Introduction

Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia and is associated with increased morbidity and mortality due to stroke and thromboembolism. In patients with AF, strokes are usually more severe, resulting in longer hospital stays, worse disability and considerable healthcare costs. The prevention of stroke therefore is crucial in the management of AF. Stroke risk stratification tools can be used to determine patients at higher risk of stroke, and if no contraindications are present oral anticoagulation (OAC) therapy can be initiated. Despite the strong evidence for the benefit of OAC in stroke prevention in patients with AF, the use of thromboprophylaxis remains inadequate. The key measures to prevent stroke in patients with AF include: adequate stroke risk assessment and thrombo-prophylaxis; prompt initiation of OAC and avoidance of interruptions; earlier detection of AF; and education to overcome the under-usage of OAC in elderly patients.

Newer drugs such as dabigatran, a direct thrombin inhibitor and rivaroxaban, a direct factor Xa inhibitor are anticipated to soon replace warfarin altogether, negating the need for regular dose monitoring and adjustment.}

This review is targeted at clinicians who are exposed to patients with atrial fibrillation, including general practitioners, general physicians and cardiologists. Although this is not a systematic review, information was obtained through literature search engines such as PubMed, from current guidelines on the management of atrial fibrillation and from recent review articles. Examples of search terms used included “atrial fibrillation”, “AF”, “stroke prevention”, “oral anticoagulation”, “oral anticoagulants”, “OAC”, “warfarin”, “barriers to anticoagulation”, “stroke risk assessment”, “bleeding risk assessment”. Prevention of stroke in atrial fibrillation is a vast topic with a wealth of literature. This article does not attempt to evaluate all the evidence in this area, but rather to give an overview of some of the new developments and measures to prevent stroke in patients with AF.
Atrial Fibrillation and Stroke

AF occurs in approximately 1-2% of the general population. The prevalence of AF increases with advancing age and is expected to increase by 2.5-fold over the next fifty years, as the population ages. AF is associated with increased morbidity and mortality as a result of stroke and thromboembolism. Patients with AF are five times more likely to develop a stroke than patients in sinus rhythm, and when stroke occurs it is more likely to be severe. AF related strokes have higher mortality and morbidity, with longer hospital stays and increased disability, as well as considerable healthcare costs. In the United Kingdom AF accounts for almost 1% of total National Health Service expenditure, estimated at £459 million excluding costs of nursing care and hospitalizations where AF is a secondary diagnosis.

Stroke Risk Stratification

Given the adverse implications of stroke, both to the patient and to the healthcare system, the prevention of stroke in AF should therefore be a key component of the management of AF. As the risk of stroke in AF is not homogeneous, all patients diagnosed with AF should undergo a stroke ‘risk assessment’.

The risk of stroke in AF is variable and dependent on multiple risk factors, which are cumulative in adding to the overall stroke risk. Various risk stratification models exist to try and identify patients at higher risk of stroke, namely the CHADS score (see Table 1, C = Congestive heart failure, H = Hypertension, A = Age over 75 years, D = Diabetes, S = Prior Stroke or transient ischaemic attack) and more recently, the CHA\_DS\_2-VASc score which is more inclusive of common stroke risk factors (see Table 2, as per CHADS\_2 plus additionally V = Vascular disease, A = Age 65-75 years, Sc = Sex category female). Patients are given a score which is a total of the individual risk factors and then, could be (perhaps artificially) stratified into low, intermediate or high risk strata.

Guidelines recommend OAC therapy (such as warfarin) or aspirin in patients with an intermediate risk of stroke, and OAC in those with a high risk of stroke. Patients with a low risk of stroke may not need any anticoagulation. The CHADS\_2 scoring system is well known and readily used, as it is simple and easy to remember, and based on the original validation of this scheme, patients with a score of 0 are low risk, 1-2 are intermediate risk and ≥3 are high risk. However there is concern that with CHADS, the risk of stroke is under-estimated as this scheme does not include many common stroke risk factors, and secondly, far too many patients are placed within the “intermediate risk” category whereby ambiguity exists as to whether these patients should receive aspirin or warfarin.

