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Leo M, Betts T. Have a high index of suspicion for atrial fibrillation.
Practitioner 2014;258 (1775)15-20

Dr Milena Leo
MD
Clinical Fellow

Dr Tim Betts
MD FRCP
Consultant Cardiologist and Electrophysiologist,
Oxford Heart Centre, John Radcliffe Hospital, Oxford, UK

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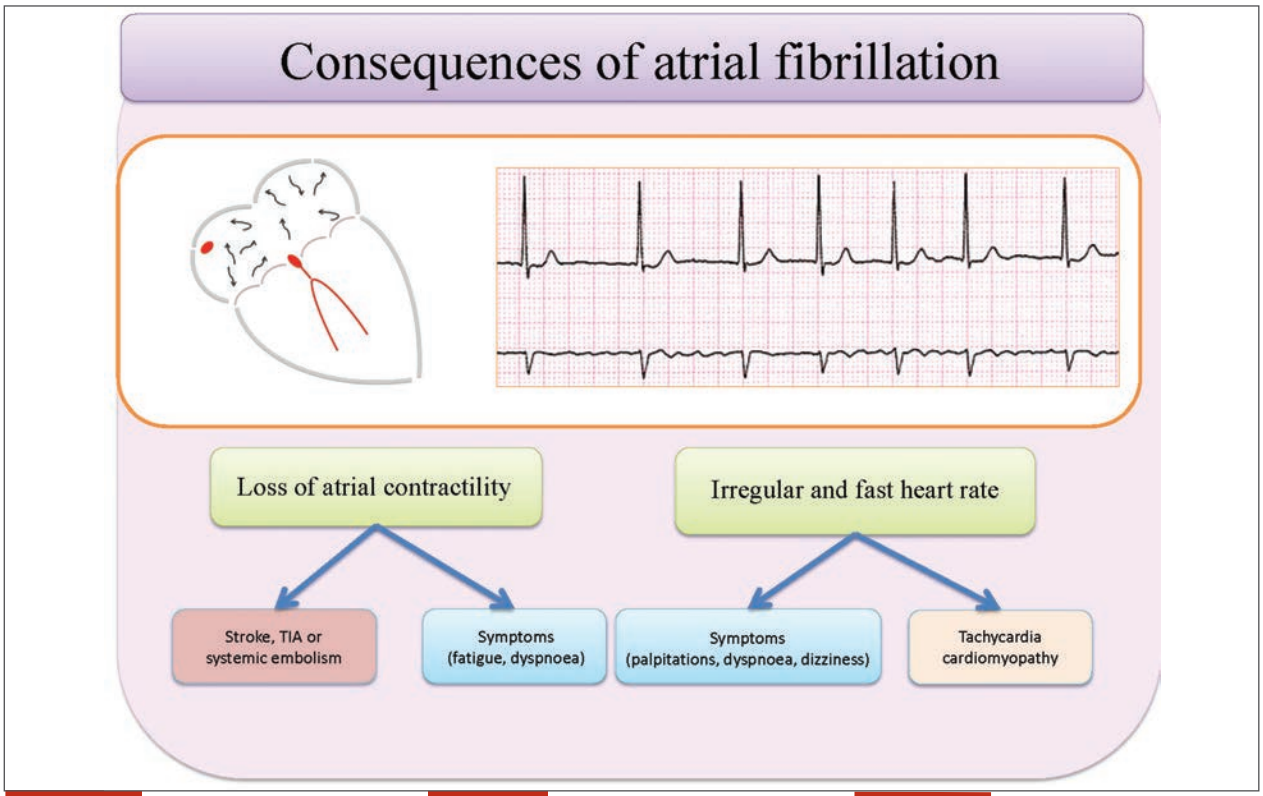
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AUTHORS
Dr Milena Leo
MD
Clinical Fellow

Dr Tim Betts
MD FRCP
Consultant Cardiologist and Electrophysiologist

Oxford Heart Centre, John Radcliffe Hospital, Oxford, UK



What are the symptoms of atrial fibrillation?

ALTHOUGH THE FIRST RECORDED DESCRIPTION OF ATRIAL FIBRILLATION (AF) IS IN THE *YELLOW EMPEROR'S* *Classic of Internal Medicine,* believed to date between 1696 and 2598 BC, only in the last century has this cardiac dysrhythmia been recognised as a very common condition associated with increased cardiac and cerebrovascular morbidity and mortality.

