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Recent advances in the treatment of atrial fibrillation

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Atrial fibrillation is the most common cardiac arrhythmia seen in clinical practice, occurring in paroxysmal, persistent or permanent forms. New anti-arrhythmic agents are being trialled for the pharmacological treatment of affected patients. Catheter ablation is an effective therapeutic intervention for the treatment of patients with symptomatic, drug-refractory paroxysmal atrial fibrillation.

Key points

- The two main aims of treatment of patients with atrial fibrillation (AF) are symptom control and reduc - tion in thromboembolic risk.
- Once AF has been diagnosed, either a rate control or rhythm control treatment strategy may be reasonable.
- Symptomatic patients often derive much greater symptom relief from rhythm control, which may be achieved pharmacologically or with electric cardioversion.
- The decision to opt for rate control is based on symptoms and likelihood of long-term sinus rhythm maintenance.
- In the small proportion of patients in whom rate control is difficult to achieve pharma - cologically, permanent pacing followed by atrioventricular nodal ablation improves symptoms and quality of life.
- Catheter ablation is a highly efficacious strategy for maintaining sinus rhythm in patients with symptomatic paroxysmal AF who have failed one or more anti-arrhythmic drugs.

Atrial fibrillation (AF) is the most common cardiac arrhythmia in humans. Its incidence increases with age from 0.1% in patients younger than 55 years of age to 9.0% in patients aged over 80 years. The lifetime risk of developing AF is one in four and its incidence doubles with each decade of life over the age of 55 years, independent of known predisposing conditions. With the ageing population, the prevalence of AF is expected to reach epidemic proportions.[1] AF causes significant impairment in quality of life, primarily from symptoms such as palpitations, fatigue, breathlessness or chest discomfort, often resulting in curtailment of employment, or social or recreational activities. Furthermore, AF is associated with a four to fivefold increase in the risk of stroke, a tripling of the risk of heart failure and an increased risk of mortality.[2] About 15% of strokes are attributed to AF and these tend to be associated with higher morbidity and mortality, greater disability, longer hospital stays and lower rates of discharge of patients to their own homes.[3]

Three different types of AF are recognised: paroxysmal, persistent and permanent forms (Table 1). Persistent and permanent forms of AF are invariably associated with underlying structural heart disease. When paroxysmal AF occurs in the absence of structural heart disease or clinical risk factors for AF it is termed 'lone AF'. In general, management decisions in patients with AF are based on the nature and severity of symptoms and on thromboembolic risk, rather than arrhythmia classification.

The GP frequently encounters patients of AF either as part of long-term management with other comorbidities, as a new diagnosis

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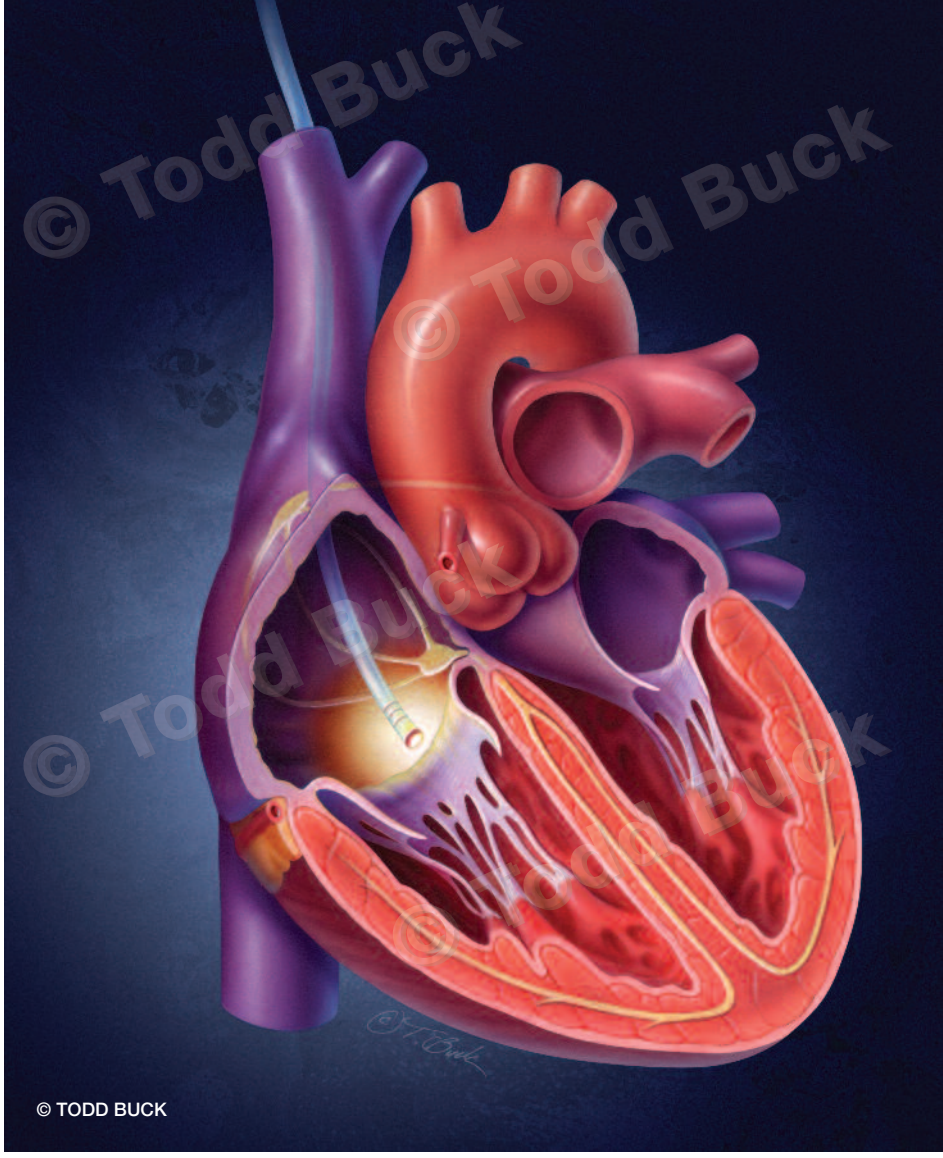
in the investigation of breathlessness and palpitations or as an incidental finding. Significant advances in the pharmacological and percutaneous interventional treatment of patients with AF have occurred over the past decade that GPs should be aware of so they can be better able to answer the question 'what do I do with my patient with AF today?'

