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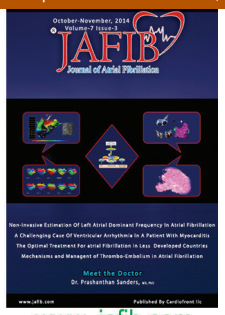

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How To Follow Atrial Fibrillation Ablation Patients?

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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.[1,2] 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.

Disclosures:
None.

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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, atrio-esophageal fistula), arteriovenous fistula and hematoma resulting from vascular access, and phrenic nerve injury[1-3] (table I). A recent single-centre cohort analysis reported late complications in 4% of the patients submitted to AF ablation.[4] 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.[5,6] 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.[1-3]

From a clinical point of view, some patients with mild (<50%) or moderate stenosis (50-70%) are asymptomatic.[7] Symptoms caused by PV stenosis depend on the severity and the number of the affected veins and range from persistent cough, to chest pain, hemoptysis, 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.[8] It has been shown that stent angioplasty is superior to balloon dilation in treating this complication.[7,8] However, even with stent implantation, restenosis may occur in 30% to 50% of patients.[8] Also, prompt referral for intervention and use of larger stents seem to be associated with lower restenosis rates and, therefore, with long-term patency.[8]

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

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

Transthoracic echo before discharge
outpatient clinic at 4 weeks and every 6 months thereafter
antiarrhythmics3-6 months;anticogulation 3-6 months
proton pump inhibitors for 1 week
patients with hypertension - ARB/ACEI
EKG (every regular appointment or if symptoms recurrence)
Event recorder or Implantable loop recorder
Holter recording 1st month and every 4 months

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.[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[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%.[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 of the ablation procedure.[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.[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.[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.[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.[1,18,19]

Follow-Up And Long-Term Management

Post-Procedural Anticoagulation

There is consistent evidence that a continuous warfarin strategy reduces periprocedural thromboembolic complications without increasing the risk of major bleeding events.[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.[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.[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 2: CHA_2DS_2-VASc score and risk of stroke in atrial fibrillation

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease[a]	1
Age 65-74	1
Sex category (i.e. female sex)	1
Maximum score	9
Score CHA_2DS_2-VASc	**Annual risk of thromboembolic events (%/y)**
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8

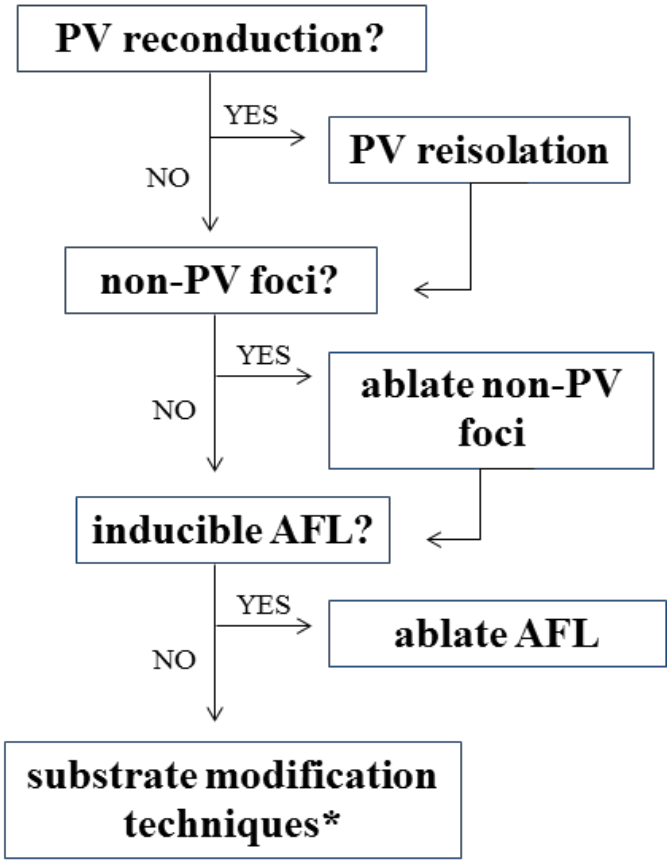

Figure 1: An approach to a redo procedure after atrial fibrillation recurrence

about continuation of oral anticoagulation with warfarin or newer anticoagulants thereafter should be based on the risk factors for stroke[1] (figure 2). Among patients at high $CHADS_2Vasc$ score anticoagulation should be maintained life-long after the procedure even if the ablation appears to have eliminated AF.[1,2] For patients with $CHADS_2Vasc \leq 1$, duration of anticoagulation has been suggested to be continued for at least 3 months.[20]

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 asymptomatic episodes.[24] 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.[25]

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, telemedicine transmissions, 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.[1,26] 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.[27] 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.[28]

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, is 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.[1,26]

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.[25] 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.[25,29-32] On an average, patients with nonparoxysmal AF are about 60% more likely to have AF recurrence after radiofrequency ablation than those with paroxysmal AF.[30]