The CHA\_DS\_2-VASc stratification tool includes more risk factors than CHADS\_2 and has been shown to be superior at identifying the “truly low risk” patient and secondly, to minimise stratification to the “intermediate risk” category. In a Danish study of 73,538 patients with non-valvular AF, the rates of thrombo-embolism per 100 person-years in “low risk” patients were found to be 1.67 (95% confidence interval [CI] 1.47-1.89) with CHADS\_2 and 0.78 (0.58-1.04) with CHA\_DS\_2-VASc at 1 year follow up. The study also demonstrated that the risk of thrombo-embolism depended on the specific risk factor, with age ≥75 years and previous thrombo-embolism posing the greatest risk.

The European Society of Cardiology recommends the CHADS\_2 stratification tool as a quick initial screening, and patients with a score ≥2 should be given OAC unless contraindicated. In patients with a score of 0 or 1 a more detailed risk assessment is required by way of the CHA\_DS\_2-VASc score. In patients with a score of 0 (ie a “truly low” risk of stroke) no anticoagulation is preferred. In patients with a CHA\_DS\_2-VASc score of 1, aspirin or OAC is recommended and OAC (whether with well-controlled warfarin or one of the new oral anticoagulant drugs, see later) is preferred.

Oral Anticoagulation Therapy

Traditional oral anticoagulants include vitamin K antagonists such as warfarin or phenindione.
Warfarin requires dose-adjustment according to the international normalized ratio (INR), which should be maintained between 2 and 3. An INR greater than 3 confers a greater risk of bleeding whilst an INR less than 2 confers greater risk of thromboembolism. Extensive studies have demonstrated the benefit of vitamin K antagonists. A meta-analysis showed that adjusted-dose warfarin and antiplatelet agents reduce stroke by 64% [95% CI 49-74] and 22% [95% CI 6-35%], respectively. Dose-adjusted warfarin was found to be more efficacious than antiplatelet therapy with a relative risk reduction of 39%. The disadvantages of using warfarin include the increased bleeding risk, the need for intensive monitoring of INR and the potential drug and food interactions. Studies have shown that patients receiving OAC remain in therapeutic range approximately 60% of the time, and in clinical practice less than 50% of the time. Furthermore a 10% rise in time out of the desired INR range was associated with a significant increased risk of mortality (odds ratio (OR) 1.29, p<0.001), ischaemic stroke (OR 1.10, p=0.006) and other thrombo-embolic events (OR 1.12, p<0.001).

**Bleeding Risk Assessment**

The main concern with OAC is the risk of intracranial haemorrhage which is greatest in patients of advanced age and those with hypertension. In a systematic review, other factors associated with higher risk of bleeding complications include: history of myocardial infarction or ischaemic heart disease, cerebrovascular disease, anaemia or a history of bleeding, and the use of antiplatelet therapy.

The HAS-BLED score (H = Hypertension, A = Abnormal renal/liver function, S = Stroke, B = Bleeding history or predisposition, L = Labile INR, E = Elderly, D = Drug/alcohol concomitantly, see Table 3) is a new and easy-to-use bleeding risk assessment tool that predicts patients at high risk of bleeding. Patients are given a score of 1 for Table 1. CHADS2 Stroke Risk Stratification Tool

<table>
<thead>
<tr>
<th>CHADS2 risk factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥ 75 years</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/transient ischaemic attack</td>
<td>2</td>
</tr>
<tr>
<td>Maximum</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 2. CHA2DS2-VASc Stroke Risk Stratification Tool

<table>
<thead>
<tr>
<th>CHA2DS2-VASc risk factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥ 75 years</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/transient ischaemic attack/thromboembolism</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease (previous myocardial infarction, peripheral arterial disease, aortic plaque)</td>
<td>1</td>
</tr>
<tr>
<td>Age 65-74 years</td>
<td>1</td>
</tr>
<tr>
<td>Sex category (female)</td>
<td>1</td>
</tr>
<tr>
<td>Maximum</td>
<td>9</td>
</tr>
</tbody>
</table>
Each factor present and the total is calculated. Patients with a score of ≥3 are deemed at high risk of bleeding and therefore close monitoring and regular review is required.\(^{11}\)