DIAGNOSIS OF AF

The clinical diagnosis of AF is suspected by the presence of a classic irregularly irregular pulse and is confirmed with an ECG. It is important to be aware that for short periods of time, the rhythm during AF can be relatively regular and thus mimic sinus rhythm at the pulse. This may particularly occur when AF is either very rapid or slow. Conversely, the presence of multiple ventricular or atrial ectopic beats can mimic AF. Therefore, ECG confirmation is essential. This demonstrates the presence of rapid oscillations or fibrillatory waves (best seen in leads V_1 or II on the ECG) that vary in amplitude, shape and timing, accompanied by an irregular and often rapid ventricular response (Figure 1). When AF is intermittent, ECG confirmation of diagnosis can be more difficult. For patients with frequent symptoms (episodic palpitations), AF can be detected by 24-hour Holter monitoring or longer periods of monitoring (usually by seven-day event recorder or seven-day Holter monitor). In patients with infrequent episodes of AF, one strategy is to request that they present for an ECG at the time of symptoms. Alternatively, an implantable monitor (loop recorder) may be useful in occasional cases.[4]

RISK FACTORS FOR AF

AF is frequently associated with cardiovascular or noncardiovascular risk factors. When these factors are absent the diagnosis of 'lone AF' may be made (Table 2). The Atherosclerosis Risk in Communities (ARIC) study showed that about 57% of cases of new-onset AF could be attributed to common cardiovascular risk factors.[5] When a patient presents with AF, a search for these risk factors is important as part of an overall management strategy. As part of this initial evaluation, in addition to the ECG, an echocardiogram and routine blood tests are mandatory.



ANTICOAGULATION FOR AF

The unco-ordinated atrial activity during AF predisposes patients to thrombus formation, especially in the left atrial appendage. Issues relating to anticoagulation include: the assessment of risk of thromboembolism, the potential benefit to be gained from anticoagulation, the risk of bleeding and patient preference for anticoagulation.

Thromboembolism risk

Patients with nonvalvular AF have a five to eight times increased risk of stroke; however, the risk is not uniform and is influenced by the presence of certain risk factors. These risk factors have been combined to formulate stroke risk stratification schema.

Traditionally, the $CHADS_2$ score (cardiac failure, hypertension, age over 75 years and

TABLE 1. TYPES OF ATRIAL FIBRILLATION

Type	Definition
Paroxysmal	Self-terminating atrial fibrillation episodes lasting less than one week, usually lasting 48 hours
Persistent	Episode of atrial fibrillation that either lasts longer than seven days or needs cardioversion to restore sinus rhythm
Longstanding persistent	Atrial fibrillation that has lasted for one year or longer and a rhythm-control strategy is used
Permanent	Atrial fibrillation refractory to cardioversion or when cardioversion is deemed inappropriate and the presence of atrial fibrillation is accepted by the patient (and physician) to be due to patient frailty and/or associated medical comorbidities

diabetes are assigned one point, and prior stroke or embolic event are assigned two points) has been used to categorise the risk of AF. Low-risk patients (score of 0) are recommended to take aspirin alone; those at intermediate risk (score of one) are recommended to take either aspirin or warfarin; and high-risk patients (score of two or more) are recommended to take warfarin (target INR 2 to 3). However, the $CHADS_2$ score has been found to have only moderate predictive value for thromboembolic risk. Furthermore, about 65% of patients would be classified as being at intermediate risk, with uncertainty as to which agent to prescribe (aspirin or warfarin). With the use of $CHADS_2$ scoring, low-risk patients still have an appreciable risk of stroke (1.67 per 100 person years).[1]

Recently, the CHA_2DS_2VASc score (one point each for cardiac failure/left ventricular dysfunction and hypertension, two points for age 75 years or older, one point for diabetes, two points for stroke, and one point each for vascular disease, age 65 to 74 years and sex category [female]; Table 3) has been advocated as a better predictor of low risk than the $CHADS_2$ score.[6] Patients with a CHA_2DS_2VASc score of zero have a very low risk of events (0% in one study).[1]

