Anticoagulation for Stroke Prevention in Atrial Fibrillation

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Disclosures

• No disclosures to report
Learning Objectives

1. Define the clinical implications of inadequate anticoagulation in patients with atrial fibrillation

2. Evaluate potential obstacles and solutions regarding treatment regimens for critically ill patients with limited financial resources
Atrial Fibrillation (AF)

• Common cardiac arrhythmia

• Clinical implications
  – Hospitalizations
  – Hemodynamic abnormalities
  – Heart failure
  – Thromboembolic events
  – Dementia
  – Mortality

January et al, J Am Coll Cardiol 2014.
AF and Stroke

• Thromboembolism occurring with AF
  – Greater risk of recurrent stroke
  – More severe disability
  – Mortality

• Stroke prevention
  – Control risk factors
  – Appropriate use of antithrombotic therapy

January et al, J Am Coll Cardiol 2014.
## Stroke Risk Stratification

Adapted from January et al, J Am Coll Cardiol 2014.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Score</th>
<th>CHA₂DS₂-VASc</th>
<th>CHA₂DS₂-VASc†</th>
<th>Adjusted Stroke Rate (% per y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive HF</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>1</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Age ≥75 y</td>
<td>2</td>
<td>2</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
<td>3</td>
<td>3.2</td>
<td></td>
</tr>
<tr>
<td>Stroke/TIA/TE</td>
<td>2</td>
<td>4</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>Vascular disease (prior MI, PAD, or aortic plaque)</td>
<td>1</td>
<td>5</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td>Age 65-74 y</td>
<td>1</td>
<td>6</td>
<td>9.8</td>
<td></td>
</tr>
<tr>
<td>Sex category (i.e., female sex)</td>
<td>1</td>
<td>7</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td>Maximum score</td>
<td>9</td>
<td>8</td>
<td>6.7</td>
<td></td>
</tr>
</tbody>
</table>

- **Adjusted Stroke Rate (9)**: 15.20

Adapted from January et al, J Am Coll Cardiol 2014.
## CHA$_2$DS$_2$-VASc Score

### 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation

<table>
<thead>
<tr>
<th>Score</th>
<th>Recommendation</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Reasonable to omit antithrombotic therapy</td>
<td>B</td>
</tr>
<tr>
<td>1</td>
<td>No antithrombotic therapy or treatment with an oral anticoagulant or aspirin may be considered.</td>
<td>C</td>
</tr>
</tbody>
</table>
| $\geq 2$ | Oral anticoagulants recommended:  
- Warfarin  
- Dabigatran, Rivaroxaban, Apixaban | A, B |

AHA: American Heart Association; ACC: American College of Cardiology; HRS: Heart Rhythm Society; LOE: Level of Evidence

Antithrombotic Therapy

• Antiplatelets
  – Aspirin
  – Aspirin + Clopidogrel

• Anticoagulants
  – Warfarin
  – Novel oral anticoagulants (NOACs)
    • Dabigatran, Rivaroxaban, Apixaban, Edoxaban
  – Parenteral anticoagulants
    • Heparin, Enoxaparin
Antiplatelet Therapy

• Aspirin
  – Not as effective compared to anticoagulation
  – Lower bleeding risk compared to warfarin

• Aspirin + Clopidogrel
  – Not more effective than anticoagulation
  – Adjusted-dose warfarin significantly better
  – Increased bleeding risk compared to aspirin monotherapy

Oral Anticoagulants

Adapted from Nature Reviews Drug Discovery 2009.

Factor XIIa ➔ Factor XIa

→ Tissue factor

Factor VIIa

→ Factor IXa

→ Factor VIIIa

Warfarin

→ Factor IXa

Rivaroxaban
Apixaban
Edoxaban

Factor Xa

→ Factor Va

Factor Va

→ Thrombin

Thrombin ➔ Fibrin

Dabigatran
Safety & Efficacy

• Warfarin (Coumadin®)
  – Reduces risk of stroke and mortality compared with aspirin or no therapy
  – Safe in AF and valvular heart disease

• NOACs vs. Warfarin
  – As effective or better in preventing stroke
  – Lower rate of major bleeding

