Tailoring Therapy: Which Drug for which Patient

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February 2015
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AF and NICE

- Dabigatran and rivaroxaban approved 2012
- Apixaban approved 2013
- Need to implement NICE guidance
- Need to ensure patients benefit from these new drugs
- Ensure safe prescribing
- Need to reduce avoidable strokes
- Manage the entry of these new drugs
Safe Introduction of the New Oral Anticoagulants (NOACs)

Challenges

• Politics

• Lack of experience with NOACs
  – On job learning

• Lack of clarity on place of NOACs

• Demanding / mis-informed patients

• Securing funding
Commissioning a Specialist Anticoagulant Decision Unit

- Convened a meeting of all the key stakeholders
- Agreed criteria for NOAC use
- Agreed who could initiate NOACs
- Agreed to commission a specialist service
- Agreed referral pathways
- Agreed responsibilities of GPs and specialist clinic
GP diagnoses patient with AF and refers to NOAC service

NOAC clinic decides on anticoagulation option with patient in line with Bucks criteria

- Start warfarin
- Prescribe
- Counsel patient
- Alert Card
- Information Pack

- Start NOAC,
- Prescribe
- Counsel patient,
- Anticoagulant Alert Card
- Information pack

If warfarin and NOAC unsuitable, consider referral to cardiologist

Refer into usual A/C clinic

- Second contact by phone at 2 weeks:
  - Address issues/concerns/compliance
  - Discharge to GP for continuation
- If switching NOAC, repeat above stages
- If switched to warfarin, refer to A/C clinic
Patient with AF identified requiring A/C

Non-urgent - refer to NOAC

Recent TIA or stroke
- Stroke Team starts A/C
- Refers to NOAC Clinic

CHA2DS2VASC≥ 6 but no TIA or stroke:
- refer to NOAC clinic for urgent initiation

NOAC clinic agrees anticoagulation with patient in line with Bucks criteria

- Start warfarin
- Prescribe
- Counsel patient
- Anticoagulation Alert Card
- Information pack

If warfarin and NOAC unsuitable, consider referral to Cardiologist

- Prescribe
- Counsel patient
- Anticoagulant Alert Card
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The Consultation

• Open and welcoming
• Involve relative / carer
• Why the patient is here
• 30 minute structured consultation
• Educate on stroke risks
• Purpose of information gathering
• Shared decision making
• Information about anticoagulants
• Follow up arrangements
• Helpline
Safety Checks

- Age
- Weight
- BP
- U&Es
- FBC
- LFTs
- PMH
- Bleeding history
- Drug History
- Over the counter medicines
Stroke risk assessment with CHA\textsubscript{2}DS\textsubscript{2}-VASc

<table>
<thead>
<tr>
<th>CHA\textsubscript{2}DS\textsubscript{2}-VASc criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure/ left ventricular dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥75 yrs</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/transient ischaemic attack/TE</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease (prior myocardial infarction, peripheral artery disease or aortic plaque)</td>
<td>1</td>
</tr>
<tr>
<td>Age 65–74 yrs</td>
<td>1</td>
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<tr>
<td>Sex category (i.e. female gender)</td>
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</table>

<table>
<thead>
<tr>
<th>CHA\textsubscript{2}DS\textsubscript{2}-VASc total score</th>
<th>Rate of stroke/other TE (%/year)*</th>
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<tbody>
<tr>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>1</td>
<td>1.3</td>
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<td>6.7</td>
</tr>
<tr>
<td>9</td>
<td>15.2</td>
</tr>
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* Theoretical rates without therapy: assuming that warfarin provides a 64% relative reduction in TE risk (2.7% ARR), based on Hart et al.

TE = thromboembolism

Balancing the risk – the HASBLED score

One point for each of:

- **H**ypertension is SBP >160mmHg
- **A**bnormal renal function (Cr >200 or dialysis/transplant)
- **A**bnormal liver function (cirrhosis or Bil*2 + ALT/ALP*3)
- **S**troke
- **B**leeding (history or predisposition e.g. bleeding diathesis or anaemia)
- **L**abile INR (TTR<65%)
- **E**lderly (>65yrs)
- **D**rugs: Alcohol >8 units per week
- **D**rugs that increase bleeding risk: NSAIDs, Aspirin, SSRI
The Risk of Stroke Versus Risk of Bleeding

• Some of the risk factors for bleeding are modifiable (which is a very good reason to do the assessment and take action prior to anticoagulation)

  - Hypertension
  - Labile INR (for some)
  - Drugs
  - Alcoholic drinks

• Explain risks versus benefits in plain English to patient / carer
The Shared Decisions

First agree to anticoagulate!
Stroke Prevention: Anticoagulant Effect

Meta-analysis of stroke or systemic embolism

<table>
<thead>
<tr>
<th>Category</th>
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<tbody>
<tr>
<td>W vs Placebo</td>
<td>1</td>
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<tr>
<td>W vs W_{low dose}</td>
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<tr>
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</tr>
<tr>
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<td>1</td>
</tr>
<tr>
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<td>1</td>
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<tr>
<td>W vs Dabigatran 150</td>
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<tr>
<td>W vs Apixaban 5</td>
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Modified from
Camm AJ. EHJ
2009;30:2554-5
## Stroke Prevention: Anticoagulant Effect

