Management of Acute Ischemic Stroke

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Chief, Neurointerventional Radiology
Acute Ischemic Stroke

• Impact

  - #1 cause of adult disability
  - #2 cause of dementia
  - #3 cause of death in the United States
    - 2nd cause of death worldwide
An estimated 795,000 Americans will suffer a new or recurrent stroke this year…

…that’s one every 40 seconds
**Two Types of Stroke**

**Ischemic Stroke**
- Type of condition in which oxygen is deficient
- Often caused by a blood clot or plaque buildup that blocks blood flow

**Hemorrhagic Stroke**
- Bleeding
- Occurs when a blood vessel ruptures, causing blood to leak into the surrounding tissue
Two Types of Stroke

87% of strokes are ischemic; only 1% of these patients get intervention.

13% of strokes are hemorrhagic:
- 10% intracerebral
- 3% subarachnoid

4 out of every 5 families will be touched by stroke

87% of strokes are ischemic; only 1% of these patients get intervention.

35-40% of Ischemic Strokes are Considered “Large Vessel”

- This subset of ischemic stroke comprises blockages in the:
  - Internal Carotid Artery (ICA)
  - Middle Cerebral Artery (MCA)
  - Vertebral / Basilar Artery

- If left untreated, patient prognosis with these types of stroke is poor

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>53% 1</td>
</tr>
<tr>
<td>MCA</td>
<td>27% 2</td>
</tr>
<tr>
<td>Basilar Artery</td>
<td>89-90% 3</td>
</tr>
</tbody>
</table>

1. Jansen O. et al.
2. Purlan A et al. PROACT II Trial
## Physiological Impact of Stroke

**Time = Brain**

Estimated Pace of Neural Circuitry Lost in a Typical Large Vessel Acute Ischemic Stroke

<table>
<thead>
<tr>
<th>Time</th>
<th>Neurons Lost</th>
<th>Synapses Lost</th>
<th>Myelinated Fibers Lost</th>
<th>Accelerated Aging</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 second</td>
<td>32,000</td>
<td>230 million</td>
<td>218 yards</td>
<td>8.7 hours</td>
</tr>
<tr>
<td>1 minute</td>
<td>1.9 million</td>
<td>14 billion</td>
<td>7.5 miles</td>
<td>3.1 weeks</td>
</tr>
<tr>
<td>1 hour</td>
<td>120 million</td>
<td>830 billion</td>
<td>447 miles</td>
<td>3.6 years</td>
</tr>
<tr>
<td>Avg. stroke</td>
<td>1.2 billion</td>
<td>8.3 trillion</td>
<td>4470 miles</td>
<td>36 years</td>
</tr>
</tbody>
</table>

US Prevalence of Stroke by Age and Sex\textsuperscript{1}

Stroke kills more women than breast, ovarian, uterine and cervical cancer combined\textsuperscript{2}

Race is a Risk Factor for Stroke

African-Americans have a risk of first-ever stroke that is almost twice that of Caucasians

TIA’s (Transient Ischemic Strokes)

- “Mini-Stroke” – symptoms can be similar to a stroke but resolve on their own in a short period of time

- ~5 million Americans have been diagnosed with having had a TIA; true prevalence is probably greater because many TIA’s go undiagnosed

- A meta-analysis shows that patients with TIA have a 10-17% risk of stroke within 90 days

- Within 1 year of TIA, ~12% of patients will die

Stroke is a Leading Cause of Death

Death Rate (per 100,000 population)

- Diseases of the Heart: 193.6
- Malignant Neoplasms: 186.2
- Chronic lower respiratory diseases: 44.7
- Cerebrovascular diseases: 41.9

Stroke accounts for 1 of every 18 deaths in the United States, that’s 1 every 4 minutes

There are Over 7 Million Stroke Survivors...  

...two thirds of which are living with moderate to severe disability.

- 35% had depressive symptoms
- 26% were dependent in activities of daily living
- 26% were institutionalized in a nursing home
- 19% had aphasia
- 50% had some hemiparesis
- 30% were unable to walk without assistance
- 30% were unable to walk without assistance

The Total Estimated Cost of Stroke is $48 Billion

- Lost productivity due to mortality and morbidity: $15 Billion
- Hospitalization Costs: $16 Billion
- Rehabilitation: $4.5 Billion
- Physician Costs: $4 Billion
- Medications & Other Costs: $3.5 Billion

The lifetime cost of stroke to a single patient is more than $140,000.
Risk Factors for Stroke