**Anticoagulation Services**

The standard and availability of anticoagulation services are key in the management of OAC in patients with AF. Well-managed anticoagulation involves strict adherence to the recommended INR ranges, quick identification and response to out-of-range INR levels and a service that is readily used by clinicians.\(^{29}\)

Some studies show that patients with access to anticoagulation services have better anticoagulation control when compared to patients managed in the community.\(^{30, 36}\) In one study they found...

#### Table 3. HAS-BLED Bleeding Risk Tool

<table>
<thead>
<tr>
<th>HAS-BLED risk factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Abnormal liver/renal function (1 point each)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1</td>
</tr>
<tr>
<td>Labile INR</td>
<td>1</td>
</tr>
<tr>
<td>Elderly (age&gt;65 years)</td>
<td>1</td>
</tr>
<tr>
<td>Drugs/alcohol (1 point each)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Maximum</td>
<td>9</td>
</tr>
</tbody>
</table>

Hypertension = systolic blood pressure >160mmHg, Abnormal kidney function = chronic dialysis or renal transplantation, or serum creatinine >200 μmol/L, Abnormal liver function = chronic hepatitis disease (eg cirrhosis) or biochemical evidence of significant hepatic derangement (eg bilirubin > 2 x upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/ alkaline phosphatase > 3 x upper limit normal), Bleeding = previous bleeding history and/or predisposition to bleeding eg bleeding diathesis, anaemia, Labile INR = unstable/high INR or <60% duration within therapeutic window, Drugs/alcohol = concomitant use of drugs eg antiplatelets, non steroidal agents, or alcohol abuse. INR = international normalized ratio. Adapted from ESC guidelines for the management of atrial fibrillation.\(^{11}\)

#### Table 4. Summary of Measures to Prevent Stroke in Atrial Fibrillation

<table>
<thead>
<tr>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detect and diagnose AF earlier possibly with the use of opportunistic screening of elderly patients in primary care</td>
</tr>
<tr>
<td>Utilize risk stratification tools (such as CHADS(_2) and CHA(_2)DS(_2)-VASc) to identify patients at intermediate/high risk of stroke</td>
</tr>
<tr>
<td>Ensure patients at high/intermediate risk are prescribed OAC safely once the bleeding risk has been established</td>
</tr>
<tr>
<td>Encourage physicians and general practitioners to make a decision for OAC based on the stroke and bleeding risk stratification tools</td>
</tr>
<tr>
<td>Once a decision for OAC has been made ensure prompt initiation of treatment and avoidance of interruptions</td>
</tr>
<tr>
<td>Improve provision of anticoagulation services to ensure uptake by clinicians, stricter adherence to recommended INR range and provision to identify and respond quickly to patients with an INR out of range</td>
</tr>
<tr>
<td>Be aware of barriers to anticoagulation and improving awareness as to the increased benefit of anticoagulation in elderly patients</td>
</tr>
<tr>
<td>New OAC agents are available, overcoming some of the disadvantages of warfarin</td>
</tr>
</tbody>
</table>
that patients who self-manage their anticoagulation spend a greater amount of time within the therapeutic INR range compared to those who did not although this was not statistically significant.\textsuperscript{36} In a recent meta-analysis patients who self-test or self-manage (self-adjust dosing) their OAC were found to have a significantly reduced risk of thrombo-embolism (Peto odds ratio [OR] 0.58 [95% CI 0.45 – 0.75]) and mortality (Peto OR 0.75 [95% CI 0.63-0.87]), with no increased risk of bleeding (Peto OR 0.89 [95% CI 0.75-1.05]).\textsuperscript{31}

Of the twenty two trials analysed only five were deemed high quality and the rate of randomization was less than 50%.