In June 2014, NICE published updated guidelines for the management of AF, in the light of new evidence, including stroke and bleeding risk stratification and the role of new antithrombotic agents and ablation strategies.[1]

AF is a very heterogeneous condition. There are a number of aspects to consider, including aetiology, comorbidities, symptoms, stroke risk and other potential detrimental effects such as tachycardia cardiomyopathy. There are a variety of different treatment strategies and therapies.

For these reasons, a personalised package of care and information is necessary. Fortunately, there are a number of accessible information resources for patients and physicians, including the Atrial Fibrillation Association website, see Useful information box, p20.

How should risk stratification be carried out?

What are the treatment approaches?

WHEN TO CONSIDER AF

Thirty-three million individuals across the globe have AF, with more than five million new cases each year. The prevalence is around 1.5% in the general population but it increases with age, approaching 8% in those over 65 years old and is higher than 10% in the over-80s. The lifetime risk of AF for men and women over the age of 40 is approximately 25%.

The condition affects around 800,000 people in the UK, of which it is estimated that 250,000 are undiagnosed. With such a high prevalence, GPs will be faced with identifying and managing AF on a regular basis.

The chaotic atrial electrical activation during AF translates into »

the loss of atrial contractility and an irregular and often fast ventricular rate. A rapid heart rate may result in palpitations, dyspnoea or chest tightness, whereas the loss of atrial contractility may lead to fatigue and reduced exercise capacity.

Presentation can range from the truly asymptomatic, with AF diagnosed by chance, to those with vague, non-specific symptoms who turn out to have an irregular pulse on palpation, to clear-cut rapid, irregular palpitations with severe compromise. As up to one third of patients have no recognisable symptoms, a high index of suspicion is required.

'As up to a third of patients have no recognisable symptoms, a high index of suspicion is required'

The lack of an organised atrial contraction during AF can result in some stagnant blood in the left atrium, with an increased risk of thrombus formation that may subsequently dislodge, resulting in a five-fold increased risk of ischaemic stroke, transient ischaemic attack or systemic embolism. AF strokes are larger, more disabling and have a higher mortality rate than those with other causes.

It is important to note that the risk of stroke is not related to the presence or absence of symptoms, or whether the AF is paroxysmal (intermittent) or persistent.

Indeed, it is not clear whether there is a safe burden of AF, and there is good evidence that episodes lasting more than 5-6 minutes confer an increased risk of stroke.

Although it can occur in the absence of structural heart disease or identifiable risk factors, so-called lone AF, half of patients with AF have associated cardiovascular disease, including hypertension, valvular heart disease, congestive heart failure, coronary artery disease, pericarditis, obstructive sleep apnoea and cardiomyopathy. Moreover, physiological stressors such as surgical procedures, pulmonary embolism, chronic lung diseases, hyperthyroidism, and alcohol ingestion can induce AF in individuals with a predisposition.

DIAGNOSIS

An irregular pulse is the textbook diagnostic sign, however with the advent of automatic blood pressure monitoring, pulse palpation may no longer be part of a routine assessment and is limited by being a very infrequent, brief encounter.

With this in mind, blood pressure monitors for use in primary care have been developed that can simultaneously detect pulse irregularity and display an AF icon.

NICE has concluded that the WatchBP Home A blood pressure monitor is cost saving and could provide significant clinical benefits when used for opportunistic AF detection in asymptomatic patients being screened or monitored for hypertension, and that it would be particularly beneficial for older patients at higher risk of stroke.[2]

When an irregular pulse is detected it should precipitate further assessment with a 12-lead ECG.

In patients with intermittent palpitations that may represent AF, prolonged ECG monitoring, ideally with 7-28 day event monitors, can be used to increase the chance of diagnosis. The choice of monitor should be based on the frequency of symptoms. A 24-hour monitor should only be used if symptoms occur every day.

INVESTIGATION

A comprehensive physical examination should be undertaken, including blood pressure measurement, cardiovascular examination to look for valvular heart disease or heart failure and lung examination looking for signs of lung disease or pulmonary oedema. Blood tests, including urea and electrolytes, liver function tests, full blood count, blood glucose and thyroid function tests should be carried out.

A transthoracic echocardiogram should be performed when there is a suspicion of structural or functional heart disease based on physical examination, if a rhythm control strategy with class IC antiarrhythmic drugs (propafenone, flecainide) or electrical cardioversion are being considered, for patients under 60 years of age or in rare instances for refinement of clinical risk stratification for antithrombotic therapy.

