HOW WOULD I MANAGE A 60-YEAR-OLD WOMAN PRESENTING WITH ATRIAL FIBRILLATION?

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When approaching the initial and long-term management of patients with atrial fibrillation (AF), consideration should be made to certain points. Firstly, is the diagnosis of AF certain? It is important to document the arrhythmia, and also to distinguish between chronic and paroxysmal AF, as there are important management differences between the two conditions. Secondly, a search should be made for the underlying aetiological or predisposing factor for AF, and any associated complications (such as heart failure, stroke and thromboembolism). Finally, in acute presentations of AF, consider whether or not there were any 'acute' precipitating factors, for example, infection, and whether the haemodynamic status of the patient merits urgent intervention.

Initial and long-term management of AF depends upon the subtype of AF one is dealing with. In general AF can be subdivided into acute or chronic. Chronic AF can in turn be described as paroxysmal or sustained (persistent or permanent).

When faced with a new patient with atrial fibrillation ask:

- **Is it atrial fibrillation?**
- **Why?...what is the underlying cause?**
- **Why now?...are there any precipitating factors?**

INITIAL PRESENTATION

A 60-year-old woman initially presenting with AF may do so acutely or, alternatively, as a more chronic rhythm disorder. The history should include the following: the date of the first episode; information about acute precipitating factors or chronic conditions linked to AF; how she finds relief from her symptoms; the typical duration of, and interval between, episodes; the duration of the current or last episode and previous drug treatment.

Some patients with AF have few symptoms, but many will present with haemodynamic-related symptoms (such as tiredness, fatigue, reduced exercise tolerance and complaints related to heart failure). Some will have more serious complications, such as heart failure or thromboembolism. If the patient complains of angina, it should be established whether the angina occurs only during attacks of AF and if they are related to an uncontrolled ventricular rate or whether angina occurs independently of the arrhythmia.

A careful history and clinical examination will often reveal underlying medical problems associated with AF, such as hypertension, ischaemic heart disease, valvular heart disease and cardiomyopathy. Nevertheless, common non-cardiac factors such as excessive alcohol intake, thyroid disease, chest disease, and any infection or pyrexial illness can precipitate AF.

Acute AF usually describes an acute episode of AF related to an acute curable cause or an acute attack of AF. When faced with a patient who presents with acute, rapid AF, there has to be an assessment of the patient's clinical and haemodynamic status, and urgent heart rate slowing.

Amongst the more chronic forms of AF, a careful history may distinguish between paroxysmal, persistent and permanent (long-standing) AF, which can further assist management or 'control' strategies. For example, a history of intermittent palpitations associated with documented AF (see investigations) may suggest a diagnosis of paroxysmal AF, where the episodes are generally self-terminating and thus the main objective of management is the prevention of paroxysms and long-term maintenance of sinus rhythm, with appropriate antithrombotic therapy. In sustained AF, the objective of management is either cardioversion to sinus rhythm (persistent AF) or heart rate control with appropriate antithrombotic therapy (permanent AF).

Atrial fibrillation - diagnosis and assessment

- **History and clinical features, e.g. paroxysmal atrial fibrillation.**
- **Document the arrhythmia eg. with a 24-hour tape or cardiomemo, if required.**
- **Echocardiography, especially in young patients.**
- **Exercise testing, if ischaemic heart disease. (Caution with interpretation if digoxin also taken.)**

INVESTIGATIONS

A full blood count is useful, especially when antithrombotic therapy is being considered. Serum levels of urea and electrolytes are relevant for consideration of some drug therapies (for example, a reduced dose of digoxin in renal impairment or of ACE inhibitors for associated heart failure). Thyroid function should be measured in all patients with AF, even if there are no symptoms suggestive of thyrotoxicosis: subclinical thyroid disease is often present in the elderly and AF may be the first presentation.

A chest X-ray may occasionally be useful in patients with AF. It can give information on heart size and the presence of heart failure, intrathoracic pathology or even pericardial disease; in the young patient with AF, the chest X-ray may provide a clue to congenital heart disease, such

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as atrial septal defect.

