How to Solidify Door-In Door-Out and Other Inter-Hospital Transfer Practices

Paul Hansen, MD
Vascular Neurologist and Neurointerventionalist
Member of Texas GETAC
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Financial Disclosure

• I do not have any relevant financial interests or relationships to disclose
Objectives

• Identify advances in guidelines and evidence based care in the prevention, diagnosis, treatment of stroke in general
• Interpret which rapidly changing areas within the stroke care spectrum make rapid triage and treatment paramount
• Identify best practices for triaging all stroke patients to the most appropriate hospital, including EMS transport and inter-facility transfer algorithms
Evolution of Stroke Therapy

• Pre-1995: aspirin and observation

• 1995- NINDS stroke trial:
  • tPA was shown to be an effective tool for treating stroke within a 3 hour presentation window
  • At 3 months, 30% more likely to have minimal symptoms

• 2008- ECASS-3 stroke trial:
  • tPA can be safely administered out to 4.5 hour window
The Endovascular explosion
What’s the difference?

• What separates the early “negative trials” from the most recent “positive trials” in regards to intra-arterial therapy?
  • Confirmation of large vessel occlusion prior to enrollment
  • Device efficacy
  • Operator experience
  • Systems efficiency
  • All of the above
<table>
<thead>
<tr>
<th>Trial</th>
<th>Imaging Required to Confirm Occlusion Prior to Randomization?</th>
<th>Device(s) Used in Intervention Arm</th>
<th>TICI 2b/3 Revascularization Rate in the Intervention Arm</th>
<th>mRS 0-2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Intervention Arm</td>
<td>Control Arm</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IMS III</td>
<td>No</td>
<td>IA Lytic (138), Merci Retriever® (95), EKOS (22), Penumbra (54), Solitaire FR (5)</td>
<td>38% ICA 44% M1 44% M2 23% multi M2</td>
<td>40.8% (N=415)</td>
<td>38.7% (N=214)</td>
</tr>
<tr>
<td>MR RESCUE</td>
<td>No</td>
<td>Merci Retriever®, EKOS, IA Lytic, Penumbra</td>
<td>24% pen (n=34) 27% nonp (n=30)</td>
<td>21% pen (n=34) 17% nonp (n=30)</td>
<td>26% pen (n=34) 10% nonp (n=20)</td>
</tr>
<tr>
<td>MR CLEAN</td>
<td>Yes</td>
<td>97% Stent Retrievers, 2% other Mechanical</td>
<td>58.7% (N=196)</td>
<td>33% (N=233)</td>
<td>19% (N=267)</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>Yes</td>
<td>86% Stent Retriever</td>
<td>72.4% (n=156)</td>
<td>53.0% (n=164)</td>
<td>29.3% (n=147)</td>
</tr>
<tr>
<td>SWIFT PRIME</td>
<td>Yes</td>
<td>100% Stent Retriever</td>
<td>88.0% (n=83)</td>
<td>60.2% (n=98)</td>
<td>35.5% (n=93)</td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>Yes</td>
<td>100% Stent Retriever</td>
<td>86.2% (n=29)</td>
<td>71% (n=35)</td>
<td>40% (n=35)</td>
</tr>
</tbody>
</table>
All of the above!

• Confirmation of large vessel occlusion prior to enrollment
• Device efficacy
• Operator experience
• Systems efficiency
What We Know

2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment

Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria (Class I; Level of Evidence A). (New recommendation):

a. Prestroke mRS score 0 to 1,
b. Acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies,
c. Causative occlusion of the ICA or proximal MCA (M1),
d. Age ≥18 years,
e. NIHSS score of ≥6,
f. ASPECTS of ≥6, and
g. Treatment can be initiated (groin puncture) within 6 hours of symptom onset.
What We Still Don’t Know

