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Current Management of Symptomatic Atrial Fibrillation

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Contents

Abstract

Atrial fibrillation (AF) is the commonest arrhythmia. It presents in distinct patterns of paroxysmal, persistent and chronic AF, and patient management aims differ according to the pattern.

In paroxysmal AF, drug treatment with β-blockers, class Ic and class III agents reduce the frequency and duration of episodes.

In persistent AF (recent onset, non-paroxysmal), early cardioversion with either pharmacological agents or by direct current (DC) cardioversion should be actively considered, in those patients who are suitable. Patients most likely to cardiovert and remain in sinus rhythm include those with duration of AF of <1 year, an acute reversible cause, left atrial diameter <50mm and good left ventricular function on echocardiography. Recent data show that maintenance of sinus rhythm after successful cardioversion is enhanced by the use of class III drugs including amiodarone and dofetilide.

In chronic or permanent AF, management is aimed at controlling the ventricular rate response with combinations of digoxin, β-blockers and calcium antagonists with atrio-ventricular nodal activity (diltiazem and verapamil).

There is some debate about the prognostic significance of AF. Certainly AF is associated with an excess mortality but this is largely accounted for by its association with serious intrinsic heart disease and the thrombo-embolic complications of the arrhythmia. Atrial fibrillation is a common default arrhythmia for the sick heart.

Atrial fibrillation (AF) is the commonest arrhythmia and occurs in approximately 5% of people over the age of 75 years and approximately 9% of people over the age of 80 years.[1] It is twice as common in men than women and appears to be increasingly prevalent. In the Framingham study[1] prevalence has increased in men aged 65 to 84 years from 3.2% from 1968 to 1970 to 9.1% from 1987 to 1989. It is present in approximately 7% of patients who are emergency admissions and occurs in approximately 40% of patients with heart failure.

Atrial fibrillation is associated with a number of potential aetiological factors but hypertension is the commonest (see table I). There is good evidence that an increase in atrial diameter is the crucial predisposition. Long term community screening echocardiographic studies in the Framingham population show that for every 5mm increase in left atrial diameter, there is a 37% increase in the risk of developing AF. This is the key pathophysiological change and is influenced by other echocardiographic changes so that a reduction in left ventricular ejection fraction of 5% confers a 34% increase in risk, and a 4mm increase in summed transverse left ventricular wall dimensions confers a 28% increase in risk. The main consequence of AF is a 4 to 5-fold increase in stroke which is markedly age related.[1,2]

However, the nature of the arrhythmia varies and has recently been re-classified by the European Society of Cardiology (ESC) Working Group on Atrial Fibrillation in to paroxysmal, persistent and permanent.[3]

In order to understand the clinical significance of AF, it is important to have an understanding of the normal physiology of atrial function. In 1682, William Harvey recognised the importance of atrial function when he said 'the blood enters the ventricles not by any attraction or dilation of the heart but by being thrown into them by the pulses of the auricles, and when I speak of pulses... I mean contractions'.[4] William Harvey clearly recognised that the atria were more than just reservoirs collecting blood from the veins - they had a contractile function.

Measurement of the contribution of atrial systole to overall cardiac function has been possible by various experimental techniques and most recently has been studied in humans by examining the trans-mitral flow velocities in sinus rhythm by 2D Doppler echocardiography. A number of factors influence atrial systole including atrial after load (ventricular end diastolic pressure), ventricular compliance (for example, left ventricular hypertrophy), and diastolic duration (for example, the effect of exercise on shortening R-R intervals).[5] Atrial systole becomes substantially more important in patients who have poor ventricular compliance, and since this increases with age, it is the elderly population who have more haemodynamic disturbance with the onset of AF.

The haemodynamic consequences of loss of atrial function predict many of the symptoms associated with its onset. Loss of atrio-ventricular synchrony is associated with a fall in blood pressure of up to 55% and this may cause faintness. Cardiac output falls by between 10 and 50% causing breathlessness and a reduction in effort tolerance.[6] Palpitation is experienced by many patients as the manifestation of the irregular tachycardia of AF. However, the most important consequence of the fibrillating atria is the potential development of intra-atrial thrombi which may embolise into the systemic circulation and cause stroke (see section 3.1).

