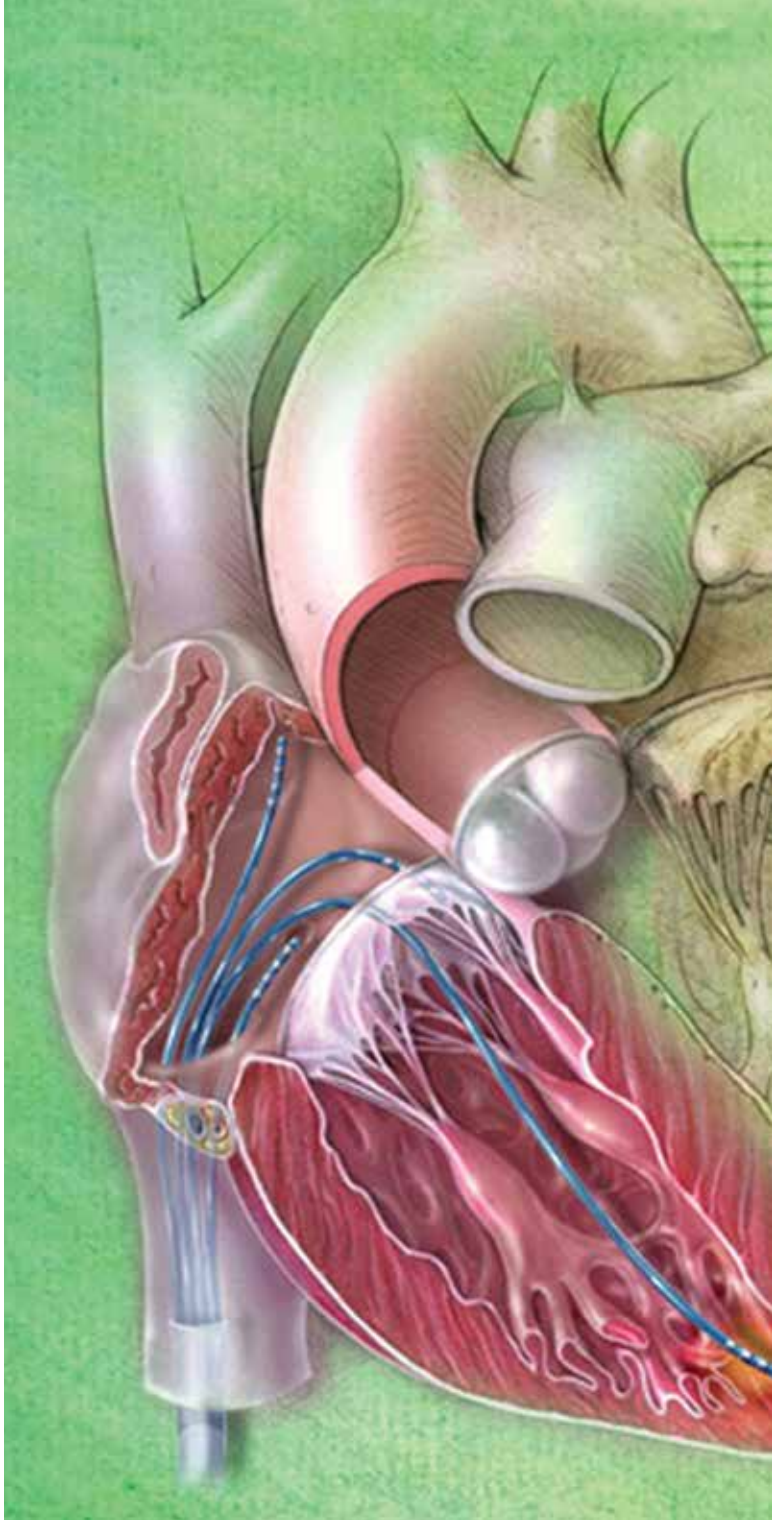
FEATURE

Atrial fibrillation

Beyond drug therapies

MALCOLM ANASTASIUS BSc(Med), MB BS, MMed(ClinEpi)
MAROS ELSIK BSc(Med), MB BS, PhD, FRACP, FCSANZ

Atrial fibrillation is the most common, clinically relevant arrhythmia encountered in general practice with treatment options that continue to expand. This article provides a brief overview of the various types of atrial fibrillation and focuses predominantly on the currently available nonpharmacological treatment modalities.

