Management of atrial fibrillation

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Cite this as: *BMJ* 2009;339:b5216
doi: 10.1136/bmj.b5216

Atrial fibrillation is the commonest sustained arrhythmia encountered in clinical practice. Its prevalence increases with age, rising from 0.7% in people aged 55-59 years to 18% in those older than 85 years.[1] Consequently, the public health burden associated with atrial fibrillation is increasing.[w1] The therapeutics of atrial fibrillation is evolving. In recent years, publication of several randomised controlled trials and meta-analyses have improved our understanding of the advantages and inconveniences of rate and rhythm control strategies, and effective, new non-pharmacological treatments have been introduced. New antiarrhythmic and anticoagulant drugs are expected in the near future.

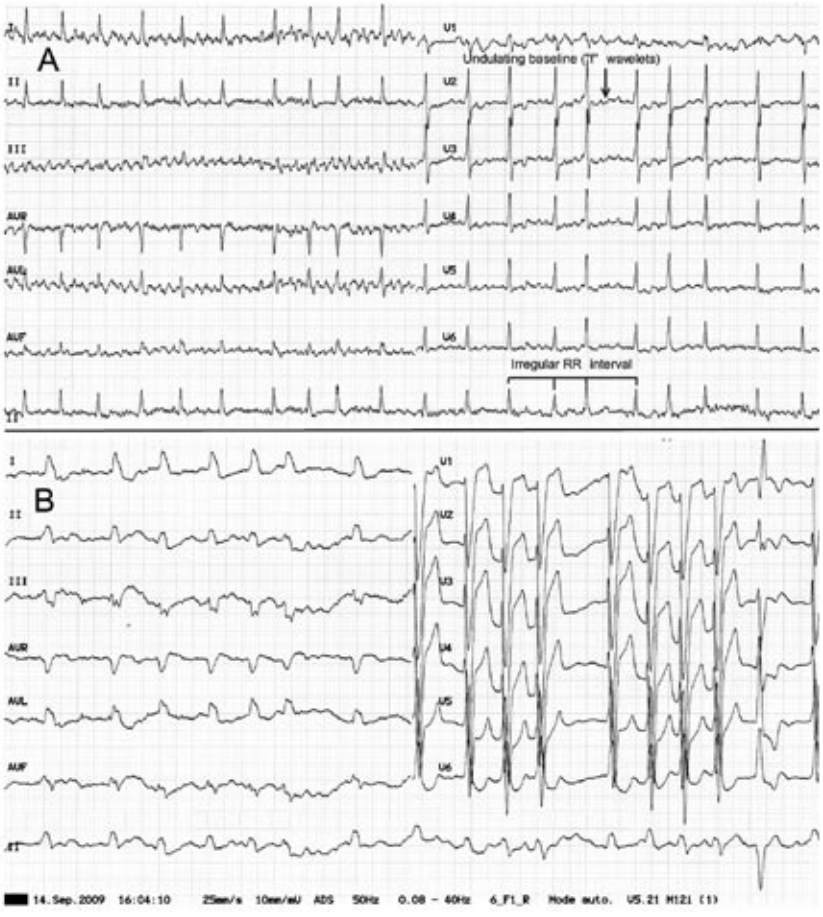

Fig 1 | Top panel (A): Typical electrocardiogram of patient with atrial fibrillation. Bottom panel (B): Atrial fibrillation in patient with concomitant left bundle branch block causing enlarged and abnormal QRS complexes

Clinical manifestations of atrial fibrillation: what is important to know?

Atrial fibrillation is characterised by a chaotic electrical activity in the atria that induces an irregular and usually rapid contraction of the ventricles (figure 1). Patients may be asymptomatic; may have mild symptoms, such as palpitations, weariness, and reduced effort capacity; or may present with syncope, heart failure, or angina. Many of the presenting symptoms, as well as their intensity, are related to the degree of associated tachycardia. Aside from tachycardia, the major complication of atrial fibrillation is systemic embolism, usually cerebral.

Atrial fibrillation may be self limiting (paroxysmal, which may recur) or sustained (termed "persistent" if lasting more than seven days). "Permanent" atrial fibrillation refers to persistent atrial fibrillation in which cardioversion has failed or restoration of sinus rhythm is no longer considered possible (table 1). An individual can have different types of atrial fibrillation over time—for example, it can evolve from paroxysmal to persistent.

