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## THE CONTEMPORARY MANAGEMENT OF ATRIAL FIBRILLATION

-  Atrial fibrillation is the commonest sustained cardiac arrhythmia
-  Untreated atrial fibrillation is a significant risk factor for stroke and other morbidities
-  Treatment involves rhythm and/or rate control and prevention of thromboembolism
-  Choice of either warfarin or aspirin should be based on the individual's stroke risk stratification and risk of bleeding

### INTRODUCTION

Atrial fibrillation (A FIB) is the commonest sustained cardiac arrhythmia and if left untreated is a significant risk factor for stroke and other morbidities. A FIB is associated with increasing age. The estimated prevalence of A FIB is 0.4% - 1% in the general population; this increases to 10% in those > 80 years of age,<sup>1</sup> where it is responsible for approximately 25% of all strokes.<sup>2</sup> Furthermore, A FIB-associated stroke has a worse outcome. Therefore, because of the aging population, A FIB is a huge and expensive public health problem in developed countries. Updated management guidelines for A FIB have been issued recently by the UK National Institute for Health and Clinical Evidence (NICE) and by a joint task force from the American College / European Society of Cardiology and American Heart Association.<sup>2,3</sup> This bulletin summarises these guidelines and reviews the management of A FIB in primary care.

### PATHOPHYSIOLOGY

The most frequent histopathological changes in A FIB are atrial fibrosis and loss of atrial muscle mass. There are many possible causes for these findings, including: coronary artery disease causing atrial ischaemia; age-related atrial fibrotic changes; alcohol and caffeine; changes in autonomic tone such as increased sympathetic activity; activation of the renin-angiotensin-aldosterone system (frequently seen in hypertension); valvular disease causing elevated atrial pressure and endocrine abnormalities such as hyperthyroidism. A FIB may also develop postoperatively, especially with surgery above the diaphragm; and it may also be familial. **Many of these factors may be present in the older population,** predisposing to the development of A FIB.

### DIAGNOSIS

Physical examination may suggest A FIB on the basis of irregular pulse, irregular jugular venous pulsation and variation in the intensity of the first heart sound. Atrial flutter is an important differential diagnosis but this may present with a regular rhythm. **A clinical diagnosis of A FIB should be confirmed by ECG.** Other tests such as echocardiography will be useful in identifying additional pathology such as valvular and/or ventricular disease. Transoesophageal echocardiography is required in order to identify the presence of a thrombus. It is important to identify predisposing factors, if present, as these may require treatment as well (e.g. hyperthyroidism).

## MANAGEMENT

There are **3 objectives in the treatment of A FIB – correction of the rhythm disturbance, rate control and prevention of thromboembolism**. The rhythm control strategy attempts restoration and maintenance of sinus rhythm. With rate control the ventricular rate is controlled with no commitment to restore or maintain sinus rhythm. **Regardless of whether the rate control or rhythm control strategy is pursued, all patients with A FIB should be evaluated for oral antithrombotic therapy to prevent thromboembolism**. However, surveys from Ireland and elsewhere suggest that many patients receive no or inappropriate antithrombotic therapy.<sup>4,5</sup>

## ORAL ANTITHROMBOTIC THERAPY

Oral antithrombotic **therapy is recommended for all patients with A FIB**, unless there are specific contraindications, in order to prevent thromboembolism and in particular stroke. **The selection of the antithrombotic agent should be based upon the absolute risk of stroke and bleeding and the relative risk and benefit for a given patient**. Table 1 describes the stroke risk stratification (which should be used to assess stroke and embolism risk in all A FIB patients) and Table 2 outlines the preferred antithrombotic treatment according to risk of stroke.

