AETIOLOGY, PATHOPHYSIOLOGY, AND CLINICAL FEATURES

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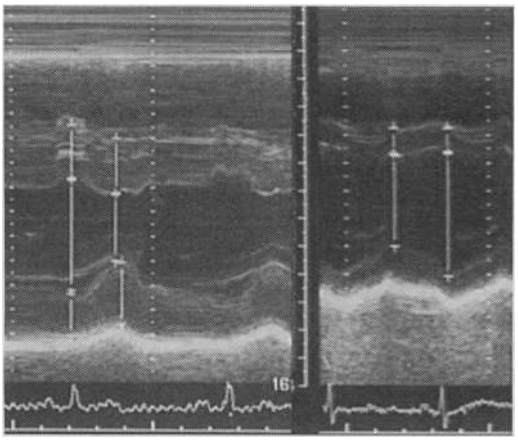
Aetiology

Causes of atrial fibrillation

Cardiac causes	Non-cardiac causes
Common	
Ischaemic heart disease	Thyrotoxicosis
Hypertension	Acute infections, especially pneumonia
Rheumatic heart disease	Excess alcohol intake
Sick sinus syndrome	Lung carcinoma
Pre-excitation syndromes (for example, Wolff-Parkinson-White)	Other intrathoracic pathology (for example, pleural effusion)
	Postoperative problems, especially after thoracotomy or coronary artery bypass
Less common	
Cardiomyopathy or heart muscle disease	Pulmonary thromboembolism
Pericardial disease, including effusion and constrictive pericarditis	
Atrial septal defect	
Atrial myxoma	

Left ventricular hypertrophy is considered to be present if the left ventricular mass index is >131 g/m² in men and >110 g/m² in women



M mode echocardiograms showing left ventricular hypertrophy (left) and normal heart (right).

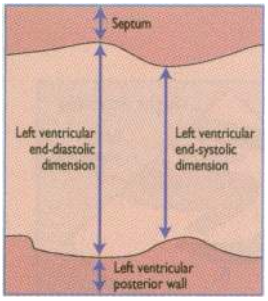


Diagram showing measurements for calculating left ventricular mass index.

Ischaemic heart disease

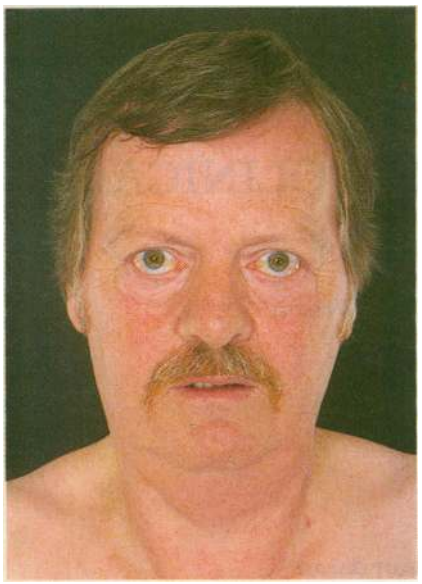
Ischaemic heart disease is probably the most common underlying cause of atrial fibrillation in Britain. In addition, the fast ventricular rate due to atrial fibrillation may cause angina, leading to cardiac ischaemia and heart failure. Atrial fibrillation may complicate acute myocardial infarction in 10-15% of cases and is often a marker of extensive myocardial damage and a poor prognosis, with increased mortality. If atrial fibrillation occurs with an acute myocardial infarction, it tends to occur in the first 24 hours and is usually self limiting. Patients should be observed unless fast atrial fibrillation occurs or the patient is haemodynamically compromised.

Atrial fibrillation is also a marker of underlying ventricular dysfunction and a compromised myocardium. Many years after myocardial infarction, ventricular scarring and dilatation often predispose to atrial fibrillation and congestive heart failure.

