A New Frontier in Anticoagulation:
Practical Issues and Considerations for Atrial Fibrillation Stroke Prevention in the Primary Care

DATE & TIME
February 7, 2013
9:45am — 11:15am

FACULTY
Kelley Branch, MD, MS
Bruce Stambler, MD

LOCATION
Broward County Convention Center
1950 Eisenhower Blvd
Fort Lauderdale, FL 33316-4205
Session 2: A New Frontier in Anticoagulation:
Practical Issues and Considerations for Atrial Fibrillation Stroke Prevention in the Primary Care

Learning Objectives

1. Apply the CHADS2 and HAS-BLED risk stratification tools in clinical practice to determine stroke and bleeding risk in patients with AF.
2. Incorporate current ACCP guideline recommendations and evidence-based approaches for stroke prevention in patients with AF while taking into account the benefit risk ratio of novel anticoagulants for each patient.
3. Recognize the importance of drug interactions, renal dysfunction, storage and handling in the application of novel anticoagulants in clinical practice.
4. Devise strategies to improve patient adherence and optimize outcomes in AF patients on novel anticoagulants undergoing surgery or experiencing bleeding.
5. Implement strategies for safe transitioning of AF patients to and from novel anticoagulants to improve patient outcomes.

Faculty

Bruce S. Stambler, MD
Professor of Medicine
Case Western Reserve University
Cleveland, Ohio

Dr Stambler received his MD from Duke University School of Medicine, Durham, North Carolina. He completed his internship and residency in medicine and his cardiology fellowship at Beth Israel Hospital, Boston, Massachusetts. He completed his fellowship in cardiac electrophysiology at Massachusetts General Hospital, Boston, Massachusetts. Dr Stambler is a practicing cardiac electrophysiologist at University Hospitals Case Medical Center and is professor of medicine at Case Western Reserve University in Cleveland, Ohio. Dr Stambler is a fellow of the American College of Cardiology, the Heart Rhythm Society, and the American Heart Association.

Kelley R. Branch, MD, MS
Assistant Professor in Cardiology
University of Washington Medical Center
Seattle, Washington

Dr Branch is assistant professor in cardiology at the University of Washington in Seattle, Washington. Dr Branch has been part of the University of Washington Medical Center faculty since 2004 and his research focus is in advanced cardiac imaging with a focus on cardiac computed tomography (CT) and magnetic resonance imaging. He also obtained a master’s degree in epidemiology and clinical trials at the University of Washington. He is the current medical director of the coronary care unit and general inpatient cardiology as well as the associate director of the clinical trials service unit at the University of Washington. Dr Branch’s recent awards include the American College of Cardiology (ACC)/Merk Fellowship Award, the Cardiology Teaching Excellence Award, the University of Washington School of Medicine Outstanding Continuing Medical Education Teacher. His most recent research has been focused on the use of cardiac CT in the emergency department, radiation reduction techniques for cardiac CT and myocardial perfusion using CT. Dr Branch’s research support included a National Institutes of Health KL2 Mentored Training Grant. He has been invited to many national and international meetings to lecture on cardiac CT and cardiac imaging. He is a fellow of the ACC.

Faculty Financial Disclosure Statements

The presenting faculty reports the following:
Dr Stambler has served on speakers’ bureaus for Boehringer Ingelheim, Janssen, and Sanofi.
Dr Branch has no financial relationships to disclose.

Education Partner Financial Disclosure Statement

The content collaborators at Horizon CME have reported the following:
Acronym List

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACCP</td>
<td>American College of Chest Physicians</td>
<td>ECT</td>
<td>Ecarin clotting time</td>
</tr>
<tr>
<td>aPTT</td>
<td>activated Partial Thromboplastin Time</td>
<td>PCC</td>
<td>Prothrombin Complex Concentrate</td>
</tr>
<tr>
<td>CrCl</td>
<td>Creatinine Clearance</td>
<td>TT</td>
<td>Thrombin Time</td>
</tr>
</tbody>
</table>

Suggested Reading List


SESSION 2
9:45 AM – 11:15 AM

A New Frontier in Anticoagulation: Practical Issues and Considerations for Atrial Fibrillation Stroke Prevention in Primary Care

SPEAKERS
Bruce S. Stambler, MD
Kelley R. Branch, MD, MS

A New Frontier in Anticoagulation: Practical Issues and Considerations for Atrial Fibrillation Stroke Prevention in Primary Care

Bruce S. Stambler, MD
Professor of Medicine
Case Western Reserve University
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Kelley R. Branch, MD, MS
Assistant Professor in Cardiology
University of Washington Medical Center
Seattle, Washington

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• Implement strategies for safe transitioning of AF patients to and from novel anticoagulants to improve patient outcome

Drug List

<table>
<thead>
<tr>
<th>Generic Drug Name</th>
<th>US Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>amlodipine</td>
<td>Valsartan, Norvasc</td>
</tr>
<tr>
<td>apixaban</td>
<td>Eliquis</td>
</tr>
<tr>
<td>atorvastatin</td>
<td>Lipitor</td>
</tr>
<tr>
<td>dabigatran</td>
<td>Pradaxa</td>
</tr>
<tr>
<td>digoxin</td>
<td>Lanoxin</td>
</tr>
<tr>
<td>dronedarone</td>
<td>Mutlaq</td>
</tr>
<tr>
<td>glipizide</td>
<td>Glucotrol</td>
</tr>
<tr>
<td>glyburide</td>
<td>Diabeta, Glynase, Micronase</td>
</tr>
<tr>
<td>isosorbide dinitrate</td>
<td>Isoptin</td>
</tr>
<tr>
<td>lisinopril</td>
<td>Prinivil, Zestril</td>
</tr>
<tr>
<td>metformin</td>
<td>Glucophage</td>
</tr>
<tr>
<td>metoprolol tartrate</td>
<td>Lopressor</td>
</tr>
<tr>
<td>rivaroxaban</td>
<td>Xarelto</td>
</tr>
<tr>
<td>tinzaparin</td>
<td>Z zieci</td>
</tr>
</tbody>
</table>

Demographic Question

How many patients with atrial fibrillation do you see each week?

