Lifelong Learning

CPD ARTICLE NUMBER ONE

Recent Advances in the Treatment of Atrial Fibrillation

Atrial fibrillation occurs in paroxysmal, persistent or permanent forms. New anti-arrhythmic agents are being trialed for the pharmacological treatment of affected patients, and catheter ablation is an effective therapeutic intervention for the treatment of patients with symptomatic, drug-refractory paroxysmal atrial fibrillation.

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, independent of known predisposing conditions. With ageing population, the prevalence of AF is expected to reach epidemic proportions. 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.

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 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 suffering from AF either as part of long-term management with other comorbidities, as a new diagnosis 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. Being aware of these advances enables doctors to better answer the question 'what do I do for 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 V1 or II on the ECG) that vary in amplitude, shape and timing, accompanied by an irregular and often rapid ventricular response (Figure 1). When

Key points

- The two main aims of treatment of patients with atrial fibrillation (AF) are symptom control and reduction 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 pharmacologically, 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 to respond to one or more anti-arrhythmic drugs.

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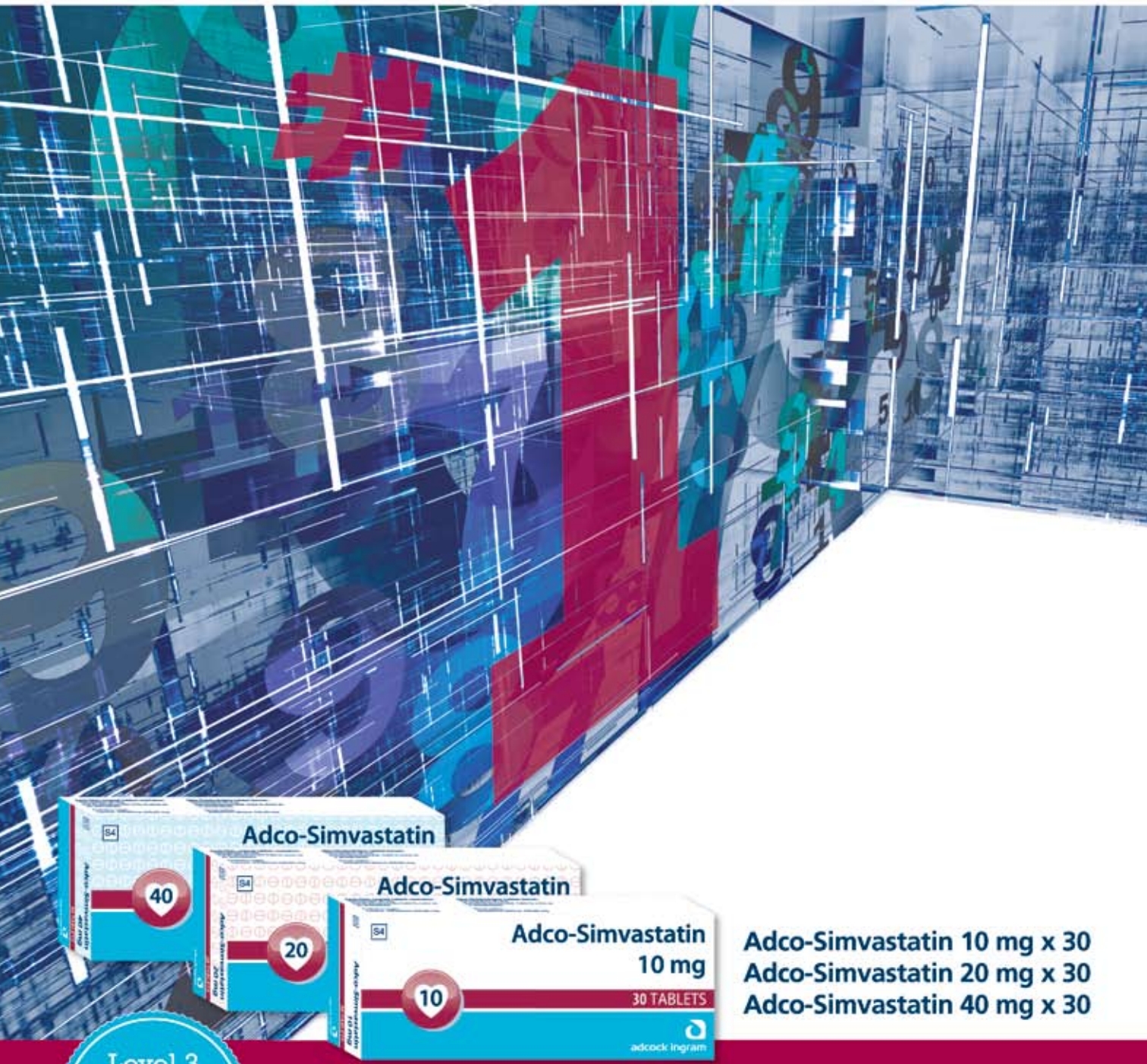