Hypertension

Hypertension accounted for about half of the cases of atrial fibrillation in the Framingham study. Hypertension contributes to the complications of stroke and thromboembolism in such patients, especially if left ventricular hypertrophy is present. Electrocardiography is useful for screening for left ventricular hypertrophy (for example, with the criteria of Sokolow and Lyon—S wave in V1 and R wave in V5 or V6 of ≥35 mm), and if the electrocardiogram is abnormal the echocardiogram will invariably show left ventricular hypertrophy. Left ventricular hypertrophy on echocardiography is defined by calculating the left ventricular mass index.

Atrial fibrillation may be secondary to left atrial dilatation, which occurs in hypertensive patients, as a consequence of reduced left ventricular compliance. In addition, hypertension may be associated with underlying coronary artery disease, which itself is a risk for atrial fibrillation and thromboembolism.



Patient with goitre and thyrotoxic eye disease (published with patient's permission).

Atrial fibrillation due to alcohol

Alcohol may account for a third of new cases of atrial fibrillation (up to two thirds in patients aged under 65)

Atrial fibrillation can occur with acute and chronic alcohol ingestion

Most (about 90%) cases of atrial fibrillation convert spontaneously to sinus rhythm within 24 hours

Mechanisms

Alcohol ingestion results in release of catecholamines from the adrenal medulla, especially noradrenaline

Alcohol causes release of cardiac stores of adrenaline

Plasma acetaldehyde, the main metabolite of ethanol, raises catecholamine concentrations systemically and in the myocardium

Alcohol (or its metabolites) directly affects the heart, with prolonged PR, QRS, and QT times, facilitating atrial arrhythmias

Withdrawal of alcohol results in increased release of catecholamines

Alcohol excess is associated with hypertension

Rheumatic heart disease

In a survey of emergency admissions of patients with atrial fibrillation, rheumatic heart disease (predominantly mitral valve disease) was present in 15% of cases. Rheumatic valve disease, especially mitral valve stenosis, is particularly important as it increases the thromboembolic risk of patients with chronic atrial fibrillation about 18-fold. Up to a fifth of patients with mitral stenosis and atrial fibrillation develop embolic events, which in most (60-75%) cases affect the cerebral circulation. This risk of stroke and thromboembolism for patients in atrial fibrillation is three to seven times that of patients with mitral stenosis in sinus rhythm. Echocardiography in such cases may show left atrial thrombus, although transthoracic echocardiography is not a sensitive or reliable method of detection.

Thyroid disease

Thyrotoxicosis is an important and curable cause of atrial fibrillation. About 10-15% of patients with untreated thyrotoxicosis develop atrial fibrillation. Thyrotoxicosis may be underdiagnosed, however, as thyroid function tests are often neglected, particularly in elderly people, in whom classic signs of thyrotoxicosis may not be obvious. One clinical clue may be the failure of digoxin to control the ventricular rate without the addition of β blockers. Hyperthyroidism (affecting about 1% of the population) may also coexist with both ischaemic and rheumatic heart disease. Thyroid function tests should therefore be routinely checked in atrial fibrillation of recent onset.

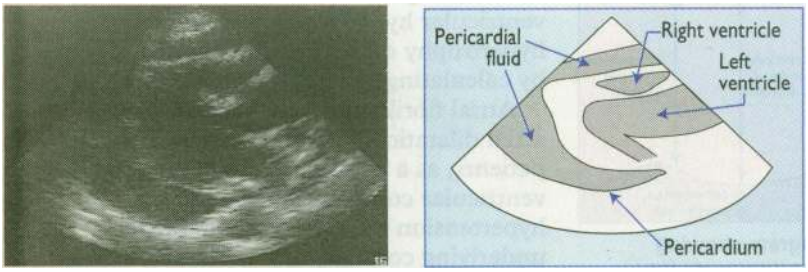
Rarely, hypothyroidism may cause heart muscle disease and heart failure. Myxoedema is also associated with hyperlipidaemia and an increased risk of heart disease.