Post-procedural atrial tachycardias have been considered to be associated with circumferential ablation using antral PV isolation and additional atrial ablation lines.[33] Most of these tachycardias originate from reentry circuits in the left atrium and are responsible for complains of worsening symptoms. Rhythm control is usually difficult with antiarrhythmic drugs (AAD) and early recurrence is common after external cardioversion.[9,10,33] 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.[33] 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 maneouvers 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%.[1,33]

AAD are commonly used during the first 3 months after AF ablation.[1,34] 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.[34]

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

Table 3: Late complications after cateter ablation to treat atrial fibrillation

	incidence	clinical manifestations	preventive management
PV stenosis	0-38%	persistent cought, dyspnea, hemoptysis	avoid lesions inside the PV, angioplasty and stenting of PV stenosis
Post-ablation atrial tachyarrhythmias	5-31%	early onset of important palpitations and fatigue	initial suppression with antiarrhythmics, may resolve by 3 months, repeat ablation after 6 months
Vascular acess complications	0-13%	groin hematoma, arteriovenous fistula, bleeding	manual compression, surgical repair
Phrenic nerve injury	0.48-11%*	dyspnea, hiccups, atelectasis, pleural effusion, cough, and thoracic pain	high output pacing along the superior vena cava or right PV to capture phenic nerve during energy applications
Thromboembolism/Stroke	0.9-7%	occur within 24h to 2 weeks after ablation. Clinical presentation depends on occlusion location	anticoagulation pre- and post-procedure (restart 6h after ablation and continued for at least 3 months). ACT of 250-300s during ablation
Pericadial effusion with cardiac tamponade	0.2-6%	chest pain, hypotension, dyspnea	echocardiography, pericardial drainage (some require surgery)
Atrio-esophageal fistulae	<1%	2-4 weeks after ablation, fever, chills, recurrent neurological events, septic shock, deat	monitoring of esophageal temperature during RF, limiting power to 25 W in the posterior wall of the left atrium, proton pump inhibitors, emergent surgical intervention

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

recorder to track atrial arrhythmic events. AF burden, progression to persistent AF and atrial tachyarrhythmia-free results were better in the reablation group after 3 years follow-up.[35]

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

PV to left atrial reconduction of previously isolated PV seems to be the major determinant of clinical AF recurrence.[36] Check for PV reconduction is a primary goal of the redo procedure. In fact, repeat PV isolation provides effective treatment for many instances of recurrent AF.[37] If no evidence of PV reconduction, greater attention should be paid to non-PV foci, commonly located at the superior vena cava, coronary sinus, ligament of Marshall, crista terminalis and left atrial posterior wall, as well as greater use of substrate modification techniques, including empirical linear ablation lines in the mitral isthmus, posterior wall, anterior wall and/or left atrial roof. Post-AF ablation atrial flutters should be also ablated, assuring the block across ablation lines created in order to minimize de risk of future pro-arrhythmia.

Upstream Pharmacological Therapy

Some studies have investigated the role of various non-AAD upstream therapies (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, statins) in preventing AF recurrences after catheter ablation, reporting conflicting results. Whereas there is a general consensus on the use of anticoagulation therapy and AAD following AF ablation, no definite data are available on the proper long-term management of upstream therapy after catheter ablation.

Attention to control of hypertension and a regimen of optimal heart failure therapy remains an integral part of AF management after the ablation procedure. There is a rational for the prevention of AF via inhibition of renin angiotensin aldosterone system (RAAS). Potential benefits may be associated with substrate modification (left atrial and PV dilation, atrial fibrosis and conduction velocity slowing), improvement of haemodynamic function (lower intra-atrial pressure, reduce blood pressure and left ventricular dysfunction) and reduction of initiators of AF (modify stretch-activated ion channels, reduce stretch-induced atrial automaticity).[2] However, in a prospective registry of 616 consecutive patients undergoing catheter ablation of paroxysmal or persistent AF, angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) showed no impact on the maintenance of sinus rhythm on long-term outcome of AF ablation.[38] The use of RAAS inhibitors for AF recurrence prevention is still up for debate because the data regarding reverse atrial remodeling remains conflicting. Larger randomized prospective studies are needed to conclusively answer that question.

There is some evidence suggesting that statins may have a role in the primary prevention of AF due to pleiotropic effects in relation with anti-inflamatory effects, improvement of endothelial function and antioxidant properties.[39] 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).[40] 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.

Conclusion:

In conclusion, AF ablation have emerged as a successful therapeutic option. However, it is a complex procedure that is associated with potential major complications and with risk of arrhythmia recurrences. Management of patients after hospital discharge requires commitment from the health team. Experience must be gained in the diagnosis and management of post-procedure complications (occurring in 3-7%), including delayed complications such as stroke, cardiac tamponade, esophageal injury, PV stenosis, and late hematoma/pseudoaneurysm or arteriovenous fistula.

Most of the authors maintain anticoagulation therapy and AAD during the first 3-6 months after successful AF ablation. The risk-benefit decision regarding the use of anticoagulation should be based on the actual risk scores. The role of ACEI/ARB after AF ablation stills controverse. The use of statins (without standard indications) is not recommended. Finnaly, the development of standard follow-up programmes in order to prevent delayed complications and to optimize the success of catheter ablation reintervention may contribute to improve the long-term results of AF ablation.

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