Anticoagulation Myth Buster

1. **Myth: “Antiplatelet agents (such as aspirin or clopidogrel) can be used to reduce stroke risk in patients with Atrial fibrillation (AF)”**

   NICE guidance CG180 (2014) states³ **“Do not offer aspirin monotherapy solely for stroke prevention to people with AF”.** This is reiterated in NICE AF Quality Standard (QS93) which states that ‘Adults with atrial fibrillation should not prescribed aspirin as monotherapy for stroke prevention’⁴.

   This is based on evidence that warfarin is far more effective at stroke prevention than aspirin, with one meta-analysis concluding that warfarin reduces stroke risk by approximately 64% and aspirin by only 22% in patients who have AF³. Trials such as BAFTA⁴ and AVERROES⁵ have demonstrated that oral anticoagulant therapies offer much greater protection from stroke with similar bleeding rates compared to antiplatelet monotherapy.

   When considering dual antiplatelet therapy (aspirin and clopidogrel); there is evidence that this is more effective at preventing stroke than aspirin monotherapy, but less effective than anticoagulant therapy. Dual antiplatelet therapy was associated with a greater risk of major bleeding than either aspirin monotherapy or warfarin monotherapy, hence, this option is not recommended in NICE guidance and should not be used in routine clinical practice for the prevention of AF-related stroke⁶⁷⁸.

2. **Myth: “Aspirin should always be continued with anticoagulants if a patient has cardiovascular disease (CVD)”**

   The use of oral anticoagulants (OAC) with antiplatelet therapy increases the absolute risk of major bleeds⁷. OAC monotherapy is recommended in AF patients with stable cardiovascular disease (CVD) without acute coronary syndrome (ACS) and/or coronary intervention in the previous 12 months⁷, please refer to cardiology or haematology specialist advice in these circumstances.

   British Society of Haematology guidelines, written before the introduction of Direct acting anticoagulants (DAOCs), (2011)⁹ advise:
   - Patients with peripheral artery disease or previous ischaemic stroke on antiplatelet therapy should stop this agent if warfarin is commenced.
   - Patients receiving an antiplatelet agent as primary prophylaxis for CVD on developing an indication for warfarin should stop their antiplatelet agent.
   - Patients on antiplatelet as secondary prophylaxis with stable ischaemic heart disease (often defined as >12 months following ACS) should stop their antiplatelet agent while being treated with warfarin.
   - Patients on a single antiplatelet agent <12 months following an ACS, who require to start warfarin therapy should continue aspirin therapy until 12 months post ACS, unless they are regarded as having a high bleeding risk.
   - When combined warfarin and single antiplatelet agent are indicated, consideration should be given to use of aspirin given the higher bleeding risk associated with clopidogrel.

   Patients on antiplatelet agents, following an ACS or stent placement, who develop an indication for warfarin should be carefully assessed for bleeding risk and discussed with their cardiologist, with a view to introducing warfarin and minimizing the duration of triple therapy. Specialist advice on the use of antiplatelet therapies in combination with anticoagulants, including DOACs can be found within European society of cardiology guidance⁸.

   These recommendations pre-date the introduction of DOACs, but a similar approach should be taken when considering the appropriateness of continuing or discontinuing antiplatelet therapy when a DOAC is to be initiated.
3. **Myth: “Newer and direct oral anticoagulant agents, e.g. dabigatran and rivaroxaban, do not interact with other medication”**

DOACs have fewer potential interactions with other medicines compared with warfarin, however there remain certain drug-drug interactions for each DOAC that should be investigated prior to initiation. Key interactions which should be considered include: antifungal agents, rifampicin, phenytoin, anti-retrovirals, anti-epileptic medication and anti-rejection medication. Please refer to a pharmacist for any specific advice.