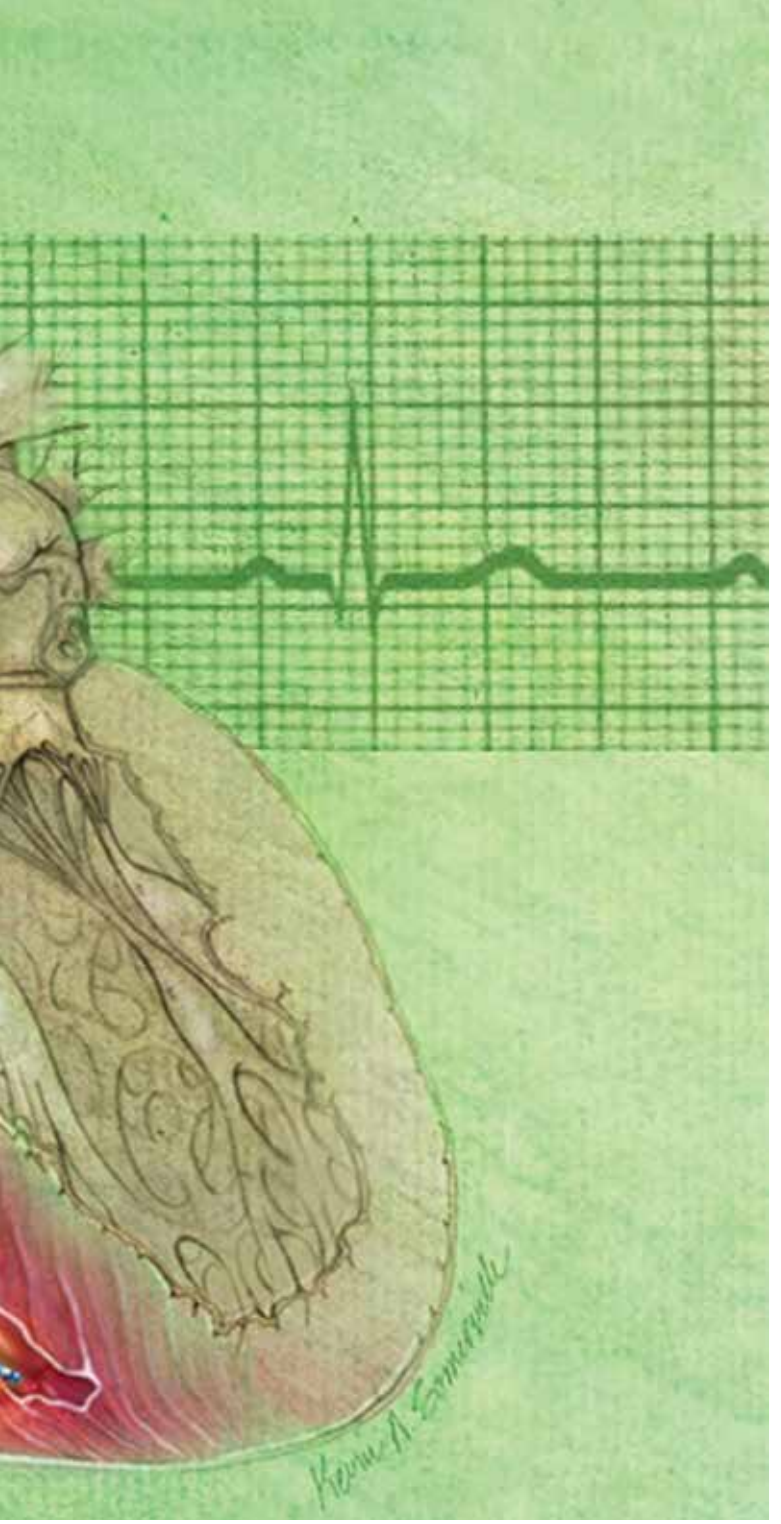


© KEVIN A. SOMERVILLE

The prevalence of atrial fibrillation (AF) in the general population is approximately 1%, being relatively uncommon in the young but increasing with age to rates of above 9% in people over the age of 80 years.[1] Symptoms due to AF vary widely. Patients can present with symptoms including palpitations, awareness of an irregular pulse, chest pains, dyspnoea, reduced exercise capacity, dizziness, syncope, lack of energy and heart failure. Some patients can be asymptomatic whereas others present with transient ischaemic attacks, strokes or other thromboembolic complications as their first symptom of AF. Hospitalisations are frequent in patients with AF.

