Atrial fibrillation

Management of older patients

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The primary care management of atrial fibrillation requires a careful assessment of age-based factors and the risk of stroke, while balancing the increased risk of treatment-related adverse events and medication misadventure.

Nonvalvular atrial fibrillation (AF) goes hand in hand with advancing age, which is an independent and nonmodifiable risk factor for AF, stroke and other cardiovascular risk factors, all adding to the risk of AF-related stroke. AF affects about 2% of the population and an estimated 5% of those aged 55 years and older.[1-3] It causes significant symptoms that can reduce quality of life and is associated with an increased risk of stroke, poorer outcomes after stroke and increased mortality.

AF is routinely detected and managed in general practice, accounting for one of the highest frequencies of repeat GP visits per year and highest management ratios (ratio of the proportion of encounters at which the condition is managed to the prevalence of the condition among patients at clinical encounters).[4] With population ageing, the burden of AF and attributable stroke is increasing in Australia. The complexity of management of AF also increases in older patients.

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KEY POINTS

- GPs are central to the long-term primary care management of patients with atrial fibrillation (AF), noting that the target population of older people is both expanding and further rapidly ageing, rendering decision-making even more complex.
- A patient-centred treatment plan should focus on three key goals: detecting AF to enable early treatment initiation, managing the dysrhythmia to optimise cardiac function and prevent symptoms, and preventing thromboembolism to reduce stroke risk.
- An individualised, evidence-based approach to AF management requires comprehensive assessment of age-related factors to identify treatment goals, the risk-benefit profile of available treatments, and any medication management issues, with documentation of decision-making and regular reassessment to identify any changes.
- An integrated care approach can help GPs optimise AF management in older people, drawing on the collective expertise and support of the wider healthcare team, particularly as both risk assessments and treatment goals change with increasing age.

This article reviews the primary care management of AF in older people, flagging key treatment goals and guideline recommendations. Clinical considerations and practical management strategies are also discussed.

Burden of AF in primary care

AF has significant anatomical, haemodynamic and thrombotic consequences and causes symptoms such as palpitations, dyspnoea, angina, fatigue, generalised weakness, presyncope or syncope and reduced exercise tolerance, which can adversely affect quality of life.[5] AF is also associated with a five- to sevenfold increased risk of stroke and poorer neurological outcomes after stroke.[6] AF-related strokes are more severe, disabling and likely to be fatal than strokes caused by other conditions.[7,8] In addition, AF itself increases mortality, being reported as the underlying or associated cause in 9% of total deaths.[2]

Given the clinical consequences of AF, it is not surprising that

1% of all GP consultations in Australia are directly related to AF, and it accounts for 2.4% of all chronic problems managed in general practice.[4] A higher proportion of consultations involve AF as a secondary diagnosis or comorbid condition. It is among the circulatory and endocrine or metabolic disorders that encompass the 'other most common' adult conditions (hypertension, lipid disorders, diabetes, obesity, thyroid disorders and diagnosed ischaemic or cardiovascular heart disease) managed in general practice and which are key risk factors for AF.[9]

AF and age

Much of the complexity of AF management relates to the impact of patient age, as well as the increasing burden in primary care. The prevalence of diagnosed AF increases from 2% in the general adult population to 10% in those aged over 65 years, and about 20% in those aged 80 years or older.[1,10-12] The incidence and prevalence of AF doubles for each advancing decade of life.[13] Australian data modelling predicts a doubling in the number of AF cases among older age groups from 2014 to 2034.[3]

The risk of AF-related stroke also significantly increases with advancing age. It rises from 1.5% for those aged 50 to 59 years to 23.5% for those aged 80 to 89 years, with about 40% of strokes in patients aged over 80 years directly attributable to AF.[14]

Fundamentals of primary care management of AF in older people

GPs are central to AF management, drawing on specialist consultation as appropriate. AF is a major reason for referral to cardiologists (13% of referrals), second only to one of its key risk factors, ischaemic heart disease (15%).[4] However, optimal management of older patients with AF requires additional expertise and resources within an integrated care approach (Figure).[15] This may involve geriatricians (regarding geriatric syndromes), allied health professionals, including physiotherapists (mobility and falls risk), occupational therapists (functional ability and independence in self-care), social workers (financial and social support) and pharmacists (medication management, drug-related problems and medication adherence assessments), and practice nurses (point-of-care assessments, monitoring, patient education and care co-ordination).