• **Class IIb recommendations for EVT** (2015 Update to the AHA Guidelines)
  • Extended time window (>6 hours)
  • Large infarcts (ASPECTS <6)
  • Mild strokes (NIHSS <6)
  • Distal (M2/M3, ACA) and posterior circulation occlusions
  • Pediatric (<18 yrs old)
  • Various procedural approaches (including aspiration catheters, anesthetic management)
  • Appropriate triage mechanisms (including bypass of PSCs for high suspicion LVO patients)
What We Still Don’t Know

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  • Distal (M2/M3, ACA) and posterior circulation occlusions
  • Pediatric (<18 yrs old)
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  • Appropriate triage mechanisms (including bypass of PSCs for high suspicion LVO patients)
DAWN in Full Daylight

DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo

Tudor G. Jovin MD & Raul G. Nogueira MD on behalf of the DAWN investigators
Study background

- Current evidence suggests that benefit of thrombectomy rapidly decays over time and may no longer exist beyond 7.3 hours from stroke onset (or TLSW)\(^1\)

- Indeed, the current AHA and ESO guidelines define a rigid therapeutic window of 6 hours as level 1a evidence\(^2,3\)

- This treatment paradigm disregards individual variations in compensatory mechanisms for ischemia led by but not restricted to collateral flow.

- Growing evidence supports a physiologic rather than a purely time based approach where patients with Clinical-Core Mismatch (e.g. significant clinical deficits but still limited infarct size) may benefit from reperfusion regardless of time to treatment.\(^4\)

- **Wake-up strokes, strokes with unclear onset time, and witnessed late** presenting strokes (> 6 hours) represent a large proportion of LVOS (~40%) yet no proven treatment options exist for this population.

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2. Powers et al, Stroke. 2015  
3. Wahlgren et al, Int. Stroke. 2016 et.al  
**Study Objective**

To demonstrate superior functional outcomes at 90 days with Trevo plus medical management compared to medical management alone in appropriately selected patients treated six to 24 hours after last seen well.

**Study Design**

<table>
<thead>
<tr>
<th>Study design</th>
<th>Global, multi-center, adaptive, population enrichment, prospective, randomized, open, blinded endpoint (PROBE), controlled FDA IDE trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient population</td>
<td>• Acute ischemic stroke (AIS) with large vessel occlusion</td>
</tr>
<tr>
<td></td>
<td>• Able to be randomized between six to 24 hours after time last known well</td>
</tr>
<tr>
<td></td>
<td>• Clinical imaging mismatch (CIM) defined by age, core, and NIHSS</td>
</tr>
<tr>
<td>Target vessel</td>
<td>Intracranial ICA, M1 segment of the MCA</td>
</tr>
<tr>
<td>Randomization</td>
<td>1:1 Trevo + medical management vs. medical management alone</td>
</tr>
<tr>
<td>Sites</td>
<td>Up to 50 sites worldwide (30 US and 20 international)</td>
</tr>
<tr>
<td>Sample size</td>
<td>500 maximum subjects: 250 in the treatment arm and 250 in the control arm. Minimum sample size is 150 subjects.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>24 hours (-6/+24), day 5-7/discharge, day 30 (± 14), and day 90 (± 14)</td>
</tr>
</tbody>
</table>
Study Methods: Workflow

6-24h

- Age ≥18
- NIHSS ≥10
- Pre-mRS 0-1
- TLSW to Randomization: 6-24h

NCCT/DWI:
<1/3 MCA Territory

CTA/MRA:
ICA-T and/or MCA-M1
(Tandem Occlusions Allowed)

RAPID CTP/DWI CIM:

A. ≥80 y/o:
1. NIHSS ≥10 + core <21cc

B. <80 y/o:
2. NIHSS ≥10 + core <31cc
3. NIHSS ≥20 + core <51cc

1:1 Randomization:
- CIM subgroup
- ICA-T vs M1
- 6-12 vs 12-24h

Control
90-day mRS

Thrombectomy

- U-W mRS
- mRS 0-2

Informed Consent
## Study endpoints

<table>
<thead>
<tr>
<th><strong>Primary endpoint</strong></th>
<th><strong>90-day disability assessed by the modified Rankin scale (mRS)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Assessed via <strong>Utility-Weighted mRS</strong></td>
</tr>
<tr>
<td></td>
<td>• Nestled <strong>Dichotomous mRS 0-2</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Secondary endpoints</strong></th>
<th>• “Early response” at day 5-7/discharge, defined as a NIHSS drop of ≥10 points from baseline or NIHSS score 0 or 1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• All cause mortality rates</td>
</tr>
<tr>
<td></td>
<td>• Median final infarct size at 24 (-6/+24) hours from randomization</td>
</tr>
<tr>
<td></td>
<td>• Revascularization rates at 24 (-6/+24) hours from randomization</td>
</tr>
<tr>
<td></td>
<td>• Treatment arm: reperfusion rates post device and post procedure by angiography core lab measurement of modified TICI &gt; 2b</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Primary safety endpoint</strong></th>
<th><strong>Stroke related mortality at 90 days</strong></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>Secondary safety endpoint</strong></th>
<th>• Incidence of SICH, by ECASS III definition, within 24 (-6/+24) hours post randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Incidence of neurological deterioration from baseline NIHSS score through day 5-7/discharge</td>
</tr>
<tr>
<td></td>
<td>• Incidence of procedure-related and device-related serious adverse events through 24 (-6/+24) hours post randomization</td>
</tr>
</tbody>
</table>
DAWN Enrollment

- Suffice it to say that demographics, history, comorbidities were controlled between the two groups
- If anyone wants more extensive review, there is an alternate (much longer) presentation that includes a longer section on DAWN
CEC adjudicated safety outcomes

- sICH rate: 4.8% (P=0.3)
- Trevo: 3.2% (MM)

- Neurological deterioration: 10.5% (P<0.01)
- Trevo: 22.1% (MM)

- Stroke related mortality: 13.0% (P=0.6)
- Trevo: 18.0% (MM)
### Co-primary endpoints

<table>
<thead>
<tr>
<th></th>
<th>Trevo</th>
<th>MM</th>
<th>Treatment benefit (95% CI)</th>
<th>Bayesian probability of superiority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 90 weighted mRS</td>
<td>5.5 ± 3.8</td>
<td>3.4 ± 3.1</td>
<td>2.1</td>
<td>&gt;0.9999*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(1.20, 3.12)</td>
<td></td>
</tr>
<tr>
<td>Day 90 mRS (0-2)</td>
<td>48.6%</td>
<td>13.1%</td>
<td>35.5%</td>
<td>&gt;0.9999*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(23.9%, 47.0%)</td>
<td></td>
</tr>
</tbody>
</table>

**NNT for 90-day functional independence = 2.8**

*Similar to p<0.0001*
Primary outcome

- TREVO
  - mRS 0/uW mRS 10: 9%
  - mRS 1/uW mRS 9.1: 22%
  - mRS 2/ uW mRS 7.6: 17%
  - mRS 3/ uW mRS 6.5: 13%
  - mRS 4/ uW mRS 3.3: 13%
  - mRS 5-6/ uW mRS 0: 26%

- CONTROL
  - mRS 0/uW mRS 10: 4%
  - mRS 1/uW mRS 9.1: 5%
  - mRS 2/ uW mRS 7.6: 16%
  - mRS 3/ uW mRS 6.5: 34%
  - mRS 4/ uW mRS 3.3: 36%

Probability of superiority >0.9999

73% relative risk reduction of dependency in ADL’s
NNT for any lower disability 2.0
90 Day mRS 0-2 by TLSW to Randomization

<table>
<thead>
<tr>
<th>Time Window</th>
<th>Trevo Percentage</th>
<th>MM Percentage</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-12h</td>
<td>55.1%</td>
<td>20.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12-24h</td>
<td>43.1%</td>
<td>7.4%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Secondary effectiveness endpoints

