MANAGEMENT OF ATRIAL FIBRILLATION

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Heart 2006;92:1177–1182. doi: 10.1136/hrt.2005.071555

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Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterised by uncoordinated atria activation with consequent deterioration of atrial mechanical function. It is the most common arrhythmia encountered in the clinical practice of the developed countries,^{1 w1} and accounts for 1% of all National Health Service expenditure in the United Kingdom.^{w2}

The prevalence and incidence of AF increases with advancing age, affecting approximately 5% of individuals older than 65 years and nearly 10% of those aged older than 80 years.² So common is this problem that it is expected that more than five million Americans will be living with AF by the year 2050.^{w1} AF also coexists with common cardiovascular conditions, such as hypertension, heart failure, coronary artery disease and diabetes mellitus, and with an increasingly older general population, AF (and its co-morbidities) will become an increasing health care burden.^{2 w3 w4} Indeed, hospitalisation rates for AF have increased by 2–3 fold.^{w4} In the Framingham Heart Study, AF was associated with a 1.5- to 1.9-fold mortality risk, even after adjustment for the pre-existing cardiovascular conditions.^{w5} AF also confers a substantial morbidity from stroke, thromboembolism, heart failure and impaired quality of life; indeed, stroke survivors associated with AF have more severe strokes with greater disability, longer hospital stays and lower rates of discharge to their own home.²

The aim of this review is to provide a practical and clinically useful approach to the management of AF. The current 2001 American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) consensus guidelines¹ for the management of patients with AF will be updated in late 2006, and the evidence-based UK National Institute for Health and Clinical Excellence (NICE) guidelines are available (www.nice.org.uk) in their final form from June 2006. The extensive literature on the electrophysiology and pathophysiology of AF is the subject of many detailed and comprehensive reviews, and is not considered in this overview.

SCREENING FOR ATRIAL FIBRILLATION

With such a common and important condition, is it worth screening for AF? This was recently addressed in the SAFE (Screening for Atrial Fibrillation in the agEd) study,³ which determined the most cost-effective method of screening for AF in the population aged 65 years and over, as well as its prevalence and incidence in this age group. Also, SAFE was designed to evaluate the relative cost-effectiveness of different methods of recording and interpreting the ECG within a screening programme. This contemporary UK study reported that the baseline prevalence of AF was 7.2%, with a higher prevalence in males (7.8%) and patients aged ≥ 75 years, with an incidence of 0.69–1.64% per year, depending on screening method. In terms of a screening programme for AF, the SAFE study suggests that the only strategy that improved on routine practice was opportunistic screening, rather than targeted screening.

Another randomised trial of two approaches to screening for AF in general practice found that nurse-led screening identified a substantial number of patients who could benefit from antithrombotic treatment.⁴ Certainly, an ECG should be performed on all patients in whom a diagnosis of AF is suspected—for example, patients who present with palpitations, breathlessness, dyspnoea, syncope/dizziness or chest discomfort—or where an irregular pulse is present. Also, patients with risk factors such as hypertension or heart failure should at the very least have pulse palpation—and an ECG, if necessary—during review visits. If a screening project is to be implemented, an opportunistic strategy may be the best option.

ASSESSMENT OF THE PATIENT WITH ATRIAL FIBRILLATION

Assessment of the patient with AF includes a careful history and physical examination, with attention to co-morbidities and complications associated with AF. The clinical presentation of AF can be classified on the basis of the temporal pattern of the arrhythmia.¹

Recurrent AF occurs when a patient develops two or more episodes of AF, which may be paroxysmal or persistent in nature. Paroxysmal AF is diagnosed if the episodes terminate

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spontaneously within seven days, but is termed “persistent” if electrical or pharmacological cardioversion is required to terminate the arrhythmia. Permanent AF occurs when the patient remains in AF, where the cardioversion is not successful or deemed inappropriate—for example, because of persistence of the AF for > 12 months.

