Atrial Fibrillation in the Emergency Department
Disclosures

• Edward Jauch, MD MS

• Research support
  – National Institutes of Health funding (multiple trials)
  – Novo Nordisk (drug in kind) STOP-IT Study
  – Genentech (drug in kind) PRISMS Study
  – Cleveland Clinic (lab in kind) Genomics Study

• None related to this subject
Disclosures

• Brett Cucchiara, MD
• Research Support
  – National Institutes of Health (multiple trials)
  – Bristol Myers Squibb
• None related to this subject
Webinar Overview

• Review epidemiology of atrial fibrillation
• Review existing guidelines for overall management
• Discuss risk assessment tools
  – Future cardioembolic risks
  – Treatment risk assessment
• Integration of management with primary care
Outline

• Epidemiology
• Signs and Symptoms
• Management
Epidemiology

• Most frequently diagnosed arrhythmia
• Affects 2.7 million people in the US with 12 million by 2050
• Incidence increases with age
  – 4% over age of 60 years
  – 8% over age of 80 years
Prevalence of Atrial Fibrillation

Epidemiology

• Atrial fibrillation carries risk
  – 1.5-1.9 higher risk of death
  – Thromboembolic events primary risk (5x stroke risk)
  – Associated with worse New York Heart Association Heart Failure classification

(CDC Fact Sheet, 2010)
Atrial Fibrillation Hospitalization 2000-2006
Classification

- Paroxysmal  Lasts < 7 days
- Persistent   Duration exceeds 7 days
- Permanent   Persists > 1 year

Diagram:
- First diagnosis of AF
  - Paroxysmal
  - Persistent
  - Permanent
  - Paroxysmal
  - Persistent
  - Permanent
Prevalence of Afib and Anticoagulation in the Emergency Department

- Prevalence in ED population of 1.10%
- 64% with prior afib history
  - 40% on warfarin (61% out of range)
  - 28% antiplatelet therapy
  - 5% warfarin and antiplatelet
  - 27% none (24% eligible)

(Scott. Stroke. 2002;33:2664-2669)
Patients with Afib in the ED

• 3 year period in province of Ontario
• 12,772 index ED visits (discharged home)
  – Repeat visits within 14 days (10.3%)
    • 0.7% mortality
    • 67.6% no followup / 19.4% PCP / 12.8% “specialist”
    • “Specialist” followup HR 0.61 (p=0.003)
  – 90 day mortality 3.3%
    • Filled warfarin rx HR 0.70

Signs and Symptoms

- Irregular or rapid heartbeat
- Palpitations
- Lightheadedness
- Extreme fatigue
- Shortness of breath
- Chest pain

- Asymptomatic

(CDC Fact Sheet, 2010)
Risk Factors

- Hemodynamic stress (valve disease, LV dysfn)
- Atrial ischemia
- Inflammation (myocarditis, pericarditis)
- Noncardiovascular respiratory causes
- Alcohol and drug use
- Endocrine disorders (hyperthyroidism, diabetes)
- Genetic factors
- Advancing age
Management

- Rate control
- Rhythm control
- Anticoagulation
- Unstable patients - Cardiovert
- Referral

(CDC Fact Sheet, 2010)
Rate Control

• Why is rate control important?
  – Ischemia, MI, hypotension can occur
  – Long term: Cardiomyopathy
• Goals
  – Rest HR < 80 bpm
  – $24^\circ$ monitor < 100 bpm average
  – HR < 110 in 6 minute walk
Rhythm Control

• Indications
  – Symptoms of persistent atrial fibrillation
  – To avoid long term anticoagulation
  – Excessive bleeding risk
  – Personal preference
Anticoagulation

- Critical for moderate to high risk patients
- Multiple options now available
- Tailor to patient characteristics, risk of stroke, risk of bleeding, etc
# CHADS\textsubscript{2} Scoring

<table>
<thead>
<tr>
<th>Item</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure history?</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension history?</td>
<td>1</td>
</tr>
<tr>
<td>Age &gt; 75 years?</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus history?</td>
<td>1</td>
</tr>
<tr>
<td>Stroke symptoms or TIA or thromboembolism?</td>
<td>2</td>
</tr>
<tr>
<td>Patient has none of the above</td>
<td>No risk</td>
</tr>
</tbody>
</table>

(Singer DE. *Chest*. 2008 Jun;133(6 Suppl):546S-592S)
## CHADS\textsubscript{2} Scoring