Pre and 24 hour median core size

P = 0.02

NIHSS early responders

P < 0.001

47.7%

140% Improvement

19.2%
Secondary effectiveness endpoints

24 hour revascularization rates

100% relative improvement

P < 0.001

76.6% (Trevo) vs. 38.4% (MM)

All cause mortality

P = 1.0

18.7% (Trevo) vs. 18.2% (MM)
Conclusions

- Thrombectomy with Trevo in DAWN-eligible patients is associated with improvement in clinical outcomes across the entire range of utility weighted mRS and with higher rates of functional independence (mRS 0-2) compared to standard medical therapy (48.6% vs 13.1%, probability of superiority >0.999, NNT = 2.8)

- For every 100 patients treated with endovascular therapy, 49 will have a less disabled outcome as a result of treatment, including 36 who will be functionally independent

- The treatment effect size in DAWN is the highest out of any stroke trials to date and suggests that the presence of Clinical-Core Mismatch is a critical predictor of treatment effect independent of time to presentation

- Treatment effect persisted throughout 24 hours from TLKW; however, earlier treated patients do better

- Thrombectomy with the Trevo device in patients presenting beyond 6 hours of TLSW had comparable safety profile to thrombectomy performed within 6 hours
Open door for further expansion of time windows?

Physiological definition of eligibility vs time-based definition of eligibility
What We Still Don’t Know

• **Class IIb recommendations for EVT (2015 Update to the AHA Guidelines)**
  - Extended time window (>6 hours)
  - Large infarcts (ASPECTS <6)
  - **Mild strokes (NIHSS <6)**
  - Distal (M2/M3, ACA) and posterior circulation occlusions
  - Pediatric (<18 yrs old)
  - Various procedural approaches (including aspiration catheters, anesthetic management)
  - Appropriate triage mechanisms (including bypass of PSCs for high suspicion LVO patients)
• A small study published by Dr. Raul Nogueira’s department at Emory evaluated 32 consecutive LVO patients with presenting NIHSS ≤ 5. They were divided into a medical arm (22) vs interventional arm (10).

• All patients had a MRS 0-2 making them all good IA candidates other than the low NIHSS

• Rescue thrombectomy was performed on 9 of the medical arm patients due to rapid late deterioration

• In the patients who crossed over, median time to deterioration was 5.2 hours
Too good to intervene? Thrombectomy for large vessel occlusion strokes with minimal symptoms: an intention-to-treat analysis

Diogo C Haussen, Mehdi Bouslama, Jonathan A Grossberg, Aaron Anderson, Semir Belagaje, Michael Frankel, Nicolas Bianchi, Leticia C Rebell, Raul G Nogueira

**Table 2. Outcome data of the studied groups.**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Thrombectomy (n=19)</th>
<th>Medical (n=22)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial hemorrhages</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1.00</td>
</tr>
<tr>
<td>NIHSS score at discharge, median (IQ)</td>
<td>1 (0–3)</td>
<td>2 (0.5–4.5)</td>
<td>0.31</td>
</tr>
<tr>
<td>NIHSS score increasing &gt;6/10 death</td>
<td>1 (0)</td>
<td>5 (2)</td>
<td>0.83</td>
</tr>
<tr>
<td>NIHSS shift</td>
<td>-7.5</td>
<td>0</td>
<td>0.01</td>
</tr>
<tr>
<td>90-Day mRS</td>
<td></td>
<td></td>
<td>0.15</td>
</tr>
<tr>
<td>0</td>
<td>4 (40)</td>
<td>5 (23)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3 (30)</td>
<td>7 (32)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3 (30)</td>
<td>5 (23)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0 (0)</td>
<td>1 (5)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>5–6</td>
<td>0 (0)</td>
<td>4 (18)</td>
<td></td>
</tr>
<tr>
<td>90-Day mRS 0–2</td>
<td>10 (100)</td>
<td>17 (77)</td>
<td>0.15</td>
</tr>
<tr>
<td>90-Day mortality</td>
<td>0 (0)</td>
<td>3 (14)</td>
<td>0.53</td>
</tr>
<tr>
<td>Discharge score</td>
<td>9 (90)</td>
<td>16 (73)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

*Results are shown as number (%) unless stated otherwise.

