Atrial fibrillation 1: classification and clinical implications

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Atrial fibrillation is a common arrhythmia that has significant clinical implications. It increases the risk of stroke and mortality. Various cardiac and extra-cardiac pathologies can lead to the development of atrial fibrillation. Determining the underlying cause is essential in assessing the prognosis and guiding the management.

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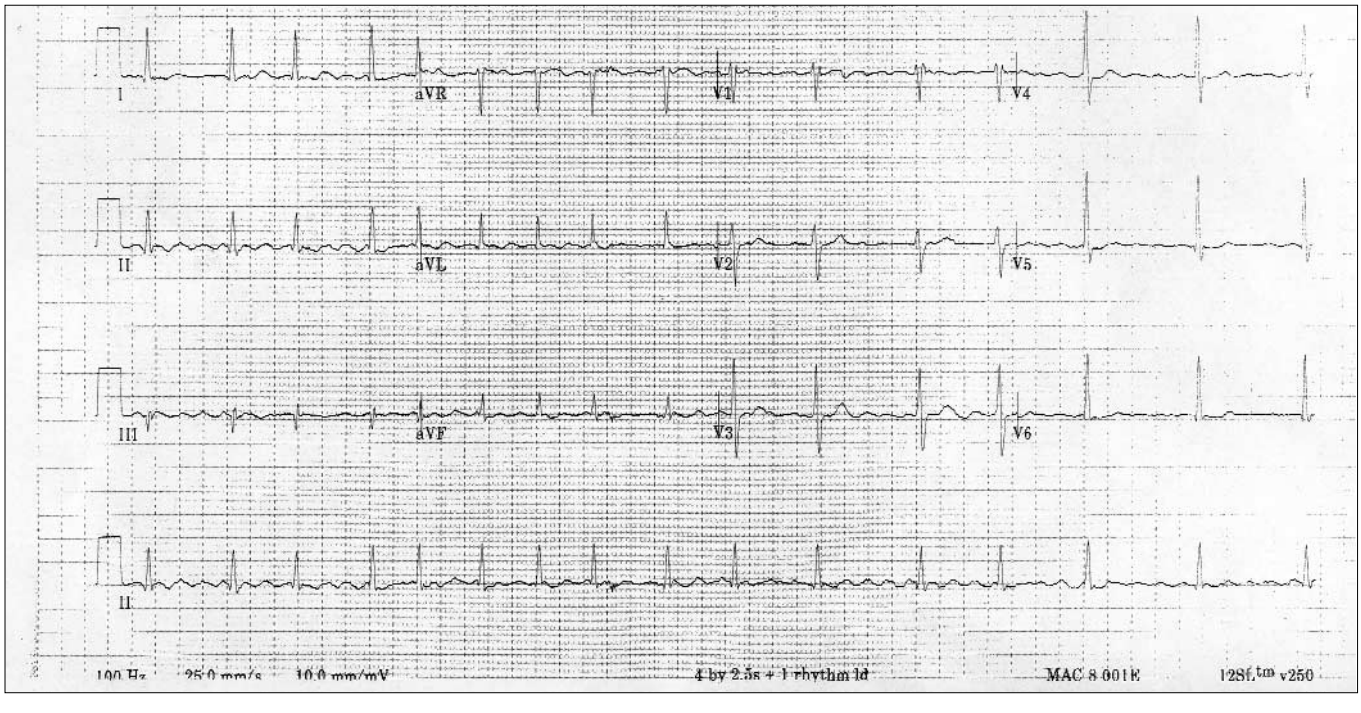
Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, and it is by no means a benign condition. People with AF have a mortality rate that is twice as high as that among those with sinus rhythm, but the optimal strategy for the management of this condition has not been completely established. This is because AF has multiple aetiologies and risk factors, various clinical presentations, and a variable pattern of behaviour. The incidence and prevalence of AF increase with age. The biennial prevalence ranges from 6.2 and 3.8 cases per 1000 in men and women respectively aged 55–64 years, up to 75.9 and 62.8 per 1000 in men and women aged 85–94 years. Men are 1.5 times more likely to develop AF than women (Benjamin et al, 1994).

DEFINITION AND MECHANISMS OF ATRIAL FIBRILLATION

AF is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with consequent deterioration of atrial mechanical function. On the electrocardiogram (ECG), AF is characterized by the replacement of consistent P waves with rapid fibrillatory waves that vary in shape, size and timing, associated with an irregular, frequently rapid ventricular response (*Figure 1*). The latter depends on electrophysiological properties of the atrioventricular (AV)

Figure 1. Atrial fibrillation with uncontrolled ventricular response. Heart rate is approximately 110/min.



node, the level of vagal and sympathetic tone, and the action of drugs.