It is important that the arrhythmia should be documented before the initiation of any treatment, ideally with a 12-lead 'standard' ECG. The ECG may also provide a clue to the aetiology or electrophysiological features that may have caused the AF, for example, the presence of prior myocardial infarction, left ventricular hypertrophy or pre-excitation syndromes (such as the delta wave in Wolff-Parkinson-White syndrome). If symptoms are intermittent and are suggestive of paroxysmal AF, a 24-hour ambulatory ECG should provide the diagnosis if they occur on a daily basis. However, if symptoms occur less frequently, a patient-activated event recorder ('Cardiomemo') would be far more likely to be effective. Exercise testing may occasionally be needed in order to clarify the severity of underlying cardiac ischaemia, although caution in interpretation of the ST segments may be needed in patients taking digoxin or if left ventricular hypertrophy is present.

Most cardiologists would request a transthoracic echocardiogram for the initial evaluation of most patients with AF, to establish the presence of structural heart disease (including valvular abnormalities, congenital anomalies, chamber dimensions, pericardial thickening or effusions) and ventricular function. Although transthoracic echocardiography is adequate for assessing chamber size, the detection of atrial thrombi or the assessment of left atrial appendage anatomy and/or function requires transoesophageal echocardiography (TOE), especially if a prosthetic mitral valve is present or when transthoracic imaging is inadequate. Recently, TOE has been employed to guide cardioversion of AF, by simplifying and shortening anticoagulation regimens in patients where left atrial thrombi have been excluded.

Invasive electrophysiologic studies usually have a limited role in the routine evaluation of patients with AF, and should be reserved for those patients with associated electrophysiological abnormalities (including pre-excitation, sinus node dysfunction, etc.) who could potentially benefit from the investigation and a curative electrophysiological procedure.

Usefulness of echocardiography in patients with atrial fibrillation

- **Refining thromboembolic risk stratification in patients unsuitable for cardioversion (Echocardiography may help determine which patients require warfarin or aspirin)**
- **To identify patients suitable for consideration of cardioversion to sinus rhythm**
- **To help classify those patients with 'lone' atrial fibrillation**
- **Helpful in the diagnosis of patients with congenital heart disease, such as an atrial septal defect.**
- *(particularly transoesophageal echocardiography)* **Helpful in excluding intracardiac thrombus, especially in patients with atrial fibrillation and stroke or thromboembolism, and possibly, pre-cardioversion.**

Atrial fibrillation - 'standard investigations'

Blood tests
- **Full Blood Count - especially when anticoagulants considered.**
- **Urea and electrolytes - baseline, and for consideration of drug therapy (e.g. reduced dose of digoxin in renal impairment).**
- **Thyroid function tests.**

ECG and Ambulatory ECG recording
- **12-lead ECG.**
- **Consider 24-hour Holter monitor - if patient presents with syncope, and paroxysmal atrial fibrillation or if sick sinus syndrome suspected.**
- **Consider Cardiomemo - if symptoms only intermittent and infrequent.**

Chest X-ray

Echocardiography
- **Standard trans-throracic echocardiography and Doppler.**
- **Consider transoesophogeal echocardiography - if prosthetic mitral valve *in situ*, endocarditis or atrial thrombi suspected.**

MANAGEMENT

The objectives of management of the patient with AF are largely dependent upon the type of patient and the variety of AF, whether paroxysmal, persistent or permanent. In most patients, consideration of antithrombotic therapy is necessary, although in a 60-year-old woman, long-term prophylactic anticoagulation would not be needed in the absence of risk factors (such as previous cerebrovascular events, structural heart disease, etc) unless cardioversion is being considered.

Paroxysmal AF

If the patient has paroxysmal AF, the aims of management are to control symptoms due to paroxysms of AF and to prevent thromboembolic complications. Where relevant, general measures should always be considered, for example the withdrawal of caffeine or alcohol, if these have been identified as precipitants, and consideration of associated conditions which may benefit from atrial pacing, for example, sick sinus syndrome. If a patient is experiencing only mild and infrequent symptoms, it may be possible to avoid antiarrhythmic drugs with their potential for toxicity. Many patients with paroxysmal AF will have asymptomatic paroxysms, but there is increasing evidence that frequent, uncontrolled paroxysms of fast AF may lead to impairment of cardiac function (the so-called 'tachycardia-induced cardiomyopathy') and a higher progression to sustained AF.[1]