Hereditary / non-modifiable

- Increasing age
- Family history of stroke
- Prior TIA
- Prior ischemic stroke
- Prior heart attack

Modifiable

- High blood pressure
- High cholesterol
- Smoking / tobacco use
- Diabetes
- Physical inactivity / obesity
- Afib
- Carotid Artery Stenosis
- End-stage renal disease

So a stroke comes into the hospital. Now what?
Emergency Medical Services: American Heart Association Recommendations

- Onset time of stroke symptoms
  - Time of onset is very important
  - Clock time at onset of symptoms is preferred over "duration"
- Notification to hospital of triage
  - Obtaining telephone numbers of witness or family
National Institute of Neurological Disorders and Stroke (NINDS) Recommended Treatment Times

ED Door-to-MD 10 minutes
ED Door-to-Stroke Team notification 15 minutes
ED Door-to-CT scan 25 minutes
ED Door-to-Drug 60 minutes
ED Door-to-Admission 3 hours
What Are Signs and Clinical Presentation of Stroke?

Symptoms of stroke vary depending on the part of the brain that is affected:

- Sudden numbness or weakness of the face, arm, or leg
- Sudden trouble seeing in one or both eyes
- Sudden confusion or trouble speaking
- Sudden trouble with walking, dizziness, or loss of balance
- Sudden, severe headache with no known cause
Conditions that Mimic Stroke

- Alcohol Intoxication
- Migraines
- Epilepsy
- Psychogenic disorders
- Brain tumor
- Encephalitis
- Vertigo
- Hypo- or Hyperglycemia

Immediate Diagnosis and Management

- **Stat CT Head Scan**
  - Standard diagnostic tool to rule out hemorrhagic stroke
  - Subtle or early signs of infarct
    - Hyperdense vessel sign – indicative of thrombus or embolus
    - Loss of gray-white differentiation
      - Detected in many large vessel anterior circulation occlusions
Immediate Diagnosis and Management

- Lab Work
- EKG
- Maintain O$_2$ saturation $\geq$ 95%
- Neurological Exam – Stroke Assessment including National Institute of Health Stroke Scale (NIHSS)
Stroke Assessment
National Institute of Health Stroke Scale (NIHSS)

Severity scoring: range 0-42
0 = normal, 42 = worst score
NIHSS is used to measure severity and quantify objective changes in the assessment

1. Level of consciousness, following commands
2. Gaze preference
3. Visual acuity – partial/complete hemianopsia or total blindness
4. Facial palsy – smile/raise your eyebrows
National Institute of Health Stroke Scale (NIHSS) – cont’d

5. Motor arm – hold up your arms for 10 secs
6. Motor leg – hold up your leg for 5 secs
7. Limb ataxia – in 1 or 2 limbs
8. Sensory – do you feel this
9. Best language – aphasia or mute
10. Dysarthria – slurred or unintelligible
11. Extinction/Inattention – to double simultaneous stimulation, partial or profound neglect
NIHSS:
Stroke Severity & Vessel Location

- NIHSS $\geq 12$ $\rightarrow$ 91% Positive Predictive Value of Large Vessel Stroke
  

- NIHSS 5-9 $\rightarrow$ 36% Large Vessel

- NIHSS 10-14 $\rightarrow$ 44% Large Vessel

- NIHSS 15+ $\rightarrow$ 100% Large Vessel

Large Vessel Strokes

- ICA, ICA-T, MCA, vertebrobasilar arteries
- Poor natural history in large vessel stroke
- Mortality rates from published literature
  - ICA-T: 53%  
    Jansen, 1995
  - MCA: 30-35%  
    Chambers, 1987
  - Basilar: 89-92%  
    Brückmann H, 1986 & Brandt, 1996
Evidenced Based Stroke Treatment

**Stroke**

- **Imaging**
  - **Hemorrhagic?**
    - SAH?
    - Aneurysm?
    - Hypertensive ICH?
    - Investigate for cause
    - Other
  - **SAH Management**
  - **Risk Factor Modification**
  - **ICH Management**
  - **Risk Factor Modification**
  - **Specific Cause Management and Treatment**

- **Ischemic?**
  - **Consider Thrombolysis Thrombectomy**
  - **Atrial Fibrillation, Mechanical Valve, Mural Thrombus?**
  - **Carotid Atherosclerosis?**
  - **Small Vessel?**
  - **Intracranial Atherosclerosis?**
  - **Sinus Thrombosis?**
  - **Dissection?**
  - **Other**
  - **Risk Factor Modification**
    - Antithrombotic
    - Statin
    - ACE Inhibitor
  - **Risk Factor Modification: Warfarin, or aspirin if contraindicated**
  - **CEA or Stent**
  - **Anticoagulation**
  - **Treat specific cause, consultation**
Ischemic Stroke: Basic Criteria for Endovascular Rx

