Atrial fibrillation: current perspectives

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Dramatic advances in basic and clinical cardiac electrophysiology have rendered many arrhythmias amenable to cure by catheter ablation and have relegated anti-arrhythmic drugs to a subsidiary role. Unfortunately, however, the commonest sustained cardiac arrhythmia, atrial fibrillation (AF), remains incompletely understood and consequently difficult to manage. Nevertheless, important advances in our knowledge have recently been made; these will be reviewed in this article.

Classification

AF incorporates a range of subsets of which the mechanism and response to therapeutic intervention vary. A consensus on nomenclature has recently been achieved in an attempt to ensure appropriate management:

- An AF event is either the first detected or a recurrent episode.
- Paroxysmal AF describes episodes that terminate spontaneously within seven days.
- AF is termed persistent if it lasts longer than seven days or requires cardioversion by any means to restore sinus rhythm.
- Permanent AF is the term used when cardioversion has failed or has not been attempted.

Mechanisms

Arrhythmias

The mechanism of virtually all tachyarrhythmias can be described as:

- re-entrant, where wavefronts of electrical activation propagate continuously around lines of electrical conduction block, or
- focal, where activation wavefronts spread from a discrete source of repetitive electrical discharge.

AF, however, consists of multiple, irregular, constantly varying wavefronts that cannot be easily analysed under physiological conditions in the human heart. As a consequence, much of our understanding has come from experimental studies in animal models and
caution is necessary in extrapolating these data to humans. The source of these wavefronts can be a single re-entrant wavefront or an ectopic focus. The importance of this observation is that the focal origin provides a much simpler target for potentially curative radiofrequency ablation procedures in a proportion of patients.

Remodelling and ion channels

The natural history of paroxysmal AF is for the episodes to become more frequent, then persistent and ultimately permanent. AF per se induces changes in the atria that facilitate the development and maintenance of further episodes of AF. This process is termed remodelling. Electrical remodelling is caused by changes in the expression of atrial transmembrane ion channels, and in the long term can lead to fibrotic change (structural remodelling). The molecular biology of these ion channels is an area of intense research as they are subject to genetic variation that underlies familial AF in some cases and may also explain individual susceptibility to the development of AF. Furthermore, these channels represent a target for novel anti-arrhythmic drug strategies.

Management

Anticoagulation

Stroke prevention is a major aim of the treatment of all types of AF and is laid out clearly in international practice guidelines (Table 1). Both aspirin (300 mg) and warfarin (international normalised ratio (INR) 2–3) prevent strokes, but the benefit of warfarin is greater especially in high-risk groups. Although ischaemic strokes may occur as a result of embolism from the left atrium, the pathogenesis is complex and the indication for anticoagulation should be determined by the overall stroke risk rather than the presence of AF at the time of assessment. Hence, no distinction should be made between paroxysmal, persistent and permanent AF. A therapeutic INR should be maintained for at least a month before and after planned DC cardioversion. The decision whether or not to continue warfarin long term depends on the patient’s overall stroke risk.

Rate control versus rhythm control

Several recent publications have ignited considerable debate about the value of restoring sinus rhythm. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial compared the strategy of rhythm control (using anti-arrhythmic drugs and DC cardioversion) with ventricular rate control alone. All-cause mortality was similar with either strategy, but the rhythm control group had a significantly higher rate of hospitalisation and adverse drug effects. One interpretation of these results is that either strategy is acceptable. An alternative interpretation, however, is that both strategies are equally bad. Intuitively, restoration and maintenance of sinus rhythm should be better than palliation by ventricular rate control, but current anti-arrhythmic drugs are of limited efficacy and have considerable toxicity.

Ventricular rate control

The aim of ventricular rate control is to improve both cardiac function and symptoms. This is achieved in most cases with drugs that increase the refractory period of the atrioventricular (AV) node: digoxin, beta-blockers and calcium-blockers such as verapamil and diltiazem. Although digoxin is useful for controlling the ventricular rate at rest, it has limited efficacy during conditions of sympathetic nervous system predominance including exertion. Beta-blockers and verapamil are more useful in these circumstances and a combination of drugs may be necessary to achieve adequate rate control. Assessment of rate control should include Holter monitoring and/or exercise testing.

In some patients ventricular rate control by drugs may not be achieved. In extreme cases a tachycardia-induced cardiomyopathy may develop. An effective solution is catheter ablation of the AV node, although this has disadvantages including dependency upon a permanent pacemaker. Survival is the same as with standard medical therapy and symptoms are greatly improved. Indeed,
in patients with normal ventricular function, survival is identical to that of the general population.\textsuperscript{10}

**Maintenance of sinus rhythm**

Device therapy. Specific situations in which pacemakers reduce the burden of AF are sick sinus syndrome and vagally-mediated AF. Aside from these clear indications, there are other novel pacemaker strategies to suppress AF. A comprehensive review of this interesting field has recently been published.\textsuperscript{11}

A further innovation is the internal atrial defibrillator; this aims to prevent remodelling and lessen the tendency to develop persistent AF by detecting episodes of AF rapidly and restoring sinus rhythm through a low energy internal shock. Although effective, these devices are not popular due to the pain of repeated shocks.

Drug treatment. The evidence for anti-arrhythmic drugs for the maintenance of sinus rhythm has been comprehensively reviewed.\textsuperscript{4} Drugs with proven efficacy include flecainide, sotalol, propafenone and amiodarone. The choice of drug is largely governed by the presence of structural heart disease and comorbidity. Flecainide should be avoided in the presence of coronary artery disease or impaired left ventricular systolic function. Sotalol and propafenone are beta-adrenergic receptor antagonists and may therefore cause adverse effects related to that property. Although the efficacy of amiodarone is fractionally higher than that of the other anti-arrhythmic drugs, its side effect pro-
file should lead to caution over long-term use. Unfortunately, many patients with AF will remain symptomatic despite the administration of anti-arrhythmic drugs or be intolerant of them.

Curative catheter ablation. Based on the observation that ectopic foci in the pulmonary veins were responsible for some cases of AF and that by ablating these foci AF was curable, there has been a large increase in the number of catheter ablation procedures. Later it was recognised that multiple foci may coexist in one patient, and techniques have evolved to isolate all possible sources of ectopy (ie all four pulmonary veins, the coronary sinus and the venae cavae). Many aspects of this procedure remain contentious, in particular the need to prove electrical isolation of the pulmonary veins or whether a purely empirical, anatomical approach is sufficient (Figs 1(a) and (b)). Published results are excellent using both approaches, but they are time-consuming and can be complicated by stroke and pulmonary vein stenosis. Numerous questions remain, including the identification of suitable patients and long-term safety and efficacy.

Permanent AF is not amenable to catheter ablation using the techniques described above as the dominant arrhythmia mechanism is multiple wavelet re-entry. To restore sinus rhythm in these patients, a dramatic alteration of the atria is required so that the multiple re-entry wavefronts cannot be supported. This is achieved in the surgical maze, in which multiple lines of conduction block are created in both atria, dividing them into much smaller electrical compartments. This procedure is remarkably successful (99% AF-free), but it is a major undertaking requiring cardiopulmonary bypass, with significant morbidity and mortality (2–3%). The development of non-fluoroscopic catheter systems (eg non-contact mapping) and the success of ablation in paroxysmal AF has reawakened interest in a less invasive catheter maze procedure (Fig 2), bringing with it the prospect of an acceptable cure for this most intractable of arrhythmia.
References