1. None
2. 1-10
3. 11-20
4. 21-30
5. Over 30

Presenter Disclosure Information

The following relationships exist related to this presentation:
• Dr Stambler has served on speakers’ bureaus for Boehringer Ingelheim, Janssen, and Sanofi.
• Dr Branch has no financial relationships to disclose.

Off-Label/Investigational Discussion
• In accordance with pmICME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.
Pre-Activity Question 1
Which of the following factors is NOT a component of the CHADS\(_2\) score for stroke risk assessment in patients with nonvalvular atrial fibrillation?

1. Hypertension
2. Dyslipidemia
3. Heart failure
4. Diabetes mellitus
5. Age ≥75 years

Pre-Activity Question 2
Which of the following factors is NOT a component of the HAS-BLED score for bleeding risk assessment in patients with nonvalvular atrial fibrillation?

1. Hypertension
2. History of stroke
3. Renal insufficiency
4. Age ≥55 years
5. Use of alcohol

Pre-Activity Question 3
A 77-year-old male patient with nonvalvular atrial fibrillation has been maintained on dabigatran at 150 mg twice daily for 14 months. He has a CHADS\(_2\) score of 3 (with no history of prior TIA or stroke) and a HAS-BLED score of 2. He has an estimated creatinine clearance of 38 ml/min. He has had worsening knee pain and is in need of arthroscopic surgery. An appropriate preoperative management approach for his dabigatran would be to:

1. Continue dabigatran through surgery without interruption
2. Hold the dabigatran for 12 hours before surgery
3. Hold the dabigatran for 24-48 hours before surgery
4. Hold the dabigatran for 4-5 days before surgery
5. Hold the dabigatran for a minimum of 7 days before surgery

The Consequences of Atrial Fibrillation

Thromboembolism
- Stroke: 4.5 times increased risk
- Microemboli: reduced cognitive function
- Prothrombotic state

Hospitalizations
- Most common arrhythmia requiring hospitalization
- 2.3 times increased risk for hospitalization

Mortality
- Increased risk independent of comorbid CV disease
- Sudden death in HF and HCM

Impaired Hemodynamics
- Loss of atrial kick
- Irregular ventricular contractions
- Tachycardia-induced cardiomyopathy
- HF

- Enormous contributor to the growing cost of medical care

Epidemiology of Stroke in Atrial Fibrillation
- Stroke is the most common and devastating complication of AF
- AF increases stroke risk 4- to 5-fold
- Incidence of all-cause stroke in pts with AF is 5% per year
- Approximately 25-20% of all strokes are due to AF

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Strokes per 1000 PY</th>
<th>Strokes per 1000 PY attributable to Chronic AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 - 69</td>
<td>4.5</td>
<td>21.2</td>
</tr>
<tr>
<td>70 - 79</td>
<td>9.5</td>
<td>48.9</td>
</tr>
<tr>
<td>80 - 89</td>
<td>14.5</td>
<td>71.4</td>
</tr>
</tbody>
</table>

AF=Atrial fibrillation, PY=Patient years

Atrial Fibrillation and Stroke Severity
- Strokes due to AF are associated with greater mortality and disability compared with non-AF related stroke
  - Higher mortality (AF vs. non-AF): OR = 1.84, CI: 1.34-2.57
  - Larger infarcts (52 ml vs. 16 ml, p=0.05)
  - More severe hemorrhagic transformation (25% vs. 5%, p=0.002)

AF=Atrial fibrillation, m=Milliliters
Ability to Predict the Risk of Stroke and Bleeding in Atrial Fibrillation

Stroke Risk Assessment Tools

**CHA2DS2-VASc**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac 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>Diabetees</td>
<td>1</td>
</tr>
<tr>
<td>Vascular disease (MI, peripheral arterial disease, aortic valve disease)</td>
<td>1</td>
</tr>
<tr>
<td>Age 65-74 years</td>
<td>0</td>
</tr>
<tr>
<td>Sex category (female)</td>
<td>1</td>
</tr>
</tbody>
</table>

**CHADS2**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac 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>Diabetees</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>2</td>
</tr>
</tbody>
</table>

**Annual Risk of Stroke (%)**

- **The CHA2DS2-VASc score may be useful when determining risk in a patient with a CHADS2 score of 0 or 1**
- **HAS-BLED study has not yet been validated in other data sets**
- **Score of ≥ 3 indicates ‘high risk’, and some caution and regular patient review is needed following initiation of oral anticoagulant therapy.**
- **INR = International normalized ratio**
- **Hypertension defined as uncontrolled, systolic blood pressure >160 mm Hg**
- **Renal disease is defined as being on dialysis, kidney transplant, or a creatinine >2.6 mg/dL. Liver disease is defined as cirrhosis, bilirubin >2x upper limit of normal, or AST/ALT/alkaline phosphatase >3x upper limit of normal.**
- **Labile INR is defined as unstable and/or high INRs**
- **Drugs/alcohol use refers to concomitant use of drugs, such as antiparallel agents, anti-inflammatory drugs, or alcohol abuse, etc.**

**HAS-BLED Bleeding Risk Score***

<table>
<thead>
<tr>
<th>Letter</th>
<th>Clinical Characteristic</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>Abnormal renal and liver function (1 point each)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>S</td>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>Bleeding</td>
<td>1</td>
</tr>
<tr>
<td>L</td>
<td>Labile INR</td>
<td>1</td>
</tr>
<tr>
<td>E</td>
<td>Elderly (age &gt;65 years)</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>Drugs or alcohol (1 point each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

*Maximum of 9 points

**Annual Risk of Stroke (%)**

- **The CHA2DS2-VASc score may be useful when determining risk in a patient with a CHADS2 score of 0 or 1**

**Efficacy and Limitations of Warfarin for Stroke Prevention in Atrial Fibrillation**

- **HAS-BLED score ≥3 indicates “high risk” of bleeding**
  - Caution and regular review needed following initiation of oral anticoagulant
  - Address correctable bleeding risk factors (e.g. uncontrolled HTN, co-administration of NSAIDs or aspirin, etc.)
- **If HAS-BLED score exceeds CHADS2 score, the risk of major bleeding may outweigh potential benefit of oral anticoagulant**
  - Use in the Euro Heart Survey on AF population could have prevented 12.1% (4/33) of major bleeds
- **HAS-BLED requires validation in other patient cohorts**
  - Not yet adopted by the ACC/AHA/HRS AF guidelines

