Practical management of common atrial arrhythmias 4: persistent atrial fibrillation

This is the last 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 persistent atrial fibrillation.

Atrial fibrillation (AF) exists in approximately 500 000 people in the UK. It is growing in incidence, consumes 1% of the NHS budget, reduces longevity and greatly increases health-care consumption (see first article in this series on cardioversion). AF is defined as persistent if it has been present for more than 7 days' duration and permanent (or chronic) if the rhythm has been accepted and restoration of sinus rhythm is considered unlikely, impossible or undesirable. Paroxysmal AF is discussed in the third article of this series. Treatment strategies can be broadly broken down into 'rate control', aiming to control the ventricular rate, and 'rhythm control', attempting to restore and maintain sinus rhythm. Prevention of cardiac thromboembolism is a key consideration no matter which strategy is pursued, and this receives regular attention and update (Iqbal et al, 2005; National Collaborating Centre for Chronic Conditions, 2006).

Rationale for treatment

Many cases of persistent AF are related to underlying cardiac disorders, with hypertension being present in nearly 60% of new cases and with approximately half having underlying structural heart disease (Benjamin et al, 1998). Untreated patients are often symptomatic as a result of rapid ventricular rates and loss of atrioventricular synchrony, but many patients with persistent AF have few or no symptoms. Patients with AF have an approximately twofold increase in mortality compared with those in sinus rhythm, primarily as a result of an increased risk of stroke and heart failure. This increased mortality persists even after adjusting for pre-existing cardiovascular conditions (Benjamin et al, 1998).

The left atrium is smooth walled apart from the left atrial appendage which has a pectinate lumen with the mouth often narrower than the body. This anatomy encourages the development of thrombus. As asymptomatic patients with persistent AF are at increased risk of stroke, and AF is present in one third of patients admitted with stroke, screening for this condition is worthwhile. The NHS GP Quality Outcomes Framework provides 30 points for management of AF in primary care and the National Institute for Health and Clinical Excellence has issued a clinical guideline on AF which recommends screening with pulse checks (National Institute for Health and Clinical Excellence, 2006).

General measures

AF is diagnosed by a standard 12-lead electrocardiogram. It is important to distinguish AF from atrial flutter, which usually has characteristic flutter waves and is far more amenable to curative catheter ablation (see second article in this series on common atrial flutter). If the onset of the arrhythmia is uncertain, it may be necessary to organize a period of cardiac monitoring to assess whether AF is paroxysmal or persistent, as these conditions have very different management strategies (see third article in this series on paroxysmal AF).

Initial assessment should focus on symptoms attributable to AF and identifying risk factors for the development of AF such as alcohol excess, hypertension, heart failure, valvular heart disease and thyroid disease. Thyroid function and serum electrolytes should be measured routinely. An echocardiogram is essential to exclude structural heart disease, but should only be performed once the ventricular rate is adequately controlled to allow accurate assessment of left ventricular function.

Specific measures

The cornerstones of AF management are to reduce or abolish symptoms and to prevent complications, particularly stroke. Restoration and maintenance of sinus rhythm per se has not yet been shown to improve mortality but it may be the best way to control symptoms. It has been shown, however, that a strategy using antiarrhythmic drugs to maintain sinus rhythm has no

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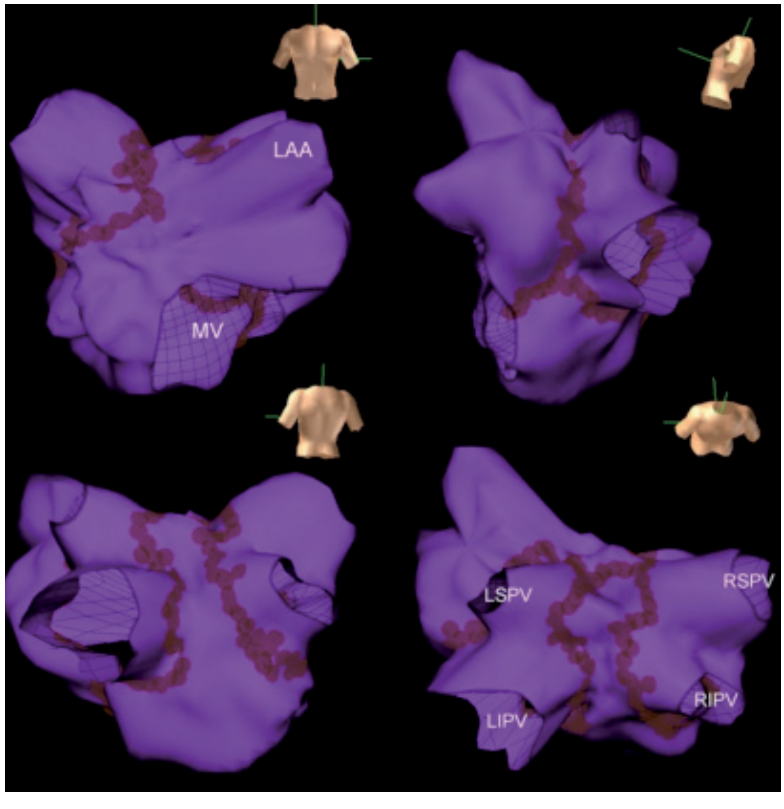
prognostic benefit over using drugs to control the ventricular rate (Van Gelder et al, 2002; Wyse et al, 2002).

