

These guidelines have been withdrawn

MOH clinical practice guidelines are considered withdrawn five years after publication unless otherwise specified in individual guidelines. Users should keep in mind that evidence-based guidelines are only as current as the evidence that supports them and new evidence can supersede recommendations made in the guidelines.

CLINICAL PRACTICE GUIDELINES

Management of Atrial Fibrillation



Singapore
Heart
Foundation
Your Heart We Care



Singapore Cardiac
Society



Clinical Neuroscience
Society Singapore

Aug 2004



Ministry
of Health



College of Family
Physicians Singapore



Chapter of Physicians
Academy of Medicine
Singapore

National Committee
On Cardiac Care

MOH Clinical Practice Guidelines 8/2004

Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
Ia	Evidence obtained from meta-analysis of randomised controlled trials.
Ib	Evidence obtained from at least one randomised controlled trial.
IIa	Evidence obtained from at least one well-designed controlled study without randomisation.
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study.
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Grades of recommendation

Grade	Recommendation
A (evidence levels Ia, Ib)	Requires at least one randomised controlled trial, as part of the body of literature of overall good quality and consistency, addressing the specific recommendation.
B (evidence levels IIa, IIb, III)	Requires availability of well conducted clinical studies, but no randomised clinical trials on the topic of recommendation.
C (evidence level IV)	Requires evidence obtained from expert committee reports or opinions, and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL PRACTICE GUIDELINES

**Management of Atrial
Fibrillation**

MOH Clinical Practice Guidelines 8/2004

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Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

Foreword

Atrial fibrillation is the most common arrhythmia you are likely to encounter in your clinical practice. Patients may experience palpitations, dizziness, fatigue and shortness of breath – symptoms that may be debilitating for badly affected patients. Furthermore, atrial fibrillation can give rise to clot formation and a subsequent thromboembolic stroke.

The prevalence of atrial fibrillation increases with age and as our population ages, the number of patients with atrial fibrillation will increase. It is timely to publish these clinical practice guidelines on the management of atrial fibrillation.

These guidelines provide useful information on the evaluation of patients with atrial fibrillation. The three main goals of treatment of atrial fibrillation are discussed in detail: (i) control of the ventricular rate, (ii) reestablishment of sinus rhythm, and (iii) prevention of thromboembolism. Special considerations like post-operative atrial fibrillation and atrial fibrillation in patients with acute myocardial infarctions or other conditions are covered.

I am grateful to the workgroup for drafting these guidelines on an important topic. I hope you will find their work of use in your own practice.

PROFESSOR K SATKU
DIRECTOR OF MEDICAL SERVICES

Contents

	Page
Executive summary of recommendations	1
1. Introduction	2
2. Definition of AF	4
3. Clinical Presentation and Importance of AF	8
4. Evaluation of the AF patient	9
5. Management of Atrial Fibrillation	14
6. Rhythm Control	16
7. Maintenance of Sinus Rhythm	23
8. Rate Control during AF	28
9. Prevention of Thromboembolic Complication	34
10. Special Considerations	40
11. Clinical Quality Improvement	46
References	47
Self-assessment (MCQs)	57
Workgroup members	61

Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated. Where differences exist between this executive summary and the main text, please take reference from the main text.

A Rate control with anticoagulation should be the recommended strategy for most patients with atrial fibrillation (AF). Specific drug classes that should be used as part of this strategy include beta-blockers, non-dihydropyridine calcium channel blockers, and digoxin. (pg 15 and 28-30)

Grade A, Level Ia

C Synchronized direct current cardioversion is recommended for termination of rapid AF that renders the patient hemodynamically unstable. (pg 18)

Grade C, Level IV

A Adequate anticoagulation is needed if the AF has lasted > 48 hours. A delayed strategy of adequate anticoagulation for 3-4 weeks prior and 4 weeks post cardioversion or an early strategy using transesophageal guidance to exclude intracardiac thrombi followed by acute anticoagulation and cardioversion and post cardioversion anticoagulation may be used. (pg 16)

Grade A, Level Ib

A & C All patients with AF should be risk stratified for risk of thromboembolism and given the appropriate antithrombotic strategy. Patients with AF and additional risk factors should receive anticoagulation with warfarin to an adjusted INR of 2-3. Older patients (> 75 years old) may have a lower target INR of 1.6-2.5. Lone AF patients with no risk factor who are young may be given aspirin only. (pg 35-37)

**Grade A, Level Ia
and Grade C, Level IV**

B Rhythm control may be appropriate for patients who are symptomatic especially in those with no significant underlying heart disease. Conversion to sinus rhythm may be achieved by electrical or pharmacologic means. (pg 15)

Grade B, Level III

1 Introduction

1.1 Background Information

Atrial fibrillation (AF) is the most common sustained arrhythmia.

AF may be associated with structural or ischemic heart disease but a substantial proportion may have no underlying heart disease detectable clinically (Lone AF). The most important reason for treating AF is that, if untreated, it can result in hemodynamic impairment and thromboembolic events. These can occur even in the relatively asymptomatic patient.

Atrial flutter is a much less common arrhythmia compared to AF. The rhythm may alternate between AF and atrial flutter, AF may trigger atrial flutter, or atrial flutter may degenerate into AF. However its etiology and management is similar.

Figure 1 ECG showing AF with a rapid ventricular response

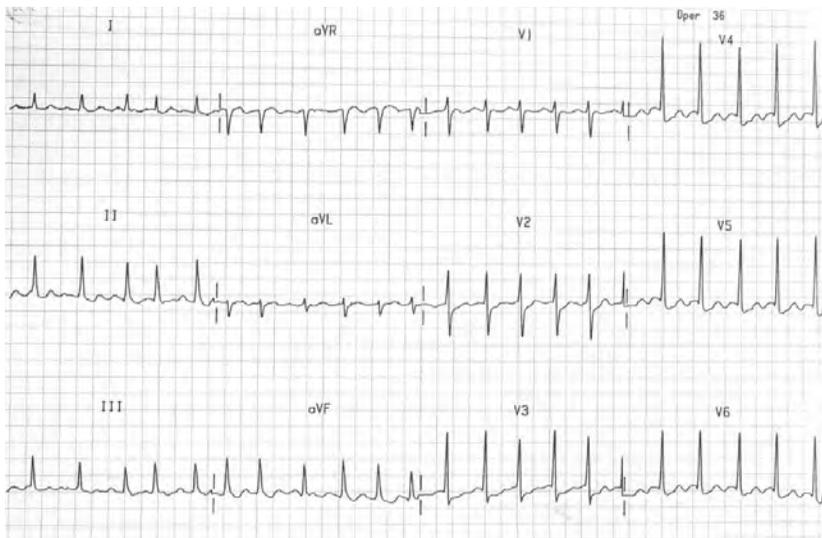


Figure 2 ECG showing atrial flutter with 2:1 ventricular response



1.2 Development of Guidelines

These guidelines have been produced by a committee of cardiologists, cardiothoracic surgeons, neurologists and a family physician appointed by the Ministry of Health. They were developed using the best available current evidence and expert opinion.

1.3 Review of Guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supercede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review 3 to 5 years after publication, or if new evidence appears that requires substantive changes to the recommendations.

2 Definition of AF

2.1 Definition

AF is a supraventricular tachyarrhythmia characterized by irregular, disorganized electrical activity of the atrium during which P waves on the ECG are absent and the baseline consists of irregular waveforms that continuously change shape, duration, amplitude and direction. In the absence of advanced or complete atrioventricular block, the resulting ventricular response is frequently rapid and irregular.

2.2 Classification of AF

There are many possible classifications of AF but a recent International Consensus on nomenclature and classification of AF has suggested the following:¹

First detected episode of AF

This is the first time AF is detected. The patient may or may not be symptomatic and the duration of the episode may be uncertain. The importance of recognizing this is that if the episode is brief or related to a precipitating factor, long-term prophylactic treatment may not be necessary.

Acute AF

Acute AF is AF with onset within 24-48 hrs and is distinguished by a high chance of successful cardioversion, either spontaneously or using antiarrhythmic drugs. Also anticoagulation may not be necessary if the onset of the AF can be accurately determined.

Paroxysmal AF

Paroxysmal AF is characterized by recurrent episodes of AF alternating with sinus rhythm. The hallmark of paroxysmal AF is that most of the episodes terminate spontaneously ≤ 7 days.

Persistent AF

In persistent AF, the atria continue to fibrillate for over 48 hrs or until cardioversion is performed. The distinction between persistent and paroxysmal AF is not absolute but generally persistent AF has persisted for more than 7 days.

Permanent AF

In permanent AF attempts at restoration of sinus rhythm have failed or the AF has lasted for more than 1 year and the probability of successful cardioversion is considered so low that no attempt is made and the patient is left in AF.

2.3 Epidemiology

The prevalence of AF increases with age and as our population ages, the number of patients with AF will increase rapidly. At present AF occurs in about 0.5-1% of the general population. It has been estimated that the number of patients with AF will increase 2.5-fold over the next 50 years.² Its prevalence increases with age and occurs in 0.1% of patients < 55 years old, 5% of patients \geq 65 years old and about 10% of patients \geq 80 years old.²

Risk for developing atrial fibrillation

In the Framingham study,^{3,4} the lifetime risk of AF was found to be 1 out of 4 for men and 1 out of 5 for women. The odds ratio of AF for each decade of advancing age was 2.1 for men and 2.2 for women ($p < 0.0001$). In addition, diabetes, hypertension, congestive heart failure and valve disease were all significantly associated with risk for AF in both sexes. Myocardial infarction was significantly associated with the development of AF in men.

2.4 Etiology of atrial fibrillation

The etiologic causes of AF are shown in Table 1. AF in the elderly may be related to the sick sinus syndrome. Lone AF is AF occurring in the absence of any known etiology or underlying structural heart disease.