**Bleeding Risk Assessment Tool**

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<td>S</td>
<td>Stroke</td>
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<tr>
<td>B</td>
<td>Bleeding</td>
<td>1</td>
</tr>
<tr>
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<td>Labile INR</td>
<td>1</td>
</tr>
<tr>
<td>E</td>
<td>Elderly (age &gt;65 years)</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>Drugs or alcohol (1 point each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

*Maximum of 9 points

**Mobile and Web-Based Tools**

**FOCUS-AF CALCULATOR:**

- Free iPhone App
- The American College of Cardiology put together a tool kit for helping clinicians better manage atrial fibrillation.

**Weighing The Risks Ischemic vs. Bleeding**

- HAS-BLED score ≥3 indicates “high risk” of bleeding
  - Caution and regular review needed following initiation of oral anticoagulant
  - Address correctable bleeding risk factors (e.g. uncontrolled HTN, co-administration of NSAIDs or aspirin, etc.)
- If HAS-BLED score exceeds CHADS2 score, the risk of major bleeding may outweigh potential benefit of oral anticoagulant
  - Use in the Euro Heart Survey on AF population could have prevented 12.1% (4/33) of major bleeds
- HAS-BLED requires validation in other patient cohorts
  - Not yet adopted by the ACC/AHA/HRS AF guidelines
**Efficacy of Warfarin on Stroke in AF**

Compared with Control in 6 Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Patients</th>
<th>Number of Events</th>
<th>Number of Patient-years</th>
<th>RRR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFASAK I</td>
<td>9</td>
<td>413</td>
<td>19</td>
<td>398</td>
</tr>
<tr>
<td>SPAF I</td>
<td>8</td>
<td>263</td>
<td>19</td>
<td>245</td>
</tr>
<tr>
<td>BAATAF</td>
<td>3</td>
<td>487</td>
<td>13</td>
<td>435</td>
</tr>
<tr>
<td>CAFA</td>
<td>6</td>
<td>237</td>
<td>9</td>
<td>241</td>
</tr>
<tr>
<td>SPINAF</td>
<td>7</td>
<td>489</td>
<td>23</td>
<td>483</td>
</tr>
<tr>
<td>EAFT</td>
<td>20</td>
<td>507</td>
<td>50</td>
<td>405</td>
</tr>
<tr>
<td>Combined</td>
<td>53</td>
<td>2396</td>
<td>114</td>
<td>2207</td>
</tr>
</tbody>
</table>

*All stroke (ischemic and hemorrhagic)*  
RRR=Relative risk reduction  

**Warfarin’s Narrow Therapeutic Window**

Balancing Efficacy and Safety

<table>
<thead>
<tr>
<th>INR</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>0.6</td>
<td>0.9</td>
</tr>
<tr>
<td>0.8</td>
<td>1.2</td>
</tr>
</tbody>
</table>


**Benefits & Limitations of Warfarin**

- Established therapeutic efficacy  
- Delayed onset/offset  
- Unpredictable dose response  
- Narrow therapeutic range  
- Drug–drug, drug–food interactions  
- Monitoring  
  - Expense  
  - Inconvenience  
- Adverse effects (primarily bleeding)  
- Slow reversibility


**Warfarin Remains Underutilized**

Retrospective cohort study of 171,393 patients to assess the utilization of warfarin within 30 days of an AF/flutter diagnosis among different risk strata*  

<table>
<thead>
<tr>
<th>CHADS2 Score</th>
<th>Low Risk</th>
<th>Moderate Risk</th>
<th>High Risk</th>
<th>Total (N = 171,393)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>22.9 %</td>
<td>56.5 %</td>
<td>40.1 %</td>
<td>40.1 %</td>
</tr>
<tr>
<td>1</td>
<td>30.4 %</td>
<td>50.7 %</td>
<td>40.0 %</td>
<td>40.0 %</td>
</tr>
<tr>
<td>2</td>
<td>36.3 %</td>
<td>49.0 %</td>
<td>40.2 %</td>
<td>40.2 %</td>
</tr>
<tr>
<td>3</td>
<td>43.0 %</td>
<td>40.4 %</td>
<td>39.7 %</td>
<td>39.7 %</td>
</tr>
<tr>
<td>4</td>
<td>46.1 %</td>
<td>42.1 %</td>
<td>40.8 %</td>
<td>40.8 %</td>
</tr>
<tr>
<td>5</td>
<td>42.1 %</td>
<td>40.8 %</td>
<td>40.0 %</td>
<td>40.0 %</td>
</tr>
<tr>
<td>6</td>
<td>43.0 %</td>
<td>40.2 %</td>
<td>39.7 %</td>
<td>39.7 %</td>
</tr>
</tbody>
</table>

*Hatched area represents the proportion of patients with uninterrupted therapy over 180 days following initial warfarin prescription  

**The Use of Novel Anticoagulants for Stroke Prevention in Atrial Fibrillation**
Sites of Action for the Novel Anticoagulants

**Intrinsic**
- XI
- IX
- VIII
- VII

**Extrinsic**
- TF
- V
- VIIIa
- Fibrinogen
- Fibrin Clot

**Xa Inhibitors**
- Apixaban
- Betrixaban*
- Edoxaban
- Rivaroxaban

**Mechanism of Action**
- Thrombin inhibitor
- Factor Xa inhibitor
- Factor Xa inhibitor
- Factor Xa inhibitor

**T1/2**
- Dabigatran: 14-17 hours
- Rivaroxaban: 5-9 hours
- Apixaban: 12 hours
- Betrixaban: 12 hours
- Edoxaban: 19-24 hours
- Rivaroxaban: 6-12 hours

P-values are for superiority. The 110 mg twice daily is not presented as this dose was not approved by the FDA.

