Management of atrial arrhythmias 3: paroxysmal atrial fibrillation

This is the third in a series of four practical articles highlighting the important management steps for non-cardiologists and non-cardiac electrophysiologists dealing with patients with atrial fibrillation and common atrial flutter. This article will deal with care pathways and management principles for paroxysmal atrial fibrillation.

Atrial fibrillation (AF) is the most commonly encountered arrhythmia in general and hospital practice. Paroxysmal AF (PAF) is defined as AF occurring in episodes that spontaneously terminate within 7 days and should be distinguished from persistent and permanent AF which are discussed in detail in the fourth article in this series. PAF is potentially curable if managed appropriately and physicians or GPs should consider prompt referral to a cardiac arrhythmia specialist.

Pathophysiology

AF is characterized on the electrocardiogram (ECG) by replacement of P waves with rapid irregular oscillations (fibrillatory waves) which represent multiple chaotic electrical wavefronts meandering around the atria. In permanent AF these wavefronts are self-perpetuating constantly colliding with each other, splitting or reforming such that the impulses are diverted into different random paths (Moe and Abildskov, 1959). In PAF, however, there is usually a single source (focal trigger) that generates high frequency wavefronts that cannot be conducted by the atrial myocardium uniformly, such that they fractionate into multiple wavefronts. The key difference from permanent AF, however, is that if the focal trigger is blocked then the episode of AF will terminate (Haissaguerre et al, 1998).

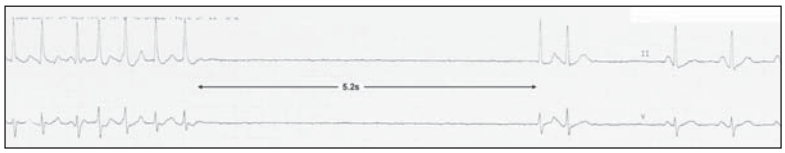
The commonest location of these triggers is the junction between the pulmonary veins (PV) and the left atrial myocardium as the electrical properties of the cells at this transition site promote the generation of rapid atrial ectopics. PAF and permanent AF should not be considered as separate conditions, however. AF that is initiated by rapid PV activity will eventually lead to changes in the atrium that will allow AF to be sustained even in the absence of triggers (Wijffels et al, 1995). This pathological entity (remodelling) is well recognized clinically as the natural history of PAF is to become permanent if untreated (Kopecky et al, 1987). It is for this reason that early appropriate treatment of PAF is essential to prevent development of persistent and permanent AF which is much more difficult to manage.

Clinical features and diagnosis

The symptoms of PAF are caused by the sudden change from a regular and relatively slow ventricular rate to a rapid irregular rate of varying intensity. It is the irregularity of these palpitations that is the key feature suggesting AF rather than a regular tachycardia such as atrial flutter or ventricular tachycardia. The heart rate in AF is determined by atrioventricular node (AVN) function. Young patients with a healthy AVN are able to conduct AF very rapidly such that the palpitations are likely to be more severe. In patients with sinoatrial node (SAN) dysfunction when a paroxysm of AF terminates there can be a prolonged period of asystole causing syncope or presyncope (*Figure 1*). The combination of AVN dysfunction, SAN dysfunction and AF characterizes sick sinus syndrome (also called sinoatrial node disease or tachy-brady syndrome). Other symptoms related to the loss of cardiac output caused by rapid ventricular rates are dyspnoea, exercise intolerance, fatigue and chest pain, the severity of which may depend on the presence of other cardiac disease such as ischaemia and left ventricular impairment.

Diagnosing PAF depends on recording the cardiac rhythm during a symptomatic episode. This may be a resting 12-lead ECG for a patient who presents to accident and emergency or to his/her GP or more likely on an ambulatory (Holter) monitor for a patient with sus-

Figure 1. A cardiac monitor tracing of a patient with sinoatrial node disease. The electrograms are surface electrocardiogram leads II (top) and V5 (bottom). The termination of a paroxysm of atrial fibrillation is seen followed by a 5.2 s pause caused by impaired sinoatrial node function. Eventually sinus rhythm returns. In this patient paroxysms of atrial fibrillation could be associated with dizzy spells or collapse.



