



An update on antithrombotic medicines: What does primary care need to know?



Key practice points

- Patients with atrial fibrillation who have a very low risk of stroke are unlikely to benefit from antithrombotic treatment
- Aspirin monotherapy should not be prescribed solely for stroke prevention; anticoagulation is the preferred treatment
- On balance dabigatran appears at least as effective and may be safer than warfarin for the prevention of ischaemic stroke and systemic embolism
- Dabigatran should NOT be prescribed to patients with valvular heart disease

The number of antithrombotic medicines is increasing, as is the challenge for general practitioners in advising patients about treatment options and managing patients when antithrombotic medicines are initiated in secondary care, e.g. following a percutaneous coronary intervention.

Antithrombotic treatment recommendations for patients with non-valvular atrial fibrillation depend on the patient's risk of ischaemic stroke which can vary by 20-fold depending on their age and clinical features.¹

Managing stroke risk in patients with non-valvular atrial fibrillation

The individual stroke risk for patients with non-valvular atrial fibrillation needs to be assessed to determine if they are likely to benefit from anticoagulant treatment.¹

Previous guidance on the management of stroke risk has changed

Previously, all patients with atrial fibrillation were offered antithrombotic treatment and those with a CHA₂DS₂-VASc score of 0 (see: "Atrial fibrillation management tools: CHA₂DS₂-VASc and HAS-BLED") were offered aspirin in preference to an anticoagulant. It is now recommended that these patients **should not** be treated with either an anticoagulant or an antiplatelet at this time.² Furthermore, aspirin monotherapy should generally not be prescribed for the purpose of stroke prevention in any patients with atrial fibrillation: anticoagulation is preferred.³

Guidance now recommends that anticoagulation be considered for all patients who have a CHA₂DS₂-VASc score ≥ 1 .⁴ Where it is uncertain if a patient will benefit from anticoagulant treatment discussion with a cardiologist or neurologist may be beneficial.

Always consider the risk of bleeding before discussing anticoagulation treatment with a patient. This risk, however, should not be overstated. Risk factors for bleeding in patients taking anticoagulant treatment include:⁴

- Increasing age
- Uncontrolled hypertension
- History of myocardial infarction, ischaemic heart disease or cerebrovascular disease
- Anaemia
- A history of bleeding
- The use of other medicines that increase bleeding risk, e.g. aspirin or other antiplatelet medicines and non-steroidal anti-inflammatory drugs (NSAIDs)

There are a number of tools available that can be used to assess the risk of bleeding in patients with atrial fibrillation. The HAS-BLED tool is used to identify modifiable risk factors that can be managed in patients undergoing anticoagulation treatment.²

Warfarin or dabigatran to prevent thromboembolism?

If anticoagulant treatment is appropriate the decision needs to be made whether warfarin or dabigatran is the preferred treatment option (Table 1). Patient preference plays a significant role in this decision.

On balance the evidence suggests that dabigatran, dosed appropriately, is at least as effective and may be safer than warfarin for the prevention of ischaemic stroke and systemic embolism.

Dabigatran should NOT be prescribed to patients with valvular heart disease: patients with mechanical heart valves who take dabigatran are at an increased risk of bleeding or experiencing a thromboembolic event compared to what their risk would have been if they had been prescribed warfarin.⁸

Atrial fibrillation management tools: CHA₂DS₂-VASc and HAS-BLED

The CHA₂DS₂-VASc stroke risk assessment tool uses risk factors to calculate a score out of nine. This tool is helpful for identifying patients at very low risk of stroke who may not benefit from treatment with an anticoagulant.² Figure 1 shows the annual stroke risk for patients with a CHA₂DS₂-VASc score of 0 – 6.