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*VTE = venous thromboembolism;

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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]

TABLE 1
Types of atrial fibrillation

Type	Definition
Paroxysmal	Self-terminating atrial fibrillation episodes lasting less than one week, usually 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 co-morbidities.

Risk factors for AF

AF is frequently associated with cardiovascular or non-cardiovascular 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.

Anti-coagulation for AF

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

Thromboembolism risk

Patients with non-valvular 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 CHADS2 score (cardiac failure, hypertension, age over 75 and 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 CHADS2 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 CHADS2 scoring, low-risk patients still have an appreciable risk of stroke (1.67 per 100 person years).[1]

Recently, the CHA2DS2VASc 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 CHADS2 score.[6] Patients with a CHA2DS2VASc score of zero have a very low risk of events (0% in one study).[1] 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 CHA2DS2VASc score has as yet not been widely adopted in cardiology practice, with many still favouring the CHADS2 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

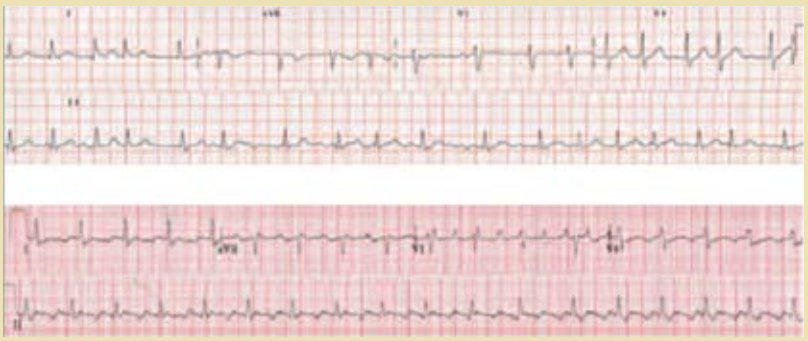

Figure 1. ECGs showing atrial fibrillation (top) and atrial flutter (bottom).

TABLE 2

Common factors for atrial fibrillation and associated common diagnostic tests

Risk factors	Common diagnostic test
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 (eg, 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

CHA2DS2VASc scoring system and associated risk of thromboembolic stroke[1]

Factor	CHA2DS2 VASc 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**

*CHA2DS2 VASc 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%

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), although apixaban has not yet been approved for AF treatment in South Africa. These drugs are given in fixed doses without coagulation monitoring.

Dabigatran

The major advantage of dabigatran etexilate (direct thrombin inhibitor) is that it does not require INR monitoring and does not have many of the food and drug interactions of warfarin.[10] Dabigatran 150mg twice daily was found to be better than warfarin for stroke risk reduction with a similar risk of major bleeding, and dabigatran 110mg twice daily was found to be similar to warfarin for stroke risk reduction with significantly less major bleeding.[11,12] For the prevention of stroke and systemic embolism in patients with non-valvular AF, the recommended daily dose of dabigatran is 300mg taken orally as a 150mg cap-

TABLE 4

Commonly used anti-arrhythmic drugs for atrial fibrillation and some of their more common side effects

