Advances in Neuro-Endovascular Care for Acute Stroke

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Overview

• Stroke Facts
  – Definition, demographics, types
• Telestroke
  – IV tPA delivery data
• Thrombectomy for Large Vessel Occlusion (LVO)
  – MR CLEAN, DEFUSE 3 and friends
• The Future of Stroke Care
  – What about mobile stroke units (MSUs)?

STROKE FACTS
Stroke

• Injury to the brain as a result of a blocked or ruptured blood vessel.
• Someone in the U.S. has a stroke about once every 40 seconds.
• Stroke accounts for 1 of every 20 deaths in the U.S. Stroke ranks 5th among all causes of death in the U.S., killing nearly 133,000 people a year.
• Each year, about 795,000 people suffer a new or recurrent stroke.
• Stroke is a leading cause of serious long-term disability in the U.S.


Dariush Mozaffarian et al. Circulation. 2016;133:e38-e360
Cerebrovascular Disease: Pathogenesis

Ischemic Stroke (87%)
- Atherothrombotic Cerebrovascular Disease (20%)
- Cryptogenic (30%)
- Embolism (20%)
- Lacunar (25%)
- Small vessel disease

Hemorrhagic Stroke (13%)
- Intracerebral Hemorrhage (77%)
- Subarachnoid Hemorrhage (23%)

Ohio State Horseshoe

Seating capacity = 106,000 per game
Ischemic stroke = 690,000 per year
Hemorrhagic stroke = 105,000 per year

References:
Tissue Plasminogen Activator for Acute Ischemic Stroke
The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group
1995;333:1581-1687

In this illustration, 1 of the mortalities in the Actinase (r-PA) group could be due to SICH.
- Patients treated with Actinase (r-PA)
- Patients treated with placebo
- Patients with symptomatic intracranial hemorrhage (SICH)
### Telestroke

**The Ohio State University Wexner Medical Center**

#### Telestroke Protocol

**Telestroke** is a telemedicine program that connects patients with stroke specialists remotely, allowing for early intervention and treatment. It leverages technology to provide immediate access to expertise, potentially saving lives and improving outcomes. This protocol outlines key steps and criteria for patients to be eligible for Telestroke treatment.

#### Eligibility Criteria

1. **Inclusion Criteria**
   - Age 18 years and older
   - Recent onset of neurological symptoms (within 6 hours)
   - Systolic blood pressure ≤ 180 mmHg or diastolic blood pressure ≤ 110 mmHg
   - Glasgow Coma Scale (GCS) ≥ 8
   - National Institutes of Health Stroke Scale (NIHSS) ≤ 25

2. **Exclusion Criteria**
   - Seizures
   - Severe head injury
   - Known drug or alcohol abuse
   - Known cancer (active or within 5 years of diagnosis)
   - Known history of stroke or TIA
   - Known history of cardiomyopathy
   - Known history of coagulopathy
   - Known history of brain tumor
   - Known history of serious mental illness
   - Known history of head trauma
   - Known history of serious systemic illness
   - Known history of serious infection
   - Known history of serious bleeding disorder
   - Known history of serious metabolic disorder
   - Known history of serious renal disease
   - Known history of serious pulmonary disease
   - Known history of serious hepatic disease
   - Known history of serious neurologic disease

#### Procedure

1. **Initial Evaluation**
   - Immediate neurological examination
   - Immediate laboratory tests (e.g., CT scan of the head)
   - Immediate intervention if indicated

2. **Follow-up Evaluation**
   - Repeat neurological examination
   - Repeat laboratory tests
   - Repeat imaging studies

3. **Discharge Planning**
   - Education on stroke prevention
   - Referral to rehabilitation services

#### Telestroke Benefits

- Immediate access to stroke specialists
- Reduced time to treatment
- Improved outcomes
- Cost savings

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**For more information, visit [Telestroke Program](#) or contact (800) 262-4257.**
Regional thrombolysis use 2007 to 2010.


Table 2. The 20 Regions With the Highest Proportion of Ischemic Stroke Patients Treated With Thrombolysis From 2007 to 2010

### Telestroke – Current Status

- Started in 2011 with an ODH grant and 3 sites.
- Largest Telestroke Network in Ohio.
- 26 Telestroke sites to date

### Comprehensive Stroke Center: Telestroke Consults

**Within our 25 spoke hospital network:**

- 3173 telestroke consultations performed
- 1557 patients transferred from the originating spokes
- 712 patients (22%) received t-PA
- 51% of patients stayed at their local hospital

Data from (first go-live) 05/18/11 through 10/31/16.
THROMBECTOMY FOR LVO
TICI

- Grade 0 = No perfusion.
- Grade 1 = Perfusion past the initial obstruction, but limited distal branch filling with little or slow distal perfusion.
- Grade 2a = Perfusion of less than ½ of the vascular distribution of the occluded artery (e.g., filling and perfusion through 1 M2 division).
- Grade 2b = Perfusion of ½ or greater of the vascular distribution of the occluded artery (e.g., filling and perfusion through 2 or more M2 divisions).
- Grade 3 = Full perfusion will filling of all distal branches.
STUDIES SUPPORTING THROMBECTOMY