CARDIOLOGY TODAY 2014; 4(3): 6-12

Dr Anastasius is a Cardiology Registrar at Concord Hospital, Sydney. Dr Elsik is a Consultant Cardiologist and Electrophysiologist at Concord Hospital, Macquarie University Hospital and Sydney Adventist Hospital, Sydney, NSW.



Key points

- **Atrial fibrillation is the most common clinically relevant arrhythmia, which in most patients originates from abnormal 'triggers' within the pulmonary veins.**
- **Medical therapy and nonpharmacological approaches are often used together to treat symptoms of arrhythmia and prevent thromboembolic complications.**
- **Catheter ablation of atrial fibrillation utilising a pulmonary vein isolation (PVI) is a commonly used and highly effective procedure to treat symptomatic patients, especially if used early.**
- **An ablation of the atrioventricular node and a pacemaker insertion can be useful in improving symptoms in patients who remain symptomatic despite all other treatment attempts.**
- **Left atrial appendage occlusion devices can be effective in reducing thromboembolic complications if anticoagulation is contraindicated.**

Types of atrial fibrillation

Awareness of the types of AF is useful to understanding the aetiology of AF and the available treatment options. The current AF classification is based predominantly on the duration of each arrhythmic episode:[2]

- **paroxysmal AF:** episodes lasting less than seven days
- **persistent AF:** episodes lasting more than seven days
- **longstanding persistent AF:** episodes lasting more than 12 months
- **permanent AF:** when the doctor and patient agree not to pursue restoration of sinus rhythm, and accept that AF will not resolve.

Paroxysmal AF

Paroxysmal AF is predominantly a disease of the pulmonary veins. It is now recognised that 'sleeves' of left atrial myocardial cells extend into the proximal portions of the pulmonary veins. In 95% of AF cases, the arrhythmia is triggered by an abnormal focus of rapidly firing myocardial cells within the proximal portions of the pulmonary vein. These pulmonary vein 'triggers' initiate AF, which subsequently spreads to involve both atria.[3]

Nonparoxysmal (persistent, permanent) AF

Nonparoxysmal AF is a complex and chronic rhythm disorder. AF becomes longer lasting as a result of abnormalities in atrial tissue that promote AF reinitiation and maintenance. In persistent and permanent AF, these changes in the atrial 'substrate' often become more important than pulmonary vein triggers in maintaining arrhythmia (Figure 1). The mechanisms responsible are thought to include multiple re-entrant wavelets, nonpulmonary vein triggers and independent rotors. In this setting, atrial enlargement, replacement myocardial fibrosis, ischaemia, activation of the autonomic nervous system and renin-angiotensin-aldosterone system, and numerous extrinsic factors contribute to adverse atrial remodelling, which further contributes to reinitiation and maintenance of AF (Figure 2).[1]

The natural history of AF is such that it becomes more frequent over time and about 25% of patients with paroxysmal AF will develop permanent AF within five years.