Drug	Side effects	Contraindications	Caveats
Rhythm control drugs			
Flecainide	Ventricular pro-arrhythmia (or ventricular fibrillation) in patients with structural heart disease. Atrial pro-arrhythmia (eg,) atrial flutter with 1:1 conduction when used without concurrent atrioventricular nodal blocking	Absolutely contraindicated in patients with left ventricular dysfunction or coronary heart disease	Reasonable first choice for maintaining sinus rhythm in patients with paroxysmal and persistent atrial fibrillation, normal ventricular function and no structural heart disease. Should be used in combination with atrioventricular nodal blocking agent (eg, β-blocker or calcium channel blocker such as verapamil
Sotalol	Bradycardia, depression of cardiac pump function, atrioventricular block, ventricular proarrythmia (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 AF
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 (eg onset of atrial fibrillation with stress or exercise)
Calcium channel antagonists (non-dihydropyridine)	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 arrhymthmias		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 a sole agent if the patient has a hypotensive response to other rate controlling drugs. Monitor digoxin levels and digoxin toxicity

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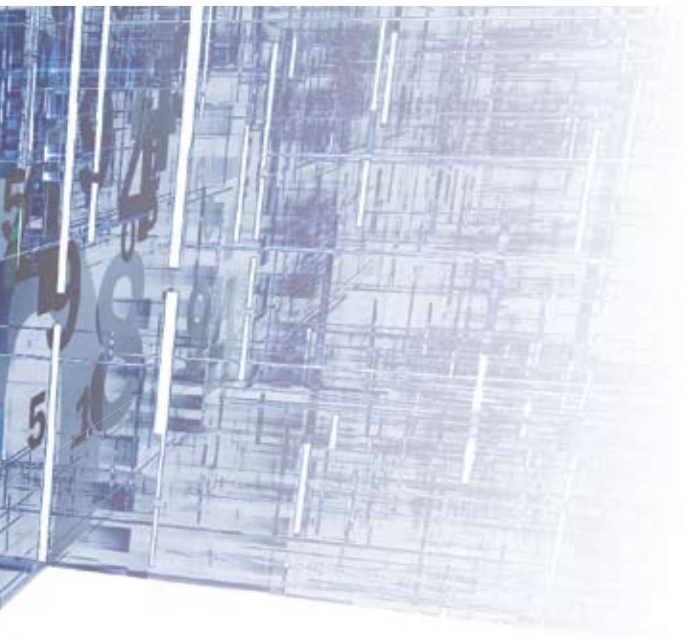

* "The **LDL cholesterol goal** in **very high risk patients** is now **1.8 mmol/L** and in **high risk patients** is **2.5 mmol/L**"

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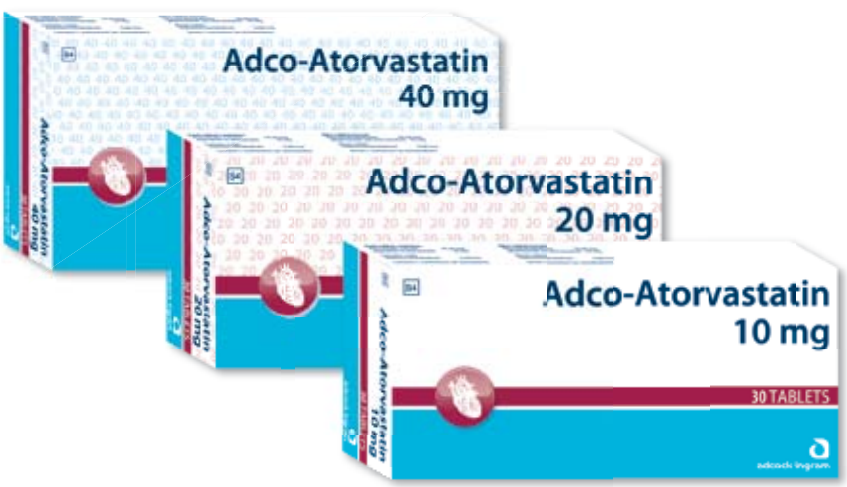

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sule twice daily. Dabigatran is excreted renally and is contraindicated in patients with severe renal impairment (creatinine clearance less than 30mL/min).