# NOACs vs. Warfarin

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran (RE-LY)</th>
<th>Rivaroxaban (ROCKET-AF)</th>
<th>Apixaban (ARISTOTLE)</th>
<th>Edoxaban (ENGAGE AF-TIMI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHADS₂ score (mean)</td>
<td>2.1</td>
<td>3.5</td>
<td>2.1</td>
<td>2.8</td>
</tr>
<tr>
<td>Dose</td>
<td>150 mg BID</td>
<td>20 mg daily</td>
<td>5 mg BID</td>
<td>60 mg daily</td>
</tr>
<tr>
<td>Stroke/systemic embolism</td>
<td>↓</td>
<td>↔</td>
<td>↓</td>
<td>↔</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>↓</td>
<td>↔</td>
<td>↔</td>
<td>↔</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>↔</td>
<td>↔</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Intracranial bleeding</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>GI major bleeding</td>
<td>↑</td>
<td>↑</td>
<td>↔</td>
<td>↑</td>
</tr>
</tbody>
</table>

# Oral Anticoagulants

<table>
<thead>
<tr>
<th></th>
<th>Warfarin</th>
<th>Dabigatran</th>
<th>Xa inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing</strong></td>
<td>Once daily</td>
<td>Twice daily</td>
<td>Once or twice daily</td>
</tr>
<tr>
<td><strong>Dose adjustment</strong></td>
<td>Based on INR</td>
<td>Renal</td>
<td>Renal, age, weight</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>Routine</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Drug interactions</strong></td>
<td>Numerous</td>
<td>Less than Warfarin</td>
<td>Less than Warfarin</td>
</tr>
<tr>
<td><strong>Food interactions</strong></td>
<td>Numerous</td>
<td>None</td>
<td>Minimal to none</td>
</tr>
<tr>
<td><strong>Reversal agent</strong></td>
<td>Vitamin K</td>
<td>Idarucizumab</td>
<td>None approved</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>$4/month</td>
<td>~ $400/month</td>
<td>~ $400/month</td>
</tr>
</tbody>
</table>

Parenteral Anticoagulants

- Heparin, Enoxaparin (Lovenox®)

- To bridge or not to bridge?
  - Consider risk of thromboembolism vs. bleeding
  - Bridging beneficial in patients with mechanical heart valves

Inadequate Anticoagulation

- About half of patients with AF are being treated with anticoagulation

- Patients on warfarin spend less than two-thirds of the time within the therapeutic INR range

- One missed NOAC dose can increase risk of thromboembolism due to short half-life

January et al, J Am Coll Cardiol 2014.
Barriers to Anticoagulation

- Knowledge gaps
- Bleeding risk
- Drug-specific concerns
- Financial limitations
  - Drug acquisition
  - Drug monitoring

Drug Acquisition

• Warfarin
  – Generic availability

• Enoxaparin
  – Sanofi Patient Connection

• NOACs
  – Insurance formulary status
  – Patient assistance programs
<table>
<thead>
<tr>
<th>NOACs</th>
<th>Cost/Month</th>
<th>Patient Assistance</th>
</tr>
</thead>
</table>
| Dabigatran (Pradaxa®) | ~ $420 | Pradaxa Savings  
  • Insured – as little as $0/month  
  • Uninsured – 30-day free trial |
| Rivaroxaban (Xarelto®) | ~ $430 | Janssen CarePath  
  • Insured – $0 copay/month  
  • Uninsured – 30-day free trial  
  Johnson & Johnson Patient Assistance Foundation |
| Apixaban (Eliquis®) | ~ $430 | Eliquis 360 Support  
  • Insured – $10/month (up to 24 months)  
  • Uninsured – 30-day free trial |
| Edoxaban (Savaysa®) | ~ $350 | Savaysa Support  
  • Insured – $4/month |
Drug Monitoring

• Monitor warfarin at least weekly during initiation and monthly when stable

• Health centers/clinics
  – Federally Qualified Health Center
  – County healthcare assistance
  – Anticoagulation clinics
Summary

• AF confers an increased risk of stroke

• Anticoagulation therapy can prevent the majority of ischemic strokes in AF patients

• Selection of antithrombotic therapy should be based on discussion of risks and benefits and patient’s preferences
Learning Assessment

Which score is recommended in current guidelines to assess stroke risk in patients with nonvalvular atrial fibrillation?

A. ATRIA
B. CHADS\textsubscript{2}
C. CHA\textsubscript{2}DS\textsubscript{2}-VASc
D. HAS-BLED
Learning Assessment

Which score is recommended in current guidelines to assess stroke risk in patients with nonvalvular atrial fibrillation?

A. ATRIA
B. CHADS$_2$
C. CHA$_2$DS$_2$-VASc
D. HAS-BLED
Learning Assessment

Which oral anticoagulant is recommended for patients with nonvalvular atrial fibrillation and a prior stroke?

A. Apixaban
B. Rivaroxaban
C. Warfarin
D. All of the above
Which oral anticoagulant is recommended for patients with nonvalvular atrial fibrillation and a prior stroke?

A. Apixaban
B. Rivaroxaban
C. Warfarin
D. All of the above