4. **Myth: “DOACs cannot be reversed and are therefore unsafe”**

Currently only dabigatran has a specific reversal agent, idarucizumab. However, it is important to recognise that DOACs have a significantly shorter duration of action than warfarin (see below), therefore the duration of any bleeding is likely to be significantly shorter. If a patient does experience a bleed, the cause and severity should be assessed. If urgent treatment is required, the oral anticoagulant agent (OAC) may be discontinued and supportive measures started; e.g fluid replacement and / or transfusions. (Refer to local or hospital guidance on management of bleeding on anticoagulant therapy for further information). There are reports that Prothrombin Complex Concentrate (PCC) has been used successfully to reverse or partially reverse bleeding.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Approximate half life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>40 hours</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>13-18 hours</td>
</tr>
<tr>
<td>Apixaban</td>
<td>12 hours</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>5-13 hours</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>10-14 hours</td>
</tr>
</tbody>
</table>

5. **Myth: “I cannot give anticoagulation to an elderly or frail patient in case they fall”**

NICE guidance (2014) states that anticoagulation therapy should not be withheld solely because the person is at risk of falls.

The risk of intracranial haemorrhage (ICH) on warfarin occurring as a consequence of a fall is often lower than perceived. Modelling suggests that a patient with an annual stroke risk of 5% (CHA₂DS₂VASc score 4-5) would need to fall approximately 295 times in a year for the falls risk to outweigh the stroke reduction benefit of warfarin. Clinical trial data demonstrates that the risk of ICH is lower with DOACs than with warfarin. Risk of falls is therefore not a contraindication to initiating oral anticoagulation with warfarin or a DOAC.

6. **Myth: “My patient is renally impaired, they cannot have an OAC”**

The degree to which OAC agents are cleared by the kidney varies, and, as shown by the table below, dose adjustments are necessary at various levels of renal impairment. Care should be taken to consider patients age and renal function prior to deciding the most appropriate agent.

<table>
<thead>
<tr>
<th>Degree of Impairment</th>
<th>Warfarin</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-49mL/min</td>
<td>Closely monitor INR</td>
<td>Dose reduce</td>
<td>Dose reduce</td>
<td>Continue normal dosing</td>
<td>Dose reduce</td>
</tr>
<tr>
<td>15-29mL/min</td>
<td>Contraindicated</td>
<td>Dose reduce</td>
<td>Consider dose reduction (see SPC)</td>
<td>Dose reduce</td>
<td></td>
</tr>
<tr>
<td>&lt;15mL/min</td>
<td>Contraindicated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The Cockcroft-Gault equation is the standard method for estimating creatinine clearance (CrCl) and drug dose adjustment in adults using the patient’s age, weight, sex and serum creatinine. Current CrCl calculators embedded within GP IT systems provide estimated glomerular filtration rates (eGFR), which do not give a reliable estimate of CrCl for the adjustment of DOAC doses and thus should not be used.

We recommend use of the MD+CALC Cockcroft-Gault equation which recognises the need to adjust for bodyweight in obese patients (BMI > 30) and will calculate a modified estimate of CrCl with a range that is based on ideal bodyweight (IBW) and actual body weight (ABW). This can be accessed using the link: https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation or it can be downloaded as an app.

7. Myth: “I need to give heparin to my patients with AF (bridging), when they are not taking warfarin or DOACS”

Many minor surgical interventions may not require interruption of anticoagulation therapy. When temporary cessation of anticoagulant therapy is required, replacing oral agents with subcutaneous heparin / low molecular weight heparin (LMWH) does not seem to be beneficial, except in patients with mechanical heart valves. Evidence from a randomized trial of 1,884 patients with AF, demonstrated that interruption of anticoagulation was non-inferior to heparin bridging for arterial thromboembolism and resulted in a lower risk of major bleeding.

In view of this, the general recommendation is that anticoagulant therapy in patients with AF should be withheld without bridging in patients at low risk of stroke. However many centres do still recommend bridging with LMWH for high risk patients on warfarin, with warfarin stopped 5 days before surgery.

In view of the short half-life of DOACs, there is no need for bridging with LMWH – the recommendations on when to stop therapy before surgical interventions are specific to each DOAC and should be followed carefully. These recommendations can be found in the Summary of Product Characteristics for each individual DOAC.