**Barriers to Anticoagulation**

Despite the strong evidence of the benefit of OAC in patients with AF, the use of thromboprophylaxis still remains inadequate.\textsuperscript{12, 16, 17} In the UK it is estimated that only 56% of patients eligible for OAC are actually receiving it.\textsuperscript{12} A recent literature review reports the following as barriers for the use of OAC in patients with AF: age, risk of bleeding, risk of falls, co-morbidities including cognitive impairment and alcohol use, and the patient’s ability to comply with treatment.\textsuperscript{37} Physicians were found to be less likely to use OAC in patients aged over 70 years compared to those aged less than 70 years, despite having no contra-indications to warfarin.\textsuperscript{37} In two studies, 50 to 60% of physicians agreed that the benefit of anticoagulation therapy outweighed the risks in elderly patients with AF.\textsuperscript{38, 39}

The reluctance of physicians to use OAC in elderly patients with AF is an important barrier in the prevention of stroke. Evidence exists to support the use of warfarin in elderly patients with AF,\textsuperscript{40, 41} as they have the highest risk of stroke.\textsuperscript{4-6} In fact the benefit of warfarin has been shown to increase with advancing age,\textsuperscript{40} and the risk of intracranial bleeding to be not significantly different in patients receiving warfarin compared to antiplatelets.\textsuperscript{41}

**Novel Oral Anticoagulants**

Novel therapies have been developed to overcome the limitations of vitamin K antagonists.\textsuperscript{18} These include dabigatran etexilate, a direct thrombin inhibitor and rivaroxaban, a direct factor Xa inhibitor.\textsuperscript{18}

Dabigatran is available orally in doses of 110mg or 150mg twice daily, and peak plasma concentrations are achieved 2-3 hours following oral administration. There are few drug/food interactions and dose monitoring is not required. However there are a few limitations: currently no antidote exists to reverse its effect in patients with massive haemorrhage; its half life is 12 – 17 hours which means that patients who miss doses may not be adequately anticoagulated; it is mainly excreted renally and should be used cautiously in patients with renal failure; its absorption is dependent upon pH which is reduced in patients taking proton pump inhibitors.\textsuperscript{18}

Dabigatran has recently been approved in the USA, Canada, Japan and Europe for stroke prevention in AF.\textsuperscript{42} The Randomized Evaluation of Long Term Anticoagulant Therapy (RE-LY) trial demonstrated non inferiority of dabigatran as compared to warfarin.\textsuperscript{43} 113 patients with AF were randomized to receive either a fixed dose of dabigatran (110mg or 150mg twice daily) or dose adjusted warfarin. Patients were followed up for 2 years where the primary outcome was stroke or systemic embolism. The study showed patients receiving dabigatran 110mg twice daily had similar rates of stroke and systemic embolism as patients receiving warfarin (1.69%, 1.53% respectively, relative risk with dabigatran 0.91; 95% CI 0.74-1.11, p<0.001 for non-inferiority), but lower rates of major haemorrhage (2.71%, 3.36% per year respectively). Patients receiving dabigatran 150mg twice daily had similar rates of stroke or systemic embolism when compared to patients receiving warfarin (1.11%, 1.53% respectively, relative risk 0.66, 95% CI 0.53 – 0.82, p<0.001 for superiority), and similar rates of major haemorrhage (3.11%, 3.36% per year respectively). A recent study has shown that dabigatran can be used in patients undergoing cardioversion.\textsuperscript{44}

Rivaroxaban, an oral direct inhibitor of factor Xa has been shown to be a potential alternative to warfarin in patients with non valvular AF.\textsuperscript{45} Rivaroxaban does not require dose adjustment and has little food or drug reaction.\textsuperscript{46} It is primarily excreted via the liver and therefore should be used
cautiously in patients with hepatic impairment. In the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF), a randomized double blind study, 14,264 patients were randomized to receive oral rivaroxaban (20mg daily) or dose adjusted warfarin. They found that the occurrence of stroke or systemic embolism in patients taking rivaroxaban and warfarin was comparable (1.7%, 2.2% per year respectively, hazard ratio in the rivaroxaban group 0.79; 95% CI 0.66-0.96; p<0.001 for non inferiority). Furthermore the rates of intracranial bleeding were significantly lower in patients taking rivaroxaban compared to warfarin, (0.5% v 0.7% per year; hazard ratio 0.67; 95% CI 0.47-0.93, p=0.02) although major gastrointestinal bleeding was higher in patients taking rivaroxaban (3.2%, 2.2%, p<0.001).