The need for optimal management of AF to maintain good circulatory health, improve quality of life and prevent stroke is clear, underpinned by evidence from more 'inclusive' clinical trials involving 'real world' patients and advances in diagnostics, risk assessment, rhythm management and anticoagulation therapies. However, clinical advances have not kept pace with the rapidly ageing population and the evolving AF burden in the 'old' old, in whom comorbidities and frailty have an additive negative impact on health.[5] Very old age also independently predicts poor short- and long-term outcomes after stroke, reflecting increased hospitalisations for AF-related adverse events among older age groups.[14,16]

Nevertheless, arbitrary age thresholds used in clinical guidelines, often derived from the inclusion and exclusion criteria in clinical trials, do not correlate well with actual medication behaviour and treatment response in real-world patients.[17] Treatment planning needs to be individualised as much as possible.

Treatment goal: AF screening and diagnosis

The incidence of AF increases sharply after the age of 65 years.[18] With a mean life expectancy of 85.3 years in Australia, there are at least 20 years of optimal health, independent functioning and quality of life to be preserved.[19] Early detection of AF enables early prophylaxis and treatment to improve cardiovascular function, prevent long-term complications, such as structural cardiac changes and heart failure, and avoid stroke. Also potentially amenable to early intervention are the pathophysiological mechanisms underpinning cognitive impairment and dementia in AF, such as cerebral microinfarction, AF-related cerebral hypoperfusion, inflammation, microhaemorrhage, brain atrophy and systemic atherosclerotic vascular disease.[20,21] Further, initiation of new therapies is less complex in the 'young' old than in the 'old' old, before cognitive and functional changes reduce the capacity to adhere to pharmacotherapy and lifestyle measures, manage treatment changes and self-monitor.

Reliance on patients presenting with AF symptoms to prompt diagnostic investigation can miss up to 40% of AF cases, as symptoms such as palpitations, chest discomfort, dizziness or syncope, dyspnoea and fatigue are both nonspecific and common in older people.[22-25] Paroxysms of AF may be asymptomatic ('silent' AF), with poor correlation between AF and symptoms, particularly in the very old in whom sedentary living reduces the likelihood of acute vagally or adrenergically stimulated AF. Nevertheless, asymptomatic or subclinical AF is associated with a 2.5-fold increase in stroke risk compared with no AF.[26]

In the absence of AF screening, the first clinical manifestation of AF may be stroke.[24] Half of all AF cases identified in patients with ischaemic stroke or transient ischaemic attack are asymptomatic.[27] GPs are uniquely placed to screen and initiate management for AF. In Australia, more than 90% of adults aged 65 years and over see their GP at least annually, and around 70% see their GP two or more times per year.[28]

Approach to screening and diagnosis

A proactive approach to detecting AF in older people is warranted and endorsed by current Australian guidelines.[15] These recommend opportunistic point-of-care screening in the clinic or community for people aged 65 years and over by pulse palpation or an ECG rhythm strip. In primary care, the GP, practice nurse or GP-based pharmacist can incorporate pulse palpation into standard consultations or targeted services. For screening, a medical-quality single-lead ECG trace is preferred to pulse-taking or pulse-based devices such as photoplethysmography and blood pressure oscillometry.

Detection of an irregular pulse should be followed by a diagnostic ECG or ECG rhythm strip using a handheld ECG to

confirm the diagnosis of AF. Given the episodic nature of AF, innovative wearable 'rhythm monitoring' technology is also being explored, although uncertainty remains about its diagnostic accuracy, the clinical significance of short asymptomatic bursts of AF and its feasibility in older people and overall cost-effectiveness.[29] However, any method that might help AF detection in older people should be considered as an option, particularly when routine access to health services is restricted, such as in regional and rural areas and for patients with reduced mobility.

A diagnostic work up should assess serum levels of potassium, sodium, magnesium and calcium. Abnormalities may underly the cardiac arrhythmia or predispose to drug toxicity (e.g. for digoxin).[15]

Recommendation on screening and prevention – screening for silent AF

Opportunistic point-of-care screening in the clinic or community should be conducted in people aged 65 years or more (GRADE quality of evidence, moderate; strength of recommendation, strong).[15]

Treatment goal: dysrhythmia management

Treating the underlying dysrhythmia in AF by controlling the cardiac rhythm, rate or both is a key goal. Current guidelines recommend a strategy of either rhythm control with classic antiarrhythmic drugs or rate control.[15] Although rhythm control seems inherently preferable, antiarrhythmic drugs reduce the risk of AF recurrence by only 50% and do not reduce stroke risk and mortality more than rate control. Rate control may be preferred in older people when AF is relatively asymptomatic or when restoration or maintenance of normal sinus rhythm may not be possible because of prolonged, irreversible cardiac changes (e.g. atrial enlargement due to long-standing AF).[30] For 'young' old patients experiencing frequent and symptomatic paroxysms of AF, particularly after physical activity, or left ventricular dysfunction, rhythm control is preferred and is advantageous in enabling physical activity for broader health benefits.[15]