Table 1 Etiologic causes of AF

Cardiac

Common

- Hypertension
- Ischemic heart disease & acute myocardial infarction
- Valvular heart disease
- Sick sinus syndrome
- Lone AF
- Cardiomyopathy
- Post cardiac surgery

Less common

- Pericarditis & myocarditis
- Cor pulmonale
- Preexcitation syndrome
- Tachycardia induced tachycardia (e.g. PSVT, atrial flutter)
- Atrial septal defect
- Acute pulmonary embolism

Non-cardiac

- Alcohol
- Thyrotoxicosis
- Diabetes mellitus
- Sepsis, especially pneumonia in the elderly
- Other intrathoracic abnormalities (e.g. pleural effusion)

The ALFA⁵ study showed a changing pattern of the underlying disease responsible for AF. The most common underlying disease was hypertension, found in 60% of AF cases, followed by coronary artery disease (16%), cardiomyopathy (dilated or hypertrophic, 9%), and valvular heart disease, particularly mitral stenosis and mitral regurgitation (15%). Hyperthyroidism accounted for only 3% of all cases of AF and 30% of the total number of AF cases had history of congestive heart failure. Of particular interest, 29% of all cases had idiopathic AF, and half of the patients in the paroxysmal AF group had no identifiable heart disease.

2.5 Pathophysiology of AF

The pathophysiology of AF is now believed to be related to the electrical trigger that initiates or drives the arrhythmia and an abnormal myocardial substrate that allows AF to be maintained and perpetuated. A spectrum of triggers may initiate AF, ranging from premature atrial ectopics, atrial flutter to atrial tachycardia. Ectopic atrial foci, frequently located in the pulmonary veins, have been shown to trigger AF in up to 80% of cases.⁶

However in many patients for AF to persist, the atrial tissue must be remodeled to allow the propagation of multiple wavelets of electrical depolarization throughout the atria. Fibrosis, hypertrophy, fatty infiltration and perhaps ischemia of atrial tissue may allow for abnormal atrial electrical activation and the maintenance of AF wavelets.

3 Clinical presentation and importance of AF

Most patients with AF present with symptoms of palpitations, chest pain, dyspnoea, fatigue, lightheadedness or rarely syncope. Some may present with complications of AF such as heart failure or stroke. The symptomatic presentation may be related to the ventricular rate, as rapid AF may present with palpitations, while slow AF may present with giddiness and syncope. The perception of symptoms is however poorly understood, as the same ventricular rate may cause one patient only to be dimly aware of “something wrong” while another may experience profound discomfort. Occasionally chest pain may be the only presentation.

The AF may also be asymptomatic and as much as 25% of patients may have no symptoms.⁷ Such asymptomatic episodes, however, can still result in adverse atrial remodeling and increase the risk for thromboembolic stroke.

There is increasing awareness that AF is not entirely a benign arrhythmia and is associated with significant morbidity and mortality. It may cause disabling symptoms of decreased cardiac output (e.g. malaise, effort intolerance). If associated with a prolonged uncontrolled ventricular rate, it can result in aggravation of myocardial ischemia and heart failure due to tachycardia induced cardiomyopathy. More importantly, AF is associated with an increased risk of systemic thromboembolism and stroke, even in asymptomatic patients. The annual incidence of ischemic stroke in patients with nonvalvular AF is 5%, which is two to seven times higher than the incidence in the general population. Studies have also suggested an increased risk for ventricular arrhythmias and doubling of mortality in patients with AF.⁸

AF is also of clinical importance because it may signify underlying heart disease. It is hence important to exclude underlying structural heart disease, especially hypertensive, valvular and ischemic heart disease. Finally, AF is an important cause for hospitalisation and health care expenditure. In Singapore, 2.9% of patients admitted acutely to the National Heart Centre were found to have AF.

4 Evaluation of the AF patient

All patients with AF, whether symptomatic or asymptomatic, need to be further evaluated. The initial evaluation of a patient with AF must include the following:

1. Confirming the diagnosis of AF
2. Classifying the type of AF
3. Identifying factors (both reversible and irreversible) that contribute to or cause AF
4. Looking for underlying structural or ischemic heart disease and estimating left ventricular function
5. Establishing the risk of thromboembolism and additional adverse outcomes
6. Assessing adequacy of control of ventricular rate during AF
7. Assessing the need to convert to sinus rhythm
8. Deciding on the most effective treatment strategy

The initial evaluation of a patient with suspected AF is to confirm the diagnosis with a 12 lead ECG.⁹⁻¹⁰ The episodes may, however, be transient and documentation with ECG during symptoms, transtelephonic ECG monitoring or 24-hour ambulatory Holter ECG recordings may be needed.

Once AF is confirmed it is important to determine the onset and duration of the arrhythmia, frequency of attacks and define the associated cardiac and non-cardiac conditions. The pattern and factors associated with the AF allows us to classify the AF and determine how we should manage the patient. Potential non-cardiac precipitants of AF include thyrotoxicosis, sepsis especially pneumonia in the elderly, and electrolyte disturbances. These triggers should be sought during history taking. Alcohol consumption, anxiety, excessive caffeine intake and exercise can precipitate AF. Similarly vagally-mediated episodes may be suggested if the attacks occur during sleep, at rest, after a large meal or after being started on drugs such as beta-blockers.

Patients who present with AF should also undergo thorough evaluation to look for possible underlying heart disease such as hypertension, ischemic heart disease, valvular heart disease, and cardiomyopathy. Patients are defined as having lone AF, when there is no structural

heart disease, hypertension, diabetes or previous stroke. This is a diagnosis of exclusion and requires completely normal blood tests and a normal echocardiogram. Patients with lone AF are usually younger and are likely to present with paroxysmal rather than persistent or chronic AF.

The next important step is to determine the risk for possible complications from AF. A history of hypertension, diabetes, advanced age, heart failure and previous thromboembolic events are important as their presence identify patients at high risk of thromboembolic events. Patients with rapid AF may progress to heart failure and tachycardia induced cardiomyopathy.

The physical examination of a patient with AF is directed towards confirming the rhythm and looking for signs of associated conditions and complications of AF. The pulse is irregularly irregular and usually rapid but can be slow especially if on drugs or associated with the sick sinus syndrome. Other physical findings include a first heart sound of varying intensity, absence of “a” wave in the jugular venous pressure and pulse deficit. The blood pressure must be measured but systolic measurements may be variable. Physical signs for the etiology of AF also include looking for a goiter, signs of thyrotoxicosis and auscultation of the heart for valvular heart disease or cardiomyopathy. Complications to look for include heart failure and previous stroke.

4.1 Basic Investigations

The most basic investigation is an ECG. This is needed to confirm the diagnosis of AF. The ECG documentation is usually obtained by a standard 12-lead ECG or through a rhythm strip obtained from Holter monitoring or transtelephonic ECG recordings.

A chest X-ray is also useful. It provides information about cardiac chambers sizes, presence of heart failure and assessment of pulmonary pathology.

Hyperthyroidism should be excluded and thus the thyroid function test should be done in all patients with new onset AF even in those patients without symptoms or signs of hyperthyroidism. Serum electrolytes and full blood count should be routinely done.

All patients with AF should at least have one baseline transthoracic echocardiogram. This test is very useful for documentation of structural heart disease, assessment of cardiac chamber sizes, in particular left atrial and left ventricular size and function. Structural heart disease due to cardiomyopathies, pericardial or valvular heart disease and intracardiac shunt can all be diagnosed with this test. The information obtained from the echocardiogram can help decide whether to cardiovert, control the ventricular rate, anticoagulate or use antiarrhythmic drugs for the patient with AF. The presence of left atrial thrombus is often sought but the ability of this test to detect thrombus is very low.

4.2 Additional Investigations

Ambulatory ECG monitoring

In patients who have frequent episodes of palpitations, 24-hour Holter monitoring or transtelephonic event recorders may be useful to confirm the diagnosis of paroxysmal AF.

In addition, 24-hour ambulatory Holter ECG may be useful for:

- Quantifying the frequency and duration of symptomatic and asymptomatic AF episodes
- Looking for associated sinus node dysfunction or sick sinus syndrome
- Assessing adequacy of rhythm or rate control in patients with AF
- Assessing time of onset of AF (e.g. at night in vagally-mediated AF)
- Identifying patients with frequent atrial ectopics and nonsustained atrial tachycardia who may be suitable for curative therapy with catheter ablation

Transtelephonic event recorders

This may be useful when the AF episodes are infrequent and brief. It is also useful for monitoring asymptomatic episodes.

Exercise stress test

In patients who have history of AF precipitated by exertion, the exercise stress test may be useful. The exercise stress test should also be done

if there is any suspicion that the patient has ischemic heart disease or that myocardial ischaemia has precipitated the arrhythmia. Hence, in older patients (≥ 40 years old) and patients with significant coronary risk factors, exercise stress test should be routinely performed. In addition, exercise testing can be used to explore the safety of using certain antiarrhythmic drugs (especially class Ic antiarrhythmic drugs) and to assess the rate control during exercise. A routine coronary angiogram is, however, not indicated unless the stress test is positive or the pretest likelihood for coronary artery disease is very high.

Transesophageal echocardiogram (TEE)

Transesophageal echocardiogram is of greatest use in establishing the risk for embolic stroke, most notably before cardioversion in patients who present with AF.¹¹ This technique provides superior visualization of left atrial structures, in particular, in the detection of left atrial appendage thrombus compared to transthoracic echocardiogram. Additional information obtained from the TEE such as left atrial and left atrial appendage spontaneous echo contrast (smoke), left atrial appendage flow velocity, and aortic plaque can be used to further stratify the stroke risk. At present its main use is to screen for left atrial thrombus before elective cardioversion in patients who did not receive the conventional 3 weeks oral anticoagulation with warfarin or in whom anticoagulation is contraindicated.

Electrophysiological study (EPS)

Electrophysiological study is rarely needed for establishment of diagnosis. However it can be considered in patients with history of syncope where the EPS can be used to exclude sick sinus syndrome. In patients with rapid preexcited AF associated with the Wolff-Parkinson-White syndrome, catheter ablation can cure the patients and eliminate the risk for sudden death. It can also define specific types of focal AF (especially those in the pulmonary veins) that are amenable to curative therapy with catheter ablation.

Table 2 Clinical evaluation

Confirm diagnosis of AF
Determine pattern of AF attacks
Determine underlying etiology or precipitating factors
Determine risk for complications from AF

BASIC EVALUATION

History and physical examination
Electrocardiogram (ECG)
Chest X-ray (CXR)
Full blood count
Serum electrolytes
Thyroid function test
Transthoracic 2D – echocardiogram

ADDITIONAL INVESTIGATIONS

Holter monitoring
Transtelephonic event recorder
Exercise stress testing
Transoesophageal echocardiogram
Electrophysiological study

5 Management of Atrial Fibrillation

The management of AF is influenced by the clinical presentation, duration of the AF episode, underlying medical history or heart disease, response to previous therapy and risk of complications from AF.