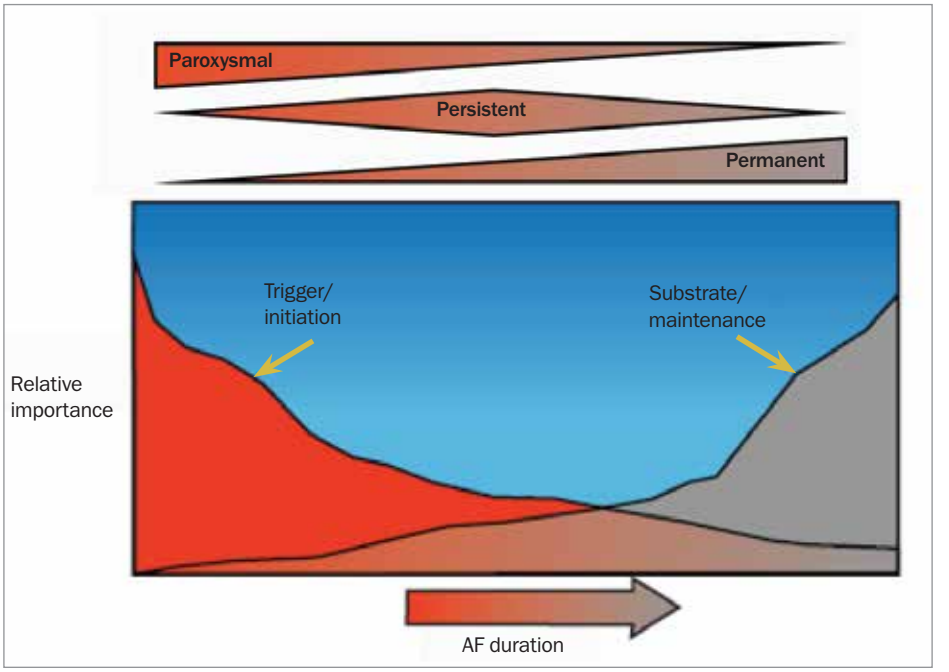


Figure 1. Mechanisms in paroxysmal, persistent and permanent atrial fibrillation (AF). Triggers are most important in paroxysmal atrial fibrillation whereas substrate abnormalities are necessary for maintaining permanent atrial fibrillation.

Reproduced with permission from Crandall M, et al. Mayo Clin Proc 2009; 84: 643-662.[1]

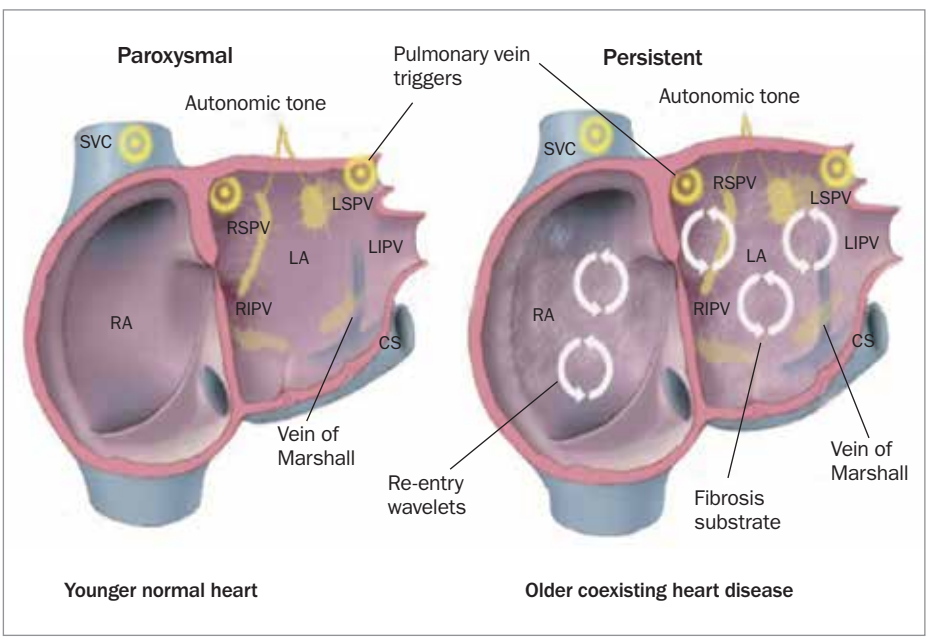


Figure 2. Differences between paroxysmal and persistent forms of atrial fibrillation. Persistent atrial fibrillation is associated with a larger left atrium, fibrosis and re-entrant wavelets. Common to both are triggers in the proximal pulmonary veins.

Abbreviations: CS = coronary sinus; LA = left atrium; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RA = right atrium; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein; SVC = superior vena cava.

