FUTURE DIRECTIONS OF STROKE CARE

Jawad F. Kirmani MD
Director Stroke & Neurovascular Center
New Jersey Neurological Institute

Mohammad Moussavi, MD, Spozhmy Panezai, MD, Siddharat Mehta, MD, Daniel Korya, MD, Mohammad Hussein, MD Florence Chukwuneke RN, Martin Gizzi MD, PhD
OUTLINE

- Concept #1 Gotta have a Window!
- Concept #2 Bridges are Useless!
- Concept #3 Different Folks Same Strokes!
- Concept #4 Never mix your Meds!
- Concept #5 Stenting is for the Heart!
- Cases
- Conclusion
Concept #1: Gotta have a window!

- Acute Stroke intervention has traditional “Time Windows”
Intravenous Thrombolysis

624 patients with ischemic stroke within 3 hours

Intravenous tPA (0.9 mg/kg) vs placebo

Follow-up 3 months

tPA  placebo

Favorable outcome  42%  27%
Symptomatic ICH  6.4%  0.6%
Death at 3 month  17%  21%

NINDS trial

Intravenous Thrombolysis

700 patients with ischemic hemispheric infarct <6 hours of onset

rt-PA 0.9 mg/kg vs placebo

Follow-up 90 days

Favorable outcome
- rtPA: 40.3%
- Placebo: 36.6%

Any parenchymal hemorrhage
- rtPA: 11.8%
- Placebo: 3.1%

ECASS 2
821 patients with ischemic stroke within 3 to 4.5 hours

Intravenous tPA (0.9 mg/kg) vs placebo

3 months follow-up

<table>
<thead>
<tr>
<th></th>
<th>tPA</th>
<th>placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable outcome</td>
<td>52%</td>
<td>45%</td>
</tr>
<tr>
<td>Symptomatic ICH</td>
<td>2.4%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Death at 3 month</td>
<td>7.7%</td>
<td>8.4%</td>
</tr>
</tbody>
</table>

Intravenous Thrombolysis
IA

180 patients with occlusion of MCA within 6 hours of onset

IA Prourokinase (9mg) Vs. Placebo
Follow-up 3 months

Prourokinase
Recanalization: 66%
Hemorrhagic transformation: 10%
Favorable outcome: 40%

Placebo
Recanalization: 18%
Hemorrhagic transformation: 2%
Favorable outcome: 25%

PROACT - II
Prolyse in Acute Cerebral Thromboembolism Trial
Stroke. 1998;29:4-11.
114 patients with occlusion of MCA within 6 hours of onset - Japan - 2007

IA Urokinase Vs. Placebo
Follow-up 3 months

Urokinase
- Recanalization: 73%
- Symptomatic ICH: 9%
- Favorable outcome: 49%

Placebo
- Recanalization: 2%
- Symptomatic ICH: 2%
- Favorable outcome: 39%

MELT

Stroke. 2007;38:2627-2628.
151 patients with occlusion of large intracranial vessels within 8 hours of onset and ineligible for IV-tPA

Merici Retriever device
Follow-up 3 months

Merici-1
Recanalization 46%
Symptomatic ICH 7.8%
Favorable outcome 28%

NINDS - tPA
Recanalization
Symptomatic ICH 6.4%
Favorable outcome 30% >Placebo

**MERCI-1**

125 patients with occlusion of large intracranial vessels within 8 hours of onset and ineligible for IV-tPA

### Mechanical

- **Penumbra system**
- **Follow-up 3 months**

<table>
<thead>
<tr>
<th></th>
<th>Penumbra</th>
<th>NINDS - tPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recanalization</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>Symptomatic ICH</td>
<td>11.2%</td>
<td>6.4%</td>
</tr>
<tr>
<td>Favorable outcome</td>
<td>25%</td>
<td>42%</td>
</tr>
</tbody>
</table>

164 patients with occlusion of large intracranial vessels +/- lytics

Merci Retriever device-8h
Follow-up 3 months

MULTI-Merci (L5 & others) NINDS - tPA

Recanalization 68%
Symptomatic ICH 10% 6.4%
Favorable outcome 36% 42%
Mortality 34% 21%

MULTI-MERCII

Stroke. 2008; 39: 1205-1212
60 patients with occlusion of large intracranial vessels +/- lytics

