Therapy for Acute Stroke
and
Systems of Care for TIA

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Acute Stroke Therapy

- Intravenous tPA
  - FDA approved in 1996 (3 hour window)
  - Cost-effective
  - Better efficacy with earlier treatment
  - Treatment rates vary from <1%-20%
MERCI® Retrieval System
Acute Stroke Therapy

- Endovascular therapy
  - Several thrombectomy devices with FDA 510K clearance
  - Encouraging cohort study data
  - CMS reimbursement
  - Randomized trials required to establish efficacy
  - No data on cost-effectiveness
DRG Reimbursement for Acute Stroke Therapy

- Standard medical therapy - about 6K
- IV tPA - about 12K
- Endovascular therapy - >20K
Your loved one is in the ER with a large stroke:

MD: “There is a large blood clot in the brain, we have an FDA cleared device (Merci) that can probably pull out the clot. That could be a good option or we can enroll in a clinical trial: 50% get the device, 50% do not.

So, what will it be? Merci or No Merci?”
Endovascular Stroke Therapy

• Randomized Trials
  – Lack of equipoise made clinical trials very challenging
  – Selection bias, extremely slow recruitment
  – All 3 randomized trials failed to establish efficacy of thrombectomy devices
Audience Response Question:

Should there be changes in reimbursement?

A. Suspend all reimbursement for thrombectomy
B. Reimburse only if enrolled in a randomized trial
C. No changes yet; let’s wait for more data
October 26, 2013 10 am: Stroke Code in ER

61yo female, healthy but recent stressors; 2 hr episode of L sided weakness; BP 160/90, neuro exam now nl, routine labs ok, non-con CT nl

Resident calls attending: Attending asks “do you think she had a TIA?”

Resident: “I have no idea.”

Attending sees patient obtains more history, “some features are atypical, but ABCD² score is 4; I think it might be a TIA, but maybe not. Let’s get an MRI”
What is the diagnosis? Should the patient be admitted?

MRI / MRA negative except for:

DWI
How Should TIA Be Defined?

In 2002 the TIA Working Group proposed a new definition:

“A brief episode of neurological dysfunction caused by focal brain or retinal ischemia with clinical symptoms … without evidence of acute infarction”

TIA: New technology triggers a change in terminology to emphasize tissue status, rather than time

New AHA endorsed definition of TIA:

*A transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction*

Stroke Risk After TIA: ABCD\(^2\) Score

Score points for each of the following:

- Age \(\geq 60\) (1)
- Blood pressure \(\geq 140/90\) on initial evaluation (1)
- Clinical:
  - Focal weakness (2)
  - Speech impairment without weakness (1)
- Duration
  - \(\geq 60\) min (2)
  - 10-59 min (1)
- Diabetes (1)

Final Score 0-7

ABCD$^2$ Score and Stroke Risks

Figure: Short-term risk of stroke by ABCD$^2$ score in six groups combined (n=4799)

After adjustment for ABCD² score, patients with acute infarction had substantially higher 7 day stroke risk:

OR for positive DWI: 14.9 (7.4- 30.2)

Incorporation of imaging evidence of infarction into ABCD² improved predictive power: optimal weighing of 3 points

### Stroke Risk at 7 days

<table>
<thead>
<tr>
<th>ABCD²</th>
<th>N</th>
<th>DWI positive</th>
<th></th>
<th>N</th>
<th>DWI negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1</td>
<td>20</td>
<td>0.0 (0.0- 0.0)</td>
<td></td>
<td>225</td>
<td>0.0 (0.0- 0.0)</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
<td>1.5 (0.0- 8.2)</td>
<td></td>
<td>329</td>
<td>0.0 (0.0- 0.0)</td>
</tr>
<tr>
<td>3</td>
<td>135</td>
<td>2.2 (0.5- 6.5)</td>
<td></td>
<td>469</td>
<td>0.2 (0.0- 1.2)</td>
</tr>
<tr>
<td>4</td>
<td>228</td>
<td>5.3 (2.7- 9.2)</td>
<td></td>
<td>577</td>
<td>0.7 (0.2- 1.8)</td>
</tr>
<tr>
<td>5</td>
<td>241</td>
<td>9.5 (6.0- 14.3)</td>
<td></td>
<td>454</td>
<td>0.7 (0.1- 1.9)</td>
</tr>
<tr>
<td>≥6</td>
<td>192</td>
<td>12.5 (8.0- 18.6)</td>
<td></td>
<td>268</td>
<td>0.4 (0.0- 2.1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>884</td>
<td>7.1 (5.5- 9.1)</td>
<td></td>
<td>2322</td>
<td>0.4 (0.2- 0.7)</td>
</tr>
</tbody>
</table>

Duration of Transient Symptoms and Proportion with Negative DWI

Pooled Data from 10 MRI Studies; N=818

<table>
<thead>
<tr>
<th>Duration of Symptoms (Hours)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>64.7</td>
</tr>
<tr>
<td>1-2</td>
<td>67.0</td>
</tr>
<tr>
<td>2-3</td>
<td>60.3</td>
</tr>
<tr>
<td>3-6</td>
<td>72.6</td>
</tr>
<tr>
<td>6-12</td>
<td>62.1</td>
</tr>
<tr>
<td>12-18</td>
<td>51.7</td>
</tr>
<tr>
<td>18-24</td>
<td>49.3</td>
</tr>
</tbody>
</table>

Technology Needed:
- Serum marker “troponin for TIA”

NSA Recommendations for Systems of Care for TIA

- Goal: identify dedicated models of care for TIA that assure the best possible patient outcomes in diverse healthcare settings.