The treatment has three main goals. These are (i) control the ventricular rate (ii) reestablish sinus rhythm and (iii) prevent thromboembolism.

Management strategies available include:

- Observe and wait for spontaneous resolution
- Immediate cardioversion in the hemodynamically unstable patient
- Anticoagulation to prevent thromboembolism
- Rate control with rate limiting drugs
- Rhythm control by conversion and maintenance of sinus rhythm with antiarrhythmic drugs
- Hybrid therapy with drugs and nonpharmacological therapies such as pacing, defibrillator or catheter ablation

Patients who present with the first attack of AF not associated with severe symptoms or hemodynamic instability and terminating spontaneously may not require any long-term prophylactic treatment, unless they have significant risk factors for thromboembolism.

Patients who present with hemodynamically unstable AF, however, require immediate treatment with electrical cardioversion.

More frequently patients have history of recurrent paroxysmal AF. In this group of patients the immediate priority will be rate control and to decide if conversion back to sinus rhythm is possible or necessary. The most important issue remains the assessment for the risk of thromboembolism and careful risk stratification is vital.

Precipitating factors when present need to be treated accordingly. For example, AF which is precipitated by exercise may be treated with beta blockers while AF occurring at night or during rest may be vagally-mediated and beta blockers should be avoided. Similarly if alcohol is a precipitating factor, this must be stopped. Thyrotoxicosis should always be looked for and treated appropriately.

Long-term anticoagulation should be considered in all patients with AF regardless of presentation of the AF if risk factors for embolic complications are present.

In some cases when drug therapy alone is unable to achieve rate control or maintain sinus rhythm, non-pharmacological therapies with pacemakers, defibrillators or catheter ablation should be considered.

In patients who have bradyarrhythmias associated with AF, pacemakers are needed. The use of dual chamber pacemakers have been shown to reduce the risk of recurrent AF and thromboembolism. Newer pacemakers with pacing prevention algorithms and anti-tachycardia pacing, dual site pacing and biatrial pacing may also be useful.

5.1 Rhythm control versus heart-rate control

In patients with AF, restoration and maintenance of sinus rhythm can improve symptoms, possibly reduce the risk of thromboembolic stroke and correct the unfavourable remodeling process associated with arrhythmia (e.g. heart failure, cardiomyopathy).¹²⁻¹⁴ Treatment strategy of heart-rate control, however, has now been shown to be at least as effective as the rhythm-control strategy^{12,13,15} in reducing morbidity and mortality. The AFFIRM trial¹⁰ showed no difference in stroke or mortality when rhythm control was compared to rate control. The most important limitation with the rhythm control strategy using presently available antiarrhythmic drugs is its lack of efficacy in maintaining sinus rhythm as >50% of the patients develop recurrent AF during follow-up. Moreover, antiarrhythmic drugs used to restore sinus rhythm may have significant side effects and may be even proarrhythmic and cause serious life threatening arrhythmias, while drugs used to control heart rate are generally easier and safer to use.¹⁴⁻¹⁶

A Hence rate control with chronic anticoagulation is the recommended strategy for the majority of patients with atrial fibrillation.¹⁷

Grade A, Level Ia

B Rhythm control is appropriate when based on other special considerations, such as patient's age, symptoms, exercise tolerance, and preference.¹⁷

Grade B, Level III

6 Rhythm Control

Restoring the patient to sinus rhythm through pharmacologic or electric cardioversion not only relieves symptoms but may reduce the risk of embolism (if sinus rhythm can be maintained) and cardiomyopathy. Although many patients who experience new-onset AF will spontaneously convert within 24 to 48 hours in up to 50-70% of patients, this is less likely to occur if the AF has persisted for more than a week and drugs or electrical cardioversion will be necessary. However the longer the duration of antecedent AF, the lesser the probability of a successful cardioversion. Hence restoration of sinus rhythm should be done early if it is considered the treatment of choice and provided it can be performed safely.

6.1 Anticoagulation prior to cardioversion

Patients who develop acute AF (< 48 hours) can be cardioverted (using either method) without the need for prior long-term anticoagulation. Intravenous bolus heparin is recommended prior to cardioversion, followed by continuous infusion in a dose adjusted to keep APTT at 1.5 to 2 times the reference control value. This should be followed by at least another four weeks of oral anticoagulation (keeping INR 2-3) even if the procedure is successful.

A Patients with persistent AF should be anticoagulated first for 3-4 weeks (keeping INR 2-3) prior to any attempt of cardioversion. After successful cardioversion, a further four weeks of oral anticoagulation at therapeutic range (INR 2-3) is required. An alternative approach to cardioversion in patients with persistent AF without prior oral anticoagulation is to perform transesophageal echocardiography immediately before DC cardioversion to exclude intra-atrial thrombus. When no intracardiac thrombus is visualized, DC cardioversion can be performed after intravenous heparin bolus injection and subsequent heparin infusion.¹¹

Grade A, Level Ib

Post-procedural oral anticoagulation is still recommended for further four weeks even when no intracardiac thrombus is found during the procedure. Clinical experience with the use of subcutaneous administration of low molecular weight heparin instead of the

unfractionated heparin in the above situations is promising but the data on its use is limited at this moment.¹⁴

6.2 Cardioversion

B Cardioversion in patients without hemodynamic instability, but with significant symptoms due to AF is acceptable.^{13,14}

Grade B, Level III

C Similarly, cardioversion in patients with first episode of recent onset AF and low likelihood of recurrence^{13,14,16} is also recommended.

Grade C, Level IV

i) Pharmacological cardioversion:

B Pharmacologic cardioversion can be used for patients with persistent AF of recent onset.^{14,17}

Grade B, Level III

Pharmacologic cardioversion using antiarrhythmic drugs can be successful in up to 80% of patients with persistent AF, especially when initiated within 7 days of AF onset.

Several antiarrhythmic agents have been shown to be effective in converting AF into sinus rhythm with varying efficacy. Class IC antiarrhythmics (Propafenone, Flecainide) are recommended for acute conversion of AF but can only be used in patients without ischemic heart disease, left ventricular dysfunction, congestive heart failure, or major conduction disturbances. Class IC antiarrhythmics may also cause organization of the AF into atrial flutter and the slower atrial rate can result in 1:1 AV conduction and a rapid ventricular response. Combining beta blockers, digoxin or calcium channel blockers with these agents may prevent this complication. Amiodarone is modestly effective for cardioversion and the effect may take days or weeks to occur especially if given orally. However it is considered the safest and most effective drug in patients who have underlying structural heart disease or heart failure. Long term use of amiodarone is, however, associated with significant side effects and toxicity and regular monitoring of liver and thyroid function tests (at least 6 monthly) must be done.

Dofetilide and ibutilide are newer agents that have been shown to be effective for pharmacological conversion of AF or atrial flutter. Quinidine is also effective but may provoke serious side-effects such as hypotension or Torsades de pointes. Digoxin, calcium channel blockers or beta-blockers have not been proven to be effective as agents for restoration of sinus rhythm in AF or atrial flutter, although they can be effective in controlling the ventricular rate. Sotalol while useful for rate control and maintaining sinus rhythm, has not been shown to be very effective in acutely converting AF to sinus rhythm.

Hospitalization may be required to monitor for possible serious side effects and proarrhythmia during the initial phase of pharmacological cardioversion especially in patients who have underlying structural heart disease, ischemic heart disease or a history of heart failure. Oral pulse therapy with propafenone (300 to 600 mg stat) or flecainide (150 to 200 mg stat) may be given in an attempt to convert AF to sinus rhythm.

ii) Electrical cardioversion:

C Synchronized direct current cardioversion is recommended for termination of rapid AF that renders the patient hemodynamically unstable.^{14,17}

Grade C, Level IV

B Electrical DC cardioversion for patients with hemodynamically stable persistent AF is recommended when early recurrence is unlikely.^{14,17}

Grade B, Level III

C Repeated DC cardioversion followed by prophylactic drug therapy in patients who relapse into AF without antiarrhythmic agents after successful cardioversion can also be attempted.^{14,16,17}

Grade C, Level IV

C Patients with paroxysmal AF who exhibit alternation between AF and sinus rhythm over short periods of time and those who have permanent AF of long (> 1 year) duration should, however, not undergo external electrical cardioversion.

Grade C, Level IV

Internal cardioversion with percutaneous electrode catheters, or via an implantable atrial defibrillator, are currently being evaluated.

The initial energy used to convert AF using monophasic waveform shocks is at least 200 joules, with successive increments till maximum of 360 joules. The initial energy used for atrial flutter conversion is much smaller, such as 50 joules.¹⁴ Defibrillator using the newer biphasic waveform may need less energy (100 joules) for initial electrical DC cardioversion.

