Cardiogenic Stroke: 
A Neurologist View

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Disclosure

I have one relevant relationship I need to disclose:

I am currently working on a stroke-related research project named *Socrates*, which is funded by AstraZeneca. This relationship will in no way affect the discussion we will be having about Cardiogenic Stroke.
Objectives

- Define Cardiogenic Stroke and discuss its causes.
- Discuss treatment options for the different types of Cardiogenic Stroke.
- Discuss new research in Atrial Fibrillation and other types of Cardiogenic Stroke.
~795,000 Strokes Annually

- Ischemic stroke: 88%
- Intracerebral hemorrhage: 9%
- Subarachnoid hemorrhage: 3%
Cerebral Ischemia

Thrombosis

Cardioembolic

Aortic Embolism

Artery to Artery

Hypotension
Cardioembolic Stroke

- Accounts for substantial proportion of overall stroke burden\(^1\)
  - 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

- Aortic Embolism
Atrial Fibrillation (AF)

- ≈ 50% of cardioembolic strokes

SURGE in AF related stroke
Afib

- Embolization from left atrial appendage and left atrium
- Increased risk with left atrial enlargement
- Risk same for paroxysmal vs persistent afib
  - How much afib is enough?
Afib

- Overall risk:

  - 5% annual risk of stroke
  - However, risk varies based on patient's risk factors:
    - CHADS\textsubscript{2} score
      - Congestive Heart Failure – 1 point
      - Hypertension – 1 point
      - Age > 75 years – 1 point
      - Diabetes Mellitus – 1 point
      - Stroke/TIA symptoms – 2 points

<table>
<thead>
<tr>
<th>CHADS\textsubscript{2} Score</th>
<th>Annual 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>
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<td>6</td>
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- **Stroke/TIA symptoms - 2 points**

A fibr

<table>
<thead>
<tr>
<th>CHA₂DS₂-VASc Score</th>
<th>Annual Stroke Risk %</th>
<th>95% Confidence Interval</th>
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<td>9</td>
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<td>10.6–52.6</td>
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</table>

- Female sex - 1 point

Detecting Afib

- Based on characteristics of stroke
- AT LEAST 24 hours of monitoring after event
- In Cryptogenic embolic stroke,

\[ EMBRACE \]

\[ CRYSTAL AF \]


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**Get longer study...**

**Loop monitor**

**30-day Holter**

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<th>Months since Randomization</th>
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<td>102</td>
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<td>57</td>
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<tr>
<td>29</td>
</tr>
<tr>
<td>8</td>
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Treatment

- Aspirin
  - RR – 21%
- Warfarin
  - RR – 68%

Effectively reduces annual risk – 5% to 1.4%

- Aspirin + Clopidogrel
  - Better than Aspirin
  - But not as good as warfarin
  - Increased risk of bleed ~ similar to warfarin

Treatment

Renal Impairment
Significant Liver Disease
Mechanical Valves
Anticipated Reversal of Anticoagulation
Treatment

HAS-BLED

<table>
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<th>HAS-BLED Score</th>
<th>Bleeding Risk</th>
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<tr>
<td>4</td>
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<td>5</td>
<td>9.1%</td>
</tr>
<tr>
<td>≥6</td>
<td>Increased</td>
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**Recommendation**

- None
- None
- None
- Caution warranted
- Caution warranted
- Caution warranted
- Caution warranted

**Drugs**

- NSAIDs/antiplatelets or excess alcohol use

Infective Endocarditis

- Stroke often presenting feature
- Risk Factors
  - Valvular issues related to Rheumatic Heart Disease
  - Bicuspid Aortic Valve
  - Prosthetic Valve
  - IV Drug use (although more often right sided involvement)
- Clinical Picture
  - Weight loss
  - Fever
  - New murmur
  - Systemic embolization

- Detection
  - Transesophageal Echo!
  - MRI better than CT
Multiple cortical and subcortical microbleeds on a T2* sequence.

