Atrial fibrillation in the elderly

COLIN BERRY, ALAN RAE, JAQUELINE TAYLOR, ADRIAN J BRADY

Abstract

Atrial fibrillation (AF) is the commonest sustained arrhythmia affecting elderly people. It will become increasingly prevalent in Western societies, given the growing proportion of elderly people in these populations.

AF may lead to a variety of embolic phenomena, notably stroke. Furthermore, AF may complicate other conditions, such as hypertension and heart failure. AF is associated with an increased risk of death.

The management of AF can be a difficult problem, particularly in symptomatic, elderly patients. Results from recent large, multicentre clinical trials in sustained AF have demonstrated that a rate control strategy with conventional drugs, is at least as effective, and possibly superior, to rhythm control by chemical or electrical cardioversion over a three-year period. Whether these results can be extrapolated to longer time periods than the trials' durations (approximately 3.5 years) is not known.

Results from clinical trials of a new oral anticoagulant, ximelagatran, indicate that this agent is as good an anticoagulant as warfarin in sustained AF. Other results are awaited from on-going trials on the tolerability and side-effect profile of this drug. The possibility of an alternative anticoagulant which does not share warfarin's need for routine monitoring of its anticoagulant effect, nor share warfarin's potential for adverse interactions with other drugs, is very attractive, particularly in elderly patients.

In the longer term, radiofrequency ablation techniques might provide a more widely available, curative therapy, for elderly patients with AF.

Key words: atrial fibrillation, rate control, rhythm control, anticoagulation, radiofrequency ablation, elderly.

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Introduction

Atrial fibrillation (AF) is disorganised atrial depolarisation resulting in loss of effective atrial contraction. It is the commonest sustained arrhythmia in the elderly and is associated with considerable morbidity and an increased risk of death. AF may be paroxysmal (intermittent), persistent or sustained. A diagnosis of persistent AF indicates the potential for restoration of sinus rhythm, whereas that of sustained AF implies that this is the final established cardiac rhythm.

Recent multinational guidelines are now available for the management of AF. The purpose of this article is to discuss some important aspects of AF and review recent developments in the management of this condition, with particular regard to elderly patients.

Electrocardiography of AF

AF is characterised by disorganised waves of electrical activation, with a rate of 350–600 beats per minute (bpm). The ventricular response is also irregular, with a usual rate between 100–160 bpm in patients with normal atrio-ventricular conduction. In the elderly, however, the ventricular rate response may be slower, and is often less than 100 bpm. This relatively slower rate is probably due to fibrotic change within the conducting system of the heart.

Conversely, Wolff-Parkinson-White (WPW) syndrome can present in the elderly.[2] This is believed to be due to fibro-calcific change within the atrioventricular (AV) node, which unmasks a latent accessory pathway. The risk of death from AF and malignant arrhythmias arising from 1:1 atrioventricular conduction in WPW is not affected by age,[3] and ambulant elderly patients who are diagnosed with WPW should therefore undergo similar management to younger patients.[2,4]

Epidemiology

AF is the commonest occurring sustained arrhythmia in the community, with a prevalence of 0.4% in those aged less than 65 years, rising to approximately 10% in those greater than 75 years.[1,5] In North America, the prevalence of AF is projected to rise two to three fold by the year 2050,[6] this being largely due to improved life expectancy. In the Cardiovascular Health Study,[7] AF was present in 9.4% of patients who had cardiovascular disease (CVD), and 1.6% without CVD. In this population, heart failure, valvular heart disease, hypertension, and advancing age, were independently associated with the presence of AF.