Earlier Detection of Atrial Fibrillation

Patients with AF are commonly asymptomatic and may only be diagnosed during presentation related to complications of AF, including heart failure, stroke or thrombo-embolism. An irregular pulse should raise the suspicion of AF and a 12 lead electrocardiogram (ECG) should be performed to confirm the diagnosis. Often AF begins with paroxysms that are short and rare, which progress to longer and more frequent attacks which may become continuous. In paroxysmal AF about 1 in 12 paroxysms are actually symptomatic. Studies of patients with pacemakers confirm that the burden in AF can vary between patients and that many paroxysms are asymptomatic. Theoretically earlier detection of AF allows for earlier risk stratification and use of thromboprophylaxis and hence reduction in risk and occurrence of stroke; However, this is difficult to put into practice.

Screening patients following ischaemic stroke with holter monitoring has been found to detect new onset AF or atrial flutter in 5% of patients. Performing a 12 lead ECG would detect AF in 6.7% of patients, a 24 hour holter would detect 10.6% and a 7 day event loop recorder would detect 15.6%. In the UK, incentivized screening programmes in primary care were piloted and 1.4% of patients were found to have a new diagnosis of AF through opportunistic pulse palpation.

Earlier Initiation of OAC and Avoiding Interruptions

Once patients have been identified as requiring OAC, it is recommended that treatment should be initiated promptly. However in the UK, it is common practice for non-specialists to refer to a specialist clinic for a decision on appropriate anticoagulation. This creates unnecessary delays and places patients at a higher risk of stroke and thrombo-embolism. A survey of accident and emergency consultants in the UK found that half were reluctant to make a decision on appropriate anticoagulation, and preferred to refer to a medical or cardiology team.

Patients receiving OAC may need to undergo surgical procedures for which interruption of therapeutic anticoagulation is essential. Although evidence is lacking in the absolute risk of stroke following interruption of anticoagulation in patients with AF, it is recommended that the interval without anticoagulation should be kept to a minimum and that anticoagulation should be re-started on the evening of (or the morning after) the surgery assuming there is adequate haemostasis. Furthermore it has been recognized that not all procedures will require anticoagulation therapy to be stopped.

Anti-Arrhythmics and the Role for Catheter Ablation

Rhythm control can be achieved with pharmacological, electrical or more invasive means such as catheter ablation. The rhythm-control strategy has been largely reserved for symptomatic patients, and furthermore catheter ablation is generally considered for symptomatic patients with paroxysmal AF who are resistant to at least one anti-arrhythmic agent.

Restoring sinus rhythm in a patient with AF will theoretically reduce the risk of stroke. However studies to date comparing the rhythm versus rate control strategy, such as the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study and the Atrial Fibrillation and Congestive Heart Failure (AF-CHF) study, show...
no significant difference in mortality or stroke risk. Patients undergoing catheter ablation often require more than one procedure, and remain at risk of recurrence.

Current studies are under way to evaluate the role of catheter ablation in the treatment of AF. The Catheter Ablation versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation (CABANA) trial is a randomized, parallel, open label trial evaluating percutaneous left atrial catheter ablation for the purpose of elimination of atrial fibrillation, as compared with current state-of-the-art therapy with either rate or rhythm control drugs [CABANA; clinicaltrials.gov; identifier NCT00911508]. The primary outcome is mortality and secondary outcomes include stroke, bleeding, cardiovascular hospitalization, arrhythmias and recurrent AF. It is expected to complete in 2015.

