Striking out Stroke

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Providence Stroke Program
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The legal stuff…

No disclosures.

Learning Objectives: Striking Out Stroke

• Strike 1: How are you (PCP) at preventing the first stroke?

• Strike 2: How do I (ST) determine who gets acute stroke treatment?

• Strike 3: How do we (PCP + ST) prevent the next stroke?
U.S. Stroke Stats

- >795K new strokes/year
  - 185K of those are recurrent strokes
- >133K (17%) deaths/year (#5 cause)
- ~7.2M survivors, 4.5M disabled (#1 cause)
- >$40 billion/yr

Strike 1: Preventing First Stroke


Figure Legend:
Adjusted Stroke Incidence Rate Ratios vs Calendar Time
Models are adjusted for age, sex, race and center, hypertension, diabetes, coronary heart disease, cholesterol-lowering medication use, and smoking. Dots represent adjusted incidence rate ratio point estimates from model run using a categorical calendar time variable, plotted at midpoint of each 3-year calendar time category, with 1999-2001 as the reference category. The dotted line represents the linear trend in adjusted incidence rate ratios and the shaded area represents the 95% CI with 2000 as the reference point. Models included all study data, but plots exclude time periods in which there were few events.
Primary Prevention: No Surprises

- Physical activity lowers risk 25-30%
  - 40 min moderate exercise 3-4x/week (IB)
- BP reduction more important than agent (IA)
  - Target <140/90 (**130/80)
- Diabetic stroke risk lower by BP control and statin
  - Benefit of aspirin or tight glycemic control unclear (IIB)
- Statin for those with high 10-year risk (1A)
  - [http://my.americanheart.org/cvriskcalculator](http://my.americanheart.org/cvriskcalculator)
- Smoking is bad, healthy diets are good
- AF with CHADS-VASc ≥2 need anticoagulation (IA)
Primary Prevention: Other

- Asymptomatic Carotid Disease (CEA/CAS):
  - Stroke risk is low, medical management is good
  - Ongoing study (CEA vs CAS vs BMM)
  - No indication for general screening

- PFO
  - Antiplatelet, closure not recommended (IIIIC)

- OSA
  - Screen, study, treat (IIBC)

- Aspirin:
  - 10-year CV risk >10%
Primary Prevention—Challenge

Stroke Awareness

**Background and Purpose**—Although time-dependent treatment is available, most people delay contacting emergency medical services for stroke. Given differences in the healthcare system and public health campaigns, exploring between-country differences in stroke preparedness may identify novel ways to increase acute stroke treatment.

**Methods**—A survey was mailed to population-based samples in Ingham County, Michigan, US (n=2500), and Newcastle upon Tyne, UK (n=2500). Surveys included stroke perceptions and stroke/nonstroke scenarios to assess recognition and response to stroke. Between-country differences and associations with stroke preparedness were examined using t tests and linear mixed models.

**Results**—Overall response rate was 27.4%. The mean age of participants was 55 years, and 58% were female. US participants were better in recognizing stroke (70% versus 63%, d=0.27) and were more likely to call emergency medical services (55% versus 52%, d=0.11). After controlling for demographics and comorbidities, US participants remained more likely to recognize stroke but were not more likely to respond appropriately. A greater belief that medical treatment can help with stroke and understanding of stroke was associated with improved stroke recognition and response.

**Conclusions**—Overall, stroke recognition and response were moderate. US participants were modestly better at recognizing stroke, although there was little difference in response to stroke. Future stroke awareness interventions could focus more on stroke outcome expectations and developing a greater understanding of stroke among the public. *(Stroke. 2015;46:3220-3225. DOI: 10.1161/STROKEAHA.115.009997.)*
Strike 2: Improved Treatment

Less morbidity/mortality due to:

• Better treatments
• Better processes
• Better access
Stroke Mortality by State: 2016

24th highest stroke mortality

Age-Adjusted Death Rates
History of acute stroke revascularization therapy

- 1995  NINDS  iv tPA (<3hr)
- 1999  ProAct  ia tPA
- 2008  ECASS III: iv tPA (<4.5hr)
- 2012  IMS (tPA + device)
- 2014…
# Outcomes from iv tPA

<table>
<thead>
<tr>
<th>Outcome</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>NI/Near NI</td>
<td>8.3</td>
</tr>
<tr>
<td>Improved</td>
<td>2.0</td>
</tr>
<tr>
<td>Worse (NNH)</td>
<td>33</td>
</tr>
</tbody>
</table>