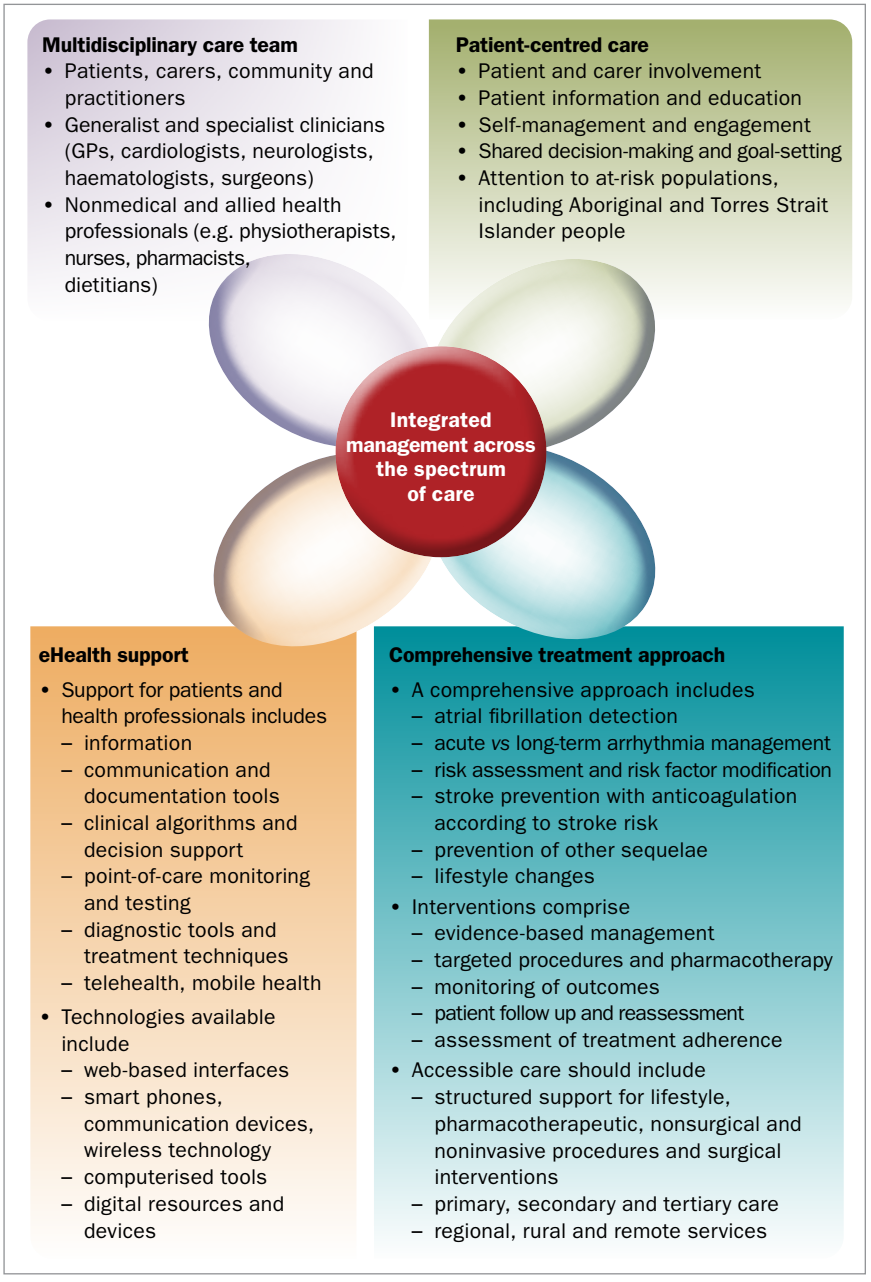

Figure. Integrated care in the management of patients with atrial fibrillation.
Adapted from NHFA CSANZ Atrial Fibrillation Guideline Working Group, et al (2018).[15]

The approach chosen should be individualised, communicated in the treatment plan and monitored by ECG, measurement of ventricular rate and surveillance for emergent cardiomyopathy or overt heart failure. This is important at both the 'macro' level of decision-making (rhythm versus rate control) and the 'micro' level (choice of pharmacological agent).

