

# Management of atrial fibrillation: an overview of the NICE guidance on AF management

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## Abstract

**T**his article aims to provide an overview of the management of atrial fibrillation (AF), with reference to the recently published National Institute for Health and Clinical Excellence (NICE) guidelines on AF management (<http://www.nice.org.uk/CG36/guidance/pdf/english>). This article is not meant to cover the whole guideline nor be a systematic review, as the full guideline contains all the search strategies and appraised evidence tables, and represents a comprehensive assessment of the evidence behind the recommendations in the NICE guideline (also available at <http://rcplondon.ac.uk/pubs/books/af/index.asp>).

**Key words:** atrial fibrillation, NICE, guidelines.

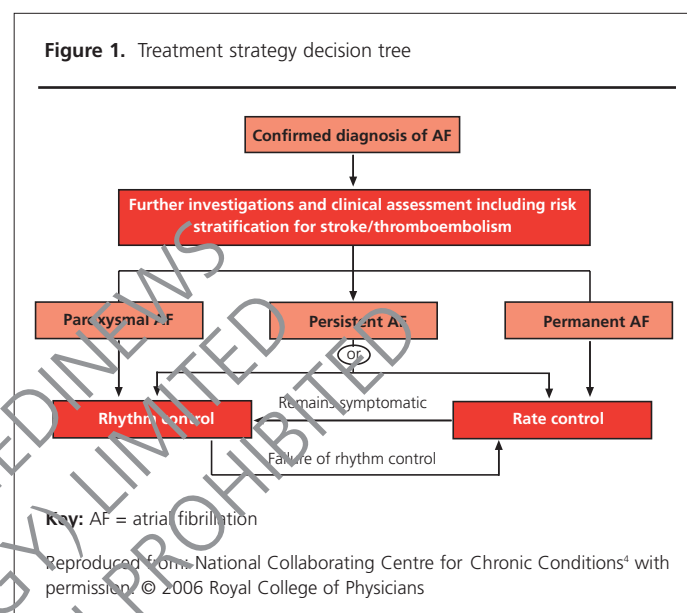
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## Introduction

The management of atrial fibrillation (AF) has, for many years, varied significantly between physicians, with often much debate as to the optimal approach to be taken. Since AF is associated with a substantial excess of both morbidity and mortality it is clear that a streamlined guideline-based approach to management is necessary.<sup>2</sup>

Notably, AF and its complications now consume 1% of the UK National Health Service budget.<sup>3</sup> Hence, the recent publication of evidence-based guidelines from the National Institute for Health and Clinical Excellence (NICE) could not be more appropriate.<sup>4</sup> Other guidelines are also available, such as the joint American College of Cardiology/American Heart Association/European Society of Cardiology guidelines (recently updated in 2006) and the American College of Chest Physicians guidelines on antithrombotic therapy for AF.<sup>5,6</sup> Some aspects of these guidelines merit comment.

Most guidelines on AF management are largely 'expert con-



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sensus-based' i.e. formulated by a large group of cardiology experts following a review of the published evidence. The NICE guidelines on AF management are different as the methodology was based on systematic reviews of the world literature performed (by an information specialist) following definition of the guideline scope.<sup>4</sup> The scope itself underwent public consultation and was modified in line with suggestions from stakeholders to address key areas pertaining to AF management that are applicable to UK clinical practice. These systematic reviews were then critically appraised (by a health services researcher) and cost-effectiveness analyses applied (by a health economist). The distilled, appraised evidence thus gathered was then debated by a multi-disciplinary Guideline Development Group (GDG), which consisted of cardiologists (only three), general physicians, nurses, pharmacists, general practitioners and two lay representatives (one of whom had AF). The recommendations were then formulated. The GDG was led by a Chair (a physician who was a non-cardiologist) and a Clinical Adviser (a cardiologist with special interest in AF management). Invited experts, including a stroke physician, cardiac surgeon and a haematologist, also contributed where evidence for some sections were being debated.

The draft NICE guideline then underwent two rounds of public stakeholder consultation, which was followed by the formal publication of the guideline in June 2006. The remit of the NICE guideline on AF management was to be practical and pragmat-

ic which would be applicable for more than 80% of AF patients for over 80% of the time in the UK setting.

### Classification

AF is now generally classified according to the temporal pattern of presentation as: i) recent onset (within 48 hours); ii) paroxysmal; iii) persistent (duration seven days or more); or iv) permanent (duration greater than one year or refractory to cardioversion attempts).<sup>4,5,7</sup> This simple classification (see figure 1) merely offers an idea of the likely time course of AF and may help guide management objectives.

In reality, management of patients with AF should be guided by many considerations, including symptoms, haemodynamic stability and associated co-morbidities (such as hypertension and heart failure).

### Symptoms

Patients with AF can present with a wide variety of symptoms and many are asymptomatic. Where AF is suspected, it is important to confirm the diagnosis before initiating management strategies. Patients presenting with any of the following: breathlessness/dyspnoea, palpitations, syncope/dizziness, chest discomfort, and stroke/transient ischaemic attack etc, should have manual pulse palpation performed to assess for the presence of an irregular pulse that may indicate underlying AF. This should then be confirmed electrocardiographically.<sup>4</sup>

### Investigation of AF

The assessment of the patient with AF needs to be methodical. As always, a thorough history taking and clinical examination are essential and may alert the physician to potential causes for AF and the impact on the patient's lifestyle.