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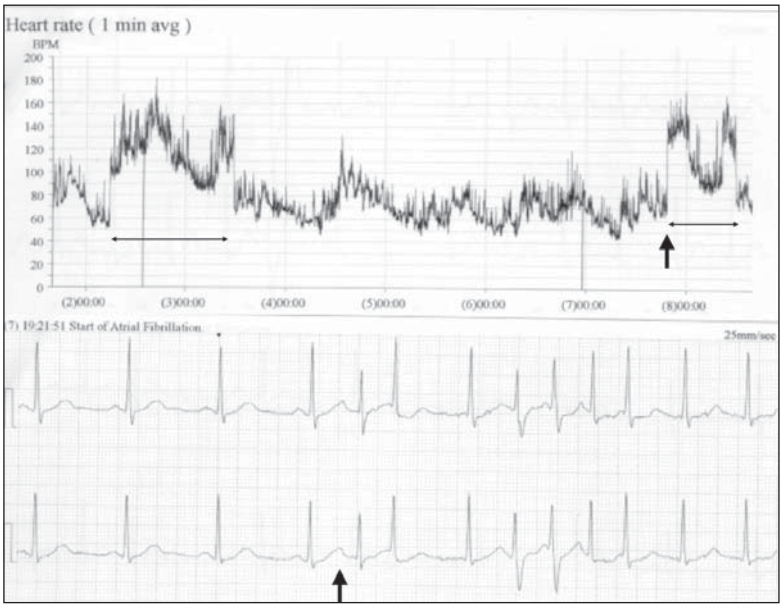
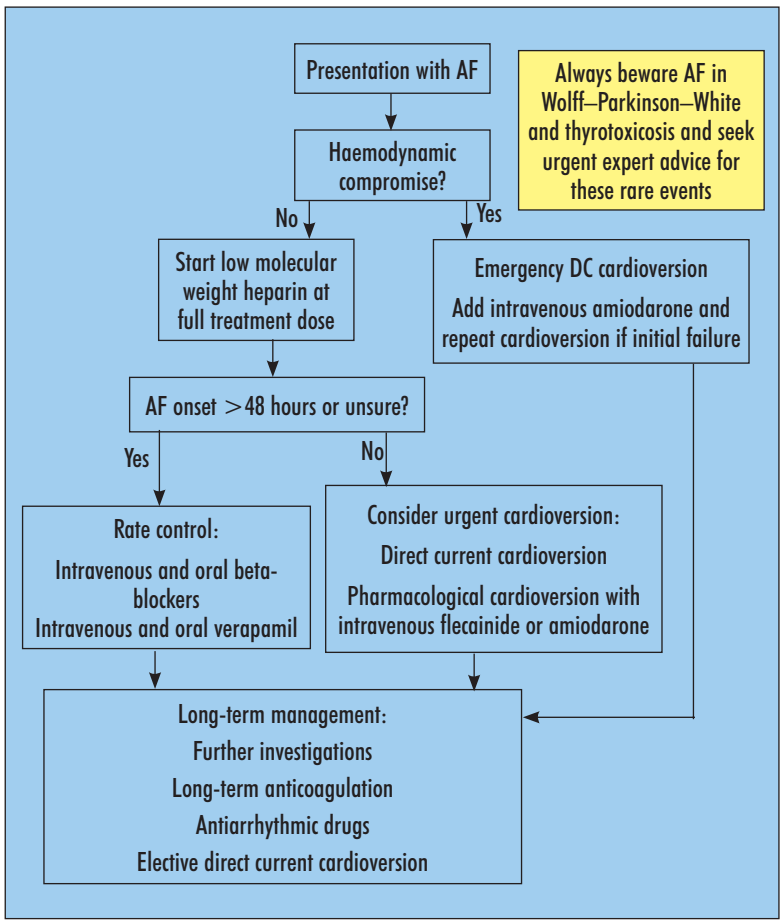