The Early treatment of Atrial fibrillation for Stroke prevention Trial (EAST) is a randomized, prospective, open label study that is expected to complete in 2017 [EAST; clinicaltrials.gov; identifier NCT01288352]. EAST hopes to test the hypothesis that early, structured rhythm control therapy based on anti-arrhythmic drugs and catheter ablation can prevent AF related complications when compared to usual care (following the 2010 ESC guidelines for the management AF). The primary outcomes include stroke, bleeding, cardiovascular hospitalization, arrhythmias and recurrent AF. It is anticipated that these large trials will help establish a role for catheter ablation in the management of AF.

Special Considerations

OAC Following Stroke

1. Acute Infarct

OAC following a minor stroke or TIA is more effective than aspirin in prevention of further ischaemic events and therefore current guidelines recommend that unless there are clear contraindications, long-term OAC should be initiated following ischaemic stroke. However, OAC will increase the risk of developing intracerebral haemorrhage (ICH) which can potentially have devastating effects to the patient causing increased mortality and morbidity. The main factors that increase the risk of ICH include dose intensity, advanced age and hypertension. Other possible factors include size of infarct, associated cerebrovascular disease, concomitant antiplatelet therapy, tobacco or alcohol consumption, ethnicity, dialysis and vascular abnormalities detected by cerebral imaging (amyloid angiopathy, leukoaraiosis or microbleeds). Guidelines therefore recommend appropriate management of uncontrolled hypertension, and cerebral imaging, such as computed tomography or magnetic resonance imaging (MRI) to exclude ICH prior to initiation of OAC. Unfortunately no robust evidence exists as to the optimal timing of OAC; however most guidelines recommend that in the absence of ICH, anticoagulation should begin after 2 weeks. The American Heart Association/American Stroke Association (AHA/ASA) guidelines for the prevention of stroke in patients with stroke or transient ischemic attack recommend delaying OAC (more than 2 weeks) in patients with larger infarcts, hemorrhagic transformation and uncontrolled hypertension.

2. Hemorrhagic Transformation

In an acute infarct there is a risk of hemorrhagic transformation which may be a complication of thrombolysis treatment or indeed a natural course of the stroke. Hemorrhagic transformation may or may not give rise to neurological deterioration depending on its type, and one case series suggests that OAC may be safe in selected patients. Current guidelines differ in their guidance in situations where hemorrhagic transformation has occurred. The ESC and NICE guidelines state that OAC should be stopped. The AHA/ASA guidelines recommend that the decision for OAC should be made on a case-by-case basis depending upon various factors including size of hemorrhage, status of the patient and the indication for anticoagulation. Furthermore the introduction of OAC should be delayed by more than 2 weeks.

3. Intracerebral Haemorrhage

Unfortunately no robust evidence exists as to the risks and benefits of oral anticoagulation in...
patients who have had an intra-cerebral hemorrhage, and randomized controlled trials would not be ethical. Eckman et al. applied a decision-analysis model to evaluate the role of anticoagulation in patients following intra-cerebral hemorrhage. They determined that OAC should largely be avoided in survivors of ICH, and only considered in patients with a deep hemorrhage (affecting the thalamus or basal ganglia), with a particularly high risk of thromboembolism or low risk of ICH recurrence.

The ESC and NICE guidelines recommend that OAC should not be given in the presence of an intracranial hemorrhage, although they do not elaborate as to whether there would be any situations where OAC may be considered. The AHA/ASA guidelines recommend that for patients who develop ICH, anticoagulants and antiplatelets should be discontinued during the acute period for 1 to 2 weeks, and clotting abnormalities may be corrected. However the decision to restart anticoagulation depends upon balancing the risk of recurrent ICH against the risk of ischemic stroke. Furthermore if anticoagulation is to be restarted this should be done within 7-10 days.

4. Patients who Develop a Stroke Despite Adequate Anticoagulation

In patients who have developed an ischemic stroke despite adequate anticoagulation (ie INR between 2-3) current guidelines agree that it may be re-instated with a higher target INR range of 3-4. However, this recommendation is not evidence-based. As mentioned previously an INR greater than 3 will increase the risk of bleeding. Adding in an antiplatelet agent is discouraged as there is no evidence to suggest this would be beneficial, as there is an increased risk of ICH.