Excess alcohol intake

Atrial fibrillation due to an excess intake of alcohol often occurs after holidays or at weekends, giving rise to the term "holiday heart syndrome." Alcohol can thus precipitate atrial fibrillation in healthy people (with otherwise normal hearts), who may have no subsequent risk of atrial fibrillation. Chronic excess intake of alcohol can also be associated with a dilated heart (alcoholic heart muscle disease) and atrial fibrillation.

Pneumonia

Pneumonia is commonly associated with atrial fibrillation in medical patients admitted urgently, being present in about 7% of cases. It is often difficult to know, however, whether the pneumonia is complicating pre-existing atrial fibrillation or is the precipitant of atrial fibrillation. Pneumonia as a precipitant of atrial fibrillation occurs predominantly in elderly patients, who thus have an acute precipitating cause for atrial fibrillation. The pneumonia should therefore be treated, and cardioversion to sinus rhythm after treatment of the acute episode should be considered.

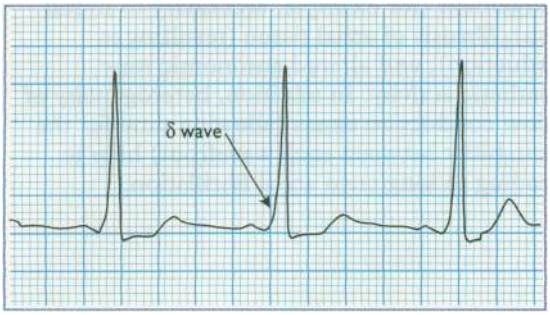


Two dimensional echocardiogram (and diagram) showing large pericardial effusion.

Other causes

Other cardiac causes of atrial fibrillation include congenital heart disease (especially atrial septal defect), the sick sinus syndrome, and the pre-excitation syndromes associated with accessory pathways in the conducting system of the heart (such as the Wolff-Parkinson-White syndrome). Idiopathic dilated and hypertrophic cardiomyopathy and pericardial diseases (such as pericardial effusion) are also associated with atrial fibrillation.

An atrial septal defect should be considered in a young patient with atrial fibrillation, especially if a pulmonary ejection systolic murmur in association with a split, second heart sound is heard. The Wolff-Parkinson-White syndrome is recognised by a short PR interval (<0·12 seconds in an electrocardiogram) and a δ wave in the electrocardiogram when the patient is in sinus rhythm, and should be suspected in a young patient presenting with fast atrial fibrillation.



Electrocardiogram showing short PR interval and δ wave in Wolff-Parkinson-White syndrome.

Non-cardiac causes of atrial fibrillation are also often encountered, and causes of single, isolated episodes include pneumonia (and other acute infections); lung tumours and other intrathoracic conditions, such as pleural effusions; pulmonary thromboembolism; and surgery. When atrial fibrillation occurs postoperatively, it is usually after cardiothoracic surgery, although any surgery with general anaesthesia may precipitate atrial fibrillation. The incidence of supraventricular arrhythmias after cardiothoracic surgery is 20%. Atrial fibrillation after cardiothoracic surgery often requires treatment in the short term. In contrast, atrial fibrillation after non-cardiothoracic surgery is usually self limiting, often reverting spontaneously to sinus rhythm.

Features of "idiopathic" or "lone" atrial fibrillation

Diagnosis of exclusion
No history of cardiovascular disease or hypertension
No abnormal cardiac signs on physical examination
Normal chest *x* ray film and electrocardiogram (apart from the atrial fibrillation) with no previous myocardial infarction or left ventricular hypertrophy
Normal atria, valves, and left ventricular size (and function) on echocardiography

Idiopathic or "lone" atrial fibrillation

Some patients with atrial fibrillation have no predisposing factor or cardiac lesions. The condition in these patients is classified as "lone" or "idiopathic" atrial fibrillation. Lone atrial fibrillation can be either paroxysmal or persistent, and is present in between 3% and 11% of all patients with atrial fibrillation.

