Afib + Cryptogenic Stroke: A Neurologist View

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Objectives

- Discuss the Risks of Cardioembolic Stroke
- Review Afib Related Stroke
- Review Prevention Strategies for Afib Related Stroke
- Review Approach to Evaluating Cryptogenic Stroke
CASE

• 64 year old male
  • HPI:
    • Transient loss of vision on left side
  • PMH –
    • No medical issues
• MEDS
  • None
• SOCIAL:
  • Avid cyclist with over 100 miles week
Case

- July 2012

  - Referred to ophthalmologist – “Amaurosis Fugax”

  - Referred to neurologist
    - MRI
Ischemic stroke: 88%
Intracerebral hemorrhage: 9%
Subarachnoid hemorrhage: 3%

~795,000 Strokes Annually
Cerebral Ischemia

Small Vessel Dz 25%

Cardioembolic 25%

Large Artery Dz 25%
Cardioembolic Stroke

- Accounts for substantial proportion of overall stroke burden

  - High prevalence
  - Greater severity of stroke
  - Less favorable prognosis
  - High recurrence risk

Cardioembolic Causes

1. Atrial Fibrillation
2. Valvular disease
3. Heart Failure
4. Patent Foramen Ovale
Atrial Fibrillation (AF)

- >50% of cardioembolic strokes
- 2.7 million Americans
- 33 million worldwide
  - 2-3% at age 60
  - 8-10% at age 80

- Given increased risk of AF with age…
SURGE in AF related stroke
Afib

- Embolization from left atrial appendage and left atrium
Fig 1. LAA morphology types based on Wang’s classification with Kimura’s quantitative limits.
Afib

- Embolization from left atrial appendage and left atrium

- Risk same for paroxysmal vs persistent afib
  - How much afib is enough?
Device-detected atrial fibrillation and risk for stroke: an analysis of >10 000 patients from the SOS AF project (Stroke prevention Strategies based on Atrial Fibrillation information from implanted devices)

Giuseppe Boriani¹*, Taya V. Glotzer², Massimo Santini³, Teena M. West⁴, Mirko De Melis⁴, Milan Sепsi⁵, Maurizio Gasparini⁶, Thorsten Lewalter⁷, John A. Camm⁸, and Daniel E. Singer⁹

Treatment

- Aspirin
  - RR – 21%
- Warfarin
  - RR – 68%
  - Effectively reduces annual risk – 5% to 1.4%
- Aspirin + Clopidogrel
  - Better than Aspirin\(^1\)
  - But not as good as warfarin\(^1\)
  - Increased risk of bleed ~ similar to warfarin\(^1\)

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Treatment

Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors

Stuart J. Connolly, M.D., Truman J. Milling, Jr., M.D., John W. Eikelboom, M.D., C. Michael Gibson, M.D., John T. Curnutte, M.D., Ph.D., Alex Gold, M.D., Michele D. Bronson, Ph.D., Genmin Lu, Ph.D., Pamela B. Conley, Ph.D., Peter Verhamme, M.D., Ph.D., Jeannot Schmidt, M.D., Saskia Middeldorp, M.D., Alexander T. Cohen, M.D., Jan Beyer-Westendorf, M.D., Pierre Albaladejo, M.D., Jose Lopez-Sendon, M.D., Shelly Goodman, Ph.D., Janet Leeds, Ph.D., Brian L. Wiens, Ph.D., Deborah M. Siegal, M.D., Elena Zotova, Ph.D., Brandi Meeks, B.Eng., Juliet Nakamya, Ph.D., W. Ting Lim, M.Sc., and Mark Crowther, M.D., for the ANNEXA-4 Investigators*
# Afib

<table>
<thead>
<tr>
<th>CHADS\textsubscript{2} Score</th>
<th>Annual Stroke Risk %</th>
<th>95% Confidence Interval</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>0</td>
<td>1.9</td>
<td>1.2–3.0</td>
<td>No antithrombotic</td>
</tr>
<tr>
<td>1</td>
<td>2.8</td>
<td>2.0–3.8</td>
<td>Antiplatelet or anticoagulation</td>
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<td>2</td>
<td>4.0</td>
<td>3.1–5.1</td>
<td>Anticoagulation</td>
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<tr>
<td>3</td>
<td>5.9</td>
<td>4.6–7.3</td>
<td>Anticoagulation</td>
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<td>4</td>
<td>8.5</td>
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<td>6</td>
<td>18.2</td>
<td>10.5–27.4</td>
<td>Anticoagulation</td>
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<table>
<thead>
<tr>
<th>CHA_{2}DS_{2}-VASc Score</th>
<th>Annual Stroke Risk %</th>
<th>95% Confidence Interval</th>
<th>Recommendation</th>
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<td>0.6–1.0</td>
<td>No antithrombotic</td>
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<tr>
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<td>1.7–2.4</td>
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<td>5.5–6.3</td>
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<td>7</td>
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<td>22.4</td>
<td>16.3–30.8</td>
<td>Anticoagulation</td>
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<td>9</td>
<td>23.6</td>
<td>10.6–52.6</td>
<td>Anticoagulation</td>
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### Treatment