Pathophysiology

Hypotheses for the aetiology of AF include enhanced automatic-

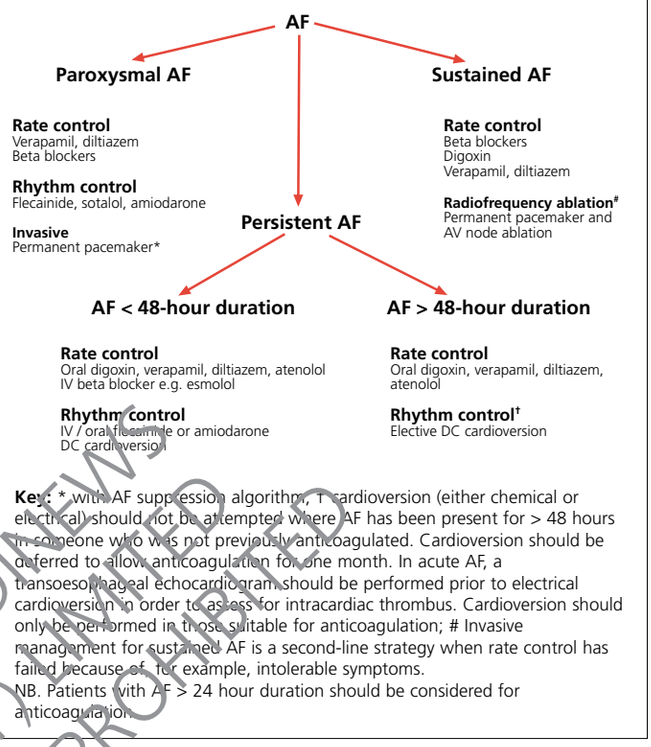
Table 1. Causes of atrial fibrillation (AF)

Factors associated with the development of AF	
Cardiac	**Non-cardiac**
Hypertension	Increasing age
Coronary heart disease	Alcohol excess
Mitral valve disease	Hyperthyroidism
Heart failure	
Atrial septal defect	

Table 2. Health problems due to atrial fibrillation

Cardiac	Non-cardiac
Exercise-intolerance	Thrombo-embolic events
Heart failure	Reduced quality of life

Figure 1. Management strategies for atrial fibrillation (AF)



Key: * with AF suppression algorithm, † cardioversion (either chemical or electrical) should not be attempted where AF has been present for > 48 hours in someone who was not previously anticoagulated. Cardioversion should be deferred to allow anticoagulation for one month. In acute AF, a transoesophageal echocardiogram should be performed prior to electrical cardioversion in order to assess for intracardiac thrombus. Cardioversion should only be performed in those suitable for anticoagulation; # Invasive management for sustained AF is a second-line strategy when rate control has failed because of, for example, intolerable symptoms.
NB. Patients with AF > 24 hour duration should be considered for anticoagulation.

ity of one or more atrial foci and re-entry circuits, often arising in atrial tissue around the pulmonary veins, or fractionation of depolarisation wave fronts within the atria leading to multiple wavelets and disorganised atrial conduction.[1] AF is probably more common in the elderly, because of age-related fibrotic changes within the atrial myocardium and conducting tissues. The risk of developing AF is more common in people with structural heart disease, such as left atrial dilatation, and left ventricular hypertrophy[5,8] (table 1).

AF can result in a reduction in cardiac output. Loss of sequential atrioventricular conduction leads to a loss of co-ordinated atrial filling and emptying. Atrial contraction may contribute up to 30% of the cardiac output. Furthermore, a rapid, irregular ventricular rate will also result in impaired ventricular filling, contraction and a reduced ejection fraction. These abnormalities may lead to a reduction in exercise capacity and symptoms, particularly in patients with underlying cardiac disease.

In some patients, AF may be due to sick sinus syndrome, otherwise known as the tachycardia bradycardia syndrome.[9] Patients with sick sinus syndrome may present with symptoms due to AF with a rapid, or slow, ventricular response. In some of these patients, AF may be paroxysmal, rather than sustained.

Morbidity and mortality

AF is associated with a reduced quality of life.[10] It is also associated with an increased risk of health problems, such as heart failure , and stroke,[11] and is a common finding in hospitalised, elderly patients[12] (table 2). AF may also be an incidental finding in the elderly, when the ventricular rate may be normal, or even slow.

AF is also associated with cognitive impairment in older patients.[13] The Rotterdam study has shown that both Alzheimer's disease and vascular dementia are commoner in patients with AF.[14] Case control studies in patients with AF have shown consistently poorer performance in neuropsychological tests.[15] The mechanism is likely to be due to a combination of silent cerebral infarction and leukoariosis due to white matter hypoperfusion, both of which are commoner in patients with AF than controls in sinus rhythm.[16,17]

Thrombo-embolism

AF greatly increases the risk of thrombo-embolic events and death.[11] The annual risk of a stroke in lone AF increases with age, approaching 20% in patients > 80 years.[18,19] Importantly, the risk of thrombo-embolism with either paroxysmal AF or sustained AF is comparable. The annual risk of thrombo-embolic stroke is 5% in non-valvular AF,[19-21] five times that of age-matched controls in sinus rhythm.[20] The stroke rate is much higher if transient ischaemic attacks and subclinical strokes are included.[22] The risk of a thrombo-embolic stroke in patients with mitral valve disease is higher still. For example, the annual thrombo-embolic risk in patients with AF and rheumatic heart disease is reported to be 17-fold greater than that of age-matched controls.[18-23]

