Practical tips in initiating and maintaining anticoagulation

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Questions to ask:

• What is the diagnosis?
• Which anticoagulant?
• How to choose?
• How to initiate?
• How to switch between anticoagulants
• Follow up?
Diagnosis requiring anticoagulation

Prevention of stroke in Atrial Fibrillation (AF)
Treatment of venous thromboembolism
Replacement heart valves, bioprosthetic and mechanical
Arterial Embolus
Arterial disease
Cardiac problems
and many others
Which anticoagulant?

- Vitamin K antagonists
  - Warfarin, sinthrome, acenocoumarol, phenindione
- Non Vit K antagonists (NOACs)
  - Dabigatran
  - Rivaroxaban
  - Apixaban
  - Edoxaban
- LMWH (including fondaparinux)
How to choose in VTE?

- Traditionally LMWH and then initiation with warfarin, continuing with LMWH for 5/7 and until INR >2.0 for 2 days
- LMWH only if active malignancy
- Now – NOACs most likely to be used as first line treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Treatment</th>
<th>Continued</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>LMWH 5/7</td>
<td>150mg twice daily</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>15mg BD 21 days</td>
<td>20mg OD (10mg od if equipoise)</td>
</tr>
<tr>
<td>Apixaban</td>
<td>10mg BD 7/7</td>
<td>5 mg BD for 6 months [2.5 mg BD if equipoise]</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>LMWH 5/7</td>
<td>60 mg once daily (30mg OD reduced dose depending on risk factors)</td>
</tr>
</tbody>
</table>
How to choose in AF? (ESC guidance)

1. **Mechanical heart valves or moderate or severe mitral stenosis**
   - Yes
   - No

2. **Estimate stroke risk based on number of CHA₂DS₂-VASc risk factors**
   - \( 0 \)
   - \( 1 \)
   - \( \geq 2 \)

3. **No antiplatelet or anticoagulant treatment (IIIB)**
   - OAC should be considered (IIaB)

4. **Oral anticoagulation indicated**
   - Assess for contra-indications
   - Correct reversible bleeding risk factors

5. **LAA occluding devices may be considered in patients with clear contra-indications for OAC (IIbC)**

6. **NOAC (IA)\(^c\)**

7. **VKA (IA)\(^c,d\)**

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AF = atrial fibrillation; LAA = left atrial appendage; NOAC = non-vitamin K antagonist oral anticoagulant; OAC = oral anticoagulation; VKA = vitamin K antagonist.

\(^a\)Congestive heart failure, Hypertension, Age \( \geq 75 \) years (2 points), Diabetes, prior Stroke/TIA/embolus (2 points), Vascular disease, age 65–74 years, female Sex.

\(^b\)Includes women without other stroke risk factors.

\(^c\)IIaB for women with only one additional stroke risk factor.

\(^d\)IB for patients with mechanical heart valves or mitral stenosis.
Initiation of Warfarin for VTE

- Decide on initiation dose (in hospital use the warfarin chart for guidance)
- Consider the age of the patient (e.g., Elderly and frail needs less warfarin as compare to young patient)
- Ensure adequate warfarin counselling – involve family member
- Try to give consistent doses
- In hospital - Daily INR’s only required on Day 1-4, and following dosing tables on the warfarin chart
- Have they been on warfarin before – what dose did they take
- What other drugs are they taking? (HIV and rifampacin reduce the INR whereas medication - amiodarone may increase the INR)
- When INR >2.0 do not dose reduce but continue until INR nearly 2.5 and then stop LMWH
Initiation of warfarin for AF

- As for VTE – but cover with LMWH not required (although mentioned in NICE update 2014 – only for symptomatic patients in hospital)
- Start on 5mg – standard, INR on day 5 and 8
- Frail and elderly (or those who had low dose previously) 2mg/3mg – if frail and also on interacting drugs - ?amiodarone
- Dosing by following TAIT – adjust if not starting on 5mg
# NOACs and AF