Regardless of the temporal classification, the management of patients with AF should broadly be guided by symptoms, the presence or absence of haemodynamic compromise, and associated co-morbidities. However, the clinical subtypes of AF can help define the objectives of management and therapeutic strategies. For example, the objective of management in paroxysmal AF is the reduction of paroxysms and the long term maintenance of sinus rhythm, and hence anti-arrhythmic drugs (or non-pharmacological approaches—see later) are used. In persistent AF, the management objective is restoration of sinus rhythm, and hence cardioversion (either pharmacological or electrical) is attempted. In permanent AF, the objective is heart rate control, and hence drugs (or non-pharmacological approaches) are used. In all patients with AF, appropriate antithrombotic treatment use is mandatory, based on risk factors for stroke and thromboembolism. Nonetheless, this approach is a simplistic one, as even permanent AF can be successfully eliminated by catheter and surgical ablation, even in the setting of significant structural heart disease. The (sometimes artificial) classification system purely gives an idea of the time course of the AF but not the ultimate clinical outcome, and re-emphasises the fact that the management of AF should be guided by symptoms.

AF may be related to a wide range of acute and non-acute, cardiac and non-cardiac causes. However, AF can present as an isolated arrhythmia^{w3} without other structural heart disease, and approximately 40–50% of paroxysmal AF cases and 20–25% of permanent AF cases occur in patients without demonstrable underlying causes (often referred to as “lone AF”).^{2 w3} Strictly speaking, “lone” AF is defined as AF without “overt” structural heart disease, as defined by essentially normal clinical history and examination, ECG (apart from AF), chest x ray and, in more recent series, an echocardiogram. There are implications of labelling patients with this diagnosis, as this group is often considered as being “at low risk”, although recent data have been inconclusive.

The diagnosis of AF requires documentation of the arrhythmia by an ECG. In patients with suspected paroxysmal AF, a 24-hour Holter monitor is useful for diagnosis in those with symptomatic episodes less than 24 hours apart, while an event recorder ECG (“cardiomemo” or transtelephonic monitor) is more appropriate for making a diagnosis in patients with symptomatic episodes more than 24 hours apart. Sometimes, a seven day Holter can also be useful; these devices often give better quality ECG and pick up asymptomatic episodes, when compared to event recorders.

Most cardiologists would perform an echocardiogram as part of the assessment of AF patients, usually for the diagnosis of underlying structural heart disease. The NICE guidelines suggest that a transthoracic echocardiogram (TTE) should be performed where a baseline echocardiogram is important for planning long term management strategies (for example, for younger patients), as well as those being considered for a rhythm control strategy, or where there may be associated underlying structural/functional heart disease that influences management (for example, deciding on cardioversion or choice of antiarrhythmic drug). On

occasion, an echocardiogram is useful in those where refinement of clinical risk stratification for thromboprophylaxis is needed, but when the need for anticoagulation treatment has already been established on appropriate clinical risk stratification criteria, a TTE should not be routinely performed. In patients with AF, transoesophageal echocardiography (TOE) should be performed where TTE demonstrates an abnormality (for example, valvular heart disease, atrial septal defect) that warrants more comprehensive assessment, or (less commonly) where TTE is technically difficult and there is still the need to exclude cardiac abnormalities. TOE is also used in those being considered for TOE-guided cardioversion.

RATE CONTROL

The aims of this approach are to minimise the symptoms associated with the excessive tachycardia and the haemodynamic consequences associated with the fast heart rate, as well as the prevention of tachycardia-associated cardiomyopathy.^{w6} The rate is generally considered controlled when the ventricular response ranges between 60–90 beats per minute (beats/min) at rest and < 110 beats/min during exercise.^{w7}

In patients with permanent AF, who need treatment for rate control, β blockers or rate-limiting calcium antagonists should be administered as the preferred initial monotherapy in all patients. The β blockers may provide an additional benefit in patients with concomitant ischaemic heart disease, and some (for example, carvedilol, bisoprolol, metoprolol, nebivolol) have proven benefits in patients with systolic heart failure who are optimised on treatments for heart failure.⁵ The non-dihydropyridine (or rate-limiting) calcium channel blockers (diltiazem, verapamil) are also effective in reducing ventricular rate, even in hyperadrenergic states.^{w8} Digoxin should only be considered for use as monotherapy in sedentary (and usually, elderly) patients, and generally has limited efficacy in patients who are in hyperadrenergic states, such as thyrotoxicosis, fever, acute volume loss, the post-operative state, and during exertion.^{w8}

Where monotherapy inadequately controls the heart rate, combination therapy should be considered. Indeed, β blockers or rate-limiting calcium channel blockers could be co-administered with digoxin for improved heart rate control.⁶ On occasion, amiodarone (a III class antiarrhythmic drug) is useful for rate control in the setting of left ventricular systolic dysfunction, being well tolerated, and may be of similar efficacy to diltiazem in controlling ventricular rate.^{w9 w10} The effectiveness of amiodarone has to be tempered by the long term irreversible adverse effects of amiodarone (for example, pulmonary fibrosis, etc). Amiodarone also has a dropout rate of 30–40% because of side effects.