#### HAS-BLED

<table>
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<tr>
<th>HAS-BLED Score</th>
<th>Bleeding Risk</th>
<th>Recommendation</th>
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<tr>
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<td>3.4</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>4.1</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>5.8</td>
<td>Caution warranted</td>
</tr>
<tr>
<td>4</td>
<td>8.9</td>
<td>Caution warranted</td>
</tr>
<tr>
<td>5</td>
<td>9.1</td>
<td>Caution warranted</td>
</tr>
<tr>
<td>≥6</td>
<td>Insufficient Information</td>
<td>Caution warranted</td>
</tr>
</tbody>
</table>

**Drugs**
- NSAIDs/Antiplatelets
- Excess alcohol use

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Apixaban in Patients with Atrial Fibrillation

Stuart J. Connolly, M.D., John Eikelboom, M.B., B.S., Campbell Joyner, M.D., Hans-Christoph Diener, M.D., Ph.D., Robert Hart, M.D., Sergey Golitsyn, M.D., Ph.D., Greg Flaker, M.D., Alvaro Avezum, M.D., Ph.D., Stefan H. Hohnloser, M.D., Rafael Diaz, M.D., Mario Talajic, M.D., Jun Zhu, M.D., Prem Pais, M.B., B.S., M.D., Andrzej Budai, M.D., Ph.D., Alexander Parkhomenko, M.D., Ph.D., Petr Jansky, M.D.
Afib
(N=5599)

Apixaban
(N=2808)

Aspirin
(N=2791)
Major Bleed
- Apixaban: 1.4%/yr
- Aspirin: 1.2%/yr

Intracranial Bleed
- Apixaban: 0.4%/yr
- Aspirin: 0.4%/yr

Extracranial Bleed
- Apixaban: 1.1%/yr
- Aspirin: 0.9%/yr
Large Artery 25%
Cardioembolic 25%
Small Vessel Dz 25%
Cryptogenic Stroke

- 20-40% of all Strokes
- 120,000 to 180,000 patients per year
- Most are embolic…

Saver, J. Cryptogenic Stroke: NEJM 374;21
Get longer study...

AF Recommendations

1. For patients who have experienced an acute ischemic stroke or TIA with no other apparent cause, prolonged rhythm monitoring (≈30 days) for AF is reasonable within 6 months of the index event (Class IIa; Level of Evidence C). (New recommendation)
Sequential Evaluation for afib

- Meta-analysis between 1980 – 2014
- 50 studies, > 11,000 patients

- ER – EKG – 7.7%
- In hospital telemetry – 5.1%
- Ambulatory Holter (first 30 days) – 10.7%
- Second Ambulatory Evaluation (Insertable monitor) – 16.9%

- Overall Yield: 23.7%
Quick View - Aug 11, 2016
To: Pima Heart

DOB: Sep 30, 1949
ICM Implant: Jul 15, 2016

Device status
- Device status: OK
- Battery status: OK

Findings
- Episode details received

Recordings memory
- Episodes: 0
- Patient triggered recordings: 0

Detection settings
- Atrial fibrillation [AF]: Low
- High vent. rate [HR]: ON
- Bradycardia: ON
- Sudden rate drop: ON
- Asystole duration [s]: 3
- Patient trigger: ON

Ven. arrhythmia since Jul 17, 2016
- High vent. rate episodes per day: 0

Atr. arrhythmia since Jul 17, 2016
- Atrial burden (% of day): 0.7
- Atrial fibrillation episodes per day: 5
- Mean vent. heart rate during atr. burden [bpm]: 91

Brady/Asyst. since Jul 17, 2016
- Bradycardia episodes per day: 8
- Sudden rate drop episodes per day: 16
- Asystole episodes per day: 0
- Patient triggered recordings per day: 0

Sensing
- Sensing amplitude mean (mV): 0.57
- Noise (% of day): 0.0

Long term trends
- Heart rate
- Patient activity
- Atrial fibrillation
- Sudden rate drop
- Asystole burden
- RR variability

Note: The graph shows long-term trends for heart rate, patient activity, atrial fibrillation, sudden rate drop, asystole burden, and RR variability. The x-axis represents time, and the y-axis represents the measured values.
## Recordings - Episode 81:

<table>
<thead>
<tr>
<th>General</th>
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<tbody>
<tr>
<td>Episode number</td>
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<tr>
<td>Episode type</td>
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<tr>
<td>Detection</td>
</tr>
<tr>
<td>Termination</td>
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<tr>
<td>Duration</td>
</tr>
<tr>
<td>Device settings no.</td>
</tr>
<tr>
<td>Mean ven. rate / RR interval [ms]</td>
</tr>
</tbody>
</table>