Reproduced with permission from Crandall M, et al. Mayo Clin Proc 2009; 84: 643-662.[1]

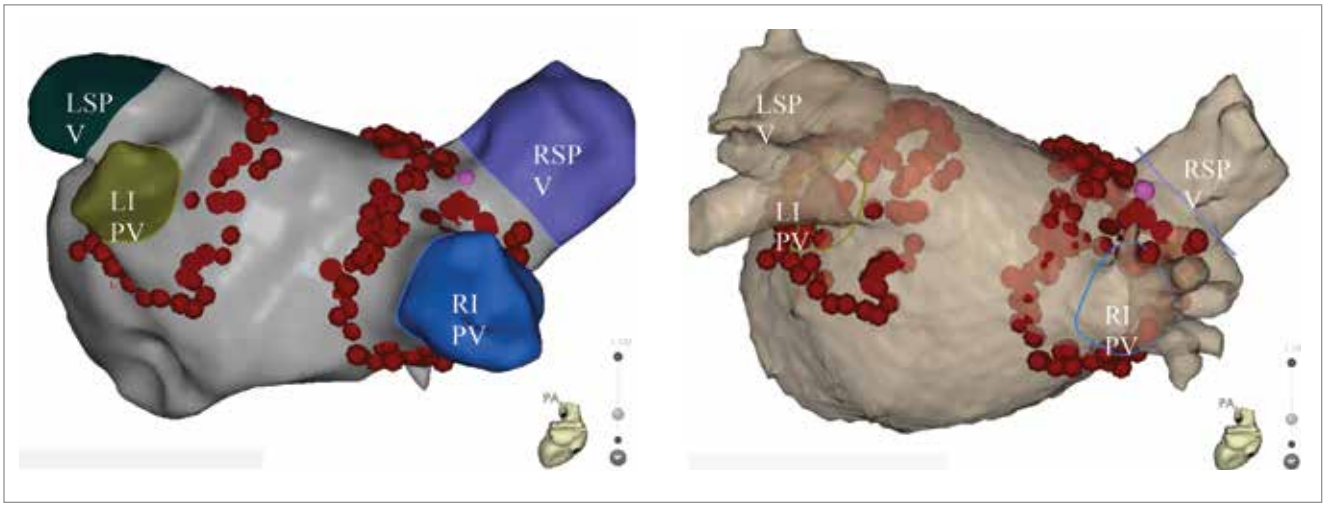
Management goals and nonpharmacological treatment strategies

The treatment of AF – cardiac rhythm management and anticoagulation – is focused on managing two distinct aspects of the condition. In treating the rhythm abnormality in AF, a decision is made to focus on either a rhythm-control strategy (aiming to restore and maintain sinus rhythm) or a rate-control strategy (accepting AF, but ensuring that the ventricular rate is adequately controlled). The decision to pursue one strategy or another is determined predominantly by symptoms and the length of AF, as well as the age of patients and their comorbidities.

Rhythm-control strategy

In symptomatic patients, usually of a younger age, a strategy of attempting to maintain sinus rhythm should be considered. The first-line approach involves medical therapy, using antiarrhythmic drugs such as sotalol, flecainide or amiodarone either alone or in combination with other drugs. Patients who remain symptomatic from AF despite medical therapy should be considered for ablative therapy.

Catheter ablation is now a standard procedure and regarded as a class I indication for the treatment of AF in appropriately selected patients who remain symptomatic despite use of at least one class I (e.g. flecainide) or class III (e.g. amiodarone, sotalol) antiarrhythmic medication. The procedure is aimed at restoring and maintaining sinus rhythm and improving patient's quality of life. Catheter ablation of AF does not eliminate the need for anticoagulation and is not an alternative to anticoagulation. The CHA_2DS_2-VASc score determines the need for anticoagulation.



Figures 3a and b. a (left). 3D map of the left atrium showing the pulmonary veins (posterior view). The ablation lesions (red circles) surround the left superior and left inferior pulmonary veins, as well as the right superior and right inferior pulmonary veins, respectively, to create pulmonary vein isolation. b (right). A preprocedure CT scan of the left atrium showing pulmonary veins from the same patient. This image demonstrates the close correlation between the 3D map created at the time of the procedure and the actual CT scan. Corresponding ablation lesions (red circles) are also shown.

Catheter ablation of paroxysmal AF

Catheter ablation focusing on pulmonary vein isolation (PVI) is the key ablation procedure for AF. It is performed under sedation or general anaesthesia in a cardiac catheter laboratory. A preprocedure transoesophageal echocardiography is used to exclude an intracardiac thrombus and a CT scan of left atrium and pulmonary veins is obtained to guide the ablation.