The primary success rate in cardioversion of AF varies from 65% to 90%. It is improved by concomitant administration of antiarrhythmic agents such as Class III agents (e.g. sotalol, amiodarone, ibutilide) or Class IC agents (e.g. flecainide, propafenone). Patients receiving this procedure must be sedated and fasted. Good intravenous access and airway management is important. The electrolyte and anticoagulation status must be checked before cardioversion. Complications of electrical DC cardioversion include thromboembolism, various arrhythmias, myocardial injury, heart failure and skin burn. Electrical DC cardioversion in patients with implanted pacemakers and/or cardioverter-defibrillators can be performed safely, provided the paddles of the external defibrillator are placed at least 6 inches from the device. The device should be interrogated immediately after the cardioversion.^{14,16}

Recommendations for pharmacological or electrical DC cardioversion for patients with AF	Grade	Level of evidence
1. Immediate cardioversion for patients with clinical (heart failure, acute coronary syndrome) or hemodynamic (hypotension, pulmonary edema) instabilities due to rapid ventricular response secondary to AF.	C	IV
2. Cardioversion in patients without clinical or hemodynamic instability, but have unacceptable symptoms due to AF.	B	III
3. Cardioversion in patients with first episode of recent onset AF and low likelihood of recurrence.	B	III
4. Electrical DC cardioversion for patients with persistent AF when early recurrence is unlikely.	C	IV

Recommendations for pharmacological or electrical DC cardioversion for patients with AF (con't)	Grade	Level of evidence
5. Pharmacologic cardioversion for patients with persistent AF.	C	IV
6. Repeated cardioversion followed by prophylactic drug therapy in patients who relapse to AF without anti-arrhythmic agents after successful cardioversion.	C	IV

Table 3 Recommended drugs and typical doses for conversion to sinus rhythm

Drug	Dosage	Potential Adverse Effects
Amiodarone	iv 5 to 7 mg/kg over 30-60 mins then 900-1200 mg per day until 10 g total or Oral 600-800 mg per day until 5-10 gm total	Photosensitivity, pulmonary toxicity, polyneuropathy, GI upset, bradycardia, Torsades de pointes (rare), hepatic toxicity, thyroid dysfunction
Flecainide	iv 150 mg over 10-20 mins or Oral 200 mg stat and up to 300 mg per day	Ventricular tachycardia, congestive heart failure, 1:1 atrial flutter, hypotension
Propafenone	Oral 300-600 mg stat and up to 900 mg per day	Ventricular tachycardia, congestive heart failure, 1:1 atrial flutter, asthma

6.3 Rhythm control with non-pharmacological therapies

Non-pharmacological therapies for maintenance of rhythm include permanent pacing, catheter ablation or surgical ablation.

Permanent pacing

Dual chamber pacing has been shown to reduce the incidence of AF in patients with sick sinus syndrome.^{18,19} The risk for thromboembolism and mortality is also decreased. However the PA3 study suggests that in patients with medically refractory AF who do not have bradycardia, conventional atrial pacing at 70 bpm in the short term is not effective in preventing AF.²⁰ The role of Bachman's bundle pacing, inter-atrial septal pacing, dual site or biatrial pacing remains investigational.^{21,22} Newer pacing algorithms such as atrial overdrive pacing (or dynamic atrial overdrive, atrial preference pacing) and anti-tachycardia pacing for atrial flutter may have a role but requires further evaluation.²³

Catheter ablation

Catheter ablation may be considered in young patients with paroxysmal AF especially those whose ECGs or Holter show frequent atrial ectopics and bursts of rapid atrial tachycardia degenerating into AF.²⁴ These have been found to be due to rapidly firing foci in the pulmonary veins and less frequently in the superior vena cava and coronary sinus. In carefully selected patients, long-term maintenance of sinus rhythm may be possible in 70-80% of patients. Patients with atrial flutter or supraventricular tachycardia degenerating into AF are also candidates for ablation.

Surgical ablation

Surgical ablation of AF using the "Maze" procedure introduced by Cox et al²⁵ can restore sinus rhythm, atrial transport function and prevent thromboembolism. The mechanism by which the procedure prevents AF involves creation of barriers to conduction within the right atrium and left atrium, which limits the amount of myocardium available to propagate reentrant wavefronts, thereby inhibiting AF. Isolation of the pulmonary veins may prevent initiation of AF by isolating potentially arrhythmogenic foci within or near the pulmonary veins from the remainder of the atrium.

B Hence in patients with highly symptomatic AF who require open-heart operation for valvular, ischemic or congenital heart disease, consideration should be given to performing a concomitant Maze operation for AF.

Grade B, Level III

The additional mortality and morbidity of the procedure should be less than 10%. In some patients (about 10-20%) however, sinus node dysfunction may develop and these patients may require a permanent pacemaker implantation.

7 Maintenance of Sinus Rhythm

7.1 Pharmacological therapy to prevent recurrence of atrial fibrillation (AF)

B Prophylactic drug therapy is not indicated in the case of a first detected episode of AF which has resolved.¹⁴ However, be it paroxysmal or persistent, AF is often a chronic disorder and recurrence is likely in most patients. Maintenance of sinus rhythm is desirable in some patients to suppress symptoms and prevent tachycardia-induced cardiomyopathy but as discussed earlier, it has not been proven to reduce thromboembolism, heart failure or death. For patients with significant risk or side effects from antiarrhythmic drugs, they should not be placed on rhythm maintenance therapy as the risk with presently available antiarrhythmic drugs outweighs the benefits.

Grade B, Level IIa

Figure 3 on page 25 outlines the decision tree for pharmacological management of patients with recurrent paroxysmal and persistent AF.

Table 4 on page 26 summarises the recommended drugs and typical doses used to maintain sinus rhythm and their adverse effects. Several studies have shown the superiority of amiodarone over sotalol and Class IC drugs in maintenance of sinus rhythm, but it is generally reserved as the drug of last resort because of potentially serious long-term extracardiac side effects.²⁶⁻²⁹ We recommend that with Class IC drugs, QRS widening should not exceed 150% of the pre-treatment QRS duration. With Class III drugs, except amiodarone, the corrected QT interval should not exceed 0.52 seconds in sinus rhythm. Plasma potassium and magnesium levels and renal function should be checked periodically, as renal insufficiency predisposes to drug accumulation and proarrhythmia.

Figure 4 on page 27 shows the preferred drugs to use in the presence of ischemic heart disease, heart failure and hypertensive heart disease.

Outpatient initiation of anti-arrhythmic drugs can be safely done in selected patients.¹⁴ Proarrhythmia is uncommon in patients with normal ventricular function and normal baseline QT intervals, without heart failure or renal failure and profound bradycardia.^{30,31} Class IC drugs

may precipitate ventricular fibrillation and must be avoided in the Brugada Syndrome, a syndrome characterised by partial right bundle branch block and ST elevation in leads V1 to V3. Sotalol must be used with caution in elderly females, abnormal baseline QT interval, hypokalemia, renal dysfunction or hypothyroidism. However it can be safely given in the outpatient setting if left ventricular and renal function are normal, baseline uncorrected QT interval is < 420 ms and serum electrolytes are normal.^{31,32} Amiodarone can generally be given safely in outpatients but should also be closely monitored with regular ECGs.

Recommendations	Grade	Level of evidence
1. Base selection of antiarrhythmic drug predominantly on safety.	B	IIa
2. Treat precipitating or reversible causes of AF before initiation of anti-arrhythmic drug therapy.	C	IV
3. Administer pharmacological therapy to maintain sinus rhythm to prevent progression of tachycardia-induced cardiomyopathy due to AF.	C	IV
4. Outpatient initiation of anti-arrhythmic drug therapy is appropriate in selected patients.	B	IIa
5. Administer pharmacological therapy to maintain sinus rhythm in asymptomatic patients to prevent atrial remodeling.	C	IV
6. Administer pharmacological therapy to maintain sinus rhythm to prevent heart failure or thromboembolism in selected patients.	C	IV

Figure 3 Pharmacological management of recurrent paroxysmal or persistent AF

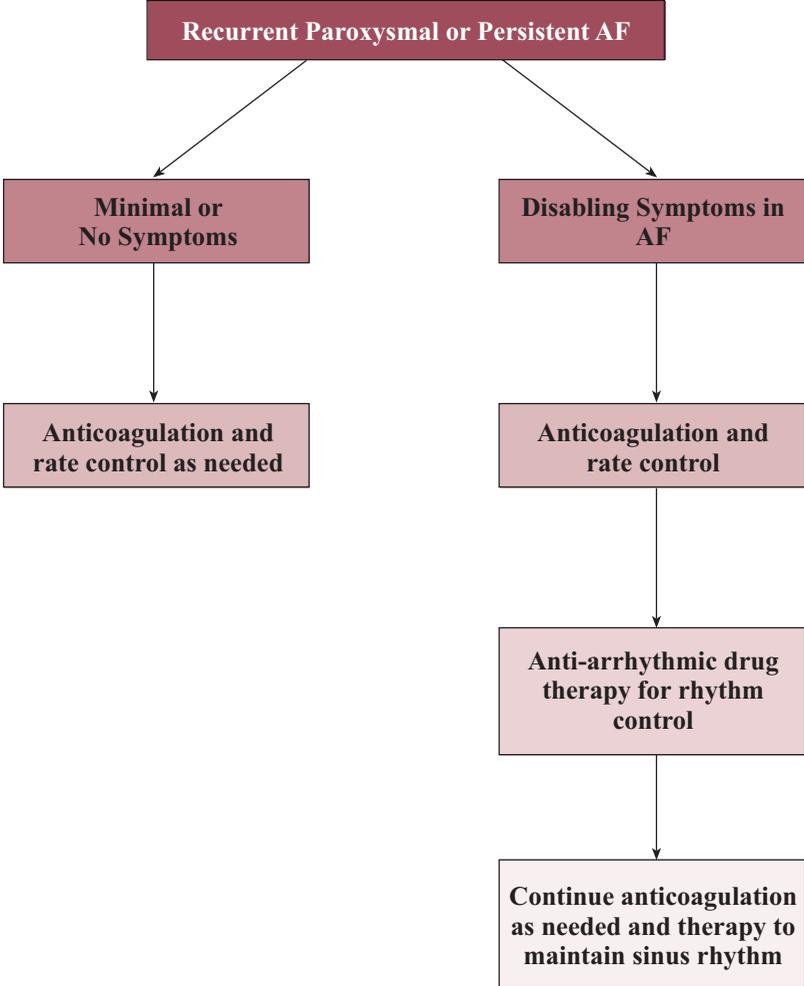
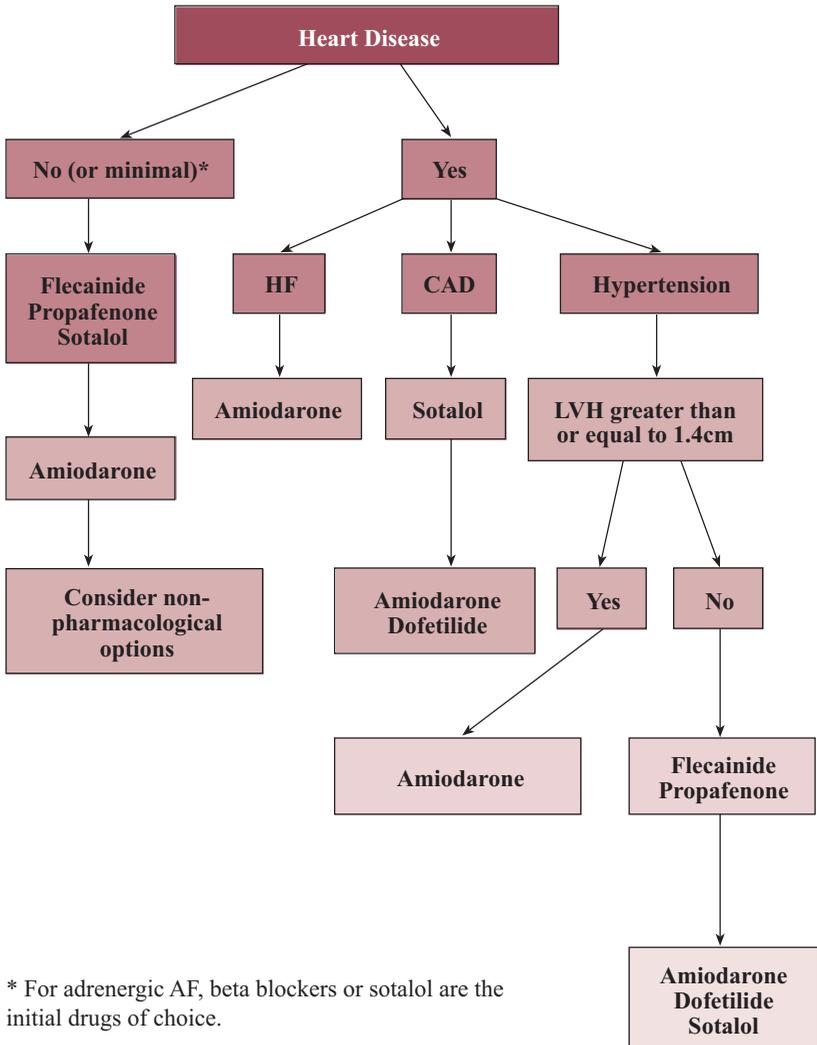