Trevo Retriever device-8h
Follow-up 3 months

Recanalization 92%
Symptomatic ICH 5%
Favorable outcome 55%

Trevo
NINDS - tPA

5% 6.4%
92% 42%

TREVO

113 patients with occlusion of large intracranial vessels +/- lytics-8h

Solitaire vs Merci Retriever device
Follow-up 3 months

<table>
<thead>
<tr>
<th></th>
<th>Salitaire</th>
<th>Merci</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recanalization w/o symptomatic ICH</td>
<td>61%</td>
<td>24%</td>
</tr>
<tr>
<td>Recanalization</td>
<td>83%</td>
<td>48%</td>
</tr>
<tr>
<td>Symptomatic ICH</td>
<td>1.7%</td>
<td>11%</td>
</tr>
<tr>
<td>Good mental/motor functioning</td>
<td>58%</td>
<td>33%</td>
</tr>
<tr>
<td>Mortality</td>
<td>17%</td>
<td>38%</td>
</tr>
</tbody>
</table>

SWIFT

BUT WHAT ABOUT MR. H?

- 71 y.o. AAM
  - HTN, Cigs, Et-OH
- Presented 17 hours after onset of progressive
  - Aphasia
  - Right Homonymous Hemianopsia
  - Right sided Hemiparesis
- Initial NIHSS 17
CLINICAL COURSE

- Initial CT
  - Normal
  - ? Subtle Early changes
- Admitted Pending MRI results
- Loaded with Plavix 300mg
- Fluid Bolus to elevate BP
- @ 24 hours NIHSS=24
  - Somnolent
  - Right Hemineglect
MRI

- Small deep DWI Lesion
- Large PWI Lesion
ANGIOGRAPHIC RESULT
OUTCOME

- Improvement began within 15 minutes
- 4hrs Post NIHSS=6
- DWI Same
- PWI Normal
- POD#3 D/C to Home
  - NIHSS=3
RESULTS-SNC NJ DATA

- 40 Patients
  - 24 Men
  - Mean age: 62.5 ± 15 years
    - Range: 25-91
  - Average Time-to-Tx: 12.2 ± 14 hours
    - Range: 8-68 hours

RESULTS

- Mean NIHSS: 19.5 ± 6.1
  - Range: 7-28

- Vessel Occlusion:
  - MCA: 15
  - ICA: 5
  - Tandem ICA+MCA: 12
  - BA: 8

TREATMENT

- IA Lysis/IA GIIb IIIa
  - Alone: 4
  - Combination: 17

- Embolectomy
  - Alone: 8
  - Combination: 19

- PTA/Stenting
  - Alone: 5
  - Combination: 16

- Combination: 22

RESULTS- RECANALIZATION

- TIMI 2/3 82.5%
- TIMI 3 53.9%

RESULTS - ADVERSE EVENTS

- Symptomatic ICH 2 (5%)
- All ICH 6 (15%)

RESULTS- CLINICAL OUTCOMES

- NIHSS Improvement @ D/C: 8.0 ± 6.6
- Death @30 days: 5 (12.8%)
RESULTS- FOLLOW-UP

- Death 10%
- mRankin ≤2 45.9%

CONCEPT # 2 BRIDGING IS USELESS!

“BRIDGING” from Intravenous to Neurointerventional therapeutic options may not be a helpful strategy for stroke patient treatment.
81 patients with occlusion of MCA within 3 hours of onset

IV t-PA followed by Angiography, then +/- IA t-PA or EKOS
Follow-up 3 months

IMS-2
- Recanalization: 60%
- Symptomatic ICH: 10%
- Favorable outcome: 46%
- Recanalization of EKOS vs IA-tPA: 73% vs 56%

NINDS - tPA
- Recanalization: 6.4%
- Symptomatic ICH: 42%

Stroke. 2007; 38: 2127-2135
Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke


N Engl J Med
Volume 368(10):893-903
March 7, 2013
Enrollment by CTA and Treatment Group

All Subjects
n=656

Baseline CTA
n=306

No Occlusion
n=24

NIHSS<20
n=23

NIHSS≥20
n=1

Occlusion
n=282

NIHSS<20
n=194

NIHSS≥20
n=88

No Baseline CTA
n=350

NIHSS<20
n=235

NIHSS≥20
n=115

Time Intervals to Treatment (Minutes)

Time from Onset to IA Therapy: 249 minutes
Primary and Secondary Safety End Points.