1. Paroxysmal Atrial Fibrillation

Paroxysmal atrial fibrillation (PAF) by definition means that the patient has episodes of AF inter-linked with episodes of sinus rhythm. The usual

Table I. Relative risk of the development of atrial fibrillation[1]

Risk factor	Relative risk
Male sex	1.5
Hypertension	1.5
Diabetes mellitus	1.5
Heart failure	
men	4.5
women	5.9
Valvular heart disease	
men	1.8
women	3.4

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symptom of this is palpitation. However, there is wide variation in the frequency and duration of paroxysms. Some patients have a single episode of AF only, some have occasional prolonged episodes and some have frequent short episodes. With time many patients recognise increasingly frequent and prolonged episodes of AF, and eventually they remain in AF, that is, they develop chronic or permanent AF.

The diagnosis of PAF is made clinically by patients presenting with episodic irregular palpitation but can only be confirmed by electrocardiographic (ECG) evidence of AF during symptoms. 24 hour ambulatory ECG recording or telemetry are often used.

Several patterns of PAF have been recognised, including predominantly nocturnal episodic AF (so-called vagotonic) and exercise-related AF (adrenergic mediated). The vagotonic episodes occur more often in males, are not associated with underlying heart disease, are preceded by a slowing of the heart rate in sinus rhythm and are often reverted to sinus rhythm by exercise. Adrenergic-related PAF occurs with equal frequency in both sexes and is often associated with underlying heart disease; paroxysms predominate during the day and are preceded by an increase in heart rate.[7]

In some patients PAF is a manifestation of sick sinus syndrome which is characterised by episodes of bradycardia and atrial tachycardias of different types.

The management of PAF is aimed at both preventing recurrent AF and reducing the frequency of episodes. In order to prevent recurrent AF, it is important to identify any precipitating causes. 'Monday morning' or 'holiday' AF[8] occurs in association with binge drinking of alcohol, and thyrotoxicosis may cause episodic as well as persistent AF. These precipitating causes need to be considered both when taking the patient history and ordering appropriate investigations.

There are no drug treatments which are 100% effective in preventing recurrence of AF. A number of drugs may help in this regard, especially β-blockers, class Ic antiarrhythmic drugs (flecainide and propafenone) and class III drugs (amiodarone, ibutilide, dofetilide and azilimide). When AF is part of a sick sinus syndrome, atrial pacing may be effective in reducing paroxysms.[9]

1.1 Preventing Atrial Fibrillation After Cardiac Surgery

Atrial arrhythmias, especially AF, are a common complication of cardiac surgery occurring in up to 20 to 40% of patients.[10-12] In this situation AF is adrenergically mediated and associated with high ectopic counts. β-Blockers, including sotalol, propanolol, atenolol and metoprolol, administered peri-operatively, have been shown to reduce the frequency of AF complicating cardiac surgery. Sotalol has become known as the β-blocker with antiarrhythmic properties because of its class III properties but these are only measurable at dosages of >160 mg/day.[13] In earlier studies, sotalol 160 mg/day[14] was effective in reducing the frequency of ectopic beats and halved the incidence of atrial arrhythmias generally, including AF. In randomised controlled trials, sotalol 120 to 240 mg/day reduced the frequency of AF significantly more than placebo[14] and metoprolol[15] but not significantly more than propanolol.[12] The most recent trial in this setting[16] with sotalol used dosages of 160 to 240 mg/day and again showed a significant reduction in the frequency of post-operative AF from 38% in the placebo group to 12.5% ($p < 0.01$).

Other agents have been tested in this situation. Amiodarone given as an infusion over 24 hours on the day after cardiac surgery reduced the incidence of AF from 47% (placebo) to 35% ($p = 0.01$) and in the amiodarone group the arrhythmia developed on average a day later.[17] Pre-treatment with oral amiodarone 600 mg/day for a week before cardiac surgery followed by 200 mg/day until hospital discharge halved the incidence of AF from 53% (placebo) to 25% ($p < 0.005$).[18] Thus, short term treatment with this drug, which minimises the risk of adverse effects, is useful in this setting.

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1.2 Reducing Paroxysms of Atrial Fibrillation

In the setting of cardiac surgery (section 1.1), the common complication of AF was reduced by drug treatment. However, in patients with established PAF, therapy is aimed more at reducing symptomatic attacks. Again, β-blockers have proven efficacy in this situation.