Class I and Class III antiarrhythmic drugs are appropriate choices for patients with paroxysmal AF. The class IC antiarrhythmics, flecainide and propafenone, have an antiarrhythmic efficacy similar to the Class 1A agents, but are usually better tolerated due to less extracardiac toxicity. However, Class I agents should be avoided in the patients with poor cardiac function. Furthermore, interactions with drugs that prolong the QT interval (some antihistiminics,

tricyclic antidepressants, some macrolide antibiotics, etc.) and electrolyte abnormalities (hypokalaemia, hypomagnesaemia) will cause proarrhythmia, especially polymorphic ventricular tachycardia (*torsades des pointes*).[2]

Sotalol, another commonly prescribed drug, combines both Class II (beta blockade) and Class III antiarrhythmic effects, although at the low doses (<160mg/day) commonly used in the United Kingdom, much of its activity is more likely to related to its beta-blocking activity.[3] Thus, commonly used beta-blockers, such as atenolol or metoprolol, have been prescribed as alternatives to sotalol, especially if paroxysmal AF is related to an adrenergic stimulus (stress, exercise, alcohol, etc.), thus avoiding the potential toxicity associated with sotalol. Amiodarone has potentially serious, albeit relatively rare, side-effects but is of particular value in paroxysmal AF for treating patients who have proved to be refractory to other measures, the elderly and those with poor left ventricular function. In paroxysmal AF, low doses may be effective with little risk of side-effects or proarrhythmia.[2]

Digoxin should be avoided in paroxysmal AF as the evidence would suggest that this drug makes paroxysmal AF worse. Indeed, retrospective analyses have suggested that paroxysms of AF are more frequent and last longer, and the initial heart rate appears no better controlled whether or not digoxin is being taken.[4] The mechanism for this is unclear but digoxin increases vagal tone, moderating the speed of atrio-ventricular conduction, and also reduces the atrial refractory period. This latter property may paradoxically render the atrium more susceptible to AF and may reduce or even prevent the chance of reversion to sinus rhythm. However a recent double-blind placebo controlled trial of digoxin in symptomatic paroxysmal AF found a small effect in reducing the frequency of symptomatic AF episodes, probably due to a reduction in ventricular rate or irregularity rather than to an antiarrhythmic action.[5] Rate-limiting calcium channel blockers and beta blockers may help control ventricular rate in paroxysmal AF, but also may not change the frequency of episodes.

Antithrombotic therapy should be considered in patients with paroxysmal AF, since evidence from the AF investigators' meta-analysis[6] suggests that patients with paroxysmal AF have a stroke rate similar to patients with chronic AF. Nevertheless, there have been no definitive trials looking specifically at the benefits of antithrombotic therapy in patients with paroxysmal AF *per se*, and the range of thromboembolic risk in such patients are likely to be wide, as the patient with one short paroxysm once a year is likely to be at much less risk when compared to a patient with paroxysmal AF who is having daily lengthy paroxysms. However, it would seem reasonable to consider antithrombotic therapy based on patients' co-morbidity, age and the presence of structural heart disease.[6] Indeed, patients with paroxysmal AF who have risk factors (hypertension, diabetes, heart failure, cardiac impairment, etc) for stroke and thromboembolism, as shown in the AF investigators' meta-analysis[6] should be started on antithrombotic therapy.

Persistent AF

In persistent AF, the management objective for these patients is cardioversion. Persistent AF can be related to paroxysmal AF, where an episode lasts more than 48 hours and spontaneous conversion to sinus rhythm does not occur; that time window presents the duration beyond which formal anticoagulation should be taken prior to cardioversion. In these patients, appropriate use of antiarrhythmic therapy to maintain sinus rhythm, and anticoagulation to reduce the risk of thromboembolism post-cardioversion, should be considered. The patient with acute AF and haemodynamic collapse or those who are highly symptomatic will require urgent or early cardioversion. It should be noted that a high percentage of episodes of new-onset AF will spontaneously terminate within 24 and 48 hours even without specific therapy.