1) Large Vessel Occlusion (CT/MR angiography)

2) Salvageable tissue (time window, imaging studies)

Neurovascular and Spine Associates
Acute Stroke Protocol

Acute Stroke at Home/Work
- 911; Paramedics Arrive
- Transport to Hospital
  - Call Ahead to ED
  - Patient Arrival in ED
    - Stroke Pager Called
    - Stroke CT ordered
    - Labs drawn
    - Family located

Stroke CT Obtained

Hemorrhage

Ischemic Stroke

IV t-PA Eligible?

IV t-PA

Large Vessel Occlusion?

No

Medical Therapy

Yes

Embolectomy / IA lytic

Large Vessel Occlusion?

Yes

Embolectomy / IA lytic

No

Treat Cause

Neurovascular and Spine Associates

Stroke CT = noncon CT, CTA (chest through brain), CTP, post-contrast CT
CT Angiography

Intravenous bolus of iodinated contrast is given through peripheral IV. A rapid scan is then performed from the heart to the top of the head, tracking the contrast through the arteries.

Hemorrhagic Stroke: helps identify aneurysms, vascular malformations
Ischemic Stroke: helps identify large vessel occlusions/stenoses
CT Angiography – Extracranial Vessels

LightSpeed16
Ex: 25001
Reformatted
Se: 839/21
Im: 43/44
Sag: R15.7 (COI)
512 x 512
STANDARD

120.0 kV
0.0 mA
Tilt: 0.0
ET: 0.5 s
GP: 0.5 s
TS: 27.50 mm/s
SPR: 1.375:1
W:534 L:216

DFOV: 22.6 x 22.6cm

Neurovascular and Spine Associates
CT Angiography – Extracranial Vessels

Neurovascular and Spine Associates
CT Perfusion

An intravenous bolus of iodinated-contrast is given through a peripheral IV. Serial images are then taken over time at a given location (or “slice”) of the brain, watching the contrast “wash in and wash out.”

\[
\text{CBF} = \frac{\text{CBV (ml/100 gm)}}{\text{MTT (sec)}}
\]
The Ischemic Penumbra

Mean Transit Time

Cerebral Blood Volume

Neurovascular and Spine Associates
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    - Family located

Stroke CT Obtained

Hemorrhage
- Treat Cause

Ischemic Stroke
- IV t-PA Eligible?
  - Yes
  - IV t-PA
  - Large Vessel Occlusion?
    - Yes
    - Embolectomy / IA lytic
    - No
    - Medical Therapy
  - No
  - Large Vessel Occlusion?
    - No
    - Medical Therapy
    - Yes
    - Embolectomy / IA lytic

Stroke CT = noncon CT, CTA (chest through brain), CTP, post-contrast CT
Consider Thrombolysis
Thrombectomy

0

4.5

IV t-PA

Time from stroke symptom onset (hr)
Intravenous t-PA -vs- placebo (N=312 each group)
- 0.9 mg/kg t-PA IV (10% bolus, 1 hr infusion)
- within 90-180 mins of symptom onset
- CT exclude hemorrhage

Clinical benefit seen in both large vessel and small vessel stroke syndromes.

- symptomatic intracranial hemorrhage
  6% -vs- 0.6% (t-PA -vs- placebo)
- 3% hemorrhage-related death

**NEJM 333:1581 (1995)**
Acute Stroke Protocol

Stroke CT = noncon CT, CTA (chest through brain), CTP, post-contrast CT

Acute Stroke at Home/Work
- 911; Paramedics Arrive
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- Call Ahead to ED
- Patient Arrival in ED
  - Stroke Pager Called
  - Stroke CT ordered
  - Labs drawn
  - Family located

Stroke CT Obtained

Hemorrhage
- Treat Cause

Ischemic Stroke
- IV t-PA Eligible?
- No
  - Large Vessel Occlusion?
  - No
    - Medical Therapy
  - Yes
    - IV t-PA
      - Yes
        - Large Vessel Occlusion?
          - Yes
            - Embolectomy / IA lytic
          - No
            - Embolectomy / IA lytic
      - No
        - No
          - Ischemic Stroke
            - Yes
              - Embolectomy / IA lytic
            - No
              - Medical Therapy
Consider Thrombolysis Thrombectomy

Small and large vessel ischemic strokes.