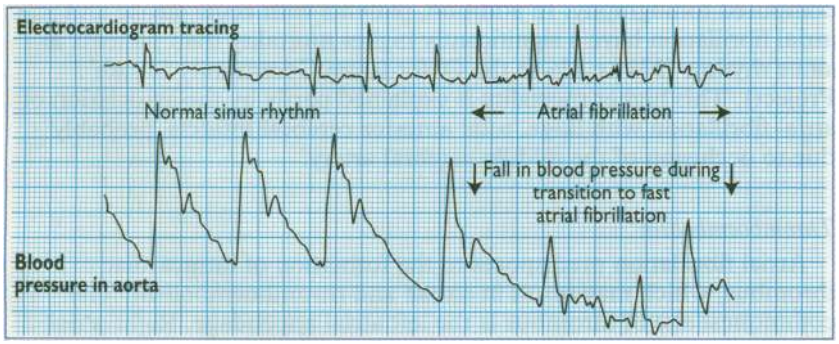
Young patients (aged under 60 years) with lone atrial fibrillation are generally accepted to be at a low thromboembolic risk, and antithrombotic treatment may not be justified. Data from the Framingham study, however, suggest a fivefold increase in the incidence of stroke in elderly patients (aged over 65) with the condition, and antithrombotic treatment should be considered.

Pathophysiology and electrophysiology

Haemodynamic disturbances

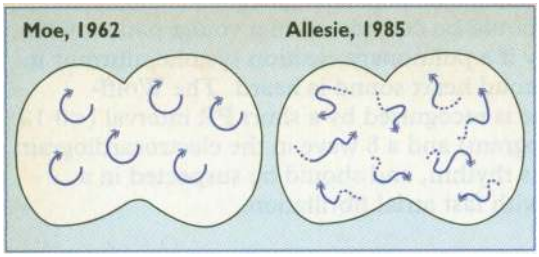
Fast ventricular rate
Reduced diastolic filling period, especially with sudden changes to a very rapid heart rate, results in a further reduction in cardiac output (especially with valvar stenosis or reduced left ventricular compliance—for example, in left ventricular hypertrophy)
Reduced atrial transport (lack of organised atrial mechanical activity with a concomitant decrease in stroke volume and cardiac output)
Atrial dilatation and loss of atrial systole, leading to intra-atrial stasis, which favours formation of thrombi
Onset of a rapid ventricular response may also lead to some mitral incompetence, thus further reducing forward flow

The haemodynamic disturbance of atrial fibrillation results essentially from the absence of atrial systole ("atrial kick") and from the rapidity and irregularity of the ventricular response, with a consequent loss of cardiac output (a loss of about 10% in normal individuals, with a greater loss at fast ventricular rates). This is more important in patients with increasing age or with progressive impairment of left ventricular contraction, or with both, in whom atrial systole contributes increasingly towards the overall stroke volume.



Blood pressure trace showing fall in blood pressure after onset of fast atrial fibrillation.

A rapid heart rate reduces the diastolic filling interval, and the additional loss of the sequential atrioventricular contraction mechanism in atrial fibrillation may lead to a dramatic reduction in cardiac output and to other haemodynamic disturbances. This is substantiated by evidence of a much improved cardiac output after cardioversion of atrial fibrillation to sinus rhythm.



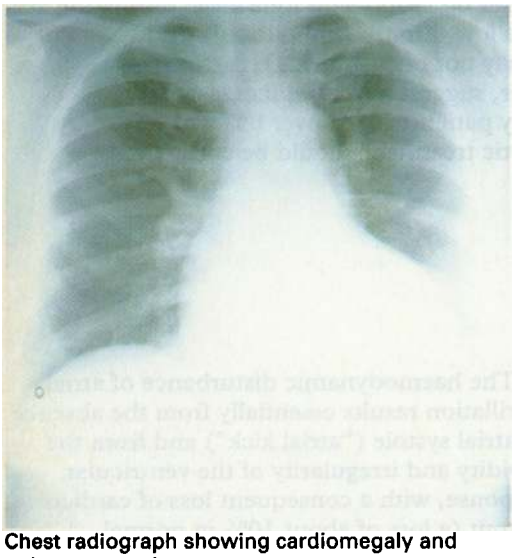
Electrophysiology of atrial fibrillation: Moe's model, multiple coexisting re-entrant wavefronts of activation within atria; and Allesie's model, multiple wavelets continually sweeping around atria in irregular, shifting patterns.