One way to assess drug efficacy is to compare the length of time to recurrence of the arrhythmia with drug treatment compared with placebo. Using this technique, sotalol showed a dose responsive prolongation of time-to-first-recurrence in patients with paroxysmal supraventricular tachycardias, including AF.[19] A more recent study in patients with PAF also showed a dose-response relationship in prolonging the period of sinus rhythm before relapse to AF; however, in this study sotalol 80mg twice daily was no better than placebo, whereas both 120mg and 160mg twice daily prolonged time to first recurrence.[20] This trial used trans-telephonic monitoring of heart rhythm to confirm relapse. However, this technique relies on patients recognising clinical symptoms. Other studies have shown that asymptomatic episodes of AF occur despite drug treatment and therefore, some of the benefit of treatment is to reduce symptoms presumably by shortening attacks rather than abolishing the arrhythmia completely.[21] Adverse effects from high dose sotalol are considerable and in the latest trial[20] occurred in 29% of patients receiving 160mg twice daily compared with 6% of those receiving placebo. Indeed, many patients will not tolerate dosages in excess of 80mg twice daily. At this latter dosage, sotalol has little class III activity. The question then is, are other β-blockers of benefit?

Unfortunately, there are very few clinical trials directly comparing different β-blockers in patients with PAF. In one recent trial,[22] atenolol 50mg once daily was compared with sotalol 80mg twice daily in a nonblind, randomised, crossover study. Both treatments significantly reduced the symptomatic and asymptomatic episodes of PAF as measured using prolonged ambulatory ECG monitoring but there were no significant differences between treatments. Sotalol (3±0.4 mg/kg) has also been compared with propafenone (13±1.5 mg/kg) and placebo in a double-blind controlled study in patients with PAF.[23] Over 12 months of follow-up, AF recurred in 73% patients receiving the placebo compared with 45% in those receiving propafenone ($p < 0.005$ vs placebo), and 30% in those receiving sotalol ($p < 0.005$ vs placebo). In addition, sotalol was significantly superior to propafenone.

Class Ic agents, flecainide[24,25] and propafenone[26,27] are effective in reducing recurrence in patients PAF. Class III agents including amiodarone and azimilide have also been shown to reduce relapse rate in patients with PAF. Azimilide is a new anti-arrhythmic drug which blocks both Ikr and Iks channels and is currently undergoing clinical trials. Results show that azimilide in a dosage of 100 to 125 mg/day prolonged time to first recurrence from 17 days to 60 days ($p < 0.005$) versus placebo.[28]

1.3 Which Drug Treatment Is Best for Paroxysmal Atrial Fibrillation?

There are few comparative drug treatment trials in patients with PAF but one important new study[29] showed that long term amiodarone 200 mg/day (after initial loading) was better than propafenone 300mg twice daily and sotalol 160mg twice daily. Recurrence of AF over a 16 month follow-up period occurred in 35% of patients receiving amiodarone and 63% of patients receiving either of the other agents. Figure 1 shows the relative efficacy of the current drugs used to reduce relapses of PAF.

When assessing which drug to use in a patient with PAF, it is important also to appreciate the dangers of antiarrhythmic drug therapy. All antiarrhythmic drugs are also pro-arrhythmic and torsade de pointes is the major serious pro-arrhythmia seen. Torsades de pointes is found with quinidine (class Ia), class Ic drugs and class III drugs, and probably accounts for the excess mortality seen with quinidine[30] and flecainide[31] in the Cardiac Arrhythmia Suppression Trial (CAST) study. Overall, torsade de pointes seems to occur in approximately <1% of patients receiving low dose amiodarone,[32] but in 3 to 5% of patients receiving

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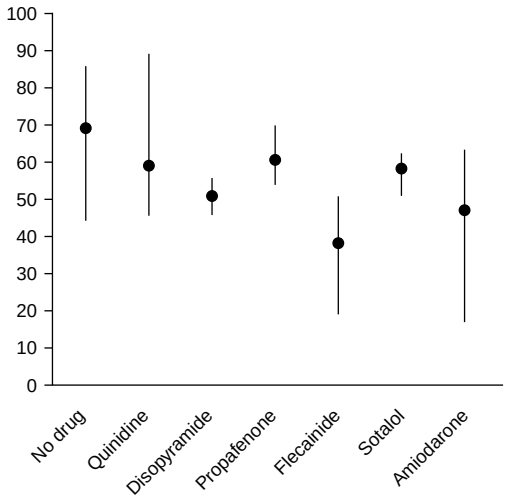

Fig. 1. Relapse rate for paroxysmal atrial fibrillation with antiarrhythmic drugs as reported in the literature. No. of studies 3 to 10.[3]

sotalol and dofetilide.[33] The precise characteristics of the patients most liable to torsades de pointes are unknown, but elderly female patients with impaired left ventricular function seem to be most susceptible and most events seem to occur early during dose titration. Because of this it is recommended that newer class III drugs such as dofetilide be started in hospital.[33] The other important pro-arrhythmic effect, seen in patients with atrial flutter in particular, is conversion from flutter with 2 : 1 atrio-ventricular block to flutter with 1 : 1 conduction. Each individual drug has its own idiosyncratic safety profile; although amiodarone has the lowest rate of pro-arrhythmia, it has more serious adverse effects ranging from photosensitivity of the skin to thyroid, liver and pulmonary dysfunction.