Time from stroke symptom onset (hr)

IV t-PA

IA pro-UK

0

4.5

6
Intraarterial Thrombolysis – PROACT Trial

180 pts with acute MCA stroke presenting within 3-6 hours randomized 2:1 to IA pro-urokinase or placebo; primary outcome mRS at 90 days
PROACT-II: mRS ≤ 2

* OR 2.13 (1.02-4.42), p=0.043
PROACT-II: Conclusions

- IA r-ProUK for M1 or M2 occlusions, given under 6 hours, provides 60% relative benefit and 15% absolute benefit (mRS ≤ 2)
- Symptomatic intracranial hemorrhage risk increased (10% IA lytic, 2% control)
- No change in mortality
- MCA recanalization rate 67% (vs. 18% in placebo and ~25-30% with IV tPA alone)
- Natural history of M1/M2 occlusions: 75% disability at 90 days
Consider Thrombolysis
Thrombectomy

Small and large vessel ischemic strokes.

Time from stroke symptom onset (hr)

0
4.5
6
24

IV t-PA

IA pro-UK

Thrombectomy

Large vessel ischemic strokes.
“Stent-retriever”: Self-Expanding Non-Detachable Stent
Newer Technologies = Better Recanalization

Solitaire FR

Trevo

Separator 3-D

Penumbra Max System
<table>
<thead>
<tr>
<th></th>
<th>MR CLEAN</th>
<th>ESCAPE</th>
<th>EXTEND-IA</th>
<th>SWIFT PRIME</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>500 patients</td>
<td>316</td>
<td>70</td>
<td>196</td>
</tr>
<tr>
<td></td>
<td>- 233 IAT</td>
<td>- 165 IAT</td>
<td>- 35 IAT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 267 Control</td>
<td>- 150 Control</td>
<td>- 35 Control</td>
<td></td>
</tr>
<tr>
<td><strong>Device Usage</strong></td>
<td>Open Label</td>
<td>Open Label</td>
<td>Solitaire</td>
<td>Solitaire</td>
</tr>
<tr>
<td></td>
<td>- Mostly stent</td>
<td>- 86% Stent</td>
<td>(provided free</td>
<td></td>
</tr>
<tr>
<td></td>
<td>retrievers</td>
<td>Retriever</td>
<td>by Covidien)</td>
<td></td>
</tr>
<tr>
<td><strong>Enrollment Time Window</strong></td>
<td>6 hrs from symptom onset</td>
<td>12 hrs from symptom onset</td>
<td>4.5 hrs from symptom onset</td>
<td>6 hrs from symptom onset</td>
</tr>
<tr>
<td><strong>Key Selection Criteria</strong></td>
<td>- CTA LVO</td>
<td>- CTA LVO</td>
<td>- CTA LVO</td>
<td>- CTA LVO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- ASPECTS ≥ 6</td>
<td>- Mismatch</td>
<td>- ASPECTS ≥ 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Moderate/Good</td>
<td>with ischemic</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Collaterals</td>
<td>core &lt; 70 ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>on CTP</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline NIHSS</strong></td>
<td>- 17 IAT</td>
<td>- 16 IAT</td>
<td>- 17 IAT</td>
<td>17 both IAT and Control</td>
</tr>
<tr>
<td></td>
<td>- 18 Control</td>
<td>- 17 Control</td>
<td>- 13 Control</td>
<td></td>
</tr>
<tr>
<td><strong>Median ASPECTS</strong></td>
<td>9 both IAT and Control</td>
<td>9 both IAT and Control</td>
<td>Not applicable</td>
<td>9 both IAT and Control</td>
</tr>
<tr>
<td></td>
<td>MR CLEAN</td>
<td>ESCAPE</td>
<td>EXTEND-IA</td>
<td>SWIFT PRIME</td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>mRS ≤ 2 @ 90 Days</td>
<td>IAT: 32.6% Control: 19.1%</td>
<td>IAT: 53% Control: 29.3% NNT: 4</td>
<td>IAT: 71% Control: 40%</td>
<td>IAT: 61.1% Control: 35.5%</td>
</tr>
<tr>
<td>Revas Rate of IAT</td>
<td>58.7% TICI 2b/3</td>
<td>72.4% TICI 2b/3</td>
<td>86% TICI 2b/3</td>
<td>88% TICI 2b/3</td>
</tr>
<tr>
<td>Mortality at 90 Days</td>
<td>IAT: 21% Control: 22%</td>
<td>IAT: 10% Control: 19%</td>
<td>IAT: 9% Control: 20%</td>
<td>IAT: 12.2% Control: 25.8%</td>
</tr>
<tr>
<td>sICH</td>
<td>IAT: 7.7% Control: 6.4%</td>
<td>IAT: 3.6% Control: 2.7%</td>
<td>IAT: 0% Control: 6%</td>
<td>IAT: 1.0% Control: 3.1%</td>
</tr>
</tbody>
</table>
SWIFT-PRIME

- Multicenter International Randomized Control Trial comparing Solitaire + IV tPA vs. IV tPA alone in patients with large vessel occlusion.