It has been suggested that electrical activation in AF originated from multiple reentrant wavelets that arc around the atrium (Moe, 1962). These wavelets range from a few large loops to many small circuits. Small circuits are easier to sustain and less likely to terminate spontaneously. The wavelength of a circuit is the product of the conduction velocity and the refractory period. Slow conduction results from fibrosis, inflammation, ischaemia and autonomic tone, while short refractoriness could be the result of thyrotoxicosis. Atrial enlargement helps sustain AF by accommodating more wavelets. It has been discovered that some episodes of AF are initiated by rapid, repetitive firing foci of atrial myocytes in muscle sleeves located in the pulmonary veins (Haissaguerre et al, 1998). Patients may have more than one pulmonary vein focus capable of generating AF. Foci also occur in the right atrium and infrequently in the superior vena cava or coronary sinus (Chen et al, 1999).

Pharmacological or electrical cardioversion of AF has a higher success rate when AF has been present for less than 24 hours, whereas a longer duration of AF reduces the likelihood of restoring and maintaining sinus rhythm. This might be explained by the fact that AF induces anatomical and electrical remodelling of the atria. Wijffels et al (1995) have supported the notion that AF tends to perpetuate itself by conducting an experiment on an animal model. They used an automatic atrial fibrillator that detected spontaneous termination of induced AF and re-induced the dysrhythmia by delivering a burst of electrical stimuli.

Initially, electrically-induced AF terminated spontaneously. After repeated inductions, however, the episodes became progressively more sustained until AF persisted at a more rapid atrial rate. This was related to a phenomenon known as electrophysiological remodelling, defined as progressive shortening of effective refractory periods associated with increasing episode duration. Restoration of electrical refractoriness by DC cardioversion might explain the higher success rate of early intervention. After a long period of persistent AF, recovery of atrial contraction can be delayed for days or even weeks after sinus rhythm has been restored. This has important implications for the duration of anticoagulation after cardioversion.

TABLE 1.
Causes of atrial fibrillation

Cardiac causes	Ischaemic heart disease	
	Rheumatic heart disease	
	Hypertension	
	Heart failure	
	Cardiomyopathy	
	Valvular disease	
	Myocarditis	
	Pericarditis	
	Tachycardia-bradycardia syndrome	
	Left atrial myxoma	
	Cardiac surgery	
Non-cardiac causes	Metabolic	Diabetes mellitus
		Obesity
	Endocrine	Thyrotoxicosis
		Phaeochromocytoma
	Toxic	Alcohol abuse
		Carbon monoxide poisoning
	Respiratory	Chronic obstructive pulmonary disease
		Pulmonary embolism
		Pneumonia
	Autonomic	Post-prandial atrial fibrillation
		Exercise-induced atrial fibrillation

CAUSES AND PREDISPOSING FACTORS

AF develops when any pathological process such as inflammation, infiltration, scarring or stretching take place in the atrial tissue. The underlying pathologies range from autonomic imbalance through organic heart disease to metabolic disorders (*Table 1*).

Valvular heart disease, heart failure, hypertension and diabetes mellitus predispose people of both sexes to AF. Myocardial infarction and coronary heart disease are associated with AF in men (Benjamin et al, 1994) (*Figure 2*). Other conditions that increase the risk are obesity, cardiomyopathy, alcohol ingestion, thyrotoxicosis and, in susceptible persons (Coumel, 1992), increased vagal tone (causing post-prandial AF) or increased sympathetic tone (causing exercise-related AF). Familial cases are rare and have been associated with abnormalities of chromosome 10. 'Lone' AF accounts for 17% of all cases with AF. It applies to young individuals (under 60 years of age) without clinical, electrocardiographic or echocardiographic evidence of cardiopulmonary disease (Kopecky et al, 1987).

CLASSIFICATION OF ATRIAL FIBRILLATION

Various classification systems have been proposed for AF. One scheme is based on the ECG

