated with lower restenosis rates and, therefore, with long-term patency.

Post-procedural atrial tachycardias are relatively common and have been considered to be largely associated with circumferential ablation

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using wide-area circular lesions around the PV, or when additional ablation lines are incorporated in the procedure, creating an electrophysiologic milieu for both small and macroreentry circuits.\textsuperscript{9,10} From a clinical point of view, these arrhythmias are characterized by: early onset of significant symptoms (frequent palpitations and fatigue) after ablation, refractory to management with rate-controlling drugs, limited amenability with antiarrhythmic drugs, and high recurrence rate after cardioversion.

Vascular access complications (hematoma, femoral pseudoaneurysm, arteriovenous fistula or retroperitoneal bleeding) are influenced by the number and size of sheats used, the need for anticoagulation before and after the procedure, and the operator experience. Incidence has been described in up to 13\% of the cases\textsuperscript{1-3,11} and may require adequate manual compression or surgical repair.

The incidence of thromboembolism associated with AF ablation is reported to be between 0.9\% and 7\%.\textsuperscript{1,3,12} A thromboembolic phenomenon leading to stroke is a serious complication of AF ablation that typically occurs between 24 hours and the first 2 weeks after the ablation procedure.\textsuperscript{13} In fact, a portion of the left atrium is burned during the procedure and the atria are often stunned after ablation. There is an increased risk of thromboembolism immediately following, and for several weeks after ablation, justifying optimal anticoagulation monitoring in order to achieve a safe level of thromboembolism prevention.

Cardiac tamponade is the most common life-threatening complication observed in patients undergoing AF ablation. The intense intraprocedural and post-procedural anticoagulation regimen recommended, together with extensive catheters manipulation, high levels of radiofrequency energy and the contact force exerted by the ablation catheter on the interface with cardiac tissue may expose patients to an excessive risk for bleeding. Delayed pericardial effusion (occurring >1h after ablation) leading to hypotension or cardiac shock is relatively rare in patients undergone a recent AF ablation.\textsuperscript{14,15} However, attention should be given to chest pain, fatigue, dyspnea, tachycardia, and hypotension. Echocardiography confirms the diagnosis and pericardial drainage needs to be performed in most of the cases. Also, anticoagulation may be temporarily discontinued if the bleeding situation is maintained, and, in some cases, surgery is required in order to repair rupture of the atrial tissue.

A very rare, but potentially fatal, late complication is the atrio-esophageal fistulae, formed from thermal injury from posterior wall of the left atrium causing damage of the esophagus. Although the incidence of the fistula is less than 1\%, high mortality adds significance to the problem, making it one of the most feared complications of AF ablation.\textsuperscript{16,17} The observation that esophageal ulcerations may be observed on endoscopy following AF ablation has led to prophylactic use of proton pump inhibitors for one to four weeks after ablation in many centres. However, there are no data available available to demonstrate that this approach reduces the incidence of an atrio-esophageal fistula. Therefore, current guidelines and consensus reports list no objectives on this issue.\textsuperscript{1}

Phrenic nerve paralysis is another complication of AF ablation using cryoablation or radiofrequency energy, resulting from direct thermal injury to the right phrenic nerve. Although uncommon with radiofrequency energy (<1\%), its incidence with the use of the cryoballoon system ranges from 4.7\% to 11\%, with a complete resolution noted in >80\% of the cases.\textsuperscript{1,18,19}

### Follow-Up And Long-Term Management

#### Post-Procedural Anticoagulation

There is consistent evidence that a continuous warfarin strategy reduces peri-procedural thromboembolic complications without increasing the risk of major bleeding events.\textsuperscript{20,21} Also, the use of dabigatran with the dose held on the day before the procedure and restarted immediately after AF ablation, seems to be safe and well tolerated, with no evidence of a higher risk of thromboembolic or bleeding complications compared to warfarin.\textsuperscript{22} Regarding the use of warfarin or new anticoagulants (direct thrombin inhibitors or factor Xa inhibitors), it has been recently suggested that both dabigatran and rivaroxaban are equally safe and effective when compared to warfarin.\textsuperscript{23}

Low molecular weight heparin should be used 4-6h after sheat removal as a bridge to resumption of oral anticoagulation with warfarin or new anticoagulants.

