Hot Topics: Current PFO Recommendations and Loop Monitoring/Cryptogenic Stroke.

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Disclosure

- I certify that I do not carry a conflict of interest, financial or material, regarding the information to be discussed today.
Objectives

• Epidemiology

• Cardiac Causes of stroke
  – Atrial Fibrillation
  – Patent Foramen Ovale

• Approach to Cryptogenic stroke
  – Cardiac Rhythm Monitoring

• Treatment options
690,000 Ischemic strokes/year

240,000 TIA/year

Annual Risk/Year
≈3-4%

Wikimedia Commons
• Patent Foramen Ovale (PFO)
• Atrial Fibrillation (AF)

Stroke Frequency by Mechanism:
- Cryptogenic
- Lacunar
- Cardiogenic
- Atheros. CVD
- Hemorrhage
- Other
Atrial Fibrillation (AF)
Question 1:

- 68 year old female with atrial fibrillation, CAD, hypertension, diabetes and a prior mitral valve repair. Which of the following is the best anticoagulant for ischemic stroke prophylaxis?

a) Dabigatran
b) Rivaroxaban
c) Warfarin
d) Apixaban
e) Any of the above are reasonable treatment options
Atrial Fibrillation

• > 2.7 million Americans

• Leading Cardiac arrhythmia in the elderly

• May be responsible for > 70,000 ischemic strokes/year (10-12%)

Stroke 2014; 45:00-00

Favoriteplus.com

Gopixpic.com
Left Atrial Appendage (LAA)
LAA Thrombus
# Atrial Fibrillation Classification

**JACC** 2014; 64 (21): 2246-80

## TABLE 3 Definitions of AF: A Simplified Scheme

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal AF</td>
<td>• AF that terminates spontaneously or with intervention within 7 d of onset.</td>
</tr>
<tr>
<td></td>
<td>• Episodes may recur with variable frequency.</td>
</tr>
<tr>
<td>Persistent AF</td>
<td>• Continuous AF that is sustained &gt;7 d.</td>
</tr>
<tr>
<td>Long-standing persistent AF</td>
<td>• Continuous AF &gt;12 mo in duration.</td>
</tr>
<tr>
<td>Permanent AF</td>
<td>• The term &quot;permanent AF&quot; is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm.</td>
</tr>
<tr>
<td></td>
<td>• Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of AF.</td>
</tr>
<tr>
<td></td>
<td>• Acceptance of AF may change as symptoms, efficacy of therapeutic interventions, and patient and clinician preferences evolve.</td>
</tr>
</tbody>
</table>

## Symptoms when rhythm changes to atrial fibrillation

- Symptoms only with rapid ventricular rates
- No symptoms at all
Atrial Fibrillation: Thromboembolism Protection

• Antithrombotic therapy: Based on shared decision-making, discussion of the risks of stroke and bleeding and patient’s preference (Ic)

• CHA$_2$DS$_2$-VASc score is recommended to assess stroke risk (Ib)

• Same strategy applies to atrial flutter (Afl) (Ic)

• JACC 2014, doi:10:1-16/j.jacc.2014.03.021
• Favoriteplus.com
CHA$_2$DS$_2$-VASc score

- **C**: Congestive Heart Failure
  - (Systolic dysfunction, LVEF $\leq 40\%$)
- **H**: Hypertension
- **A**: Age $\geq 75$
- **D**: Diabetes mellitus
- **S**: Prior Stroke, TIA or thromboembolism
- **V**: Vascular Disease:
  - Myocardial infarction, peripheral arterial disease, aortic plaque
- **A**: Age $\geq 65$
- **S**: Sex = Female

2 Points
CHA$_2$DS$_2$-VASc score

- Score = 0: No anticoagulation (IIa b)

- Score = 1: No anticoagulation or Aspirin 75-100 mg daily (IIb c)

- Score ≥ 2: Anticoagulation
  - Warfarin (Ia)
  - NOAC’s (Ib)

JACC 2014, doi:10.1-16/j.jacc.2014.03.021
### (c) Adjusted stroke rate according to CHA$_2$DS$_2$-VASc score