### Meta-analysis of stroke or systemic embolism

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Agree the right drug for the patient

- Stroke risk
- Risk of ICH
- Bleeding risk
- Extreme age
- Extreme weight
- Co-morbidities
- Renal function
- Liver function
- TTR

- Risk of side effects
- Need for MDS
- Lack of licensed antidotes for NOACs
- Mitral stenosis or mechanical heart valve
- Adherence with complex regimens
- Compliance issues
- Lack of long term safety data
Checking Renal function

CrCl = (140 – age) x weight (kg) x 1.2 for men

Serum creatinine

- NOTE: eGFR does not allow for weight
- Use IBW or actual if underweight
Locally Agreed Criteria for NOAC Use

NEW PATIENTS

• High risk of interactions with warfarin leading to unacceptable INR fluctuations which cannot be addressed.
• Co-morbidities which make INR control challenging e.g. unstable severe COPD or recurrent cellulitis
• Regular INR monitoring is difficult or impractical after exploring all possible alternatives eg. immobile patients requiring home visits from phlebotomy
• Adherence to variable and complex warfarin dosage regimens is likely to be poor
• Secondary prevention of AF patients with recent stroke or TIA. To be referred by secondary care stroke service
Locally Agreed Criteria for NOAC Use (2)

EXISTING WARFARIN PATIENTS

• Poor INR control (TTR < 65%) despite evidence of compliance

• Allergy to or intolerable side effects from warfarin which would require warfarin withdrawal
<table>
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<th>Patient Characteristic</th>
<th>If NOAC to be used then drug choice</th>
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<td>Mechanical valve or valvular AF</td>
<td>NOACs contra- indicated</td>
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| Severe renal impairment (CrCl <30 ml/min)                                              | NOACs not recommended  
Dabigatran contraindicated. Apixaban and rivaroxaban – Use with caution.                                                                                       |
| Dyspepsia or upper GI symptoms                                                        | Apixaban preferred  
Dyspepsia occurs in 10% of patients on dabigatran                                                                                                                                                                             |
| Recent GI bleed                                                                        | Apixaban preferred. Higher rates of GI bleeding with dabigatran & rivaroxaban compared to warfarin.                                                                                                                                  |
| Recent ischaemic stroke on warfarin                                                   | Dabigatran (at a dose of 150mg bd) is the only NOAC shown to be superior to warfarin in reducing ischaemic stroke                                                                                                                   |
| Recent ACS                                                                             | Rivaroxaban or Apixaban Preferred                                                                                                                                                                                                     |
| Moderate or severe heart failure                                                      | Dabigatran preferred.  
Peripheral oedema reported with rivaroxaban. No data available for apixaban.                                                                                                                                             |
| Poor compliance with twice daily dosing                                               | Rivaroxaban preferred as only NOAC that is once daily administration                                                                                                                                                                |
| Patient requiring a compliance aid e.g. dosette box                                  | Rivaroxaban or apixaban preferred.  
Dabigatran not stable in a compliance aid                                                                                                                      |
Initiation of **ANY** anticoagulant needs full counselling
Doses for AF(1)
(see SPC for full dosing and prescribing information)

**Dabigatran**
- 150 mg BD
- 110 mg BD e.g. if high risk of bleeds, CrCl 30 - 50 ml/min plus other bleeding risk factor, over 75 & considered a moderate risk of a bleed, over 80, very low body weight
- Do not added to Dosette box
- Best with or after food

**Rivaroxaban**
- 20 mg OD
- If CrCl 15 – 49 ml/min 15 mg OD
- Best taken with or after food
Doses for AF (2)
(see SPC for full dosing and prescribing information)

Apixaban

- 5 mg BD

- All patients with creatinine clearance 15 - 29ml/min should receive 2.5 mg twice daily of apixaban.

- In addition if they meet two of the following criteria they should receive the lower dose: serum creatinine 133 micromol/L, age ≥ 80 years or body weight ≤ 60kg.
Side Effects of NOACs

One in Five people stop NOACs due to SEs

**Dabigatran**
Bleeding, dyspepsia, GI bleeding, diarrhoea (liquid stools), malaise, headaches, hallucinations

**Apixaban / Rivaroxaban**
Bleeding, malaise, headaches, insomnia, reduced cognition, hallucinations, mucous membrane bleeding, dyspepsia, loss of appetite, constipation, oedema, pruritis
Avoiding the Pitfalls (1)

• NOACs are anticoagulants
  - Major side effect is bleeding
• Omitted doses cause patient harm
  - Short Half Lives all about 12 hours
• Only ONE anticoagulant at a time
  - No LMWH, fondaparinux or warfarin
Avoiding the Pitfalls (2)

• Avoid antiplatelets
  - same rules as with warfarin
  - include OTC medicines
• Report any possible side effects to MHRA
• Prescribe correct dose for renal function calculated using Cockcroft & Gault
Summary

• Specialist NOAC clinic pathways in Bucks
• Patient risk assessment
• Shared decision making
• Selecting the correct drug and dose for the patient
• Avoiding pitfalls