Stroke: Time is Brain

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Impact and Improvements

- In 2013, stroke dropped to the FIFTH leading cause of death
- 795,000 per year
- One stroke every 40 sec
- One death every 4 min
- Remains the leading cause of disability

Number of deaths for leading causes of death

<table>
<thead>
<tr>
<th>Disease/Medical Condition</th>
<th>Number of Deaths</th>
</tr>
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<tbody>
<tr>
<td>Cancer: GLO-01</td>
<td>501,599</td>
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<tr>
<td>Chronic lower respiratory: 199,919</td>
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<tr>
<td>Accidents/Cerebrovascular: 136,157</td>
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<tr>
<td>Heart/Lower respiratory: 126,978</td>
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<tr>
<td>Rheumatic/Infectious: 84,767</td>
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<tr>
<td>Diabetes: 56,976</td>
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<tr>
<td>HIV/AIDS: 54,879</td>
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<tr>
<td>Nephritis/malignant neoplasms: 45,132</td>
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<tr>
<td>Intentional self-harm (suicide): 43,144</td>
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</tbody>
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Source: Deaths, Final Data for 2013 and 2014, Long-Term

PREVENTABLE
Impact and Improvements

- Trade-Off in Mortality reduction through better acute stroke care is increase in survivors with disabilities
  - Estimated 73.7 billion dollars in economic costs in 2010
  - Incalculable human and social costs to patients and families

The Clock Is Ticking...how fast?

- In the typical LARGE VESSEL, supratentorial acute ischemic stroke:
  - **PER MINUTE:**
    - 1.9 million neurons are lost
    - 14 billion synapses
    - 7.5 miles of myelinated fibers
    - Brain ages 3.1 weeks
  - **PER SECOND:**
    - 32,000 neurons
    - 23 million synapses
    - 238 yards of myelinated fibers
    - Brain ages 8.7 hours

Stroke to Date

- IV tPA has been our only pharmacologic therapy of benefit
  - 3-4.5 hour time window
  - Risk of cerebral and systemic hemorrhage
  - Early reperfusion in only 13-50% of large vessel occlusions
    - Works best on clots 5 mm or less in length
Large Vessel Occlusions

- Problem of larger clots
  - Clots longer than 8mm, < 1% likelihood of recanalization.
- 15-30% of acute strokes presenting within the first 6 hours are “LVO”
  - Proximal MCA
  - Proximal ACA
  - Distal ICA
  - Basilar artery


Changes in Acute Stroke Therapy

- Previously, IV tPA was the main go-to therapy
- Multiple prior trials had failed to show that catheter-based interventions were effective
  - Intra-arterial tPA
  - Mechanical thrombectomy
- October 2014: first of several trials published that have led to a change in acute stroke triage and management
  - Mechanical thrombectomy for LVO strokes in the anterior circulation within 6 hours, used IN ADDITION to IV tPA within the 3-4.5 hour time window.
### New Triage Patterns and Same Old Story

<table>
<thead>
<tr>
<th>New Triage</th>
<th>Unchanged Issues</th>
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<tbody>
<tr>
<td>• Need a way to rapidly assess patients who may benefit from endovascular treatment and get them to a stroke center with an interventionalist</td>
<td>• Fingertip glucose</td>
</tr>
<tr>
<td>• Triage protocols are key</td>
<td>• Get the meds, are they on warfarin or any new anticoagulants?</td>
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<tr>
<td>• CT Angiogram cornerstone to treatment</td>
<td>• Blood pressure targets:</td>
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<tr>
<td></td>
<td>- SBP &lt; 220, DBP &lt; 120 for non-tPA patients</td>
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<tr>
<td></td>
<td>- SBP &lt; 185, DBP &lt; 110 for tPA patients</td>
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### What can YOU do?

- Determine time **LAST SEEN NORMAL**
- Determine if patient is on warfarin or not
- Field draw of labs if there is time
- Fingertip glucose most important lab
- Start 16 or 18 gauge IV with Luer Lock hub
  - New treatment algorithms involving CT angiography, check with your local COPs
  - Please call in and notify receiving hospital if unable to obtain IV access

### STROKE ASSESSMENT TOOLS

- Stroke assessment tools help EMS identify a stroke quickly and transport the individual to the appropriate center
- Pre-hospital stroke assessment training raises the accuracy of stroke identification
- Paramedics demonstrated a sensitivity of 61-68% without stroke assessment training and 88-97% with training
What can YOU do?