Where urgent pharmacological rate control is indicated, intravenous treatment should be with either an intravenous β blocker (for example, esmolol or metoprolol) or rate-limiting calcium antagonist (for example, verapamil). Intravenous amiodarone is a useful alternative where β blockers or calcium antagonists are contraindicated or ineffective.

RHYTHM CONTROL

The perceived reasons for the restoration and maintenance of sinus rhythm in patients with AF include the relief of symptoms with better exercise tolerance and quality of life, the possible reduction of thromboembolic risk, and the

avoidance of tachycardia-induced cardiomyopathy. However, limited efficacy and adverse effects associated with the use of antiarrhythmic treatment, as well as frequent asymptomatic recurrence of AF, represent serious drawbacks to this approach. In the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) study, antiarrhythmic drug and digoxin use were important predictors of increased mortality, while anticoagulation use significantly reduced mortality.⁷

Rhythm control in AF aims to restore sinus rhythm and reduce recurrences of AF, and secondly to achieve long term maintenance of sinus rhythm. In patients with persistent AF, cardioversion can be performed electrically (by a synchronised direct current (DC) shock) or pharmacologically. The latter uses an intravenous antiarrhythmic agent and is best performed using a class Ic drug (for example, flecainide) in the absence of structural heart disease.⁸ In the presence of structural heart disease, amiodarone is the drug of choice for cardioversion. Where there is some concern about a successful restoration of sinus rhythm (for example, previous cardioversion failure or early recurrence of AF), concomitant amiodarone or sotalol should be used pre-cardioversion, to improve the success of electrical cardioversion.⁹ An antiarrhythmic drug is usually not required post-cardioversion to maintain sinus rhythm in patients with persistent AF where a precipitant (for example, chest infection, fever, etc) has been corrected and cardioversion has been performed successfully, and there are no other risk factors for recurrence. In patients with persistent AF and structural heart disease, a β blocker can be used post-cardioversion to help maintain sinus rhythm, but amiodarone is an alternative. In the absence of structural heart disease, a β blocker, a class Ic agent, sotalol or amiodarone could be administered, utilising an approach balancing drug tolerance, therapeutic effectiveness and side effects. Digoxin is no better than placebo for pharmacological cardioversion, and does not help in the maintenance of sinus rhythm.

In patients with paroxysmal AF who have infrequent paroxysms or few symptoms, or where symptoms are induced by known precipitants (for example, alcohol, caffeine), a “no drug treatment” strategy or a “pill-in-the-pocket” strategy could be considered.¹⁰ Based on one randomised trial,¹⁰ this “pill-in-the-pocket” strategy is best used in those who have no history of left ventricular dysfunction, or valvular or ischaemic heart disease, but have a history of infrequent symptomatic episodes of paroxysmal AF, a systolic blood pressure > 100 mm Hg and resting heart rate > 70 beats/min, and have the ability to understand how and when to take the medication.

In patients with symptomatic paroxysms (with or without structural heart disease, including coronary artery disease) a β blocker should be the initial treatment option. Where β blockers are ineffective, a class Ic agent (for example, flecainide or propafenone) could be used in the absence of structural heart disease. It should be noted that the only strong evidence for the danger of class I antiarrhythmic drugs is in patients who have had myocardial infarction, but this has been interpreted as being the result of myocardial scarring and the proarrhythmic tendency of these drugs. Where neither β blockers nor class Ic agents achieve symptomatic suppression, sotalol or amiodarone can be tried. However, referral for non-pharmacological approaches (see later) could also be considered.

In patients with paroxysmal AF and coronary artery disease, where standard β blockers do not achieve symptomatic suppression, sotalol could be tried (but proarrhythmia may be problematic at the usual doses of sotalol with class III effects—that is, 240–480 mg/day), or if that fails to help, amiodarone. In patients with paroxysmal AF with poor left ventricular function, where β blockers do not adequately suppress paroxysms, amiodarone would be the drug of choice. Digoxin is of limited use in the management of paroxysmal AF, with no significant reduction in paroxysms (and may even cause more frequent paroxysms), although heart rate control during paroxysms may be slightly better compared to no treatment.

RATE CONTROL OR RHYTHM CONTROL?