Patient population
- Greater than 18 years with no upper age limit
- NIHSS greater than or equal to 2

Imaging
- Exclude hemorrhagic stroke by CT
- Occlusion by CTA, MRA or DSA

Intervention
- Intra-arterial thrombectomy within 6 hours with or without IV rtPA in patients with intracranial occlusion in anterior circulation artery (ICA, M1, M2, A1 or A2)

Primary outcome
- Modified Rankin scale (mRS) at 90 days

Secondary outcome
- NIHSS 24 hours, 5 and 7 days
- ADL measured by Barthel index

Imaging outcomes
- CTA or MRA 24 hours to measure persistence of recanalization
- CT 5-7 days to measure final infarct volume

MR CLEAN
Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands
Study Stats

- Size: 500 study participants
  - Mean age: 65 years (23 to 96 years)
  - Men: 58.4%
  - 95% of patients in both groups had pre-stroke mRS 2 or better
  - Mean NIHSS: 17
- 267 patients (53.4%) assigned to control
- 233 patients (46.6%) assigned to intervention
  - 196 underwent IA therapy
    - 195 patients underwent mechanical thrombectomy
      - 190 with stent-retriever
    - 88 patients (37.8%) had general anesthesia
    - 30 patients (12.9%) underwent concurrent carotid stent
    - 24 patients (10.3%) received additional IA thrombolytic
    - 1 patient (0.4%) underwent IA tPA only

Results

- Primary
  - Median mRS at 90 days: 3 in Intervention and 4 in Control.
- Secondary
  - mRS 0-3 at 90 days: 51% in Intervention and 35% in Control.
  - Persistent vessel patency: 75% in Intervention and 33% in Control.

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
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<tbody>
<tr>
<td>mRS 0-1 90 days</td>
<td>27 (12%)</td>
<td>16 (6%)</td>
</tr>
<tr>
<td>mRS 0-2 90 days</td>
<td>76 (33%)</td>
<td>51 (19%)</td>
</tr>
<tr>
<td>mRS 0-3 90 days</td>
<td>119 (51%)</td>
<td>95 (36%)</td>
</tr>
<tr>
<td>NIHSS 24 h median</td>
<td>13 (0-20)</td>
<td>16 (12-21)</td>
</tr>
<tr>
<td>NIHSS 5-7 days median</td>
<td>8 (2-17)</td>
<td>14 (7-18)</td>
</tr>
<tr>
<td>Persistent vessel patency</td>
<td>141/187 (75.4%)</td>
<td>68/207 (32.9%)</td>
</tr>
<tr>
<td>Infarct volume median</td>
<td>49ml (22-96)</td>
<td>79ml (34-125)</td>
</tr>
</tbody>
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Safety

- 13 patients (5.6%) had clinical evidence of new ischemic stroke in different vascular territory in 90 days in intervention group, compared to 1 patient (0.4%) in control group
- Procedure-related complications
  - Embolization to new territory in 20 patients (8.6%)
  - Vessel dissection in 4 patients (1.7%)
  - Vessel perforations in 2 patients (0.9%)

Serious adverse events

![Image of table]
EXTEND IA
Extending the Time for Thrombolysis in Emergency Neurological Deficits—Intra-Arterial

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

- **Patient population**
  - Greater than 18 years with no upper age limit
  - NIHSS no lower limit
  - Pre-stroke mRS less than 2 (functional independence)

- **Imaging**
  - Exclude hemorrhagic stroke by CT
  - Ischemic core of less than 70 ml with salvageable tissue
  - Occlusion by CTA, MRA or DSA

- **Intervention**
  - Solitaire thrombectomy started within 6 hours and completed in 8 hours in patients who had received IV rtPA within 4.5 hours of stroke onset with ICA, M1 or M2 occlusion

- **Primary outcome**
  - Reperfusion at 24 hours defined by percent reduction in perfusion-lesion volume between initial and 24-hour CT perfusion studies
  - Early neurological improvement defined by decrease in NIHSS by 8 or more or a score of 0 or 1 3 days after intervention

- **Secondary outcome**
  - mRS at 90 days
  - Symptomatic hemorrhage
  - SAH
  - Parenchymal hematoma within 36 hours after treatment with increase in NIHSS by 4 or more points
  - Death due to any cause

ESCAPE
Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

- **Patient population**
  - Greater than 18 years with no upper age limit
  - Functional independence before stroke onset

- **Imaging**
  - CT
    - Exclude hemorrhagic stroke
    - ASPECTS (Alberta Stroke Program Early Computed Tomography Score), used in ASPECTS to identify patients with small infarct core defined by ASPECT score 6-10
    - CTA evaluated for occlusion AND also assesses for moderate-to-good vascular collateralization in setting of LVO, which was defined as filling of at least 50% of the MCA pial artery circulation

- **Intervention**
  - Intra-arterial thrombectomy within 6 hours with or without IV rtPA in patients with intracranial occlusion in anterior circulation artery (ICA, M1, M2)

- **Primary outcome**
  - Modified Rankin scale (mRS) at 90 days

- **Secondary outcome**
  - Early recanalization and reperfusion
  - Intracranial hemorrhage
  - Angiographic complications
  - Neurological disability at 90 days
  - Death

- **Imaging outcomes**
Trends over time in complete reperfusion rates in active arms of coronary (diamond) and cerebral (square) reperfusion trials, without sample size weighting and with spontaneous reperfusion rates placed in 1980 as anchor, pre-reperfusion therapy era, values.