The large AFFIRM study (Wyse et al, 2002) compared rate control with rhythm control, using cardioversion and antiarrhythmic drugs, in patients over the age of 65 years. There were increased hospitalizations and adverse drug effects, and a trend towards increased mortality in the rhythm control arm, with no difference overall in the rate of cerebrovascular events. The majority of strokes in the rhythm control arm occurred in patients who had stopped taking warfarin as they were believed to be in sustained sinus rhythm.

As the majority of patients with AF are elderly and have few symptoms, a rate control strategy will usually therefore be the preferred option. In younger patients without cardiac disease and those with significant symptoms attributable to AF, the decision is less clear cut, and improvements have been shown in quality of life measures with a rhythm control strategy (Singh et al, 2005). It is therefore important that the decision is tailored to the individual patient. However, patients should be informed that most drugs used to maintain sinus rhythm have a worse side-effect profile than those used to control ventricular rate, and that the decision on management strategy has no bearing on the decision to anticoagulate.

Figure 1. The purple represents the endocardial surface of the left atrium recreated by the non-contact system, with the left atrial appendage (LAA), mitral valve (MV), and left superior (LSPV), left inferior (LIPV), right superior (RSPV) and right inferior (RIPV) pulmonary veins. The torso indicates the orientation of each view. Each brown mark represents a radiofrequency lesion. The standard set of lesions is applied to encircle the ipsilateral veins in pairs, to create lines between the left and right pulmonary veins across the roof and extending from the left inferior pulmonary vein to the MV annulus.



Rhythm control

Pharmacological

Initial rhythm control attempts will usually involve an attempt at electrical cardioversion, which is discussed in detail in the first article in this series. However, only 30% of patients will still be in sinus rhythm at the end of 1 year without antiarrhythmic therapy (Golzari et al, 1996). Antiarrhythmic medication with serial cardioversions maintains long-term sinus rhythm in approximately 30–40% (Van Gelder et al, 1996). The Vaughan-Williams classification of antiarrhythmic drugs is still in clinical use and the most commonly used agents belong to class Ic (sodium channel blockers, e.g. flecainide, propafenone), class II (beta-blockers) and class III (potassium channel blockers, e.g. sotalol, amiodarone). In younger patients with no cardiac disease, class Ic drugs are usually first-line agents. Beta-blockers are effective (Van Gelder et al, 1996) and, as they are already indicated for heart failure and coronary artery disease, should be first-line agents for patients with these conditions.

Sotalol is often used but is probably no more effective than standard beta-blockers (Kuhlkamp et al, 2000; Plewan et al, 2001), and is well known to be proarrhythmic with an increased risk of torsades de pointes secondary to QT interval prolongation. Although amiodarone is often poorly tolerated because of its well known side-effect profile, it is the most effective agent at maintaining sinus rhythm (Singh et al, 2005), and is useful in selected patients. Digoxin has no role in the maintenance of sinus rhythm. The pharmacological maintenance of sinus rhythm is discussed in more detail in the third article in this series on paroxysmal AF.

In most patients, attempts to maintain sinus rhythm will be unsuccessful in the long term and at this stage a rate control policy should be adopted. Once this occurs, it is important that potentially toxic drugs, such as amiodarone and sotalol, are substituted for safer rate control agents as discussed below.

