Improving anticoagulant prescribing for AF

Duncan Petty PhD, MRPharmS, IP and Matthew Fay FRCP

KEY POINTS
- OACs and NOACs are effective in preventing strokes in AF
- there is concern about underprescribing – 40 per cent of patients with AF and eligible for OACs do not receive treatment
- barriers to OAC use include increasing patient age, bleeding risk, falls risk, co-morbidities and poor adherence
- QOF provides limited incentive to increase OAC use but it allows aspirin at lower levels of risk
- risk stratification tools include CHADS2 and CHA2DS2-VASc – the latter includes additional risk factors and only patients with a CHA2DS2-VASc score of 0 can be considered truly low risk
- for most patients with no absolute contraindications the benefits of OACs outweigh the risks
- all anticoagulants can cause bleeds but severe bleeds with well-controlled warfarin or NOACs are relatively rare
- minor bleeding is relatively common but not necessarily a reason to permanently discontinue treatment
- most patients should be offered warfarin first line

Anticoagulants are effective at preventing strokes in AF, but there is concern that GPs are not adequately prescribing them. Here, the authors discuss the barriers to prescribing anticoagulants and how to increase their use.

Atrial fibrillation (AF) is a leading preventable cause of stroke.¹ People with nonvalvular AF are five times more likely than those without to have a stroke.² AF strokes often result in long hospital stays and a greater chance of being discharged into a long-term care facility.³ Oral anticoagulants (OACs) and novel oral anticoagulants (NOACs) are effective in preventing strokes in AF.⁴,⁵ However, there is concern that clinicians often do not adequately prescribe OAC treatment to reduce stroke risk. In the UK 40 per cent of patients with AF and eligible for OACs do not receive treatment.⁶ Of those with higher risks (CHADS2 ≥2 or more – see below) only 53 per cent were prescribed OACs.⁷

Barriers to prescribing OACs
The decision to use anticoagulant drugs in patients with AF involves a consideration of the potential benefits vs the risks, inconveniences and costs.⁷

There are numerous barriers to prescribing OACs. A recent systematic review identified: increasing patient age, bleeding risk (or perceived bleeding risk), falls risk, co-morbidities (eg chronic alcoholism or cognitive impairment) and poor adherence as barriers to prescribing OACs.⁸

Advanced age, especially over 80 years, is the most common reason for withholding OACs,⁸,⁹ but increasing age is also the biggest stroke risk in non-valvular AF.¹⁰,¹¹

Overestimation of bleeding risk is a key barrier to OAC prescribing. For example, older people are often denied OACs most commonly because of perceived risks of bleeding following previous bleeds and from falls, despite both stroke risk and OAC benefits increasing with age. In one cohort study of a PCT population, 51 per cent of AF patients had a high stroke risk (CHADS2 ≥2 or more – see below) but only 27 per cent of the untreated population had absolute contraindications to an OAC.¹²

Prescribers can have concerns about older people’s adherence to treatment and monitoring regimens; however, whether these concerns are real or perceived and the degree to which patients are involved in subsequent decision-making is uncertain.¹³,¹⁴,¹⁵

Clinicians seeing higher numbers of people with AF seem more able to discuss the risks and benefits of intervention with OACs.¹⁶ Longer duration as a registered doctor is associated with poorer ability to estimate stroke risk.¹⁷

Healthcare systems also create barriers to the prescribing of OACs. Little has been published on these barriers but lack of experience and training in managing OAC therapy is a main barrier cited.¹⁸ Others may include lack of facilities for INR
monitoring, difficulties in attending INR monitoring clinics and lack of clarity about responsibility for initiating OAC treatments. Patients need to be given the opportunity to consider the risks and benefits and the different options available. The NHS has produced a decision support tool to help patients make an informed decision on whether they wish to take an OAC for stroke prevention in AF.19

Increasing OAC use
The Quality and Outcomes Framework (QOF) has provided limited incentive to increase OAC prescribing but it allows aspirin at lower levels of risk, thereby acting to deny effective treatments to patients.

Knowledge is necessary to change behaviour but on its own is often insufficient. Prescribers need to have knowledge on what are true contraindications to OAC and skills in the use of tools to assess stroke risk. They also need to know how to minimise bleed risk from OACs and how to help patients who are ambivalent about treatment to come to an informed decision.

Computerised decision support software is often not sophisticated enough to guide prescribers to the best decision for an individual patient. General practice software systems such as SystmOne provide CHADS\textsubscript{2} (see below) scores for individual patients, indicate if a patient has previously declined treatment or if they have a ‘contraindication’ and suggest treatment; but reasons for treatment being declined or contraindicated are subjective and only as good as the skills and knowledge of the person who made the decision.