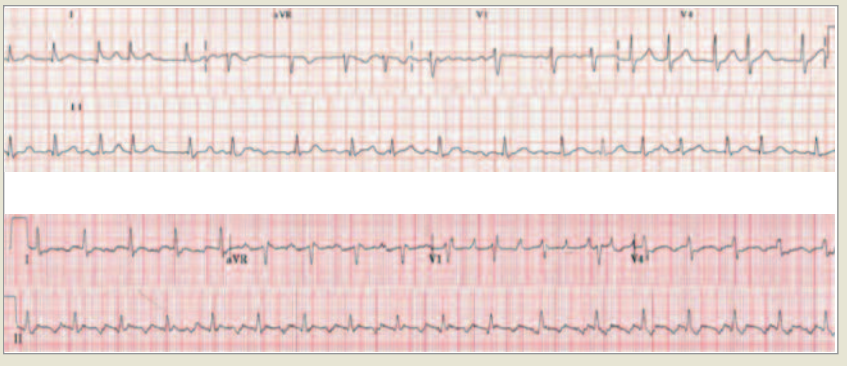


Figure 1. ECGs showing atrial fibrillation (top) and atrial flutter (bottom).

Patients with a score of one or more require anticoagulation with warfarin (INR 2 to 3; Table 3). It is important to note that the CHA_2DS_2VASc score has as yet not been widely adopted in cardiology practice with many still favouring the $CHADS_2$ score.

Bleeding risk

Many clinical risk factors have been reported to be associated with an increased risk of bleeding but the recently reported HAS-BLED scoring system has been used as a simple risk assessment tool in major international guidelines.[7] In this system, one point is given for uncontrolled hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, being elderly (over 65 years) and drugs or alcohol use. A score of three or more suggests a high risk of bleeding that requires caution when considering anticoagulation.

Patient preference

The risks and benefits of anticoagulation should be discussed thoroughly with patients, and their perceptions and expectations taken into account, along with factors such as patient compliance, cognitive function, alcohol intake, recreational drug use, pharmacological drug interactions, mobility, risk of falls and accessibility to monitoring services.

Frequent re-assessment of stroke risk is also important. The amount of time spent in the therapeutic range (INR 2 to 3) has a key influence on the level of protection against ischaemic stroke and risk of major haemorrhage. Good anticoagulation control (time in therapeutic range 70% or more) is associated with a low risk of stroke and bleeding events.[8]

Anticoagulants

Warfarin

Warfarin provides a 62% relative risk reduction for stroke and a 26% relative risk reduction for overall mortality compared with no anticoagulation.[9] The

benefit of aspirin is less, with a relative risk reduction of 22% compared with no anticoagulation.

A number of new anticoagulants have emerged, targeting the single coagulation enzymes thrombin (dabigatran) or factor Xa (apixaban and rivaroxaban). These drugs are given in fixed doses without coagulation monitoring.

Dabigatran

Dabigatran etexilate (direct thrombin inhibitor) may soon be available on the Pharmaceutical Benefit Scheme under authority prescription as an alternative to warfarin for patients with AF. Its major advantage is that it does not require INR monitoring and it does not have many of the food and drug interactions of warfarin.[10] Dabigatran 150 mg twice daily was found to be better than warfarin for stroke risk reduction with a similar risk of major bleeding, and dabigatran 110 mg twice daily was found to be similar to warfarin for stroke risk reduction with significantly less major bleeding.[11,12] Dabigatran is excreted renally and therefore is not a good option for patients with renal failure (creatinine clearance less than 15 mL/min). If used in patients with renal impairment, a reduced dose of 75 mg twice daily is recommended. The most common side effect of dabigatran is dyspepsia. Dabigatran has a half-life of eight to 14 hours and, as yet, there is no agent capable of reversing its anti-coagulant effect.

Rivaroxaban and apixaban

Rivaroxaban and apixaban are highly selective, reversible direct oral factor Xa inhibitors, which are rapidly absorbed after oral administration (maximum effect within two to four hours).[13] Rivaroxaban is prescribed once daily and apixaban is prescribed twice daily in patients with AF. They must be used with caution in patients with severe renal failure as between one-quarter and one-third of the ingested drug is excreted renally.

TABLE 2. COMMON RISK FACTORS FOR ATRIAL FIBRILLATION AND ASSOCIATED COMMON DIAGNOSTIC TESTS

Risk factors	Common diagnostic tests
Hypertension	Measurement of resting and ambulatory blood pressure
Diabetes	Measurement of fasting blood glucose level
Valvular heart disease	Echocardiography
Congestive heart failure	Clinical examination, chest x-ray and measurement of B-type natriuretic peptide
Obesity	Body mass index
Sleep apnoea	Clinical history and sleep studies
Thyroid disease	Thyroid function tests
Ischaemic heart disease	ECG and exercise stress test (stress echocardiography, nuclear scan, angiography)
Pulmonary disease (e.g. smoking, chronic obstructive pulmonary disease, chronic thromboembolic pulmonary hypertension)	Chest x-ray and pulmonary function tests
Pericarditis	Pleuritic chest pain and concave up ST-elevation on ECG

TABLE 3. CHA_2DS_2VASc SCORING SYSTEM AND ASSOCIATED RISK OF THROMBOEMBOLIC STROKE[1]

Factor	CHA_2DS_2VASc score*	Stroke risk (% per year)*
Congestive heart failure/left ventricular dysfunction	1	1.3
Hypertension	1	1.3
Age 65 to 74 years	1	1.3
Age ≥75 years	2	2.2
Diabetes	1	1.3
Stroke/transient ischaemic attack/thromboembolism	2	2.2
Vascular disease (previous myocardial infarction, aortic plaque, peripheral arterial disease)	1	1.3
Female sex	1	1.3
Maximum score	**9**	**15.2**

* CHA_2DS_2VASc score 1 = 1.3% stroke risk per year; 2 = 2.2%; 3 = 3.2%; 4 = 4%; 5 = 6.7%; 6 = 9.8%; 7 = 9.6%; 8 = 6.7%; 9 = 15.2%.