To confirm the diagnosis of AF, an electrocardiogram (ECG) should be performed in all patients in whom AF is suspected because an irregular pulse has been detected, whether symptomatic or not. A blood workup (full blood count, electrolytes and thyroid function tests) and chest X-ray are essential; an echocardiogram is often useful.

In patients with suspected paroxysmal AF, which is undetected by standard ECG recording, the NICE guidelines suggest that a 24-hour ambulatory ECG monitor should be used in those with suspected asymptomatic episodes or symptomatic episodes less than 24 hours apart. However, a seven-day Holter or an event recorder ECG should be used in those with symptomatic episodes more than 24 hours apart.

### Rate control or rhythm control

Theoretically, restoration of sinus rhythm should offer the premise of improved haemodynamics and symptom relief, whilst potentially reducing the thromboembolic tendency and stroke risk. Unfortunately, this is often unrealistic. The tendency in many patients with AF is towards recurrence (often asymptomatic) even if rhythm control succeeds initially. Even when using an aggressive serial cardioversion strategy for relapse, approximately half the patients remain in sinus rhythm at one year.<sup>8</sup> At five

years, only 25% remain free of AF.<sup>9</sup> These recurrences may be asymptomatic and thereby still confer an increased risk of stroke, of which the clinician may be unaware. This knowledge means that many patients should be considered for long-term anticoagulation even if rhythm control has apparently succeeded.<sup>10</sup>

As to whether rhythm or rate control should be offered as first line, some data from clinical trials are available. Large studies such as the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial<sup>11</sup> suggest that rate control is not an inferior strategy to rhythm control. There was no difference in the primary end point of overall mortality at five years and no significant difference in the composite secondary outcome measure of death, disabling stroke, disabling anoxic encephalopathy, major bleeding and cardiac arrest, between the study arms.

Importantly, a rhythm control strategy was associated with a higher rate of hospitalisations and more frequent adverse drug reactions. An interesting post-hoc analysis of the predictors of survival in the AFFIRM study showed that anticoagulation therapy and sinus rhythm were potent predictors of survival. However, a greater mortality associated with anti-arrhythmic drug use offset the survival advantage of maintaining sinus rhythm.<sup>12</sup> This implies that survival would be improved if better drugs or techniques to maintain sinus rhythm were available.

Of course, extrapolating such clinical trial data to the 'real world' can be fraught with difficulties. To help guide clinical decisions, the NICE guidelines have suggested that rhythm control should be offered to the following patients as the preferred initial option: those with lone AF, or AF secondary to a corrected precipitant (e.g. alcohol); patients with symptoms despite optimal rate control; and patients with heart failure. However, these categories are not mutually exclusive from those where a rate control strategy is the preferred option. Thus, associated co-morbidities and patient choice should be considered.

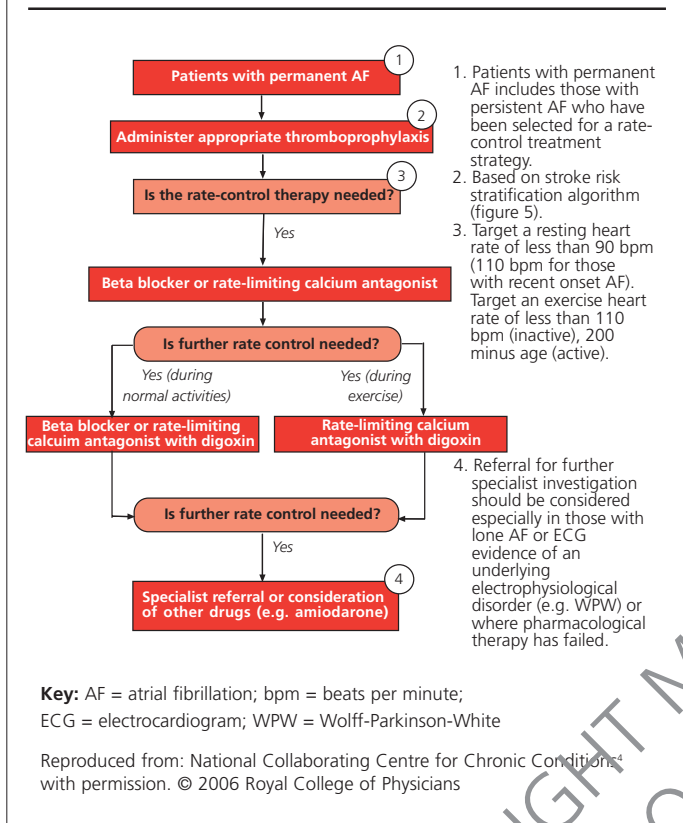
### Drug therapy for atrial fibrillation

The crux of management of acute AF is primarily an assessment of haemodynamic stability. In those with life-threatening features (haemodynamic compromise, severe cardiac decompensation, angina etc), emergency electrical cardioversion should always be considered irrespective of duration of onset.<sup>4,13</sup> In the more stable patient, a rate-limiting calcium channel blocker or beta blocker should be tried as first line, but where these are inappropriate (e.g. pulmonary oedema), intravenous amiodarone is preferred.