Table 4 Recommended drugs and typical doses for maintenance of sinus rhythm

Drug	Daily Dosage	Potential Adverse Effects
Amiodarone	100-400 mg	Photosensitivity, pulmonary toxicity, polyneuropathy, GI upset, bradycardia, Torsades de pointes (rare), hepatic toxicity, thyroid dysfunction.
Flecainide	200-300 mg	Ventricular tachycardia, congestive heart failure, enhanced AV nodal conduction (conversion to atrial flutter).
Propafenone	300-900 mg	Ventricular tachycardia, congestive heart failure, enhanced AV nodal conduction (conversion to atrial flutter).
Sotalol	80-320 mg	Torsades de pointes, congestive heart failure, bradycardia, exacerbation of chronic obstructive or bronchospastic lung disease.

Figure 4 Anti-arrhythmic drug therapy to maintain sinus rhythm in recurrent paroxysmal or persistent AF



* For adrenergic AF, beta blockers or sotalol are the initial drugs of choice.

HF = heart failure
 CAD = coronary artery disease
 LVH = left ventricular hypertrophy

8 Rate Control During AF

A When restoration of sinus rhythm is not possible or is not attempted in patients with AF, control of the ventricular rate is essential. Regardless of the type of AF, rate control is crucial to improve cardiac output. If the rate is controlled, diastolic filling time, stroke volume and cardiac output increases. Additionally control of the ventricular rate during AF is an acceptable alternative.

Grade A, Level Ia

In 2 recent randomized trials, the therapeutic strategies of rate versus rhythm control yielded similar clinical results, although exercise tolerance was better with rhythm control.^{12,13}

Drugs that block atrioventricular (AV) nodal conduction can be used to achieve rate control both at rest and during exercise or other types of cardiovascular stress. Recommended drugs are digoxin, beta blockers or calcium channel blockers. Ablation and pacemaker implantation are alternatives for patients whose symptoms are refractory to drugs. (See Table 5 on page 33)

Criteria for rate control

There are no definite criteria agreed but the rate is generally considered controlled when the ventricular response ranges between 60 and 90 beats per minute at rest and between 100 and 120 beats per minute during moderate exercise. The heart rate response should be measured both at rest and during exercise to assess the control of the rate with pharmacological agents to the physiological range.

8.1 Pharmacological agents to control heart rate in patients with AF with a rapid ventricular response

Digoxin

In the past, digoxin was the first-line agent for AF, but even with intravenous digoxin, the onset of therapeutic effect takes at least 60 minutes, and its peak effect does not develop till 6 hours later. It is however still very useful in patients with heart failure and AF.³³ According to a recent meta-analysis,³⁴ digoxin administered alone slows

the resting heart rate more than placebo. Its efficacy is reduced in states of high sympathetic tone, such as during febrile states, sepsis and during exercise which are common precipitants of paroxysmal AF. A combination of digoxin and atenolol has been shown to be especially effective for ventricular rate control.³⁵ Digoxin must be used with caution in the elderly and in patients with renal dysfunction.

Nondihydropyridine Calcium Channel Blockers

Nondihydropyridine calcium channel blockers (verapamil, diltiazem) are used to control ventricular rate and are especially helpful if beta blockers are contraindicated. Verapamil and diltiazem reduced heart rate both at rest and during exercise significantly better than placebo in several trials, with preserved or improved exercise tolerance in most patients.³⁶ Intravenous verapamil and diltiazem are effective in emergency settings^{37,38} but the response is transient, and repeated doses or a continuous intravenous infusion may be required. These agents should be used cautiously in patients with heart failure but are preferred over beta-blockers for long-term use in patients with chronic obstructive pulmonary disease.

Beta-Blockers

Beta blockers are considered first-line therapy for controlling heart rate in AF especially in states of high adrenergic tone (e.g. postoperative AF) but may have serious adverse effects. They may worsen heart failure symptoms and cause bronchospasm in patients with asthma. In 7 of 12 comparisons with placebo, beta-blockers were effective at controlling resting heart rate, with nadolol and atenolol being most efficacious. All 9 comparisons demonstrated good rate control with beta-blockers, but exercise tolerance was compromised in 3 of 9 studies.³⁴ Atenolol provided better control of exercise-induced tachycardia than digoxin alone.³⁶ Beta-blockers should be initiated cautiously in patients with history of heart failure.³⁹

Sotalol

Sotalol provides excellent rate control during AF recurrence.^{32,40} However it should not be used in patients with preexisting prolonged QT interval especially in older women or patients with renal dysfunction or hypothyroidism.

Amiodarone

Intravenous amiodarone is effective and well tolerated in critically ill patients or patients with heart failure and hypotension due to rapid AF. Although not yet sufficiently evaluated in this indication, it is considered a suitable alternative agent for heart rate control when conventional measures are ineffective.⁴¹ Oral amiodarone has not been investigated properly in this indication and should not be used as a first-line agent because of the side effects associated with its chronic administration. Oral amiodarone also interacts with digoxin, raising its serum concentrations.

Combination Therapy

Combinations of these agents may often be required to achieve adequate rate control, but care should be taken to avoid excessive slowing. Addition of other drugs to digoxin is commonly required to control AV nodal conduction during exercise and to achieve consistent, adequate heart rate control. In general, the combination of digoxin and beta-blockers appears to be more effective than the combination of digoxin and diltiazem.³⁵

8.2 Nonpharmacological regulation of AV nodal conduction and pacing

Permanent pacing

Ventricular pacing may prove useful for patients with marked variability in ventricular rates and for those who develop intermittent resting bradycardia during treatment with medications prescribed to control rapid ventricular rates during exertion.

AV Nodal Ablation and Permanent pacing

AV nodal ablation and permanent pacemaker implantation provide a highly effective means of improving symptoms in selected patients with AF.⁴²⁻⁴⁴ This approach should be considered for those who experience rate-related symptoms not adequately controlled with medications or have developed a tachycardia-induced cardiomyopathy. A meta-analysis of 21 studies (total 1,181 patients) concluded that AV nodal ablation and permanent pacemaker implantation significantly

improved cardiac symptom scores, quality-of-life measures, and healthcare utilization.⁴⁴ For patients with impaired left ventricular function before ablation, this treatment significantly improved left ventricular ejection fraction. Two small randomized trials compared the effects of AV nodal ablation with antiarrhythmic medications on quality of life and symptoms in patients with AF.^{43,44} Significantly more patients with both forms of AF experienced improvement in symptoms and quality of life after AV nodal ablation.

Use of catheter ablation to modify AV nodal conduction by eliminating posterior atrial inputs to the AV node has been reported to decrease the ventricular rate during AF and to improve cardiac symptoms without requiring pacemaker implantation.^{45,46} This technique however still incurs risk of inadvertent complete AV block and hence AV nodal modification without pacemaker implantation is only rarely used for patients with rapid ventricular rates during AF.

Although the symptomatic benefits of AV nodal ablation have been clearly demonstrated, the limitations of this technique include the continued need for anticoagulation, loss of AV synchrony, and lifelong pacemaker dependency. There is a small but real risk of sudden death (< 2%) due largely to Torsades de pointes.⁴⁴ Patients with impaired diastolic ventricular compliance who are most dependent on AV synchrony for maintenance of cardiac output (such as those with hypertrophic or restrictive cardiomyopathies) may experience persistent symptoms after AV nodal ablation and permanent single chamber pacemaker implantation. Thus, patients must be counseled regarding each of these considerations before proceeding with this irreversible treatment.

C Hence catheter ablation for rate control should not be done without prior attempt at medical therapy to control AF.

