

CME General Internal Medicine for the Physician – I

The management of atrial fibrillation

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Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia. It is responsible for 30% of hospital admissions for arrhythmia and is a common cause of stroke. Its prevalence increases with age (0.5%: 50–59 years; 8.8%: 80–89 years), with an incidence of 0.2% per year in men aged 30–39 years and 2.3% per year in men aged 80–89 years. It may be associated with cardiac pathology such as rheumatic heart disease, coronary heart disease (CHD), hypertension and cardiomyopathies. When found without such associated conditions, it is called 'lone' AF. It frequently complicates non-cardiac conditions such as hyperthyroidism, fever, the post-surgical period, hypoxia and acute ethanol intoxication. In these situations, treatment of the underlying condition may be enough to restore sinus rhythm. However, chronic alcohol abuse can result in a dilated cardiomyopathy of which AF may be the presenting manifestation.

The management of AF is changing rapidly, with developments in ablation techniques and implantable devices showing considerable promise. The concept that AF leads to ultrastructural remodelling of the atria, which then further encourages the recurrence and establishment of AF, promotes the application of these and other therapies earlier and more aggressively in the course of the disease than has hitherto been the case.

Classification

Camm's classification of AF (Table 1) is clinically based. The trend to chronicity within the classification predicts the natural history of lone AF and the increasing difficulty encountered in

managing AF when associated with increasingly important structural heart disease.

Pathophysiology of atrial fibrillation

During AF, the process of atrial depolarisation is rapid and disorganised and is responsible for the various clinical manifestations of the condition:

- an irregular and usually rapid ventricular response rate
- loss of atrial contraction
- decreased efficiency of ventricular filling, and thus of cardiac output
- thrombus formation within the atria.

The ventricular response rate and regularity depend upon the function of the atrioventricular (AV) node and His-Purkinje system, which in turn influence the heart rate and the extent to which

Table 1. Clinical classification of atrial fibrillation.

Acute	<48 hours' duration
Paroxysmal	Self-terminating at least once
Persistent	>48 hours with no spontaneous termination
Permanent	Resistant to pharmacological & DC cardioversion

Table 2. Therapies available for the treatment of atrial fibrillation (AF)

Therapy	Therapeutic effect
Drugs	<ul style="list-style-type: none"> • Restore sinus rhythm • Maintain sinus rhythm • Control ventricular response rate • Prevent thromboembolism
Implantable devices	<ul style="list-style-type: none"> • Prevent AF by: <ul style="list-style-type: none"> – avoiding atrial bradycardia – resynchronising atrial activation • Terminate AF
Surgery	<ul style="list-style-type: none"> • Create linked atrial compartments ('maze'), preventing development & perpetuation of AF
Catheter ablation	<ul style="list-style-type: none"> • Control ventricular response rate by: <ul style="list-style-type: none"> – modifying AV nodal conduction – destroying AV nodal conduction & implanting a pacemaker • Destroy or isolate triggers which initiate AF • Linear ablation to create a catheter 'maze'
Hybrids of the above	

AV = atrioventricular.

cardiac output falls during AF. The risk of thrombus formation depends on a number of factors (see below).

Management goals and strategies

- 1 Termination of AF and maintenance of sinus rhythm.
- 2 Control of ventricular rate.
- 3 Prevention of thromboembolism.

The ideal is to restore and maintain sinus rhythm when the symptoms and risks associated with AF would be removed. This can be difficult to achieve, so other strategies are often required. The therapies available to treat AF are listed in Table 2.

Termination of atrial fibrillation and maintenance of sinus rhythm

The restoration of sinus rhythm secures all the management goals, but it is limited both by a high recurrence rate of AF and by the difficulties associated with achieving sinus rhythm.

Cardioversion

Sinus rhythm can be restored either pharmacologically or by DC cardioversion. The former can be achieved

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without the general anaesthesia required for DC cardioversion. Although usually administered intravenously, at least the class 1c agents (flecainide and propafenone) are as effective orally. A meta-analysis of studies of readily available anti-arrhythmic drugs showed that flecainide and propafenone are effective in restoring sinus rhythm from AF. The evidence is moderate for quinidine, only suggestive for disopyramide and amiodarone, while suggesting negative efficacy for sotalol.

The chance of anti-arrhythmic drug therapy successfully restoring sinus rhythm diminishes significantly if the AF has lasted more than 12–24 hours. Thus, once safety and efficacy have been established intravenously, the patient should take the drug orally as soon as AF recurs – thus achieving earlier therapy and usually avoiding the need for presentation to hospital. If there is significant associated structural disease, drug therapy should be restricted to amiodarone or β -blockade. DC cardioversion is also less likely to be effective with increased duration of AF, but this effect is measured in months rather than hours.