Figure 2. A 7-day Holter recording of a patient with paroxysmal atrial fibrillation. The top part is the mean 1-minute heart rate recorded over the whole 7 days (day 2 to 8 on the recording). There are two paroxysms of atrial fibrillation where the heart rate is persistently elevated (marked with double-ended arrows), the first lasting just over 24 hours and the second 16 hours. The larger arrows mark the onset of the second burst of atrial fibrillation and the surface electrograms recorded at this point are shown below. Sinus rhythm is interrupted by an atrial ectopic that triggers atrial fibrillation.

Figure 3. Immediate hospital management of patient presenting in atrial fibrillation (AF).



pected PAF (*Figure 2*). It is essential that patients wear the monitor for an appropriate length of time, e.g. it is a waste of resources to order a 24-hour monitor on a patient with palpitations occurring once a week. Continuous ambulatory recording can be performed for up to 1 week and if symptoms are less frequent than this then an event recorder should be used, i.e. a cardiac monitor that is only attached to the patient during the symptomatic episode to record and store the cardiac rhythm. Whatever type of recorder is used patients should keep a careful diary of their symptoms which can then be correlated to their cardiac rhythm. Implantable cardiac recorders should only be used to investigate patients who have syncope.

PAF occurs in an apparently structurally normal heart (lone PAF) in approximately half of all cases, however, underlying conditions that promote AF such as hypertension, ischaemic heart disease, any form of structural heart disease or hyperthyroidism are commonly found and should be screened for and treated (Levy et al, 1999). All patients with a new diagnosis of AF should have an echocardiogram and thyroid function testing performed with other appropriate investigations guided by clinical evaluation. In some patients paroxysms of AF may be linked to autonomic activity either during exercise (adrenergic-mediated AF) or bradycardia (vagally-mediated AF) which is seen usually in young men and occurs at times of relative parasympathetic overdrive, i.e. after meals or during sleep (Attuel et al, 1988). Identification of such a clear link to the autonomic nervous system should strongly influence treatment choices as outlined below.

Emergency management

Figure 3 details the hospital management of a patient presenting acutely with an episode of AF. If a patient is haemodynamically compromised, i.e. there is evidence of cardiogenic shock or exacerbation of an underlying condition such as angina, then emergency direct current cardioversion to sinus rhythm should be attempted as soon as possible.

Long-term management

General considerations

The key aspects of managing any form of AF are the relief of symptoms and prevention of stroke. An additional feature in PAF is to prevent progression to symptomatic permanent AF. Maintenance of sinus rhythm is the 'curative' approach; however, it should only be a therapeutic goal to achieve the above aims. It is crucial that any precipitating factors such as alcohol, caffeine or stress are removed and that underlying conditions such as hypertension, left ventricular failure or hyperthyroidism are treated effectively. If patients are truly asymptomatic and paroxysms of AF are an incidental finding then treatment with antiarrhythmic drugs or catheter ablation cannot be recommended. Maintenance

of sinus rhythm can be achieved with antiarrhythmic drugs, catheter ablation, atrial defibrillators or permanent pacemakers. Drugs to suppress or catheter ablation to destroy the AVN are a purely palliative but often effective approach. *Figure 4* outlines the main aspects of managing PAF.

Antiarrhythmic drugs

Many drugs maintain sinus rhythm (rhythm control); amiodarone, quinidine, flecainide, propafenone, disopyramide and sotalol (Roy et al, 2000; The AFFIRM Investigators, 2003) by modifying the sodium, potassium and calcium ion channels such that the atrial myocyte action potential is prolonged. Alternatively drugs such as digoxin, verapamil, dilatiazem and β blockers can be used to suppress AVN function and keep the ventricular rate low (rate control). Several trials have suggested that there is no benefit of rhythm over rate control in AF and that it may be harmful (Falk, 2005), but only one of these four studies included patients with PAF (Wyse et al, 2002).