Apixaban is metabolised in the liver, in part by the cytochrome P450 enzymes; therefore, it is not recommended in patients taking an antifungal drug of the azole class, anti-epileptic drugs (e.g. phenytoin, carbamazepine), the antibiotic rifampicin or certain HIV drugs such as protease inhibitors. Of note, there are currently no agents capable of reversing the anticoagulant effect of rivaroxaban or apixaban.[13]

In phase III trials of rivaroxaban and apixaban, compared with warfarin, in patients with AF, apixaban reduced the risk of stroke, systemic embolism, mortality and major bleeding, and rivaroxaban was found to be noninferior to warfarin for stroke and systemic embolism with no difference in risk of major bleeding.[13] Both agents reduced the risk of intracranial haemorrhage. Due to their efficacy and ease of use, it is probable that these agents will gradually replace warfarin to a large extent in patients with AF.

Of all newer anticoagulants mentioned, a key point is that compliance is crucial because these drugs have a relatively short half-life, such that patients may be left without anticoagulation if more than one dose is missed.

PHARMACOLOGICAL MANAGEMENT OF AF

Pharmacological management of patients with AF is directed either at rhythm control or rate control. Rhythm-control drugs act by altering the electrical properties of the atria such that they can no longer sustain the presence of AF. Rate-control drugs slow conduction through the atrioventricular (AV) node and therefore reduce ventricular rate response.

Either strategy may be reasonable as no significant difference in mortality or thromboembolic risk has been demonstrated between the two approaches; however, symptomatic patients frequently derive much greater symptom relief from rhythm control. In addition, even in minimally symptomatic patients an initial attempt at rhythm control may be worthwhile taking into account such issues as patient preference, age and comorbidities. Rhythm control may be achieved either pharmacologically or with electric cardioversion. After cardioversion, anti-arrhythmic drugs may be used to maintain sinus rhythm (Table 4).

Pharmacological management of patients with AF is directed either at rhythm control or rate control.

Amiodarone is the most effective anti-arrhythmic drug available but should be used as a last resort because of its troublesome side effects. Flecainide should not be used in patients with structural heart disease, particularly coronary artery disease where it may lead to malignant ventricular arrhythmias. It must also be combined with an AV nodal-blocking agent because it may organise AF into atrial flutter, which may lead to conduction down the AV node rapidly leading to haemodynamic compromise.

In patients with no structural heart disease and infrequent episodes of symptomatic AF, a 'pill-in-the-pocket' approach with an oral agent such as flecainide may be effective. When the patient becomes aware of an episode of AF they can take a single oral dose of flecainide (50 to 100 mg) together with a rate-control agent such as a β-blocker. When pharmacological rhythm control fails, catheter ablation is an option in some patients.

The choice to opt for rate control is based on both symptoms and the likelihood of long-term sinus rhythm maintenance (e.g. the presence of marked atrial enlargement or other significant structural heart disease reduces this likelihood; see the flowchart on page 23). Rate control is also the default option when rhythm control fails. Commonly used drugs and important caveats are shown in Table 4.

In general, the target in rate control is symptom control rather than a particular heart rate. However, for patients who remain symptomatic the best method for assessing pharmacological response is 24-hour Holter monitoring. Heart rate may appear well controlled when the patient is at rest in the office, but monitoring may show poor control with minor activity. Holter monitoring also allows correlation of the heart rate with symptoms. It is important to be aware that persistently elevated heart rates (even in asymptomatic patients) may result in a decline in left ventricular function. This is termed tachycardia-mediated cardiomyopathy and may occur when the average 24-hour heart rate is above about 100 beats per minute. Tachycardia-mediated cardiomyopathy is usually reversible when better rate control is achieved.