**Table 1: Stroke risk stratification<sup>2,3</sup>**

High Risk Factors	Moderate Risk Factors	Low Risk Factors
•Previous stroke/ TIA/embolism	•Age > 75 years	•Female gender
•Mitral stenosis	•Hypertension	•Age < 75 years
•Prosthetic heart valve	•Heart failure	•Coronary artery disease
	•LV ejection fraction <35%	•Thyrototoxicosis
	•Diabetes	

**Table 2: Recommended Antithrombotic Treatment according to stroke risk<sup>2,3</sup>**

Risk Factors	Recommended Therapy
No / low risk factors	Aspirin 75-300mg daily
One moderate-risk factor	Aspirin 75-300mg daily <b>OR</b> Warfarin (INR 2.0-3.0, target 2.5)
Any high-risk factor or > 1 moderate-risk factor	Warfarin (INR 2.0-3.0, target 2.5)

**Warfarin is recommended for patients in the high risk category and for those with more than one moderate risk factor**. Before initiating treatment, each patient should be individually assessed for his/her stroke risk as outlined in Table 1 and should also be assessed for the risk of bleeding with warfarin. The following factors may pose a particular risk for bleeding with warfarin: older patients (>75 years); patients with uncontrolled hypertension; those already taking other antiplatelet agents such as aspirin, clopidogrel or NSAIDs; those on multiple medications; patients with a history of prior bleeding, e.g. from peptic ulcer, or those with a past history of poorly controlled anticoagulation therapy. However, even these patients may be able to take warfarin if closely monitored. If warfarin is appropriate, aspirin, clopidogrel or similar agents should not be co-administered purely for thromboprophylaxis as they provide no additional benefit. INR (International Normalised Ratio) should be checked weekly in patients receiving warfarin until it stabilises; thereafter it should be checked monthly. **The stroke risk stratification for each patient should be reviewed on a regular basis in order to ensure that antithrombotic therapy is appropriate for the individual's current risk of stroke (Table 1).**

## RHYTHM VERSUS RATE CONTROL

Studies comparing outcomes of rhythm vs. rate control strategies in A FIB patients found no difference in the incidence of mortality or stroke between the groups. **Rhythm control** is recommended for patients with paroxysmal A FIB and for younger patients (<65 years) with persistent A FIB who are: symptomatic; presenting for the first time with isolated A FIB; have congestive heart failure or those where A FIB is secondary to a treated or corrected predisposing factor. Cardioversion is usually undertaken in a hospital setting and may consist of pharmacological and/or electrical treatment. Pharmacological agents include the anti-arrhythmic agents flecainide or amiodarone. **Irrespective of the type of procedure, patients must undergo adequate anticoagulation before cardioversion is undertaken**. In emergency situations, patients should be heparinised. **Follow-up consists of appropriate thromboprophylaxis** (even if in sinus rhythm) and a  $\beta$ -blocker. Patients should be evaluated at 1 and 6 months to see if sinus rhythm is maintained. If A FIB has recurred, the patient should be re-evaluated to see if further rhythm control is warranted; otherwise they should be considered for rate control.

**Rate control** is recommended as first-line treatment in older patients (> 65 years) and those who have: A FIB of > 1 year's duration; coronary artery disease; contraindications to anti-arrhythmic agents or those who have had multiple previous failed attempts at cardioversion. As well as thromboprophylaxis, patients should be treated with a  $\beta$ -blocker or rate-limiting calcium antagonist (e.g. verapamil or diltiazem) in order to achieve a target of a resting heart rate of < 90bpm and an exercise heart rate of <110bpm. **Some patients achieve these targets without the need for any pharmacological treatment.**

It is important to note that the updated guidelines recommend that digoxin should only be added if inadequate control is achieved with either of the above drugs. **Digoxin should only be considered for monotherapy in predominantly sedentary patients** as it does not control the increased heart rate that may occur with exercise.

## MANAGEMENT OF ATRIAL FIBRILLATION IN CLINICAL PRACTICE

A recent Irish study investigated the use of antithrombotic therapy in clinical practice.<sup>6</sup> Although 87/100 (87%) of the A FIB patients studied were receiving oral antithrombotic therapy, 35 of them were receiving suboptimal therapy according to the stroke risk stratification in Table 1. **Patients >75 years were more likely to be receiving suboptimal therapy compared with younger patients.** The authors concluded that the benefits and suitability of antithrombotic therapy for patients of all ages needed to be more comprehensively communicated to prescribers.

