Atrial fibrillation

This is the second in a series of articles discussing common arrhythmias seen in hospital. This article addresses the most common arrhythmia, atrial fibrillation.

Atrial fibrillation

Atrial fibrillation is the most common arrhythmia with a prevalence of over 10% in those over the age of 65 years (Heeringa et al, 2006). Its prevalence is increasing as the population ages and it is associated with many medical conditions (*Table 1*). The electrocardiogram from a patient with atrial fibrillation shows loss of organized atrial activity with an irregularly irregular ventricular rate (*Figure 1*). Chaotic electrical activity is initiated from rapidly firing electrically active foci, usually located in the pulmonary veins, and is sustained by multiple constantly varying re-entrant wave-fronts within the atrial myocardium (the so-called 'wavelet hypothesis'). Re-entrant activity is promoted when there is atrial dilatation, wall thinning and myocardial fibrosis, as can occur in patients with heart muscle or valve disease. Coordinated atrial contraction and relaxation is replaced by continuous mechanically ineffective twitching. This leads to stasis of blood and possible clot formation in the atria and left atrial appendage with potential for embolization and stroke.

Table 1. Common conditions associated with atrial fibrillation

Alcohol (dependence and binge)
Hyperthyroidism
Hypertension
Mitral valve disease
Left ventricular failure of any cause
Acute myocardial infarction
Cardiac surgery
Exacerbations of lung disease
Obstructive sleep apnoea

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Patients may present with uncomfortable persistent palpitations, fatigue, pre-syncope or syncope. Angina may occur in those with coronary disease because uncontrolled high ventricular rates increase myocardial oxygen consumption. Patients may present in acute heart failure and pulmonary oedema because cardiac mechanical action is less efficient in atrial fibrillation, leading to impairment of left ventricular ejection fraction and loss of atrioventricular mechanical coupling. In those with pre-existing ventricular dysfunction, this may be sufficient to trigger decompensation.

Uncontrolled fast ventricular rates can cause a 'tachycardia cardiomyopathy' over time leading to chronic heart failure. The first presentation may be with stroke or other arterial embolism. Not infrequently, atrial fibrillation is an incidental finding in an asymptomatic patient. Nonetheless, death rates are doubled for those in atrial fibrillation compared to the general population, while hospitalizations increase and quality of life diminishes (Camm et al, 2010).

Management strategies

Symptomatic atrial fibrillation presenting suddenly for the first time is termed 'acute' atrial fibrillation. Atrial fibrillation is paroxysmal if it terminates spontaneously within 7 days. Any atrial fibrillation that persists beyond 48 hours should be considered for anticoagulation (Camm et al, 2010). Atrial fibrillation is 'persistent' when it lasts for longer than 7 days or requires termination with drugs or direct current (DC) cardioversion (Camm et al, 2010). The term 'long-standing persistent atrial fibrillation' is used when it has persisted for more than a year, but the plan remains to try and restore sinus rhythm (Camm et al, 2010). In contrast, 'permanent atrial fibrillation' is when atrial fibrillation has been accepted by both the medical team and patient, with a plan to manage symptoms and ameliorate stroke risk (Camm et al, 2010).

Medical therapy for atrial fibrillation has traditionally been classified according to Vaughan-Williams based on the primary mechanism of the drug's antiarrhythmic effect. Many medications, however, have multiple mechanisms of action. *Table 2* gives a simplified adaptation of this classification including those therapies commonly used in clinical practice. Class I and III agents are for restoring sinus rhythm by action on myocardial tissue ('rhythm control'). Class II and IV agents are mainly used for controlling the ventricular

Figure 1. Atrial fibrillation. There is loss of organized atrial activity (no P waves are seen) and the ventricular rate is irregularly irregular.