AF is an independent risk factor for cardiac and all-cause mortality.[12,24,25] Overall, the risk of death conferred by AF is at least double that of age-matched controls in sinus rhythm,[1] and tends to increase with advancing age.[24,26]

Management

Rate or rhythm control

The management strategies for AF include either to attempt to

Table 3. Drugs which may be used for 'rate control' or 'rhythm control' in the elderly

Drug	Class	Mechanism of action	Indication	Comment/cautions in the elderly
Rate control				
Beta blockers	Non-β1 selective: atenolol 25–100 mg daily	Anti-sympathetic nervous system	Rapid atrial fibrillation	May cause lethargy or postural hypotension
	β1-selective: bisoprolol 2.5–10 mg daily			Can be useful when angina and/or hypertension are also present
Calcium antagonist	Diltiazem 90–400 mg daily	Slow calcium channel antagonist (AV node blocker)	Rapid atrial fibrillation	Can be useful when angina and/or hypertension are also present
	Verapamil 40–360 mg daily			Avoid in heart failure
				Diltiazem may cause diarrhoea, verapamil may cause constipation
Digitalis glycoside	Digoxin 87.5–250 µg daily	Slows AV node conduction	Rapid atrial fibrillation	Less effective control of heart rate, particularly during exercise, than beta blockers. Reasonably well tolerated Caution in renal dysfunction
Rhythm control				
Anti-arrhythmic agents	Amiodarone 100–200 mg daily	Prolongation of action potential duration	Chemical cardioversion of AF to sinus rhythm	Wide side effect profile
				Chronic therapy: consider checking TFTs/LFTs and PFTs at 6–12 month intervals
	Sotalol 40–160 mg twice daily	Prolongation of action potential duration	Adjunctive therapy to maintain sinus rhythm in longer term	Can be effective and is reasonably well tolerated. Caution in those with heart failure and coronary heart disease
	Flecainide	Sodium channel inhibitor	Should only be used in conjunction with a cardiologist or physician	Should only be used in patients without CHD. A stress test to screen for the presence of inducible cardiac ischaemic should be performed prior to the prescription of flecainide in elderly patients

Key: AF = atrial fibrillation; AV = atrioventricular; TFT = thyroid function tests; LFT = liver function tests; PFT = pulmonary function tests; CHD = coronary heart disease

control the ventricular rate – 'rate control', or to restore and maintain sinus rhythm – 'rhythm control'[1] (figure 1). Rate-limiting drug therapies, such as beta blockers, digoxin, or verapamil, can be used to achieve a normal heart rate during rest and daily activities (table 3). In some symptomatic patients, the ventricular rate may still not be well controlled and, in this case, an invasive strategy, involving implantation of a permanent pacemaker and AV node ablation, may be needed.

Rhythm control

For patients with recent onset AF (e.g. < three months), and those who are symptomatic, rhythm control may be the preferred option. This strategy can involve either electrical cardioversion, or anti-arrhythmic medication, alone, or in combination (figure 1 and table 3), together with warfarin therapy.

Elderly patients are less likely to tolerate anti-arrhythmic drugs, such as amiodarone and sotalol. These drugs should be used with caution, and in conjunction with a cardiologist. Flecainide carries a risk of provoking ventricular arrhythmias and sudden death in patients with coronary heart disease (CHD). It should not be used in patients with coronary disease. CHD is common in elderly patients and is often subclinical. Flecainide should generally be avoided in elderly patients. If other drugs have failed and flecainide is being considered, a stress test should be performed to exclude inducible myocardial ischaemia, together with an echocardiogram to establish normal LV function.

Cardioversion

Our current practice for a patient presenting with recent onset AF is to start warfarin if the patient is not already anticoagulated and attempt elective electrical cardioversion one month later. If sinus rhythm is not restored, or if it is, but then the rhythm subsequently reverts to AF, then the patient would usually be offered a repeat cardioversion. In this case, amiodarone would be com-

menced and electrical cardioversion performed six weeks later. The amiodarone is then continued afterwards. In this case, the duration of therapy will vary dependent on whether the drug is tolerated and sinus rhythm maintained.