Recommendation on arrhythmia management – rhythm control versus rate control

A rhythm-control or a rate-control strategy should be selected, documented and

TABLE 1. CONSIDERATIONS FOR THE USE OF RHYTHM AND RATE CONTROL AGENTS IN OLDER PEOPLE WITH ATRIAL FIBRILLATION – RHYTHM CONTROLLERS

Therapeutic class and agent	Guideline recommendations[15]	Practical considerations
Class Ic antiarrhythmic agents, e.g. flecainide (sodium channel blocker)	• Flecainide can be considered in the maintenance of sinus rhythm in patients without left ventricular systolic dysfunction, moderate left ventricular hypertrophy, or coronary artery disease (QoE, high; SoR, strong) • Membrane-active antiarrhythmic agents (e.g. sotalol or flecainide) should not be used in patients managed with a rate-control strategy (QoE, low; SoR, strong) • AV nodal blocking medication is recommended for patients treated with flecainide (QoE, low; SoR, strong)	• Highly effective but should be used in conjunction with an AV nodal block agent to avoid 1:1 conduction of atrial flutter • Should not be used in LV systolic dysfunction, moderate LV hypertrophy or coronary artery disease • Should not be continued in patients transitioning to a rate-control strategy because of potential proarrhythmic side effects • All Class I antiarrhythmic drugs are generally not recommended in older people; use with caution and monitor PR, QRS and QT duration
Class Ia antiarrhythmic agents, e.g. disopyramide, quinidine*	-	• Effective but suggested increased mortality • Not recommended for maintaining sinus rhythm EXCEPT for disopyramide, which may have a role in vagally mediated AF and hypertrophic obstructive cardiomyopathy • All Class I antiarrhythmic drugs are generally not recommended in older people; use with caution and monitor PR, QRS and QT duration
Class III antiarrhythmic agents (potassium channel blockers), e.g. dofetilide*	-	• No overall negative inotropic effect and few noncardiac adverse effects • Causes QT prolongation and torsades de pointes • No effect on mortality • Dose adjustment required in renal impairment

Abbreviations: AF = atrial fibrillation; AV = atrioventricular; LV = left ventricular; QoE = GRADE quality of evidence; SoR = GRADE strength of recommendation.
* Not available in Australia.

communicated for all AF patients, and this strategy should be reviewed regularly (GRADE quality of evidence, low; strength of recommendation, strong).[15]

Choice of medication for dysrhythmia

Currently available pharmacotherapeutic options for dysrhythmia include:

- rhythm controllers (e.g. flecainide)
- rate controllers (e.g. beta-adrenoceptor antagonists, the centrally acting calcium channel blockers diltiazem and verapamil, and digoxin)
- dual-action agents possessing both rhythm and rate control properties (e.g. amiodarone and sotalol).

Specific considerations apply to the use of each option in older patients, particularly those with heart, renal or hepatic disease (Tables 1 to 3).[30] Although the safety of rhythm controllers in older people has been a concern, with some studies suggesting an increase in mortality, more recent studies suggest that a more liberal approach towards prescribing a rhythm control strategy for older patients with AF may be warranted and seems safe.[31] Pharmacological rate control also requires careful consideration and may not always be appropriate. Instead, catheter ablation of the atrioventricular node with permanent pacing should be considered, although the efficacy is lower in 'old' old patients because of AF permanency, frailty and comorbidities such as heart disease, sleep apnoea and obesity.

Treatment goal: stroke risk assessment and stroke prevention

Antiarrhythmic strategies do not obviate the risk of atrial thromboembolism and therefore do not reduce the risk stroke in patients with AF. The risk of stroke remains high in older people as advancing age itself is a core risk factor. Using the guideline-advocated CHA_2DS_2-VA stroke risk prediction score, where a threshold of 1 to 2 points confers a higher risk of stroke and 1 point is assigned for age 65 to 74 years and 2 points for age 75 years or over, then anticoagulation is indicated, or at least should be considered, in almost all older people with AF (Table 4).[15]

With stroke risk following a continuum rather than a dichotomous classification, risk scoring systems such as the CHA_2DS_2-VA score can reliably identify patients who should not receive anticoagulants because of a low risk of thromboembolism. They can also identify modifiable risk factors for management, although even well

TABLE 2. CONSIDERATIONS FOR THE USE OF RHYTHM AND RATE CONTROL AGENTS IN OLDER PEOPLE WITH ATRIAL FIBRILLATION – RATE CONTROLLERS