AF=Atrial Fibrillation, FDA=US Food and Drug Administration, GI=Gastrointestinal, MI=Myocardial infarction, TTR=Time in therapeutic range

*Not currently FDA approved

**Characteristics of the Novel Anticoagulants**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Betrixaban*</th>
<th>Edoxaban*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of action</td>
<td>Thrombin inhibitor</td>
<td>Factor Xa inhibitor</td>
<td>Factor Xa inhibitor</td>
<td>Factor Xa inhibitor</td>
<td>Factor Xa inhibitor</td>
</tr>
<tr>
<td>T1/2</td>
<td>14-17 hours</td>
<td>5-9 hours</td>
<td>12 hours</td>
<td>19-24 hours</td>
<td>6-12 hours</td>
</tr>
<tr>
<td>Regimen</td>
<td>BID</td>
<td>QD</td>
<td>BID</td>
<td>QD</td>
<td>QD</td>
</tr>
<tr>
<td>Peak to trough</td>
<td>2.5</td>
<td>12 (QD)</td>
<td>3-5</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Renal excretion of absorbed drug</td>
<td>~80%</td>
<td>36%-45%</td>
<td>25%-30%</td>
<td>~15%</td>
<td>35%</td>
</tr>
</tbody>
</table>

Potential for drug interactions:
- p-glycoprotein CYP3A4 = cytochrome P450 3A4
- PGP= P-glycoprotein

*Not currently FDA approved

**ARISTOTLE**

*Patients with AF+1: TIA/CVA/embolism, >75 years, History CHF or LVEF ≤40, DM, MI*

18,201 patients with AF randomized to rivaroxaban (15-20 mg daily) for a median of 1.6 years

P-value for superiority: P<0.001

**RE-LY Trial**

18,113 patients with nonvalvular AF randomized to warfarin (goal INR 2-3), dabigatran (150 mg BID), or dabigatran (110 mg BID) for a median of 2 years

150 mg twice daily

Warfarin INR 2.0-3.0 TTR=67%

P-value for superiority: P<0.001

**ROCKET AF Trial**

14,264 patients with nonvalvular AF randomized to warfarin (goal INR 2-3) or rivaroxaban (15-20 mg daily) for a median of 1.6 years

Hazard ratio 0.88 (95% CI 0.75 -1.03)

P-value for superiority: P<0.001

**Guideline Recommendations for Antithrombotic Therapy in Atrial Fibrillation**

- G=Giastrointestinal, MI=Myocardial infarction, TTR=Time in therapeutic range
- PGP= P-glycoprotein

*Not currently FDA approved

**Am J Health Syst Pharm** 2008;65:1520-1529.


**Chest.** 2001;119:95S-107S, Gulseth MP et al.

**Gut.** 2009;58:1234-1243.

**Am J Health Syst Pharm.** 2010;67:1855-1858.

**Am J Health Syst Pharm.** 2010;67:1855-1858.


**Am J Health Syst Pharm.** 2010;67:1855-1858.
### ACC/AHA/HRS 2011 AF Guidelines

**Antithrombotic therapy recommendations to prevent stroke**

<table>
<thead>
<tr>
<th>Less Validated or Weaker Risk Factors</th>
<th>Moderate-Risk Factors</th>
<th>High-Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>Age ≥ 75 years</td>
<td>Previous stroke</td>
</tr>
<tr>
<td>65-74 years of age</td>
<td>HTN</td>
<td>TIÁ or embolism</td>
</tr>
<tr>
<td>CAD</td>
<td>HF</td>
<td>Mitral stenosis</td>
</tr>
<tr>
<td>Thyrotoxicosis</td>
<td>LVEF ≤ 35%</td>
<td>Prosthetic heart valve</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ACC=American College of Cardiology, AHA=American Heart Association, HRS=Heart Rhythm Society

### ACCP 2012 AF Guidelines

**Antithrombotic therapy recommendations to prevent stroke**

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>CHADS2 Score</th>
<th>Recommended Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factors</td>
<td>0</td>
<td>ASA 81-325 mg QD</td>
</tr>
<tr>
<td>1 moderate-risk factor</td>
<td>1</td>
<td>ASA 81-325 mg QD or Warfarin (INR 2.0-3.0) or Dabigatran 150 mg BID</td>
</tr>
<tr>
<td>Any high-risk factor or &gt;1 moderate-risk factor</td>
<td>2</td>
<td>Warfarin (INR 2.0-3.0, target 2.5) or Dabigatran 150 mg BID</td>
</tr>
</tbody>
</table>

OAC* ≥ 2

Dabigatran 150mg twice daily preferred over a vitamin K antagonist

ACCP=American College of Chest Physicians, OAC=Oral anticoagulant


### Dosing, Boxed Warnings, Drug Interactions, and Storage of the Novel Anticoagulants

#### Indications for Use

**Novel Anticoagulants**

- Apixaban, Dabigatran and Rivaroxaban
  - “...indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.”
  - Not approved for use in patients with prosthetic heart valves

#### Dosing of the Novel Anticoagulants

- **Apixaban:**
  - 5 mg twice daily for most patients
  - 2.5 mg twice daily in patients with any 2 of the following: age ≥ 80 years, Body weight ≤ 60 kg, and Serum creatinine ≥ 1.5 mg/dL
  - Avoid use if Cr Cl < 15 ml/min
  - Peak plasma concentrations can be achieved in 3.5 hrs and steady state achieved in 3 days

Boxed Warnings

Apixaban:
- "WARNING: Discontinuing apixaban in patients without adequate continuous anticoagulation increases risk of stroke"
- "Discontinuing apixaban places patients at an increased risk of thrombotic events. An increased rate of stroke was observed following discontinuation of apixaban in clinical trials in patients with nonvalvular atrial fibrillation. If anticoagulation with apixaban must be discontinued for a reason other than pathological bleeding, coverage with another anticoagulant should be strongly considered."