In most cases, atrial fibrillation is associated with hypertension, coronary disease, heart failure, valvular diseases, or cardiomyopathies that result in a dysfunctional heart

SUMMARY POINTS

- Atrial fibrillation is common and highly variable in its clinical presentation and evolution; it causes substantial morbidity and mortality, including impaired quality of life, heart failure, systemic emboli, and stroke
- The first priority is to control heart rate (if tachycardia is present) and provide adequate antithrombotic treatment for preventing complications of embolism
- Patients with moderate to high risk of stroke require warfarin long term for preventing emboli; aspirin is adequate in patients with low risk of stroke
- When a patient should but cannot take warfarin, aspirin plus clopidogrel can be an intermediate option
- For long term treatment of atrial fibrillation, rate control matches rhythm control in terms of mortality and major cardiovascular events but has fewer adverse events related to the treatment and fewer hospital admissions
- Consider referring for rhythm control younger patients with lone atrial fibrillation, patients with symptomatic atrial fibrillation, and patients with atrial fibrillation secondary to a corrected precipitant
- If antiarrhythmic drugs fail to maintain sinus rhythm, percutaneous catheter ablation is an alternative for rhythm control

muscle. Correct recognition and treatment of underlying conditions is essential.

How should we investigate a patient presenting with atrial fibrillation?

Diagnosis of atrial fibrillation requires electrocardiographic documentation. In patients with suspected symptoms but in sinus rhythm at the time of consultation, ambulatory electrocardiography (a 24 hour monitor or an event recorder) may be needed. History taking and physical examination are important for defining whether the atrial fibrillation is paroxysmal or persistent and which symptoms it produces, and for enabling detection of possible causes and precipitating factors, as well as any underlying heart disease (table 2).

US and UK guidelines recommend transthoracic echocardiography in all patients with atrial fibrillation to identify underlying heart disease and to assess signs associated with increased risk of recurrence and embolism (dilated atria, presence of thrombus).[2 3] The US guidelines also recommend measurement of serum electrolytes, blood count, and renal, hepatic, and thyroid function in all patients at least once. Sometimes referral will be needed for specialised investigations, such as transoesophageal echocardiography in patients in whom a cardioversion without previous anticoagulation is being considered, electrophysiological study in patients with wide QRS complex tachycardia, or exercise testing when ischaemia is suspected (table 2).

Table 1 | Classification of atrial fibrillation*

Type	Definition	Recurrence
Recent onset or first detected	First diagnosed episode (sometimes an incidental diagnosis and precise duration is not known)	May or may not recur
Paroxysmal	Terminates spontaneously in <7 days	Tends to recur
Persistent	Sustained beyond 7 days; rarely terminates spontaneously	Often recurs
Permanent	Cardioversion has failed or restoration of sinus rhythm is no longer considered possible	Established

*Adapted from joint guidelines from the American College of Cardiology, American Heart Association, and European Society of Cardiology.[2]

Table 2 | Investigations in patients with atrial fibrillation

Investigation	Purpose
Basic evaluation (history)	
Presence of symptoms, type, intensity	To assess clinical impact
Date of onset or discovery, frequency, duration	To characterise as paroxysmal or persistent
Antecedents, cardiac and non-cardiac diseases, cardiovascular risk factors, alcohol and drugs intake	To look for possible causes, precipitating factors, and possible underlying heart disease
Any previous treatment and response	To plan future treatment
Basic evaluation (physical examination)	
Blood pressure	To rule out hypertension
Heart rate	To establish degree of tachycardia
Heart murmurs, signs of heart failure	To consider probability of heart disease
Enlarged or nodular thyroid	To consider lung and thyroid diseases (possible causes of atrial fibrillation)
Signs of respiratory disease	
Basic evaluation (other)	
Transthoracic echocardiography	To identify heart disease: valvular disease, left ventricle size, hypertrophy, and function
	To establish precise risk of recurrence and of embolism: atrial size, presence of thrombus in left atria (low sensibility)
Blood tests: electrolytes, thyroid function	To identify possible causes or precipitating factors
Blood tests: blood count, renal and hepatic function	To adequately establish dose of drugs and follow side effects
Additional testing	
24 hour electrocardiographic monitoring or event recorder	To diagnose the type of arrhythmia if unknown, and to assess adequacy of rate control
Six-minute walk test	To assess adequacy of rate control
Exercise testing	To evaluate ischaemia if suspected, reproduce exercise induced atrial fibrillation, assess adequacy of rate control
Transoesophageal echocardiography	To identify thrombus in left atrium (high sensibility) and guide cardioversion accordingly
Electrophysiological study	To clarify the mechanism of wide QRS complex tachycardia (accessory pathway?) and to study further any patient considered for ablation of atrial fibrillation, of atrioventricular node, or of other supraventricular arrhythmias
Chest radiography	To identify lung diseases if suggested by clinical findings