During the procedure, catheters are guided into the left atrium. Sophisticated mapping equipment is used to construct a 3D map of the left atrium and the pulmonary veins, which is then used to locate and guide the catheters to specific ablation sites (Figures 3a and b). An ablation catheter is used to deliver radiofrequency energy to the left atrium, which causes heating of the tissue. With healing, this leads to scar formation at the ablation sites. In this way an ablation is used to electrically 'isolate' the pulmonary veins from the atria (hence the term pulmonary vein isolation). As a result, the pulmonary vein triggers are unable to conduct electrical impulses to the atria, thus preventing AF initiation, and favouring the maintenance of sinus rhythm. Cryotherapy ablation resulting in tissue freezing is an alternative approach to PVI used in some centres.

Catheter ablation of persistent AF

For patients with persistent AF, PVI is performed together with additional ablation targeting abnormal atrial substrate. The techniques for this vary among operators, however, in most cases, linear ablations in the left atrium will be performed with or without ablation of complex fractionated atrial electrograms. These ablations are used to target regions of high frequency atrial activity due to areas of abnormal conduction, intrinsic rotors, neural activity or micro re-entry, which are thought to be responsible for maintaining and reinitiating AF in patients with nonparoxysmal AF. Ablation of persistent AF is typically performed in a stepwise fashion rather than all at once. As a result, patients with nonparoxysmal AF are more likely to need repeat procedures to achieve and maintain sinus rhythm.

Outcomes of catheter ablation

Success of catheter ablation is typically defined as freedom from AF. The main aim is to reduce AF-related symptoms. Recurrence of AF after PVI can occur early (within three months) due to ablation-related inflammation but this does not preclude long-term success. The success rate of catheter ablation for patients with paroxysmal AF has been reported to be between approximately 60% and 80%, with a generally reported mean of approximately 70% after the first procedure. Antiarrhythmic medications may be stopped in many but not all patients after catheter ablation.

In the treatment of patients with paroxysmal AF, a meta-analysis of randomised controlled trials comparing PVI ablation with drug therapy alone showed a statistically significant lower recurrence of atrial arrhythmia – 23.2% (PVI) versus 76.6% (drug therapy alone).[4] Studies with five-year follow-up data have shown that in patients with paroxysmal AF sinus rhythm was achieved in 80 to 92% of patients after repeat ablation procedure.[5]

In patients with persistent AF, the single procedure success rate using various ablation techniques (PVI alone, PVI with additional ablations) showed a mean single procedure success rate of 47% (drug free). Repeat ablation procedures (targeting abnormal atrial substrate) have been shown to improve success rates up to 65%.[6]

The success rate of catheter ablation is highest in younger patients (less than 70 years of age) without structural heart disease. The predictors of reduced success of catheter ablation in the long term include persistent AF, older age, severe left atrial enlargement, obesity, sleep apnoea and structural heart disease. The likelihood of success diminishes in people with persistent AF and a duration of more than three years, and ablation is less likely to be offered in these patients. For this reason, catheter ablation should be considered earlier rather than later in patients with symptomatic AF. Age is not an absolute barrier to catheter ablation, however, the primary success rates of the procedure fall as age increases, and procedure-related complications increase.

Most commonly encountered complications following catheter ablation of AF are related to the access site and include bleeding, haematoma, deep venous thrombosis and vascular damage. Less common but more serious complications can include cardiac tamponade (about 1%), stroke and transient ischaemic attack (0.5 to 1%), and pulmonary vein stenosis (<1%). The risk of death is about 0.1%, and atrioesophageal fistula (about 0.02%) is a feared but rare complication.[7] Postprocedural pericarditis is common and treated in a standard way. Atrial flutter is not uncommonly seen postablation and this may need to be treated with further ablation.

PVI is considered a class I indication for the treatment of patients with symptomatic paroxysmal AF. Due to the increased complexity of ablation needed to treat persistent AF, PVI should ideally be considered and offered earlier rather than later in symptomatic patients.

Rate-control strategy

A rate-control strategy can be an alternative to a rhythm control strategy in all forms of AF, but especially in patients with persistent and permanent AF. Medications acting on the atrioventricular (AV) node, such as beta blockers, nondihydropyridine calcium antagonists and digoxin, are most commonly used in this setting to control the ventricular rate. If symptoms persist after pharmacotherapy, an atrioventricular node ablation (AVNA) and a pacemaker insertion can be considered.