In younger patients (< 60 years) with lone AF, our strategy is usually to attempt electrical cardioversion, which may be preferable to many years of sustained AF. In older patients with lone AF, our threshold for undertaking electrical cardioversion would usually be higher, largely because of a higher rate of AF recurrence in older patients after this procedure.[10]

Recent randomised trials

The AFFIRM study was designed to compare the strategies of either rate control or rhythm control in patients with AF and a high risk of stroke or death.[27] Four thousand and sixty patients were randomised to either pharmacological rate or rhythm control groups. The average age of the study population was 70±9(SD) years. Sixty-nine per cent of patients had been in AF for two or more days, and 64% of patients had experienced recurrent AF. Many patients had coexisting hypertension, CHD and heart failure. The anti-arrhythmic drugs that were most commonly used in the rhythm control group included amiodarone, sotalol, propafenone and flecainide. The drugs that were used in the rate control group were digoxin, beta-blockers, verapamil and diltiazem. Approximately 5% of patients in this group who continued to be symptomatic due to inadequate rate control, underwent AV node ablation.

The mean follow-up period was 3.5 years, with a maximum of six years. The prevalence of sinus rhythm in the rhythm control group was 82%, 73% and 63% at one, three and five years, respectively. Warfarin was administered in 85% and 70% of the rate and rhythm control groups, respectively. Fewer people died in the rate control compared to the rhythm control groups (310 *vs.* 365; p=0.08). The annual ischaemic stroke rate was approximately 1% in each group. Cardiovascular events tended to be less in the rate control group. In our own centre, we found that electrical cardioversion for sustained AF is associated with a poor rate of long-term maintenance of sinus rhythm, particularly in those who are elderly with or without structural heart disease.[10]

Rate control of AF

Beta blockers and the rate-limiting calcium antagonists, verapamil and diltiazem, may be better at controlling the ventricular rate-response during exercise than digoxin, and are now an alternative first-line therapy to digoxin (table 3). Digoxin and beta blockers can be particularly useful in the management of patients with AF and heart failure.[28] Given the age of the AFFIRM population, and the high prevalence of co-morbid health problems, the results of this trial are applicable in ordinary clinical practice. The AFFIRM results demonstrated equality, or slight superiority, for rate control and warfarin therapy, versus rhythm control over a 3.5-year period. Taken together, these data suggest that rate control should be the preferred strategy in most elderly patients with sustained AF. Whether these results are maintained in the longer term (i.e. for longer than the follow-up period of the AFFIRM trial) is not known.

Table 4. Risk factors for bleeding complications with oral anticoagulation

Risk factor	Potential clinical characteristic
History of bleeding	Gastrointestinal blood loss, epistaxis, haematuria
Drugs which cause bleeding	Non-steroidal anti-inflammatory drug therapy
Drugs which potentiate warfarin effect	Erythromycin, amiodarone
Co-morbid health problems	Heart failure, liver disease
Poor compliance	Cognitive impairment, lack of carer support
Psycho-social problems	Excess alcohol
Trauma	Recurrent falls

Failed rate control

For patients who are still symptomatic due to an uncontrolled heart rate, an invasive strategy may be preferred (figure 1). The options in this case involve pacemaker-based strategies. Advances in pacemaker technology have led to the development of devices that incorporate AF suppression algorithms. These pacemakers act to prevent the onset of AF when atrial ectopic beats occur, and may be useful in patients with a history of bradycardia and either previous persistent AF, or paroxysmal AF.

In patients with severe, refractory symptoms, the definitive strategy may be permanent pacemaker implantation followed by radiofrequency AV node ablation. This is a relatively straightforward and safe (procedure-related risk of death 0.1%) to perform. The mode of pacing should aim to maintain AV synchrony in those in sinus rhythm who experience paroxysmal AF. This is best attained with a dual chamber (pacing and sensing) mode switching device.[29,30] For those in sustained AF, a single ventricular (pacing and sensing) mode is satisfactory.

Anticoagulation

The issue of anticoagulation for AF is particularly difficult in the elderly, as few patients over the age of 80 years have been included in clinical trials of anticoagulation in AF. Furthermore, it is often difficult to achieve the 'tight' levels of anticoagulation control reported in clinical trials in ordinary clinical practice. Nevertheless, the current guidelines recommend that all patients with AF should be considered for some form of thromboprophylactic drug therapy.[1,11]

Patients with 'lone AF', without risk factors for stroke, and who are 60 years or less, are at a very low annual risk (< 1% per annum) of thrombo-embolism and do not require anticoagulation. Many of these patients with 'lone AF' are given low-dose (75 mg) aspirin. Younger patients with 'lone AF' may also be offered elective electrical cardioversion. In this case, warfarin is required for at least four weeks before and six weeks after the cardioversion procedure.