Grade C, Level IV

Recommendations for Heart Rate Control in Patients With AF	Grade	Level of Evidence
Administer intravenous beta-blockers or calcium channel antagonists (verapamil, diltiazem) in the acute setting to slow the ventricular response to AF in the absence of conduction over an accessory pathway, exercising caution in patients with hypotension or heart failure.	A	Ib
Perform immediate electrical cardioversion in patients with acute paroxysmal AF and a rapid ventricular response associated with acute myocardial infarction, symptomatic hypotension, angina, or cardiac failure that does not respond promptly to pharmacological measures.	C	IV
Administer a combination of digoxin and a beta-blocker or calcium channel antagonist to control the heart rate at rest and during exercise in patients with AF. The choice of medication should be individualized and the dose modulated to avoid bradycardia.	A	Ia
Employ nonpharmacological therapy to control heart rate when pharmacological therapy is insufficient.	B	IIb
Administer digoxin as the sole agent to control heart rate at rest in patients with persistent AF.	B	IIb

Tables 5 Recommended intravenous or oral drugs and typical doses for heart rate control in AF

Drug	Loading Dosage	Potential Adverse Effects
Digoxin	iv 0.25-1 mg or Oral 0.0625 to 1.0 mg	Digitalis toxicity, heart block, bradycardia.
Verapamil	iv 0.075-0.15 mg/kg over 2 mins or Oral 80-240 mg	Hypotension, heart block, heart failure.
Diltiazem	iv 10-20 mg or Oral 60-200 mg	Hypotension, heart block, heart failure.
Propranolol	iv 0.05-0.15 mg/kg or Oral 20-80 mg	Hypotension, heart block, bradycardia, asthma, heart failure.
Atenolol	Oral 25-100 mg	Hypotension, heart block, bradycardia, asthma, lethargy.
Bisoprolol	Oral 2.5 to 10 mg	Hypotension, heart block, bradycardia, asthma.
Esmolol	iv 0.5 mg/kg over 1 min	Hypotension, heart block, bradyardia, asthma, heart failure.
Sotalol	Oral 80-320 mg	Torsades de pointes, congestive heart failure, bradycardia, asthma.
Amiodarone	iv 150-300 mg over 1 hour or Oral 200-600 mg	Hypotension, bradycardia, Torsades de pointes, pulmonary toxicity, hyperthyroidism, hypothyroidism, skin photosensitivity, corneal deposits, warfarin interaction, proarrhythmia.

9 Prevention of Thromboembolic Complication

AF is associated with a significantly increased risk of thromboembolism, the most important being cardioembolic stroke. In the Framingham study,⁴⁷ there was a nearly fivefold excess of stroke when AF was present. AF was also shown to be associated with a four to fivefold increased risk of peripheral arterial thromboembolism.⁴⁸

A The appropriate drug for prevention of thromboembolism depends on the risk of stroke, presence or absence of active bleeding, and patient-specific traits. Oral anticoagulation is highly effective in stroke prevention for patients with AF. Compared to patients taking aspirin, patients receiving oral anticoagulant were significantly less likely to experience any ischemic stroke or cardiovascular events.⁴⁹⁻⁵¹ The degree of benefit associated with oral anticoagulation was similar in patients with paroxysmal or permanent AF.⁴⁹⁻⁵²

Grade A, Level Ia

9.1 Stroke risk stratification

In patients with AF, the risk of thromboembolism is stratified according to the presence or absence of a number of risk factors.⁵³⁻⁵⁴

High-risk factors include:

- Prior stroke/transient ischaemic attack/systemic embolism
- Prosthetic heart valve
- Rheumatic mitral stenosis
- Age > 75 years

Moderate-risk factors include:

- Age 60-75 years
- History of hypertension
- Congestive heart failure
- Poor left ventricular function (LVEF \leq 35%)
- Diabetes mellitus
- Coronary artery disease
- Thyrotoxicosis

Low risk factors include:

- Age < 60

Specific stroke risk calculations have also been proposed to estimate the risk. These include the CHADS2 stroke risk classification scheme⁵⁴ and the Framingham risk of stroke score.⁵⁵

9.2 Antithrombotic strategy

A Antithrombotic therapies are best tailored according to the patient's risk of stroke and of bleeding during anticoagulation. In general, AF patients with additional risk factors should be considered for long-term anticoagulation with adjusted-dose warfarin, unless they are at low risk of stroke or have a specific contraindication to the use of warfarin.^{14,17}

Grade A, Level Ia

In AF patients with any high-risk factor, long-term oral anticoagulation with adjusted dose warfarin is recommended unless contraindicated (target INR 2.5; range 2.0-3.0). Anticoagulation is especially important in patients with previous stroke. Thus, although anticoagulant use is associated with a similar two-thirds risk reduction compared to control in both primary and secondary stroke prevention, a much larger absolute risk reduction was found in AF patients who had already suffered from a minor stroke or transient ischaemic attack (TIA) (4% vs. 12%) compared to AF patients without a prior cerebrovascular event (1.4% vs. 4.5%).⁵⁰

A Patients with AF who are 60-75 years old with any one of the other moderate risk factors (history of hypertension, congestive heart failure or echocardiographically confirmed poor left ventricular function, diabetes mellitus, coronary artery disease, and thyrotoxicosis) have been demonstrated to have increased thromboembolic risks. Such patients should also be anticoagulated to an INR of 2.0-3.0.

Grade A, Level Ia

C For those at intermediate risk, the patient's preference, the individual risk of bleeding during anticoagulation, and access to high-quality anticoagulation monitoring are crucial factors in the decision to use warfarin rather than aspirin. Thus, for non-valvular AF patients who are < 60 years old who have one of the moderate risk factors or who are 60-75 years with no other risk factor, a careful assessment and risk stratification is recommended. Either aspirin (100 mg per day) or warfarin may be appropriate.

Grade C, Level IV

Occasionally there may be male patients who are > 75 years old with no other risk factors and these may be considered for either aspirin or warfarin. An echocardiogram will be useful in further risk stratification in the above group of patients, as patients with impaired left ventricular function or dilated left atrium should be considered for anticoagulation.⁵⁶

C In those AF patients considered at low risk, or when warfarin is contraindicated (e.g. significant bleeding or fall risks, thrombocytopenia, recent surgery or trauma active peptic ulcer disease, or patients unlikely to comply with the diet and monitoring regimens required in warfarin therapy), 100-300 mg aspirin daily may be used. Alternative antiplatelet agents for patients unable to take aspirin include ticlopidine 250 mg twice daily (with mandatory full blood count monitoring for the first 3 months of therapy), clopidogrel 75 mg daily, and dipyridamole up to 75 mg three times daily. Thus AF patients < 60 years with no risk factors (lone AF) and normal left atrial size have a very low annual rate of stroke (1%), and therefore do not require anticoagulant therapy and long term aspirin may be used if needed.

Grade C, Level IV

Although it is well established that both the risk of stroke and the prevalence of AF increases with age, advanced age may also exclude an AF patient from anticoagulant therapy because of increased risks of falls, bleeding, and warfarin sensitivity. It is also important to take into consideration whether adequate monitoring and support is available for patients put on long-term oral anticoagulation, and that the local incidence of haemorrhagic stroke is higher in Singapore than that of most Western countries. It is hence very important to risk stratify the patients further and decide on whether anticoagulation or aspirin therapy is preferable as shown in Table 6 on page 38.

The combination of low-intensity, fixed-dose warfarin (INR < 1.5) plus aspirin is not effective for stroke prevention in high-risk AF patients, and is not recommended.⁵⁷ Ximelagatran, a new oral direct thrombin inhibitor, has recently been compared with warfarin and the results are promising but further studies are needed.

A The need for anticoagulation and risk for complications (see Table 7 on page 39) from anticoagulation should be evaluated at regular intervals and if any contraindications develop, the need and safety for anticoagulation should be reassessed.

Grade A, Level Ia

9.3 Type and level of anticoagulation

Warfarin is the anticoagulant of choice unless contraindicated due to active bleeding, recent hemorrhagic stroke, or known coagulation defects. The systemic effect of warfarin can take several days and requires slow, careful titration to reach the desired INR level of 2 to 3 for AF.

C Adjusted-dose warfarin, with a target INR of 2.5 (range 2.0-3.0), is usually recommended in AF patients. A lower target INR of 2.0 (range 1.6-2.5) may be preferred in patients who are frail, elderly (>75 years old) or judged to have an increased risk of haemorrhagic complications, but nevertheless expected to benefit from warfarin.¹⁴

Grade C, Level IV

C A higher target INR of 3.0 (range 2.5-3.5) may be chosen for patients with mechanical prosthetic heart valves, anti-phospholipid antibody syndrome, or have recurrent stroke despite anticoagulation.

Grade C, Level IV

The exception is a bileaflet mechanical valve in the aortic position, for which an INR of 2.0-3.0 may be adequate. In some of these patients who suffer from recurrent thromboembolic events despite adequate anticoagulation, low-dose aspirin (e.g. 100 mg per day) may be added to warfarin therapy.

Monitor the INR at least weekly during initial dosing and then every 6-8 weeks once stable therapeutic INR is achieved. In patients with a proven record of excellent compliance and stable INRs, follow-up INR monitoring may be extended to once every 8-12 weeks and the patient advised to come immediately for a review if there is any spontaneous bruising or bleeding. The dose of warfarin may need to be adjusted after any change in drugs which have interaction with warfarin, e.g. amiodarone, that is commonly used in patients with AF. Most surgical or invasive procedures require a temporary discontinuation of warfarin, usually about 5 days, until the INR is < 1.5 before the procedure can be done. The anticoagulation can be restarted once there is no evidence of bleeding.

Table 6 Recommendations for antithrombotic therapy in patients with AF

	Age		
	< 60	60-75	> 75
No risk factor	Aspirin or no treatment	Aspirin or anticoagulate INR 2.0-3.0	Anticoagulate INR 1.6-2.5
<i>History of:</i> Hypertension Diabetes mellitus Thyrotoxicosis Coronary artery disease Significant valvular heart disease (except mitral stenosis) Heart Failure LVEF \leq 35%	Aspirin or anticoagulate INR 2.0-3.0*	Anticoagulate INR 2.0-3.0	Anticoagulate INR 1.6-2.5
<i>History of:</i> Stroke/TIA LA thrombus Mitral stenosis	Anticoagulate INR 2.0-3.0	Anticoagulate INR 2.0-3.0	Anticoagulate INR 1.6-2.5
<i>History of:</i> Mechanical prosthetic valve	Anticoagulate INR 2.5-3.5	Anticoagulate INR 2.5-3.5	Anticoagulate INR 2-3

* Preferable to anticoagulate if have hypertension, history of heart failure or LVEF \leq 35%.