For patients with infrequent but symptomatic paroxysms that last over 6 hours, who have been shown to have a structurally normal heart, a 'pill in the pocket' approach can be used (Camm and Savelieva, 2007). Patients carry with them a tablet of either flecainide (300 mg) or propafenone (600 mg) which they self administer after 30 minutes of palpitations. They should then rest until their symptoms subside or at least for several hours. If they experience deterioration in the symptoms, particularly severe dizziness or collapse, they should attend hospital as an emergency. If paroxysms are more frequent then pharmacological prophylaxis can be tried. The initial medication should be a standard β blocker starting at a low dose and building up to reduce the common side effects of β blockade. Verapamil or diltiazem are alternatives if β blockers are contraindicated.

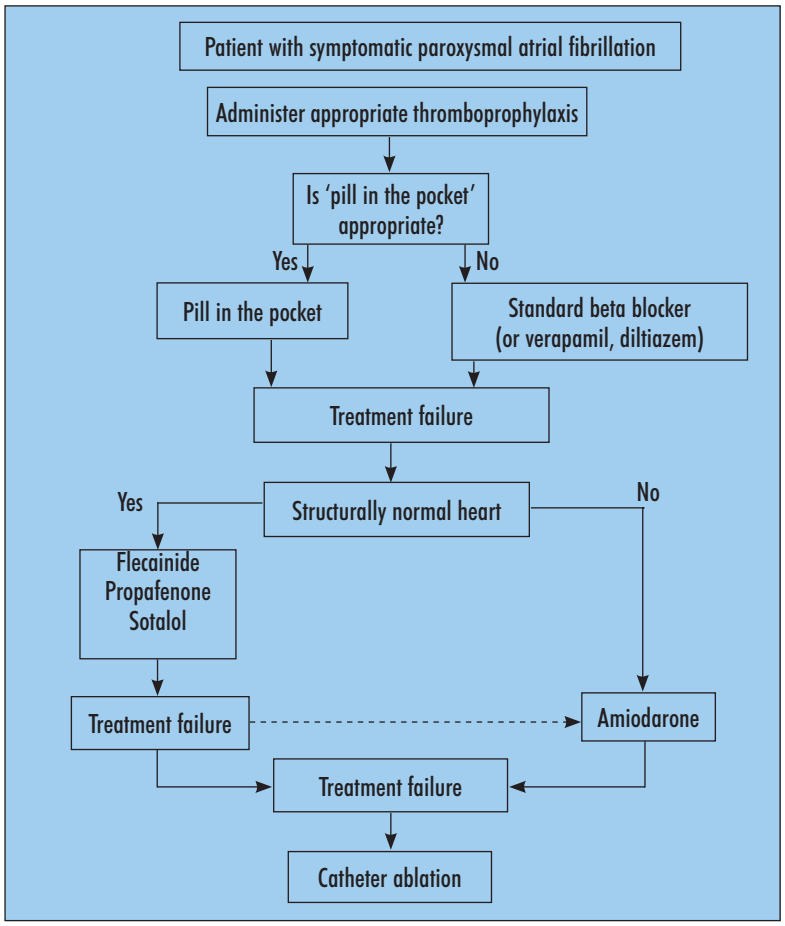
The escalation of drug therapy should be done under the supervision of a hospital consultant and depends on the presence of structural heart disease. For patients with a normal heart a choice can be made between flecainide (initially 50 mg twice daily up to a maximum of 150 mg twice daily), propafenone (150 mg three times daily up to 300 mg three times daily) or sotalol (40 mg twice daily up to 160 mg twice daily). Flecainide or propafenone can be used in combination with a β blocker. All of these can safely be started as an outpatient providing left ventricular function is normal, there is no known AVN disease and a baseline ECG does not show a prolonged QT interval or wide QRS. It is good practice to perform an ECG 1 week after starting or increasing the dose to check for QRS widening (flecainide or propafenone) or QT prolongation (sotalol).