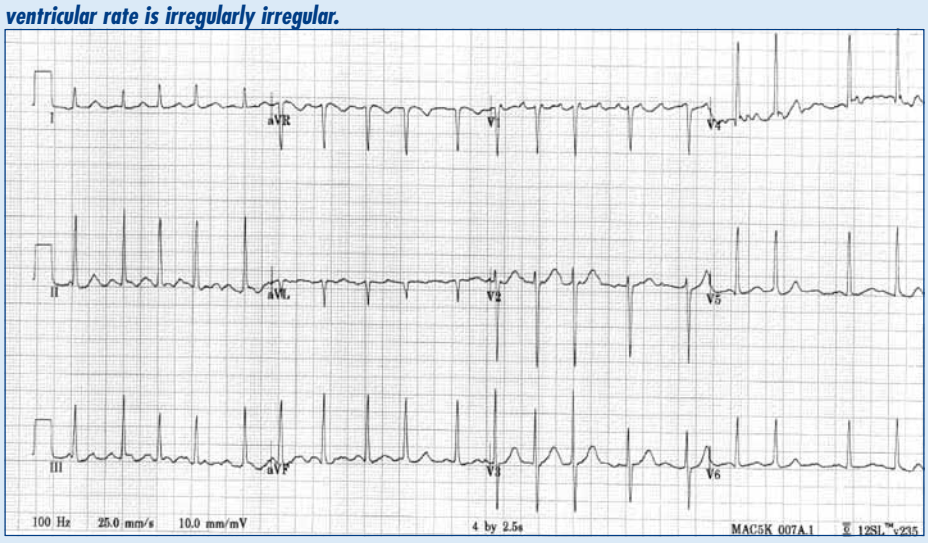

Table 2. Simplified Vaughan-Williams classification of antiarrhythmics

Class	Action	Main target tissue	Examples
I	Sodium channel blockade	Atrial and ventricular myocardium	Flecainide
			Lidocaine*
			Propafenone
II	Beta adrenoreceptor blockade	Sinus and atrioventricular node	Bisoprolol
			Metoprolol
			Esmolol †
			Sotalol ‡
III	Potassium channel blockade	Atrial and ventricular myocardium	Amiodarone
			Dronedarone
			Sotalol ‡
IV	Calcium channel blockade	Sinus and atrioventricular node	Verapamil
			Diltiazem

* (ventricular only); † (intravenous only, short acting); ‡ acts in both class II and III

response to atrial fibrillation by increasing the refractoriness of the atrioventricular node and thereby reducing impulses conducted to the ventricle ('rate control'). Digoxin may be used with class II and IV agents to achieve adequate rate control. These agents may be used for both acute and chronic atrial fibrillation although the dose and mode of delivery may differ.

Acute atrial fibrillation with a rapid ventricular rate can be initially managed with class II and IV drugs to increase the degree of block at the atrioventricular node. Beta-blockers or calcium-channel blockers, alone or with digoxin, are commonly used to achieve a ventricular rate of 60–80/minute. A combination of beta-blocker and calcium-channel blocker should only be used with caution: this may result in excessive bradycardia either as a result of high grade atrioventricular block, or as a result of sinus arrest should atrial fibrillation terminate, so facilities for emergency pacing should be available if this combination is used in the acute situation.

When ventricular function is severely impaired, or the patient is haemodynamically compromised, beta-blockers or calcium-channel blockers may not be tolerated, and restoration and maintenance of sinus rhythm may be required either by DC cardioversion if instant conversion needed (discussed below), or by amiodarone if the arrhythmia can be tolerated for a few hours. Amiodarone does have a modest rate-slowing effect on the atrioventricular node, but is not usually used for this because of the availability of other drugs to achieve this with less concerning side-effect profiles. However, amiodarone is the most effective drug available for maintaining sinus rhythm. Unlike many other antiarrhythmic drugs, amiodarone may safely be given to patients with ischaemic heart disease or heart failure.

Once the patient is stabilized, subsequent management requires anticoagulation and a decision for either a 'rhythm control' strategy (using class I or III antiarrhythmic drugs, DC cardioversion, or left atrial catheter ablation either alone or in combination), or a 'rate control' strategy (using class II or IV antiarrhythmic drugs with or without digoxin, or ablation of the atrioventricular node with pacemaker implantation) (*Figure 2*) (Lafuente-Lafuente et al, 2009). Clinical considerations will dictate the appropriate strategy for an individual patient. Any underlying disease, such as hypertension or thyroid disorder, must also be managed.