**CONCLUSIONS**

We demonstrate a shift towards a lower NIHSS in patients with a LVO stroke presenting with mild symptoms who underwent primary thrombectomy as compared with those who received best medical therapy alone. Despite the overall perception that this condition is benign, nearly a quarter of patients primarily given medical treatment did not achieve independence at 90 days. Further studies evaluating the role of endovascular reperfusion for acute ischemic stroke with mild symptoms are warranted.
What We Still Don’t Know

• **Class IIb recommendations for EVT (2015 Update to the AHA Guidelines)**
  - Extended time window (>6 hours)
  - Large infarcts (ASPECTS <6)
  - **Mild strokes (NIHSS <6)** further RCT will be necessary
  - Distal (M2/M3, ACA) and posterior circulation occlusions
  - Pediatric (<18 yrs old)
  - Various procedural approaches (including aspiration catheters, anesthetic management)
  - **Appropriate triage mechanisms (including bypass of PSCs for high suspicion LVO patients)**
Appropriate stroke triage

• “Getting the right patients to the right places”
Identifying LVO patients

• Definitive diagnosis requires vessel imaging (CTA, MRA)

• Until mobile imaging, the clinical exam is the best proxy in the field
  • More severe the stroke → greater likelihood of LVO
  • Prehospital prediction score needs:
    • Fast and easy
    • Reliable in the field
    • Acceptable prediction of LVO
3-item stroke scale

Cortical signs

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disturbance of consciousness</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>0</td>
</tr>
<tr>
<td>mild</td>
<td>1</td>
</tr>
<tr>
<td>severe</td>
<td>2</td>
</tr>
<tr>
<td>Gaze and head deviation</td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>0</td>
</tr>
<tr>
<td>incomplete gaze/head deviation</td>
<td>1</td>
</tr>
<tr>
<td>forced gaze/head deviation</td>
<td>2</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>0</td>
</tr>
<tr>
<td>moderate</td>
<td>1</td>
</tr>
<tr>
<td>severe</td>
<td>2</td>
</tr>
</tbody>
</table>

Score (total) 0–6

# LA motor score (LAMS)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Facial droop</strong></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td><strong>Arm drift</strong></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Drifts down</td>
<td>1</td>
</tr>
<tr>
<td>Falls rapidly</td>
<td>2</td>
</tr>
<tr>
<td><strong>Grip strength</strong></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
</tr>
<tr>
<td>Weak grip</td>
<td>1</td>
</tr>
<tr>
<td>No grip</td>
<td>2</td>
</tr>
</tbody>
</table>

RACE scale

Cortical signs

Table 1. RACE Scale

<table>
<thead>
<tr>
<th>Item</th>
<th>RACE Score</th>
<th>NIHSS Score Equivalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial palsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Moderate to severe</td>
<td>2</td>
<td>2–3</td>
</tr>
<tr>
<td>Arm motor function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal to mild</td>
<td>0</td>
<td>0–1</td>
</tr>
<tr>
<td>Moderate</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>3–4</td>
</tr>
<tr>
<td>Leg motor function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal to mild</td>
<td>0</td>
<td>0–1</td>
</tr>
<tr>
<td>Moderate</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>3–4</td>
</tr>
<tr>
<td>Head and gaze deviation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1</td>
<td>1–2</td>
</tr>
<tr>
<td>Aphasia* (if right hemiparesis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Performs both tasks correctly</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Performs 1 task correctly</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Performs neither tasks</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Agnosia† (if left hemiparesis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient recognizes his/her arm and the impairment</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Does not recognize his/her arm or the impairment</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Does not recognize his/her arm nor the impairment</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Score total 0–9