In patients in whom PAF is inadequately controlled, it is possible to offer electrophysiological testing with ablation. There is a form of PAF/flutter that has been identified to be related to a focus in the pulmonary veins.[34] Ablation in this territory then abolishes the tendency to the paroxysmal arrhythmia, although pulmonary vein stenosis is an important adverse effect in a substantial minority (approximately 15%). This is probably a rare form of PAF and most patients with the condition will not be cured with focal ablation. Alternative ablative techniques mimicking the maze procedure may offer some help in symptomatic patients but results thus far are disappointing with average success rates of 40 to 50% for left atrial and only 20% for right atrial maze ablation (oral communication, American Heart Association Conference, 2000). Figure 2 describes the management algorithm for patients with PAF recommended by the ESC Working Group on Atrial Fibrillation.

2. Persistent Atrial Fibrillation

Persistent AF describes atrial fibrillation which once developed persists until corrected. It is often caused by an acute cardiac insult, for example, acute myocardial infarction, cardiac surgery or pulmonary embolism. It may be the first and only presentation of AF but it may be the first manifestation of chronic or permanent AF.

In any patient who presents acutely with AF the possibility of cardioversion back to sinus rhythm must be considered. Direct current (DC) cardioversion is not always successful and factors that have been shown to predict successful cardioversion, and particularly the maintenance of sinus rhythm in the longer term, include: (i) recent onset of AF (<12 months duration); (ii) known acute and reversible cause (e.g. thyrotoxicosis); (iii) the absence of significant heart disease on echocardiography (good left ventricular function and no mitral valve disease); and (iv) an atrial diameter of <50mm on echocardiography.

Thus, in a patient with recent onset AF, the first management decision is whether cardioversion is likely to succeed and sinus rhythm be maintained. With careful selection of patients using the factors described in the previous paragraph, successful cardioversion is possible and sinus rhythm can be maintained in the majority (>70%) for several years and, in many, without long term anti-arrhythmic drug therapy.[35]

Newer improved techniques for cardioversion include the use of biphasic shocks[36] and internal

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defibrillation by catheter positioned in the pulmonary artery[37] or coronary sinus that have the potential of increasing the number of patients successfully cardioverted, although do not influence the long term maintenance of sinus rhythm. However, in the population of patients selected for cardioversion and enrolled in clinical trials, maintenance of sinus rhythm without anti-arrhythmic drug therapy is depressingly low, occurring only in about a third of patients.[38]

Pre-treatment and persistent long term treatment with class III anti-arrhythmic drug therapy (amiodarone) is associated with a higher maintenance rate of normal sinus rhythm after DC cardioversion[39,40] of about 50% after 3 years in 1 non-randomised trial.[39] Similar results have been found with dofetilide producing a virtual doubling of the maintenance rate at 12 months after DC cardioversion compared with placebo. All these trials show that early relapse occurs most commonly in the first 6 to 8 weeks after cardioversion, which corresponds with the time the atria take to re-establish full tonic function.[41]

The standard approach to cardioversion is electrical DC counter shock. This requires a general anaesthetic and all its associated mortality, morbidity and costs. Pharmacological cardioversion is an increasingly viable alternative.

2.1 Pharmacological Cardioversion

In patients with AF of less than 48 hours duration, flecainide 2 mg/kg administered intravenously over half an hour has a very high cardioversion success rate.[42] High dose oral flecainide is as effective as the intravenous preparation but it takes longer to work.[43] Other studies have shown that high dose oral propafenone or intravenous propafenone[44] can also be used as can intravenous or oral amiodarone.[45] Similarly, ibutilide given intravenously to patients with AF complicating surgery, was effective in 48% of patients compared with 15% of placebo recipients.[46] The striking ob-