Anticoagulation

Anticoagulation should be an urgent consideration given the stroke risk (Hughes et al, 2008). The European Society of Cardiology has modified the commonly used 'CHADS$_2$' to become the CHA$_2$DS$_2$-VASc score to help assess stroke risk (*Table 3*). Bleeding risk can also be assessed via the HAS-BLED score (*Table 4*) (Camm et al, 2010) – scores ≥3 indicate a high bleeding risk and require regular review of the choice of anticoagulant (Pisters et al, 2010).

Warfarin remains the most commonly used anticoagulant in the UK. Combinations of aspirin and clopidogrel are inferior to warfarin in preventing thromboembolic events (ACTIVE Writing Group et al, 2006). Selected cases with ischaemic heart disease may need both warfarin and aspirin but most can be managed on warfarin alone. Those with recently implanted intracoronary stents may need warfarin and clopidogrel together. The risk of bleeding is significantly elevated with 'triple' therapy (aspirin, clopidogrel and warfarin) and the time spent on all three should be minimized (Rubboli et al, 2011). This may dictate the use of bare metal stents rather than drug-eluting stents, except in cases in which the risk of in-stent restenosis is considered to overwhelm all other considerations.

Newer direct orally active thrombin inhibitors (ximelagatran, dabigatran) and factor Xa inhibitors (apixaban, rivaroxaban) have been developed which do not require regular dose adjustments. They have similar or greater efficacy at preventing thromboembolism, for a similar or lower bleeding

Figure 2. An action algorithm for acute atrial fibrillation.

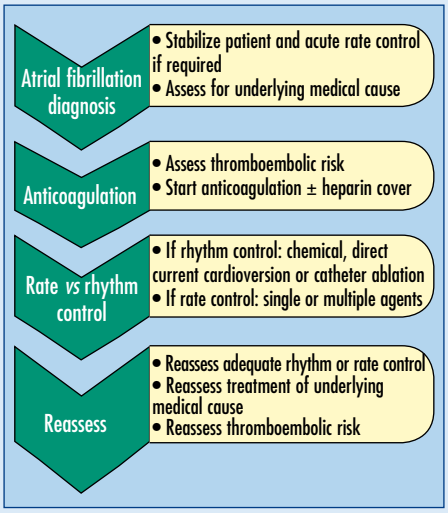

Table 3. CHA$_2$DS$_2$-VASc score

CHA$_2$DS$_2$-VASc score*	Annual stroke risk (%/year)	Suggested medication
0	0	Aspirin or nothing (preferred)
1	1.3	Aspirin or warfarin (preferred)
2	2.2	Warfarin
3	3.2	
4	4.0	
5	6.7	
6	9.8	
7	9.6	
8	6.7	
9	15.2	

* score 1 point for cardiac failure, hypertension, diabetes, vascular disease, age 65–74 years, female. Score 2 points for age ≥75 years, previous stroke, transient ischaemic attack or thromboembolic event. Maximum score is 9 because age can contribute 0, 1 or 2 points. Adapted from the European Society of Cardiology guidelines (Camm et al, 2010).

Table 4. HAS-BLED bleeding risk score

Letter	Characteristics	Definition	Score
H	Hypertension	Systolic blood pressure >160 mmHg	1
A	Abnormal renal and liver function	Dialysis, renal transplantation or creatinine >200 mmol/litre; cirrhosis of alanine transaminase/aspartate transaminase >3 x upper normal limit	1 point each (1 or 2)
S	Stroke		1
B	Bleeding	Previous bleeding or predisposition to bleeding	1
L	Labile INRs	INRs out of range >40% of time	1
E	Elderly >65 years of age		1
D	Drugs or alcohol	Concomitant use of non-steroidal anti-inflammatory drugs, antiplatelet agents or alcohol abuse	1 point each (1 or 2)

Adapted from the European Society of Cardiology guidelines (Camm et al, 2010). INR = international normalized ratio.

risk. Ximelagatran was withdrawn by the manufacturer as a result of concerns about liver toxicity. The introduction of these drugs into widespread clinical use for the prevention of complications of atrial fibrillation has major cost implications, although some of this expense may be recouped by closing anticoagulation clinics.