<table>
<thead>
<tr>
<th>CHADS\textsubscript{2} Score</th>
<th>Stroke Risk (%/yr)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.9</td>
<td>1.2-3.0</td>
</tr>
<tr>
<td>1</td>
<td>2.8</td>
<td>2.0-3.8</td>
</tr>
<tr>
<td>2</td>
<td>4.0</td>
<td>3.1-5.1</td>
</tr>
<tr>
<td>3</td>
<td>5.9</td>
<td>4.6-7.3</td>
</tr>
<tr>
<td>4</td>
<td>8.5</td>
<td>6.3-11.1</td>
</tr>
<tr>
<td>5</td>
<td>12.5</td>
<td>8.2-17.5</td>
</tr>
<tr>
<td>6</td>
<td>18.2</td>
<td>10.5-27.4</td>
</tr>
</tbody>
</table>

(Singer DE. *Chest.* 2008 Jun;133(6 Suppl):546S-592S)
### CHADS<sub>2</sub> Score Utilization

<table>
<thead>
<tr>
<th>CHADS&lt;sub&gt;2&lt;/sub&gt; Score</th>
<th>Stroke Risk</th>
<th>Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Low</td>
<td>No treatment (or aspirin 75-325 mg / day)</td>
</tr>
<tr>
<td>1</td>
<td>Moderate</td>
<td>Oral anticoagulation Warfarin with INR 2-3 or new oral anticoagulant (or aspirin 75-325 mg / day)</td>
</tr>
<tr>
<td>2 or higher</td>
<td>Moderate to High</td>
<td>Oral anticoagulation Warfarin with INR 2-3 or new oral anticoagulant</td>
</tr>
</tbody>
</table>

(Singer DE. *Chest*. 2008 Jun;133(6 Suppl):546S-592S)
Low Risk CHADS$_2$ Scores

Kaplan-Meier estimate of probability of remaining free of thromboembolism with CHADS2 score 0 and 1. Only patients with CHADS2 scores 0 and 1 were included.

(Olesen. BMJ. 2011:342:d124)
# CHA$_2$DS$_2$VASc Scoring

<table>
<thead>
<tr>
<th>Item</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure history?</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension history?</td>
<td>1</td>
</tr>
<tr>
<td>Age 65 - 75 years?</td>
<td>1</td>
</tr>
<tr>
<td>Age $&gt;75$ years</td>
<td>2</td>
</tr>
<tr>
<td>Stroke symptoms or TIA or thromboembolism?</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus history?</td>
<td>1</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>1</td>
</tr>
<tr>
<td>Female sex</td>
<td>1</td>
</tr>
</tbody>
</table>

More sensitive and places $\sim30\%$ of those in CHADS$_2$ 0-1 into higher score where anticoagulation is recommended.

(Lip GY. *Stroke*. 2010;41:2731-8)
**CHA$_2$DS$_2$-Vasc Score**

<table>
<thead>
<tr>
<th>CHA$_2$DS$_2$-Vasc Score</th>
<th>Annual Stroke Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>~0%</td>
</tr>
<tr>
<td>1</td>
<td>1.3%</td>
</tr>
<tr>
<td>2</td>
<td>2.2%</td>
</tr>
<tr>
<td>3</td>
<td>3.2%</td>
</tr>
<tr>
<td>4</td>
<td>4.0%</td>
</tr>
<tr>
<td>5</td>
<td>6.7%</td>
</tr>
<tr>
<td>6</td>
<td>9.8%</td>
</tr>
<tr>
<td>7</td>
<td>9.6%</td>
</tr>
<tr>
<td>8</td>
<td>6.7%</td>
</tr>
<tr>
<td>9</td>
<td>15.2%</td>
</tr>
</tbody>
</table>
Stroke Prevention in AFib

• Currently approved medications are oral anticoagulants (vitamin K antagonists such as warfarin) and aspirin\(^1\)

• Vitamin K antagonists are effective in preventing stroke among AFib patients with a 68% relative reduction versus placebo

(SPAF Trial. *Arch Intern Med* 1994;154:1449-1457)
Limitations of Vitamin K Antagonists

• Narrow therapeutic window
• Wide variation in metabolism, with numerous food and drug interactions
• Need for regular coagulation monitoring and dose adjustment
• Slow onset/offset
Warfarin for Atrial Fibrillation

Anticoagulation in Patients with AFib in PC Practice

- No Warfarin: 65%
- INR Above Target: 6%
- INR in Target Range: 15%
- Subtherapeutic INR: 13%

New Antithrombotic Agents

- Tissue Factor
- Plasma Clotting Cascade
- Prothrombin
- Thrombin
- Fibrinogen
- Fibrin
- Thrombus
- Collagen
- ADP
- Thromboxane A₂
- Conformational Activation of GPIIb/IIa
- Platelet Aggregation