Numerous randomised trials have compared a strategy of rate control versus rhythm control in patients with recurrent AF, as reviewed by Lim *et al.*¹¹ These trials^{w11–14} have broadly concluded that a rate control strategy is not inferior to a rhythm control strategy, although the latter may be less cost effective and associated with a tendency to more stroke, hospital readmissions and drug adverse effects.

However, there is clearly the need to individualise management strategies. For example, in young patients without structural heart disease and recurrent AF, a rhythm control approach may well be the best. In contrast, there is no trial evidence to suggest that cardioversion of AF in critically ill patients in the absence of haemodynamic compromise is associated with a better outcome.

Certainly, some patients with persistent AF will satisfy criteria for either an initial rate control or rhythm control strategy. The strategy to adopt should take into account any co-morbidities, symptoms and patient preferences. Indeed, the randomised trials—as reviewed by the NICE guidelines—suggest that a rate control strategy should be the preferred *initial* option in the following patients with persistent AF: those aged over 65 years; those with coronary artery disease; those with contraindications to antiarrhythmic drugs; patients without congestive heart failure; and patients unsuitable for cardioversion. In contrast, a rhythm control strategy should be the preferred initial option in the following patients with persistent AF: symptomatic patients; younger patients; those presenting for the first time with lone AF; and those with AF secondary to a treated/corrected precipitant. These indications are not mutually exclusive, and in appropriate circumstances, the possibility of restoring sinus rhythm (for example, using catheter ablation) can be considered, especially in symptomatic patients.

Of note, a large proportion of patients with recent-onset AF will experience spontaneous cardioversion within 24–48 hours.^{w15} In patients with AF who have undergone cardioversion, it is important to emphasise that anticoagulation should be continued for the long term in patients at high risk of AF recurrence or with co-existent stroke risk factors.

NON-PHARMACOLOGICAL APPROACHES

The limited efficacy and proarrhythmic risks of antiarrhythmic drugs have led to the exploration of a wide spectrum of alternative non-pharmacological therapies to treat AF. In some patients, non-pharmacological therapies may render AF responsive to previously ineffective pharmacological agents. Combinations of approaches may also be required in treating AF in selected patients (a so-called “hybrid” approach). Thus, these strategies should be considered for patients who failed

Figure 1 Practical guidelines for antithrombotic treatment in non-valvular atrial fibrillation. Assess risk, and reassess regularly. Note that risk factors are not mutually exclusive, and are additive to each other in producing a composite risk. *An echocardiogram is not needed for routine risk assessment but refines clinical risk stratification in case of moderate or severe left ventricular dysfunction and valve disease. †Owing to lack of sufficient clear cut evidence, treatment may be decided on an individual basis, and the physician must balance the risks and benefits of warfarin versus aspirin; as stroke risk factors are cumulative, warfarin may (for example) be used in the presence of two or more risk factors. Referral and echocardiography may help in cases of uncertainty. Since the incidence of stroke and thromboembolic events in patients with thyrotoxicosis appears similar to other aetiologies of AF, antithrombotic treatments should be chosen based on the presence of validated stroke risk factors. CVA, cerebrovascular accident; INR, international normalised ratio; TIA, transient ischaemic attack. Reproduced from Lip and Boos,¹⁹ with permission from the BMJ Publishing Group.

drug treatment either because of continued AF or were intolerant of the drugs per se.

For example, the Maze procedure is a surgical method based on mapping studies of animal and human AF that successfully controls AF in more than 90% of selected cases.^{w16} Modifications of the Maze procedure (Maze III) involve encircling the pulmonary veins, and may prevent initiation of AF by isolating potentially arrhythmogenic foci. Surgeons currently tend to use the procedure for patients who have drug-refractory AF undergoing surgery for concomitant cardiac disease (frequently valve disease).^{w17} Given the success of the surgical approach, several ablation strategies have been designed, following the recognition that the pulmonary veins are a common source of rapidly depolarising arrhythmogenic foci that induce paroxysmal AF.^{w18} Ablation of these foci eliminates or reduces the frequency of recurrent AF in more than 60% of patients, although there is still a small recurrence rate following the procedure, necessitating the need for antiarrhythmic drugs. In a recent small randomised trial, pulmonary vein isolation (PVI) with radiofrequency ablation was compared with antiarrhythmic drug therapy as initial treatment for symptomatic AF—after one year of follow up, PVI patients had better outcomes in terms of AF recurrences and hospitalisations, as well as a better quality of life at six months.¹² The

substantial enthusiasm for PVI needs to be tempered by another recent study, where at the six month follow-up period, only 54% and 82% of patients remained free from arrhythmia-related symptoms after circumferential pulmonary vein ablation and after segmental pulmonary vein ablation, respectively.¹³ Frequently, asymptomatic episodes do occur and may be significantly increased after catheter ablation, especially among previously symptomatic patients—thus, follow-up based on symptoms only would substantially overestimate the success rate of ablation procedures.¹⁴ For now, PVI may perhaps be considered for patients resistant to pharmacological treatment, especially those who are younger and have lone AF.