Therapeutic class and agent	Guideline recommendations[15]	Practical considerations
Selective beta-adrenoceptor antagonists (beta-blockers), e.g. metoprolol, atenolol, bisoprolol (excluding sotalol, which is a dual rhythm and rate controller [see Table 3])	• Beta adrenoceptor antagonists or non-dihydropyridine calcium channel antagonists should be the first-line agents for long-term control of the ventricular rate (QoE, moderate; SoR, strong)	• Can be used alone or in combination with centrally acting calcium channel blockers • Adverse effects include extreme slowing of AV conduction, hypotension, reduced exercise tolerance and acute worsening of heart failure; should not be used in LV systolic dysfunction because of negative inotropic effect • Agents with low lipophilicity (atenolol, nadolol) have fewer central nervous system side effects but should be avoided in patients with significant renal impairment • Agents with longer half-lives and controlled-release formulations (metoprolol, bisoprolol) enable once-daily dosing to support adherence (and are relatively safe in heart failure) • Possibly lower risk of AF recurrence after cardioversion but less effective than classic antiarrhythmic agents in maintaining sinus rhythm (therefore not indicated for rhythm control)
Beta- and alpha-adrenoceptor antagonists (beta- and alpha-blockers), e.g. carvedilol	-	• Less potent beta-adrenergic blocker than others and therefore may have less adverse effects related to beta blockade • Particularly useful for patients with coexisting hypertension or angina
Centrally acting calcium channel blockers (non-dihydropyridines), e.g. diltiazem, verapamil	• Calcium channel antagonists should be avoided in patients with left ventricular systolic dysfunction (ejection fraction <40%) (QoE, low; SoR, strong)	• Can be used alone or in combination with beta-adrenergic blockers (combination therapy may cause severe bradycardia or severe prolongation of AV conduction including different degrees of AV block) • Should not be used in patients with LV systolic dysfunction because of negative inotropic effects • Verapamil increases serum digoxin levels; use combination with caution • Verapamil reduces gut motility and causes constipation more than other calcium channel blockers • Diltiazem may induce oedema
Class V antiarrhythmic agents (cardiac glycosides), e.g. digoxin	• Digoxin can be considered for control of the ventricular rate in patients with suboptimal rate control on, or with contraindications to, first-line agents (QoE, low; SoR, weak) • When digoxin is used, serum concentration should be monitored, with the goal of maintaining levels of <1.2 ng/mL (QoE, moderate; SoR, strong)	• Useful as second-line agent, particularly in combination with beta-blockers or calcium antagonists or when the latter agents are contraindicated • Most likely to benefit older patients who are not physically active or are immobile or disabled • Avoid using alone due to slow onset of action and weak long-term rate control (particularly during exertion) • Risk of death related to serum digoxin concentration and highest in patients with concentrations ≥1.2 ng/mL

Abbreviations: AF = atrial fibrillation; AV = atrioventricular; LV = left ventricular; QoE = GRADE quality of evidence; SoR = GRADE strength of recommendation.

controlled risk factors still contribute to the overall risk of stroke.

The failure to assess and recognise the high risk of stroke in older people with AF, while overestimating any potential risk of treatment-related bleeding has resulted in continued underutilisation of prophylactic anticoagulants, leaving patients susceptible to devastating AF complications.[32-34] Cautious prescribing has been underpinned by fears of bleeding after decades of reliance on the pharmacologically complex and practically challenging vitamin K antagonist, warfarin. There are specific concerns about iatrogenic intracranial haemorrhage and life-threatening major bleeds in older people in whom frailty, falls risk and multimorbidities complicate decision-making.[32,35] However, although studies have shown that frail older patients with AF are significantly less likely to receive an

TABLE 3. CONSIDERATIONS FOR THE USE OF RHYTHM AND RATE CONTROL AGENTS IN OLDER PEOPLE WITH ATRIAL FIBRILLATION – DUAL ACTION RHYTHM AND RATE CONTROLLERS

Therapeutic class and agent	Guideline recommendations[15]	Practical considerations
Class III antiarrhythmic drugs (potassium channel blockers), e.g. amiodarone, dronedarone*	• Amiodarone can be considered for maintenance of sinus rhythm as a second-line agent or as a first-line agent in patients with LV systolic dysfunction, moderate LV hypertrophy or coronary artery disease (QoE, high; SoR, strong) • Amiodarone should not be administered as a first-line agent for chronic rate control, given its toxicity profile (QoE, low; SoR, strong)	• Rhythm control: effective agent possessing class III as well as class I, II and IV antiarrhythmic actions • Rate control: considered a last-line option for chronic rate control given long-term side-effect and toxicity profile • Less frequent side effects in terms of proarrhythmia, bradycardia or hypotension • Amiodarone contains iodine moiety; may cause thyroid dysfunction (hypo- or hyperthyroidism) • May be considered in older patients refractory to other agents • Dronedarone (noniodinated analogue of amiodarone) is generally safer than amiodarone but less effective; it may increase risk of cardiovascular events in patients 75 years and over with hypertension and diabetes
Class III antiarrhythmic agents (methane-sulfonanilide beta-blockers), e.g. sotalol	• Sotalol may be considered for maintenance of sinus rhythm but requires close monitoring of QT interval (QoE, high; SoR, strong) • Membrane-active antiarrhythmic agents (e.g. sotalol or flecainide) should not be used in patients managed with a rate-control strategy (QoE, low; SoR, strong) • Beta-adrenoceptor antagonists may be considered for the maintenance of sinus rhythm (QoE, moderate; SoR, weak)	• Modest efficacy in maintaining sinus rhythm • Requires close monitoring of QT interval, particularly in older people, women and people with impaired renal function • Avoid in structural heart disease (LV dysfunction, LV hypertrophy, coronary artery disease) • Should not be used in patients starting (or transitioned to) a rate-control strategy because of potential proarrhythmic side effects (e.g. torsades de pointes)