For the prevention of stroke and systemic embolism in patients with non-valvular AF who have moderate renal impairment (creatinine clearance 30 to 50mL/min), a reduced dose of 220mg dabigatran given as a 110mg capsule twice daily may be considered. The reduced dose should also be used in those aged over 75 and may be considered in those patients with an increased risk of bleeding (eg, taking concomitant aspirin or who have experienced a recent gastrointestinal bleed).

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 anticoagulant effect.

Rivaroxaban and apixaban

Rivaroxaban and apixaban are highly selective, 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. 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 (eg, phenytoin, carbamazepine), the antibiotic rifampicin or certain HIV drugs such as protease inhibitors. 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 non-inferior 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

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).

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 (50mg to 100mg) with a rate control agent such as a beta blocker. When pharmacological rhythm control fails, catheter ablation is an option in some patients.

The choice to opt for rate control is based both on symptoms and the likelihood of long-term sinus rhythm maintenance (eg, the presence of marked atrial enlargement or other significant structural heart disease reduces this likelihood; see the flowchart on page 21). 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 in some countries. 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 to be 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.

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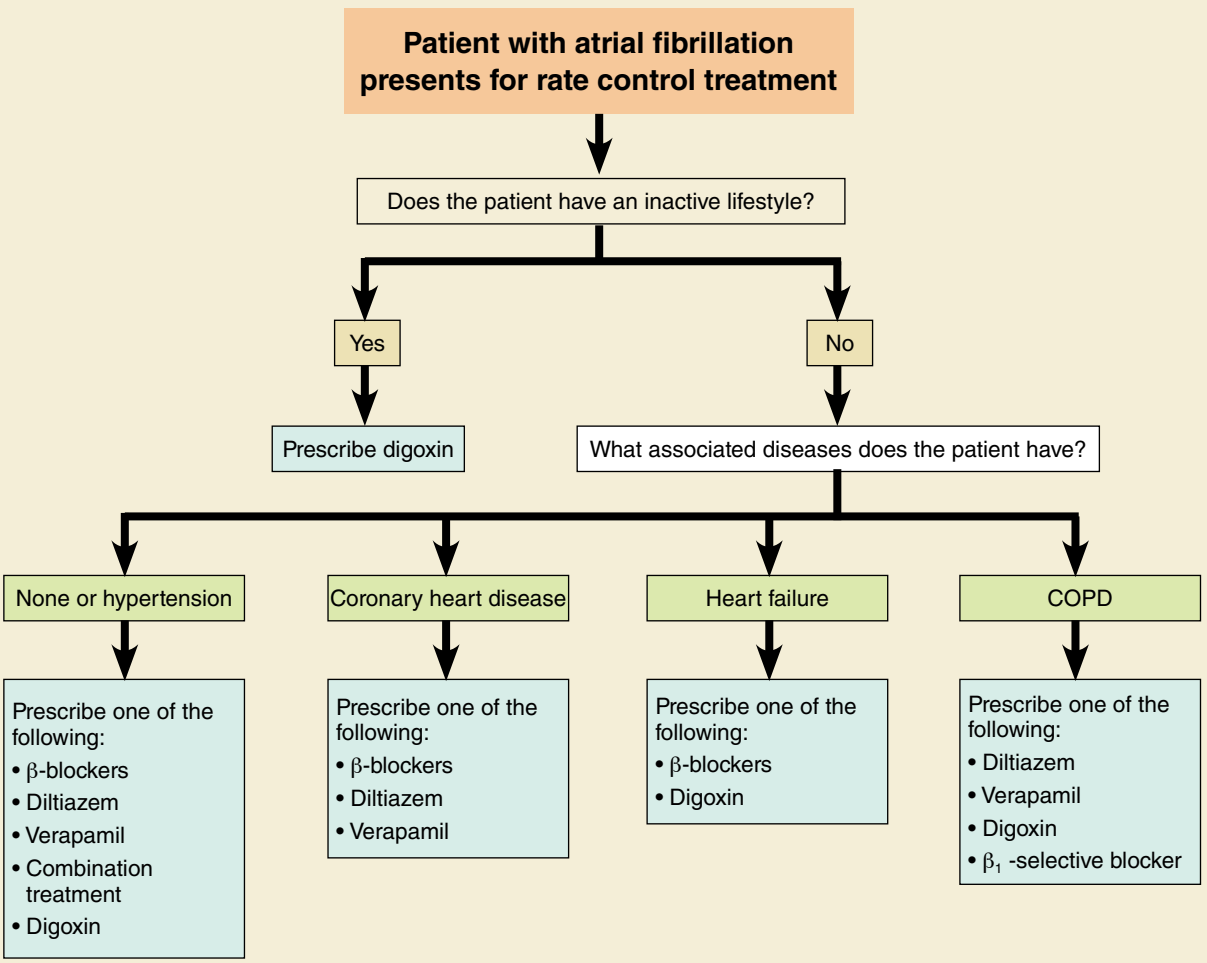
Choosing a rate control agent for patients with atrial fibrillation