Anti-thrombotic therapy is associated with increased risk of hemorrhage.
Infective Endocarditis

- Vegetations most at risk for embolizing
  - Large + Mobile vegetations
  - Mitral Valve
  - Staph Aureas
Multiple macular spots of varying sizes over both feet (A) and hand (B), which were nontender and noncompressible.
Prosthetic valves

- High risk especially
  - Caged ball
  - Tilting disc
  - Mitral position
- Warfarin
  - INR 2.5-3.5
  - Stroke despite therapeutic INR
    - Add aspirin 81mg
Heart Failure

- Mechanism
  - Thrombus formation
  - Borderzone Infarcts
Figure 1 Examples of borderzone infarcts on diffusion-weighted MRI

Heart Failure

Secondary Prevention

Aspirin vs
Clopidogrel vs
Extended release dipyridamole-ASA vs
Warfarin

ANYTHING GOES

Patent Foramen Ovale
PFO

- 20-25% of population with PFO

- In cryptogenic stroke…

- ~50% of population with PFO
PFO

- Transthoracic Echo (TTE)
  - With agitated bubble study

- Transesophageal echocardiogram (TEE)
  - Atrial Septum
  - Aortic arch
  - Left atrial appendage
  - Aortic valve
PFO

Amplatzer

StarFlex
Cumulative number of patients recruited in studies of different designs over a period of 16 years for the comparison of closure vs medical treatment.

Closure of Patent Foramen Ovale versus Medical Therapy after Cryptogenic Stroke

John D. Carroll, M.D., Jeffrey L. Saver, M.D., David E. Thaler, M.D., Ph.D., Richard W. Smalling, M.D., Ph.D., Scott Berry, Ph.D., Lee A. MacDonald, M.D., David S. Marks, M.D., and David L. Tirschwell, M.D., for the RESPECT Investigators*

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Closure Group</th>
<th>Medical-Therapy Group</th>
<th>Hazard Ratio (95% CI)</th>
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<td>Overall</td>
<td>9/499 (1.8)</td>
<td>16/481 (3.3)</td>
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<tr>
<td>Age</td>
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<td>18–45 yr</td>
<td>4/230 (1.7)</td>
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<td>46–60 yr</td>
<td>5/262 (1.9)</td>
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<td>Sex</td>
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<tr>
<td>Male</td>
<td>5/268 (1.9)</td>
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<tr>
<td>Female</td>
<td>4/231 (1.7)</td>
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<td>Shunt size</td>
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<tr>
<td>None, trace, or moderate</td>
<td>7/247 (2.8)</td>
<td>6/244 (2.5)</td>
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<td>Substantial</td>
<td>2/247 (0.8)</td>
<td>10/231 (4.3)</td>
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<td>Atrial septal aneurysm</td>
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<td>Absent</td>
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<td>Index infarct topography</td>
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<td>Superficial</td>
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<td>Small deep</td>
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<td>Other</td>
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<td>Planned medical regimen</td>
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<td>Anticoagulant</td>
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<td>Antiplatelet</td>
<td>5/367 (1.4)</td>
<td>13/359 (3.6)</td>
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</table>
PFO

- Medical Treatment
  - Aspirin
  - Clopidogrel
  - Extended Release Dipyridamole-ASA
  - Warfarin – IF DVT or hyper-coagulable state
- Closure reasonable to consider
  - Recurrent events
    - Young Age
    - Large PFO
    - Atrial Septal Aneurysm
Aortic Arch Atherosclerosis

- Thromboembolism
- Cholesterol emboli
- TEE better than TTE
- Plaques >4mm
- Aggressive risk factor Control
- Anti-platelet vs warfarin
- Arch Related Cerebral Hazard Trial (ARCH)\(^1\)
  - ASA-Clopidogrel combo may be better

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
- Heart failure
  - No warfarin as primary treatment
  - Secondary stroke prevention best antithrombotic unknown
- PFO
  - Most of the time closure not better than medical therapy
  - Antiplatelet agent
- Aortic atheromas
  - TEE
  - Best antithrombotic unknown