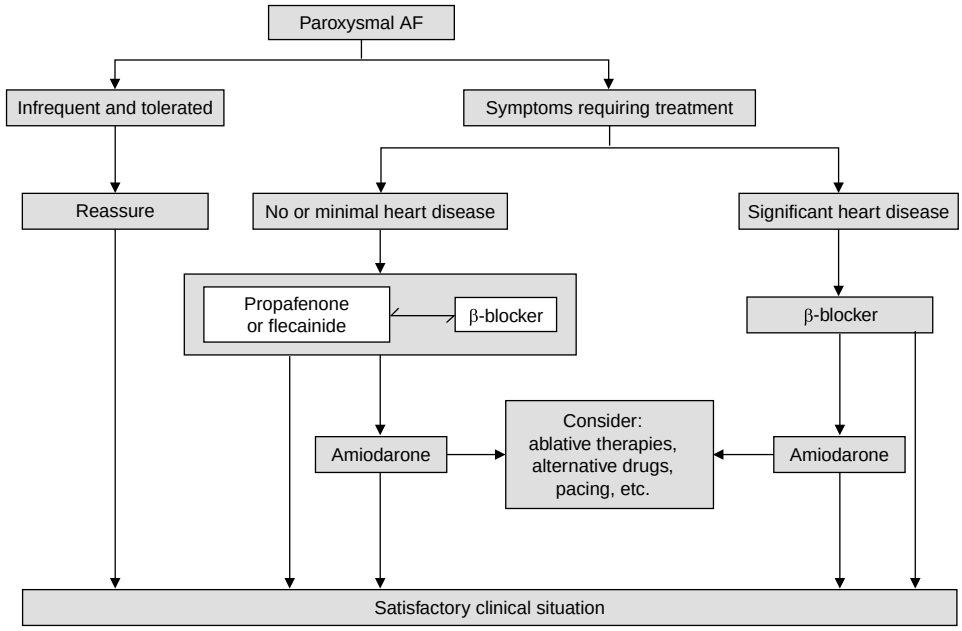

Fig. 2. Management algorithm for patients with paroxysmal atrial fibrillation (AF).

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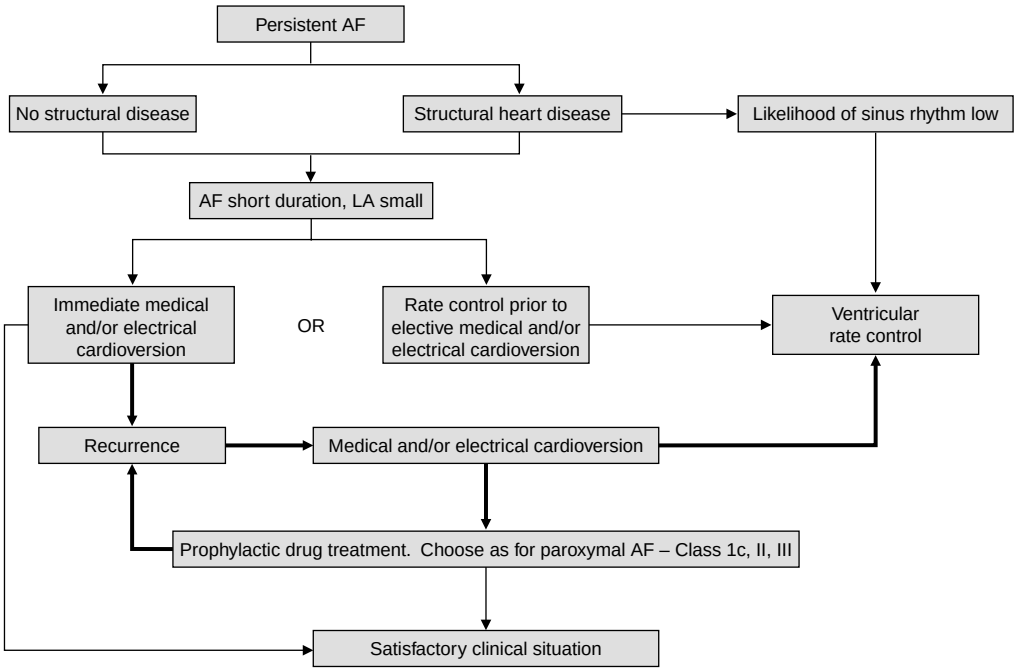

Fig. 3. Management algorithm for patients with persistent atrial fibrillation (AF). **LA** = left atrium.

servation with these drugs is the poor result when the AF has been present for longer that 48 hours.