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in patients with heart failure[17] or permanent AF with pre-existing cardiovascular disease[18] have shown an increase in 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]

Non-pharmacological management

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 (eg, 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, 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 non-randomised studies, the single procedure success rate of catheter ablation in patients taking no anti-arrhythmic 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-

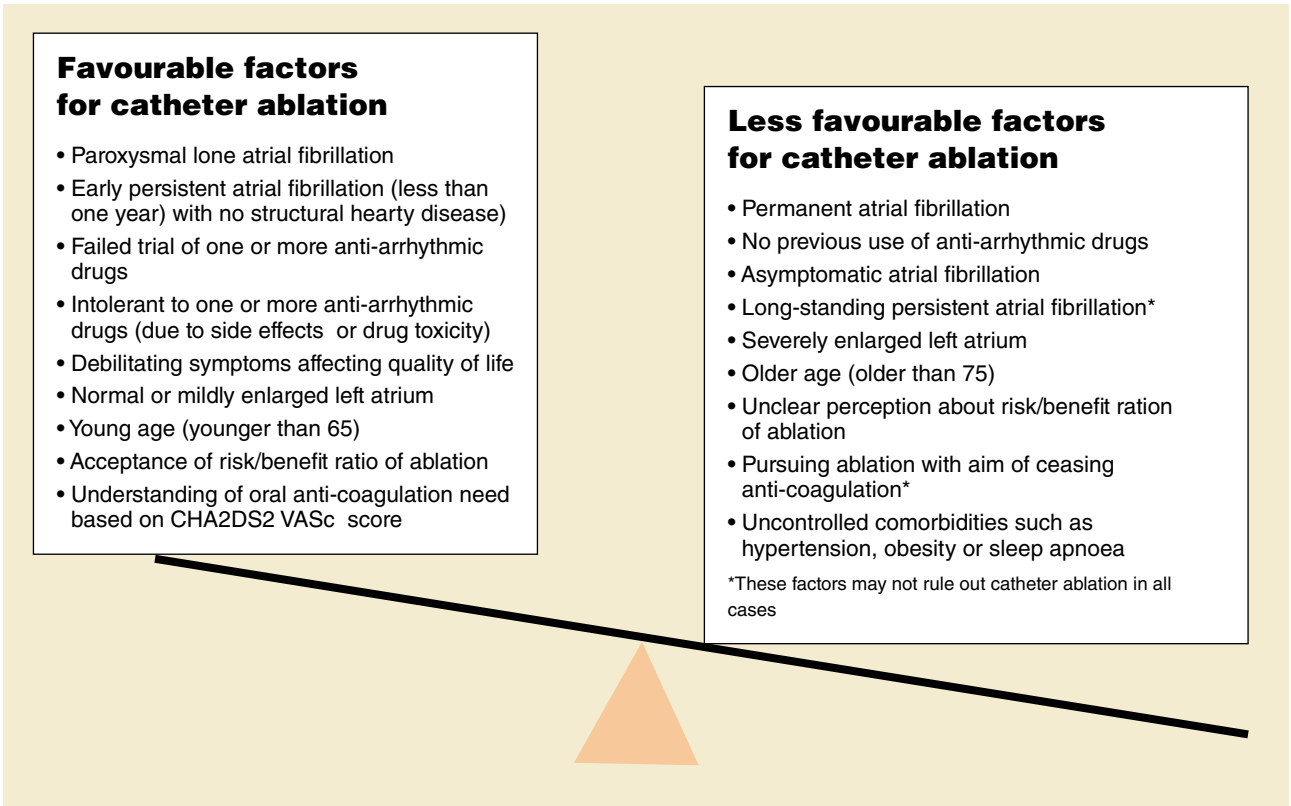

Figure 2. Factors influencing referral for catheter ablation

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 increase.

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 anti-arrhythmic drug (eg, flecainide, sotalol or amiodarone). 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 2). 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

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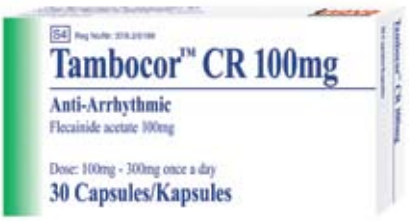
Controlled-release Tambocor Now Available in SA

iNova Pharmaceuticals has introduced Tambocor CR, a controlled-release version of the anti-arrhythmic drug Tambocor (flecainide acetate). Indicated for the treatment of atrial fibrillation (AF) in the patient with no structural heart disease, Tambocor has achieved international support as an anti-arrhythmic drug with a heritage spanning 30 years.[1,2,3] Tambocor is the anti-arrhythmic market leader in France, Italy, Germany and Spain.[4]

New Tambocor CR's controlled-release formulation offers the potential for improved patient compliance thanks to once-daily dosage.[1,5,6] Steady-state plasma concentrations over a 24-hour period ensure better drug coverage and therapeutic success. Furthermore, Tambocor CR helps reduce QRS variation compared with normal Tambocor immediate release tablets.[5] With proven efficacy in the prevention of paroxysmal AF recurrences, Tambocor CR is a noteworthy therapeutic choice, said researchers.[8]