Saver JL et al, Stroke 2007; 38:2279-2283

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**Diagram:**

- **Normal or nearly normal**
- **Better**
- **No major change**
- **Worse**
- **Severely disabled or dead**

**Early course:**
- **No early worsening with brain bleeding**
- **Early worsening with brain bleeding**
Interventional Stroke Treatment

- >15yrs studies using different devices
  - Good technical success/TICI 2b, 3
  - No clinical/functional improvement

**Concentric: corkscrew**

**Penumbra: suction**
Then Came Stent-retrievers

11/2014 MR. CLEAN study: significant improvement in outcomes for major stroke.

What was different?

Patient selection:
- Under 6hr, CTA positive for large vessel occlusion
- Up to 24hr, CTA positive AND CTP appropriate
Arterial Circulation of the Brain, Including Carotid Arteries

- Basilar artery
- Middle cerebral artery
- Internal carotid artery
CBF<30% volume: 18 ml

Mismatch volume: 87 ml
Mismatch ratio: 5.8

Tmax>6.0s volume: 105 ml

Slab 2

Total CBF<30% volume: 29 ml
Total Tmax>6.0s volume: 133 ml
Total Mismatch difference: 104 ml
Total Mismatch ratio: 4.6
## Some Stentriever Data

<table>
<thead>
<tr>
<th>Study</th>
<th>Endo +/- tPA</th>
<th>tPA only</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SWIFT PRIME</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS score 0-2 at 90d</td>
<td>60.2%</td>
<td>35.5%</td>
<td>.0008</td>
</tr>
<tr>
<td>Mortality</td>
<td>9.2%</td>
<td>12.45%</td>
<td>.50</td>
</tr>
<tr>
<td>Mean chg NIHSS at 27h (pts)</td>
<td>8.5</td>
<td>3.9</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
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<tbody>
<tr>
<td><strong>EXTEND-IA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS score 0-2 at 90 d</td>
<td>71%</td>
<td>40%</td>
<td>.01</td>
</tr>
<tr>
<td>Reperfusion at 24 h</td>
<td>100%</td>
<td>37%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Neurologic improvement at 3 d</td>
<td>80%</td>
<td>37%</td>
<td>.002</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Study</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ESCAPE</strong> (some &gt;6h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS score 0-2 at 90d</td>
<td>53.0%</td>
<td>29.3%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mortality</td>
<td>10.4%</td>
<td>19.0%</td>
<td>.04</td>
</tr>
</tbody>
</table>

“With standard tPA treatment of stroke, one in five patients had a good outcome. With intra-arterial intervention treatment, one in three patients had a good outcome.” (Dr. Dippel of the MR. CLEAN study group)
It takes a village…
or a Pit Crew!

- EMS: identify, transport quickly, prenotify
- ED triage: highest level, activate protocol
- ED physician: recognize and order studies
- ED HUC: activate Stroke team, CT, Pharmacy, lab
- ED RN: monitor VS, check meds, etc…
- CT tech/Radiologist: DT <25min, read<45 min
- Stroke Neurologist/Team: examine patient, review data, decide therapy
- Pharmacy: mix and deliver drug
- Lab: stat runs and reports
- CVL: prepare to receive patient

- All within 60 minutes from arrival to ED!!!
Telestroke

- Partner site
- (Patient)
- Broadband Internet
- Hub (or Home)
- (Stroke Neurologist)
Stroke Center Certification

- 1 Comprehensive Stroke Center (level III)
- 3 Primary Stroke Centers (2 endovascular capable) (level II)
- 16 Stroke-ready Tele Partner sites (level I)

Acute and Prevention Clinical Trials
Cutting edge care for Ischemic and Hemorrhagic stroke care

The Stroke Care Pyramid

- **Comprehensive Stroke Center**
  - All PSC functions plus Neurosurgeon
  - Neuroendovascular, and full spectrum of hemorrhagic stroke care

- **Primary Stroke Center**
  - Stroke Unit, coordinator, Stroke Service, continuum of inpatient care

- **Acute Stroke Ready Hospitals**
  - IV tPA, CT scanner, acute stroke expertise (via TeleStroke if needed)

- **Basic Care Hospital**
  - Assessment, identification, stabilization & transfer