- Aspirin
- Clopidogrel
- Prasugrel
- AZD6140

- Apixaban
- Rivaroxaban
- Idraparinux
- AT
- Dabigatran
- Ximelagatran
- Robert Wood Johnson Foundation
- The George Washington University
- School of Public Health and Health Services
Considerations with New Agents

• New oral anticoagulants (NOAc): dabigatran, rivaroxaban, and apixaban
• There are no published data directly comparing NOAc to each other, just to warfarin
• The follow-up duration in NOAc is limited in clinical trials and real-world adherence is unknown
• Because of the short half-life, missing NOAc medication doses may increase risk of stroke
• Treatment decisions should account for cost differences to patients
Considerations with New Agents

- Data on clinical effectiveness for dabigatran in the real world are just beginning to emerge; data on apixiban and rivaroxaban are unavailable.
- A transition from warfarin to NOAc should be managed carefully; this period may constitute increased risk of stroke or hemorrhage.
- Safety of thrombolytic use in patients with ischemic stroke on NOAc is unknown.
- There are no antidotes to emergently reverse NOAc during hemorrhage.
OAC Associated Bleeding Risk Factors

- **Patient-related factors**
  - Age
  - History of bleeding
  - Previous stroke
  - Anemia
  - Genetic factors
  - Sex
  - Uncontrolled hypertension
  - Renal insufficiency
  - Hepatic dysfunction
  - Malignancy

- **OAC treatment-related factors**
  - Inception vs OAC experience
  - Adherence
  - Intensity of anticoagulation (INR)*
  - Time in therapeutic range*
  - Dietary intake of vitamin K*
  - Management of OAC (self-monitoring, dedicated OAC clinic, usual care)*
  - Concomitant medications/alcohol
  - Antiplatelet drugs / NSAIDs
  - Other medications affecting OAC intensity
  - Excessive alcohol intake

*Vitamin K antagonist therapy only

(Lane, *Circulation*. 2012;126:860-865)
Risk with Warfarin Anticoagulation

(Oden A. Thromb Res. 2006;117:493-9)
# Bleeding Risk – HAS BLED

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (SBP &gt; 160 mm Hg)</td>
<td>1</td>
</tr>
<tr>
<td>Abnormal renal function</td>
<td>1</td>
</tr>
<tr>
<td>Abnormal liver function</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding predisposition</td>
<td>1</td>
</tr>
<tr>
<td>Labile INRs (if on warfarin)</td>
<td>1</td>
</tr>
<tr>
<td>Elderly (&gt; 65 yrs)</td>
<td>1</td>
</tr>
<tr>
<td>Drug use</td>
<td>1</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1</td>
</tr>
</tbody>
</table>

(Pisters R. Chest. 2010;138:1093-100)

**HAS-BLED Score**

≥ 3 indicates caution is warranted
Current Treatment Options

- Adjusted-dose warfarin (target INR, 2.0 –3.0) is recommended for all patients with nonvalvular atrial fibrillation deemed high risk or moderate risk for stroke who can receive it safely (Class I; LOE A).

- Antiplatelet therapy with aspirin is recommended for low-risk and some moderate-risk patients with atrial fibrillation on the basis of patient preference, estimated bleeding risk if anticoagulated, and access to high-quality anticoagulation monitoring (Class I; LOE A).

- For high-risk patients with atrial fibrillation deemed unsuitable for anticoagulation, dual-antiplatelet therapy with clopidogrel and aspirin offers more protection against stroke than aspirin alone but with an increased risk of major bleeding and might not be reasonable (Class IIb; LOE B).

New Anticoagulants

• Short half life – less bleeding
  – Subtherapeutic after missing one or two doses
• Lack of need for routine monitoring
  – No standard test to assess degree of anticoagulation
• Generally safer than warfarin
  – No antidote
• Cost of medication
  – Overall cost of care
Conclusions

• Atrial fibrillation is coming
• Many present to the ED with their index event
• Treatment options continue to expand
• Key to successful prevention
  – Identification
  – Initiation
  – Consultation and referral
ASPRIRIN

- CHADS2=0 or 1
- 81 mg to 325mg PO daily
- Lower risk for bleeding than warfarin
- No need to check INRs etc
- Lower risk of major bleeds in patients who are a fall risk
• For CHADS2 score 2 or greater and also 1 depending on patient and physician preference

