Disclosures

• IA t-PA is not labeled for clinical use
• IV t-PA is not labeled for use beyond 3 hours
• NIH
  • U10 NS058931 - NETT
• Consultant or stock ownership:
  • Concentric Medical, Ornim
• DSMB
  • HCRI, Micrus, NIH
Board Review Focus

a. Massive hemispheric infarction
b. Basilar artery occlusion and stenosis
c. Carotid artery occlusion and stenosis
d. Crescendo TIAs
e. Occlusive vasculopathies (Moyamoya, sickle cell)
f. Spinal cord infarction
Pathophysiology

• Blood Flow and Time Dependent
Pathophysiology

- Time dependent
- Focal ischemia is different from global ischemia
- Energy failure -> Ca^{++} entry and cell death
- Glutamate toxicity
- Apoptosis
Imaging

• Acute Ischemic Stroke
  – Non-contrast CT is standard of care
  – 1/3 MCA territory edema or hemorrhage excludes t-PA

• MRI
  – DWI improved sensitivity
  – DWI/PWI mismatch images penumbra
  – Currently investigational (as is CTP/CBV)
Treatment: Revascularization Therapy

• t-PA
  – IV t-PA is approved in US for AIS within 3 hours of symptom onset
  – Know the indications and contraindications and how to administer (syllabus table 1)
  – 3 to 4.5 hour window is effective (ECASS-III) but not yet approved in the US
Treatment: Revascularization Therapy

• IA Lytics
  – PROACT-II trial supports benefit from IA pro-urokinase; t-PA is used off label

• Mechanical Embolectomy
  – Devices do open vessels and have FDA clearance to open vessels
  – 3 ongoing studies to establish clinical efficacy
Massive Hemispheric Infarction

• Brain Edema
  – Mannitol and hyperventilation not validated but are important bridges to surgical interventions as necessary
  – Hemicraniectomy for hemispheric stroke is proven to reduce morality and improve outcomes (Level 1 evidence)
Hemicraniectomy

Conservative treatment:
- MRS=2: 2% (1/42)
- MRS=3: 19% (8/42)
- MRS=4: 2% (1/42)
- MRS=5: 5% (2/42)
- Death: 71% (30/42)

Surgery:
- MRS=2: 14% (7/51)
- MRS=3: 29% (15/51)
- MRS=4: 31% (16/51)
- MRS=5: 4% (2/51)
- Death: 22% (11/51)
<table>
<thead>
<tr>
<th>Outcome/patients</th>
<th>Conservative</th>
<th>Surgery</th>
<th>ARR (%)</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td><strong>mRS&gt;4 at 12 months</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>DECIMAL</td>
<td>14/18</td>
<td>5/20</td>
<td>52.8</td>
<td>25.8 to 79.8</td>
<td>0.10</td>
<td>0.02-0.43</td>
</tr>
<tr>
<td>DESTINY</td>
<td>10/15</td>
<td>4/17</td>
<td>43.1</td>
<td>11.9 to 74.4</td>
<td>0.15</td>
<td>0.03-0.73</td>
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<td>HAMLET</td>
<td>8/9</td>
<td>4/14</td>
<td>60.3</td>
<td>29.0 to 91.6</td>
<td>0.05</td>
<td>0.00-0.54</td>
</tr>
<tr>
<td>Total</td>
<td>32/42</td>
<td>13/51</td>
<td>51.2</td>
<td>33.9 to 68.5</td>
<td>0.10</td>
<td>0.04-0.27</td>
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<tr>
<td>Significance: p&lt;0.0001</td>
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<tr>
<td>Heterogeneity: p=0.74</td>
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<td><strong>mRS&gt;3 at 12 months</strong></td>
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<td>DECIMAL</td>
<td>14/18</td>
<td>10/20</td>
<td>27.8</td>
<td>-1.4 to 56.9</td>
<td>0.29</td>
<td>0.07-1.18</td>
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<tr>
<td>DESTINY</td>
<td>11/15</td>
<td>9/17</td>
<td>20.4</td>
<td>-12.2 to 53.0</td>
<td>0.41</td>
<td>0.09-1.81</td>
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<tr>
<td>HAMLET</td>
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<td>10/14</td>
<td>17.5</td>
<td>-13.9 to 48.8</td>
<td>0.31</td>
<td>0.03-3.38</td>
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<tr>
<td>Total</td>
<td>33/42</td>
<td>29/51</td>
<td>22.7</td>
<td>4.6 to 40.9</td>
<td>0.33</td>
<td>0.13-0.86</td>
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<td><strong>Death at 12 months</strong></td>
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<td>25.8 to 79.8</td>
<td>0.10</td>
<td>0.02-0.43</td>
</tr>
<tr>
<td>DESTINY</td>
<td>8/15</td>
<td>3/17</td>
<td>35.7</td>
<td>4.6 to 66.8</td>
<td>0.19</td>
<td>0.04-0.94</td>
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<td>3/14</td>
<td>67.5</td>
<td>37.7 to 97.2</td>
<td>0.03</td>
<td>0.00-0.39</td>
</tr>
<tr>
<td>Total</td>
<td>30/42</td>
<td>11/51</td>
<td>50.3</td>
<td>33.3 to 67.4</td>
<td>0.10</td>
<td>0.04-0.27</td>
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<tr>
<td>Significance: p&lt;0.0001</td>
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<tr>
<td>Heterogeneity: p=0.34</td>
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No aphasia