*aphasia
†agnosia

**LEGS score**

| **LEG STRENGTH**                  | 0 = NO DRIFT  
1= DRIFT  
2= SOME EFFORT AGAINST GRAVITY  
3= NO EFFORT AGAINST GRAVITY  
4= NO MOVEMENT  
UN= AMPUTATION OR JOINT FUSION  
RIGHT | LEFT |
|----------------------------------|-------------------------------------------------|---|
| **EYES/VISUAL FIELDS**           | 0 = NO VISUAL LOSS  
1= PARTIAL HEMIANOPIA  
2= COMPLETE HEMIANOPIA  
3= BILATERAL HEMIANOPIA (BLIND  
INCLUDING CORtical BLINDNESS) | |
| **GAZE**                         | 0 = NORMAL  
1 = PARTIAL GAZE PALSy  
2 = FORCED DEVIATION | |
| **SPEECH/LANGUAGE**              | 0 = NO APHASIA, NORMAL  
1 = MILD-TO-MODERATE APHASIA  
2 = SEVERE APHASIA  
3 = MUTE, GLOBAL APHASIA | |

Cortical signs
Cortical signs

Cincinnati Prehospital Stroke Severity Scale

2 points: Conjugate gaze deviation (≥1 on NIHSS item for Gaze)

1 point: Incorrectly answers at least one of two level of consciousness questions on NIHSS (age or current month) and does not follow at least one of two commands (close eyes, open and close hand) (≥1 on the NIHSS item for Level of Consciousness 1b and 1c)

1 point: Cannot hold arm (either right, left or both) up for 10 seconds before arm(s) falls to bed (≥2 on the NIHSS item for Motor Arm)

### FAST-ED Scale

Cortical signs

<table>
<thead>
<tr>
<th>Item</th>
<th>FAST-ED Score</th>
<th>NIHSS Score Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial palsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal or minor paralysis</td>
<td>0</td>
<td>0–1</td>
</tr>
<tr>
<td>Partial or complete paralysis</td>
<td>1</td>
<td>2–3</td>
</tr>
<tr>
<td>Arm weakness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No drift</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Drift or some effort against gravity</td>
<td>1</td>
<td>1–2</td>
</tr>
<tr>
<td>No effort against gravity or no movement</td>
<td>2</td>
<td>3–4</td>
</tr>
<tr>
<td>Speech changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mild to moderate</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Severe, global aphasia, or mute</td>
<td>2</td>
<td>2–3</td>
</tr>
<tr>
<td>Eye deviation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Partial</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Forced deviation</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Denial/Neglect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Extinction to bilateral simultaneous</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>stimulation in only 1 sensory modality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does not recognize own hand or</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>orients only to one side of the body</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FAST-ED indicates Field Assessment Stroke Triage for Emergency Destination; and NIHSS, National Institutes of Health Stroke Scale.
Which Pre-Hospital Scale is Best?

- 3- ISS
- LAMS
- RACE
- LEGS
- CPSSS
- FAST-ED
### LVO prediction: Diagnostic performance

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>PPV</th>
<th>NPV</th>
<th>+LR</th>
<th>-LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>3I SS (≥4)</td>
<td>171</td>
<td>0.67</td>
<td>0.92</td>
<td>0.86</td>
<td>0.74</td>
<td>0.89</td>
<td>8.37</td>
<td>0.36</td>
</tr>
<tr>
<td>LAMS (≥4)</td>
<td>119</td>
<td>0.81</td>
<td>0.89</td>
<td>0.85</td>
<td>7.36</td>
<td>0.85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RACE (≥5)</td>
<td>357</td>
<td>0.85</td>
<td>0.68</td>
<td>0.72</td>
<td>0.42</td>
<td>0.94</td>
<td>2.65</td>
<td>0.22</td>
</tr>
<tr>
<td>LEGS (≥4)</td>
<td>175</td>
<td>0.70</td>
<td>0.81</td>
<td>0.78</td>
<td>0.59</td>
<td>0.88</td>
<td>3.75</td>
<td>0.37</td>
</tr>
<tr>
<td>CPSSS (≥2)</td>
<td>303</td>
<td>0.83</td>
<td>0.40</td>
<td>0.71</td>
<td>0.79</td>
<td>0.46</td>
<td>1.40</td>
<td>0.40</td>
</tr>
<tr>
<td>FAST-ED (≥4)</td>
<td>741</td>
<td>0.60</td>
<td>0.89</td>
<td>0.79</td>
<td>0.72</td>
<td>0.82</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **RACE**: only score validated in prehospital setting by EMS
Any of the scores is sufficient!
Appropriate stroke triage