- Assess FAST scale (or other triage scale)
- Call in and recommend activation of the Stroke Team:
  - “We have a 76 yo man last seen normal at 2:10 pm with a FAST score of 3. He is unable to talk or move the right side. We recommend activating the Code Stroke. 16 gauge Luer lock IV in the left arm.”

CONSUMER ASSESSMENT OF STROKE

Face Drooping - Ask the person to smile. Does one side of the face droop or is it numb?

Arm Weakness - Ask the person to raise both arms. Is one arm weak or numb? Does one arm drift downward?

Speech Difficulty - Ask the person to repeat a simple sentence. Is the sentence repeated correctly? Are they unable to speak, or are they hard to understand?

Time to call 9-1-1 - If the person shows any of these symptoms, even if the symptoms go away, call 9-1-1 and get them to the hospital immediately.

What can YOU do?

- Teach the FAST score at community education events
- Encourage community members to use 911 even if symptoms resolve
What can YOU do?

- If no family member travelling with patient, please obtain cell phone number
  - May need consent for endovascular therapies
  - May need more detailed information about past medical history to make decisions in less clear cases

Neighborhood Influences on EMS Use

- Neighborhood Influences
  - Lower SES use EMS more, but with delay
  - Higher SES use EMS less!
  - Neighborhoods with greater percentage of residents >age 65 less likely to use EMS, although individually older patients more likely to use EMS.
- Presents potentially modifiable targets for education
NEW TRIALS AFFECTING THE TRIAGE

Some Vocabulary

- **TICI 2b flow**: partial recanalization of 50% or more of the distribution of the occluded vessel
- **TICI 3 flow**: full recanalization
- **mRS 0-2**: no symptoms left – some symptoms but walks unassisted and basically independent, considered a “GOOD NEUROLOGIC OUTCOME”
- **ASPECTS score**: A CT based scoring system where 10 areas are judged as showing early signs of infarction or not. 10 is good. -1 point for each “bad” area. An ASPECTS score of 7-10 usually considered “safe” for tPA.

ASPECTS Score

Examine all the images at the ganglionic and supra-ganglionic levels.
Take off 1 pt from 10 for every region that is affected

<table>
<thead>
<tr>
<th>ASPECTS</th>
<th>Size</th>
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<tbody>
<tr>
<td>8-10</td>
<td>Small core.</td>
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<tr>
<td>6-7</td>
<td>Moderate core.</td>
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<tr>
<td>0-5</td>
<td>Large core.</td>
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</table>
Endovascular therapy (any) vs. standard care for ANTERIOR strokes (ICA/MCA/ACA) within 6 hours
- 18+ years old, no upper age limit
- NIH Stroke Scale Score of 2 or more
- 90 day functional outcomes, mRS, Barthel
- IV tPA w/in 4.5 hrs for pts who qualified
- ANY endovascular! (just had to have done 5+ before)
  - Most used stentriever

What is a Stentriever?
- Removable stent
- Struts engage the clot
- Not deployed permanently
- No need to use anticoagulation or antiplatelets targeted to the stent as it does not remain in the brain
  - Choice of antithrombotic therapy then depends on the stroke

Solitaire FR Revascularization Device
MR CLEAN

- 500 patients total
  - 233 endovascular and 267 "usual care"

- IV tPA was NOT a requirement for this trial.
  - 87% of patients in the endovascular arm received IV tPA.
  - 91% of patients in the control arm received IV tPA.

- NIHSS in MR CLEAN (and in the following trials) is 17-18 for a median (14-21x vs 14-22 control).
  - Expected range for large vessel occlusions

MR CLEAN Functional Outcomes

- NNT= 7-8 for primary outcome
- OR = 1.7 for 1 pt on mRS
- OR = 2.2 for mRS 0-2

- Need to treat 7-8 people to improve chances of functional independence!

