Atrial fibrillation

Yee C Lau

Gregory YH Lip

Abstract

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with a high prevalence rate amongst the elderly. It is associated with increased mortality and morbidity, as a result of ischaemic stroke, systemic thromboembolism and heart failure. Stroke prevention is central to the initial management of AF, irrespective of the clinical subtype of AF.

The keystone of AF management remains stroke prevention. The risk of ischaemic stroke in AF is related to increasing age and co-existent comorbidities, such as hypertension, diabetes mellitus, valvular heart disease, heart failure and previous strokes. All patients with AF should be risk stratified for stroke and bleeding, with the CHA_2DS_2-VASc and HAS-BLED scores, respectively, before initiation of oral anticoagulant treatment. Until recently, the vitamin K antagonists were the mainstay of antithrombotic therapy, but non-warfarin oral anticoagulants (NOACs) are now increasingly being preferred.

The subsequent approach to management of AF is largely patient centred and symptom driven, and can be broadly described as 'rhythm control' for paroxysmal and persistent AF, using anti-arrhythmic agents, and 'rate control' for permanent AF. Rate control is usually with β-blockers or non-dihydropyridine calcium channel blockers, with or without digitalis. Rhythm control may require anti-arrhythmic drugs and/or electrophysiological procedures, such as catheter ablation.

Keywords Atrial fibrillation; non-warfarin oral anticoagulant (NOAC); stroke; thromboembolism; vitamin K antagonist

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia encountered in clinical practice. In both developed and emerging economies, the incidence of AF is increasing as a result of improved longevity and expansion of the elderly population. It is projected that by 2050, 2% of the general population will have AF, which poses an important public health problem.[1] The prevalence of AF is age-dependent, affecting <0.5% of subjects aged between 40 and 50 years, and increasing to 18% in individuals aged ≥85 years.[2,3]

Yee C Lau ***MRCP*** *is a Research Fellow at the University of Birmingham Centre for Cardiovascular Science, City Hospital, Birmingham, UK. Competing interests: none declared.*

Gregory Y H Lip ***MD FRCP*** *is Professor of Cardiovascular Medicine at the University of Birmingham Centre for Cardiovascular Science, City Hospital, Birmingham, UK. Competing interests: Prof Lip has served as a consultant for Bayer, Astellas, Merck, Sanofi, BMS/Pfizer, Daiichi-Sankyo, Biotronik, Medtronic, Portola and Boehringer Ingelheim and has been on the speakers bureau for Bayer, BMS/Pfizer, Boehringer Ingelheim, Daiichi-Sankyo, Medtronic and Sanofi Aventis.*

AF is associated with increased morbidity and morbidity due to its complications, such as ischaemic stroke, systemic thromboembolism and heart failure. AF confers a fivefold increase risk of stroke, and one in five 'cryptogenic' strokes is attributed to this arrhythmia. More importantly, stroke in association with AF generally results in higher mortality, greater disability and longer in-patient stay than stroke occurring in the absence of this arrhythmia.[4] AF confers a twofold increased risk of mortality even after adjusting for pre-existing cardiovascular conditions.[5] Finally, patients with AF have an increased risk of heart failure with a relative risk of 3.4 in both men and women.[3]

Definition and classifications of AF

AF is an atrial tachyarrhythmia characterized by rapid, chaotic and uncoordinated atrial activation with subsequent deterioration of atrial mechanical function. AF is classified into paroxysmal, persistent, long-standing persistent and permanent based on the temporal pattern of arrhythmia plus treatment strategy.

- Paroxysmal AF: recurrent, self-terminating episodes lasting less than 7 days (usually less than 24 hours).
- Persistent AF: episodes lasting for more than 7 days or requiring termination by either pharmacological or electrical cardioversion.
- Long-persistent AF: AF lasting over 1 year when decision is made for rhythm control strategy.
- Permanent AF: AF lasting for more than a year with decision made by both patient and physician not to pursue rhythm control strategy.

Risk factors for AF

In the population-based prospective Framingham Heart study, advancing age was associated with increased risk of AF (odds ratio [OR] 2.1 in men, 2.2 in women for every decade).[6] In addition, patients with congestive heart failure (OR 4.5 in men and 5.9 in women), valvular heart disease (OR 1.8 in men, 3.4 in women), myocardial infarction (OR 1.4 in men), diabetes (OR 1.4 in men, 1.6 in women) and hypertension (OR 1.5 in men, 1.4 in women) were at significantly higher risk of developing AF. At the same time, increased left atrial (LA) size is also known to precipitate and perpetuate AF.[7] Table 1 summarizes the common risk factors for developing AF.

Pathophysiology of AF – a brief overview

The pathophysiology relating to the development of AF is complex, involving structural changes to the atrium and electrophysiological alterations.