Dabigatran:
- None

Dosing of the Novel Anticoagulants Continued

- Dabigatran:
  - 150 mg twice daily if CrCl >30 ml/min (with or without food)
  - 75 mg twice daily if CrCl 15-30 ml/min (with or without food)
  - Avoid use if CrCl <15 ml/min
  - Peak plasma concentrations can be achieved in 0.5 to 2 hrs and steady state achieved in ~3 days

- Rivaroxaban:
  - 20 mg once daily with the evening meal if CrCl >50 ml/min
  - 15 mg once daily with the evening meal if CrCl 15-50 ml/min
  - Avoid use if CrCl <15 ml/min
  - Peak plasma concentrations can be achieved in 2 to 4 hrs and steady state achieved in ~6 days

Boxed Warnings Continued

Rivaroxaban:
- "Discontinuing rivaroxaban places patients at an increased risk of thrombotic events. An increased rate of stroke was observed following rivaroxaban discontinuation. If anticoagulation with rivaroxaban must be discontinued for a reason other than pathologic bleeding, consider administering another anticoagulant."
- Epidural or spinal hematomas have occurred in patients treated with rivaroxaban who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures.

Drug – Drug Interactions Continued

- Apixaban: Metabolized by CYP 3A4 and substrate of P-glycoprotein
  - Decrease dose to 2.5 mg twice daily in patients taking strong dual inhibitors of CYP 3A4 and P-glycoprotein (e.g., ketoconazole, itraconazole, ritonavir)
  - Avoid coadministration of strong dual inducers of CYP 3A4 and P-glycoprotein in patients already taking 2.5 mg twice daily

- Dabigatran: Metabolized by P-glycoprotein
  - Decrease the dose to 75 mg twice daily if coadministered with a P-glycoprotein inhibitor (e.g., dronedarone, systemic ketoconazole) and the CrCl is 30-39 ml/min
  - Avoid if coadministered with a P-glycoprotein inhibitor (e.g., dronedarone, systemic ketoconazole) and the CrCl is <30 ml/min
  - Avoid in conjunction with P-glycoprotein inducers (e.g., rifampin)

- Rivaroxaban: Metabolized by P-glycoprotein and CYP3A4
  - Avoid in conjunction with P-glycoprotein and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, etc.)
  - Avoid in conjunction with P-glycoprotein and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, St. John’s wort)
What to do for a Missed Dose?

- **Apixaban:**
  - Take as soon as possible on the same day
  - Do not double up on the dose to make up for a missed dose
- **Dabigatran:**
  - Take as soon as possible on the same day
  - Do not take the missed dose if it is within 6 hours of the next
    scheduled dose
  - Do not double up on the dose to make up for a missed dose
- **Rivaroxaban:**
  - Take as soon as possible on the same day

Storage Recommendations

- **Apixaban:**
  - Tablets in unit-of-use bottle or hospital unit-dose blister packages
  - Store at room temperature
- **Rivaroxaban:**
  - Tablets in unit-of-use bottle or blister packages
  - Store at room temperature

Storage Recommendations Continued

- **Dabigatran:**
  - Capsules packaged in two ways:
    - unit-of-use bottle (contains a desiccant in the cap)
    - unit dose blister package
  - Store in and dispense from the original bottle/package to
    protect from moisture
  - Once the bottle is opened, all capsules should be used
    within 4 months
  - If dispensed more than one bottle, open one bottle at a time
  - Do not repackage or place capsules in pill boxes/organizers

Managing the Risk of Periprocedural and Spontaneous Bleeding with the Novel Anticoagulants

Periprocedural Anticoagulant Management

- Discontinuing anticoagulants for elective surgery or invasive procedures places patients at an increased risk of stroke
  - There are no validated risk stratification schemes to estimate risk for peri-operative stroke or thromboembolism in patients with AF
- In high risk patients (ie CHADS2 >4, recent stroke/TIA), bridging may be advisable
- If anticoagulants must be temporarily discontinued, therapy should be restarted as soon as possible based on the clinical situation when adequate hemostasis has been established
- If oral medication cannot be taken after surgical intervention, consider administering a parenteral anticoagulant

NOTE: If apixaban, dabigatran or rivaroxaban must be discontinued for a reason other than pathological bleeding, consider administering another anticoagulant.


Periprocedural Anticoagulant Management Continued

- **Stop apixaban** at least 48-hours prior to elective surgery or invasive procedures with a moderate or high risk of clinically significant bleeding;
- **Stop apixaban** at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding
- **Stop dabigatran** 1-2 days (CrCl ≥ 50 mL/min) or 3-5 days (CrCl < 50 mL/min) before elective invasive or surgical procedures
- **Stop rivaroxaban** at least 24 hours before elective invasive or surgical procedures

Food and Drug Administration. Drugs@FDA – Rivaroxaban or Dabigatran or Apixaban. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm
Periprocedural Anticoagulant Management Continued

- If surgery cannot be delayed, there is an increased risk of bleeding in patients receiving anticoagulants
  - Risk of bleeding should be weighed against the urgency of intervention
  - Consider longer discontinuation times for patients undergoing major surgery, spinal puncture, or placement of a spinal or epidural catheter or port, in whom complete hemostasis may be required

Monitoring Anticoagulation

- Normally there is NO indication for anticoagulation monitoring of novel agents
- Agents can prolong various clotting tests
  - DO NOT provide a reliable and accurate prediction of a patient’s coagulation status
  - Apixaban:
    - Prolongs clotting tests: prothrombin time (PT), INR and activated partial thromboplastin time (aPTT)
    - Not recommended to monitor anticoagulation effect of apixaban

Monitoring Anticoagulation Continued

- Dabigatran:
  - The coagulation status can be assessed using the aPTT, ECT, and TT
  - The INR cannot be interpreted in the same way as with warfarin
  - The aPTT is the most widely available test with a level of 40 seconds corresponding to the lowest 10th percentile in the RE-LY trial
- Rivaroxaban:
  - The coagulation status can be assessed using the PT/INR, aPTT, HepTest, and Anti-factor Xa activity
  - Among the more widely available tests, the PT/INR is more sensitive than the aPTT

Managing Active Pathologic Bleeding

- Discontinue apixaban, dabigatran, or rivaroxaban
- Investigate the source of bleeding
- Consider transfusion of fresh frozen plasma or red blood cells
- Consider dialysis for dabigatran ONLY
  - Dabigatran can be dialyzed (protein binding is low) with removal of about 60% of drug over 2–3 hrs
  - Rivaroxaban and apixaban are not expected to be dialyzable (high plasma protein binding 92–93% and 87%, respectively)
- Consider measurement of aPTT (dabigatran) or PT/INR (rivaroxaban) to guide therapy