Catheter or surgical ablation

Radiofrequency catheter ablation is already an accepted treatment for paroxysmal AF (see third article in this series) and also offers the prospect of a complete cure in persistent AF (Steeds et al, 1999; Haissaguerre et al, 2005; Earley et al, 2006). More extensive ablation is required in persistent AF than in paroxysmal AF (*Figure 1*), and multiple procedures are often required for recurrent atrial arrhythmias, including atrial tachycardia. The medium-term success rate for restoration of sustained sinus rhythm is currently about 70% (Steeds et al, 1999; Earley et al, 2006). Complications include a 1.5% risk of pulmonary vein stenosis, a 1% risk of

cardiac tamponade, and a 1% risk of stroke (Cappato et al, 2005). Atrio-oesophageal fistula has been described and can be fatal (Pappone et al, 2004). Currently the procedure is best reserved for fit and motivated patients who remain symptomatic despite pharmacological therapy. However, as the technique evolves further, the indications for ablation will almost certainly broaden. The surgical maze procedure can be used to achieve a greater than 90% cure rate (McCarthy et al, 2000), but it is highly invasive, requiring cardiopulmonary bypass. Therefore its use is reserved for patients undergoing cardiac surgery for other indications, particularly mitral valve surgery.

Rate control

The widespread use of digoxin as the first-line agent for rate control of persistent AF continues despite its important limitations. Digoxin works by increasing vagal tone and has little effect during exercise when vagal tone is withdrawn. A cursory evaluation may show that digoxin in isolation has controlled the resting ventricular rate, but patients will have uncontrolled ventricular rates on exercise. Beta-blockers are first-line rate-control agents, particularly in patients with heart failure or coronary artery disease. If beta-blockers are contraindicated or not tolerated, rate-lowering calcium antagonists such as verapamil and diltiazem should be used instead or in combination with caution. Digoxin can be added if ventricular rate is not controlled with an adequate dose of one of these agents. Rate control is generally considered adequate if ventricular rate is <80 beats per minute (bpm) at rest and <120 bpm during exercise. If there are concerns over the adequacy of rate control during the patient's usual daily activities, Holter monitoring or exercise testing should be performed.

In patients with poorly rate-controlled symptomatic AF despite adequate pharmacological therapy, catheter ablation should be considered. In patients who are not suitable candidates for direct ablation (see above and the third article in this series), catheter ablation of the atrioventricular node with permanent pacemaker implantation should be offered. Although this procedure is irreversible and renders the patient pacemaker dependent, it can offer excellent symptomatic improvement and greatly reduce health-care costs (Fitzpatrick et al, 1996). Survival after the procedure is the same as with medical therapy (Wood et al, 2000), and is the same as the general population if left ventricular function is normal (Ozcan et al, 2001). The pacing mode after atrioventricular nodal ablation has received attention in recent years and any patient with reduced left ventricular function should receive a biventricular pacemaker (Doshi et al, 2005).

Prevention of thromboembolism

This is the major complication of AF and it is imperative that it is addressed. The mainstays of treatment are antiplatelet agents (usually aspirin) and anticoagulants (usually warfarin). Although warfarin is far more effective at preventing cerebrovascular events than aspirin, it carries an increased risk of bleeding complications and the choice of agent therefore depends on the patient's risk of stroke. There are consensus international guidelines on which patients should be anticoagulated based on large randomized trials (American College of Cardiology/American Heart Association/European Society of Cardiology, 2006; National Collaborating Centre for Chronic Conditions, 2006) (*Table 1*). It is important to re-emphasize that no study has ever shown that it is safe to stop anticoagulation with an apparently successful rhythm control strategy and therefore the decision to anticoagulate is made independently from the decision to aim for rate or rhythm control. Novel oral anticoagulants are being developed which do not require monitoring of therapeutic levels, but there remain concerns over their toxicity, and they cannot be recommended at present.

Conclusions

The management of persistent AF is summarized in *Figure 2*. For most patients a rate control strategy will be the preferred option and this will render the majority

Table 1. Guidelines for antithrombotic therapy for patients with atrial fibrillation

Risk category	Therapy
Low risk (age <65 years with no moderate or high risk factors)	Aspirin
Moderate risk (age >65 years with no high risk factors; age <75 years with hypertension, diabetes or vascular disease)	Aspirin or warfarin
High risk (previous thromboembolic event; age >75 years with hypertension, diabetes or vascular disease; evidence of valve disease or impaired left ventricular function)	Warfarin (INR 2–3)

From National Collaborating Centre for Chronic Conditions (2006). INR = international normalized ratio