If these drugs fail or for patients with structural heart disease the only alternative is amiodarone which requires a loading dose over 2 weeks followed by the lowest possible daily maintenance dose (100–200 mg). Although amiodarone is the most effective drug, patients should be counselled regarding the dermatological, thyroid and pulmonary toxicity associated with its long-term use. Monitoring of thyroid and liver function is mandatory. During randomized controlled trials 18–25% of patients stopped taking amiodarone because of side effects (Roy et al, 2000; Van Gelder et al, 2002).

Catheter ablation

Radiofrequency ablation energy is used to electrically disconnect the PV from the rest of the left atria and hence prevent the triggering of AF paroxysms. This can be achieved either by identifying and destroying the specific veno-atrial connections for each of the four PV or alternatively by creating two circumferential lines of scar that completely enclose the atrial tissue into which each ipsilateral pair of PV enter (*Figure 5*). A catheter is placed within each PV to ensure it is isolated regardless of which technique is used (*Figure 6*). This procedure is now extremely effective with 86–95% of patients achieving medium-term freedom from PAF, off antiarrhythmic drugs (Ouyang et al, 2004; Verma et al, 2005); however, it should be remembered that many patients, 49% in one study (Macle et al, 2002), will require repeat procedures. Although these procedures are considered safe a worldwide study reported the incidence of major com-

Figure 4. Long-term management of patient with symptomatic paroxysmal atrial fibrillation.



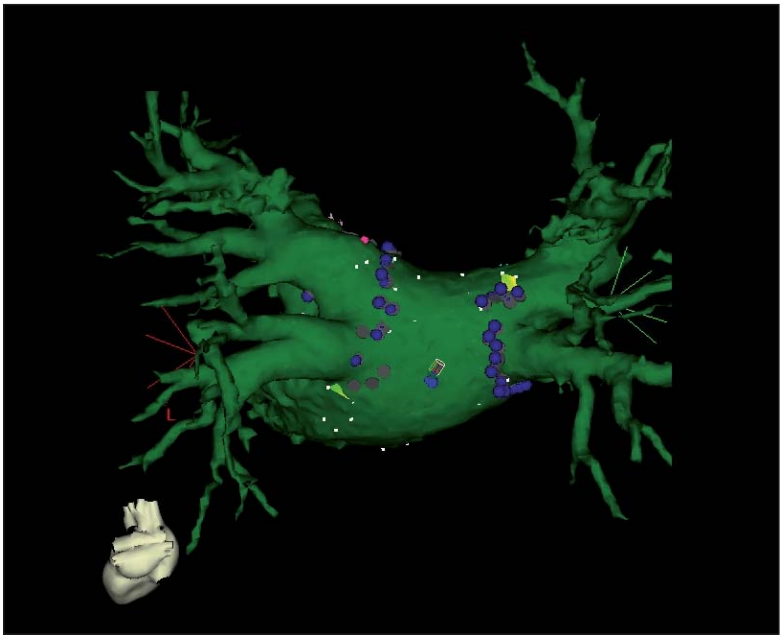
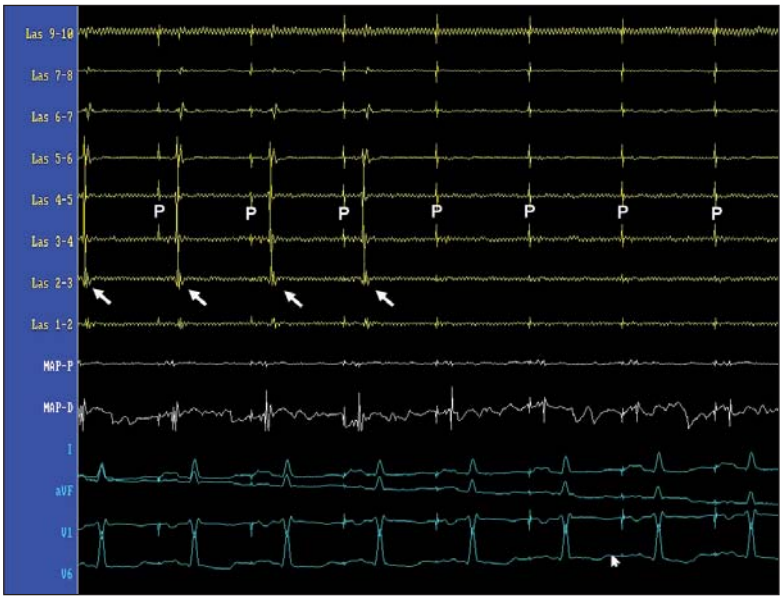