MANAGEMENT

In patients with a confirmed diagnosis of AF, three key factors need to be considered, all of which are independent of one another:

- Stroke risk
- Symptoms
- Risk of tachycardia cardiomyopathy

The following areas are emphasised in the recent NICE guidelines.

Risk stratification

The thromboembolic risk and the bleeding risk related to the initiation of anticoagulant therapy should be promptly stratified in each patient.

The CHA_2DS_2-VASc score is currently used to assess the stroke risk in patients with AF. Oral anticoagulation should be offered to patients with a CHA_2DS_2-VASc score of 2 or more, and considered for men with a CHA_2DS_2-VASc score of 1. Although female gender is considered a risk factor, this is only in patients aged 65 years or older, see table 1, p17.

The risk of severe bleeding with warfarin should also be assessed using the HAS-BLED score, see table 2, p17. A score of 3 or more indicates that caution is required when starting any anticoagulant therapy.

'Risk of stroke is not related to the presence or absence of symptoms, or whether the AF is paroxysmal or persistent'

Of note, risk of falls is not a good reason to withhold anticoagulation — modelling studies have calculated that it takes nearly 300 falls per annum before the risks of warfarin overweigh the benefits.

In some instances, such as previous life-threatening bleeds, the risks of oral anticoagulation outweigh the benefits. In these situations, percutaneous left atrial appendage occlusion is an interventional procedure currently being evaluated as an alternative,[3] see table 3, p17.

Oral anticoagulant therapy

When appropriate, oral anticoagulant therapy should be promptly initiated, choosing the best option for the patient.

Oral anticoagulant therapy can reduce the risk of having a stroke by approximately 50-70%.

Until recently, warfarin was the only available option. Although cheap and effective, the need for regular monitoring and dose adjustments, combined with multiple food and drug interactions, results in suboptimal time in the therapeutic range, a high rate of non-compliance and treatment cessation in 25-40% by three-year follow-up.

Starting in 2012, a number of drugs belonging to a new generation of novel oral anticoagulants (NOACs) have been approved by NICE for prevention of stroke and systemic embolism in patients with non-valvular (i.e. not caused by rheumatic heart disease) AF: dabigatran,[4] rivaroxaban[5] and apixaban.[6]

Their anticoagulant effect is predictable, thus they do not require regular monitoring and dose adjustments. It should be noted that their excretion is affected by renal function, their safety in the very elderly is not known and they also have side effects and still have a relatively high incidence of discontinuation. Although they do not have formal antidotes, studies show that this does not have an impact on

Table 1

CHA_2DS_2-Vasc score

CHA_2DS_2-Vasc risk factors		Score
C	Congestive heart failure/ LV dysfunction	1
H	Hypertension	1
A_2	Age ≥ 75 years	2
D	Diabetes mellitus	1
S_2	Stroke/TIA	2
V	Vascular disease (prior MI, PAD, aortic plaque)	1
A	Age 65-74 years	1
Sc	Sex category (female gender)	1
Maximum		9

Table 2

HAS-BLED score

HAS-BLED risk factors		Score
H	Uncontrolled Hypertension	1
A	Abnormal renal and/or liver function	1 or 2
S	Stroke	1
B	Bleeding tendency or predisposition	1
L	Labile INR	1
E	Elderly (age > 65 years)	1
D	Drugs (concomitant aspirin or NSAID) and/or alcohol	1 or 2
Maximum		9

Table 3

Atrial fibrillation anticoagulation chart according to thromboembolic risk and bleeding risk

HAS-BLED score (adjusted annual bleeding rate)	CHA_2DS_2-VASc score (adjusted annual stroke rate in no AC)					
	0 (0%)	1 (1.3%)	2 (2.2%)	3 (3.2%)	4 (4%)	5 or more (≥ 6.7%)
5 or more (12.5%)	AC not required	AC contraindicated	?*	?*	?*	?*
4 (8.7%)	AC not required	AC contraindicated	?*	?*	?*	?*
3 (7.2%)	AC not required	AC contraindicated	?*	?*	?*	?*
2 (1.88%)	AC not required	AC suggested	AC recommended	AC recommended	AC recommended	AC recommended
1 (1.02%)	AC not required	AC suggested	AC recommended	AC recommended	AC recommended	AC recommended
0 (1.13%)	AC not required	AC suggested	AC recommended	AC recommended	AC recommended	AC recommended

Key: AC = anticoagulant therapy; * = refer to specialist centre to consider left atrial appendage occlusion

outcome following severe bleeds.