Some patients at high risk of thromboembolism may not be candidates for long-term oral anticoagulation because the risk of bleeding complications is unacceptably high. In such cases, occlusion of the lumen of the left atrial appendage with a detachable occlusion device deployed via transseptal access to the left atrium may offer an alternative approach to reducing risk, although antiplatelet and anticoagulation therapy are required for several months after implantation until the device has endothelialized.

Rhythm control strategy

Rhythm control involves the restoration of sinus rhythm. This can be achieved electrically, using DC cardioversion, chemically with antiarrhythmic drugs from classes I or III (flecainide, propafenone, amiodarone, sotalol or dronedarone), or by using catheter ablation.

Drug cardioversion

Amiodarone is the most effective drug for achieving and maintaining sinus rhythm but toxic effects may occasionally develop, particularly with prolonged use at high doses. The iodine content of amiodarone predisposes to abnormalities of thyroid function with asymptomatic small rises in thyroid-stimulating hormone being common and clinical hypothyroidism or thyrotoxicosis occurring not infrequently with prolonged use. Liver and lung fibrosis are a concern, but are less common. Thyroid function tests, liver function tests and a chest radiograph should be documented before starting amiodarone, and thyroid and liver function checked at least every 6 months. If given acutely, intravenous amiodarone loading acts more quickly than oral medication (80–90% sinus rhythm at 24 hours). When given by prolonged infusion, administration into a central vein is necessary to avoid thrombophlebitis.

Dronedarone is a new antiarrhythmic, developed by modifying the structure of amiodarone to reduce its toxicity and improve pharmacokinetics. It is currently approved by the National Institute for Health and Clinical Excellence for patients with non-permanent atrial fibrillation not controlled by first-line therapy with risk factors for stroke but who do not have New York Heart Association class III or IV heart failure. The ATHENA trial showed that dronedarone reduced rates of cardiovascular hospitalization and death (Hohnloser et al, 2009). However, the role of dronedarone in the management of atrial fibrillation is to be revised in light of the PALLAS (Permanent Atrial Fibrillation Outcome Study Using Dronedarone on Top of Standard Therapy) trial which was halted early (Connolly et al, 2011). In PALLAS, the death (from any cause), stroke rate and heart failure events was statistically significantly increased in those patients taking dronedarone compared to placebo (Connolly et al, 2011). The reason for this remains unclear but dronedarone should be avoided in high-risk patients with non-permanent atrial fibrillation, particularly those with heart failure.

Sotalol has class II and III antiarrhythmic properties. It can prolong the QT interval and the electrocardiogram should be checked after initiating treatment. Women are more vulnerable than men to the development of torsades de pointes, which may occur even years after initiation of sotalol. Flecainide, other class I antiarrhythmic drugs and sotalol should not be used in those with ischaemic heart disease or impaired ventricular function, because use of these drugs is associated with an increased risk of mortality during follow up.

For patients with very infrequent episodes of atrial fibrillation, a so-called 'pill-in-the-pocket' approach is sometimes appropriate. The patient does not take regular antiarrhythmic medication, but self-medicates with antiarrhythmic drugs (typically flecainide 150 mg together with a beta blocker) as soon as he/she is aware of the symptoms. The first occasion that a patient tries this should be under direct medical supervision. A beta-blocker is given with flecainide to reduce the risk conversion to atrial flutter with 1:1 atrioventricular conduction which can lead to ventricular rates of 250 per minute or higher and can cause collapse. Amiodarone can be used in a similar fashion, but has a slower onset of action than flecainide, so restoration of sinus rhythm may take some time, even a day or more.

The choice of drug may be constrained by the presence of non-cardiac comorbidity. For instance, sotalol is unlikely to be well tolerated in patients with significant lung disease, because of its beta-blocking action.

Electrical cardioversion

Cardioversion is associated with a risk of thromboembolism and patients must be therapeutically anticoagulated to an international normalized ratio (INR) of greater than 2.0 for at least 3–4 weeks before elective cardioversion to reduce this risk (Camm et al, 2010). An alternative approach for patients with atrial fibrillation of acute onset within the previous 48 hours is to cardiovert early without prior anticoagulation with warfarin, provided the left atrial appendage is demonstrated to be clear of thrombus using transoesophageal echocardiography.