Abbreviations: AF = atrial fibrillation; AV = atrioventricular; LV = left ventricular; QoE = GRADE quality of evidence; SoR = GRADE strength of recommendation.
* Not available in Australia.

anticoagulant, they have also shown that these same patients are more vulnerable to adverse clinical outcomes (embolic stroke, higher mortality), with or without therapy.[36,37] Therefore, clinical guidelines reinforce that old age, frailty and falls risk per se are not absolute contraindications for anticoagulation in AF.[38] Nevertheless, Australian GPs have also expressed concern about medication safety and its likely impact on patient adherence as a major determinant in decision-making.[39]

Recommendation on stroke prevention – anticoagulation

Oral anticoagulation therapy to prevent stroke and systemic embolism is recommended in patients with nonvalvular AF whose CA_2DS_2-VA score is 2 or more, unless there are contraindications to anticoagulation (GRADE quality of evidence, high; strength of recommendation, strong).[15]

Recommendation on stroke prevention – prediction and minimisation of bleeding risk

Reversible bleeding factors should be identified and corrected in AF patients for whom anticoagulation is indicated (GRADE quality of evidence, low; strength of recommendation, strong).[15]

Choice of anticoagulant

The direct-acting oral anticoagulants (DOACs), also known as non-vitamin K antagonist oral anticoagulants (NOACs), have expanded the treatment armamentarium. They include dabigatran, rivaroxaban and apixaban. DOACs offer more pharmacodynamically and pharmacokinetically predictable treatment, without the need for routine monitoring of coagulation parameters, and with relatively lower potential for interactions with drugs, herbs and food, overcoming previously cited concerns.

Importantly, in patients aged 75 years and over, DOACs are as effective as warfarin for stroke prevention and in some cases superior, with a better safety profile overall, including lower rates of intracranial haemorrhage.[40] Limited evidence also suggests that DOACs might be superior in preventing cognitive impairment, which confers additional advantages in avoiding dementia-related treatment nonadherence.[38] DOACs are therefore recommended as first-line agents for stroke prevention in AF.[15]

Recommendation on oral anticoagulation

When oral anticoagulation is initiated in a patient with nonvalvular AF, a DOAC – apixaban, dabigatran or rivaroxaban – is recommended in preference to warfarin (GRADE quality of evidence, moderate; strength of recommendation, strong).[15]

TABLE 4. MODIFIABILITY OF CHA_2DS_2-VA RISK FACTORS[15]

CHA_2DS_2-VA risk factor		Score assigned	Modifiability*
C	Congestive heart failure	1	Nonmodifiable; congestive heart failure is difficult to reverse in most cases, although optimal management can delay progression and thereby avoid exacerbating AF and reduce accompanying morbidity
H	Hypertension	1	Modifiable to at least some extent in most patients through pharmacological and nonpharmacological management
A	Age ≥75 years	2	Nonmodifiable; stroke risk inherently increases with advancing age
D	Diabetes	1	Most patients with diabetes have type 2 diabetes, which may be modifiable through optimal pharmacological and nonpharmacological management
S	Previous stroke or TIA (or history of systemic thromboembolism)	2	Nonmodifiable; optimal AF management aims to prevent recurrence of thromboembolic events
V	Vascular disease present	1	Nonmodifiable; history of previous heart attack and existing peripheral artery disease cannot be reversed but optimal management can avoid exacerbating AF and reduce accompanying morbidity
A	Age 65 to 74 years	1	Nonmodifiable; stroke risk inherently increases with advancing age

Abbreviations: AF = atrial fibrillation; TIA = transient ischaemic attack.
* Indicates where optimal management of a risk factor may help reduce the risk of AF-related stroke, although it may not fully obviate the risk.

Other considerations regarding anticoagulants

Other considerations regarding the use of DOACs in older people are shown in Table 5. They include:

- dosage adjustment by age (e.g. dabigatran, apixaban) and renal impairment (more so with dabigatran, less so with rivaroxaban and apixaban)
- contraindications in patients with severe liver impairment (e.g. apixaban and rivaroxaban)
- limited access to specific antidotes for treating DOAC-related overanticoagulation
- the need for twice daily dosing (dabigatran and apixaban), which may reduce adherence, especially in older patients taking many medications.

Further, the DOACs dabigatran and rivaroxaban are not as well tolerated as warfarin in patients with gastrointestinal disease.