Another strategy—radiofrequency ablation of the atrioventricular node and permanent pacing—has also been used for symptomatic relief in patients with medically refractory paroxysmal AF. In a meta-analysis of 21 studies ($n = 1181$ patients),¹⁵ there were significant improvements after ablation and pacing therapy in quality of life and clinical outcome measures (except fractional shortening), and the calculated one year total and sudden death mortality rates were 6.3% and 2.0%, respectively.

The utility of atrial pacing as a treatment for paroxysmal AF in patients without conventional indications for pacing has not been proven.^{w19 w20} Other than the recognised

indications for pacemaker implantations—such as sinus node disease, symptomatic bradycardia and chronotropic incompetence—there is little evidence to suggest that particular patients with AF should be referred for pacemaker implantation.

Initial enthusiasm for internal atrial defibrillators (atrioverters) for patients with recurrent persistent AF has also been dampened by the uncomfortable shock for most patients.^{w21} Indeed, the stand-alone atrioverter is no longer available, and combined atrial and ventricular defibrillators are in use for patients with ventricular arrhythmias who also get paroxysmal AF.

ANTITHROMBOTIC TREATMENT

AF increases the risk of stroke and thromboembolism by four- to fivefold across all age groups, and accounts for 10–15% of all ischaemic strokes.¹⁶ Patients with paroxysmal and persistent AF have a risk of stroke similar to patients with permanent AF.¹⁷ The absence of AF symptoms does not confer a more favourable prognosis and anticoagulation should still be considered in patients with asymptomatic AF, who have less serious heart disease but more cerebrovascular disease.¹⁸ Patients with atrial flutter should be managed with antithrombotic treatment in a manner similar to those with AF, depending on the coexistence of stroke risk factors.

Nonetheless, this is the one area with good evidence from randomised controlled trials. In a recent meta-analysis of 13 trials ($n = 14\,423$ participants), adjusted dose of warfarin significantly reduced the risk of ischaemic stroke or systemic thromboembolism compared with placebo (relative risk (RR) 0.33, 95% confidence interval (CI) 0.2 to 0.45).¹⁶ There was no significant difference in the rate of intracranial haemorrhage (0.3% in anticoagulation group versus 0.1% per year in control group); furthermore, oral anticoagulation treatment reduced all cause mortality (RR 0.69, 95% CI 0.53 to 0.89).¹⁶ When warfarin was compared with aspirin, warfarin was superior in reducing the risk of ischaemic stroke or systemic embolism (RR 0.59, 95% CI 0.40 to 0.86). Compared with placebo, aspirin alone reduced the risk of stroke by approximately 22%, but this is broadly similar to the effect of antiplatelet treatment on stroke prevention among high risk vascular disease patients; as AF commonly coexists with vascular disease, it is likely we are seeing an effect of aspirin on vascular disease rather than on the AF per se.¹⁹ Anticoagulation use in the setting of AF and acute stroke has recently been reviewed by Lip and Boos.¹⁹

However, the risk of stroke in AF is not homogeneous, and clinical factors associated with AF contribute to this risk. For example, high risk patients are those with a history of a previous stroke or transient ischaemic attack, the elderly (aged > 75 years), and those where there is the presence of structural heart disease, hypertension, diabetes mellitus and vascular disease, or the presence of moderate to severe left ventricular systolic dysfunction on two-dimensional echocardiography. These clinical and echocardiographic criteria have informed the development of a number of risk stratification models, of different complexity, as recently reviewed by Lip and Boos.¹⁹ Of the various published risk stratification criteria, the CHADS₂ scheme (an acronym for Congestive heart failure, Hypertension, Age > 75 , Diabetes mellitus, and prior Stroke or transient ischaemic attack) successfully identified primary prevention patients who were at high risk of stroke (5.3 strokes per 100 patient-years),²⁰ and clearly emphasises the cumulative nature of stroke risk