ENDOVASCULAR THERAPY FOLLOWING IMAGING EVALUATION FOR ISCHEMIC STROKE 3 (DEFUSE 3)

- Prospective randomized Phase III multicenter controlled trial for patients with acute ischemic anterior circulation strokes due to large artery occlusion treated between 6-16 hours of stroke onset with endovascular therapy versus control.
- Primary endpoint is modified Rankin Score at 3 months.
DEFUSE 2

Initial Growth Rate: Known Onset & M1 Occlusion

- Baseline DWI Volume (ml)
- Time between Symptom Onset and Baseline MRI (hrs)


DEFUSE 3: NIH-funded, prospective, randomized, multi-center, adaptive, blinded endpoint trial

- Paradigm shift
  - From time-based selection to imaging-based selection

- Target population
  - Anterior circulation ischemic stroke; ICA or M1 occlusions (CTA/MRA)
  - Salvageable tissue on CT perfusion or MR diffusion / perfusion
  - Endovascular therapy within 6-16 hours of last known well

- Design
  - 1:1 randomization; standard medical therapy vs. endovascular
  - 45 sites
Neuroimaging Inclusion Criteria

MRA / CTA reveals
- M1 segment MCA occlusion, or
- ICA occlusion (cervical or intracranial; with or without tandem MCA lesions)

AND

Target Mismatch Profile on CT perfusion or MRI (RAPID)
- Ischemic core volume < 70 mL and
- Mismatch ratio > 1.8 and
- Mismatch volume ≥ 15 mL

RAPID Imaging

CBF (<30%) volume: 26.4 ml
Perfusion (Tmax>6.0s) volume: 129.4 ml
Mismatch volume: 103.0 ml
Mismatch ratio: 4.9
What does the future hold?

Benefits of Stroke Treatment Using a Mobile Stroke Unit Compared With Standard Management
The BEST-MSU Study Run-In Phase

Rivij Bowry, MD; Stephanie Parker, RN; Suja S. Rajan, PhD; Jose-Miguel Yamal, PhD; Tzu-Ching Wu, MD; Laura Richardson, BS; Elizabeth Noser, MD; David Persse, MD; Kamilar Jackson, RT; James C. Grotta, MD

Background and Purpose—Faster treatment with intravenous tissue-type plasminogen activator (tPA) is likely to improve outcomes. Optimizing prehospital triage by mobile stroke units (MSUs) may speed treatment times. The Benefits of Stroke Treatment Delivered Using a Mobile Stroke Unit (BEST-MSU) study was launched in May 2014 using the first MSU in the United States to compare stroke management using an MSU versus standard management (SM). Herein, we describe the results of the prespecified, nonrandomized run-in phase designed to obtain preliminary data on study logistics.

Methods—The run-in phase consisted of 8 MSU weeks when all patient care occurred on the MSU and 2 SM weeks when the MSU nurse met personnel on scene or at the emergency department to ensure compatibility with MSU patients. Telemedicine was independently performed in 9 MSU cases.

Results—Of 130 alerts, 24 MSU and 2 SM patients were enrolled. Twelve of 24 MSU patients received tPA on board; 4 were treated within 60 minutes of last seen normal, and 4 went on to endovascular treatment. There were no hemorrhagic complications. Four had primary intracerebral hemorrhage. Agreement on tPA eligibility between the onsite and telemedicine physician was 90%.

Conclusions—The run-in phase provided a tPA treatment rate of 1.5 patients per week, assured us that treatment within 60 minutes of onset is possible, and enabled enrollment of patients on SM weeks. We also recognized the opportunity to assess the effect of the MSU on endovascular treatment and intracerebral hemorrhage. Challenges include the need to control based patient selection on MSU versus SM weeks and establish inter-rater agreement for tPA treatment using telemedicine. (Stroke. 2015;46:3370-3374. DOI: 10.1161/STROKEAHA.115.010993.)
Summary

• Stroke Facts
  – Almost 800,000 patients suffer stroke a year in the U.S.

• Telestroke
  – Patients who receive Telestroke consult are much more likely to get IV tPA

• Thrombectomy for Large Vessel Occlusion (LVO)
  – Patients with LVO benefit from thrombectomy
  – The window for thrombectomy may be determined by functional imaging

• The Future of Stroke Care
  – MSUs may play a role in expediting stroke care
Thank you!

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