Potential benefits from cardioversion of AF to sinus rhythm include: improved haemodynamics at rest and with exercise, improvement of symptoms and a possible reduction in the risk of stroke and the need for anticoagulation. Nevertheless, if the underlying aetiology or trigger continue to exert an effect on the patient with persistent AF, attempts at cardioversion may be unsuccessful; treatment of the precipitating factor, such as a fever or thyrotoxicosis, may result in spontaneous reversion to sinus rhythm, or increase the chances of successful cardioversion. Predictors of refractoriness to cardioversion or unsuccessful maintenance of sinus rhythm include the following: age, duration of arrhythmia, the presence of uncontrolled hypertension, structural heart disease and the presence of other systemic diseases. Duration of AF is probably the most important predictor of successful cardioversion and the subsequent long-term maintenance of sinus rhythm.

Cardioversion may be performed by electrical or pharmacological methods. External electrical cardioversion, using a synchronised DC shock, is effective in restoring sinus rhythm, but its efficacy is highly influenced by the underlying aetiology, ranging from 20 to 90%. The highest recorded success rates for cardioversion are seen in patients with AF secondary to hyperthyroidism, and the lowest rates are seen in patients with severe mitral regurgitation. The recommended initial energy for electrical cardioversion is 200 joules and >75% of patients are successfully cardioverted with this energy. Higher energies (300-360 joules) are needed if 200 joules' shocks are unsuccessful to restore sinus rhythm. Previous enthusiasm for the superiority of antero-posterior electrode pad positions for cardioversion have been dampened by the recent randomised trial by Mathew *et al*,[7] where cardioversion success rate and energy requirements were similar in the antero-anterior and antero-posterior positions. An alternative to electrical cardioversion is pharmacological (or chemical) cardioversion, especially for patients with recent onset AF. In general, drugs that are usually prescribed for paroxysmal AF or to maintain sinus rhythm after electrical cardioversion are also effective for pharmacological cardioversion, such as the Class I and III agents. Digoxin is no better than placebo in cardioversion of AF.

It is important to prevent thromboembolism after cardioversion of AF, the American College of Chest Physicians has published a set of recommendations regarding anticoagulation.[8] (Table 1.)

Permanent AF

In permanent AF the arrhythmia has been present for a long time, cardioversion has not been indicated, or one or several attempts at cardioversion has failed to restore sinus rhythm. The objectives of management in such patients are therefore heart rate control and antithrombotic therapy.

TABLE 1
Recommendations for anticoagulation for cardioversion.*

- the administration of warfarin for three weeks before elective cardioversion of AF of ≥ 48 hours' duration; continuation of warfarin therapy for four weeks after cardioversion;
- administration of intravenous heparin followed by warfarin if cardioversion cannot be postponed for 3 weeks; and
- treat atrial flutter similarly
- no anticoagulant therapy for SVT or atrial fibrillation of <48 hours' duration

*Based on the 5th ACCP Consensus Conference on AntiThrombotic Therapy.[8]

The superiority of a strategy of heart rate control and antithrombotic therapy ('rate control') over a strategy of aggressive cardioversion ('rhythm control') is still unproven, and is being tested in several large randomised trials, the largest of which is the AFFIRM study.[9] Heart rate control can be achieved by pharmacological and non-pharmacological methods.

Digoxin is commonly used for heart rate control, but is less likely to control the ventricular rate during pyrexia, stress, exercise (when vagal tone is low and sympathetic tone is high), etc. It also has little or no ability to terminate the arrhythmia or to maintain sinus rhythm post-cardioversion. The onset of rate control with digoxin is often delayed for several hours even with intravenous therapy, and this slow onset of action may be undesirable in acute situations.[10] Many patients usually require the addition of a beta-blocker or rate-limiting calcium channel blocker, (verapamil or diltiazem) for optimal rate control. If pharmacological measures fail to prevent recurrence of AF and/or control the ventricular rate, non-pharmacological strategies should be considered.[11] These include pacemakers, atrial defibrillators, catheter ablation (for either rate control or prevention of AF) and surgery.