8. Myth: “I don’t need to monitor my patients bloods when they are on a DOAC”

Although the monitoring required for DOACs differs from the close INR monitoring required for warfarin, systematic patient monitoring is still required throughout therapy with a DOAC. DOAC licensing does not specifically stipulate the details of the required monitoring. However all patients on DOACs will require renal function assessments at least annually (6 monthly if CrCl 30-60ml/min or if on dabigatran and aged >75 years or frail). It is good practice also, to monitor hepatic function, and a full blood count at least annually. Patients on DOACs should have a regular review of their adherence to therapy – recent evidence suggests that up 30-35% of patients prescribed a DOAC for the prevention of AF-related stroke, stop treatment within 6 months of initiation.

9. I have decided to put my patient on a DOAC, which one is the best? And at what dose?

Currently there are no head to head trials comparing the DOAC agents. All four currently available DOACs are licensed to treat non-valvular AF, however all have slightly different properties. Characteristics to take into account when determining the most appropriate drug and dose include: age, weight, renal function (in the form of calculated creatinine clearance), bleeding risk, previous history of bleeding, history of dyspepsia, history of stroke and need for a compliance aids.
10. Myth: “My newly diagnosed AF patient is on a DOAC already for joint replacement, so they are already anticoagulated for their AF”

Care should be taken when prescribing DOACs, as the doses used for indications such as joint replacement, acute coronary syndromes, venous thromboembolism and AF vary. Patients post-hip and knee replacement will be on a lower dose than required for the prevention of AF-related stroke hence, in this circumstance, the dose will need to be increased, please consult individual summary of product characteristics.9,10,11,12.

11. Myth: “My patient is unable to swallow therefore cannot have a DOAC”

Rivaroxaban and apixaban may be crushed and mixed with liquids if patients are unable to swallow. Dabigatran capsules must not be opened9,10,11,12.

12. Myth: “DOACS, like warfarin, can interact with food”

There are no known drug-food interactions with DOAC agents. Rivaroxaban should be taken with food to improve absorption and maximise bioavailability but the timing of apixaban, dabigatran and edoxaban dosing in relation to food is unimportant9,10,11,12.

13. Myth: “Patients with any form of valve disease are not suitable for DOACs”

Valvular heart disease can be associated with an increased thromboembolic risk, and historically patients with AF have been categorised as either “valvular” or “non-valvular”. Valvular AF refers primarily to patients with rheumatic valvular disease (predominantly mitral stenosis) or mechanical heart valves. There is no clear evidence that other valvular disease, including mitral regurgitation or aortic valve disease, affects the stroke risk in AF or impacts on the selection of an appropriate anticoagulant. Routine screening for valvular heart disease is not recommended prior to prescribing DOACs.

14. Myth: “All patients must stop anticoagulant agents prior to dental procedures”

It is advised that all dental procedures should be risk stratified, taking into account the risk of bleeding associated with the dental procedure itself, alongside the patients individual stroke risk (based on CHA2DS2VASc) and their bleeding risk (based on HASBLED)24. Where possible, modifiable bleeding risk factors should be addressed. The risk of significant bleeding during dental procedures in patients on oral anticoagulant with an INR >4 is small and thus oral anticoagulants do not routinely need to be withheld in the majority of stable patients undergoing out-patient dental surgery.25.
A recent review concluded that it is safe and possible to undertake dentoalveolar procedures whilst talking DOAC therapy\(^2\)\(^6\). It is recommended that care should be taken to consider the timing of DOAC dosing in relation to when the procedure is planned to minimise post-procedural bleeding. Dental surgeons should aim to undertake procedures when peak DOAC concentrations have reduced (ie, at least 5–6 hours post dose)\(^2\)\(^6\). Current guidance suggests achieving this by delaying the morning dose of a DOAC for procedures with a high risk of bleeding\(^2\)\(^4\)–\(^2\)\(^6\). In addition, researchers suggest waiting a minimum of four to six hours after the procedure, and ensuring haemostasis has been achieved, prior to re-starting DOAC therapy\(^2\)\(^6\).

Patients at high risk of bleeding undergoing more invasive procedures, should be considered for referral to specialist units for their procedures.

References

15. Man-Son-Hing et al. Choosing antithrombotic therapy for elderly patients with AF who are a risk for falls. Archives of Internal Medicine. 1999;vol.159(7)pp677-685  