The Stroke Prevention in Atrial Fibrillation Trials demonstrated that warfarin substantially reduced the risk of a thrombo-

Key messages

- Atrial fibrillation is common and affects up to 10% of elderly people
- This prevalence of this arrhythmia in Western populations is increasing because of increasing life expectancy
- Atrial fibrillation is associated with a reduced quality of life and an increased risk of death and stroke, especially in older patients
- Rate control strategies with traditional drugs such as digoxin, calcium channel blockers and beta blockers are as good, or even better, than rhythm control by pharmacological or electrical methods, at least in the medium term
- Ximelagatran, an orally active thrombin inhibitor, may be a future alternative anticoagulant to warfarin

embolic event, compared with either aspirin, or placebo.[31] In non-rheumatic AF, warfarin reduced the risk of stroke by 68% whereas aspirin reduced the risk by 44%. Although the risk of haemorrhage with warfarin therapy is increased in the elderly, the absolute benefit of oral anticoagulation is greatest in elderly patients with AF.[31] Despite this, anticoagulation rates are low in this group.[32]

Elderly patients should be carefully assessed for risk factors for bleeding (table 3). For those elderly patients at low risk of gastro-intestinal bleeding, warfarin can be safely administered.[33] The target INR in this group is 2-3.[1] Recent data from our centre suggest that elderly patients (> 75 years; n=128) with AF who are taking warfarin have equally good INR control and similar rates of serious bleeding complications compared with younger patients (60–69 years; n=204).[34] The presence of cognitive impairment and disability are not absolute contraindications to anticoagulant therapy, but do mean that careful consideration, assessment of risk/benefit and organisation of services are required (table 4). Falls in the elderly, usually common and often trivial, become much more sinister when patients are on warfarin. Subdural haematoma is then by no means rare, and the risks of warfarin must never be underestimated.

Duration of warfarin therapy and electrical cardioversion

Warfarin should be started at least four weeks before electrical cardioversion for persistent AF be attempted. This strategy ensures that any intracardiac thrombus which may have developed becomes organised, minimising the potential for thromboembolism after restoration of atrial contraction.

Warfarin should continue for at least four weeks after DC cardioversion, and preferably longer. In our centre, 50% of patients who were in sinus rhythm at clinic review one month after successful electrical cardioversion had reverted to AF by one year. Warfarin had been discontinued at clinic review, leaving those patients who subsequently reverted to AF without thromboprophylactic protection. In the AFFIRM study, most of the ischaemic strokes occurred after warfarin had been stopped.[27] Based on our own experiences, we continue oral anticoagulation for 3–6 months after successful cardioversion,[35] and often review the patient at one year.

An alternative oral anticoagulant has been long awaited. The future is nearly here. Ximelagatran is an orally active, long-acting thrombin inhibitor which prevents the cleavage of fibrinogen to fibrin.[36] The Stroke Prophylaxis Using an Oral Thrombin Inhibitor in Atrial Fibrillation (SPORTIF III) compared ximelagatran with warfarin, in patients with AF and one or more risk factors for stroke. Preliminary results suggest that ximelagatran may be at least as effective as warfarin.

Future directions

AF is likely to become an even more common challenge for primary and secondary care clinicians. Rate control is likely to become the main therapeutic goal in older patients. AV nodal ablation with pacemaker insertion in symptomatic elderly patients will likely increase. Radiofrequency ablation of atrial tissue around pulmonary veins is an emerging procedure that can restore sinus rhythm and has been successfully performed in elderly patients.[37] Therapeutic advances with oral anticoagulation will hopefully facilitate community-based management of patients with AF.

Editors' note

This is the fifth article in our clinical cardiology series. Previous articles include: the future of cardiology: heart disease in older patients (*Br J Cardiol* 2003;**10**:45-8); heart disease in older patients: myocardial infarction (*Br J Cardiol* 2003;**10**:123-7); thrombolytic therapy for acute ischaemic stroke (*Br J Cardiol* 2003;**10**:197-205); percutaneous coronary intervention in the elderly (*Br J Cardiol* 2003;**10**:293–6).

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