*Adapted from joint guidelines from the American College of Cardiology, American Heart Association, and European Society of Cardiology.[2]

SOURCES AND SELECTION CRITERIA

We searched the Cochrane database of systematic reviews, *Clinical Evidence*, and the US National Guideline Clearinghouse up to 20 September 2009. We also used personal databases (www.nodo3.net/) and reference collections. We selected well conducted systematic reviews, meta-analyses, and large randomised controlled trials. When no study of those types was available, we considered small randomised controlled trials and cohort studies

What are the general principles of the treatment?

Managing acutely unwell patients

Current guidelines for atrial fibrillation agree in several aspects.[2 3 w2] Patients presenting with rapid atrial fibrillation and acute symptoms (hypotension, syncope, chest pain, dyspnoea, heart failure, or neurological symptoms) require urgent control of their heart rate and possibly emergency cardioversion, in a hospital setting.

Managing patients who are stable at presentation

For patients who are haemodynamically stable and have few or tolerable symptoms the initial management is to slow down the heart rate to the normal range and provide adequate treatment to prevent emboli. Subsequent long term management will focus on rate control or rhythm control. Additionally, adequate treatment of cardiovascular risk factors, especially of hypertension, and avoiding hypokalaemia when using diuretics, can contribute to reduce recurrences of atrial fibrillation.

Which drugs should be used to control heart rate?

Table 3 lists the most common drugs used for controlling heart rate. A systematic review of randomised trials found that first generation calcium channel blockers, β blockers, digoxin, or a combination of these drugs are more effective than placebo in slowing tachycardia associated with atrial fibrillation.[4] Digoxin seemed less effective at controlling heart rate during exercise than β blockers or diltiazem (mean difference 15 to 30 beats/min higher with digoxin). In the AFFIRM trial,[5] a large randomised trial that studied rate versus rhythm control, β blockers were the most effective drugs for slowing heart rate, but frequent treatment changes or combination with other drugs were often needed to achieve adequate rate control.

A randomised trial found that intravenous diltiazem was better than intravenous digoxin (90% versus 74% of patients were well controlled at 24 hours) for rapid rate control of acute, symptomatic, uncomplicated atrial fibrillation.[w4] In patients with decompensated heart failure, current US guidelines recommend intravenous administration of digoxin or amiodarone to slow heart rate, and avoidance of acute use of calcium channel blockers or acute large doses of β blockers as both are negative inotropes.[2]

Table 3 | Drugs commonly used to control heart rate in atrial fibrillation

Drug	Dose range	Use in heart failure	Major and common side effects
β blockers			
Atenolol	25-100 mg daily	Negative inotropes. Avoid in acute decompensated heart failure. Recommended in chronic, stable systolic heart failure	Hypotension, bradycardia, atrioventricular block, heart failure, bronchospasm, impotence, asthenia, depression
Bisoprolol	2.5-10 mg daily		
Metoprolol	Intravenously 2.5-5 mg (up to three doses) or orally 25-200 mg every 12 hours		
Any other β blocker at appropriate doses			
Calcium channel blockers			
Diltiazem	Intravenously 0.25 mg/kg ororally 120-360 mg daily, in two to three doses	Negative inotropes. Use caution in decompensated heart failure	Hypotension, bradycardia, atrioventricular block, heart failure
Verapamil	120-360 mg daily in two to three doses		
Digoxin	Intravenously 0.25 mg every two hours, up to 1-1.5 mg, or orally 0.125-0.5 mg daily	Positive inotrope. Improves symptoms of heart failure	Bradycardia; intoxication (nausea, abdominal pain, vision changes, confusion, various arrhythmias)

How do we choose an antithrombotic treatment?