The GRASP-AF (Guidance on Risk Assessment and Stroke Prevention in Atrial Fibrillation) tool is useful for auditing current prescribing for stroke prevention in AF.20 It can provide benchmarking data and helps identify suboptimally treated individuals. It does not remove the need for somebody to act on the data produced.

To prevent AF-related stroke it is not only important to minimise the risk of cardioembolic stroke through anticoagulation, but also to reduce the risk of intracerebral haemorrhage induced by anticoagulation. This can be facilitated through risk assessment of stroke and bleeding risk.

Risk scoring
The decision to prescribe aspirin, OAC or nothing for patients with AF is guided by risk stratification tools. Current, but outdated, guidance from NICE simply categorises risk of stroke into low, moderate or high.21 Aspirin is generally regarded as ineffective in prevention strokes from AF.22,23 Guidance by the Royal College of Physicians of Edinburgh recommends not to use aspirin for stroke prevention in patients with AF.24

The CHADS\textsubscript{2} risk tool is widely used in primary care. CHADS\textsubscript{2} assigns one point each for congestive heart failure (C), high blood pressure (H), age 75 or older (A) and diabetes (D), and two points for a previous stroke or transient ischaemic attack (S\textsubscript{2}).10 The total score gives an individual patient’s annualised stroke risk.

One of the deficiencies in all scoring systems is that there is a step progression of risk, where in reality risk is a continuum.
This is seen in the CHADS2 tool where a significant number of patients with a score of 0 or 1 can go on to have a stroke. In the Euro Heart Survey on AF a large proportion of patients (60 per cent) had an ‘intermediate’ risk (CHADS2 = 1) and were therefore offered either warfarin or aspirin according to current (outdated) guidelines. It is likely that many patients in this category have previously been offered aspirin on the assumption that it is as effective as and safer than warfarin, and because it is easier to monitor.

The CHA2DS2-VASc Scoring System (see Table 1) includes additional stroke risk factors not considered in the CHADS2 score. Those with a risk score of 2 or greater are clearly at significant risk of AF-related stroke and therefore should be offered an OAC if there are no absolute contraindications.

The annual adjusted risk of stroke using the CHA2DS2-VASc scoring system is shown in Table 2. Warfarin gives a mean 64 per cent relative risk reduction across all levels of risk.

With CHA2DS2-VASc no patients classified as ‘low risk’ had a thromboembolic event (thus identifying ‘truly low risk’ patients). In contrast, 1.4 per cent of those categorised as ‘low risk’ with CHADS2 had a thromboembolic event.

In practice, patients with a CHADS2 score of 0 or 1 could have an additional risk score applied using CHA2DS2-VASc. Only patients with a CHA2DS2-VASc score of 0 should be considered ‘truly low risk’. They should not be offered any stroke prevention treatment.

It should be noted that a failing of the common risk scoring tools is that all risk factors other than age over 75 and previous stroke are rated the same at 1 point. For instance, hypertension brings a relative adjusted risk of 2.0 per cent (95% CI 1.6–2.5) and increasing age 1.5 per cent per decade (95% CI 1.3–1.7).

**Risk of anticoagulation**

Patients with absolute contraindications to any form of anticoagulation should not be offered treatment. A guide to absolute and relative contraindications can be found on the Atrial Fibrillation Association website. Importantly these also apply to antplatelets. In studies comparing aspirin with warfarin for stroke prevention in AF the percentage of patients experiencing a major extracranial bleed were 2.1 and 2.2 per cent with warfarin and aspirin respectively and 0.85 and 0.41 per cent respectively for intracranial bleeds.

Patients at higher risk of a bleed can be assessed using a tool such as HAS-BLED. Factors such as high blood pressure, taking other GI irritant drugs (such as NSAIDs or SSRIs) and alcohol intake, for example, increase bleed risk but the risks can be reduced by managing these factors.

For most patients with no absolute contraindications the benefits of OACs outweigh the risks. Clinicians should be skilled in explaining the benefits as well as risks in a balanced way and helping patients come to an informed decision about treatment.

AF strokes tend to be more severe than other types of stroke. A quarter are fatal and 80 per cent of people suffering an AF stroke can no longer go on living independently and they will end up in care or needing a carer.

All anticoagulants can cause bleeds, but severe bleeds with well-controlled warfarin or NOACs are relatively rare. In trials of warfarin annual intracerebral bleed rates were between 0.38 and 0.60 per cent per annum. NOACs produce lower rates (0.10–0.50 per cent per annum) against a background incidence of 0.17 per cent on no treatment.

Major bleeds (ie those requiring a healthcare intervention or hospitalisation) occur at a rate of between 3.1 and 3.4 per cent per annum with warfarin and either the same or better with NOACs depending on the drug against a background of 1.4 per cent with no treatment.

Minor bleeding, which includes bruising, nose bleeds, bleeding gums and heavier periods in women, is relatively common but not necessarily a reason to permanently discontinue treatment.