In summary, the DOACs are not devoid of risk.[41] Further, knowledge gaps exist regarding optimal dosing in very old patients, especially those with mild-to-moderate renal failure or very low or very high body mass index, and those concurrently taking medications predisposing to metabolic drug interactions (all DOACs are eliminated by either CYP metabolic enzymes or permeability glycoprotein transporters).[38]

In practice, optimal patient-centred, individualised anticoagulation decisions in older people require comprehensive assessment, meaningful engagement, integration into existing systems and processes, and possibly overcoming health professional and patient misperceptions about treatment options.[33,42-44] An integrated, multidisciplinary care approach can help overcome some of these challenges to individualised, risk-based decision-making (Figure).[32,41]

Drawing on multidisciplinary expertise can facilitate:

- full assessment of the patient's AF-related stroke risk to ascertain the benefit of anticoagulation in the individual relative to treatment risks
- rigorous assessment of the potential for bleeding, identifying and addressing any modifiable risk factors (e.g. under lying conditions, drug interactions)
- thorough review of the patient's medical history (comorbidities, baseline kidney function, cognitive status, mobility and falls risk, nutritional status and life expectancy)[40] and medication history (drug regimen, polypharmacy and medication adherence) to identify potential treatment contraindications, drug interactions and adverse events and any need for dosage adjustment
- careful consideration of the pharmacological properties of all available anticoagulant options against the individual patient's characteristics
- ongoing review of the patient's predicted treatment risk versus benefit profile, taking into account changing risks and treatment goals over time as the patient ages from 'young' old to 'old' old, as well as the occurrence of any strokes and bleeds and coagulation parameters
- identification of alternative approaches, such as percutaneous left atrial appendage closure in older patients with contraindications to oral anticoagulants.[42]

TABLE 5. PHARMACOLOGICAL PROPERTIES OF DIRECT ORAL ANTICOAGULANTS (DOACS) AVAILABLE IN AUSTRALIA*

Feature	Dabigatran	Rivaroxaban	Apixaban
Pharmaceutics			
Route of administration	Oral, swallow whole with or without food	Oral	Oral, swallow whole with or without food
Formulation	• 75, 110 and 150 mg capsules • Keep in original packaging, do not transfer capsule to a dose administration aid	• 10, 15 and 20 mg tablets • Can be used in dose administration aids	• 2.5 and 5 mg tablets • Can be used in dose administration aids
Bioavailability	Low (6.5%)	High (80 to 90%)	Moderate (50%)
Pharmacodynamics			
Therapeutic class	Direct thrombin inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
Pro-drug	Yes (dabigatran etexilate); pro-drug is activated via intestinal and hepatic esterases	No	No
Pharmacokinetics			
Absorption	Slight delay with food	Absorption increases with food; doses over 10 mg must be taken with food	Unaffected by food
Distribution: volume	60 to 70 L	50 L	21 L
Distribution: protein binding	Low (35%)	High (90%)	High (90%)
Metabolism: hepatobiliary	Low (20%), no hepatic metabolism by P450 isoenzymes, including CYP3A4	Moderate to high (69%), mostly via CYP3A4, CYP2J2	Moderate to high (75%), mostly via CYP3A4, CYP3A5
Excretion: renal	High (80 to 90%)	Moderate (65%) (1/3 of active drug)	Limited (25%)
Half-life (healthy adults)	12 to 17 hours	5 to 9 hours	8 to 12 hours
Drug interaction substrates	P-glycoprotein	CYP3A4, P-glycoprotein	CYP3A4, P-glycoprotein
Dosing recommendation in AF	Twice daily	Once daily	Twice daily
Standard dose	150 mg twice daily	20 mg once daily	5 mg twice daily
Adjustment by age	>74 years: 110 mg twice daily	None	>79 years plus another risk feature (see footnote): 2.5 mg twice daily†
Adjustment by renal function	• CrCl 30 to 50 mL/min: 110 mg twice daily • CrCl <30 mL/min: avoid	• CrCl 30 to 49 mL/min: 15 mg once daily • CrCl 15 to 29 mL/min: 15 mg once daily (use with caution) • CrCl <15 mL/min: avoid	• Serum creatinine level >132 mcmol/L plus another risk feature (see footnote): 2.5 mg twice daily† • CrCl <25 mL/min: avoid
Adjustment by hepatic function	Avoid in hepatic impairment expected to have any impact on survival	Avoid in moderate to severe hepatic impairment (Child-Pugh classes B and C)	Avoid in severe hepatic impairment (Child-Pugh class C)
Adjustment by body weight	Not required	Not required	<61 kg plus another risk feature (see footnote): 2.5 mg twice daily†
Monitoring of coagulation	• Not required routinely • Assays include ECT, dTT (aPTT), direct thrombin inhibitor assay	• Not required routinely • Modified anti-Xa assay	• Not required routinely • Modified anti-Xa assay
Antidote or reversal agent	• Idarucizumab (monoclonal antibody fragment) • Removed by dialysis	• Andexanet alfa (recombinant coagulation factor Xa) • Not removed by dialysis	• Not removed by dialysis