Both methods can be complicated by thromboembolism, the likelihood of which also increases with:

- the duration of AF
- the presence of structural heart disease
- age.

If AF has been present for less than 24 hours, it is safe to cardiovert immediately by either method, reverting to DC cardioversion if initial drug therapy fails. If AF duration is uncertain and there is no urgent need for cardioversion, either a trans-oesophageal echocardiogram should be performed to ensure that the left atrium is free of thrombus or cardioversion be postponed to allow a day or two of heparin therapy or for two months of warfarin therapy to achieve an INR of 2–3. Warfarin should be continued for at least two months after successful cardioversion, even if sinus rhythm is maintained, because of the delay in restoration of atrial mechanical function after cardioversion.

Key Points

AF is the commonest sustained cardiac arrhythmia

Various possible clinical presentations including as an incidental finding, palpitations, heart failure and peripheral thrombo-embolism especially stroke

Occurs either as 'lone' AF, complicating reversible non-cardiac pathology and in association with structural heart disease

Classically, lone AF begins as paroxysmal AF, progressing to persistent and ultimately permanent AF in keeping with atrial remodelling

Individual therapy should aim at restoration of sinus rhythm whenever appropriate and emphasising ventricular rate control if not; consideration should always be given to whether (or which) anticoagulation therapy is required

New ablation, surgical and implantable device therapies need to be remembered

Maintaining sinus rhythm

Prophylactic drug therapy should be considered after cardioversion. If, based upon past history and a normal echocardiogram, a long interval is likely before any recurrent AF, it would be reasonable not to use prophylactic therapy. Otherwise, prophylactic therapy prolongs the intervals between AF recurrences, with choice of prophylaxis influenced by the presence or absence of structural heart disease. There is strong evidence that disopyramide, flecainide, propafenone, quinidine and sotalol (in contrast to its role in terminating AF) are effective in maintaining sinus rhythm in patients with paroxysmal AF. There is little evidence on the use of amiodarone for maintenance of sinus rhythm after cardioversion of AF – which may be corrected by clinical trials now in progress. Combination therapy, especially of class 1 drugs and β -blockade, may be useful.

Control of ventricular rate

This therapeutic strategy accepts the continuation of AF, so consideration must also be given to the thromboembolic risk. If sinus rhythm cannot be restored, a relatively physiological ventricular rate should be attained, first, for acute improvement in cardiac output and symptoms; secondly, to avoid the gradual development of a dilated

cardiomyopathy caused by an unremitting tachycardia (the so-called 'tachycardia myopathy') which is underestimated in AF patients with uncontrolled ventricular rates. AV nodal and His-Purkinje conduction are the sole determinants of the ventricular rate in most patients with AF. Therapies to control the ventricular rate are all directed at the AV node and fall into the two categories of drug therapy and catheter ablation.

Drug therapy

Three groups of drugs are used to control ventricular response rate to AF:

- digoxin
- β -blockers
- calcium antagonists.

They all prolong the refractory period of the AV node by different mechanisms, so can be used together to produce additive effects. The choice of drug depends upon individual patient assessment for contraindications or other therapeutic requirements. For example, if the patient is also hypertensive, β -blockade or calcium antagonism might be considered first instead of digoxin – although, unless there is renal failure, digoxin is useful in most patients. However, combination therapy is usually required, especially as digoxin is of limited value in controlling the ventricular response rate during exercise. For

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this reason, the efficacy of rate control therapy should ideally be assessed from the heart rate trend in a 24-hour ECG recording.

Catheter ablation

When drugs fail to control the ventricular response rate during AF, catheter ablation techniques should be considered, especially if there has been evidence of heart failure. There are two approaches to catheter ablation for this indication:

- 1 The option with which there is more experience is that of complete destruction of the AV node followed by implantation of a rate responsive pacemaker. The heart rate is then controlled by appropriate programming of the pacemaker.
- 2 The realisation that the AV node usually has two inputs into the His-Purkinje system has enabled catheter ablation to modify AV nodal function by selectively destroying one (usually the slowly conducting) of these inputs. With one possible AV nodal route removed, the ventricular response rate is thus reduced without the need for a pacemaker.