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<th>DESTINY</th>
<th>HAMLET</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>5/7</td>
<td>1/8</td>
<td>58.9</td>
</tr>
<tr>
<td></td>
<td>3/4</td>
<td>2/7</td>
<td>46.4</td>
</tr>
<tr>
<td></td>
<td>6/6</td>
<td>2/8</td>
<td>65.1</td>
</tr>
</tbody>
</table>

Total 14/17 5/23 58.2 34.1 to 82.3

Significance: p<0.0001
Heterogeneity: p=0.85

Aphasia

<table>
<thead>
<tr>
<th></th>
<th>DECIMAL</th>
<th>DESTINY</th>
<th>HAMLET</th>
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<tbody>
<tr>
<td></td>
<td>9/11</td>
<td>4/12</td>
<td>48.5</td>
</tr>
<tr>
<td></td>
<td>7/11</td>
<td>2/10</td>
<td>43.6</td>
</tr>
<tr>
<td></td>
<td>2/3</td>
<td>2/6</td>
<td>33.3</td>
</tr>
</tbody>
</table>

Total 18/25 8/28 44.2 20.2 to 68.1

Significance: p=0.0003
Heterogeneity: p=0.92

% ARR (95% CI)
Massive Hemispheric Infarction

• Brain Edema
  – Mannitol and hyperventilation not validated but are important bridges to surgical interventions as necessary
  – Hemicraniectomy for hemispheric stroke is proven to reduce morality and improve outcomes (Level 1 evidence)
  – Follow Na⁺
  – No indication for corticosteroids
  – Posterior fossae strokes should be treated with suboccipital decompression if brainstem is compressed
  – ? Role of hypothermia
Basilar Artery Occlusion/Stenosis

- Brainstem signs
- Prior TIAs suggest intracranial atherosclerosis as cause
- Treat with t-PA if eligible
- Endovascular (lytic/thrombectomy) not tested in randomized trials
- Role of stenting under investigation
Carotid Disease

- Symptomatic vs. asymptomatic determines future risk
- NASCET/ECST trials established benefit for CEA > 70% and > 50% stenosis
- SAPPHIRE established non-inferiority to CEA in high-risk patients
- CREST (2010) shows similar benefit from surgery (excess MI) and stenting (excess stroke)
Carotid Disease

