Stroke Systems and Cryptogenic Stroke

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Disclosures

* I am a speaker and/or consultant to any company that has made, is making, or will make a NOAC
* I am a consultant for Medtronic
What is a Stroke System of Care?

- A comprehensive, diverse, longitudinal system that addresses all aspects of stroke care in an organized and coordinated manner.
- Spans the spectrum of stroke care from primary prevention, calling 9-1-1, acute care, secondary prevention, rehabilitation, return to the community.
- As with any system, it is only as strong as its weakest link.
- This talk will focus the roles of different types of stroke centers and Emergency Medical Services.
Pictorial Stroke System of Care

Primary Prevention/Secondary Prevention

Public Education

Calling 911

EMS elements

Transportation to hospital

Stroke Centers

Acute Care

Secondary Prevention

Rehabilitation

Return to the community
Characteristics of Different Stroke Centers

**Comprehensive Stroke Center**
- Academic Medical Center
- Tertiary Care facility

**Primary Stroke Center**
- Wide range of hospitals;
- standard stroke care; stroke unit;
- use TPA

**Acute Stroke Ready Hospital**
- Rural hospitals; basic care;
- drip and ship;
- use tele-technologies
**Numbers of Types of Stroke Centers in the US**

<table>
<thead>
<tr>
<th>Type of Stroke Center</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comprehensive Stroke Center</td>
<td>About 95 now</td>
</tr>
<tr>
<td></td>
<td>150-200 total</td>
</tr>
<tr>
<td>Primary Stroke Center</td>
<td>About 1070 now</td>
</tr>
<tr>
<td></td>
<td>1200-1500 total</td>
</tr>
<tr>
<td>Acute Stroke Ready Hospital</td>
<td>Very few now</td>
</tr>
<tr>
<td></td>
<td>500-700 total</td>
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</tbody>
</table>

> 5000 total acute care hospitals in the U.S.
The Comprehensive Stroke Center

- Provides complete care to patients with the worst, most severe, most complex strokes
  - Large ischemic strokes (might need ICP interventions, surgery, etc.)
  - ICH
  - SAH
  - Multi-system disease
  - Cryptogenic strokes
- Might require surgical or endovascular therapy
- Might require NICU level care
- Has all services available 24/7, 365 days/year
Why did we specifically highlight cryptogenic stroke for CSCs??

- By definition they are the most challenging to Dx and Rx
- They require specialists in many different areas
  - Vascular neurology, vascular neurosurgery, neuroradiology, cardiology, hematology, etc.
- Often require extensive testing
- Often affect younger patients with high life expectancy
“Common” Causes of “Cryptogenic” Stroke

- Cardiac etiologies:
  - Paroxysmal Afib, SBE with negative Cx, papillary fibroelastoma
  - Subtle arterial dissections, CNS vasculitis (isolated)
  - Hypercoagulable state in setting of cancer (see this often)
  - Metabolic disorders: Hyper-homocysteine, Fabry’s disease
  - Plaque in aortic arch
  - HIV (often not tested for), CNS infection
  - Drug abuse (often not tested for)
  - Genetic etiologies (CADASIL, CARASIL, MELAS, etc.)
  - Hemoglobinopathies
Risk of Recurrent Stroke After Cryptogenic Stroke

Younger patients = 1-3% per year

Older patients = 5-10% per year

This is similar to recurrent stroke risk in typical stroke populations
Risk of Recurrent Stroke in Cryptogenic Stroke Patients

- Very few specific focused studies
- Best surrogate likely PFO Studies
  - Fairly large number of enrolled patients
  - Reasonable work-up and follow-up
- Standard therapy—usually ASA
- Major limitation is young patient age
  - 20-40 years
### Table 2. Comparison of Aspirin and Warfarin in Preventing the Primary Outcome of Recurrent Ischemic Stroke and Death Over 2 Years Among Patients Whose NT-ProBNP Was ≤750 pg/mL or >750 pg/mL

<table>
<thead>
<tr>
<th>Treatment by NT-ProBNP</th>
<th>Number at Risk (Number of Events)</th>
<th>Rate Per 100 Person-Years</th>
<th>Hazard Ratio*</th>
<th>95% Confidence Interval</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤750 pg/mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>477 (49, 13)</td>
<td>6.8</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>502 (63, 17)</td>
<td>8.5</td>
<td>1.21</td>
<td>0.87, 1.69</td>
<td>0.24</td>
</tr>
<tr>
<td>&gt;750 pg/mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>28 (7, 9)</td>
<td>45.9</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>21 (4, 2)</td>
<td>16.6</td>
<td>0.30</td>
<td>0.12, 0.84</td>
<td>0.02</td>
</tr>
</tbody>
</table>

NT-proBNP indicates amino terminal pro-B-type natriuretic peptide.
*Adjusted for age, sex, and natural logarithm of NT-proBNP level as a continuous variable.
†Stroke, death.
Biomarkers and Recurrent Stroke Risk with Therapy

Longstreth et al., Stroke, 2013
The ESUS Paradigm

* Embolic Strokes of Uncertain Source

* Really??? How do you know they are embolic strokes?

When does ESUS become just SUS???
ESUS or just SUS???
ESUS or just SUS??
**Assumption #1**

- A significant % of these strokes are due to either:
  - 1. Afib, or........
  - 2. Another mechanism that is responsive to anticoagulation therapy

**Assumption #2**

- Treatment with an anticoagulant will be effective and safe for these other etiologies

**Assumption #3**

- The rate of recurrent events will be high enough to show a treatment benefit, and.......
- Enough patients will survive long enough to show overall benefit
* Preferred therapy = single antiplatelet agent... UNLESS:
  * Monitoring shows Afib...... NOAC
  * TTE with large LA or LAA...... NOAC/Anticoagulation
  * Elevated BNP...... NOAC?? Limited data........
  * Body scan shows cancer...... SQ Lovenox
  * PFO...... antiplatelet therapy, ? closure
  * Failure of 2 antiplatelet agents...... consider NOAC
Implications

* The treatment of patients with cryptogenic stroke is always a challenge
  * Selection of the proper medication is an educated guess
* Other paths forward
  * Risk stratification
  * Use of biomarkers
* Due to the complexity of the work-up, most of these patients probably benefit from the resources of a CSC
By their very nature, patients with a cryptogenic stroke are probably best evaluated and treated at a CSC

The thoroughness of the work-up (and the accuracy of the diagnosis) may vary greatly if the patient is not evaluated at a CSC

Although up to 30% of these patients may have paroxysmal Afib, what about the other 70%??

While we all agree that the best way to treat a stroke is to prevent the stroke, this is a greater challenge without a clear etiology