AV node ablation and a permanent pacemaker

In patients with AF and rapid ventricular rates refractory to all other therapy, an AVNA can be useful. AVNA does not eliminate AF, but permanently prevents rapid atrial signals reaching the ventricles. A permanent pacemaker is then needed to maintain a physiological heart rate. The procedure is most commonly considered and performed in the elderly, in patients refractory to medical therapy and in patients who are unsuitable or refractory to ablative therapy, as well as in patients in whom rapidly conducted AF results in a tachycardia-induced cardiomyopathy.

AVNA is performed under local anaesthesia and sedation in a cardiac catheter laboratory. An ablation catheter is inserted under x-ray guidance to the AV node, where radiofrequency energy is used to ablate the AV node. The end result is an irreversibly slow ventricular or junctional escape rhythm, necessitating the insertion of a permanent pacemaker. The strategy is also called 'pace and ablate'.

AVNA and pacing facilitates more consistent control of ventricular rate at physiological heart rates. Studies show improvement in exercise capacity and quality of life, as well as a reduction of palpitations, effort dyspnoea and fatigue compared with pharmacotherapy. These benefits have been described in patients with normal cardiac function, as well as in those with left ventricular dysfunction.[8,9]

Following the procedure, antiarrhythmic and rate-control medications can in many cases be ceased, reducing the potential risk of side effects. The need for anticoagulants is, however, unchanged as the atria continue to fibrillate.

Patients with paroxysmal AF require a dual-chamber permanent pacemaker to maintain AV synchrony. Patients with permanent AF require a single-chamber right-ventricular permanent pacemaker.

Complications associated with the procedure include spontaneous recurrence of AV nodal conduction and the need for redo procedure, as well as access site complications. The overall complication rate is reported at 1 to 2%, mostly related to the access site. Major complications occur in fewer than 1% of patients. The presence of a permanent pacemaker does require regular follow up. It is recognised that permanent right-ventricular pacing can induce or worsen left-ventricular dysfunction in some patients, who may then need a biventricular pacemaker to improve cardiac function.[8]

Thromboembolic risk management

Left atrial appendage thrombus is the predominant source of emboli in patients with nonvalvular AF and embolic stroke. Warfarin has been the mainstay of anticoagulation and thromboembolic risk reduction for many years. The introduction of novel oral anticoagulants has increased treatment options; however, anticoagulation remains a difficult challenge in some patients. Percutaneous left atrial appendage (LAA) occlusion devices may provide a nonsurgical, nonpharmacological alternative for these patients.

Percutaneous left atrial appendage occlusion

Percutaneous occlusion of the LAA with a specific device is a potential alternative to use of oral anticoagulants in the prevention of thromboembolic events. Two devices (the Watchman device [Figure 4] and the Amplatzer cardiac plug) are currently on the market. They are inserted into the LAA to occlude it and prevent thrombus formation and embolisation.

Patients who may benefit from this procedure are those with recurrent ischaemic strokes despite well-controlled optimal oral anticoagulation, previous intracranial haemorrhage, recurrent gastrointestinal bleeding, comorbidities that increase the risk of haemorrhage (such as cerebral amyloid angiopathy and