In an emergency, immediate cardioversion without transoesophageal echocardiography may be required to help reverse catastrophic clinical decline if the acute onset of atrial fibrillation is associated with severe pulmonary oedema, haemodynamic instability or cardiogenic shock, circumstances in which the ventricular rate is often rapid and may be difficult to slow down with drugs. Patients undergoing acute or emergency cardioversion who have not been on warfarin should receive unfractionated or low molecular weight heparin (enoxaparin 1.5 mg/kg daily or equivalent) before cardioversion.

DC cardioversion for atrial fibrillation requires deep sedation or general anaesthesia, electrocardiogram and blood pressure monitoring, and the delivery of an electric shock that is synchronized to the R wave. A biphasic shock waveform is used to maximize the likelihood of success, as the defibrillation threshold is lower than for a monophasic shock. Failure to synchronize the delivery of the shock to the R wave on the electrocardiogram may trigger ventricular fibrillation which can be refractory to further shocks. *Table 5* lists factors for consideration for successful DC cardioversion (Lip et al, 1996).

Traditionally, defibrillation energies are titrated upwards from 100 J. However, this often necessitates multiple shocks before sinus rhythm is achieved. The authors' approach is to start with the maximum energy level of 200 J with the defibrillator pads applied in the antero-posterior configuration (Camm et al, 2010). This configuration is more effective than the anterior-left lateral configuration that is frequently used because it reduces the distance between the defibrillation pads thereby increasing the electrical field strength. It also directs the electrical field selectively through the atrial mass, since both atria are virtually midline structures with the right atrium more or less anterior to the left atrium. Sinus rhythm is achieved with the first shock in most cases.

A second shock, and subsequent shocks, can be applied, but after three failed shocks further attempts are likely to be futile. In large patients, manual pressure can be applied to the sternal pad (through a thick wadding of dry blanket, with rubber shoes and rubber gloves being worn by the operator) to reduce the distance between the pads and thereby further increase the field strength. In patients in whom external DC cardioversion fails to restore sinus rhythm, particularly those in whom obesity may have been a factor in the failure, catheter-based internal cardioversion can be used.

After cardioversion for atrial fibrillation, the return of effective atrial contraction may be delayed for hours or days despite restoration of sinus rhythm, a phenomenon known as 'atrial myocardial stunning'. This stunning is caused by the previous atrial fibrillation and not by the DC shock, as it does not occur in patients receiving shocks for ventricular tachyarrhythmias.

Thromboembolism may occur several days after cardioversion as increasingly strong atrial contractions dislodge a preformed thrombus from the lumen of the left atrial appendage into the left atrial lumen whence it embolizes. Therapeutic anticoagulation should therefore be continued either with heparin or warfarin to a target INR of 2.0–3.0, for at least 1 week and preferably 1 month and until continued sinus rhythm can be confirmed. If the CHA_2DS_2-VASc score is 2 or more then warfarin may be continued long term even when sinus rhythm has been restored and maintained because subsequent recurrences of atrial fibrillation may be clinically silent and remain undetected for some time, during which the patient is exposed to significant thromboembolic risk.

DC cardioversion carries a 0.1% risk of inducing malignant arrhythmias including ventricular tachycardia and ventricular fibrillation. Atrial fibrillation recurs following DC cardioversion in 70–85% of patients by 1 year. The recurrence rate can be reduced to 30–50% by long-term antiarrhythmic drug treatment (Lafuente-Lafuente et al, 2009). The most effective agent is amiodarone.