It is also important to consider electrophysiological abnormalities, such as Wolff-Parkinson-White syndrome, as an underlying diagnosis, particularly in younger patients without evidence of structural or ischaemic heart disease. In this situation, atrio-ventricular node-blocking agents (e.g. diltiazem, verapamil, or digoxin) should not be used as these may exacerbate the ventricular rate and are potentially dangerous. Here it would be appropriate to consider intravenous flecainide for attempting pharmacological cardioversion.<sup>4,14</sup>

It is generally accepted that a resting heart rate below 90 bpm is optimal whilst, on exertion, the heart rate should not

**Figure 2.** Rate-control treatment algorithm for permanent (and some cases of persistent) atrial fibrillation



advised. This drug is also useful in those with paroxysmal AF and frequent relapses (despite adequate doses of first-line anti-arrhythmic agents, such as class 1c drugs (e.g. flecainide, propafenone and sotalol). Sadly, the potent nature of amiodarone means side effects are common, particularly with prolonged exposure.<sup>18</sup> This drug is, therefore, usually initiated only under specialist guidance so that patients can be followed-up in the long-term.

### Cardioversion

In persistent AF, cardioversion can be performed electrically or pharmacologically. Electrical cardioversion may be initially successful in 75–93% of patients but this depends strongly on the duration of AF (success rates are particularly poor after one year), left atrial size and co-existing structural heart disease.<sup>4,19-21</sup> Pharmacological cardioversion can be achieved using a number of drugs but, in the UK, the most commonly used agents are flecainide and amiodarone. There is often little to choose (apart from speed of action) between oral and intravenous administration, with successful cardioversion reported in up to 80% with oral flecainide therapy, rising to 90% with intravenous administration.<sup>4</sup> As relapse following cardioversion is common, anti-arrhythmic drugs are often required to improve the likelihood of long-term maintenance of sinus rhythm. Beta blockers are the most commonly used drugs for this purpose, although long-term amiodarone is required in some patients (particularly those who are heavily symptomatic with AF), whilst flecainide and other class I drugs are used in younger patients without structural or ischaemic heart disease.<sup>4</sup>

### Side effects

All anti-arrhythmic drugs have side effects but the problem is particularly pertinent with class I and III drugs. These alter the fluctuation of potassium or sodium channels of atrial cells and can thereby modify the refractory period, resulting in QT and QRS prolongation.<sup>22</sup> This can potentially lead to the life-threatening arrhythmias, including 'torsades de pointes', in up to 5% of patients.<sup>22,23</sup> Several factors have been identified as conferring increased risk for this, including the following: hypokalaemia or hypomagnesaemia, congenitally prolonged QT intervals, bradycardia, congestive heart failure, female sex, pauses associated with the conversion of AF to sinus rhythm, and concomitant use of medications, especially those which interfere with the hepatic metabolism of anti-arrhythmic drugs, such as erythromycin.<sup>23</sup>

It is therefore advisable that caution be used in prescribing these drugs and a 12-lead ECG sought after treatment initiation, to assess for QT prolongation. Additionally, some class Ic drugs can convert AF into atrial flutter with 1:1 atrioventricular nodal conduction, with resultant haemodynamic instability. Thus, concomitant use of atrioventricular nodal blocking agents, such as beta blockers or rate-reducing calcium channel blockers, is usually recommended.

### Treatment algorithms

The algorithms from the NICE guideline for the management of

exceed 110 bpm in the sedentary patient or '200 minus age' in the ambulatory patient.<sup>4,15</sup> For many years, the mainstay of drug therapy for rate control in AF was the cardiac glycoside, digoxin. This drug is of limited efficacy, however, in the context of hyperadrenergic states, namely thyrotoxicosis, fever, peri-operatively and – most importantly – during exercise.<sup>16,17</sup> Thus, digoxin monotherapy is only likely to offer adequate rate control in elderly sedentary patients.<sup>4</sup> The algorithm for rate control for permanent AF from the NICE guideline is illustrated in figure 2.

Beta blockers are particularly effective at controlling ventricular rate and should be used as first-line agents. Additionally, beta blockade also reduces the chance of recurrence following successful cardioversion, and these drugs are useful first-line agents in paroxysmal AF. In the peri-operative setting, beta blockers reduce the likelihood of developing AF in those deemed at risk.

The rate-limiting, non-dihydropyridine calcium channel blockers (diltiazem, verapamil) are also frequently used to optimise rate control in those unable to take or tolerate a beta blocker. Although digoxin is no longer considered first line, it remains a useful adjunct in patients who remain tachycardic at rest and can be used in combination with either beta blockers and calcium channel blockers as combination therapy.<sup>4,15</sup> Despite these drugs, some will continue to have poor control of ventricular rate. In these circumstances, agents such as amiodarone are