Reversal of Anticoagulation Effect

- Specific reversal agents (“antidotes”) for new anticoagulant agents are unavailable but being investigated
- Consider prothrombin complex concentrate (PCC) for reversal although clinical trial data is limited
- Consider administration of recombinant Factor VIIa, or concentrates of coagulation factors although clinical trial data is limited
- Protamine sulfate and vitamin K are NOT expected to affect the anticoagulant activity of apixaban, dabigatran or rivaroxaban

Dabigatran Associated Major Bleeding Does Not Increase Mortality Compared to Warfarin

<table>
<thead>
<tr>
<th></th>
<th>Warfarin</th>
<th>Dabigatran</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Bleeds in RE-LY Study</td>
<td>421</td>
<td>741</td>
<td>0.0013</td>
</tr>
<tr>
<td>Transfused with red blood cells</td>
<td>50%</td>
<td>59%</td>
<td></td>
</tr>
<tr>
<td>Transfused with plasma</td>
<td>30%</td>
<td>20%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean length of ICU stay (days)</td>
<td>3.2</td>
<td>1.9</td>
<td>0.03</td>
</tr>
<tr>
<td>Surgery to stop bleeding</td>
<td>14%</td>
<td>9%</td>
<td>0.09</td>
</tr>
<tr>
<td>Major Bleeds From 5 Phase III Trials</td>
<td>425</td>
<td>696</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>30-day mortality after 1st major bleed*</td>
<td>13.0%</td>
<td>9.1%</td>
<td>0.007</td>
</tr>
</tbody>
</table>

*Patients who experienced a major bleed on dabigatran had a significant 46% lower mortality rate than those who had a major bleed on warfarin.

Food and Drug Administration. Drugs@FDA – Rivaroxaban or Dabigatran or Apixaban. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

Food and Drug Administration. Drugs@FDA - Rivaroxaban or Dabigatran. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

Switching Anticoagulants

<table>
<thead>
<tr>
<th>Transitioning to and from the Novel Anticoagulants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin to Dabigatran: Stop warfarin and start dabigatran when the INR &lt; 2.0.</td>
</tr>
<tr>
<td>Rivaroxaban to Parenteral or Rapid Onset Anticoagulant: Start rivaroxaban 0-2 hrs prior to next scheduled evening administration of the drug.</td>
</tr>
<tr>
<td>Dabigatran to Parenteral Anticoagulant: Start dabigatran 0-2 hrs before time of next dose of intermittently administered parenteral anticoagulant (e.g., IV heparin, etc).</td>
</tr>
<tr>
<td>Rivaroxaban to Warfarin: Stop warfarin and start rivaroxaban as soon as the INR &lt; 3.0.</td>
</tr>
<tr>
<td>Warfarin to Apixaban: No clinical data available to guide converting patients from rivaroxaban to warfarin.</td>
</tr>
</tbody>
</table>

Summary

- Stroke is the most devastating and feared complication of AF.
- The risk of stroke in patients with AF is heterogeneous and modulated significantly by co-morbidities.
  - Risk stratification is a critical step in prevention of AF-related stroke.
  - The CHADS2 and CHA2DS2-VASc scores help to stratify this risk.
- An assessment of bleeding risk should be part of an AF evaluation before starting anticoagulation.
  - The HAS-BLED score is helpful in assessing bleeding risk, with scores ≥3 indicating high bleeding risk.
  - Clinical judgment (e.g., fall risk) still important.

Switching Anticoagulants Continued

| Warfarin to Apixaban – Rivaroxaban or Dabigatran: Discontinue anticoagulant being taken and begin the other at the next scheduled dose. |
| Dabigatran to Warfarin – When to start warfarin prior to stopping dabigatran: |
| - CrCl > 15 mL/min: Start warfarin 12 hours after last dose of dabigatran. |
| - CrCl 15-30 mL/min: Start warfarin 48 hours after last dose of dabigatran. |
| - CrCl < 15 mL/min: No recommendation can be made. |
| Apixaban to Parenteral or Rapid Onset Anticoagulant: |
| - Discontinue apixaban 12 hours after last dose of apixaban. |
| - Begin both a parenteral anticoagulant and warfarin at the time the next dose of apixaban would have been taken. |

Summary Continued

- Warfarin is highly effective in preventing stroke in at risk AF patients; however, its numerous drawbacks limit its use.
- The novel anticoagulants (apixaban, dabigatran and rivaroxaban) have: Superior (apixaban & dabigatran) or comparable (rivaroxaban) efficacy to warfarin.
- Lower risk of intracranial hemorrhage.
- Rapid onset and offset.
- No need for anticoagulation monitoring.
- A higher risk of GI bleeding (dabigatran & rivaroxaban, not apixaban).
- Limited or No reversal agents at present.
- Appropriate use of the novel anticoagulants can improve outcomes and minimize bleeding complications.
Summary Continued

• Adjust dose for apixaban, dabigatran and rivaroxaban with renal insufficiency
• Caution when using with CYP3A4 (apixaban, rivaroxaban) or P-glycoprotein (both) antagonists
• Emergent reversal
  – Dialysis with dabigatran
  – Prothrombin complex concentrate, recombinant Factor VIIa, or concentrates of coagulation factors (clinical trial data limited)
  – Use of procoagulant reversal agents has not been evaluated in clinical studies with apixaban
  – Additional reversal agents under investigation
• Dabigatran should be kept from moisture, not in pill packs

Post-Activity Question 1

Which of the following factors is NOT a component of the CHADS<sub>2</sub> score for stroke risk assessment in patients with nonvalvular atrial fibrillation?

1. Hypertension
2. Dyslipidemia
3. Heart failure
4. Diabetes mellitus
5. Age >75 years

Post-Activity Question 2

Which of the following factors is NOT a component of the HAS-BLED score for bleeding risk assessment in patients with nonvalvular atrial fibrillation?