The electrophysiological mechanism of atrial fibrillation is thought to involve several coexisting re-entrant wavefronts continuously sweeping around the atria, repeatedly encountering excitable myocardium. Several factors predispose to long term maintenance of the arrhythmia: atrial enlargement (for example, secondary to mitral valve disease, hypertension), fibrosis of atrial tissue (resulting in slowing of intra-atrial conduction), and altered autonomic tone, especially increased sympathetic activity. In addition, heterogeneity of atrial refractoriness and slow conduction times (allowing time for the myocardium to regain excitability between each wavefront) help to perpetuate the process, leading to long term atrial fibrillation.

Clinical features

Symptoms with atrial fibrillation

Often none
Limited exercise tolerance (dyspnoea, fatigue)
Angina
Palpitation
Presyncope and syncope
Heart failure
Stroke



Chest radiograph showing cardiomegaly and pulmonary oedema.

Atrial fibrillation commonly presents as reduced exercise tolerance and heart failure. Less dramatic presentations include dyspnoea, angina, palpitation, and dizziness. Syncope is rare with atrial fibrillation, unless associated with the sick sinus syndrome or pre-excitation syndromes, such as the Wolff-Parkinson-White syndrome. The symptoms may be more pronounced on exercise, as a rapid ventricular response may substantially impair exercise tolerance. Occasionally patients may present as an emergency with a combination of presyncope, syncope, fatigue, dyspnoea, and lethargy, and quite commonly with gross pulmonary oedema, angina, cerebral underperfusion, and stroke. Physical findings include a pulse that is irregular in rate, rhythm, and volume; variable intensity of the first heart sound; and absence of "a" waves in the jugular venous pulse, resulting in a single positive waveform being discerned. With fast ventricular rates, an apex-radial pulse deficit appears, as each contraction may not be sufficiently strong to transmit an arterial pulse wave through the peripheral artery. Measurement of ventricular rates (at rest and on exercise) may be useful in assessing the efficacy of drug treatment in atrial fibrillation.

Heart failure

The sudden onset of fast atrial fibrillation may often precipitate overt heart failure, particularly if left ventricular function is already compromised by coexisting heart disease—for example, valvar or ischaemic heart disease. Heart failure is associated with atrial fibrillation in about 35% of cases. In these patients, atrial fibrillation may be a marker of increased mortality and may also enhance the substantial risk of thromboembolism.

Stroke

Non-rheumatic atrial fibrillation increases fivefold the risk of stroke and is present in about 15% of patients presenting with acute stroke. The risk of stroke in someone with atrial fibrillation is about 5% a year, and epidemiological evidence suggests that this risk increases with age, raised blood pressure, and other evidence of heart disease.

Patients with atrial fibrillation may also have an increased risk of recurrent stroke and have silent cerebral infarcts (often multiple) on computed tomography. In addition, patients with acute stroke and atrial fibrillation have a significantly higher mortality than patients in sinus rhythm (23% *v* 8% in the Oxfordshire Community Stroke Project). This higher mortality is explained partly by the association of atrial fibrillation with large, total anterior cerebral infarcts, probably due to occlusion of the middle cerebral artery.

Thromboembolism

Atrial fibrillation predisposes to the formation of intracardiac thrombus, which may result in stroke and thromboembolism. The commonest site of thrombus is the left atrial appendage. Right atrial thrombus with subsequent pulmonary thromboembolism is a rare complication.

Key reference

Murgatroyd FD, Camm AJ. Atrial arrhythmias. *Lancet* 1993;**341**:1317-22

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