Table 5. Checklist for safe electrical cardioversion

Anticoagulation with international normalized ratio (INR) 2.0–3.0 for at least 3 weeks or transoesophageal echocardiogram to exclude left atrial thrombus in acute onset cases	
Electrolytes normal (Na+, K+, Mg2+)	
Digoxin levels are normal (if relevant)	
Patient fasted	
Admitted to coronary care unit, anaesthetic room or designated place with continuous electrocardiographic monitoring	
Confirm still in atrial fibrillation	
Written consent	Risks: thromboembolic event, skin burns, prolonged sinus arrest, dangerous arrhythmia (ventricular tachycardia or fibrillation increased by hypokalaemia, digoxin toxicity or non-synchronized shock)
General anaesthesia	
Place cardioversion pads in anteroposterior position	
Biphasic shock to be synchronized to R wave. Start at 200 J. May need to press synchronize after each shock	
Successful if there are two or more P waves after a shock. Stop after a maximum of three shocks	
Monitor patient's blood pressure and heart rate for at least 3 hours. The patient should be fully awake and recovered before eating and drinking	
Continue anticoagulation for at least 4 weeks	

Catheter ablation

Patients in atrial fibrillation who are symptomatic despite optimal medical therapy, including agents for rate and rhythm control, can be considered for catheter ablation (Jais et al, 2008). This involves a catheter being introduced into a femoral vein with passage into the right atrium. From there, a trans-septal puncture allows access to the left atrium. Different ablation strategies have been developed but typically the four pulmonary veins are electrically isolated from the left atrium by making ablation lesions in the left atrium circumferentially around the ostia of the veins. Abnormal electrical activity arising within the veins can no longer trigger episodes of atrial fibrillation. Additional lines of lesions may be created in the left atrium, and sometimes right atrium, to create regions which remain electrically connected to each other but are too small to sustain the multiple electrical re-entrant circuits that form the anatomical substrate for sustained atrial fibrillation. This is sometimes termed a 'catheter maze' procedure. Other strategies require ablation of regions of abnormal electrical conduction, very high frequency electrical activity or of foci of autonomic innervation.

Ablation should be considered particularly in lone atrial fibrillation if pharmacological therapy has failed. It can be justified as a means to avoid the need for long-term antiarrhythmic drug therapy in young patients. Patient preference should also be considered. Referral to a cardiac electrophysiologist is recommended by the National

Institute for Health and Clinical Excellence in the UK to allow detailed discussions of the benefits *vs* the 2–4% risk of serious complications (haematoma at puncture site, thromboembolism, pulmonary vein stenosis, phrenic nerve injury, pericardial effusion and tamponade, atrio-oesophageal fistula, and a risk of death of around 0.1%) (Camm et al, 2010). Second, and possibly more, procedures are needed in 30% of cases. Specialist centres have developed considerable expertise and report excellent results in patients with paroxysmal atrial fibrillation (Jais et al, 2008; Camm et al, 2010). Success rates in persistent and permanent atrial fibrillation are more variable and specific patient and disease factors play a role. Several procedures are often required and patients should be warned of this in advance.

In atrial fibrillation patients undergoing cardiac surgery, ablation of the atrial myocardium may be carried out surgically using one of a number of tools. Usually this procedure is carried out as an adjunct to coronary or valve surgery, but may occasionally be carried out as an isolated procedure. Thoracoscopic approaches have been developed to minimize the morbidity associated with surgical access to the heart.

Rate control strategy

A rate control strategy may be chosen for those entirely asymptomatic from atrial fibrillation or those in permanent atrial fibrillation. Anticoagulation must be used appropriately.

Beta-blockers are commonly used and were effective rate-controlling agents in the AFFIRM trial (AFFIRM Investigators, 2004). Bisoprolol is a long-acting agent that is safe in the majority of patients. Those with airways disease or acute medical illness may be given metoprolol because its short half-life allows an assessment of tolerability. Low doses should be started and then quickly up-titrated to achieve adequate ventricular rate control (heart rates of 80–90 bpm). If beta-blockers are contraindicated, verapamil or diltiazem can be used. Where adequate up-titration is limited by low blood pressure, addition of digoxin to either the beta-blocker or calcium-channel blocker is usually very effective. Digoxin should not be used as a sole rate-controlling drug in most instances, as its rate-slowing effect is frequently inadequate.