- St. Jude Medical Center was one of only 2 sites in Southern California that was invited to participate in this study.
Key Inclusion Criteria

- Age 18 – 80
- Pre-stroke Modified Rankin Score ≤ 1
- NIHSS 8 – 29 at randomization
- Received IV t-PA within 4.5 hours of stroke onset
- CTA or MRA confirmation of large vessel occlusion (intracranial ICA, M1 or carotid terminus)
- Groin puncture within 6 hours of stroke onset and within 90 minutes* of qualifying imaging

*optimal target: within 70 mins
SPRIME: Reperfusion

N=83 pts
Based on all patients
with final TICI data

TICI 2B/3 rate is 88.0%

Subjects (%)

0 1 2A 2B 3
4.8% 1.2% 6.0% 19.3% 68.7%
**SPRIME: Primary endpoint**

<table>
<thead>
<tr>
<th></th>
<th>Functional independence (mRS 0-2) at 90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solitaire + IV t-PA</td>
<td>59 (60.2%)</td>
</tr>
<tr>
<td>IV t-PA</td>
<td>33 (35.5%)</td>
</tr>
</tbody>
</table>
Endovascular Acute Stroke Therapies

- Intra-arterial Thrombolytics (out to ~ 6 hours)
- Mechanical Clot Disruption (out to ~ 24 hours)
  - Retrieval device (e.g., Merci)
  - Suction catheter (e.g., Penumbra)
  - Stent retrieval (e.g., Solitaire, Trevo)
  - Balloon angioplasty and/or stent
  - Clot maceration (microcatheter, microwire)
  - Ultrasound
Acute Stroke – Case 1

30 year old man with neck injury playing tag football

abrupt onset slurred speech and double vision - ? concussion

right arm and leg weakness, tired/sleepy

found sleepy but arousable, slurred speech, R lower facial weakness, not moving R arm or leg. Time from onset – 3.5 hours.
Acute Stroke – Case 1

Taken to St. Jude Medical Center.
Neuro evaluation, non-contrast CT brain
Initial Cerebral Angiography
Merci® Endovascular Thrombectomy

Neurovascular and Spine Associates
Merci® Endovascular Retrieval System

Pre-thrombectomy

Post-thrombectomy
Complete neurologic recovery.

Cause of stroke: dissection of the vertebral artery from neck trauma, complicated by thromboembolism to the basilar tip.
Acute Stroke – Case 2

- 72 year old female
- Last known normal at 11 PM last night before going to sleep
- She woke up at 8 AM with left hemiplegia
- CTA/CT Perfusion demonstrates a right MCA occlusion with large penumbra
- NIHSS 12
Acute Stroke – Case 3
26 y.o. Female: Left Brain Stroke
26 yo Female: Left Brain Stroke

Before

After
26 y.o. Female: Left Brain Stroke
Experience with Stent Retrievers

July 2013 – January 2017:

• 161 patients treated with a stent retriever device (Solitaire or Trevo®).

• All selected with CT angiography and CT perfusion studies.

• TICI 2B or 3 recanalization in 90%.

• sICH in 2.0% (4/161), in patients treated with IV tPA + IA tPA as well.

• Early to have long-term clinical outcome data, but f/u in first 128 have shown good outcome (mRS 0-2 at 90 days) in 61%.
Conclusion:

Endovascular Therapy in Large Vessel Occlusion

- Acute Ischemic Stroke secondary to large vessel occlusion is a potentially devastating disease for which best treatment remains elusive.

- To promote best possible clinical practice, the administration of interventional stroke treatment should remain in the hands of experienced stroke experts who would maximize data collection to achieve the best possible patient outcomes.
Conclusion:
Endovascular Therapy in Large Vessel Occlusion

- Better patient outcomes with interventional stroke therapy:
  - Patient selection using advanced imaging
  - Advanced device technology
  - Faster and more complete recanalization
  - Better time management
    - Getting patients to endovascular capable hospitals
    - Moving patients more efficiently from ER door to recanalization
Thank you

Hamedfarid@gmail.com