Making the choice between warfarin and the different NOACs is a complex process[7] that should take into account not only the patient's age and comorbidities but NICE guidance based on trial entry criteria as well as patient preference and compliance, see table 4, below. It is pertinent to note that in the 2012 European Society of Cardiology Guidelines, NOACs are given preference over warfarin.[8]

NICE has produced a patient decision aid to help patients weigh up the potential advantages and disadvantages of the different treatment options so that they can discuss these factors with a health professional and come to a joint decision, see Useful information box, p20.

A major change, yet to be fully

Table 4

Head-to-head comparison of available anticoagulant drugs

	Warfarin	Dabigatran	Rivaroxaban	Apixaban
Target	Vitamin K-dependent clotting factors (II, VII, IX, X)	Thrombin	Factor Xa	Factor Xa
Dose	Variable	- 150 mg bd - 110 mg bd (> 80 years old, on verapamil, HAS-BLED ≥ 3, CrCl 30-49 ml/min)	- 20 mg od - 15 mg od (HAS-BLED ≥ 3, CrCl 30-49 ml/min)	- 5 mg bid - 2.5 mg bid (≥ 80 years old, Cr ≥ 1.5 mg/dl, weight ≤ 60 kg)
Blood tests	Required	Not required	Not required	Not required
Antagonist	IV vitamin K (takes 8 hours to have effect) IV Beriplex/Octaplex (very expensive)	Not available	Not available	Not available
Drug interactions	Cimetidine, fibrates, propafenone, amiodarone, tramadol, NSAIDs, many classes of antibiotics, azole antifungals, carbamazepine, levothyroxine	Amiodarone, dronedarone, verapamil, ketoconazole, itraconazole, voriconazole, quinidine, clarithromycin, rifampicin, carbamazepine, phenytoin, St John's Wort	Quinidine, ketoconazole, itraconazole, ritonavir, clarithromycin, rifampicin, carbamazepine, phenytoin, St John's Wort	Diltiazem, ketoconazole, itraconazole, ritonavir, clarithromycin, rifampicin, carbamazepine, phenytoin, St John's Wort
Food interactions	Green leafy vegetables, liver, cranberry juice, grapefruit juice, garlic, asparagus, alcohol	- No interaction with food - Should be taken with a full glass of water while sitting upright - Take with food to minimise dyspepsia	To be taken with food	No interaction with food
Adverse reactions	Major bleeding, skin rashes, jaundice, fever, purple toe syndrome, warfarin necrosis, osteoporosis	Major bleeding, dyspepsia, nausea, upper abdominal pain, diarrhoea, gastritis, hypersensitivity reaction	Major bleeding, abdominal pain, dyspepsia, toothache, fatigue, back pain, hypersensitivity, angioedema, Stevens-Johnson syndrome, cholestasis/jaundice	Major bleeding, drug hypersensitivity, nausea, transaminitis, ocular haemorrhage, gingival bleeding
NICE indications		Nonvalvular AF with 1 or more risk factors - previous stroke or TIA - LVEF < 40% - NYHA class ≥ II - age 75 or older - age 65 or older with one of the following (diabetes, CAD, hypertension)	Nonvalvular AF with 1 or more risk factors - congestive heart failure - hypertension - age 75 or older - diabetes mellitus - prior stroke or TIA	Nonvalvular AF with 1 or more risk factors - prior stroke or TIA - age 75 or older - hypertension - diabetes, - symptomatic heart failure
When to choose	- Mechanical valves/valvular AF - Breast feeding - Active significant bleeding/bleeding diathesis - CrCl < 30 ml/min - Patient preference	- High risk of ischaemic stroke and low bleeding risk - HAS-BLED ≥ 3 (110 mg bid) - Patient preference	- Renal impairment - GI upset/disorders - CAD/previous MI or high risk - Previous stroke - Single dose - Patient preference	- Previous GI bleeding or high risk - GI upset/disorders - Previous stroke - HAS-BLED ≥ 3 - Patient preference
When to avoid	Unstable INR because of drug or food/alcohol interactions	- CrCl < 30 ml/min - Hepatic impairment or liver enzymes > 2 x upper limit of normal	- CrCl < 30 ml/min - Hepatic disease	- CrCl < 30 ml/min - Severe hepatic impairment