• “Getting the right patients to the right places”
Reperfusion approaches for LVO

• IV r-tPA
  • “Patients eligible for intravenous r-tPA should receive intravenous r-tPA even if endovascular treatments are being considered.” (Class I, LOE A)
  • ESCAPE control: mAOL 37.3% IV tPA vs. 7% no IV tPA (median 7 hrs)

• Intra-arterial therapy
  • Mechanical thrombectomy within 6 hrs & after IV r-tPA (Class I, LOE A)
  • Mechanical thrombectomy within 6 hrs and ineligible for IV r-tPA (Class IIa, LOE C: MR CLEAN, ESCAPE, REVASCAT)
Both are time dependent

**IV tPA**

**Intra-arterial therapy**


“The right place”: Critical factors

• Time
• Distance
• Eligibility
• Quality
Who should go directly to CSCs?

**Time**
- >4.5 hrs to 24 hrs (IAT only)
- <4.5 hrs (IV and IAT)

**Distance**
- CSC equidistant
- CSC remote (e.g., >30 min Δ)

**Eligibility**
- Non IV tPA candidate
- IV tPA candidate

Suspected LVO in the field

CSC

PSC

Eligibility: Non IV tPA candidate

Eligibility: IV tPA candidate

???
EMS triage: <4.5 hrs

- **Emory University**: Transferred vs. Direct Presentation
  
  Outside transfers → ~2hr transfer delay
  
  - Transfer delay → fewer pts with favorable core infarct size and lower rate of good outcome (29% vs. 51%; p=0.003)
- **Rush University**: Transfer delay vs. IAT
  
  - Median between-hospital distance=14.7 miles → median transfer time=104 minutes
  
  - Adjusted odds of IAT decrease 2.5% per minute of transfer time
EMS triage: <4.5 hrs

• Struggle between Class I therapies
  • PSC first: Early IV r-tPA + Late IAT
    \textit{versus}
  • CSC first: Late (or no) IV r-tPA + Early IAT

• The “right place”:
  • RCT necessary (RACECAT trial) \rightarrow \text{generalizable?}
  • Quality is variable:
    • Relative distance and travel time to and between hospitals
    • Door-to-needle times at PSC and CSC
    • Door in-door out times at PSC
    • Door-to-reperfusion times at CSC

Determine the relative delays to IV tPA & IAT, and the proportion who can be treated
Measure & improve quality

- Registry of standardized performance measures
- Clinical and safety outcomes (sICH, INT, mortality)
- Time measures
- Process improvement initiatives:
  - Door to needle
  - Door in-door out
  - Door to puncture/reperfusion
PSC: Door In – Door Out Time

• Analysis of 3 high-volume PSCs → CSC$^1$
  • Median DIDO: 106 min (IQR 86-143) → 64% of total time from FMC to arterial puncture
  • Suggested best practices:
    • Initiate transfer based on accepted criteria (without waiting for CSC approval)
    • Having initial ambulance crew standby for transfer
    • Predicted 30 minute improvement in DIDO

• Analysis of PSC protocol to improve DIDO$^2$
  • Patients with LAMS score 4+
  • Notify CSC on arrival and dispatch CSC transport team (prior to imaging)
  • CTA performed concurrently with NCCT → transmitted to CSC
  • +LVO → immediate transfer
  • Full adherence to protocol: median DIDO 64 min (vs. 104.5 min), $P < 0.001$

$^2$JAMA Neurol. 2017; 74:793-800.
Most Effective DIDO reduction?