Table 7 Risk factors for bleeding complications with oral anticoagulation

Risk factor	Potential clinical characteristic
History of bleeding	Gastrointestinal blood loss, epistaxis, haematuria
Thrombocytopenia	Recurrent bleeding
Drugs which cause bleeding	Aspirin, non-steroidal anti-inflammatory drug therapy
Drugs which potentiate warfarin effect	Allopurinol Antibiotics e.g. cephalosporins, erythromycin, metronidazole Amiodarone Azole antifungals e.g. fluconazole, ketoconazole Acetaminophen (high dose) Cimetidine Cox-2 inhibitors
Herbal supplements that may potentially potentiate warfarin effect	Dong quai Danshen Ginseng Ginkgo Kava
Co-morbid health problems	Heart failure, liver disease
Poor compliance	Cognitive impairment, lack of social support
Psycho-social problems	Excess alcohol
Elderly	Recurrent falls

10 Special Considerations

10.1 Post-operative atrial fibrillation

This refers to recent onset AF after open heart surgery. The incidence of atrial arrhythmias, including AF, after open heart surgery is between 20-50%.⁵⁸⁻⁶⁹

Recommendations for prevention and management of post-operative AF ⁵⁸⁻⁶⁹	Grade	Level of evidence
1. In patients with post-operative AF, control rate with intravenous nodal blocking agents such as a short acting beta-blocker, calcium channel blocker, or amiodarone.	A	Ib
2. Treat patients undergoing cardiac surgery with an oral beta-blocker to prevent AF unless contraindicated.	A	Ia
3. In patients with persistent post-operative AF, restore sinus rhythm with pharmacological agents or DC cardioversion.	A	Ib
4. In patients with recurrent or refractory post-operative AF, attempt maintenance of sinus rhythm with a beta-blocker, especially sotalol or amiodarone.	A	Ib
5. Administer anti-thrombotic medications for persistent AF as recommended for non-surgical patients after 48 hours.	B	III

10.2 Atrial fibrillation in patients with acute myocardial infarction

The incidence of AF in patients with acute myocardial infarction varies from 10.4% to 22% depending on the population sampled.^{70,71} AF following an acute myocardial infarction is associated with increased mortality and stroke rates. Class IC antiarrhythmic drugs must not be used.⁷²

Recommendations for AF management in acute myocardial infarction^{14,72}	Grade	Level of evidence
1. Electrical cardioversion for patients who are haemodynamically unstable or who have intractable ischaemia.	C	IV
2. Intravenous beta-blockers (in patients without contraindications), digoxin or amiodarone to control rate.	C	IV

10.3 Atrial fibrillation in patients with the Wolff-Parkinson-White (WPW) syndrome

AF may induce ventricular fibrillation and sudden death in patients with WPW syndrome by rapid antegrade conduction across an accessory pathway. The incidence of sudden death in patients with WPW syndrome ranges from 0.1 to 1% per year.⁷³ Immediate cardioversion should be done in the hemodynamically unstable patient. In the more stable patient intravenous flecainide, procainamide or ibutilide may be used. If the above are unavailable, intravenous amiodarone may be used but the patient must be monitored carefully as rarely intravenous amiodarone may also accelerate the preexcited AF and result in VF. Drugs that slow AV nodal conduction such as beta blockers, digoxin, diltiazem or verapamil must not be used as this may result in acceleration of the ventricular rate down the accessory pathway, resulting in hypotension, or degeneration to ventricular fibrillation.⁷⁴⁻⁷⁶

Recommendations for management of AF and ventricular pre-excitation^{14,76}	Grade	Level of evidence
1. Catheter ablation of the accessory pathway in symptomatic patients with AF and WPW syndrome.	B	Iib
2. Immediate electrical cardioversion in patients with WPW syndrome, fast AF and haemodynamic instability.	B	III
3. Intravenous flecainide, procainamide or ibutilide in patients with WPW syndrome, haemodynamically stable AF and a wide QRS complex on the ECG (≥ 120 ms) in an attempt to restore sinus rhythm.	C	IV

10.4 Atrial Fibrillation in patients with Hyperthyroidism

AF occurs in 10% to 25% of patients with hyperthyroidism.⁷⁷

Spontaneous reversion to sinus rhythm usually follows restoration of a euthyroid state and treatment is directed towards rate control during the thyrotoxic stage.

Recommendations for management of AF in patients with hyperthyroidism^{14,78}	Grade	Level of evidence
1. Treat with a beta-blocker to control ventricular rate unless contraindicated, in which case use a calcium channel blocker (diltiazem or verapamil).	B	IIb
2. Anti-coagulate to prevent thromboembolism. Once a euthyroid state is restored, the need for anti-thrombotics are similar to patients without hyperthyroidism.	C	IV

10.5 Atrial Fibrillation in Pregnancy

In a pregnant woman who develops AF, diagnosis and treatment of the underlying condition, such as mitral stenosis, congenital heart disease, or hyperthyroidism is the first priority.

Recommendations for management of AF during pregnancy¹⁴	Grade	Level of evidence
1. Control ventricular rate with digoxin, a beta-blocker or a calcium channel blocker.	C	IV
2. Electrical cardioversion in haemodynamically unstable patients.	C	IV
3. Administered unfractionated heparin or aspirin throughout pregnancy in all patients (except those with lone AF).	C	IV

10.6 Atrial Fibrillation in patients with Hypertrophic Cardiomyopathy (HCM)

The development of AF in the setting of HCM is associated with clinical deterioration, increased mortality and stroke.

Recommendations for management of AF in patients with HCM ^{14,79}	Grade	Level of evidence
1. Administer oral anti-coagulation.	B	III
2. Prevent recurrences with disopyramide or amiodarone.	C	IV

10.7 Atrial Fibrillation in patients with heart failure

Patients with heart failure are prone to the ventricular pro-arrhythmic effects of anti-arrhythmic drugs, hence the selection of an appropriate anti-arrhythmic is based on evidence of safety of the recommended agents.^{80,81}

Recommendations for management ¹⁴	Grade	Level of evidence
1. Use amiodarone or dofetilide to maintain sinus rhythm or attempt pharmacological cardioversion.	C	IV
2. Consider non-pharmacological options to maintain sinus rhythm if drug failure occurs.	C	IV
3. Chronic oral anti-coagulant therapy unless contraindicated.	C	IV

10.8 Atrial Fibrillation in patients with stable Coronary Artery Disease

In patients with stable coronary artery disease, beta-blockers or sotalol may be considered first whilst flecainide and propafenone are not recommended as a result of the CAST study.⁸²

Recommendations for management¹⁴	Grade	Level of evidence
1. Use beta-blockers or sotalol as initial anti-arrhythmic agent if there are no contraindications.	C	IV
2. Amiodarone, may be used if beta-blockers are contraindicated or ineffective.	C	IV
3. Calcium antagonists (verapamil, diltiazem) may be used for rate control.	C	IV
4. Administer anti-thrombotic therapy (oral anti-coagulation or aspirin), the selection of which is based upon the assessment of the risk benefit ratio of stroke and bleeding for each individual patient.	C	IV

10.9 Atrial Fibrillation in patients with Hypertensive Heart Disease

Patients with left ventricular hypertrophy may have an increased risk of developing Torsades de pointes. Thus the selection of an appropriate anti-arrhythmic agent is based on the presence or absence of marked left ventricular hypertrophy.

Recommendations for management¹⁴	Grade	Level of evidence
1. Use propafenone or flecainide in the absence of CAD or marked LV hypertrophy (LV thickness of ≥ 1.4 cm).	C	IV
2. Use amiodarone or sotalol as second line agents in the absence of LV hypertrophy.	C	IV
3. Use amiodarone when marked hypertrophy (LV thickness of ≥ 1.4 cm) is present.	C	IV

10.10 Atrial Fibrillation in patients with pulmonary diseases

Supraventricular arrhythmias, including AF are common in patients with chronic lung diseases. Treatment of the underlying lung disease is of primary importance as pharmacological anti-arrhythmias therapy

and electrical cardioversion may be ineffective until the respiratory decompensation has been corrected. Beta-blockers, propafenone or adenosine must not be used in such patients.⁸³

Recommendations for management¹⁴	Grade	Level of evidence
1. Correct hypoxemia and acidosis of acute exacerbation of chronic pulmonary disease.	C	IV
2. Use a calcium channel blocker such as diltiazem or verapamil for ventricular rate control.	C	IV
3. Electrical cardioversion in haemodynamically unstable patients.	C	IV

11 Clinical Quality Improvement

The following clinical quality improvement parameters, based on recommendations in these guidelines, are proposed:

1. Percentage of patients with AF (excluding lone AF and those having contraindications to warfarin) who receive long-term anticoagulation with adjusted-dose warfarin. (see page 35)
2. Percentage of patients with AF receiving anticoagulation therapy with a therapeutic INR (target range 2-3 in patients ≤ 75 years old and 1.6-2.5 in patients > 75 years old). (see page 37)

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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category III (Self-Study) of the SMC Online CME System. Before you login to claim the CME point, we encourage you to evaluate whether you have mastered the key points in the Guidelines by completing this set of MCQs. This is an extension of the learning process and is not intended to “judge” your knowledge and is not compulsory. The answers can be found at the end of the questionnaire.

Instruction: Choose the best answer.

- 1) Minimal investigations of patients with atrial fibrillation should include the following except
 - A) Electrocardiogram
 - B) Full blood count
 - C) Serum electrolytes
 - D) 2D echocardiogram
 - E) exercise stress test

- 2) AF is associated with the following conditions except
 - A) ischaemic heart disease
 - B) hypertension
 - C) mitral stenosis
 - D) hyperlipidaemia
 - E) thyrotoxicosis

- 3) The following statements are true except
 - A) initial energy required for electrical DC cardioversion of atrial fibrillation is higher than that required for atrial flutter.
 - B) electrical DC cardioversion can be safely performed in patients with implanted pacemakers.
 - C) recent data suggest that restoring and maintaining sinus rhythm is a far superior and safer treatment than that of heart-rate control strategy.
 - D) anticoagulation therapy for further four weeks is recommended even if patients with persistent atrial fibrillation have been successfully converted to sinus rhythm by electrical DC cardioversion.
 - E) pharmacologic cardioversion can be used for patients with persistent AF of recent onset.