In comparison, oral dofetilide has been recently shown to be successful in converting AF of much longer duration than 48 hours. In the European and Australian Multicenter Evaluative Research on Atrial Fibrillation (EMERALD) study, dofetilide re-established sinus rhythm in 30% of patients compared with oral sotalol (5%) and placebo (1%).[33]

2.2 Direct Current Cardioversion

Currently, DC electrical cardioversion (DCCV) using synchronised shocks is the preferred modality in patients with AF of >48 hours duration. Guidelines recommend anticoagulation with warfarin for 3 weeks before DCCV and for 4 to 6 weeks afterwards in order to reduce the thromboembolic events associated with the return to sinus rhythm. The risk of late thromboembolic events is probably because left atrial tone takes some time to recover.[41] The embolic risk is small (<1%) when the arrhythmia has been present for <48 hours.[47]

Recently, some have advocated the use of transoesophageal echocardiography to identify patients without intracardiac thrombus who may then proceed immediately to DCCV without a period of formal oral anticoagulation. However, embolic events still occur. The Assessment of Cardioversion Using Transoesophageal Echocardiography (ACUTE) study[48] was designed to test the safety of transoesophageal echocardiography (TEE) followed by immediate DCCV compared with conventional anticoagulation for 3 to 4 weeks before DCCV. Unfortunately, the trial was terminated after less than half the patients had been randomised. The actual embolic risk in the two treatment arms

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was 5/619 (0.8%) for early DCCV a median of 1 day after transoesophageal echocardiography and 3/603 (0.5%) in the conventionally managed group when DCCV was delayed until anticoagulation had been established.[48] There were more deaths in the TEE group (2.4%) than the conventional group (1.0%; p = 0.06). All patients were anticoagulated at the time of DCCV with either intravenous heparin or warfarin and afterwards with warfarin for 6 weeks. There was no difference in the frequency of recurrent AF at 8 weeks. There is a high recurrence rate of AF in the first 6 to 8 weeks after successful DCCV and anticoagulation should be continued for at least this period.

Drugs have been used to help prevent recurrence of AF and these include β-blockers, the class Ic agents flecainide and propafenone and class III agents such as amiodarone. The optimum duration of treatment with these drugs is unknown, although the recurrence rate after 3 months therapy is much lower than in the period immediately after conversion. Whether there is a survival advantage from being maintained in sinus rhythm by repeat DCCV and anti-arrhythmic drug therapy rather than accepting AF when it recurs (as it virtually always does) and controlling the ventricular rate will hopefully be answered by the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study.[49] The Pharmacological Intervention in Atrial Fibrillation (PIAF) study compared rhythm control (cardioversion and maintenance of sinus rhythm) with amiodarone with rate control with primarily diltiazem 180 to 270mg daily. Over a follow-up period of 12 months there were no significant differences in symptoms or quality of life. However, 6 minute walking distance was better in those in sinus rhythm, but there were more hospital admissions in this group.[50] Figure 3 provides a description of the management algorithm for patients with persistent AF.

In patients with significant heart disease, especially those with mitral valve disease or significantly impaired left ventricular function, the chances of success from cardioversion to sinus rhythm which is maintained for any length of time are considerably lower than in patients without significant heart disease. In this group of patients treatment should be aimed at ventricular rate control and include anti-thrombotic therapy to reduce the risk of systemic thromboembolism associated with chronic AF.

Table II. Annual incidence of stroke in patients in atrial fibrillation: influence of associated disease and anticoagulation[61]

Risk factor	Annual incidence of stroke	
	no warfarin	warfarin
Previous CVA/TIA	11.7	5.1
Hypertension	5.6	1.9
Diabetes mellitus	8.6	2.8
Congestive heart failure	6.8	1.6
Previous myocardial infarction	8.2	3.3

CVA = cerebrovascular event; **TIA** = transient ischaemic attack.

3. Permanent Atrial Fibrillation

Heart rate is under autonomic nervous control and exhibits a diurnal variation. In AF the diurnal variation is more marked with excessive diurnal tachycardia and nocturnal bradycardia. The standard therapy used to control the ventricular rate in patients with permanent AF is digoxin, especially when there is associated heart failure. Digoxin has a low therapeutic index and is often inadequate in controlling ventricular rate during exercise. It is also often used in inadequate doses. In patients with poor rate control, simply doubling the dose does reduce inappropriate tachycardia but at the expense of bradycardia at night.[51] The addition of other drugs which have a pharmacodynamic interaction with digoxin at the atrio-ventricular node improves heart rate control.