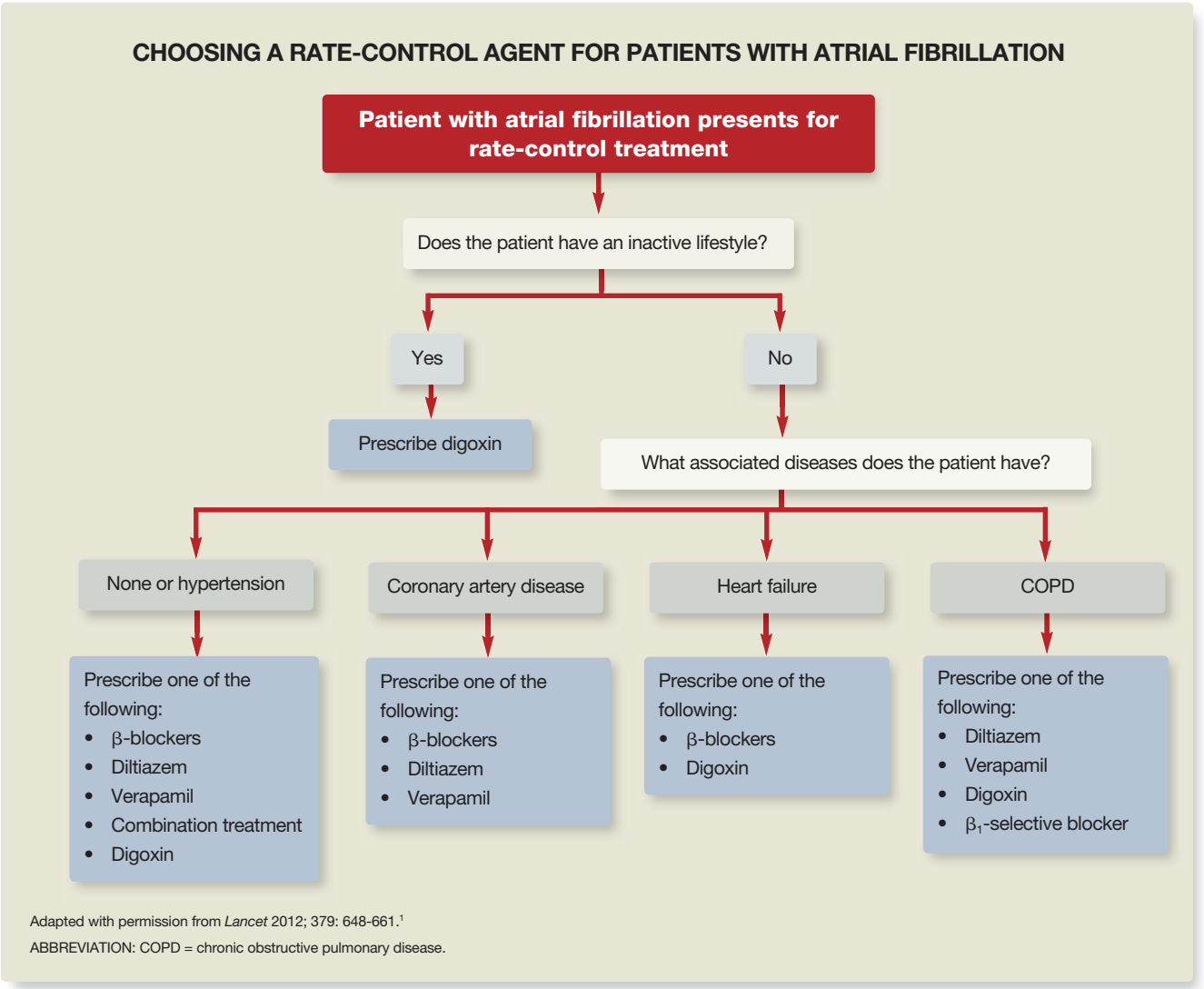
NEW ANTI-ARRHYTHMIC AGENTS

Two new anti-arrhythmic drugs are under evaluation but are as yet not available in Australia. Vernakalant, an atrial selective potassium channel-blocking agent, has been approved in Europe for the conversion of recent-onset AF. In this setting, it has been found more effective than amiodarone for conversion to sinus rhythm.[14] However, its use is contraindicated in patients with hypotension, severe heart failure, valvular heart disease, prolonged QT interval or bradycardia.

Dronedarone is similar in structure to amiodarone but with the iodine moiety removed and it therefore has a lower side effect profile. Initial studies have been encouraging,[15,16] but more recent studies in patients with heart failure[17] or permanent AF with pre-existing cardiovascular disease[18] have shown an increase in

TABLE 4. COMMONLY USED ANTI-ARRHYTHMIC DRUGS FOR ATRIAL FIBRILLATION AND SOME OF THEIR MORE COMMON OR SEVERE SIDE EFFECTS

Drug	Side effects	Contraindictions	Caveats
Rhythm-control drugs			
Flecainide	Ventricular pro-arrhythmia (or ventricular fibrillation) in patients with structural heart disease. Atrial pro-arrhythmia (e.g. atrial flutter with 1:1 conduction when used without concurrent atrioventricular nodal blocking)	Absolutely contraindicated in patients with left ventricular dysfunction or coronary artery disease	Reasonable first choice for maintaining sinus rhythm in patients with paroxysmal and persistent atrial fibrillation and normal ventricular function and no structural heart disease. Should be used in combination with atrioventricular nodal blocking agent (e.g. β-blocker or calcium channel blocker such as verapamil)
Sotalol	Bradycardia, depression of cardiac pump function, atrioventricular block, ventricular proarrhythmia (torsades de pointes)	Relatively contraindicated if renal impairment present. Avoid in patients with heart failure. Use with caution in patients with underlying conduction abnormalities	May be used as first choice in patients with paroxysmal and persistent atrial fibrillation
Amiodarone	Thyrotoxicosis (three to six monthly thyroid function tests required), sleep disturbance, cutaneous photosensitivity and tremor. Pulmonary fibrosis and liver dysfunction are rare	Use with caution in patients with underlying conduction abnormalities	First-line agent in patients with atrial fibrillation and heart failure. Second- or third-line agent for patients with paroxysmal and persistent atrial fibrillation not responding to or intolerant of other anti-arrhythmic drugs
Rate-control drugs			
β-blockers	Bradycardia, depression of cardiac pump function, heart block, exacerbation of heart failure and exacerbation of airways disease	Complete heart block or high degree atrioventricular block, asthma or reactive airways disease, decompensated heart failure	Useful for patients with atrial fibrillation associated with heightened sympathetic activity or ischaemia (e.g. onset of atrial fibrillation with stress or exercise)
Calcium channel antagonists (nondihydropyridine)	Hypotension, heart block, heart failure, constipation (with verapamil) and drug interactions	Complete heart block or high-degree atrioventricular block, decompensated heart failure	
Digoxin	Generally well tolerated when serum levels in therapeutic range. When digoxin levels are excessive may cause gastrointestinal upset, visual disturbance, heart block and ventricular arrhythmias		Not effective for rate control during activity. Can be used (with caution) in combination with either a β-blocker or calcium channel antagonist when single agent is ineffective. Use as sole agent if the patient has a hypotensive response to other rate-controlling drugs. Monitor digoxin levels and digoxin toxicity