Studies have sought to identify the problems of implementing evidence-based clinical guidance on antithrombotic therapy in general practice. Interviews with atrial fibrillation patients suggested that many of them did not see themselves as at risk of a stroke, while others felt unable to make a judgment as to whether they should be taking warfarin or not.<sup>7</sup> In addition, **patients treated by physicians in the 90 days after the physician had dealt with a warfarin-associated adverse bleeding event, had a 21% reduced odds of receiving warfarin compared with patients treated by the same physicians before exposure to the adverse bleeding event.** In contrast, a thromboembolic stroke in a patient with atrial fibrillation not on anticoagulation did not appear to influence the odds that a physician would use warfarin in subsequent patients.<sup>8</sup>

Anticoagulation therapy with warfarin is known to reduce the risk of ischaemic stroke associated with A FIB but also increases the risk for major haemorrhage and this is a major concern in clinical practice. Clinical trials reporting low risk of haemorrhage in A FIB patients usually have carefully selected participants, very few of whom are elderly. However, a recent cohort study undertaken in clinical practice, evaluated the risk of intracranial (IC) and/or extracranial (EC) haemorrhage in A FIB patients, (n=13,559 patients > 18 years), irrespective of warfarin therapy.<sup>9</sup> Results showed similar rates of haemorrhage among warfarin treated and non-treated patients: 170 haemorrhages (72 IC and 98 EC) occurred in patients on warfarin, compared with 162 (46 IC and 116 EC) in patients not taking warfarin, during approximately 15,000 patients years' follow-up; 98% of EC haemorrhages were from the GI tract. **The risk of haemorrhage (particularly IC type) increased with older age, irrespective of warfarin therapy and was most striking at age 80 years and older.** An increased risk of haemorrhage with older age remained after co-morbidities, such as existing cardiovascular disease and GI pathology, were taken into account. Of interest, **age did not have a negative impact on the control of INR.** These results suggest that prescribers may have prescribed warfarin selectively for their patients in clinical practice. However, **the findings suggest that well-managed warfarin therapy can be used safely in older patients in clinical practice.**

**Practical Advice:** Table 3 outlines the **CHADS<sub>2</sub> (Cardiac Failure, Hypertension, Age, Diabetes, Stroke [doubled]) scheme** (based on the development of ischaemic stroke in 1,733 A FIB patients on no antithrombotic therapy) that may be a useful tool for quantifying the risk of ischaemic stroke with A FIB on an individual basis. The score gives an estimation of the level of risk of A FIB-associated stroke each year, which facilitates a risk-benefit analysis.

**Table 3: Stroke risk in nonvalvular atrial fibrillation patients on no antithrombotic therapy<sup>2</sup>**

CHADS <sub>2</sub> Scoring System		CHADS <sub>2</sub> Score	Adjusted Stroke rate (% per year)
Cardiac Failure	1	0	1.9
Hypertension	1	1	2.8
Age > 75 years	1	2	4.0
Diabetes Mellitus	1	3	5.9
Prior Stroke / TIA	2	4	8.5
		5	12.5
		6	18.2

In general terms, aspirin reduces the risk of A FIB-associated stroke by 19% while warfarin reduces the risk by 61%.<sup>2</sup> The higher the CHADS<sub>2</sub> score, the greater the risk of ischaemic stroke and the more important the use of warfarin to prevent such an event. **Experts agree that aspirin is appropriate for patients with low stroke rates (< 2% per year) and that warfarin is warranted for those patients with high stroke rates (> 5% per year) - see Table 3.** There is controversy regarding the management of A FIB patients at intermediate risk (stroke rate of 3-5% per year). Reported rates of warfarin-associated haemorrhage in A FIB patients vary from 0.76% per year to approximately 10% per year for older patients; <sup>9</sup> these figures probably represent some differences in the baseline bleeding risk of the source populations. Therefore **the choice of warfarin or aspirin in the intermediate risk patient (stroke rate of 3-5% per year) should be based on an assessment of the benefit (in terms of stroke prevention) versus risk (in terms of adverse bleeding risk) in the individual patient.**