Figure 5. An image taken from a catheter ablation procedure for paroxysmal atrial fibrillation. The green image is a three-dimensional reconstruction of the patient's left atrium viewed from the posterior projection so that the four pulmonary veins are clearly seen. The ablation catheter has been moved around the pulmonary veins from within the left atria and radiofrequency ablation lesions, represented by coloured dots, have been delivered to create a continuous line of ablation that encircles the left and right pulmonary veins as pairs. By doing this the triggering atrial ectopy from the pulmonary veins cannot escape into the rest of the atria to cause atrial fibrillation.

Figure 6. Demonstration of electrical isolation of the pulmonary vein (PV) using a PV catheter. From top to bottom this figure shows eight intracardiac electrograms recorded from a PV catheter (yellow labelled Las), two intracardiac recordings from the ablation catheter (white labelled MAP) and four surface electrocardiogram leads. The right atrium is being paced via a catheter in the right atium giving the pacing spikes (P), which can be seen in all tracings. Radiofrequency energy is being delivered via the ablation catheter. The arrows show the local electrograms inside the PV which are being conducted from the left atrium. However, as ablation continues these electrograms disappear as the PV becomes electrically isolated from the rest of the left atrium.



plications (death, stroke, cardiac perforation or PV stenosis) to have occurred in 6% of patients between 1995 and 2002 (Cappato et al, 2005). The improvements in operator skill, knowledge and techniques over the past 5 years have been vast and a serious complication rate of <2% is now expected at large volume centres.

Three randomized controlled trials comparing catheter ablation to antiarrhythmic drugs in PAF have demonstrated that catheter ablation is superior with far fewer symptomatic AF recurrences and fewer admissions to hospital (Natale et al, 2000; Pappone et al, 2006; Stabile et al, 2006). There has been an exponential increase in the number of procedures performed worldwide, but there are very few high volume (greater than 100 cases per year) centres in the UK. International and UK guidelines recommend that patients should have a trial of antiarrhythmic drug therapy before being offered catheter ablation (Fuster et al, 2006; National Collaborating Centre for Chronic Conditions, 2006). Patients who refuse to take antiarrhythmic drugs or cannot tolerate them can be offered catheter ablation as a first-line treatment.

Pacemakers

PAF is common in patients who have SAN disease and use of antiarrhythmic drugs in them may cause symptomatic bradycardia. In these cases a combination of pacing and drugs is beneficial in controlling symptoms. These patients should have an atrial pacing mode of either AAI or DDD as this has been demonstrated to prevent the progression to permanent AF (Andersen et al, 1997).

Where it can be clearly established that bradycardia itself is the trigger for AF, then pacing (either AAI or DDI mode) effectively abolishes these episodes. Pacing in the atrium can suppress atrial ectopics that initiate AF. Pacemakers with specific algorithms will detect atrial pauses or ectopic activity and then pace the atrium at a rate faster than the intrinsic rate to prevent breakthrough of the potentially arrhythmogenic episodes. Alternatively this is achieved by continuously pacing the atrium at a rate just faster than the native rhythm (automatic atrial overdrive). When atrial tachycardia occurs devices can also attempt to overdrive them to restore sinus rhythm. In patients predisposed to AF both intra- and interatrial conduction is prolonged, leading to a lengthening of the atrial depolarization time, promoting both the onset and maintenance of AF. Atrial conduction time can be reduced by either simultaneously pacing both the right atrium and the left atrium via the coronary sinus (bi-atrial pacing), pacing at multiple sites in the right atrium (e.g. right atrial appendage and low atrial septum) or by pacing at the sites of known intra-atrial connection (e.g. Bachmann's bundle) (Israel and Hohnloser, 2003; Lau, 2003).