Adapted with permission from *Lancet* 2012; 379: 648-661.[1]

ABBREVIATION: COPD = chronic obstructive pulmonary disease.

mortality associated with the drug. European and Canadian guidelines have recommended dronedarone only in patients with non-permanent AF with no structural heart disease.[19,20] Given its significant limitations, it remains unclear whether this drug will be approved for use in Australia.

NONPHARMACOLOGICAL MANAGEMENT OF AF

Catheter ablation

Catheter ablation is a highly effective strategy for the control of symptomatic AF in patients who do not have advanced structural heart disease and where one or more anti-arrhythmic drugs have failed. The role of ablation in broader AF populations (e.g. patients with persistent AF or structural heart disease, or older age groups) remains under investigation and may be appropriate in selected cases.

The aim of ablation in patients with paroxysmal AF is to eliminate the initiating triggers. In patients with paroxysmal AF, these triggers are almost universally located within the pulmonary veins. By electrically isolating the pulmonary veins from the left atrium (Figure 2), these triggers (or foci of rapid electrical activity) can no longer conduct electrical activity to the atrium.

Pulmonary vein isolation can be performed with the use of radiofrequency energy (most commonly) or cryoablation. Randomised controlled trials have reported that the success of pulmonary vein isolation in maintaining sinus rhythm is between 66 and 89% at 12-month follow up.[21]

In a meta-analysis of randomised and nonrandomised studies, the single procedure success rate of catheter ablation in patients taking no anti-arrhythmic

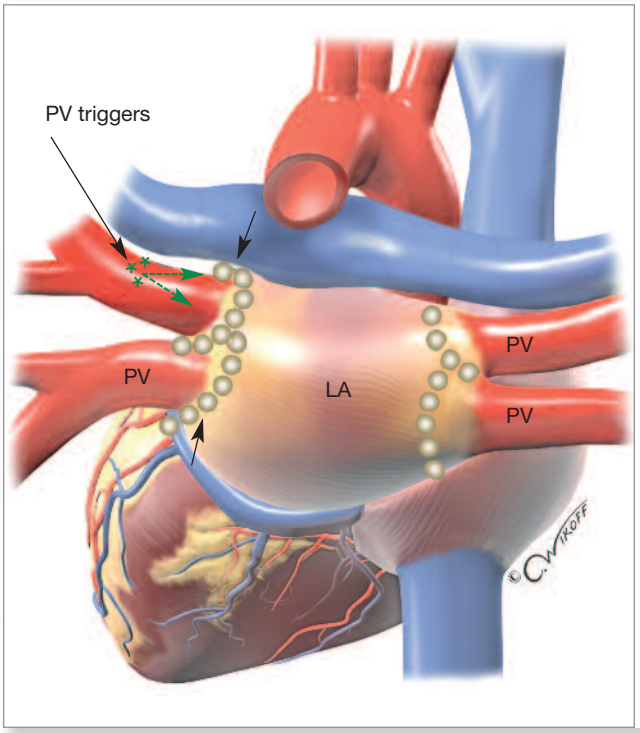


Figure 2. Pulmonary vein isolation. Continuous lines of electrical lesions (solid arrows and green dots) are placed at the junction of the pulmonary veins (PV) and left atrium (LA) so that PV triggers can no longer propagate into the LA (dotted arrows) and initiate atrial fibrillation.

drugs was 57% (95% confidence interval [CI], 50 to 64%); multiple procedure success rate off anti-arrhythmic drugs was 71% (95% CI, 65 to 77%).[22] In each trial, catheter ablation was superior to anti-arrhythmic drug use, which had an efficacy of between 9 and 58%. In a meta-analysis, the mean success rate of anti-arrhythmic drug use was 52% (95% CI, 47 to 57%).[22] Furthermore, catheter ablation has been found to be superior to anti-arrhythmic drugs in reducing AF symptoms and resulted in improved quality of life.

It is important to note that about one-third of patients may require repeat ablation owing to the phenomenon of recovered conduction to the pulmonary veins. With the continued advance in AF ablation technologies this recurrence rate is gradually decreasing.

The reported efficacy of catheter ablation for patients with persistent AF is less favourable with published mean estimates of about 47% for a single procedure.[21] However, these procedures require more extensive ablation in the atria in addition to targeting pulmonary vein triggers. Although this success rate increases with repeat procedures, there is still uncertainty about the mechanism underlying persistent AF and the best procedure to perform. Over time, it is likely that the success rate, procedural time and risk of complications of AF ablation will continue to improve, meaning that more complex ablation in patients with persistent AF will become more common.