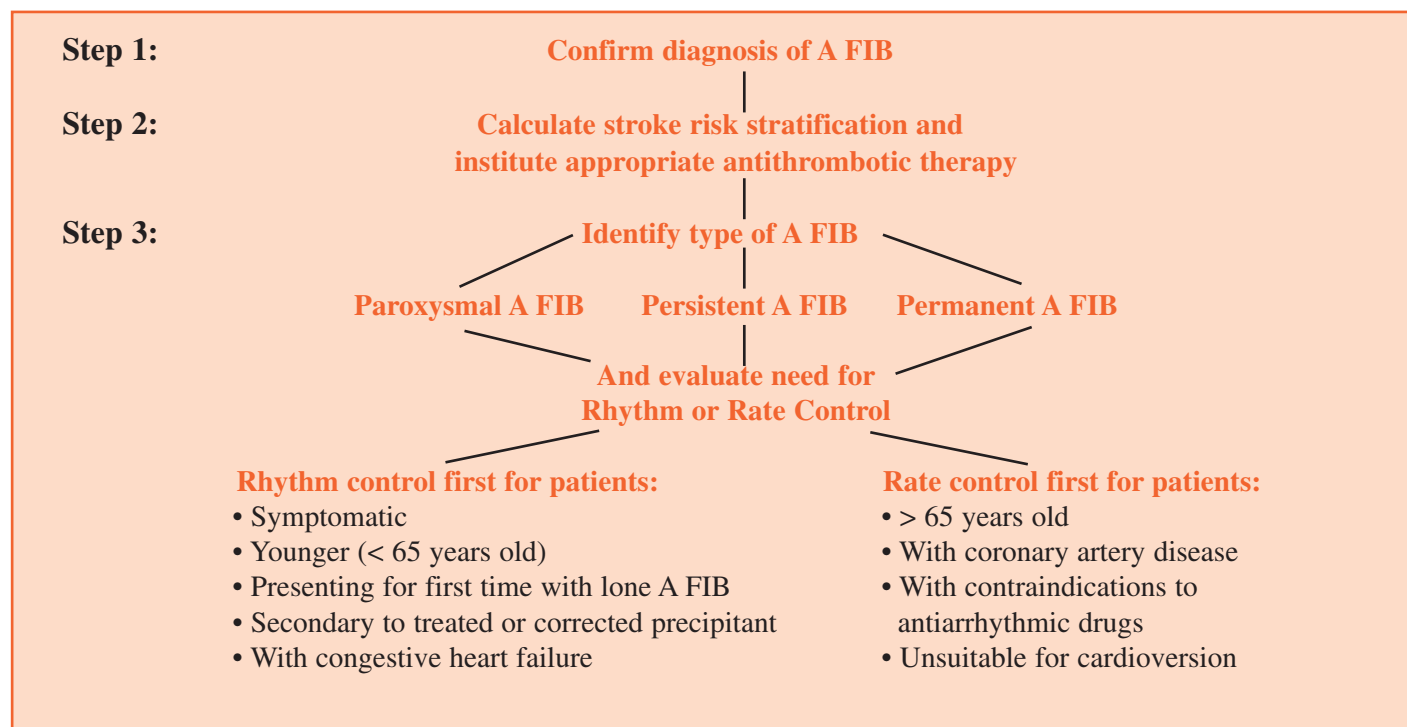
## WHEN TO SEEK SPECIALIST ADVICE

Referral to a specialist unit may be necessary for those patients with lone A FIB, those with ECG evidence of an underlying electrophysiological disorder (such as Wolff-Parkinson-White syndrome), or those in whom pharmacological therapy has failed. In addition to cardioversion, ablation therapy is available in some specialist centres and may be suitable for some patients. This consists of targeted cautery of cardiac tissue by local application of radio frequency energy in order to control the arrhythmia.<sup>10</sup> Follow-up has shown continued control at up to one year in those patients suitable for ablation therapy.

## SUMMARY

Figure 1 outlines the diagnosis and management of A FIB. Once the diagnosis has been confirmed and the patient's stroke risk stratification has been defined, it is important to explain the advantages and disadvantages of each strategy to the patient before deciding which antithrombotic therapy to use. As the risk of stroke increases with increasing number of risk factors, it is vital to use the appropriate antithrombotic therapy as per the guidelines whenever possible. Ideally, all physicians should have access to appropriate coagulation clinics in order to ensure proper titration of warfarin, especially in the initial weeks of treatment.

**Figure 1: Treatment Algorithm for Atrial Fibrillation<sup>11</sup> \***



\*Treatment algorithms for each step are available in  
 “CG36 atrial fibrillation - quick reference guide” at [www.nice.org.uk](http://www.nice.org.uk)

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