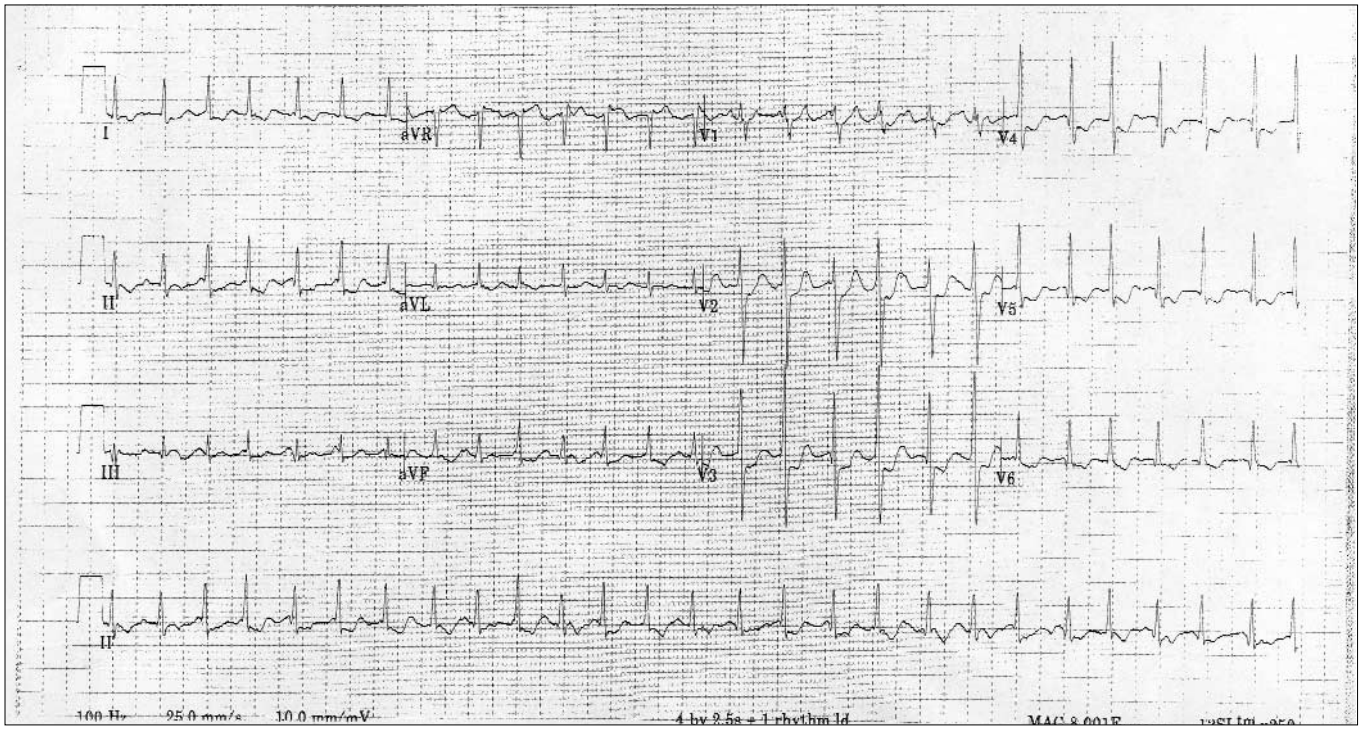


Figure 2. Fast atrial fibrillation associated with ST segment depression in the anterior leads. This could be rate-related or secondary to ischaemia induced by tachycardia. This patient had angiographic evidence of ischaemic heart disease and ST segment shift disappeared when the rhythm was converted back to sinus.

presentation (Bellet, 1971; Prystowsky and Katz, 1998), while others are based on clinical presentations and implications (Levy et al, 1995; Gallagher and Camm, 1998; Levy, 2000). None of these classifications, however, have addressed all aspects of AF. The American College of Cardiology, American Heart Association, and European Society of Cardiology have established a classification and standardized the definitions of paroxysmal, persistent, and permanent AF (Fuster et al, 2001). This classification is based on two important elements: the pattern of the evolution of the arrhythmia that may determine further treatment, and the response of this arrhythmia to medical interventions (*Table 2*).

An effort should always be made to establish whether an episode of AF is the first detected one and whether or not it is symptomatic or self-limited. It should be recognized, however, that there may be uncertainty about the duration of the episode and about previous undetected ones. When a patient has had two or more episodes, AF is considered to be recurrent. If the arrhythmia terminates spontaneously, recurrent AF is designated paroxysmal (*Figure 3*); when sustained, AF is designated persistent. In the latter case, termination with pharmacological therapy or electrical cardioversion does not change the designation. The category of persistent AF also includes cases of longstanding AF (e.g. greater than 1 year) in which cardioversion has not been indicated or attempted, usually leading to permanent AF.

The terminology defined in the preceding paragraph applies to episodes of AF that last more than 30 seconds and that are unrelated to a reversible cause. Secondary AF that occurs in the setting of acute myocardial infarction, cardiac surgery, pericarditis, myocarditis, hyperthyroidism, pulmonary embolism, pneumonia or acute pulmonary disease is considered separately, because AF is less likely to recur once the precipitating condition is resolved. In these settings, AF is not the primary problem, and treatment of the underlying disorder concurrently with management of the episode of AF usually results in termination of the arrhythmia without recurrence.