<table>
<thead>
<tr>
<th>CHA$_2$DS$_2$-VASc score</th>
<th>Patients ($n=7329$)</th>
<th>Adjusted stroke rate (%/year)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>422</td>
<td>1.3%</td>
</tr>
<tr>
<td>2</td>
<td>1230</td>
<td>2.2%</td>
</tr>
<tr>
<td>3</td>
<td>1730</td>
<td>3.2%</td>
</tr>
<tr>
<td>4</td>
<td>1718</td>
<td>4.0%</td>
</tr>
<tr>
<td>5</td>
<td>1159</td>
<td>6.7%</td>
</tr>
<tr>
<td>6</td>
<td>679</td>
<td>9.8%</td>
</tr>
<tr>
<td>7</td>
<td>294</td>
<td>9.6%</td>
</tr>
<tr>
<td>8</td>
<td>82</td>
<td>6.7%</td>
</tr>
<tr>
<td>9</td>
<td>14</td>
<td>15.2%</td>
</tr>
</tbody>
</table>
Coagulation Cascade

Intrinsic Pathway

Damaged Surface

XII → XIIa
XI → XIa
IX → IXa
X → Xa

Prothrombin (II) → Thrombin (IIa)

Fibrinogen (I) → Fibrin (Ia)

VII → VIIa
Tissue Factor

VIIIa

Va

Vka Antagonists
• Warfarin (po)

Final Common Pathway

Cross Linked Fibrin Clot
Figure 1. The vitamin K cycle and its link to carboxylation of glutamic acid residues on vitamin K–dependent coagulation proteins.

Warfarin: The Labile INR

Adapted from Blann 2003
Chronic Treatment- Warfarin

- Warfarin: goal INR is 2-3 \( \rightarrow \) Target is 2.5
CHA$_2$DS$_2$-VASc score $\geq 2$

**Choice of oral anticoagulation:**

- Valvular
- Mechanical Valve

$\}$

Warfarin (Ib)

JACC 2014, doi:10.1-16/j.jacc.2014.03.021
Valvular Atrial Fibrillation:

- Rheumatic Mitral Stenosis
- Mechanical or bioprosthetic heart valve
- Mitral valve repair
Cross Linked Fibrin Clot

Final Common Pathway

Prothrombin (II)

Fibrinogen (I)

Thrombin (IIa)

Fibrin (Ia)

XIIIa

ATIII

Direct Xa Inhibitors
- Apixaban (po)
- Rivaroxaban (po)
- Edoxaban (po)

Indirect Xa Inhibitors
- Fondaparinux (SC)

Cross Linked Fibrin Clot
Cross Linked Fibrin Clot

Final Common Pathway

Prothrombin (II)

Fibrinogen (I)

Thrombin (IIA)

Fibrin (Ia)

XIIIa

Direct Thrombin Inhibitors

- Argatroban (IV)
- Bivalrudin (IV)
- Desirudin (SC)
- Lepirudin (IV)
- Dabigatran (po)
Non Valvular Atrial Fibrillation

**Rivaroxaban (IIa b)**

- **CrCl > 50**
  - 20 mg daily

- **CrCl 15-50**
  - 15 mg daily

**Dabigatran (I b)**

- **CrCl > 30**
  - 150 mg twice daily

- **CrCl 15-30**
  - 75 mg twice daily

**Dabigatran + Dronedederone**

- **CrCl > 50**
  - 150 mg twice daily

- **CrCl 30-50**
  - 75 mg twice daily

For VTE, do not use either medication for CrCl < 30

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Non Valvular Atrial Fibrillation

Apixaban (1 a)

5 mg twice daily

2.5 mg twice daily- if 2 of the following

- Age > 80 years old
- Creatinine > 1.5 mg/dl
- Weight < 60 Kg
When do we start anticoagulation after a stroke/TIA?
High risk features → Hemorrhagic conversion

- Hemorrhagic transformation on initial imaging
- Large Infarct
- Hemorrhage tendency
- Uncontrolled hypertension
When to start anticoagulation: stroke or TIA

* Stroke 2014; 45:00-00

- No high risk features

- **Within 14 days** after the onset of neurologic symptoms (IIa B)
When to start anticoagulation: stroke or TIA

*Stroke* 2014; 45:00-00

- + High risk features
- **Delay beyond 14 days** after the onset of neurological symptoms (IIa B)
Coronary Revascularization (II b B)

- Clopidogrel (75 mg daily) + oral anticoagulant
- Without Aspirin
Do not tolerate anticoagulants

*Stroke* 2014; 45:00-00

- Aspirin alone is recommended (I A)
- Aspirin + Clopidogrel may be reasonable (IIb B)
Do not tolerate anticoagulant/antiplatelet

Stroke 2014; 45:00-00

- LA Appendage closure device (IIb B)- WATCHMAN device
Cryptogenic Stroke

R.G. González et al. (eds.), Acute Ischemic Stroke,
DOI: 10.1007/978-3-642-12751-9_2, © Springer-Verlag Berlin Heidelberg 2011