- Asymptomatic disease:
  - CEA is effective but impact on prevention is less (ca 1%/year benefit in reducing stroke)
  - SAPPHIRE and CREST included asymptomatic patients; stents are equally effective
Carotid Disease

- Stents require clopidogrel + ASA; CEA needs only one antithrombotic
- All patients should receive statin + blood pressure control
TIAs

• TIA is presence of neurological symptoms that clear within 24 hours explainable by a vascular mechanism

• TIA redefined: “Tissue based definition”:
  – Clinical TIA but with infarct seen on imaging is now classified as stroke
## TIA Risk: ABCD²

<table>
<thead>
<tr>
<th>Clinical Factor</th>
<th>Score</th>
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<tbody>
<tr>
<td>A: Age ≥ 60 years</td>
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</tr>
<tr>
<td>B: SBP &gt; 140 mm Hg or DBP &gt; 90 mm Hg</td>
<td>1</td>
</tr>
<tr>
<td>C: Clinical Symptoms</td>
<td></td>
</tr>
<tr>
<td>Unilateral weakness</td>
<td>2</td>
</tr>
<tr>
<td>Speech disturbance without weakness</td>
<td>1</td>
</tr>
<tr>
<td>D: Duration</td>
<td></td>
</tr>
<tr>
<td>&gt; 60 minutes</td>
<td>2</td>
</tr>
<tr>
<td>10-59 minutes</td>
<td>1</td>
</tr>
<tr>
<td>D: Diabetes (oral medications or insulin)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total Score</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Sum Each Category</strong></td>
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</tbody>
</table>
# TIA Risk: ABCD²

<table>
<thead>
<tr>
<th>ABCD² Score Total</th>
<th>3 month rate of Stroke</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
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<tr>
<td>1</td>
<td>2%</td>
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<tr>
<td>2</td>
<td>3%</td>
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<tr>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>5</td>
<td>12%</td>
</tr>
<tr>
<td>6</td>
<td>17%</td>
</tr>
<tr>
<td>7</td>
<td>22%</td>
</tr>
</tbody>
</table>
Crescendo TIAs

- Repetitive TIAs with increasing frequency
- Stuttering lacune: likely no specific treatment make a difference
- Thrombosis of intracranial atherosclerosis: role of heparin still controversial; role of acute stenting is being tested
Occlusive Vasculopathy

- Moyamoya disease
- Sickle Cell
Moyamoya Disease

• Non-inflammatory disease of the supraclinoid carotid arteries with development of small vessel collaterals via lenticuloostriate arteries
• Presents as TIA/Stroke or ICH in young
• EC-IC bypass (direct or indirect) is preferred method of therapy but never tested in randomized trial
Moyamoya Disease

• “Adult moyamoya” is likely atherosclerosis
• Symptomatic intracranial atherosclerosis
  – ASA is superior to warfarin (WASID trial)
  – Stenting found inferior to medical treatment (SAMPPRIS); another trial ongoing (VISSIT)
  – No role for treating asymptomatic disease
  – EC-IC bypass has not been studied
    • But has been for carotid occlusion and found ineffective (COSS, EC-IC Bypass Trial)
Sickle Cell Disease

• Most common cause of stroke in children
• MCA flow velocities > 200 cm/sec associated with higher risk of stroke
• STOP trial: randomized such patients to aggressive exchange transfusion; found benefit for transfusion in this high risk population
• Role of bone marrow tx unknown
Spinal Cord Infarction

- Rare; anterior spinal syndrome typically
- Rule out AAA
- CSF diversion (lumbar drain) anecdotal
- No role for endovascular intervention; t-PA benefit is unclear
Board Review Focus

a. Massive hemispheric infarction
b. Basilar artery occlusion and stenosis
c. Carotid artery occlusion and stenosis
d. Crescendo TIAs
e. Occlusive vasculopathies (Moyamoya, sickle cell)
f. Spinal cord infarction