New for 2018 Thrombectomy-Capable Stroke Center
ABCD2 Score

- **Age >60** 1 pt
- **Blood pressure; SBP > 140 OR DBP > 90** 1 pt
- **Clinical: weakness, one side, OR language disturbance** 2 pt
- **D(1)uration of symptoms > 60min OR** 2 pt
- **duration of symptoms 10 – 59_min** 1 pt
- **D(2)iabetes** +1 pt
- **Total ABCD2 score:** 1-7

*Johnston, SC. Lancet. 2007; 369:283-292. n=4799*
## ABCD2 Score

n=4799

<table>
<thead>
<tr>
<th>ABCD2</th>
<th>2 day risk</th>
<th>7 day risk</th>
<th>90 day risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>1.0%</td>
<td>2.2%</td>
<td>3.1%</td>
</tr>
<tr>
<td>4-5</td>
<td>4.1%</td>
<td>5.9%</td>
<td>9.8%</td>
</tr>
<tr>
<td>6-7</td>
<td>8.1%</td>
<td>11.7%</td>
<td>17.8%</td>
</tr>
</tbody>
</table>

• Lancet 2005; 366:29-36
Strike 3: Secondary Prevention
Secondary Stroke Prevention

What is the cause of the initial cerebrovascular event?

- Large vessel atherosclerosis
  - +/- CEA/CAS
- Small vessel atherosclerosis
- Unknown
- Cardioembolic
  - Warfarin
  - Dabigatran
  - Rivaroxaban, Apixiban, Edoxaban

Modified from:
The most frequent sites of arterial and cardiac abnormalities causing ischemic stroke.

Ischemic stroke etiologies

The most frequent sites of arterial and cardiac abnormalities causing ischemic stroke.
Aspirin

- Aspirin reduces risk by 15% vs. placebo
- 50-325mg safe and equally effective
- Standard to which all new agents compared
- Clopidogrel and ASA/ER DP similar to ASA in risk reduction
- Dual Anti-Platelet Therapy short term after event, then single agent
Antiplatelet Wars

• Battle I: MATCH: Clop + ASA vs. Clop (n=7599)
  – No difference in stroke or stroke/MI/death
  – Major and life-threatening bleeds significantly higher with combination

• Battle II: CHARISMA: Clop+ASA vs. Clop (15,603)

• Battle III: PRoFESS: ASA+DP vs. Clop (29,332)
  – No difference in stroke recurrence rates
  – Slightly increased ICH rate (HR 1.15, CI 1.11 to 1.42)
Conclusion?

From PRoFESS and...related trials, enlightenment might be expressed as haiku:

For stroke prevention,
use an antiplatelet drug.
Treat hypertension.

Kent, DM  Thaler, DE *NEJM* 359;12 2008
Timing of anticoagulation after stroke with atrial fibrillation

76 year-old man with atrial fibrillation presents with 8 hours of left sided weakness and slurred speech.
Timing of anticoagulation after stroke with atrial fibrillation

- 4.9% 14-day recurrence cardioembolic ischemic stroke

- Risk of hemorrhagic complication is linked to:
  - Size of stroke
  - Timing of stroke
  - Degree of anticoagulation
  - Patient age
  - History of diabetes
  - History of hypertension
  - Presence of ‘microvascular’ changes on CT/MRI

1 Stroke. 2001; 32: 2333-2337
• For most patients with a stroke or TIA in the setting of AF, it is reasonable to initiate oral anticoagulation within 14 days after the onset of neurological symptoms (Iia,B).

• In the presence of high risk for hemorrhagic conversion (ie, large infarct, hemorrhagic transformation on initial imaging, uncontrolled hypertension, or hemorrhage tendency), it is reasonable to delay initiation of oral anticoagulation beyond 14 days (IIa, B).
Comparison of NOACs to warfarin

<table>
<thead>
<tr>
<th>Agent</th>
<th>Class</th>
<th>Stroke Prevention</th>
<th>Bleeding Risk</th>
<th>Antidote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran (Pradaxa)</td>
<td>Direct thrombin inhibitor</td>
<td>Better</td>
<td>Equal</td>
<td>Praxbind (idarucizumab)</td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto)</td>
<td>oral Xa-inhibitor</td>
<td>Equal</td>
<td>Equal</td>
<td>FEIBA or Kcentra*</td>
</tr>
<tr>
<td>Apixaban (Eliquis)</td>
<td>oral Xa-inhibitor</td>
<td>Better</td>
<td>Lower</td>
<td>FEIBA or Kcentra*</td>
</tr>
<tr>
<td>Edoxaban (Savaysa)</td>
<td>oral Xa-inhibitor</td>
<td>Equal</td>
<td>Lower</td>
<td>FEIBA or Kcentra*</td>
</tr>
</tbody>
</table>