Management of atrial fibrillation: key points

- ▶ AF is the most common arrhythmia encountered in clinical practice
- ▶ The prevalence and incidence of AF increases with advancing age, and is commonly associated with many cardiac and non-cardiac disorders
- ▶ If screening for AF is to be implemented, an opportunistic strategy may be the best approach
- ▶ Assessment of the patient with AF includes a careful history and physical examination, with attention to co-morbidities and complications associated with AF
- ▶ Regardless of the temporal classification, the management of patients with AF should broadly be guided by symptoms, the presence or absence of haemodynamic compromise, and associated co-morbidities
- ▶ Antithrombotic treatment is central to the management of AF, and appropriate risk stratification and regular review is needed
- ▶ Non-pharmacological approaches for AF are being increasingly applied, especially in the symptomatic patient where drug treatment is ineffective or not tolerated

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factors. A more practical treatment guideline for antithrombotic treatment in AF, offering a balance between evidence and practical applicability, is illustrated in fig 1.

All antithrombotic agents confer a risk of bleeding. Indeed, the assessment of bleeding risk is recommended as part of the clinical assessment of AF patients before starting anticoagulation treatment, with particular attention being paid to some “high risk” categories of patients, such as the elderly, those with concomitant use of antiplatelet drugs (aspirin, clopidogrel) or non-steroidal anti-inflammatory drugs (NSAIDs), those with polypharmacy, uncontrolled hypertension, or a history of bleeding (for example, peptic ulcer, cerebral haemorrhage) and poorly controlled anticoagulation therapy. Indeed, the potential risks and benefits of antithrombotic treatment should always be explained to patients.

FUTURE PERSPECTIVES

There is increasing interest into the role of the renin–angiotensin–aldosterone system (RAAS) in AF.²¹ Certainly, RAAS blockade with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may have a role in the prevention of AF and the maintenance of sinus rhythm after cardioversion. In a recent meta-analysis of data from 11 studies in different heart diseases (pooled population of 56 308 patients),²² RAAS blockade reduced the relative risk of AF by 28% (95% CI 15% to 40%, $p = 0.0002$), especially following cardioversion (48% relative risk reduction (RRR), 95% CI 21% to 65%). These drugs even reduce major vascular events²³ and, more specifically, new strokes.²⁴

There is also great interest in the role of inflammation in the pathophysiology of AF.²⁵ Inflammation may precede the development of AF and contribute to its persistence.^{26 w22} Also, inflammation may potentially “drive” the prothrombotic or hypercoagulable state in AF.²⁵ Some interest has therefore been directed towards the n-3 polyunsaturated fatty acids (PUFAs), which may have antiarrhythmic properties related to putative anti-inflammatory effects. In one randomised trial, 2 g/day PUFA administration during hospitalisation in patients undergoing coronary bypass surgery substantially reduced the incidence of postoperative

AF (by 54.4%) and was associated with a shorter in-hospital stay.²⁷

In terms of thromboprophylaxis, new anticoagulants—such as the oral direct thrombin inhibitors (DTIs) and oral factor Xa inhibitors—show promise as alternatives to the vitamin K antagonists.^{w23} These new drugs have few drug or food interactions and, most importantly, do not need anticoagulation monitoring. However, a problem with the first DTI, ximelagatran—which had very promising data from its phase III clinical trials in AF stroke prevention—was the adverse alterations of the liver enzymes, occurring in approximately 6–7% of those undertaking chronic treatment.^{w24} Ongoing trials with other novel antithrombotic agents are still in progress. For those wishing to use an alternative to anticoagulants, closing the left atrial appendage using a percutaneous left atrial appendage occluder (PLAATO system; ev3 Inc, Plymouth, Minnesota, USA) may be feasible, with encouraging initial results.²⁸

Finally, new antiarrhythmic drugs for AF are always in development, which would hopefully overcome some of the limitations of existing agents (especially proarrhythmia).^{w25} However, their uptake in clinical practice will depend not only on their efficacy as antiarrhythmic agents, but also on their safety in acutely terminating AF and in the long term maintenance of sinus rhythm in the community.

Additional references appear on the *Heart* website—<http://www.heartjnl.com/supplemental>

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In compliance with EBAC/EACCME guidelines, all authors participating in Education in *Heart* have disclosed potential conflicts of interest that might cause a bias in the article

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