### Tachogram and Lorenz plot

![Tachogram and Lorenz plot]

### SECG

![SECG]

![SECG]
Who is at highest risk?
Higher Risk Patients

- Topographic pattern of stroke gives us insight
Higher Risk Patients

- Higher CHADs-VASc (2 or greater)

Saver, J.  Cryptogenic Stroke: NEJM 374;21
Higher Risk Patients

- Higher CHADs-VASc (2 or greater)

Table 3. Risk of Ischemic Stroke or Systemic Embolism after the 3-Month Visit, According to Baseline CHADS₂ Score and According to Whether Subclinical Atrial Tachyarrhythmias Were or Were Not Detected between Enrollment and the 3-Month Visit.

<table>
<thead>
<tr>
<th>CHADS₂ Score</th>
<th>No. of Patients</th>
<th>Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months</th>
<th>Hazard Ratio for Ischemic Stroke or Systemic Embolism with Subclinical Atrial Tachyarrhythmias (95% CI)*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>no. of patients</td>
<td>no. of events</td>
</tr>
<tr>
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<td>600</td>
<td>68</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>1129</td>
<td>119</td>
<td>4</td>
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<tr>
<td>&gt;2</td>
<td>848</td>
<td>72</td>
<td>6</td>
</tr>
</tbody>
</table>

1. Saver, J. Cryptogenic Stroke: NEJM 374;21
Higher Risk Patients

- Infarct topographic features
- Higher CHADs-VASc (2 or greater)
- Older age (>60)
- Left Atrial Cardiopathy (dilatation, strain)
Higher Risk Patients

- Higher CHADs-VASc (2 or greater)
- Older age (>60)
- Infarct topographic features
- Left Atrial Cardiopathy (dilatation, strain)
- Morphological Features of Left Atrial Appendage

Saver, J. Cryptogenic Stroke: NEJM 374;21
Fig 1. LAA morphology types based on Wang’s classification with Kimura’s quantitative limits.

http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0118822
What should we do?
Cryptogenic Stroke Treatment Algorithm

- Discharge on **cardiac telemetry for at least 30 days**
  - If multiple risk factors discharge on Oral Anticoagulation
  - If no risk factors discharge on oral antiplatelet is okay

Saver, J. Cryptogenic Stroke: NEJM 374;21
Cryptogenic Stroke Treatment Algorithm

- Initial 30 days of monitoring shows:
  - No evidence of pAF
    - Multiple risk factors
      - Subcutaneous loop monitor X 1-3 years
      - Continue OAC X 1 year then reconsider
    - No risk factors
      - Continue antiplatelet therapy
Treatment Algorithm

• Low Burden Afib (5-15 minutes/24 hours)
  • Multiple risk factors
    • Continue OAC
  • No risk factors
    • Subcutaneous loop recorder monitoring X 1-3 years
    • Switch to OAC for first year, then reconsider

• Higher burden (>15 minutes/24 hours)
  • Use OAC
CASE 1

- 64 year old gentleman with recurrent strokes!!
Case 1

- Risk Factors:
  - Age > 60
  - Multiple territory strokes
Case 1

- Loop Monitor
- Oral Anticoagulation
**Quick View - Aug 11, 2016**

**To: Pima Heart**

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**Name:**

DOB: Sep 30, 1960

Phone: -

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**BioMonitor 2-AF [SN 91504486]**

ICM implanted Jul 15, 2016

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**Last message:** Aug 11, 2016

**Last clinic follow-up:** Jul 17, 2016

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### Ven. arrhythmia since Aug 10, 2016

| High ven. rate episodes per day | 0 |

### Atr. arrhythmia since Aug 10, 2016

| Atrial burden [% of day] | 0.8 |
| Atrial fibrillation episodes per day | 1 |
| Mean ven. heart rate during atr. burden [bpm] | ... |

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Cardioembolic Strokes

- Account for large portion of stroke burden

- Afib we need to be aggressive about detection
  - Anticoagulation reduces risk of future ischemic stroke dramatically

- CHADS and HAS-BLED

- **LOOK AGGRESSIVELY**
Case 2

- 73 year old
  - Transient episode of left hand clumsiness in shower

- PMH:
  - Atrial Flutter
  - HTN
  - Dyslipidemia

- MEDS:
  - Aspirin
Case 2
Case 2

- Treatment?

- Started on Pradaxa 150mg bid
Case 2

- Returns to ER 18 months later
  - Again left hand clumsiness
Case 2
Case 2

- Treated as Pradaxa failure

- Switched to warfarin
Case 2

- 6 months later
  - Returns to ER with left sided weakness
    - AGAIN???????
Case 2
Case 2