The role of antithrombotic therapy in patients with AF has been well-established in recent clinical trials. In the pooled meta-analysis by the AF Investigators of the five initial primary prevention trials, there was an overall stoke risk reduction of 68% (95% confidence intervals 50% to 79%) with warfarin.[6] Aspirin use had no significant effect on severe strokes or mortality, although in the pooled analysis, aspirin did reduce strokes by 21% (95% CI 0-37%, p=0.05) and the combined outcome of stroke, embolism or death by 28%.[12]

Despite the compelling evidence of the benefits of stroke reduction in AF, antithrombotic therapy continues to be under-utilised. One survey of management options amongst consultant physicians in the United Kingdom reported marked disparity in treatment between cardiologists and non-cardiologists, with more cardiologists considering anticoagulation and cardioversion.[13] Other risk factors, such as poor therapy compliance, difficulty in monitoring of patients in remote areas, recurrent falls, cognitive impairment, history of gastrointestinal bleeding, active duodenal ulceration, alcoholism and risk of interaction with multiple drug therapies, need to be evaluated carefully before anticoagulation is considered, especially in the elderly.

One option to improve management of these patients with AF may be to increase the involvement of general practitioners. Indeed, general practitioners can assist in risk stratification of patients with AF, and the identification of high-risk patients with AF who would benefit most from anticoagulation. In addition, anticoagulant monitoring by general practitioners is often much better than that in hospital clinics.

Based upon largely clinical criteria from the pooled analysis of the AF Investigators, most patients with AF can be classified into high, moderate and low-risk patients.[14] (Table 2.) The most recent meta-analysis from the AF Investigators[15] of 1,066 patients from three clinical trials, suggested that echocardiography refined this clinical risk stratification scheme, with only left ventricular systolic dysfunction via two-dimensional transthoracic echocardiography independently predicting stroke risk in patients with AF. Contrary to previous reports, an isolated left atrium on the echocardiogram was not an independant risk factor for increased stroke risk on multivariate analysis. Echocardiography is therefore useful in the small group of patients who have a low risk of stroke according to clinical risk factors. Only rarely would clinicians need to proceed to TOE to assist risk stratification, but in the SPAF-III TOE substudy, stroke and thrombembolism were correlated with

TABLE 2
Risk stratification and anticoagulation in non-valvular atrial fibrillation (NVAF). (Adapted from reference 14.)

ASSESS RISK:

1. High risk (annual risk of CVA = 8-12%)

- All patients with NRAF and previous TIA or CVA.
- All patients aged 75 and over with NRAF and diabetes and/or hypertension.
- All patients with NRAF and clinical evidence of valve disease, heart failure, thyroid disease and/or impaired LV function on echocardiography.*

2. Moderate Risk (annual risk of CVA = 4%)

- All patients under 65 with NRAF and clinical risk factors: diabetes, hypertension, peripheral arterial disease, ischaemic heart disease.
- All patients over 65 with NRAF who have not been identified in high-risk group.

3. Low Risk (annual risk of CVA = 1%)

- All other patients under 65 with NRAF with no history of embolism, hypertension, diabetes or other clinical risk factors.

*Echocardiogram - not needed for routine risk assessment but refines clinical risk stratification in cases of impaired LV function and valve disease (see **1.** above); a large left atrium *per se* is not an independent risk factor on multivariate analysis.

Reassess Risk Factors At Regular Intervals

TREATMENT:

- **High Risk:** use WARFARIN (target INR 2.0-3.0) if no contraindications and possible in practice.
- **Moderate Risk:** Either WARFARIN or ASPIRIN. In view of insufficient clearcut evidence, treatment may be decided on individual cases. Referral and ECHOCARDIOGRAPHY may help.
- **Low Risk:** use ASPIRIN 75-300 mg daily

dense spontaneous echocontrast, left atrial appendage thrombus and complex aortic plaques.[16]

Thus, in our 60-year-old female patient with AF, anticoagulation would be needed in the presence of previous clinical risk factors, such as cerebrovascular events or valvular heart disease, or if moderate to severe left ventricular impairment is present on echocardiography.

CONCLUSION

AF is the most common sustained arrhythmia in adult populations. Although AF *per se* is usually not life-threatening, it leads to significant patient morbidity, economic costs, and contributes to stoke and heart failure. Clinical decisions in patients with AF are often difficult but a useful approach to the management of such patients can be based on their clinical presentation, and the clearly-defined objectives of subsequent therapeutic decisions.