• Goal INR= 2 to 3

• Must monitor INRs regularly

• Can be dangerous if fall risk or bleeding risk high
• If not a candidate for warfarin; this can reduce stroke risk greater than ASA alone
• Risk for major bleeding increased
- Direct Thrombin Inhibitor
- Alternative to warfarin for CHADS2=1 or greater in those without valvular afib
- RE-LY Trial showed superior to warfarin in preventing ischemic and hemorrhagic CVAs with reduced risk of life threatening bleeding but higher risk of GI bleeds
- No lab monitoring*
- No reversal agent available for major bleeding events
• Oral factor Xa inhibitor
• Seems to be equivalent in efficacy to warfarin for CVA prevention and no difference in major bleeding events
• Demonstrates a reduction in intracranial hemorrhage
• Note: risk of thrombotic events increased for 28 days after stopping drug so may need to bridge with another anticoagulant during this time.
• AFIB: very common arrhythmia and leading cause of embolic CVAs
• Initial Workup: H and P, trop, EKG, TSH, Echo, CXR, CMP
• Management: First must determine if stable vs unstable (medically manage vs cardiovert immediately)
• For stable Afib: rate vs rhythm control (equal in efficacy). Start with rate control and if that fails try rhythm.
• Always remember to calculate CHADS2 score and anticoagulate for CVA ppx.
Rate Control (con’t)

• Medications
  – Metoprolol / Esmolol: IV or Oral
  – Diltiazem: IV or Oral
  – Verapamil: Oral Only
  – Digoxin: Patients with hypotension
  – Amiodarone: Also for rhythm control
Rhythm Control (con’t)

- Synchronized DC cardioversion
  - Emergencies/Hemodynamic instability
  - Greater efficacy than medications

- Pharmacologic cardioversion
  - If AF < 7 days – dofetilide, flecainide, ibutilide, propaferone or amiodarone
  - If AF > 7 day – dofetilide or amiodarone
Rate or Rhythm Control?

• Affirm Study: Rate versus rhythm control
  – No difference in incidence of stroke
  – Trend towards lower mortality in the rate control group
  – See article

  – This is STILL a controversial topic!
Anticoagulation and Cardioversion

- **Afib < 48 hours**:  
  - Cardioversion (CV)  
  - No anticoagulation indicated

- **Afib > 48 hours**:  
  - Anticoagulate for 3-4 weeks before CV  
  - OR get TEE  
  - Anticoagulate for 1 month after CV
Key Points

- MI is a rare CAUSE of a-fib
- Rate control must be achieved during exercise, not just at rest
- Not every patient needs to bridge with heparin
- Unstable patients should immediately be cardioverted
Differential Diagnosis

- Narrow Complex Tachycardias
  - Atrial Fibrillation
  - Atrial Flutter
  - AVNRT
  - AVRT
  - Atrial tachycardia
  - Sinus tachycardia
  - Multifocal atrial tachycardia

SVT is a category, not a diagnosis!
Diagnostic Testing: TTE

- To assess for structural heart disease
  - EF
  - Wall motion
  - Dilation/Hypertrophy
  - Size of right and left atrium
  - Valvular disease
  - Pericardial disease
Chest X-Ray

- Look for emphasisema/COPD
- Cardiac borders
- Pneumonia
Key features of new oral anticoagulants

**Dabigatran etexilate**
- Oral direct thrombin inhibitors
- Prodrug rapid biotransformation to active drug
- Inhibit free and fibrin-bound FIIa activity
- Fixed dosing - no coagulation monitoring required
- Max inhibition of FIIa after 1–4 h
- $T_{1/2}$: dabigatran, 12–17 h
- Few food/drug interactions
- Renal excretion: 80%

**Apixaban and Rivaroxaban**
- Oral direct FXa inhibitors
- Directly acting compound – no biotransformation
- Inhibit free and fibrin-bound FXa activity, and prothrombinase
- Fixed dosing - no coagulation monitoring required
- Max inhibition of FXa after 1–4 h
- $T_{1/2}$: apixaban 12 h; rivaroxaban 6–9 h
- Few food/drug interactions
- Renal excretion: 25%, 66% resp.

**Phase III AF trials:**
- Dabigatran etexilate: RE-LY
- Apixaban: ARISTOTLE, AVERROES
- Rivaroxaban: ROCKET

**Phase II ACS trials:**
- Dabigatran: RE-DEEM
- Apixaban: APPRAISE
- Rivaroxaban: ATLAS
### Scoring Differences Between CHADS₂ and CHA₂DS₂-VASc

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>CHADS₂</th>
<th>CHA₂DS₂-VASc</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Points</td>
<td>Points</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>N/A</td>
<td>1</td>
</tr>
<tr>
<td>Age 65-74</td>
<td>N/A</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥75</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Female sex</td>
<td>N/A</td>
<td>1</td>
</tr>
<tr>
<td>Previous stroke/TIA</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

*N/A – not applicable*
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