1. Hypertension
2. History of stroke
3. Renal insufficiency
4. Age >55 years
5. Use of alcohol

Post-Activity Question 3

A 77-year-old male patient with nonvalvular atrial fibrillation has been maintained on dabigatran at 150 mg twice daily for 14 months. He has a CHADS<sub>2</sub> score of 3 (with no history of prior TIA or stroke) and a HAS-BLED score of 2. He has an estimated creatinine clearance of 58 ml/min. He has had worsening knee pain and is in need of arthroscopic surgery. An appropriate preoperative management approach for his dabigatran would be to:

1. Continue dabigatran through surgery without interruption
2. Hold the dabigatran for 12 hours before surgery
3. Hold the dabigatran for 24-48 hours before surgery
4. Hold the dabigatran for 4-5 days before surgery
5. Hold the dabigatran for a minimum of 7 days before surgery

Patient Case Discussion
**Case 1: Presentation**

HPI: A 76-year-old man presents to your office with 3 days of palpitations and shortness of breath. These symptoms are new for him and came on rather abruptly. He describes the palpitations as a sensation that his "heart is racing".

He denies complaints of chest pain, pressure, or heaviness. He denies lightheadedness, presyncope, or syncope. He has, however, noted increased fatigue which he has attributed to "less sleep than usual.

Past Medical History: Hypertension, diabetes mellitus, dyslipidemia, and obstructive sleep apnea on CPAP.

Past Surgical History: Hernia repair at age 35, tonsillectomy at age 6.

Social History: Former smoker (1.5 packs/day x 35 years, quit 2006).

Up to 3 alcoholic beverages/week. No illicit drug use

Family History: No arrhythmia history.

**Case 1: Medications**

Current Medications:

- Lisinopril 10 mg daily
- Amlodipine 5 mg daily
- Simvastatin 10 mg QHS
- Metformin 850 mg BID
- Glipizide 5 mg BID

**Case 1: Evaluation**

**Physical Exam:**

Vitals: HR=119, BP=162/78, Height=73 inches, Weight=289 lbs, BMI=38.1

General: Well appearing obese man in no apparent distress

HEENT: Unremarkable, normal thyroid examination

Nec: Preserved carotid upstrokes without bruits, JVP=4 cm water

CV: Irregularly irregular rhythm with a normal S1 and S2. No S3.

No murmurs, thrills, gallops, or rubs

Lungs: Mild end expiratory wheeze, no crackles, fair air movement

Abdomen: Obese, no organomegaly, soft, normal active bowel sounds

Extremities: No cyanosis, clubbing, or edema, 2+ distal pulses

**ECG:** Atrial fibrillation with a rate of 124 bpm. There is left axis deviation with normal intervals. There are nonspecific ST and T wave changes. No Q waves.

**Labs:** Normal basic chemicals except a BUN of 32 and creatinine of 1.6 (creatinine clearance of 73.3 ml/min). TSH of 2.4 (normal). His liver function tests are normal.

**Case 1: Question 1**

What are the patient’s CHADS2 and HAS-BLED scores?

1. CHADS2 score of 1 and HAS-BLED score of 3
2. CHADS2 score of 2 and HAS-BLED score of 2
3. CHADS2 score of 3 and HAS-BLED score of 2
4. CHADS2 score of 3 and HAS-BLED score of 3
5. CHADS2 score of 4 and HAS-BLED score of 3

**Case 1: Question 2**

Based on the patient’s CHADS2 and HAS-BLED scores, which of the following antithrombotic agents are recommended therapeutic options?

1. Aspirin (75-325 mg) only
2. Aspirin (75-325 mg) or warfarin (goal INR of 2-3)
3. Aspirin (75-325 mg) or dabigatran (150 mg twice daily)
4. Warfarin (goal INR of 2-3) or rivaroxaban (20 mg daily)
5. Warfarin (goal INR of 2-3), apixaban (5 mg twice daily), dabigatran (150 mg twice daily), or rivaroxaban (20 mg daily)
Case 1: Question 3

He started on warfarin with a goal INR of 2-3. Over the course of the subsequent 3 months, he is noted to have difficulty in maintaining his INR in the therapeutic range. The 6 most recent INR measurements have been 2.3, 2.5, 2.9, 3.7, 3.3, and 2.6. Given this, a decision is made to switch him to dabigatran at 150 mg twice daily. This should be done when he:

1. Has an INR that is <3.0
2. Has an INR that is <2.0
3. Has held his warfarin for 1 day
4. Has held his warfarin for 3 days
5. Has held his warfarin for 5 days

Case 2: Presentation

HPI: A 67-year-old woman presents to your office as a follow up to an emergency department visit the evening before for new onset atrial fibrillation. She presented with complaints of profound fatigue and palpitations for 8 hours and was found to have a rapid heart rate of 109 bpm.

Given her symptoms and the well defined timing of onset, she was cardioverted to sinus rhythm.

Past Medical History: Hypertension and coronary artery disease.

Past Surgical History: Hysterectomy at age 46.

Social History: Former smoker (2 packs/day x 40 years, quit 2010). No alcohol or illicit drug use.

Family History: Her father underwent implantation of a permanent pacemaker at age 87.

Case 2: Evaluation

**Physical Exam:**
- Vitals: HR=66, BP=118/64, Height=65 inches, Weight=188 lbs, BMI=34.4
- General: Well appearing woman in no apparent distress
- HEENT: Unremarkable, normal thyroid examination
- Neck: Preserved carotid upstrokes without bruits, JVP=5 cm water
- CV: Normal sinus rhythm with a normal S1 and S2. No 53 or 54.
- No murmurs, thrills, gurgles, or rubs
- Lungs: Clear to auscultation bilaterally without wheezes/crackles
- Abdomen: Obese, no organomegaly, soft, normal active bowel sounds
- Extremities: No cyanosis, clubbing, or edema, 2+ distal pulses

**ECG:** Normal sinus rhythm with a rate of 62 bpm. There is left axis deviation with normal intervals. There are no ischemic ST/T wave changes. There are no Q waves

**Labs:** Normal basic chemistries except a BUN of 46 and creatinine of 1.8 (creatinine clearance of 42.9 ml/min). TSH of 1.8 (normal). Her liver function tests are normal.