- Absolute difference between control and treatment arms was 14%
**EXTEND-IA**

- Test of Solitaire stentriever device and tPA
- All pts received IV tPA w/in the 4.5 hr window
- Pts randomized to endovascular arm in 6 hr window
- 35 pts tPA alone, 35 pts tPA + Solitaire
  - (stopped early due to MR CLEAN)
- No upper age limit
- No NIHSS limit
- Imaging confirmation of ICA/M1/M2 occlusion
- <70 cc core infarct on CT or MRI perfusion

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**EXTEND-IA**

- Image to puncture median 93 min (71-138 min)
- Onset to recanalization median 4.13 hr (204-277 min)
- 86% TICI 2b/3 at end of procedure
- Looking at 24+ hours, who had “complete” reperfusion (90% or more)?
  - 100% Solitaire + IV tPA pts vs. 37% of IV tPA pts (p < 0.002)
EXTEND-IA Functional Outcomes

- Modified Rankin Score of 0-2 at 3 months:
  - Solitaire + IV tPA: patients, 71%
  - IV tPA alone: patients, 40%
  - P=0.01
  - NNT = 3.2 for independence
  - NNT = 3 to be 1 or more points better on mRS

- NIH Stroke Scale scores <8 or 0-1 by day 3:
  - Solitaire + IV tPA: 80%
  - IV tPA alone: 37%
  - P = 0.002

EXTEND-IA mRS at 90 days
SWIFT-PRIME

- Test of Solitaire stentriever device and tPA
- All pts received IV tPA w/in the 4.5 hr window
- Pts randomized to endovascular arm in 6 hr window
- 98 pts tPA alone, 98 pts tPA + Solitaire
- Age limits: 18-80
- NIHSS 8-29 at randomization
- Imaging confirmation of ICA or M1/M2 occlusion
- Image to Puncture 90 MINUTES (goal 70 minutes)

SWIFT-PRIME

- ASPECTS score on CT used to exclude patients with a large “core” of stroke (ASPECTS < 6)
- OR infarct of > 1/3 MCA or > 100 cc on MRI
- Pts followed out to 90 days

SWIFT-PRIME

Trial stopped early on 2/4/15...

Due to overwhelming EFFICACY!
SWIFT-PRIME

- Image to puncture time target was 90 MINUTES or less (median 58 min, 41-83)
- Onset to first pass 4.2 hours (median 252 min, 190-300)
- 88% TICI 2b/3 at end of procedure

- Looking at 24+ hours, who had “complete” reperfusion (90% or more)?
  - 82.8% Solitaire + IV tPA pts vs. 40.4% of IV tPA pts (p < 0.0001)

SWIFT-PRIME Functional Outcomes

- Modified Rankin Score of 0-2 at 3 months:
  - Solitaire + IV tPA: 59 patients, 60.2%
  - IV tPA alone: 33 patients, 35.5%
  - P=0.0008
  - Absolute difference of 24.7%

- Improvement in NIH Stroke Scale scores at 1 day:
  - Solitaire + IV tPA: median 8.5
  - IV tPA alone: median 3.9
  - P<0.0001
  - Absolute difference of 4.6 points
SWIFT-PRIME Safety Outcomes

- No differences in:
  - Mortality
  - Subarachnoid hemorrhage
  - Intraparenchymal hemorrhage
  - Any hemorrhage
  - Any serious adverse event

SWIFT-PRIME Conclusions

- NNT = 4 to get to mRS of 0-2
- NNT = 2.6 to move down one level on the mRS
- Feasibility of rapid workflow, 90 minute goals were met

What’s In the Pipeline?

- BEST trial ongoing in China looking at Solitaire in the basilar artery
- Await further trials evaluating stentriever with and without IV tPA in the posterior circulation
  - Triage patterns will change further, infrastructure will hopefully be ready by that time
What’s In the Pipeline?

- Estimated 25% of strokes are noticed upon awakening and therefore not candidates for ANY intervention….the WakeUp Stroke.

- Ongoing research into using imaging and presence/absence collateral blood vessels to consider WUS patients for IV tPA and/or endovascular intervention.
  - Some centers doing this already case-by-case
  - Several trials ongoing

What’s In the Pipeline?

- PHANTOM-S study in Germany
  - 25 min decrease in alarm-to-treat
    - 51.8 minutes with mobile unit
    - 76.3 minutes with standard ambulance
  - 23% rate of tPA
  - c/w 22% standard rate

- Houston started in 5/14
  - 8 slice portable CT by CereTom
    - Point of Care lab
    - Telemedicine connection
    - Stroke algorithm at dispatch level

- http://www.youtube.com/watch?v=6-JtNuA4mIA