The ideal drug combination is one which blocks the sympathetic driven diurnal tachycardia and limits the excessive nocturnal bradycardia. β-blockers with intrinsic sympathomimetic activity fulfil these functions as exemplified by a study comparing pindolol with atenolol.[52] However, effort tolerance is inconsistently improved by better rate control. Xamoterol was originally developed as a mild cardiac inotropic agent and is essentially a partial agonist β-blocker with approximately

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50% sympathomimetic activity. When combined with digoxin both heart rate control and effort tolerance are improved in elderly patients.[53] Other drugs used in combination with digoxin include verapamil, diltiazem, and amiodarone (for a summary see Channer[54]).

It is important to recognise that because of the inefficient cardiac function in AF, heart rate control should be normalised not to 70 beats per minute but to 90 beats per minute.[55] In addition, since AF may be a manifestation of sick sinus syndrome, atrio-ventricular blocking drugs may exacerbate bradycardia.

In patients with permanent AF with inadequate heart rate control, radiofrequency catheter ablation of the atrio-ventricular node modulates and slows the ventricular rate response in about 75% of patients and the remainder require a permanent pacemaker.[56] This produces a regular heart rate but does not stop the atria fibrillating and as a consequence long term anticoagulation is usually required.

3.1 Reducing the Risk of Thromboembolism

Systemic embolism in association with AF has been recognised for some time. Patients in chronic or permanent AF have approximately 5 times the incidence of emboli compared with their peers in sinus rhythm.[57] Moreover, the absolute risk increases with age so that in the age range 65 to 70 years about 4% of patients per year will have an embolus compared with 8% in octogenarians.[57] Moreover, it has been recognised that there are a number of factors associated with an increased risk of embolism in the presence of AF apart from increasing age, including a history of embolism or stroke, hypertension, a history of heart failure, left ventricular dysfunction on echocardiography (table II), and an increase in left atrial dimension of more than 50mm. The corollary of this of course is

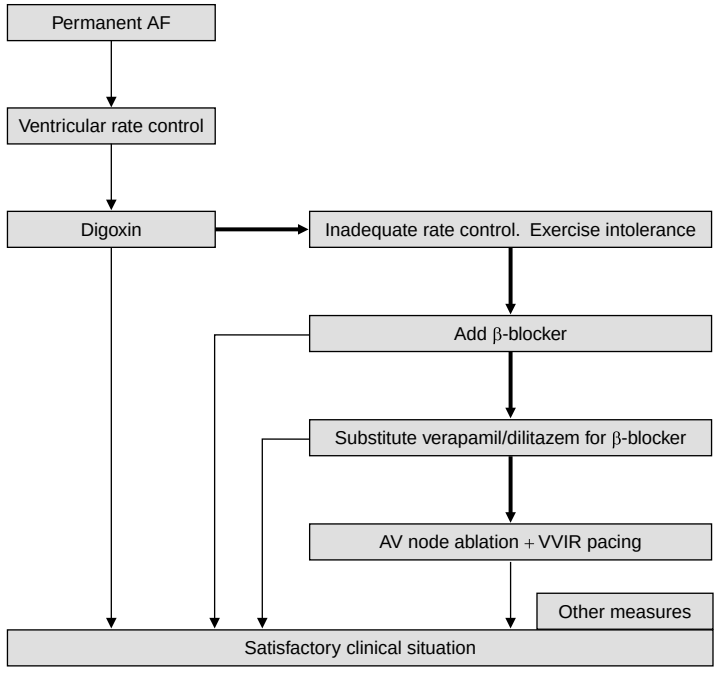

Fig 4. Management algorithm for patients with permanent atrial fibrillation (AF). **AV** = atrioventricular; **VVIR** = ventricular sensing of inhibition pacing with rate responsiveness.

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that young age (<65 years), lone AF (that is AF in the absence of organic heart disease) and PAF exposes the patient to a low risk of embolism.[58]

Clinical trial data show that warfarin reduces the risk of thromboembolism by approximately two-thirds when the international normalised ratio (INR) is in the range 2.0 to 3.0. However, there is a substantial haemorrhagic risk associated with long term warfarin usage even in the best controlled studies. The average serious haemorrhagic risk is about 1% per year but increases dramatically with INR >4.0.[59] So if the absolute risk of an embolism is <3% a year there are no major benefits in using warfarin. Aspirin (acetylsalicylic acid), by comparison, reduces the risk of thromboembolism by between 20 and 30%[60,61] but is much safer than warfarin. Thus, in high risk patients, warfarin should be used and in low risk patients aspirin should be used. Each patient must be assessed individually and their absolute risk determined to help guide management. Figure 4 describes the management algorithm of permanent or chronic AF.