Full anticoagulation is warranted whenever pharmacological or electrical cardioversion is considered, for at least three weeks before and four weeks after the procedure, except when atrial fibrillation has existed for less than 48 hours.[2] If pharmacological or electrical cardioversion is not considered, then a systematic assessment of embolic and haemorrhagic risk in each patient with atrial fibrillation should guide the choice of antithrombotic treatment.[2 w5] Several scores have been developed to help in this assessment. A large cohort study found that the CHADS-2 tool was the best of three schemes for estimating the risk of stroke in patients with atrial fibrillation not associated with valvular disease (box 1).[6] Echographic demonstration of intra-auricular thrombus or an enlarged left atrium also indicate increased risk of emboli.[7] A score for predicting the risk of bleeding in outpatients treated with warfarin has also been developed (see box 2 on bmj.com).[8]

Which patients should receive aspirin?

Systematic reviews of randomised trials show that aspirin reduces the risk of stroke by about 22-36%.[9 10] According to guidelines, aspirin is adequate for *(a)* patients at low risk of stroke (those aged under 75 years with no prior thromboembolism and no additional risk factor such as hypertension, diabetes, or heart failure) and *(b)* when warfarin is contraindicated.[2 3 11]

Box 1 | Scoring system for estimating risk of stroke patients with atrial fibrillation not associated with valvular disease*

Risk factors

Age >75 years—1 point
Hypertension—1 point
Diabetes mellitus—1 point
Congestive heart failure—1 point
History of stroke or transient ischaemic attack—2 points

Annual risk of stroke (based on points accrued)

0 points—1.9%
1 point—2.8%
2 points—4.0%
3 points—5.9%
4 points—8.5%
5 points—12.5%
6 points—18.2%

*Using the CHADS-2 tool[6]

Which patients should receive warfarin?

In well conducted systematic reviews warfarin reduced rate of stroke by 65-68% compared with placebo and 32-47% compared with aspirin, at the expense of increasing haemorrhages (2.5 to 5 major bleedings per 100 patient years, compared with one to two major bleedings in aspirin treated patients).[9 10 12] Guidelines strongly recommend warfarin for patients with atrial fibrillation and moderate to high risk of stroke, such as those with *(a)* mitral stenosis or prosthetic heart valve, *(b)* a history of prior ischaemic stroke or systemic embolism, or *(c)* two or more thromboembolic risk factors (see box 2 on bmj.com).[2 3 11]

In patients with an intermediate to low risk of stroke (no previous stroke and only one risk factor), either aspirin or warfarin is reasonable. A patient's individual characteristics and preferences should be considered. It is important to *(a)* explain clearly to patients that their disease carries a risk of embolism and stroke and that they need to take a treatment continuously to reduce this risk and *(b)* describe the relative advantages and inconveniences of aspirin and warfarin (especially the needs of regular monitoring and dose adaptations). A semiquantitative ("low, moderate, or high") or quantitative ("x cases in every 100 persons every year") estimate of patients' individual risks may be given. A large randomised trial[13] and a cohort study[w5] have found that elderly patients obtain greater net benefit from warfarin despite their higher haemorrhagic risk.

What about paroxysmal atrial fibrillation?

Cohort studies have found that thromboembolic risk in recurrent paroxysmal atrial fibrillation is closely similar to persistent or permanent atrial fibrillation.[w6] Current guidelines recommend using the same criteria to select antithrombotic treatment irrespective of the pattern of atrial fibrillation.[2 3] Anticoagulation is commonly stopped some weeks after cardioversion, but in a retrospective analysis of data from a large randomised trial this approach was associated with increased incidence of stroke.[w7]

Are there alternatives to aspirin or warfarin for preventing thromboembolic events?

Two large randomised trials, the ACTIVE trials, have studied outcomes in patients treated with aspirin plus clopidogrel. In one of them, aspirin plus clopidogrel proved inferior to warfarin in preventing embolism.[w8] The other found that in patients with atrial fibrillation who were considered unsuitable for warfarin, aspirin and clopidogrel combined reduced stroke and major cardiovascular events further than aspirin alone (relative risk 0.89).[14] However, the combination increased major bleeding by a similar magnitude.

Which long term treatment strategy: rate or rhythm control?

In rate control, in which the aim of treatment is to slow the heart rate and prevent emboli, atrial fibrillation is tolerated. In rhythm control, the objective is to restore and maintain sinus rhythm. To restore sinus rhythm, pharmacological or electrical cardioversion can be used, always after adequate anticoagulation. Pharmacological cardioversion can be tried with antiarrhythmic drugs, administered intravenously or orally; patients receive the treatment usually as inpatients but sometimes as outpatients. In electrical cardioversion, a low voltage electric current, synchronised with the R wave, is delivered through pads placed appropriately on the chest and back. The shock is painful, so it requires sedation or anaesthesia. After cardioversion, atrial fibrillation often recurs (70-85% of patients at one year[15]), so most patients need treatment with antiarrhythmic drugs to stay in sinus rhythm.