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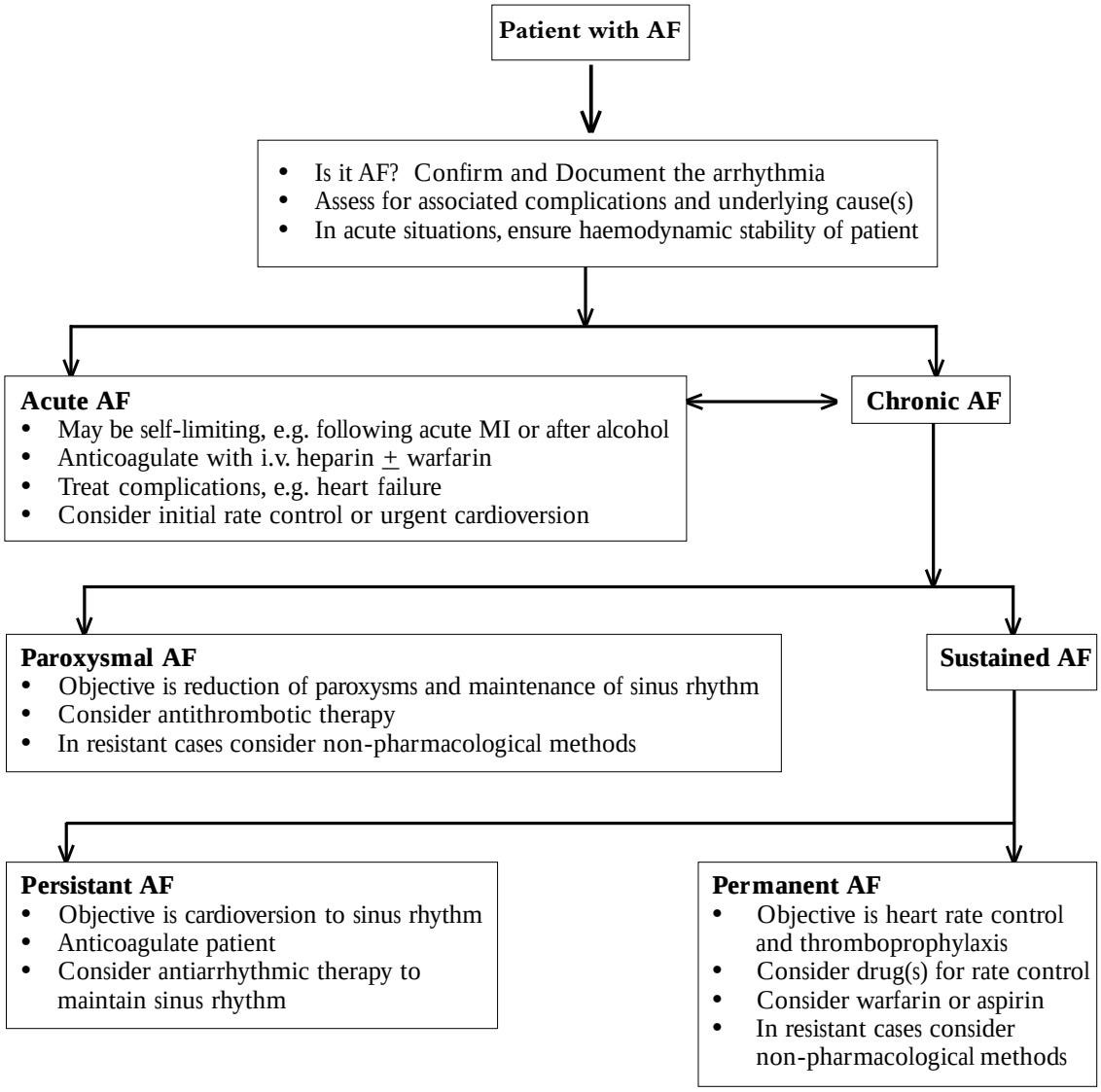
ATRIAL FIBRILLATION MANAGEMENT FLOW CHART



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