There have been no large randomized prospective trials that have assessed the safety of stopping anticoagulation in this population. However, in most studies anticoagulation was continuously maintained for at least 3-6 months after ablation in patients who did not experience recurrent AF and had no incidents of thromboembolism. Current consensus recommends that decisions

### Table 1: Clinical follow-up protocol after atrial fibrillation ablation

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transthoracic echo before discharge</td>
<td>outpatient clinic at 4 weeks and every 6 months thereafter</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>antiarrhythmics 3-6 months, anticoagulation 3-6 months</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>proton pump inhibitors for 1 week</td>
</tr>
<tr>
<td>Patients with hypertension - ARB/ACEI</td>
<td>patients with hypertension - ARB/ACEI</td>
</tr>
<tr>
<td>EKG (every regular appointment or if symptoms recurrence)</td>
<td>EKG (every regular appointment or if symptoms recurrence)</td>
</tr>
<tr>
<td>Event recorder or Implantable loop recorder</td>
<td>Event recorder or Implantable loop recorder</td>
</tr>
<tr>
<td>Holter recording 1st month and every 4 months</td>
<td>Holter recording 1st month and every 4 months</td>
</tr>
</tbody>
</table>

### Table 2: CHA\textsubscript{DS\textsuperscript{2}}-VASc score and risk of stroke in atrial fibrillation

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure/LV dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age &gt;75</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/thrombo-embolism</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease\textsuperscript{a}</td>
<td>1</td>
</tr>
<tr>
<td>Age 65-74</td>
<td>1</td>
</tr>
<tr>
<td>Sex category (i.e. female sex)</td>
<td>1</td>
</tr>
<tr>
<td>Maximum score</td>
<td>9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Score CHA\textsubscript{DS\textsuperscript{2}}-VASc</th>
<th>Annual risk of thromboembolic events (%/y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>3</td>
<td>3.2</td>
</tr>
<tr>
<td>4</td>
<td>4.0</td>
</tr>
<tr>
<td>5</td>
<td>6.7</td>
</tr>
<tr>
<td>6</td>
<td>9.8</td>
</tr>
</tbody>
</table>
Arrhythmia Monitoring

Although catheter ablation significantly reduces the burden of AF, arrhythmia recurrences are common, both early and late following AF ablation, with a high proportion of symptomatic episodes. Long-term follow-up studies have shown that a single ablation procedure may be sufficient to achieve freedom from AF in 50% of patients, and that multiple procedures may control AF in 80% of patients. 

Arrhythmia monitoring to assess the efficacy of catheter ablation is typically delayed for 3 months. The use of this blanking period, during which transient tachyarrhythmia episodes are not considered recurrences, has been employed in studies examining the efficacy of radiofrequency catheter ablation of AF. Methods to evaluate arrhythmia recurrences during follow-up include: outpatient visits (ex. once in the first 3 months after ablation and every 6 months for 2 years), ECGs, 1-7 day Holter recording, telemetric transcriptions, and event loop recorders (non-invasive or implantable). A more intensive monitoring strategy is known to be associated with a greater likelihood of AF detection.

Although early recurrence of AF carries an independent risk of treatment failure, its occurrence should not prompt immediate re-ablation attempts, as about 50% of the patients experiencing this event within the “blanking period” will not have any further arrhythmias. In our experience, the use of an external event loop recorder for the continuous detection of sudden arrhythmias during the first month after AF ablation documented sustained atrial tachyarrhythmias in 35.2% of the cases. However, the predictive positive value for the identification of patients with late arrhythmia recurrence was only 45%. Recently, in 630 patients who underwent circumferential pulmonary vein isolation and were implanted with a subcutaneous AF monitor it was suggested that the AF burden measured during the blanking period (with a calculated threshold of 65.9 hours of AF during the first 2 months) can predict the response to catheter ablation at 12 months. 

The mechanisms of AF post-ablation may be different from that of the patient’s clinical arrhythmia and may resolve completely upon resolution of the inflammatory process. Therefore, it has been suggested to treat all patients with antiarrhythmic agents for the first 3 months and delay re-ablation procedures for at least 3 months. 