*limited data
Patients to consider

- Intolerant of warfarin
- Unstable INR
- Unable to get INR
- Offer to new patients
- Cost
- Stable patients?
Outpatient Cardiac Telemonitoring for Paroxysmal afib

- 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 (IIa; C).

- PAF detection over average hosp LOS: ~3%
  - 48hr holter 2-3%
  - 30 day monitor 11-16 %
  - 6 month monitor 22%
  - 12 month 25%
  - 36 months 30%

Presented ISC, 2/2104
PFO Closure vs Medical Therapy

- Old trials slow to enroll
- 81% of the recurrent strokes were not cryptogenic
- Low recurrent event rates so not significant

- NEJM 2017;377: two studies CLOSE and RESPECT
Kaplan–Meier Cumulative Estimates of Probability of Stroke in the PFO Closure Group versus the Antiplatelet-Only Group.
<table>
<thead>
<tr>
<th>Subgroup</th>
<th>PFO Closure Group</th>
<th>Medical-Therapy Group</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value by Log-Rank Test</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>18/499 (3.6)</td>
<td>28/481 (5.8)</td>
<td>0.55 (0.30–1.00)</td>
<td>0.046</td>
<td>0.78</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–45 yr</td>
<td>6/230 (2.6)</td>
<td>10/210 (4.8)</td>
<td>0.49 (0.18–1.35)</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>46–60 yr</td>
<td>12/262 (4.6)</td>
<td>18/266 (6.8)</td>
<td>0.59 (0.28–1.23)</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Male</td>
<td>10/268 (3.7)</td>
<td>16/268 (6.0)</td>
<td>0.56 (0.25–1.23)</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>8/231 (3.5)</td>
<td>12/213 (5.6)</td>
<td>0.55 (0.22–1.34)</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Shunt size</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>None, trace or moderate</td>
<td>13/247 (5.3)</td>
<td>12/244 (4.9)</td>
<td>0.96 (0.44–2.11)</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>Substantial</td>
<td>5/247 (2.0)</td>
<td>16/231 (6.9)</td>
<td>0.26 (0.10–0.71)</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Atrial septal aneurysm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>Present</td>
<td>3/179 (1.7)</td>
<td>13/170 (7.6)</td>
<td>0.20 (0.06–0.70)</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>15/320 (4.7)</td>
<td>15/311 (4.8)</td>
<td>0.86 (0.42–1.76)</td>
<td>0.68</td>
<td></td>
</tr>
<tr>
<td>Index infarct topography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.21</td>
</tr>
<tr>
<td>Superficial</td>
<td>9/280 (3.2)</td>
<td>18/269 (6.7)</td>
<td>0.43 (0.19–0.96)</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Small deep</td>
<td>4/57 (7.0)</td>
<td>2/70 (2.9)</td>
<td>2.25 (0.41–12.32)</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5/157 (3.2)</td>
<td>8/140 (5.7)</td>
<td>0.48 (0.16–1.48)</td>
<td>0.19</td>
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</tr>
<tr>
<td>Planned medical regimen</td>
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<td></td>
<td></td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>8/132 (6.1)</td>
<td>5/121 (4.1)</td>
<td>1.32 (0.43–4.03)</td>
<td>0.63</td>
<td></td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>10/367 (2.7)</td>
<td>23/360 (6.4)</td>
<td>0.38 (0.18–0.79)</td>
<td>0.007</td>
<td></td>
</tr>
</tbody>
</table>
ASA PFO Guidelines

- For patients with ischemic stroke or TIA and PFO who:
  - Have DVT:
    - anticoagulation (IA)
    - if anticoagulation contraindicated, IVC filter reasonable (IIa,C).
    - consider PFO closure, decision based on the risk of recurrent DVT (Class IIb; Level of Evidence C).
  - Have no DVT:
    - antiplatelet therapy is recommended (Class I; LOE B).
    - no benefit for PFO closure (Class III; LOE A).
Questions?

Let’s Strike Out Stroke Together!