- 4) The following medications have NOT been shown to be useful in the pharmacological cardioversion of atrial fibrillation to sinus rhythm:
- A) amiodarone
 - B) propafenone
 - C) flecainide
 - D) digoxin
- 5) In the management of atrial fibrillation in patients with stable coronary artery disease, recommended treatment is with
- A) flecainide
 - B) propafenone
 - C) sotalol
 - D) digoxin
 - E) dofetilide
- 6) In a patient with Wolff-Parkinson-White (WPW) syndrome admitted with palpitations, a BP of 140/80 mmHg and an ECG showing atrial fibrillation with a widened QRS complex of 125 ms and ventricular rate of 130 bpm, recommended initial treatment is with
- A) IV Verapamil
 - B) IV Procainamide
 - C) IV Digoxin
 - D) Immediate electrical cardioversion
- 7) Which of the following increases the risk of AF?
- A) Increasing age
 - B) Rheumatic mitral valve disease
 - C) Congestive heart failure
 - D) Hypoxic pulmonary conditions
 - E) All of the above
- 8) Which of the following is not recommended as a first line agent for rate control in patients with AF?
- A) Metoprolol
 - B) Verapamil
 - C) Diltiazem
 - D) Digoxin
 - E) Nifedipine

- 9) The results of the AFFIRM trial suggest that rate control can serve as a primary therapy in patients at high risk for stroke.
- A) True
 - B) False
- 10) Which of the following are drugs of choice for sinus rhythm maintenance in congestive heart failure?
- A) Amiodarone
 - B) Procainamide
 - C) Quinidine
 - D) Flecainide
 - E) Propafenone

Answer

1. E
2. D
3. C
4. D
5. C
6. B
7. E
8. E
9. A
10. A

Workgroup members

The members of the review workgroup, who were appointed in their personal professional capacity, are:

Chairperson Dr Teo Wee Siong
Senior Consultant Cardiologist
Director, Electrophysiology & Pacing
Department of Cardiology
National Heart Centre

Members

Prof Chia Boon Lock
Senior Consultant
Cardiac Department
National University Hospital

Dr N V Ramani
Senior Consultant
Department of Neurology
National Neuroscience Institute

Dr Chee Tek Siong
Chee Heart Specialist Clinic
Eastshore Medical Centre

Dr Tan Kok Soon
The Heart Specialist Clinic
Mt Elizabeth Medical Centre

Dr Bernard Chan
Consultant Neurologist
Department of Medicine
National University Hospital

Dr Ruth Kam Ming Li
Senior Consultant Cardiologist
Department of Cardiology
National Heart Centre

Dr James Wong
Consultant Cardiothoracic
Surgeon
The Heart Lung & Vascular
Surgical Centre
Mt Elizabeth Medical Centre

Dr Ng Kheng Siang
Director, Arrhythmia Service
The Heart Institute (NHG)
Head, Department of Cardiology
Tan Tock Seng Hospital
Senior Consultant Cardiologist
National University Hospital

Dr Wu Dar Ching
Cardiothoracic Surgical Centre
Mt Elizabeth Medical Centre

Dr Ng Wai Lin
Consultant Cardiologist
Raffles Hospital

Dr Julian Lim
New Life Family Clinic

MOH CLINICAL PRACTICE GUIDELINES 8/2004

Management of Atrial Fibrillation



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On Cardiac Care



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Heart
Foundation
Your Heart We Care



Singapore Cardiac
Society



Clinical Neuroscience
Society Singapore

Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated. Where differences exist between this executive summary and the main text, please take reference from the main text.

A Rate control with anticoagulation should be the recommended strategy for most patients with atrial fibrillation (AF). Specific drug classes that should be used as part of this strategy include beta-blockers, non-dihydropyridine calcium channel blockers, and digoxin. (pg 15 and 28-30)

Grade A, Level Ia

C Synchronized direct current cardioversion is recommended for termination of rapid AF that renders the patient hemodynamically unstable. (pg 18)

Grade C, Level IV

A Adequate anticoagulation is needed if the AF has lasted > 48 hours. A delayed strategy of adequate anticoagulation for 3-4 weeks prior and 4 weeks post cardioversion or an early strategy using transesophageal guidance to exclude intracardiac thrombi followed by acute anticoagulation and cardioversion and post cardioversion anticoagulation may be used. (pg 16)

Grade A, Level Ib

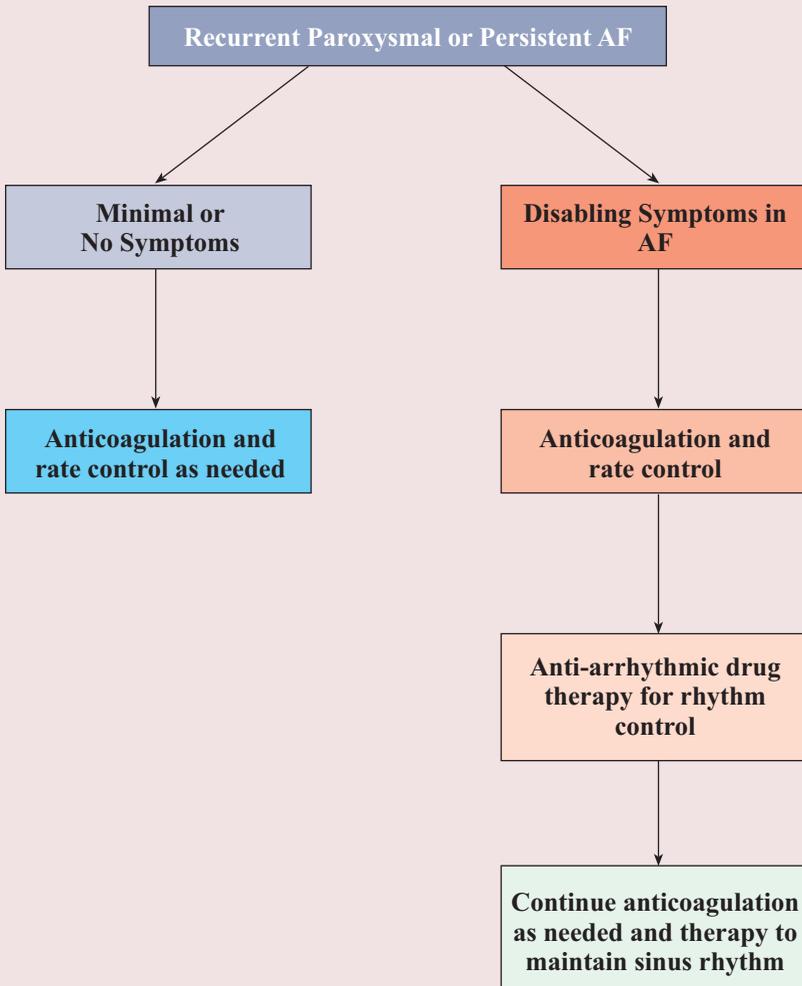
A & C All patients with AF should be risk stratified for risk of thromboembolism and given the appropriate antithrombotic strategy. Patients with AF and additional risk factors should receive anticoagulation with warfarin to an adjusted INR of 2-3. Older patients (> 75 years old) may have a lower target INR of 1.6-2.5. Lone AF patients with no risk factor who are young may be given aspirin only. (pg 35-37)

**Grade A, Level Ia
and Grade C, Level IV**

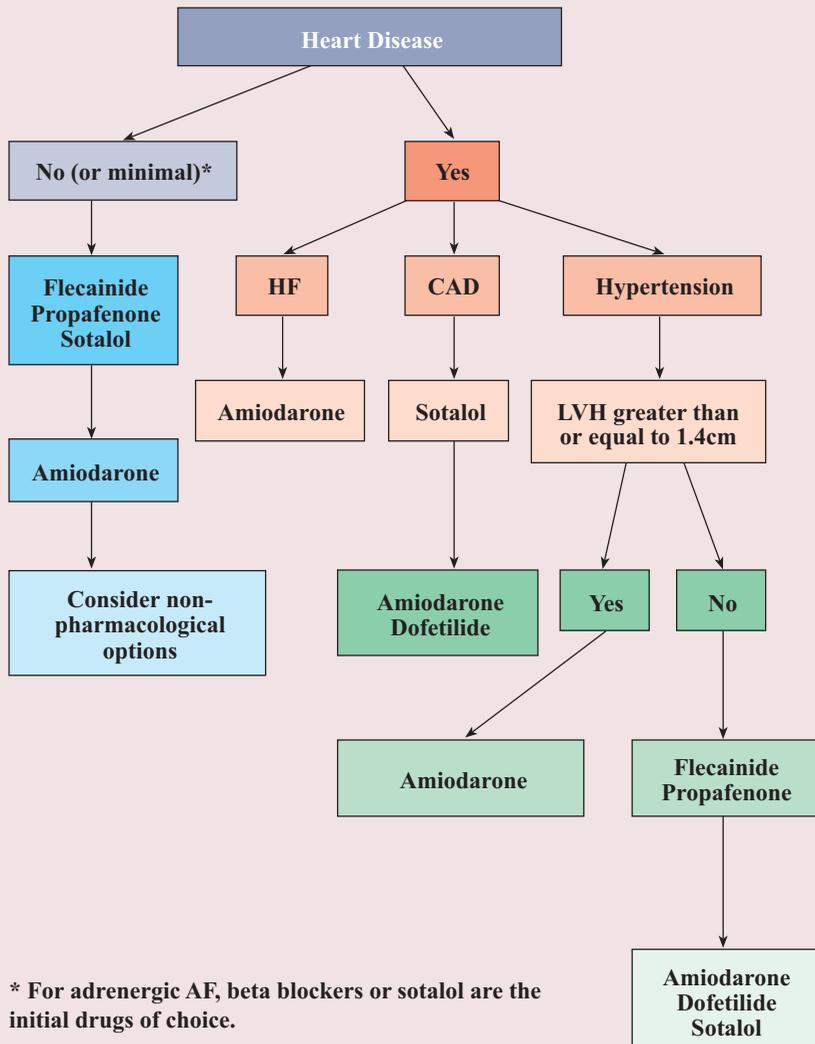
B Rhythm control may be appropriate for patients who are symptomatic especially in those with no significant underlying heart disease. Conversion to sinus rhythm may be achieved by electrical or pharmacologic means. (pg 15)

Grade B, Level III

Pharmacological management of recurrent paroxysmal or persistent AF



Anti-arrhythmic drug therapy to maintain sinus rhythm in recurrent paroxysmal or persistent AF



HF = heart failure
CAD = coronary artery disease
LVH = left ventricular hypertrophy