It is evident that managing patients with AF who have developed strokes (whether ischemic or hemorrhagic) is challenging and clinicians are advised to use their clinical judgement to try and balance the risks of bleeding with OAC against the risk of thromboembolism without. Each decision should be case-based and patients should be evaluated carefully.

OAC in Acute Coronary Syndromes and/or Percutaneous Intervention

The management of OAC in patients with AF and acute coronary syndrome (ACS) and/or percutaneous intervention (PCI) can be difficult for clinicians.

In patients without AF, dual antiplatelet therapy (aspirin and clopidogrel) is recommended for 1 year in ACS and along with stenting (clopidogrel for 4 weeks with a bare metal stent, 6-12 months following a drug eluting stent). In patients with AF a combination of OAC and antiplatelet therapy may be needed. Although this combination is known to increase bleeding risk, it will need to be balanced with the protective effects of antiplatelets in ACS and PCI.

In ACS (with or without PCI), the ESC guidelines recommend triple therapy with warfarin, aspirin and clopidogrel for 3-6 months or longer in selected patients with a low bleeding risk, followed by long term warfarin and clopidogrel (or aspirin and gastric protection). In elective PCI, drug eluting stents (DES) should be limited to clinical and/or anatomical situations where the greatest benefit will be seen. Patients with bare metal stents (BMS) should receive triple therapy for 4 weeks, followed by warfarin and clopidogrel (or aspirin and gastric protection) for one year and warfarin alone thereafter. Patients with DES should receive triple therapy for a minimum of 3 months (with a sirolimus/everolimus/tacrolimus-eluting stent) or 6 months (with paclitaxel-eluting stent), followed by warfarin and clopidogrel (or aspirin and gastric protection) for 6 months and warfarin alone.

In the ESC guidelines, triple therapy is recommended post PCI (BMS 4 weeks, DES 6-12 months) then VKA + antiplatelet, avoid DES, in stable CAD monotherapy (no acute event or PCI in preceding year).

Conclusions

Stroke and thrombo-embolism are important consequences of AF, causing considerable morbidity, mortality and associated healthcare costs.
The prevention of stroke is an essential component of the management of AF. Patients with irregular pulses should undergo an ECG to confirm the diagnosis and although routine screening is not currently recommended, pilot screening programmes (through pulse palpation of elderly patients in primary care) have shown potential cost-benefit. Once the diagnosis of AF is confirmed a stroke risk assessment should be undertaken. Utility of the CHADS\textsuperscript{2} and CHA\textsubscript{2}DS\textsubscript{2}-VASc scores are encouraged to identify patients at higher risk of stroke, which can be performed by physicians or general practitioners. Once a bleeding risk assessment (with the use of the HAS-BLED tool) has been made and the decision for OAC made, this should be initiated promptly and referral to an anticoagulation service can be made. Patients should be educated about the importance of OAC and (in the case of warfarin) the need for regular dose-monitoring or adjustment. Patients will need to be monitored to ensure they remain within the therapeutic range (INR range 2-3) and need a service provided to respond to out-of-range INR levels. Interruption of OAC therapy, for example prior to surgical procedures, should be kept to a minimum and treatment re-instated as soon as possible (usually the evening of or morning after the procedure).

Physicians and general practitioners should be educated in the benefits of OAC, particularly in the elderly age group, where the greatest benefit lies. The risk of intracranial haemorrhage in elderly patients has been shown to be less in patients receiving warfarin as compared to aspirin, whilst the benefit of stroke prevention is far greater with warfarin. Further work is clearly required to increase the use of OAC in patients with AF. Novel therapies such as the oral thrombin inhibitors (eg dabigatran and rivaroxaban) will hopefully increase usage. They negate the need for dose monitoring or adjustment and are expected to replace warfarin in the near future.

**References**

13. Fuster V, Ryden L, Cannon D, Crijns H,