Several good quality randomised trials,[16 17 w9] pooled in meta-analysis,[18 19] have compared rate and rhythm control in a variety of patients with atrial fibrillation. No study found any difference between the strategies in terms of mortality, major cardiovascular events, or stroke. Rate control was better for some secondary outcomes: it produced fewer side effects and fewer admissions to hospital. Regardless of whether patients received rate control or rhythm control, those who were in sinus rhythm reported better scores for quality of life. However, when the results were analysed on the basis of intention to treat, quality of life scores did not differ for rate control and rhythm control.[w10 w11]

Which patients should be referred for rhythm control?

Current guidelines recommend considering rhythm control in patients with *(a)* lone atrial fibrillation, especially younger patients; *(b)* symptomatic atrial fibrillation, such as frequent symptomatic paroxysmal atrial fibrillation or symptoms despite rate control; or *(c)* atrial fibrillation secondary to a corrected precipitant.[3] In addition, patients who should but cannot take warfarin might reduce their risk of stroke if sinus rhythm is restored. Nevertheless, rhythm control in those subgroups has not yet been proved in controlled trials to be better than rate control.

Rhythm control has also been recommended for patients with heart failure. However, a recent large randomised trial in patients with systolic heart failure found no difference between rate and rhythm control for any outcome, including worsening heart failure.[17]

Which antiarrhythmic drugs are used to maintain sinus rhythm?

Two meta-analyses and a systematic review[15 20 21] have found that several class I and III antiarrhythmics (table 4) are effective in reducing recurrences of atrial fibrillation, but all of them cause adverse effects, many have a proarrhythmic activity (that is, they may induce or aggravate arrhythmias), and none improve survival. Furthermore, class IA drugs were associated with increased mortality.

Amiodarone does not increase mortality, can be given to patients with heart failure, and seems to be more effective than other drugs in maintaining sinus rhythm. Unfortunately, amiodarone causes frequent and varied adverse effects, which can be severe.[22 w12] Overall, the benefit to risk ratio of antiarrhythmic drugs is low and they should be prescribed by experienced specialists.

Are there other alternatives for rhythm control?

Patients with infrequent paroxysmal atrial fibrillation may receive no treatment between episodes. If their atrial fibrillation recurs they may have repeated electrical or pharmacological cardioversion, sometimes following a "pill in the pocket" approach (that is, patients who have been given flecainide or propafenone in hospital to reduce paroxysmal atrial fibrillation, and tolerate them well, can be prescribed a single, oral loading dose of flecainide or propafenone for them to take outside hospital if they experience sudden and persistent heart palpitations). A prospective non-controlled trial found that this approach was effective and safe in patients with no underlying heart disease.[23]

Which non-pharmacological treatments can be used for atrial fibrillation?

Atrioventricular nodal catheter ablation with permanent ventricular pacing is used as a palliative approach for controlling ventricular rate in patients with symptomatic atrial fibrillation refractory to medical treatment. A meta-

ADDITIONAL EDUCATIONAL RESOURCES

For healthcare professionals

- National Institute for Health and Clinical Excellence. Atrial fibrillation. Clinical guideline CG36. www.nice.org.uk/Guidance/CG36
- ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation. (Executive summary: http://circ.ahajournals.org/cgi/content/full/114/7/700; full guidelines: http://content.onlinejacc.org/cgi/reprint/48/4/e149.pdf; pocket guidelines: www.acc.org/qualityandscience/clinical/pdfs/AF_PocketGuide.pdf)
- NHS Clinical Knowledge Summaries—source of evidence based information and practical "know how" about common conditions managed in primary care; provides answers to questions that arise in the consultation, with links to answers outlining the evidence (www.cks.nhs.uk/atrial_fibrillation)

For patients

- Shea JB, Sears SF. A patient's guide to living with atrial fibrillation. *Circulation*. 2008;117:e340-43. http://circ.ahajournals.org/cgi/content/full/117/20/e340
- Medline Plus. www.nlm.nih.gov/medlineplus/atrialfibrillation.html
- NHS Clinical Knowledge Summaries (patient information leaflet, atrial fibrillation). www.cks.nhs.uk/patient_information_leaflet/Atrial_fibrillation (Free access)
- Wikipedia. http://en.wikipedia.org/wiki/Atrial_fibrillation