Table 5

Antiarrhythmic drugs

Antiarrhythmic drug	Suitable for the following groups	Avoid in the following groups	Side effects
Sotalol (minimum dose 80 mg bd)	Hypertension, previous ischaemic heart disease	Severe lung disease or heart failure	Lethargy, fatigue, bradycardia, wheeze
Flecainide (50-150 mg bd)	Patients intolerant of beta-blockers, normal heart on echocardiography	Ischaemic heart disease, structural heart disease, Brugada syndrome, atrial flutter	Headache, paraesthesia, visual disturbances
Dronedarone (400 mg bd)	Additional risk factors including hypertension, age >70, diabetes, previous stroke/TIA, LA diameter > 50 mm, LVEF 35-40%	Persistent AF, LVEF < 35%, moderate to severe heart failure	GI disturbances. Need to monitor liver function
Amiodarone (200 mg od)	Heart failure, structural heart disease	Younger patients, liver disease thyroid disease, outdoor workers	Photosensitivity (common), thyroid dysfunction, liver toxicity, pulmonary toxicity, corneal deposits, peripheral neuropathy (all rare)

appreciated in the front line, is that aspirin is no longer recommended for thromboembolic stroke prevention in AF. It is not as effective as anticoagulants at preventing stroke yet in the elderly may have a similar risk of severe bleeds.

Dual antiplatelet therapy with aspirin and clopidogrel might be considered if anticoagulation is contraindicated or not tolerated and the patient has a CHA_2DS_2-VASc score of 2 or above, however this is likely to be superseded by percutaneous left atrial appendage occlusion.

Anticoagulant reviews

The indications for, and effectiveness of, anticoagulant therapy should be reviewed periodically in all patients with AF.

Anticoagulation should be started when the patient reaches the age of 65 or if he/she develops any of the risk factors for stroke. The need for anticoagulation and its quality should be re-evaluated in the case of bleeding or other relevant clinical events.

In patients receiving warfarin, the adequacy of anticoagulant control should be assessed by calculating the individual time in therapeutic range (TTR) at each visit. Poor control is defined as two INR values higher than 5 or one INR value higher than 8 within the past six months, two INR values less than 1.5 within the past 6 months or TTR less than 65%. In this situation, switching to a NOAC is recommended.

Rate control

Rate control is currently suggested as a first-line strategy, except in patients with AF that is of new onset, has a reversible cause, or with persistence of symptoms despite good rate control.

Rate control means the atria are left to fibrillate while aiming to keep the resting heart rate below 100 bpm to alleviate symptoms and prevent tachycardia cardiomyopathy.

‘Risk of falls is not a good reason to withhold anticoagulation’

It is a good strategy in patients whose symptoms are mainly related to rapid ventricular rate, but it will not abolish symptoms resulting from the loss of atrial contractility. Standard beta-blockers, e.g. bisoprolol, or the calcium channel blockers verapamil or diltiazem are preferred as initial monotherapy. Digoxin monotherapy is relatively ineffective.

Combination drug therapy or catheter ablation of the atrioventricular node to create complete heart block combined with insertion of a permanent pacemaker can be considered in cases of poor ventricular control. Rate control is relatively easy to achieve, yet may often end up as a compromise.

Rhythm control

Rhythm control strives to restore and maintain sinus rhythm, preserving atrial contractility as well as a normal heart rate. It is harder to achieve, yet for many patients it is the only way to abolish all symptoms. The options for rhythm control include electrical cardioversion if the AF is persistent, plus antiarrhythmic drugs and catheter ablation.

External or internal electrical cardioversion will restore sinus rhythm on the day in 90-95% of patients, however only 20-30% are still in sinus rhythm one year later. This can be increased to 50% with the addition of a long-term antiarrhythmic drug, typically amiodarone.

Once AF has been continuous for 48 hours, a minimum of three weeks of therapeutic anticoagulation is required before cardioversion.

Antiarrhythmic drugs for long-term rhythm control include standard beta-blockers (e.g. bisoprolol), flecainide, propafenone, amiodarone, sotalol or dronedarone. In selected cases (infrequent, long-lasting paroxysms of AF, no history of left ventricular dysfunction or valvular or ischaemic heart disease) a ‘pill in the pocket strategy’ with a single 200-300 mg dose of flecainide taken at the onset of the attack can be used to try to restore sinus rhythm promptly. Unfortunately, most drugs merely reduce the frequency of AF rather than eliminate it entirely and are commonly accompanied by side effects, see table 5, above.