Factors Influencing Systems of Care for TIA

- Regional and institutional differences have a major impact:
  - Limited inpatient bed availability
  - ED overcrowding
  - Presence of a stroke unit
  - Payer mix
  - Availability of stroke experts
  - Availability of brain/vascular imaging
NSA Recommendations: Triage

Healthcare systems should establish a routine TIA triage process including:

• Urgent evaluation recommended if TIA within the last 24 hours

• TIA admission policy established by representative physicians

• TIA patients who are not hospitalized should be evaluated within 24 to 48 hours by a physician with expertise in TIA
Recommendations: TIA Evaluation

Healthcare systems should establish a routine TIA evaluation protocol including:

- Description of recommended lab testing
- Protocols for head imaging, by MRI (optimal) or CT performed within 24 hrs
- Protocols for carotid imaging (MRA, CTA, or Doppler), preferably within 24 hrs
- Protocols for cardiac monitoring and/or echocardiography in appropriate patients
NSA 2011 Systems of Care for TIA

Examples: STANFORD TWO ACES

TWO ACES
Transient Ischemic Attack Work-Up as Outpatient Assessment of Clinical Evaluation and Safety

Jean-Marc Olivot, MD, PhD; Connie Wolford, NP; James Castle, MD; Michael Mlynash, MD, MS; Neil E. Schwartz, MD, PhD; Maarten G. Lansberg, MD, PhD; Stephanie Kemp, BS; Gregory W. Albers, MD

Stroke 2011; 42:1839-1843
Triage protocol

Direct Referral

n=43

Stanford ED

n=224

- ABCD2<4
- ABCD2 4-5
- ABCD2>5

MRI+MRA

Stanford TIA Clinic

Within 1-2 business day

n=200

- MRI+MRA
- MRI

NO

Symptomatic Stenosis >50%?

YES

Stanford Stroke Service

n=67=25%
Methods

- Final diagnosis defined by stroke neurologist: Probable TIA/Possible TIA/Unlikely TIA

- Follow up Stroke/MI/Vascular Death at 7, 30 and 90 days.
Hypotheses

1- Patients will have a low rate of stroke recurrence <2% at 1 week and <5% at 90 days

2- Both groups will have lower risk than predicted based on ABCD2 score *

### Outcome: Stroke/MI/Vasc Death

<table>
<thead>
<tr>
<th></th>
<th>% events at 7 and 90 days</th>
<th>% expected risk at 7 days*</th>
<th>p</th>
<th>% expected risk at 90 days*</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=265)</td>
<td>0.7 (0.2-2.7)</td>
<td>4.0</td>
<td>0.015</td>
<td>7.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Final Dx</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIA/stroke</td>
<td>1.8 (0.5-6.5)</td>
<td>4.9</td>
<td>0.44</td>
<td>8.2</td>
<td>0.032</td>
</tr>
<tr>
<td>(n=108)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIA Clinic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td>0.5 (0.9-2.8)</td>
<td>2.5</td>
<td>0.215</td>
<td>6.2</td>
<td>0.002</td>
</tr>
<tr>
<td>(n=199)</td>
<td></td>
<td></td>
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</table>

** 2 patients were lost of follow-up before 7 days
• The median (IQR) Medicare cost per patient was*:
  • $1,884 ($1,866-$1,897) for direct referrals to the TIA clinic;
  • $4,049 ($3,594-$4,756) for ED to the TIA clinic;
  • $5,804 ($4,027-$7,173) for ED to hospitalization.

• The median Medicare cost for a hospitalized patient was greater by*:
  • $3,587 (95% CI $1,450 – 5,396, p=0.006) compared to the cost for a direct referral to the TIA clinic;
  • $1,427 (95% CI $326 - $3,088, p=0.108) compared to the cost for an ED to the TIA clinic referral.

*based on a representative 15% sample of Medicare reimbursed patients from each group in the TWOACES study
Conclusion: ABCD2 based Outpatient TIA Clinic Triage Protocol

- Safe: <2% stroke/MI/vasc death rate at 90 days
- Stroke rates lower than predicted based on ABCD2
- Reduced hospitalization rate: 25% vs. prior to TWO ACES protocol, about 75%.
- Cost savings compared to routine hospital admission

Limitations:
- Small sample size, selected population, some patients did not return to clinic, insurance issues
Alternative Model: CDA triage

Direct Referral
ABCD<4 symptoms > 48 hrs

Selective MRI+MRA

Stanford TIA Clinic within 1 week

NO

Positive DWI or Symptomatic Stenosis >50% ?

YES

Clinical Decision Area*

ED Observation unit <24 hr stay
- Clinical monitoring
- MRI/MRA within 6 hrs
- Labs/EKG/Other evaluations

Hospital Admission
Call to Action

• Expand adoption of TIA Clinics
  – More cost-effective than hospital admission
  – Hospitalization reserved for high risk patients
  – Further research efforts to clarify high risk subgroups and differentiate events due to brain ischemia from non-ischemic mimics