Up to 35% of patients have recurrence of AF in the first year following catheter ablation. Multiple procedures may be considered to improve the long-term success of AF ablation. In a recent meta-analysis, the overall average number of procedures was 1.51. Left atrial enlargement, pre-existing atrial fibrosis, type of AF, age, gender, hypertension, left ventricular dysfunction, and sleep apnea syndrome have been reported as independent predictors of success after single- or multiple-procedures. On an average, patients with nonparoxysmal AF are about 60% more likely to have AF recurrence after radiofrequency ablation than those with paroxysmal AF. 

Post-procedural atrial tachycardias have been considered to be associated with circumferential ablation using antral PV isolation and additional atrial ablation lines. Most of these tachycardias originate from reentry circuits in the left atrium and are responsible for complaints of worsening symptoms. Rhythm control is usually difficult with antiarrhythmic drugs (AAD) and early recurrence is common after external cardioversion. Therefore, it often poses a more difficult clinical situation than the index arrhythmia. It has been proposed to maintain AAD therapy after electrical cardioversion and reserve a new ablation for patients in whom the arrhythmia did not disappear after a period of 3 months, because up to a third of these patients will present with resolution of their atrial tachycardia. The reablation procedure should obtain complete PV isolation and confirm bidirectional block of the previous lines. An activation mapping using tridimensional electroanatomic navigation systems is commonly complemented with detailed analysis of entrainment maneuvers to optimize the results of the procedure. Various authors have published promising results with these atrial tachycardias successfully ablated in 42% to 100% of the cases, but showing recurrence rates ranging from 21% to 44%. 

AAD are commonly used during the first 3 months after AF ablation. The therapy most commonly employed for this purpose are the drugs that were unsuccessful prior to ablation. It has been suggested that its use restricted to this period reduces the need for hospitalization or cardioversion, without exposing the patient to serious side effects associated with their prolonged use. Should we maintain AAD or repeat PV isolation to prevent arrhythmia recurrences after AF ablation? 

Pokushalov, et al, in a recent 154-patient study, compared those who underwent repeat PV isolation with patients taking AAD after recurrent paroxysmal AF. All patients received an implantable loop
Late complications after catheter ablation to treat atrial fibrillation

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Clinical manifestations</th>
<th>Preventive management</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV stenosis</td>
<td>0-38%</td>
<td>persistent cough, dyspnea, hemoptysis</td>
</tr>
<tr>
<td>Post-ablation atrial tachyarrhythmias</td>
<td>5-31%</td>
<td>early onset of important palpitations and fatigue</td>
</tr>
<tr>
<td>Vascular access complications</td>
<td>0-13%</td>
<td>groin hematoma, arteriovenous fistula, bleeding</td>
</tr>
<tr>
<td>Phrenic nerve injury</td>
<td>0.48-11%</td>
<td>dyspnea, hiccups, atelectasis, pleural effusion, cough, and thoracic pain</td>
</tr>
<tr>
<td>Thromboembolism/Stroke</td>
<td>0.9-7%</td>
<td>occur within 24h to 2 weeks after ablation. Clinical presentation depends on occlusion location</td>
</tr>
<tr>
<td>Pericardial effusion with cardiac tamponade</td>
<td>0.2-6%</td>
<td>chest pain, hypotension, dyspnea</td>
</tr>
<tr>
<td>Atrial-esophageal fistulae</td>
<td>&lt;1%</td>
<td>2-4 weeks after ablation, fever, chills, recurrent neurological events, septic shock, death</td>
</tr>
</tbody>
</table>

PV=pulmonary veins; ACT=activated clotting time; RF=radiofrequency; *=influenced by the technique and type of energy

What are the recommended steps in a redo procedure after AF recurrence? One suggested approach is shown in Figure 3.

What is the incidence of PV reconduction of previously isolated PV seems to be the major determinant of clinical AF recurrence.

In conclusion, AF ablation has emerged as a successful therapeutic option. However, it is a complex procedure that is associated with potential major complications and the primary prevention of AF due to pleiotropic effects in relation with anti-inflammatory effects, improvement of endothelial function and antioxidant properties. In a meta-analysis performed to assess the potential benefits of statins on the recurrence of AF after electrical cardioversion or ablation, statins did not reduce the risk of AF occurrence following AF ablation (4 studies including 750 patients). Thus, the role of statins post-AF ablation has not been established. Larger randomized controlled trials are required to further evaluate the role of statins after AF ablation.

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