Radiofrequency ablation is an invasive rhythm control strategy performed through femoral vein needle punctures. It aims to isolate the pulmonary veins from the left atrium »

key points

SELECTED BY
Dr Peter Saul
GP, Wrexham and Associate GP Dean for North Wales

The lifetime risk of atrial fibrillation (AF) for men and women over the age of 40 is approximately 25%. The condition affects around 800,000 people in the UK, of which it is estimated that 250,000 are undiagnosed. A rapid heart rate may result in palpitations, dyspnoea or chest tightness, whereas loss of atrial contractility may lead to fatigue and reduced exercise capacity. Half of patients with AF have associated cardiovascular disease.

There is a five-fold increased risk of ischaemic stroke, transient ischaemic attack or systemic embolism. AF strokes are larger, more disabling and have a higher mortality rate than those with other causes. The risk of stroke is not related to the presence or absence of symptoms, or whether the AF is paroxysmal or persistent.

When an irregular pulse is detected it should precipitate further assessment with a 12-lead ECG. In patients with intermittent palpitations that may represent AF, prolonged ECG monitoring can be used to increase the chance of diagnosis. In patients with a confirmed diagnosis of AF, three areas need to be considered, stroke risk, symptoms, and risk of tachycardia cardiomyopathy.

The CHA_2DS_2-VASc score is used to assess the stroke risk in patients with AF. Oral anticoagulation should be offered to those with a CHA_2DS_2-VASc score of 2 or more, and considered for men with a score of 1. The risk of severe bleeding with warfarin should also be assessed using the HAS-BLED score. A score of 3 or more indicates that caution is required when starting any anticoagulant therapy. Oral anticoagulant therapy can reduce the risk of having a stroke by approximately 50-70%. It should be started when the patient reaches the age of 65 or if he/she develops any of the risk factors for stroke.

Novel oral anticoagulants (NOACs) have been approved by NICE for prevention of stroke and systemic embolism in patients with non-valvular AF. Making the choice between warfarin and NOACs is a complex process that should take into account not only the patient's age and comorbidities but NICE guidance, patient preference and compliance. Aspirin is no longer recommended for thromboembolic stroke prevention in AF.

Rate control is currently suggested as a first-line strategy, except in patients with AF that is of new onset, has a reversible cause, or with persistence of symptoms despite good rate control. Rhythm control strives to restore and maintain sinus rhythm, preserving atrial contractility as well as a normal heart rate. It is harder to achieve, yet for many patients it is the only way to abolish all symptoms. Radiofrequency ablation is indicated in highly symptomatic patients with paroxysmal or persistent AF who have failed drug therapy and in whom a rhythm control strategy is preferred. Current techniques have a 90% success rate for paroxysmal AF and 80% for persistent AF.

electrically. The veins are often the source of ectopics that act as electrical triggers, initiating and perpetuating AF. It is indicated in highly symptomatic patients with paroxysmal or persistent AF who have failed drug therapy and in whom a rhythm control strategy is preferred.

Current techniques have a 90% success rate for paroxysmal AF and an 80% success rate for persistent AF but this is often only achieved after multiple procedures. There is a small but real risk of serious complications, such as tamponade, stroke, vascular complications and death, even in the hands of experienced doctors. There were more than 5,500 ablation procedures for AF performed in the UK in 2013.

'Evaluation should prioritise stroke risk and symptomatology'

REFERRAL

NICE advises referral at any stage if treatment fails to control the symptoms of AF or if more specialised management is needed. Referral is also appropriate when the balance of risks and benefits of anticoagulation makes for difficult decisions or there are problems with anticoagulation tolerance and/or compliance.

CONCLUSIONS

AF is a common condition but may be difficult to detect without a high index of suspicion. There is a role for screening using BP monitors with pulse regularity algorithms. Evaluation should prioritise stroke risk and symptomatology.

There are now a variety of oral anticoagulants, many of which have a predictable effect and do not require monitoring. Symptoms may be tackled using medications, ablation or pacing.

The broad spectrum of presentation and consequences means that an individualised, patient-centred approach is mandatory.

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Useful information

Atrial Fibrillation Association
www.atrialfibrillation.org.uk

NICE
A decision aid for patients with atrial fibrillation is available from the website http://guidance.nice.org.uk/CG180/PatientDecisionAid/pdf/English

Arrhythmia Alliance
www.arrhythmiaalliance.org.uk

We welcome your feedback

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editor@thepractitioner.co.uk