<table>
<thead>
<tr>
<th>Drug</th>
<th>Action</th>
<th>Dose</th>
<th>½ life hours</th>
<th>Excretion</th>
<th>Routine tests req pre initiation</th>
<th>Storage</th>
<th>Food</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban</td>
<td>Activated FXa</td>
<td>20mg od 15mg od</td>
<td>5-9</td>
<td>35% renal</td>
<td>none</td>
<td>No probs</td>
<td>Plus 39%</td>
</tr>
<tr>
<td>ROCKET-AF</td>
<td></td>
<td></td>
<td>11-13</td>
<td>65% liver</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Thrombin</td>
<td>150mg bd 110mg bd</td>
<td>12-17</td>
<td>80% renal</td>
<td>U&amp;E then yearly</td>
<td>In airtight container</td>
<td>none</td>
</tr>
<tr>
<td>RELY</td>
<td></td>
<td></td>
<td></td>
<td>20% liver</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apixaban</td>
<td>Activated FXa</td>
<td>5mg bd 2.5mg bd</td>
<td>12</td>
<td>27% renal</td>
<td>LFT</td>
<td>No probs</td>
<td>none</td>
</tr>
<tr>
<td>ARISTOTLE AVERROES</td>
<td></td>
<td></td>
<td></td>
<td>73% liver</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Activated FXa</td>
<td>60mg od 30mg od 15mg od</td>
<td>9-11</td>
<td>50% renal</td>
<td>No probs</td>
<td>No probs</td>
<td>Plus 6-22%</td>
</tr>
<tr>
<td>ENGAGE-AF</td>
<td></td>
<td></td>
<td></td>
<td>50% liver</td>
<td></td>
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</table>
Choosing the correct dose

• NOACs provide simple dosing   True/False?
• No monitoring required    True/False
• NOACs in obese patients? – what is the top limit of weight?
• No drug interactions?
Figure 4 Use of non-vitamin K antagonist oral anticoagulants according to renal function. *2 × 110 mg in patients at high risk of bleeding (per SmPC). **Other dose reduction criteria may apply (weight ≤60 kg, concomitant potent P-Gp inhibitor therapy). $2 × 2.5 mg only if at least two out of three fulfilled: age ≥80 years, body weight ≤60 kg, creatinine ≥1.5 mg/dL (133 μmol/L). Orange arrows indicate cautionary use (dabigatran in moderate renal insufficiency, FXa inhibitors in severe renal insufficiency, edoxaban in ‘supranormal’ renal function); see text for details.
Maintaining anticoagulation: Warfarin

- Ensure that Drs are aware when a patient is not eating as this may affect the INR
- INRs are taken more frequently when new drugs added or patient deteriorates
- Interacting drugs should be noted (ie antibiotics & vitamin K – when prescribing antibiotics check INR at that point as if unwell INR likely to be elevated)
- In hospital - ensure that box 4 is completed (patients normal warfarin dose) for patients admitted on warfarin to ensure safe re-anticoagulation post surgery etc
- On discharge - Patients need to know the date and time for first INR post discharge – write it down.
Maintaining Anticoagulation: Warfarin

- Regular INRs tests
- Not too often – a small dose change may take 2 weeks to affect the INR
- When patients unwell – take an INR then, before starting the antibiotics
- Advise patient to get INR done if they begin to feel unwell – not to wait till next INR
- Switch to NOACs:-
  - If TTR <65%
  - Why is TTR poor – if non compliance stay with warfarin unless eg dosset box
  - If the INR fluctuates – Variance Growth Rate (VGR) – predictive of an event
  - Unable to get to surgery for INR and require a DN
  - INR >8 x1
  - Having too many INR tests
  - Patient choice
## What is included in follow up?

<table>
<thead>
<tr>
<th></th>
<th>When</th>
<th>How</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherence</td>
<td>Each visit</td>
<td>Discussion Reinforce importance Discuss adherence aids (my therapy – dosset box)</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>Each visit</td>
<td>Any events?</td>
</tr>
<tr>
<td>Bleeding</td>
<td>Each visit</td>
<td>Nuisance bleeding Bleeding impacting on QoL</td>
</tr>
<tr>
<td>Assessing modifiable risk factors for bleeding</td>
<td>Each visit</td>
<td>Eg – hypertension, meds that increase bleeding – aspirin, labile INR, alcohol</td>
</tr>
<tr>
<td>Co-medications</td>
<td>Each visit</td>
<td>Over the counter drugs</td>
</tr>
<tr>
<td>Hb, U&amp;E, LFT</td>
<td>Yearly</td>
<td>Mainly looking at renal function</td>
</tr>
<tr>
<td></td>
<td>6 monthly</td>
<td></td>
</tr>
<tr>
<td>Check correct dose and NOAC</td>
<td>Each visit</td>
<td>Reassess that the chosen anticoagulant is a) The best for the patient b) The dose is correct</td>
</tr>
</tbody>
</table>
Figure 2 Switching between vitamin K antagonists and non-vitamin K antagonist oral anticoagulants and vice versa. TE, thromboembolic.