Stroke Frequency by Mechanism

- Hemorrhage
- Atheros.CVD
- Cardiogenic
- Lacunar
- Cryptogenic
- Other
Cryptogenic

Cardiac Rhythm Monitoring

≈28%

• Atrial Fibrillation (AF)

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Question 2

- 78 year old male is admitted with an acute ischemic stroke in the left MCA territory.
- Workup for the etiology has been unrevealing.
- During his 3 day hospital stay, telemetry monitoring and daily ECG’s were all sinus rhythm.
- A bed is now available for him at the rehab center. What is the next best step in the workup for this patient?

a) Holter monitor
b) 14 day event monitor
c) At least 30 days of event monitoring
d) Send him to rehab and let the physicians over there figure it out
Rhythm Monitoring Modalities

- **Telemetry**: 1-3 days
- **Holter**: 1-2 days
- **Loop**: 3 years
- **Event**
- **MCOT**
- **Continuous recording**
- **Triggered External**
- **Trigged Internal**
- **Patient Factor**
Atrial fibrillation monitoring post stroke or TIA

- Prolonged rhythm monitoring $\approx 30$ days (IIa C)

- Within 6 months of the index event (IIa C)
Atrial fibrillation monitoring post stroke or TIA

- 10% of pts will have new afib detected during hospitalization
- 11% more will have afib detected within 30 days
- The yield of detection increases with time
- Patient factor limits external monitors
Implantable Loop Recorder

Battery ≈ 3 years

MRI compatible
C Detection of Atrial Fibrillation by 36 Months

Hazard ratio, 8.8 (95% CI, 3.5–22.2)
P<0.001 by log-rank test

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Control</th>
<th>ICM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>220</td>
<td>221</td>
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<td>194</td>
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<td>72</td>
<td>57</td>
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<tr>
<td></td>
<td>36</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>8</td>
</tr>
</tbody>
</table>

Months since Randomization
At our institution.......  

- Telemetry monitoring during hospitalization  
- If atrial fibrillation is not documented  
- Loop recorder is implanted
How long does a person have to be in atrial fibrillation to make the diagnosis???
Duration of Atrial Fibrillation ➔ Diagnosis

- TRENDS > 5.5 Hours\(^1\)
- MOST: > 5 minutes\(^1\)
- CRYSTAL AF: ≥ 30 seconds\(^2\)
- REVEAL XT Medtronic Loop Recorder: 2 minutes

2. NEJM 2014; 370: 2478-2486
Duration of Atrial Fibrillation → Diagnosis

- 56 patients with cryptogenic stroke/TIA
- MCOT up to 21 days
- 5.3% of paroxysmal atrial fibrillation: > 30 seconds
- 23% of paroxysmal atrial fibrillation: < 30 seconds

2. Neurology 2008; 71(21) 1696-1701
Question 3

- 32 year old male with no medical history is admitted with a new left MCA ischemic stroke.
- Transesophageal echocardiogram revealed a patent foramen ovale and no cardiac thrombus.
- Arterial and venous imaging was normal.
- Which of the following is the best management for this patient?
  a) Aspirin daily
  b) Warfarin because it has been demonstrated to be superior to aspirin in secondary stroke prophylaxis
  c) Close the PFO with an occlusion device
  d) No therapy as he is young and his risk of a future event is extremely low
Patent Foramen Ovale (PFO)

1. Stroke 2014; 45:00-00

- Detected in 15%-25% of the adult population\(^1\)

- Association with ischemic cryptogenic stroke/TIA and patients < 55 years old

- PFO + prior cryptogenic event, have an increased risk of recurrence \(\approx 3.4\%-3.8\%\) yearly\(^2\)
Paradoxical Embolism

**Definition:**
- Visualization of a thrombus in the interatrial defect

**Suspect:**
- Presence of an arterial deficit
- Absence of left sided source for embolism
Patent Foramen Ovale

- Secondary Prevention
- TIA
- Ischemic Stroke
Antiplatelet Therapy

- Antiplatelet therapy is indicated for ALL patients with a PFO not on anticoagulation (Ib)
Anticoagulation versus Antiplatelet Therapy

- There is insufficient data to support that warfarin is superior to aspirin (IIb B)
Venous source of thromboembolism

- Anticoagulation is recommended (1 A)
Indication: Inferior Vena Cava Filter (IVC) Filter

- Venous source of thromboembolism + a contraindication to anticoagulation (IIa C)

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Venous source of thromboembolism

• PFO closure device (IIb C)
No Evidence of a venous thromboembolism

- PFO closure device is not indicated (III A)

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Thank You