**Identify the patient’s concerns about treatment**

Many patients will have concerns about taking OACs. It is an important role of the

### Table 1. CHA2DS2-VASc scoring system for assessing AF risk; score 2 or more = high risk (20 per cent 10 year per cent per annum) NOACs produce lower rates (0.10–0.50 per cent per annum) against a background incidence of 0.17 per cent on no treatment.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>1 point</td>
</tr>
<tr>
<td>H</td>
<td>1 point</td>
</tr>
<tr>
<td>A2</td>
<td>2 points</td>
</tr>
<tr>
<td>D</td>
<td>1 point</td>
</tr>
<tr>
<td>S2</td>
<td>2 points</td>
</tr>
<tr>
<td>V</td>
<td>1 point</td>
</tr>
<tr>
<td>A</td>
<td>1 point</td>
</tr>
<tr>
<td>Sc</td>
<td>1 point</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Score</th>
<th>Annual risk of a stroke with no treatment</th>
<th>Annual risk of a stroke on warfarin</th>
<th>NNT per annum to prevent a stroke with warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
<td>NA</td>
</tr>
<tr>
<td>1</td>
<td>1.3%</td>
<td>0.8%</td>
<td>192</td>
</tr>
<tr>
<td>2</td>
<td>2.2%</td>
<td>1.3%</td>
<td>114</td>
</tr>
<tr>
<td>3</td>
<td>3.2%</td>
<td>1.9%</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>4.0%</td>
<td>2.4%</td>
<td>63</td>
</tr>
<tr>
<td>5</td>
<td>6.7%</td>
<td>4.0%</td>
<td>37</td>
</tr>
<tr>
<td>6</td>
<td>9.8%</td>
<td>5.9%</td>
<td>26</td>
</tr>
<tr>
<td>7</td>
<td>9.6%</td>
<td>5.8%</td>
<td>26</td>
</tr>
<tr>
<td>8</td>
<td>6.7%</td>
<td>4.0%</td>
<td>37</td>
</tr>
<tr>
<td>9</td>
<td>15.2%</td>
<td>9.1%</td>
<td>16</td>
</tr>
</tbody>
</table>

**Table 2. Annual adjusted stroke risk using CHA2DS2-VASc scoring system showing numbers needed to treat (NNT) with warfarin for one year to prevent a stroke.**
Anticoagulants for AF

Prescriber 19 May 2014

MEDICINES MANAGEMENT

- true allergy to warfarin
- poorly controlled INR on warfarin despite good adherence.
- cannot adhere to blood tests, eg need for NHS transport, busy lifestyle, dementia resulting in difficulty attending or needle phobia.
- requires a monitored dosage system (eg Dosette box) – rivaroxaban or apixaban are options, dabigatran is not stable outside packaging; in this situation administration may still need to be supervised if the patient is forgetful or has cognitive impairment
- food or drug interactions with warfarin that are absent with an NOAC
- requires a monitored dosage system (eg Dosette box) – rivaroxaban or apixaban are options, dabigatran is not stable outside packaging; in this situation administration may still need to be supervised if the patient is forgetful or has cognitive impairment
- cannot adhere to blood tests, eg need for NHS transport, busy lifestyle, dementia resulting in difficulty attending or needle phobia.
- requires a monitored dosage system (eg Dosette box) – rivaroxaban or apixaban are options, dabigatran is not stable outside packaging; in this situation administration may still need to be supervised if the patient is forgetful or has cognitive impairment
- food or drug interactions with warfarin that are absent with an NOAC

Conclusion
Increasing anticoagulant prescribing in AF could have a large impact on reducing strokes. Patients need to be fully involved in decisions about whether to accept or decline treatment and assumptions should not be made about the decisions the patient may make.

The benefits as well as the risks should be explained to patients in a way they can understand, allowing them to come to an informed decision about whether to accept or decline treatment. For those who decline the decision should be revisited annually as risk continues to rise with time.

References

Declaration of interests
Dr Petty has received an honorarium from Bayer for development of DVT guidelines and a research grant; he has also accepted funding from Bristol Myers Squibb to attend a conference. Dr Fay has received honoraria from several pharmaceutical companies.

Dr Petty is lecturer-practitioner at the University of Leeds and director of Prescribing Support Services Ltd, Shipley, and Dr Fay is a GP in Shipley and an executive of the Atrial Fibrillation Association, STARs and Arrhythmia Alliance along with the West Yorkshire Stroke Research Network

Letters
If you have any issues you would like to air with your colleagues or comments on articles published in Prescriber, the Editor would be pleased to receive them and, if appropriate, publish them on our Letters page. Please send your comments to:
The Editor, Prescriber, The Atrium, Southern Gate, Chichester, West Sussex PO19 8SQ, or e-mail to prescriber@wiley.com

Table 3. Examples of when an NOAC might be a preferable choice to warfarin