Implantation of a permanent pacemaker and ablation of the atrioventricular node has a success rate approaching 100% in perfect control of the ventricular rate, as this is determined by the programmed pacemaker settings (Camm et al, 2010). It is highly effective for patients whose main concern is palpitation caused by a poorly controlled ventricular rate. It is less effective where the predominant symptom is breathlessness or fatigue. Most patients become completely pacemaker-dependent and so have a cumulative, rest-of-life risk of complications from having a permanent pacing system. This approach is not appropriate for patients under 60 years old unless all other options have been exhausted. If the patient has impaired left ventricular function careful consideration should be given to implanting a cardiac resynchronizing pacemaker before atrioventricular node ablation, as long-term right ventricular pacing will reduce left ventricular ejection fraction as a result of pacing-induced dyssynchrony, and may lead to heart failure.

Conclusions

Atrial fibrillation is common, with a wide variety of clinical presentations and several therapeutic options. In the absence of treatments that reduce the mortality from the condition, the focus is on controlling symptoms and reducing morbidity, particularly the risk of stroke. It is a chronic condition in most patients and merits regular follow up and review of management. There is a rapidly expanding array of drugs and devices to reduce thromboembolic risk, and of catheter and surgical techniques to ablate the atria, but concerns about costs will limit the use of these to a selected minority of cases for the foreseeable future. Warfarin, beta-blockers and digoxin are likely to remain the most commonly used treatments for some years to come. **BJHM**

KEY POINTS

- Atrial fibrillation can be an incidental finding or a presenting symptom; it should always be treated seriously.
- Consider anticoagulation in all patients; if the decision is made not to use warfarin, document the reasons carefully and communicate it with the patient, team members and the GP. Review the decision regarding anticoagulation regularly.
- The decision to rate control or rhythm control (whether by drug or by electricity) should be made according to the underlying cause, patient's symptoms, presentation and any comorbidities.
- Electrical cardioversion should be performed in a monitored environment, under anaesthesia. Adequate preceding anticoagulation is essential. Left atrial appendage clot must be excluded by transoesophageal echocardiography if the patient is not anticoagulated.

Conflict of interest: none.

ACTIVE Writing Group of the ACTIVE Investigators, Connolly S, Pogue J, Hart R et al (2006) Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. *Lancet* **367**(9526): 1903–12

AFFIRM Investigators (2004) The atrial fibrillation follow-up investigation of rhythm management (AFFIRM) study: approaches to control rate in atrial fibrillation. *J Am Coll Cardiol* **43**(7): 1201–8

Camm AJ, Kirchhof P, Lip GYH et al (2010) Guidelines on the management of atrial fibrillation: the Task Force for the management of atrial fibrillation of the European Society of Cardiology. *Eur Heart J* **31**(19): 2369–429

Connolly SJ, Camm AJ, Halperin JL et al (2011) Dronedarone in high-risk permanent atrial fibrillation. *N Engl J Med* **365**(24): 2268–76

Heeringa J, van der Kuip DA, Hofman A et al (2006) Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. *Eur Heart J* **27**(8): 949–53

Hohnloser SH, Crijns HJ, van Eickels M et al (2009) Effect of dronedarone on cardiovascular events in atrial fibrillation. *N Engl J Med* **360**(7): 668–78

Hughes M, Lip GY; Guideline Development Group, National Clinical Guideline for Management of Atrial Fibrillation in Primary and Secondary Care, National Institute for Health and Clinical Excellence (2008) Stroke and thromboembolism in atrial fibrillation: a systematic review of stroke risk factors, risk stratification schema and cost effectiveness data. *Thromb Haemost* **99**(2): 295–304

Jais P, Cauchemez B, Macle L et al (2008) Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. *Circulation* **118**: 2498–505

Lafuente-Lafuente C, Mahe I, Extramiana F (2009) Management of atrial fibrillation. *BMJ* **339**: b5216

Lip GY, Watson RD, Singh SP (1996) ABC of atrial fibrillation. Cardioversion of atrial fibrillation. *BMJ* **312**(7023): 112–15

Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY (2010) A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest* **138**(5): 1093–100

Rubboli A, Kovacic JC, Mehran R, Lip GY (2011) Coronary stent implantation in patients committed to long-term oral anticoagulation therapy: successfully navigating the treatment options. *Chest* **139**(5): 981–7