Intrinsic structural changes involve the proliferation and differentiation of fibroblasts into myofibroblasts, resulting in fibrosis of the atrium. This leads to electrical dissociation between muscle bundles and local conduction, with persistence and stabilization of small re-entrant circuits.[8] At the same time, intracellular changes involving inward Ca^+ and K^+ currents occur, causing shortening of atrial refractory periods.[9] The overall effect of these events is to cause electrophysiological changes in the orientations of myocyte fibres in the pulmonary vein,[10] which will perpetuate or initiate further AF.

Risk factors for the development of atrial fibrillation

Cardiac	Hypertension
	Ischaemic heart disease
	Congestive heart failure
	Rheumatic heart disease
	Sick sinus syndrome
	Pre-excitation syndromes (Wolff–Parkinson–White syndrome)
	Atrial septal defect
	Atrial myxoma
	Pericarditis and pericardial effusion
	Cardiomyopathies
	Post-operative AF (POAF)
Non-cardiac	Acute infections
	Electrolyte imbalance
	Pulmonary embolism
	Lung carcinoma
	Pleural effusion
	Thyrotoxicosis
Miscellaneous	Alcohol, excess caffeine, illicit drugs (such as cocaine, amphetamine, MDMA), emotional and physical stress

Table 1

The combination of cellular, structural and electrical remodelling provides the substrate that promotes the initiation and self-perpetuation of this arrhythmia, thereby causing AF to beget more AF.

Thrombogenesis in AF

The presence of AF results in a fivefold increase in the risk of stroke. This can be explained by components of Virchow's triad – abnormal changes in vessel wall, blood flow and blood constituents – leading to a prothrombotic state.

'Abnormal vessel wall' is recognized as gradual LA dilatation, endocardial denudation and microscopic fibro-elastic changes of the extracellular matrix, which promote thrombogenesis. 'Abnormal blood flow' due to loss of atrial systole manifests as stasis within the left atrium, spontaneous echocardiographic contrasts in the left atrium on transoesophageal echocardiography (TOE) and reduced left atrial appendage (LAA) velocities, which facilitate thrombus formation. 'Abnormal blood constituents' involving platelet activation and abnormal coagulation indices also have been shown to contribute to thrombogenesis.

Clinical features, detection and confirmation

The most common symptoms in patients with AF are palpitations, shortness of breath, chest pain, dizziness and fatigability. However, a significant proportion of patients with AF are asymptomatic (around 12–15%) and the arrhythmia is discovered by chance. Moreover, it is not uncommon to note incidental AF in patients with embolic stroke.

Detection of an irregular pulse should trigger one's suspicion of AF and allow for confirmation by electrocardiogram (ECG). A standard 12-lead ECG in AF will demonstrate loss of distinct P-wave and irregular R–R intervals. For patients with paroxysmal AF, ambulatory Holter (24 hour–7 days) monitoring or use of an implantable loop recorder may facilitate diagnosis.

Clinical evaluation including alcohol intake, illicit drugs and excessive caffeine use may help to identify possible triggers of AF development and allow immediate remedial action to be taken. Besides irregular pulse, physical examination will reveal irregular jugular venous pulsation with absence of a-wave. Signs of valvular heart disease, heart failure or even lung pathology may be present.

All AF patients should have routine haematology, biochemistry and thyroid function tests. A chest X-ray may help to identify intrinsic pulmonary pathology as well as showing enlargement of the cardiac chambers and features of heart failure.

Transthoracic echocardiography (TTE) is not helpful in making the diagnosis of AF per se, but will allow assessment of cardiac structure and function, which will help in the development of a treatment strategy.

General non-interventional management strategies

The cornerstone of management in AF is stroke prevention; after careful risk stratification of ischaemic stroke and assessment of bleeding risk, oral anticoagulants should be offered. Subsequently, the choice between rate control and rhythm control strategies will depend on the onset and pattern of AF as well as the patient's symptoms, given that AF management is patient centred and symptom-directed.[11]

Rate control is generally the first-line treatment for most people with atrial fibrillation, while rhythm control is used for the management of new-onset AF, recurrent paroxysmal AF, or AF with heart failure/cardiovascular embarrassment. A management strategy of AF is shown in Figure 1.

Rate control in new-onset AF

In haemodynamically stable, asymptomatic patients or those presenting more than 48 hours after onset, a strategy of rate control and oral anticoagulation can be offered. In the acute clinical setting, a well-controlled heart rate can be achieved by intravenous or oral use of a β-blocker and a non-dihydropyridine calcium channel blocker, such as verapamil and diltiazem. This should improve the haemodynamic status and alleviate symptoms.[11,12]

Digoxin is often used in patients with fast AF and acute heart failure owing to its negative chronotropic and positive inotropic effects.[13] It can be also used in hypotensive patients. However, it has a delayed onset of action, and not effective in patients with a high-catecholamine state (such as post-surgery or acute sepsis), myocardial ischaemia or pulmonary diseases. Combination of digoxin with a rate-limiting calcium channel blocker and a β-blocker is sometimes needed to control the ventricular rate, but a combination of verapamil and a β-blocker should be avoided owing to the risk of ventricular asystole.

Amiodarone is a useful alternative if other drugs are ineffective or contraindicated in controlling ventricular rate, especially