4. Conclusion

Physiologically, sinus rhythm is the optimal rhythm. AF is an inefficient state and exposes the patient to a long term risk of thrombo-embolism. For this reason much emphasis has been placed on cardioversion from AF to sinus rhythm whenever it is possible. Drug strategies are being developed to increase the maintenance rate of sinus rhythm. However, the risks of long term drug therapy must be weighed against the risks of AF. All anti-arrhythmic drugs have adverse effects and serious pro-arrhythmic potential.[30,31,62] The new class III drugs prolong the QT interval and this electrophysiological phenomenon increases the risk of torsade de pointes. Their use can only be justified if AF is not a benign arrhythmia.

AF complicates all forms of heart disease and is especially common in patients with impaired left ventricular function.[63] Although the presence of paroxysmal supraventricular tachycardias observed during monitoring of patients after acute myocardial infarction has been shown to be an independent predictor of late mortality,[64,65] in longitudinal studies of apparently healthy elderly people the same arrhythmias do not confer an adverse prognosis.[66-68] The adverse prognosis of the arrhythmia in the post-infarct population is linked to left ventricular dysfunction.[65,69]

Moreover, maintenance of sinus rhythm with a class III agent did not reduce mortality in patients post-infarct;[70] but did cause torsade de pointes in 3% of these patients. This suggests that preventing AF in patients with severe left ventricular function (ejection fraction <35%)[70] was irrelevant to outcome. Other data have demonstrated that patients with paroxysmal atrial tachycardia (PAT)/PAF (figs 5, 6) appear to have reduced life expectancy compared with their peers but when left ventricular function is included in multi-variate analysis, prognosis is unaffected by the arrhythmia [unpublished observation].

Nevertheless, AF confers a prognostic disadvantage. Data from the Framingham study[71] recently showed that the arrhythmia doubled the expected mortality. This effect fell to a 50 to 90% increased mortality risk after adjustment for other

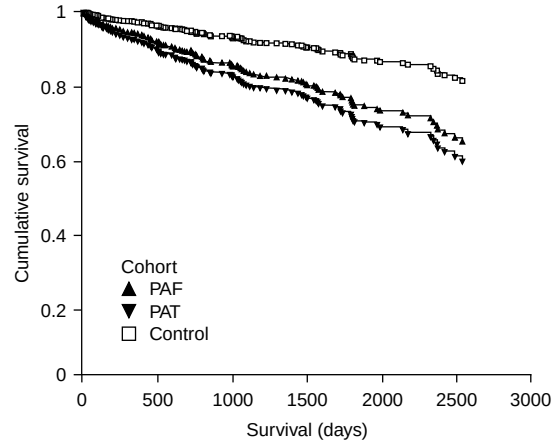

Fig. 5. Unadjusted survival of 199 patients with paroxysmal atrial tachycardia (PAT), 130 patients with paroxysmal atrial fibrillation (PAF) and 679 patients with no significant arrhythmia (control) [unpublished data].

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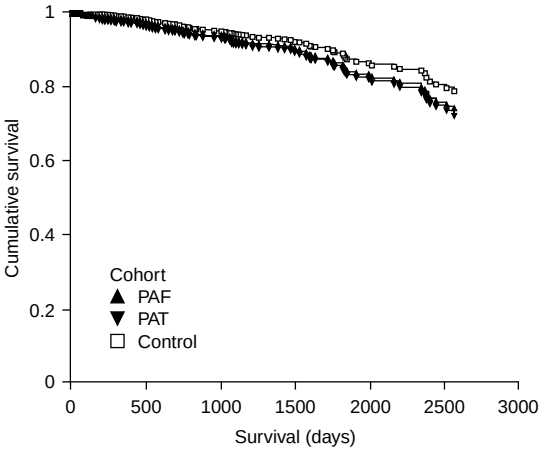

Fig. 6. Survival of patients from figure 5 with paroxysmal atrial tachycardia (PAT), paroxysmal atrial fibrillation (PAF) or no significant arrhythmia (control) adjusted for age, left ventricular function on echocardiography and in-patient status (unpublished observations).

confounding variables. However, earlier data from the same authors had already demonstrated that when ischaemic stroke was associated with AF the mortality was doubled.[72]

AF is an epiphenomenon of cardiac dysfunction; mortality and prognosis are determined by the natural history of the underlying heart disease. The major health burden associated with AF is increased risk of stroke.

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