Clinical feature	Points
Congestive heart failure	1
Hypertension	1
Age	1 or 2
■ 65 – 74 years	1
■ ≥ 75 years	2
Diabetes mellitus	1
Stroke or transient ischaemic attack	2
Vascular disease, e.g. peripheral artery disease, myocardial infarction, aortic plaque	1
Female sex	1
Total out of 9 =	

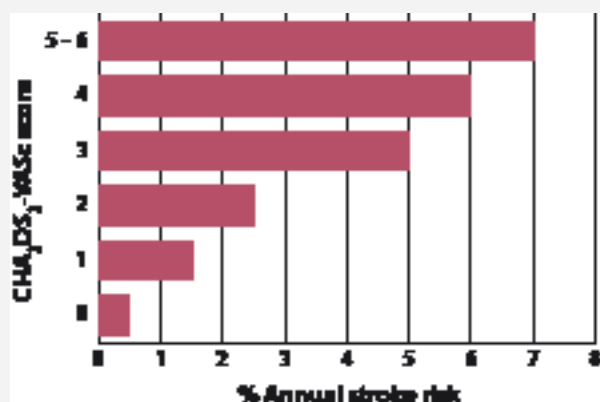


Figure 1: Annual stroke risk for patients with a CHA₂DS₂-VASc of 0 – 6

The HAS-BLED tool is used to identify modifiable risk factors in patients undergoing anticoagulation treatment.² HAS-BLED may also be useful in balancing the risks versus benefits of anticoagulation treatment in patients with atrial fibrillation who have a CHA₂DS₂-VASc score of 1.² HAS-BLED should not, however, be used to determine whether a patient should be offered anticoagulation treatment as this decision should be based on stroke risk.² A HAS-BLED score > 2 is associated with a clinically significant risk of major bleeding.¹

Risk factor	Score
Hypertension (systolic blood pressure > 160 mmHg)	1
Abnormal renal and liver function	1 point each
Stroke (past history)	1
Bleeding (previous history of bleeding or predisposition to bleeding)	1
Labile INRs (unstable, high or insufficient time with therapeutic range)	1
Elderly (aged over 65 years)	1
Drugs or alcohol (including concomitant use of aspirin, other antiplatelet medicines and NSAIDs)	1 point each
Total out of 9 =	



Table 1: The advantages and disadvantages of dabigatran, compared with warfarin, for the treatment of patients with non-valvular atrial fibrillation

The advantages of dabigatran	The disadvantages of dabigatran
<ul style="list-style-type: none"> ■ Superior stroke prevention with dabigatran 150 mg, twice daily ■ Testing and dose adjustments are not currently required ■ Onset of anticoagulation is rapid (two to three hours) compared with 48 – 72 hours with warfarin⁵ ■ Does not accumulate in the liver and safer in patients with hepatic dysfunction⁶ ■ Fewer interactions with other medicines and foods ■ A reduced risk of intracranial haemorrhage with dabigatran 110 mg, twice daily 	<ul style="list-style-type: none"> ■ An increased incidence of gastrointestinal adverse effects, e.g. dyspepsia ■ Twice daily dosing required ■ Caution required in patients with progressive chronic kidney disease (CKD) ■ A small absolute increase in risk (0.27%) of acute coronary syndrome⁷


Ticagrelor is superior to clopidogrel in patients with acute coronary syndromes

It is increasingly likely that patients who have been diagnosed with an acute coronary syndrome will receive long-term treatment with ticagrelor, twice daily, in preference to clopidogrel, once daily; both are used in combination with aspirin, i.e. dual antiplatelet treatment. The choice of anticoagulant is usually made in hospital following diagnosis of an acute coronary syndrome and treatment is then continued in the community for twelve months.

Unlike clopidogrel, ticagrelor is not a prodrug and therefore does not need to be processed by an enzyme (CYP2C19) to be activated. This explains why ticagrelor is reported to produce faster, greater and more consistent inhibition of platelet reactivity compared with clopidogrel.⁹ Due to ethnic differences in the prevalence of genetic polymorphisms in the CYP2C19 enzyme that metabolises clopidogrel it has been suggested that Māori and Pacific patients should be preferentially treated with ticagrelor over clopidogrel.¹⁰

How is ticagrelor initiated ?

Treatment with ticagrelor begins with 180 mg as a loading dose, then 90 mg, twice daily, for up to 12 months.⁵ Ticagrelor should be taken in combination with low-dose aspirin.⁵ The most frequent adverse effect is a transient dyspnoea that does not appear to be caused by bronchospasm; ticagrelor should be used cautiously in patients with asthma or COPD.⁵ Ticagrelor should be discontinued five days before elective surgery.⁵ It is recommended that renal function be tested within one month of initiation.⁵

 For further information, see: "An update on antithrombotic medicines – What does primary care need to know?" BPJ 67 (Apr, 2015).

References

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