Abbreviations: AF = atrial fibrillation; aPTT = activated partial thromboplastin time; CrCl = creatinine clearance; dTT = diluted thrombin time; ECT = ecarin clotting time.
* All three DOACs are PBS Authority subsidised in Australia.
† For apixaban, a dose of 2.5 mg twice daily is recommended in patients with at least two of the following characteristics: age >79 years; body weight <61 kg; serum creatinine level >132 mcmol/L.

Recommendations on integrated management

An integrated care approach is recommended; such an approach aims to provide patient-centred comprehensive treatment delivered by a multidisciplinary team (GRADE quality of evidence, high; strength of recommendation, strong).[15]

Targeted patient education is recommended throughout the continuum of AF management (GRADE quality of evidence, high; strength of recommendation, strong).[15]

Shared decision-making should consider patients' beliefs, values and preferences, with a goal of empowering patients to undertake self-management (GRADE quality of evidence, moderate; strength of recommendation, strong).[15]

Treatment goals should be developed in partnership with patients, and communicated with all members of the multidisciplinary team (GRADE quality of evidence, low; strength of recommendation, strong).[15]

eHealth tools and resources should be used by patients and health professionals, to support the integrated management of AF (GRADE quality of evidence, high; strength of recommendation, strong).[15]

All patients prescribed pharmacotherapy for the management of AF, including core rhythm control and anticoagulation therapies, should have their treatment adherence and persistence regularly monitored and supported using accessible and patient-centred strategies (GRADE quality of evidence, low; strength of recommendation, strong).[15]

Treatment goal: medication management to support therapeutic strategies

Initiating treatment for AF significantly increases the medication burden for patients. In addition, the risk of medication misadventure is heightened by the trilogy of old age, use of high-risk medications (antithrombotics and antiarrhythmics) and polypharmacy.[45] Polypharmacy (regularly taking five or more medicines) and hyperpolypharmacy (10 or more medicines[46]) particularly affect the oldest patients with AF, not only because of multiple comorbidities but also because of the polypharmacy required for AF alone.

Both antiarrhythmic and anticoagulant strategies comprise agents that:

- although specifically indicated for AF, are also regarded as potentially inappropriate medications (e.g. anticoagulants and digoxin as per the Beers Criteria Medication List)
- may interact with each other (e.g. amiodarone and warfarin, digoxin and warfarin, amiodarone and DOACs, calcium channel blockers and DOACs).[47]

Polypharmacy is also associated with an increase in cardiovascular death and hospitalisation, reduced quality of life and poorer physical function in older people with AF.[48] For this reason, the decision to initiate pharmacotherapy for AF must consider not only the risks of stroke, bleeding and medication misadventure but also increasing polypharmacy. Further, older patients may have physiological changes that affect drug pharmacokinetics and pharmacodynamics, homeostasis and risk of falls and bleeding, alongside increasing stroke risk.

Six- to 12-monthly re-evaluation of very old patients, including risk-benefit profile, is imperative because of their likely frequent and acute changes in clinical status.[38] Treatment adjustments may reduce patient adherence, especially if cognition is declining. Importantly, changes in one medication, whether deliberate or inadvertent through nonadherence, may significantly affect other concurrently used medications. An integrated care approach should thus support not only decision-making and monitoring of clinical outcomes but also medication management, including assessment of adherence and regular comprehensive medication review, such as a pharmacist-led home medicines review or MedsCheck.[49]

Conclusion

Optimising the management of AF in older people has significant clinical benefits, including reducing symptoms, improving functional capacity, reducing cognitive decline, preventing stroke, reducing mortality and improving quality of life. However, management decisions are complex, both in terms of treatment options, as there are no 'risk-free' agents, and in terms of the characteristics of the target population, with many potential medical, cognitive, functional, social and iatrogenic factors. There are risks and challenges along the disease management pathway, including screening for AF, dysrhythmia management and stroke prevention, compounded by concerns around medication misadventure. An integrated care approach utilising multidisciplinary expertise can support GPs in facilitating comprehensive robust risk assessments, patient-centred individualised treatment plans and therapeutic processes. Importantly, regular re-evaluation of risks and review of treatment plans as patients age, including documentation and communication of these to both patients and the broader healthcare team, will ensure that treatment goals and strategies for AF align with patients' changing needs. MT

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS. None.

Atrial fibrillation

Management of older patients

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