### Table 2. Primary and Secondary Safety End Points

<table>
<thead>
<tr>
<th>End Point</th>
<th>Endovascular Therapy (N = 434)</th>
<th>Intravenous t-PA Alone (N = 222)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within 7 days</td>
<td>52 (12.0)</td>
<td>24 (10.8)</td>
<td>0.57</td>
</tr>
<tr>
<td>Within 90 days</td>
<td>83 (19.1)</td>
<td>48 (21.6)</td>
<td>0.52</td>
</tr>
<tr>
<td>Intracerebral hemorrhage within 30 hr — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>27 (6.2)</td>
<td>13 (5.9)</td>
<td>0.83</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>119 (27.4)</td>
<td>42 (18.9)</td>
<td>0.01</td>
</tr>
<tr>
<td>Parenchymal hematoma identified within 30 hr — no./total no. (%)†</td>
<td>25/417 (6.0)</td>
<td>13/207 (6.3)</td>
<td>0.90</td>
</tr>
<tr>
<td>Type 2</td>
<td>15/417 (3.6)</td>
<td>3/207 (1.4)</td>
<td>0.12</td>
</tr>
<tr>
<td>Type 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhage — no./total no. (%)</td>
<td>48/417 (11.5)</td>
<td>12/207 (5.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>Subarachnoid</td>
<td>27/417 (6.5)</td>
<td>10/207 (4.8)</td>
<td>0.40</td>
</tr>
<tr>
<td>Intraventricular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major complication due to nonintracerebral bleeding within 5 days — no. (%)‡</td>
<td>13 (3.0)</td>
<td>5 (2.3)</td>
<td>0.55</td>
</tr>
<tr>
<td>Recurrent stroke within 90 days — no. (%)</td>
<td>22 (5.1)</td>
<td>14 (6.3)</td>
<td>0.54</td>
</tr>
<tr>
<td>Device or procedural complication — no. (%)‡</td>
<td>70 (16.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Events occurred during specified periods after the administration of intravenous t-PA. P values were obtained with the use of the Cochran–Mantel–Haenszel test. Data for events identified with the use of computed tomography exclude 32 participants for whom a scan was not obtained within 24 hours after initiation of intravenous t-PA or a postbaseline safety scan was not obtained within the defined time window (i.e., participants who died, had care withdrawn at the request of the family, or underwent imaging after the 30-hour window).
† Parenchymal hematoma type 2 was defined as a dense hematoma involving more than 30% of the infarcted area with substantial space-occupying effect or any hemorrhagic area outside the infarcted area, and type 1 as a hematoma involving 30% or less of the infarcted area.
‡ Complications included groin hematoma, vessel dissection, vessel perforation, and emboli in a previously uninvolved territory, as identified by the site investigator or as assessed centrally.

Distribution of Modified Rankin Scores, According to Study Group and Score on the National Institutes of Health Stroke Scale (NIHSS).
Adjusted Relative Risk for Predefined Subgroups, as Assessed According to the Primary Outcome of a Modified Rankin Score of 0 to 2 at 90 Days.
WHAT ABOUT MS. L

- 50 y/o F came to a Community Hospital within an hour of stroke onset affecting the left side of her body, Dysarthria. NIHSS of 7
- IVtPA given with transient improvement to NIHSS of 4
- Worsened to 7 within a couple of hours
- Then NIHSS to 10 and after 24 hours, we get a call!
CONCEPT # 3 DIFFERENT FOLKS DIFFERENT STROKES

- Not all strokes are alike. Imaging guides you to treatment decision nodes in various possible directions.
51 year old female presented with an 18 hour history of left facial droop, left upper extremity hemiplegia and lower extremity hemiparesis (NIHSS 7).

CT head showed right basal ganglia hypodensity.

Patient was out of time window for intravenous rt-PA or intra-arterial intervention.
CONCEPT # 4 DON’T MIX YOUR MEDS

- Thrombolytics can never be combined with antiplatelet agents, GIIb IIIa inhibitors, with additional thrombolytics, levonox, heparin…. List goes on
SAFETY OF IA BOLUS AND IV INFUSION OF EPTIFIBATIDIDE FOLLOWING IV TPA

28 patients, 92% recannalization rates.

3.6% Major Adverse Effects (n=1)

ISC 2012, New Orleans Moussavi M. et al
Stenting for Acute Stroke Intervention following full dose IVtPA
Phase I Study

IVtPA followed by Acute Stenting for a selected patient group

23 patients, 87% recannalization rates. 4.3% Major Adverse Effects (n=1)
CONCEPT #5: STENTING IS FOR THE HEART

- Intracranial stenting should not be tried!
CONCLUSION

- Appropriately selected patients with salvageable brain tissue may be treated safely regardless of myths surrounding rigid stroke paradigms. This is where the future of acute stroke care is going to lead us to.

   Thorough Evaluation of
   - Pathophysiology
   - Arterial Anatomy
   - Brain Substrate
“A foolish consistency is the hobgoblin of little minds”

- Ralph Waldo Emerson