Case 2: Medications

**Current Medications:**
- **Aspirin 81 mg daily**
- **Metoprolol tartrate 25 mg BID (started in the emergency department)**
- **Amlodipine 5 mg daily**
- **Atorvastatin 40 mg daily**

Dosing of the Novel Anticoagulants

- **Apixaban**:
  - 5 mg twice daily for most patients
  - 2.5 mg twice daily in patients with any 2 of the following:
    - age ≥ 80 years
    - Body weight ≤ 60 kg
    - Serum creatinine ≥ 1.5 mg/dL
  - Avoid use if Cr Cl < 15
  - Peak plasma concentrations can be achieved in 3-5 hrs and steady state achieved in 3 days

Dosing of the Novel Anticoagulants Continued

• Dabigatran:
  - 150 mg twice daily if CrCl ≥30 ml/min (with or without food)
  - 75 mg twice daily if CrCl 35–70 ml/min (with or without food)
  - Avoid use if CrCl <35 ml/min.
  - Peak plasma concentrations can be achieved in 0.5 to 2 hrs and steady state achieved in ~3 days

Food and Drug Administration. Drugs@FDA – Dabigatran. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

Dosing of the Novel Anticoagulants Continued

• Rivaroxaban:
  - 20 mg once daily with the evening meal if CrCl >50 ml/min
  - 15 mg once daily with the evening meal if CrCl 15–50 ml/min
  - Avoid use if CrCl <15 ml/min.
  - Peak plasma concentrations can be achieved in 2 to 4 hrs and steady state achieved in ~6 days

Food and Drug Administration. Drugs@FDA – Rivaroxaban. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

Case 2: Question 2

You start her on rivaroxaban at 15 mg/day. She tolerates this well without any bleeding complications.

She returns for a follow up visit 8 months later with progressive knee pain. She has been told that she needs arthroscopic surgery in the next few weeks. Her orthopedic surgeon requests that she be taken off of her anticoagulant for surgery. How should you manage her preoperative anticoagulation?

1. Stop the rivaroxaban 6 hours before surgery
2. Stop the rivaroxaban 12 hours before surgery
3. Stop the rivaroxaban for at least 24 hours before surgery
4. Stop the rivaroxaban for at least 3 days
5. Stop the rivaroxaban for at least 5 days

Case 2: Question 3

She is reintiated on rivaroxaban after her surgery without complication.

About 9 months later, she presents to her local emergency department with worsening fatigue and 3 days of melena. She is found to have a hemoglobin level of 7.6 mg/dL.

She is admitted to the hospital. Beyond stopping the rivaroxaban and transfusing her with packed red blood cells, which of the following should NOT be considered for managing her pathologic bleeding?

1. Administer fresh frozen plasma
2. Check her INR level
3. Administer prothrombin complex concentrate
4. Administer recombinant Factor VIII
5. Dialysis

Case 3: Presentation

HPI: A 64 year old man presents to your office after recently relocating to the area. He reports feeling well. He predominantly comes to establish care.

Past Medical History: Hypertension, dyslipidemia, diabetes mellitus, paroxysmal atrial fibrillation, coronary artery disease with prior percutaneous coronary intervention (age 61), peripheral arterial disease, and chronic renal insufficiency.

Past Surgical History: Femoral-femoral bypass (age 58), carotid endarterectomy (age 63).

Social History: Active smoker (1 pack/day x 45 years).
Up to 3 alcohol beverages per day. No illicit drug use.

Family History: His father died at age 54 from a myocardial infarction. His mother underwent placement of a permanent pacemaker at age 81 for “a slow heart beat”.

Case 3: Evaluation

Physical Exam:
Vitals: HR=78, BP=138/92, Height=69 inches, Weight=202 lbs, BMI=39.8
General: Mildly ill appearing man
HEENT: Unremarkable, normal thyroid examination
Neck: Bilateral carotid bruits, JVP=7 cm water
CV: Irregularly irregular rhythm with a normal S1 and S2. No S3. A 2/6 holosystolic murmur best heard at the apex. No thrills, gallops, or rubs
Lungs: Clear to auscultation bilaterally without wheezes/crackles
Abdomen: Obese, no organomegaly, soft, normal active bowel sounds
Extremities: No cyanosis, clubbing, or edema, trace distal pulses

ECG: Atrial fibrillation at a rate of 92 bpm.

Left axis deviation with a nonspecific intraventricular conduction delay.
No specific ST/T wave changes.
No Q waves.

Labs: Normal basic chemistries except a BUN of 24 and creatinine of 3.2 (creatinine clearance of 48.0 ml/min). Liver function tests are normal.
Case 3: Medications

Current Medications:
- Aspirin 81 mg daily
- Metoprolol tartrate 50 mg BID
- Digoxin 0.125 mg daily
- Isosorbide dinitrate 20 mg BID
- Simvastatin 40 mg QHS
- Glyburide 5 mg BID

Case 3: Question 1

Based on his CHADS2 score of 2, CHA2DS2-VASc score of 3, HAS-BLED score of 3, and Creatinine Clearance of 48.0 ml/min, you decide to start him on dabigatran at 150 mg twice daily. How long will it take to achieve full anticoagulation after the initial dose?

1. <1 hour
2. 2-4 hours
3. 1 day
4. 2 days
5. 4 days

Case 3: Question 2

Because of continued paroxysms of symptomatic atrial fibrillation, you decide to start him on dronedarone as antiarrhythmic therapy. What (if any) dose adjustment for the dabigatran is required?

1. Change to 150 mg daily
2. Change to 110 mg twice daily
3. Change to 75 mg daily
4. Change to 75 mg twice daily
5. No change in dose is required

Case 3: Question 3

About 6 weeks into treatment with dabigatran, he notices increased heartburn symptoms. This is not improved with the use of an over the counter proton pump inhibitor. You attribute his dyspepsia to the dabigatran and decide to switch him to warfarin. The warfarin should be started how many days before discontinuing the dabigatran?

1. 1 day
2. 2 days
3. 3 days
4. 4 days
5. 5 days

Question & Answer