TABLE 2.
Classification of atrial fibrillation

Type	Duration and character
First detected	Usually <48 hours, usually patient is still in atrial fibrillation when diagnosed
Paroxysmal	Self-terminating, <2–7 days, frequently <24 hours
Persistent	Usually more than 7 days Not self-terminating, usually electrical cardioversion needed to restore sinus rhythm
Permanent	Long standing, usually more than a year Restoration and/or maintenance of sinus rhythm not feasible

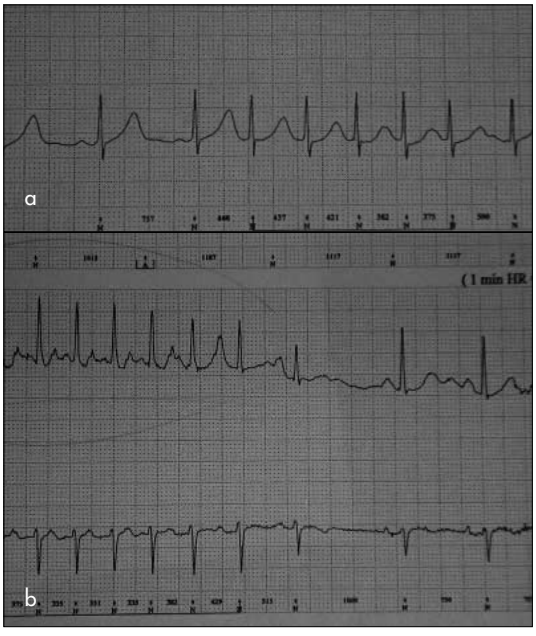


Figure 3. Traces from 24-hour electrocardiography tape. a. Sudden occurrence and (b) spontaneous conversion of paroxysmal atrial fibrillation.

CLINICAL PRESENTATIONS AND IMPLICATIONS

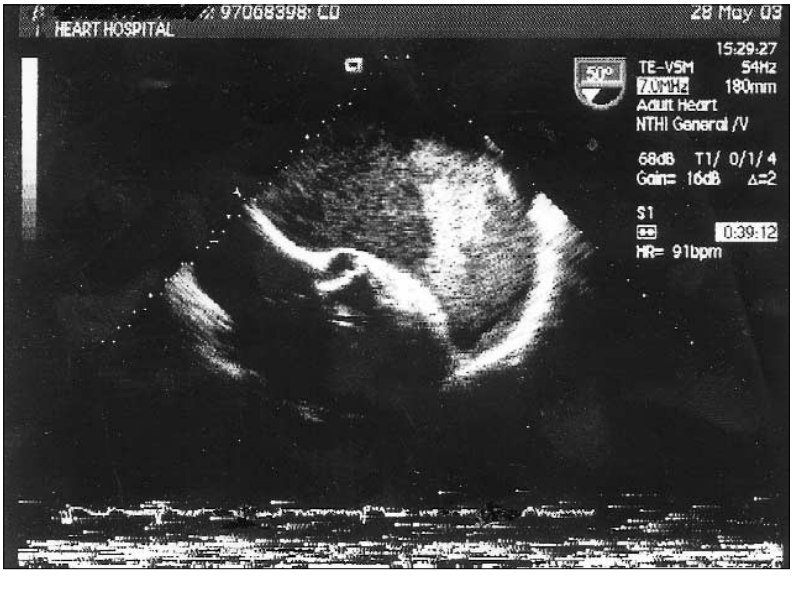
AF causes palpitation, chest pain, dyspnoea and fatigue. Some patients experience pre-syncope, especially at arrhythmia onset or termination. All patients with long-lasting episodes of AF develop left ventricular dysfunction, even those without underlying heart disease. This is often called tachycardia-induced cardiomyopathy (or tachycardiomyopathy). However, in at least one third of patients no obvious symptoms or noticeable degradation of quality of life are observed (Savelieva and Camm, 2000).

AF has significant clinical implications, namely haemodynamic deterioration, increased thromboembolic events and increased mortality. Haemodynamic impairment results from the loss of synchronous atrial contraction, rhythm irregularity and excessive ventricular rate response, and the progression of underlying cardiovascular disease. A further marked decrease in cardiac output can occur in patients with impaired diastolic ventricular filling, such as those with hypertension, mitral stenosis, or hypertrophic or restrictive cardiomyopathy.