Catheter ablation in patients with AF is a complex interventional procedure that requires skilled operators, use of specialised three-dimensional computer mapping systems and dedicated laboratory time (up to four hours per procedure). The procedure is associated with a 1 to 2% risk of major complications, including thromboembolic events (about 0.5%) such as transient ischaemic attack and stroke, and cardiac tamponade (about 1%). Other major complications may occur.

The mortality risk associated with the procedure has been estimated to be about 0.1%.[21] For these reasons, appropriate patient selection and consent is important, taking into account symptom severity, drug response and patient preference. The discussion as to whether to undergo this procedure is necessarily detailed.

Recommendations for catheter ablation

Current guidelines recommend that catheter ablation should be offered to patients with troublesome symptomatic paroxysmal AF who have either failed or are intolerant to at least one class I (e.g. flecainide) or class III (e.g. sotalol and amiodarone) anti-arrhythmic drug. Referral for catheter ablation of patients with persistent AF of less than 12 months' duration is considered reasonable if the patient has troublesome symptoms and failure of or intolerance to at least one anti-arrhythmic drug. Catheter ablation is also reasonable in selected patients with heart failure or reduced left ventricular function, especially if the onset of AF precipitates heart failure.[21]

Factors such as advancing age, the presence of structural heart disease, large left atria and long duration of persistent AF reduce the likelihood of success of catheter ablation (Figure 3). In patients undergoing ablation it is important to address associated conditions including hypertension, obesity and sleep apnoea.

In general, a desire to stop taking anticoagulants is not considered a sole indication for this procedure in the asymptomatic patient in view of the risk of late recurrences of the arrhythmia.[1]

AV node ablation and pacing

In patients with AF in whom a rate-control strategy is preferred, but who are not responding to or are intolerant of AV nodal-blocking agents, insertion of a permanent pacemaker followed by

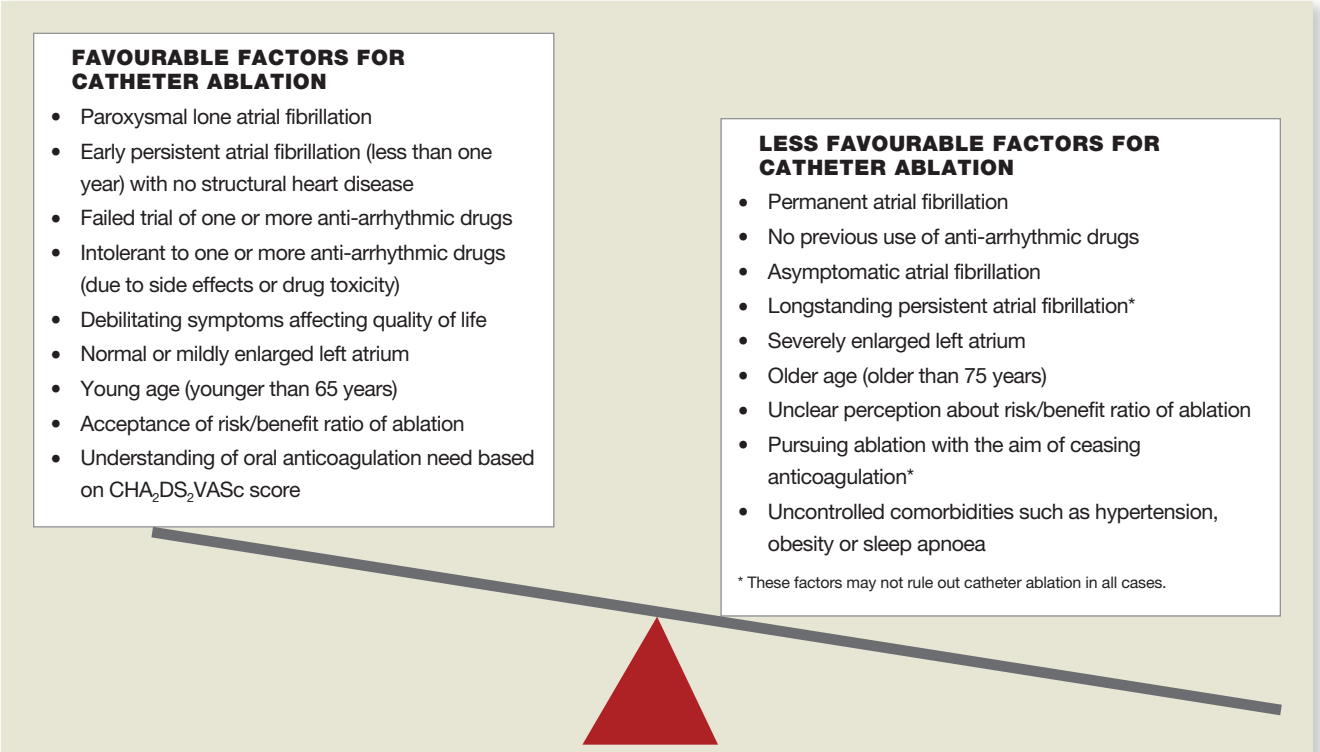


Figure 3. Factors influencing referral for catheter ablation.