Atrial defibrillators

Atrial defibrillators do not prevent AF but by promptly cardioverting each episode the atria do not remodel and therefore the progression to permanent AF is prevented.

They have been demonstrated to reduce AF burden and improve quality of life (Friedman et al, 2001; Newman et al, 2003). Most atrial defibrillators can also act as ventricular defibrillators to treat any iatrogenic VF incident. Modern atrial defibrillators also include the preventative pacing algorithms and antitachycardia pacing discussed above. Devices can fire automatically or be controlled by the patent so that shocks can be delivered after self medication with sedatives, however even though shocks are of low energy (1–2 J) they are still uncomfortable which may be unacceptable to many patients, up to 20% in one study (Geller et al, 2003). Patient selection is crucial for atrial defibrillators and it is yet to be seen whether they will still have a role in the climate of improving curative ablative approaches.

'Pace and ablate'

For patients with highly symptomatic paroxysms in which drugs or a curative ablation strategy is not effective or possible (e.g. very elderly) ablating the AVN is extremely effective in reducing symptoms (Wood et al, 2000). In the first instance a pacemaker should be implanted and then 2–3 months later the ablation procedure itself performed. Although this is a simple, very low risk procedure, it is irreversible and the patients are rendered pacemaker dependent.

Prevention of stroke

Stroke is the most devastating complication of AF with an annual incidence of 4.5% (Wolf et al, 1991). Although the vast majority of these strokes are thromboembolic, this is not simply the sequelae of sluggish blood flow in a dilated left atrium but reflects a more complex relationship reflecting risk factors common to both AF and stroke (e.g. hypertension, heart failure, diabetes) and altered platelet and endothelial function in AF. Decisions to anticoagulate then should be based on patients' overall stroke risk and no distinction should be made between PAF, persistent or permanent AF. The stroke risk stratification algorithm published in the UK guidelines for AF should be followed (National Collaborating Centre for Chronic Conditions, 2006).

Conclusions

PAF should be considered a simple arrhythmia and this article lays out a contemporary approach for its management. Chapter 8 of the *National Service Framework for Coronary Heart Disease* (DH Coronary Heart Disease Team, 2005) recommends that patients with AF who remain symptomatic despite drug treatment should be referred to a heart rhythm specialist (cardiac electrophysiologist) for further treatment, in particular catheter ablation, a potential permanent solution to many patients' debilitating symptoms.

Conflict of interest: none.

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KEY POINTS

- Paroxysmal atrial fibrillation is defined as recurrent episodes of atrial fibrillation spontaneously terminating within 7 days.
- Paroxysmal atrial fibrillation is usually caused by runs of atrial ectopic beats that emerge from the pulmonary veins.
- All patients should have an echocardiogram and their thyroid function tested.
- Asymptomatic or infrequent episodes may need no treatment.
- Prompt, appropriate investigation and treatment may prevent progression to persistent or permanent atrial fibrillation.
- Drugs to control ventricular rate or maintain sinus rhythm are recommended as first-line treatment but are not as effective as catheter ablation.
- Antiarrhythmic drugs such as flecainide, propafenone, sotalol and amiodarone should be administered under supervision of a hospital consultant.
- Patients who remain symptomatic despite drug treatment should be referred to a heart rhythm specialist (electrophysiologist).
- Catheter ablation is safe and highly effective, but repeat procedures may be needed.
- Warfarin should be prescribed for patients at risk of stroke regardless of whether atrial fibrillation is paroxysmal, persistent or permanent.

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