AF induces a hypercoagulability state, indicated by raised plasma concentration of fibrin, D-dimer and B-thromboglobulin. This, with haemodynamic stasis induced by AF, is thought to be responsible for thromboembolism (*Figure 4*). AF is considered the most common cardiac cause of systemic emboli (Wolf et al, 1987); it accounts for 15% of all cases of stroke. In patients with rheumatic heart disease, AF increases the risk of stroke by a factor of 17. Non-rheumatic AF increases the risk of stroke by approximately five-fold, to 5% per year. Apart from symptomatic stroke, AF has been associated with an increased risk of silent stroke (Petersen, 1990). Risk factors for stroke in AF include age >65 years, hypertension, previous stroke or transient ischaemic attack, diabetes, recent heart failure, and atrial or ventricular enlargement on echocardiography (Wolf et al, 1987).

Several cohort and retrospective studies have shown that the relative risk of death in subjects with AF is roughly twice that found in subjects in sinus rhythm (Onundarson et al, 1987; Krahn et al, 1995). The reduced survival relates to progression of the underlying cardiovascular disease and stroke. Patients with lone AF have a favourable prognosis with respect to thromboembolism and mortality.

Figure 4. Transoesophageal echocardiography in a patient with permanent atrial fibrillation. Note the presence of spontaneous contrast filling, a dilated left atrium and a small thrombus in the left appendage.



CLINICAL EVALUATION

The initial evaluation of a patient with suspected or proven AF includes determining the type of arrhythmia (paroxysmal or persistent), the underlying cause, and the associated cardiac and extra-cardiac factors (*Table 3*). A careful history is essential in identifying these points and serves as an effective guide to therapy. Physical examination of patients with AF reveals an irregular pulse, irregular jugular venous pulsations and variation in the loudness of the first heart sound. It might also disclose associated valvular heart disease, myocardial abnormalities or heart failure. It is important that thyroid function, serum electrolytes and haemoglobin are measured when AF is diagnosed.

The definitive diagnosis of AF requires ECG documentation during the dysrhythmia. If

episodes of paroxysmal AF are frequent, then a 24-hour Holter monitor can be used. When the episodes are infrequent, then an event recorder or an implantable recording device (Reveal device, Medtronic, USA) may be more useful.

A chest radiograph is valuable for detection of intrinsic pulmonary pathology and evaluation of the pulmonary vasculature. It might also detect the presence of heart failure. Transthoracic echocardiography should be undertaken during the initial workup of all AF patients to determine left atrium and ventricle dimensions, the left ventricular wall thickness and function, and to exclude occult valvular or pericardial disease or hypertrophic cardiomyopathy. By determining the left ventricular systolic and diastolic function, echocardiography could play an important role in guiding decisions regarding antiarrhythmic and antithrombotic therapy. Thrombus should be sought in the left atrium but is seldom detected without transoesophageal echocardiography.

An electrophysiological study is rarely needed to establish the diagnosis of AF but may be useful in defining the mechanism of arrhythmia in patients with paroxysmal AF who might be considered for curative catheter ablation. HM

Conflict of interest: none.

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TABLE 3.
Clinical evaluation of patients presenting with atrial fibrillation (AF)

Symptoms and/or signs suggestive of AF	Completed current and past medical history	Chest pain
		Dyspnoea
		Syncope
		Acute neurological symptoms
		Alcohol intake
		History of myocardial infarction
		History of rheumatic fever or valvular lesion
		History of diabetes
	General and cardiovascular physical examination	Heart rate (new-onset AF is usually fast. Tachycardia might also suggest thyrotoxicosis)
		Blood pressure measurement
		Jugular venous pressure (look for evidence of pulmonary embolism)
		Murmurs (valvular lesions)
		Respiratory examination
		Tremor (alcohol withdrawal, thyrotoxicosis)
	Investigations	Blood test (serum electrolytes, thyroid function test, haemoglobin, white cell counts)
		ECG (diagnostic of sustained AF)
		Holter ECG monitor (paroxysmal AF)
		Echocardiography (left ventricle systolic and diastolic function, valvular lesions, pericarditis)
		Exercise tolerance test/ isotope perfusion scan (ischaemic heart disease)
		Electrophysiological study (selected patients)

ECG = electrocardiogram

KEY POINTS

- Atrial fibrillation is associated with increased mortality. It is the most common cardiac cause of systemic emboli, and accounts for 15% of all causes of stroke.
- Firing foci of atrial myocytes in the pulmonary veins could generate atrial fibrillation.
- Atrial fibrillation causes anatomical and electrophysiological remodeling in the atrial tissue.
- Following a successful DC cardioversion the recovery of atrial contraction can be delayed for few weeks.
- Careful assessment of patients with atrial fibrillation is essential in determining the cause and type of the arrhythmia and consequently directing the management.