TOPICS FOR FUTURE RESEARCH

- Understand the mechanism of atrial remodelling (the changes in atrial substrate that usually precede the development of atrial fibrillation and are accentuated by its persistence) and find effective treatments for preventing or reducing it
- Clarify the utility of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers to prevent atrial fibrillation or reduce recurrences. Results of randomised trials and one meta-analysis have been contradictory[w23-w26]
- Compare new oral anticoagulants (dabigatran, rivaroxaban, factor VIIa/tissue factor inhibitors, tecarfarin) with warfarin, the current treatment of choice
- Establish the indications of percutaneous occlusion of left atrial appendage for preventing emboli
- Define the role of new antiarrhythmic drugs (dronedarone, vernakalant) in the management of atrial fibrillation
- Determine the best treatment for elderly patients
- Evaluate the effect of percutaneous catheter ablation of atrial fibrillation on mortality

Table 4 | Antiarrhythmic drugs commonly used to maintain sinus rhythm*

Drug	Maintenance dose	Use in heart failure	Major and common side effects
Class IA			
Quinidine, disopyramide	Not applicable	Avoid (owing to increased mortality)	Avoid (owing to increased mortality)
Class IC			
Flecainide	50-200 mg every 12 hours	No (negative inotropes); risk of increasing mortality in patients with structural heart disease	Heart failure, gastrointestinal and neurological side effects, blurred vision, proarrhythmia
Propafenone	150-300 mg every 8 hours		Gastrointestinal, dizziness, proarrhythmia
Class III			
Sotalol	80-160 mg every 12 hours	No (negative inotrope)	Hypotension, bradycardia, heart failure, neurological side effects , proarrhythmia
Dofetilide†	125-500 micrograms every 12 hours; monitor QTc interval; start in inpatient setting	Possible	Headache, dizziness, nausea, bradycardia, proarrhythmia
Amiodarone‡	100-200 mg daily	Yes	Bradycardia, atrioventricular block. Thyroid, dermatological, pulmonary, corneal, and liver toxicities

*Antiarrhythmic drugs should be withdrawn in any patients presenting with a long QT interval, new or increasing QRS widening, pronounced bradycardia, or unexplained syncope. β blockers might have a modest effect in preventing recurrences of atrial fibrillation, according to some randomised controlled trials.[w27 w28]

†Not available in Europe.

‡Not approved by the US Food and Drug Administration for this indication.

TIPS FOR NON-SPECIALISTS

- Patients with tachycardia plus syncope, chest pain, dyspnoea, or acute neurological symptoms should be sent immediately to hospital for urgent treatment
- Use β blockers, diltiazem, or digoxin (if heart failure is present), or a combination of these drugs at standard doses to slow heart rate in atrial fibrillation if tachycardia is present

analysis of randomised and non-randomised studies showed that this technique is highly effective and significantly improves quality of life.[24] The main limitations are a small risk of sudden death during the few months after ablation and lifelong dependency on a pacemaker.

Non-pharmacological interventions aiming to "cure" atrial fibrillation have been tried, initially using open surgery.[w13] A more successful approach has been the development of closed chest endocardial ablation, after the discovery that in many patients atrial fibrillation is triggered and/or perpetuated by extrasystoles originating in the pulmonary veins.[25] Briefly, catheters are introduced into the left atrium after a transeptal puncture, and atrial tissue is selectively destroyed (by radiofrequency or cryoenergy) to electrically isolate pulmonary veins. In experienced centres, success rates are above 70% at one year for paroxysmal atrial fibrillation. In persistent atrial fibrillation, pulmonary vein isolation alone is not sufficient to achieve acceptable success rates, and atrial substrate modification (discrete ablation and/or linear ablations) is usually necessary. Redoing procedures is required in 9-20% of patients. The rate of related major complications of ablation is below 5%.[w14] The advances obtained with endocardial catheter ablation have also led to the development of off-pump, epicardial surgical ablation, following the same principles.

Which patients should be referred for catheter ablation?