The only flecainide on the SA market, Tambocor is available in four convenient dosage forms:

- Tambocor injection,
- Tambocor 100mg tablets,
- Tambocor CR 100 mg, and
- Tambocor CR 200 mg.

References on request.

Adcock Ingram Receives FDA Accreditation for Its Wadeville Factory

Adcock Ingram says the Center for Drug Evaluation and Research of the US Food and Drug Administration (FDA) has accredited the company's Wadeville manufacturing facility, located in Germiston. Adcock's Wadeville pharmaceutical facility is also certified by SA's Medicines Control Council as a current Good Manufacturing Practice facility.

The FDA accredited Adcock's Wadeville facility following an inspection of the plant's manufacturing and testing activities. It has the capacity to produce 6 million litres of syrups and liquids, 500 000kg creams, 2 billion tablets and capsules. Last August the FDA accepted the company's research & development establishment.

Adcock's Wadeville facility is responsible for the manufacture and testing of critical medication, such as anti-retrovirals (ARVs), creams and effervescents. The Wadeville plant will be used in the manufacturing the Department of Health's ARV tender awarded to Adcock in December 2012.

"The FDA's acceptance of the Wadeville facility is evidence of the quality of systems and processes at Adcock Ingram's manufacturing plants – we strive to provide products and services that consistently exceed customer expectations. Accreditation is key to our strategy of building our business outside SA because FDA approval is a pre-requisite to accessing donor funding and so fulfil tenders in the rest of Africa. It's also a stepping stone to ensuring global best practices across all our production sites" said Adcock Ingram Medical Executive, Dr Abofele Khoele.

Recent Advances in the Treatment of Atrial Fibrillation

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AV nodal-blocking agents, insertion of a permanent pacemaker followed by 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]

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.

References are available on request.