• Appropriate triage that avoids the second transfer in the first place!
• 90-120 minute reduction in FMC to groin puncture times based on available studies
How do we do it?

• Hospital mechanisms to improve DIDO
  - Door to needle/door to reperfusion monthly meetings (ED, radiology, pharmacy, neuro, neuro IR, EMS, administration, nursing)
  - CTA on front end to identify transfers
  - Shared imaging for interventionalist review
  - Immediate accept (“just say yes” policy)
  - Stroke champion/navigator
  - Stopwatch with each patient
  - Close interaction between CSC and various PSCs for education
  - Goal of 60 min DIDO (45 min door to needle + transfer)
  - Results in our experience, **45-90 min in network, 60-120 min out of network**
  - Special case of inpatient to inpatient transfer

• Statewide Guidance in Texas
  • Governor’s Emergency and Trauma Advisory Council (GETAC) – meets quarterly to set statewide goals in line with best practices and guidelines
  • Regional Advisory Councils (RACs) – empowered to guide EMS regionally to meet the proposed guidelines, coordinate with member hospitals, report back to GETAC
Proliferation of Stroke Centers

1476 Primary Stroke Centers (up 6.4% since 2014)
170 Comprehensive Stroke Centers (up 26% since 2014)

Source: JCAHO (www.jointcommission.org); DNVP (www.dnvaccreditation.com); HFAP (www.hfap.org); & State Department of Public Health websites & www.strokecenter.org
Last accessed: October 1st, 2015
Thought Experiment Based on Transparency

Triage Based on Distance + In-Hospital Process

<table>
<thead>
<tr>
<th>Field to Puncture Time</th>
<th>Median Door-to-Puncture Times</th>
</tr>
</thead>
<tbody>
<tr>
<td>130m</td>
<td>CSC #1 120 min</td>
</tr>
<tr>
<td>120m</td>
<td>CSC #2 100 min</td>
</tr>
<tr>
<td>90m</td>
<td>CSC #3 60 min</td>
</tr>
</tbody>
</table>

Field to ER Arrival Time (minutes)

Courtesy of Dr. Brijesh Mehta (Memorial Hospital, South Florida)
Food for Thought – DFW vs Rhode Island

- Dallas – Ft. Worth Metroplex
  - Population – 7.1 million
  - Size – 9,286 mi² (Dallas county alone is 909 mi²)
  - 13 counties
  - 9 CSCs
  - 31 PSCs

- Rhode Island
  - Population – 1.1 million
  - Size – 1,212 mi²
  - 5 counties, 1 CSC, 10 PSCs
Why Is This Important?

• DAWN and low NIHSS severity trials demonstrate that there are more candidates for intra-arterial therapy than are currently being treated. Variations in vascular reserve argue for using time based cutoffs for guidance, but physiology for absolute inclusion/exclusion.

• The landmark trials demonstrate that there is a life changing treatment which currently can only be offered at certain centers. The right place matters.

• DIDO and continuing process improvement is paramount. Faster is always better to increase the number of patients who could benefit from treatment, the closest center may not always be best.
Conclusions

• DAWN, low NIHSS studies
  • Current guidelines too restrictive → must expand the eligible patient population
  • Triage algorithms must consider extend the CSC time criteria to up to 24 hours (? Of EMS vs PSC based triage)

• Appropriate patient triage for IAT
  • Utilize pre-hospital scales for identifying high suspicion LVO patients, pre-hospital notification reduces response times
  • Must capture, report and improve time and quality metrics to guide triage decisions and that information must be available to EMS
  • Various DIDO improvement mechanisms can be successful, continuous process streamlining and data collection are necessary
Thank you!