Catheter ablation for patients with atrial fibrillation has become widely used only recently and has not yet been tested in large randomised studies with a mortality end point. However, several well conducted randomised trials and systematic reviews have shown that, in both paroxysmal and persistent atrial fibrillation, catheter ablation is better than antiarrhythmic drugs at preventing recurrences of atrial fibrillation.[26 27 w14-w17] According to recent guidelines, prevention of recurrence of atrial fibrillation by ablation is justified only when atrial fibrillation is associated with disabling symptoms, and its use depends on the type of atrial fibrillation.[2]

In patients with paroxysmal symptomatic atrial fibrillation, catheter ablation may be considered after failure of a first line antiarrhythmic drug. Hence, in patients with a structurally normal heart, ablation is an alternative to amiodarone if a class IC antiarrhythmic fails. When amiodarone is the first line treatment because class IC drugs are contraindicated, ablation can be considered if amiodarone fails.

The guidelines are less clear for patients with persistent atrial fibrillation. In such patients, catheter ablation can be considered for "severely symptomatic recurrent atrial fibrillation after failure of greater than or equal to one antiarrhythmic drug plus rate control."[2] This recommendation is not based on strong evidence but is supported by small case series and randomised studies showing that restoration of sinus rhythm by catheter ablation may be associated with a significant improvement in left ventricular ejection fraction in patients with either heart failure induced by tachycardia or pre-existing heart failure.[28 w18]

Can we expect any new treatments for atrial fibrillation?

New antiarrhythmic drugs are being developed. In a randomised trial, vernakalant, a new atrial selective agent, was effective for rapid cardioversion of recent onset atrial fibrillation.[w19] In several randomised trials, dronedarone, a derivative of amiodarone, was more effective than placebo in maintaining sinus rhythm and reducing admission to hospital[29 w20] but increased mortality in patients with heart failure.[w21] The results from a study comparing dronedarone with amiodarone are expected soon.

New oral anticoagulant drugs not requiring blood tests for monitoring are being developed. In a recent large randomised trial, dabigatran, a direct thrombin inhibitor, was as good as warfarin for the primary end point of stroke or systemic embolism and was associated with comparable or lower rates of major haemorrhage.[30]

A randomised trial has shown that percutaneous occlusion of left atrial appendage is as good as warfarin in preventing stroke in patients with atrial fibrillation.[w22]

Contributors: CL-L coordinated the review and wrote the introduction and the sections on rate control, rhythm control, and antiarrhythmic drugs. IM wrote about anticoagulants and the choice of antithrombotic treatment. FE wrote about non-pharmacological treatments, ablation, and percutaneous procedures. All the authors revised the draft and approved the complete final version. CL-L is the guarantor.

Competing interests: None declared.

Provenance and peer review: Commissioned; externally peer reviewed.

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ANSWERS TO ENDGAMES, p 57. For long answers go to the Education channel on bmj.com

STATISTICAL QUESTION
Sampling I

b

PICTURE QUIZ
Flank pain and haematuria

1 The patient has a left renal injury.
2 He has a laceration through the left kidney posteriorly, with extravasation of contrast and a perinephric haematoma.
3 This is a grade 4 renal injury.
4 Renal injuries can be serious and rapid deterioration can occur. Patients should therefore be managed with close observation (at least hourly and ideally in a high dependency environment), maintenance of good intravenous access, bed rest, antibiotic prophylaxis, regular blood tests to monitor renal function and haematocrit, and delayed repeat imaging.

CASE REPORT **The vomiting baby**

1 The most common causes in a baby are regurgitation, gastro-oesophageal reflux, hypertrophic pyloric stenosis, pylorospasm, and necrotising enterocolitis. Necrotising enterocolitis is more commonly seen in preterm infants but can occasionally be seen in term infants. Also consider extraintestinal causes including sepsis, drugs or other toxic agents, intracerebral abnormalities, metabolic problems, renal pathology, and medical conditions such as kernicterus.
2 Hypertrophic pyloric stenosis, in which blood gas analysis classically shows hypochloraemic hypokalaemic metabolic alkalosis.
3 Ultrasound scanning is commonly used because it is non-invasive, does not use radiation, and can differentiate between several diagnoses—in particular, hypertrophic pyloric stenosis, gastro-oesophageal reflux disease, and duodenal anomalies. Capillary blood gas analysis and measurement of urea and electrolytes can also help confirm the diagnosis.
4 Several imaging modalities can be used depending on the associated symptoms—upper gastrointestinal contrast study, plain abdominal radiography, computed tomography, and magnetic resonance imaging.
5 The most common cause of intermittent vomiting from birth is gastro-oesophageal reflux.