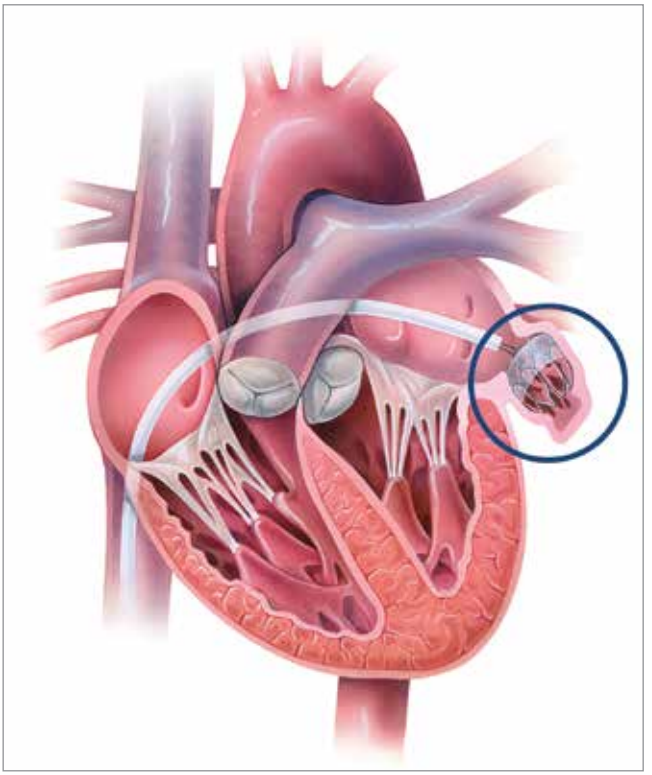


Figure 4. The Watchman device placed at the opening of the left atrial appendage.

procoagulopathic conditions) and those with specific contraindications to anticoagulation.[10]

The procedure is performed under general anaesthesia, x-ray and transoesophageal echocardiography guidance. The success rate of the procedure is about 95%. The overall procedural complication rate is 2 to 4% and includes cerebrovascular accident, device embolisation, bleeding, cardiac perforation, pericardial effusion, air embolism, thrombus on device, infection and a low risk of death.

Anticoagulation needs to be maintained for a few months after percutaneous closure of the LAA with the Watchman device to reduce the risk of thrombus formation on the device. After this time antiplatelet medications need to be continued. Following Amplatzer plug insertion in clinical trials, dual antiplatelet medications are needed initially followed by a single antiplatelet drug.

A study has shown that the Watchman device is noninferior to warfarin therapy in terms of all-cause mortality and efficacy, which was assessed by a primary composite endpoint of ischaemic stroke, cardiovascular death, haemorrhagic stroke and systemic embolism.[11] Most patients in this study had a $CHADS_2$ score of 1 or 2.[11] This procedure is approved in Australia, but is not yet widely available.

Summary

The prevalence of AF is continuing to increase and treatment options continue to evolve. Catheter ablation targeting PVI is now a standard procedure and should be considered relatively early for rhythm control in symptomatic patients. AVNA with permanent pacing has been performed for many years, and can be considered in patients with refractory symptoms who have failed other treatments. Percutaneous LAA occlusion devices have been developed as an alternative to long-term anticoagulation and are likely to become more common in clinical practice. In this setting, general practitioners should be increasingly aware of the currently available and expanding treatments in AF, the most common cardiac arrhythmia. **CT**

References

1. Crandall M, Bradley D, Packer D. Contemporary management of atrial fibrillation: update on anticoagulation and invasive management strategies. Mayo Clin Proc 2009; 84: 643-662.
2. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Heart Rhythm 2012; 9: 632-696.
3. Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998; 339: 659-666.
4. Bonanno C, Paccanaro M, La Vecchia L, Ometto R, Fontanelli A. Efficacy and safety of catheter ablation versus antiarrhythmic drugs for atrial fibrillation: a meta-analysis of randomized trials. J Cardiovasc Med 2010; 11: 408-418.
5. Ouyang F, Tilz R, Chun J, et al. Long-term results of catheter ablation in paroxysmal atrial fibrillation: lessons from a 5-year follow-up. Circulation 2010; 122: 2368-2377.
6. Brooks AG, Stiles MK, Laborderie J, et al. Outcomes of long-standing persistent atrial fibrillation ablation: a systematic review. Heart Rhythm 2010; 7: 835-846.
7. Cappato R, Calkins H, Chen SA, et al. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. J Am Coll Cardiol 2009; 53: 1798-1803.
8. Curtis AB, Worley SJ, Adamson PB, et al. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med 2013; 368: 1585-1593.
9. Wood MA, Brown-Mahoney C, Kay GN, et al. Clinical outcomes after ablation and pacing therapy for atrial fibrillation: a meta-analysis. Circulation 2000; 101: 1138-1144.
10. Lewalter T, Ibrahim R, Albers B, et al. An update and current expert opinions on percutaneous left atrial appendage occlusion for stroke prevention in atrial fibrillation. Europace 2013; 15: 652-656.
11. Holmes D, Reddy V, Turi Z, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet 2009; 374: 534-542.

COMPETING INTERESTS: None.