AV node ablation has been shown to improve symptoms and quality of life.[23] Although this represents a relatively small group, the improvement in symptoms and quality of life can be dramatic. This is particularly the case in the elderly who tend to tolerate pharmacological agents poorly. In patients with heart failure, biventricular pacing may be preferable to right ventricular pacing to prevent further deterioration of left ventricular function.[24,25]

CONCLUSION

AF is the most frequent cardiac arrhythmia encountered in clinical practice, occurring in paroxysmal, persistent or permanent forms. Recognition and treatment of underlying risk factors or associated conditions is important in the overall management strategy of these patients. Treatment is directed primarily at symptom control and reduction in stroke risk.

Catheter ablation is an excellent strategy for AF management in patients with paroxysmal AF and limited structural heart disease. It may also play a role in some patients with persistent AF. The development of newer anticoagulant agents may greatly simplify management of stroke risk in at-risk patients. MT

REFERENCES

References are included in the pdf version of this article available at www.medicinetoday.com.au.

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REFERENCES

1. Lip GY, Tse HF, Lane DA. Atrial fibrillation. Lancet 2012; 379: 648-661.
2. Benjamin EJ, Chen PS, Bild DE, et al. Prevention of atrial fibrillation: report from a national heart, lung, and blood institute workshop. Circulation 2009; 119: 606-618.
3. Steger C, Pratter A, Martinek-Bregel M, et al. Stroke patients with atrial fibrillation have a worse prognosis than patients without: data from the Austrian Stroke Registry. Eur Heart J 2004; 25: 1734-1740.
4. Hobbs FD, Fitzmaurice DA, Mant J, et al. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. Health Technol Assess 2005; 9: iii-iv, ix-x, 1-74.
5. Huxley RR, Lopez FL, Folsom AR, et al. Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: the Atherosclerosis Risk in Communities (ARIC) study. Circulation 2011; 123: 1501-1508.
6. Olesen JB, Lip GY, Hansen ML, et al. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. BMJ 2011; 342: d124.
7. Lip GY, Frison L, Halperin JL, Lane DA. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. J Am Coll Cardiol 2011; 57: 173-180.
8. Wan Y, Heneghan C, Perera R, et al. Anticoagulation control and prediction of adverse events in patients with atrial fibrillation: a systematic review. Circ Cardiovasc Qual Outcomes 2008; 1: 84-91.
9. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007; 146: 857-867.
10. Hankey GJ, Eikelboom JW. Dabigatran etexilate: a new oral thrombin inhibitor. Circulation 2011; 123: 1436-1450.
11. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009; 361: 1139-1151.
12. Roskell NS, Lip GY, Noack H, Clemens A, Plumb JM. Treatments for stroke prevention in atrial fibrillation: a network meta-analysis and indirect comparisons versus dabigatran etexilate. Thromb Haemost 2010; 104: 1106-1115.
13. Bassand JP. Review of atrial fibrillation outcome trials of oral anticoagulant and antiplatelet agents. Europace 2012; 14: 312-324.
14. Camm AJ, Capucci A, Hohnloser SH, et al. A randomized active-controlled study comparing the efficacy and safety of vernakalant to amiodarone in recent-onset atrial fibrillation. J Am Coll Cardiol 2011; 57: 313-321.
15. Hohnloser SH, Crijns HJ, van Eickels M, et al. Effect of dronedarone on cardiovascular events in atrial fibrillation. N Engl J Med 2009; 360: 668-678.
16. Connolly SJ, Crijns HJ, Torp-Pedersen C, et al. Analysis of stroke in ATHENA: a placebo-controlled, double-blind, parallel-arm trial to assess the efficacy of dronedarone 400 mg BID for the prevention of cardiovascular hospitalization or death from any cause in patients with atrial fibrillation/atrial flutter. Circulation 2009; 120: 1174-1180.
17. Kober L, Torp-Pedersen C, McMurray JJ, et al. Increased mortality after dronedarone therapy for severe heart failure. N Engl J Med 2008; 358: 2678-2687.
18. Hohnloser SH, Crijns HJ, van Eickels M, et al. Dronedarone in patients with congestive heart failure: insights from ATHENA. Eur Heart J 2010; 31: 1717-1721.
19. Camm AJ, Kirchhof P, Lip FY, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J 2010; 31: 2369-2429.
20. Gillis AM, Verma A, Talajic M, Nattel S, Dorian P. Canadian Cardiovascular Society atrial fibrillation guidelines 2010: rate and rhythm management. Can J Cardiol 2011; 27: 47-59.
21. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. Europace 2012; 14: 528-606.
22. Calkins H, Reynolds MR, Spector P, et al. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. Circ Arrhythm Electrophysiol 2009; 2: 349-361.
23. Wood MA, Brown-Mahoney C, Kay GN, Ellenbogen KA. Clinical outcomes after ablation and pacing therapy for atrial fibrillation: a meta-analysis. Circulation 2000; 101: 1138-1144.
24. Brignole M, Gammage M, Puggioni E, et al. Comparative assessment of right, left, and biventricular pacing in patients with permanent atrial fibrillation. Eur Heart J 2005; 26: 712-722.
25. Sweeney MO, Bank AJ, Nsah E, et al. Minimizing ventricular pacing to reduce atrial fibrillation in sinus-node disease. N Engl J Med 2007; 357: 1000-1008.