Accessory pathway

It is important to remember the occasional possibility that an accessory pathway may be present. In those patients, a delta wave will be seen during sinus rhythm and the ventricular response rate to AF may be very rapid and occasionally life-threatening. It will not be controlled by usual AV nodal blocking drug therapy, and the treatment of choice is catheter ablation of the accessory pathway.

Prevention of thromboembolism

AF is present in 15% of all stroke patients, in 2–8% of all transient ischaemic attacks, and it confers a 5% risk of ischaemic stroke in the absence of rheumatic heart disease. This risk is increased by the coexistence of:

- mitral stenosis

- age over 75 years
- hypertension
- impaired left ventricular function and heart failure
- diabetes mellitus
- CHD
- increased left atrial dimensions
- longer duration of atrial fibrillation.

Therefore, unless AF is completely suppressed, careful consideration must be given to prevention of thromboembolism. From the same meta-analysis mentioned earlier, 11 trials were identified that evaluated anticoagulation.

Warfarin. There was strong evidence for the prevention of stroke by warfarin compared with placebo, but at the expense of a higher bleeding rate. For every 1,000 patients with AF who are treated with warfarin for one year, 30 strokes are prevented at the expense of six major bleeds.

Aspirin. The evidence for efficacy in preventing stroke was moderately strong for aspirin, with 12.5 strokes prevented in each 1,000 patients treated for one year. The evidence for increased odds of major bleeding associated with aspirin compared with placebo was inconclusive.

The evidence from trials directly comparing warfarin and aspirin does not permit strong conclusions.

For patients at low risk of stroke (ca 1% per year) aspirin is the most cost-effective therapy, whereas warfarin appears to be the most cost-effective strategy for patients at high risk of stroke (ca 10% per year). For those at intermediate risk (3–6% per year), aspirin therapy was estimated to be the most cost-effective therapy if quality of life would be decreased by taking warfarin. If quality of life is not reduced by warfarin therapy, it is the most cost-effective strategy for this group.

New therapies

Emphasising the inadequacy of the above therapies, developments have been made in various directions, especially with catheter ablation and device therapy.

Implantable devices

Although automatic implantable atrial defibrillation has been realised, its application is limited because of the pain associated with shock delivery. Dual-site atrial pacemakers seek to resynchronise atrial depolarisation. In patients with paroxysmal AF and increased P wave duration during sinus rhythm, successful prophylaxis has been demonstrated.

Surgery

The surgical procedure in which the atria are divided and resutured into inter-connecting corridors and blind alleys has been termed the 'maze' procedure. It has not been widely practised in the UK and has most often been added to other surgery such as mitral valve replacement. It is the most effective method of restoring sinus rhythm from permanent AF but carries an estimated mortality of 2%. Promising modifications to simplify and shorten the procedure are under assessment.

Catheter ablation

It is in catheter ablation that the most exciting new development in treating AF has been made. The discovery that most episodes of AF are initiated by 'ectopic' activity originating from within the pulmonary veins has led to the application of catheter ablation to either destroy the initiating focus or electrically isolate the veins from the left atrium. Preliminary data suggest that 70% of patients can be rendered free from AF by this method. Patients with frequent paroxysms of lone atrial fibrillation are especially suitable for this therapy.

Conclusions

Patients need to be assessed individually to enable the correct therapy – usually a hybrid of different therapies – to be appropriately chosen and then monitored. Important advances, especially in the field of catheter ablation, may make a significant difference to the treatment of many patients, especially those with lone AF.

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FURTHER READING

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CME Rheumatological and immunological disorders SAQs

Answers to the CME SAQs published in *Clinical Medicine* March/April 2001

Q1	Q2	Q3	Q4	Q5	Q11	Q12	Q13	Q14	Q15
a) T	a) F	a) F	a) F	a) F	a) T	a) T	a) T	a) F	a) F
b) F	b) T	b) F	b) F	b) F	b) F	b) F	b) F	b) T	b) F
c) F	c) T	c) F	c) T	c) F	c) T	c) F	c) F	c) F	c) T
d) F	d) T	d) F	d) T	d) T	d) F	d) T	d) T	d) F	d) F
e) T	e) T	e) T	e) F	e) T	e) F	e) T	e) T	e) F	e) F
Q6	Q7	Q8	Q9	Q10	Q16	Q17	Q18	Q19	Q20
a) F	a) F	a) F	a) T	a) F	a) F	a) F	a) F	a) T	a) T
b) F	b) T	b) T	b) T	b) F	b) F	b) F	b) T	b) T	b) T
c) F	c) F	c) T	c) T	c) T	c) T				
d) T	d) F	d) F	d) F	d) T	d) T				
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