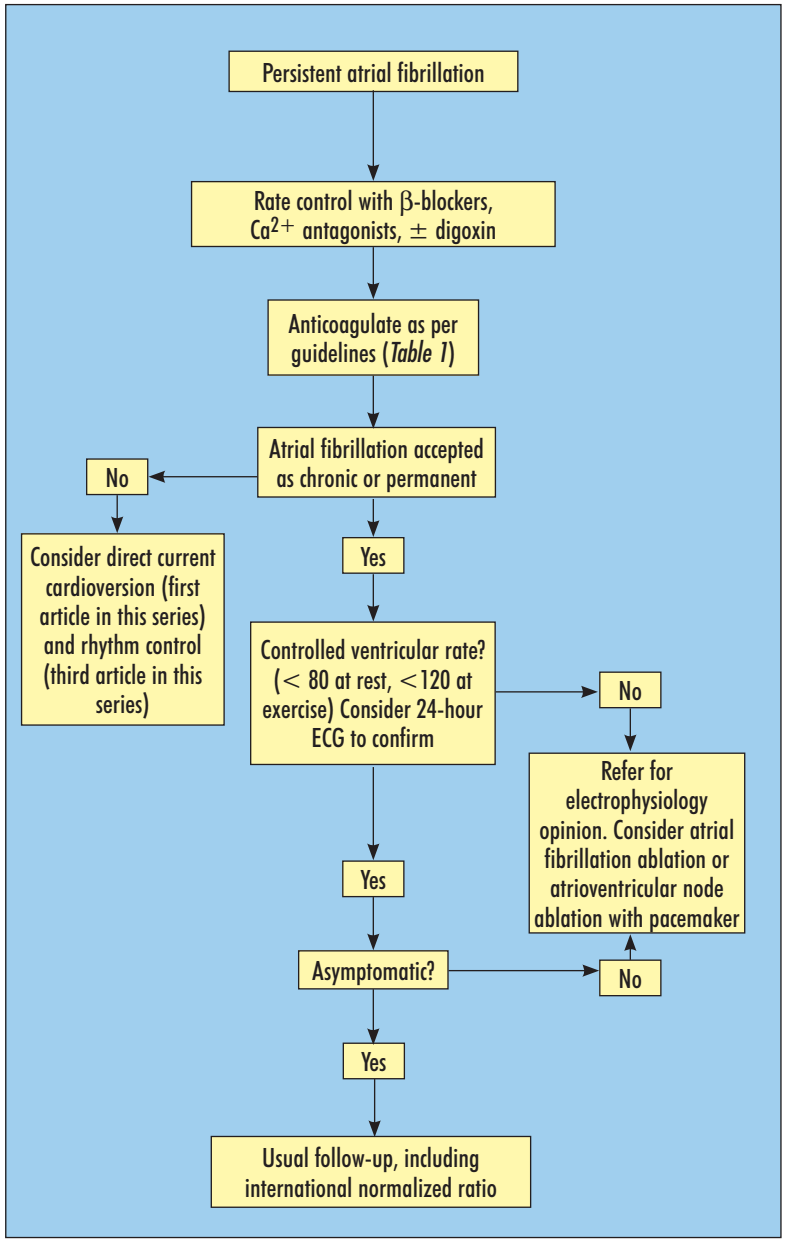
KEY POINTS

- Atrial fibrillation is common and associated with considerable morbidity and mortality.
- Restoration of sinus rhythm with cardioversion and antiarrhythmic drugs has no mortality benefit over ventricular rate control in older patients; rate control is the usual preferred strategy in the asymptomatic patient.
- For rate control, beta-blockers or calcium-channel blockers are first-line agents; digoxin should be reserved as a second-line agent only.
- In symptomatic atrial fibrillation despite standard management, referral to an electrophysiologist should be made for consideration of an ablation procedure.
- An active decision on anticoagulation should be made in all cases of atrial fibrillation, based on the guidelines derived from large trials.

asymptomatic. However in those who remain symptomatic despite adequate rate control, or in whom rate control cannot be achieved satisfactorily with pharmacological agents, a rhythm control strategy should be pursued. If this is unsuccessful, the patient should be referred to an electrophysiologist for consideration of either AF ablation or atrioventricular nodal ablation with pacemaker implantation. Although catheter ablation offers the prospect of a cure for persistent AF, current techniques carry a small risk of major complications and it cannot yet be recommended as standard management. A decision on anticoagulation should be made in all patients with AF, irrespective of the management strategy chosen. BJHM

Conflict of interest: none.

Figure 2. Management of persistent atrial fibrillation. ECG = electrocardiogram.



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