SLASH DISABILITY AND DEATH WITH PRECISION IN ACUTE STROKE CARE
stroke is deadly and disabling
stroke is preventable
stroke is treatable
only if you are prepared
65 yo with word finding difficulty

- The patient’s partner calls your office 8am:
- *She understands me, but is substituting words and keeps pausing when trying to talk. It started after dinner at 8pm last night but she didn’t improve after a good night’s rest.*
- *She just had hip surgery and only wants to leave the house if something can be done*

*is the patient eligible for treatment?*
step 1
eliminate outdated eligibility criteria

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Time from last normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV thrombolysis</td>
<td>0-4.5 hours</td>
</tr>
<tr>
<td>thrombectomy</td>
<td>0-6 hours</td>
</tr>
</tbody>
</table>

[Image of a brain scan with labels such as Dead Tissue and Penumbra]
treat patients with penumbra

**ISCHEMIC CORE =** already dead tissue

**PENUMBRA =** underperfused tissue around core at risk for dying but not dead yet

When there is a mismatch, there is an opportunity to save tissue

No mismatch = no acute therapy
mismatch identification with multimodal imaging

Baseline
CTP

CBF (< 30%): 11 ml

Hypoperfusion (Tmax>6s) 151 ml
mechanical thrombectomy reliably reperfuses the brain in large vessel occlusions (LVOs)
mechanical thrombectomy
modified Rankin Scale (mRS) measures function & independence

- **0**: No symptoms at all
- **1**: Slight disability; unable to carry out all previous activities but able to look after own affairs
- **2**: Moderate disability; requiring some help, but able to walk without assistance
- **3**: Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
- **4**: Severe disability; bedridden, incontinent Snd requiring constant nursing care and attention
- **5**: Death of the patient
endovascular trials succeed with precision in patient selection & tech
<table>
<thead>
<tr>
<th>Trial</th>
<th>MR CLEAN</th>
<th>ESCAPE</th>
<th>EXTEND-IA</th>
<th>SWIFT PRIME</th>
<th>REVASCAT</th>
<th>THERAPY</th>
<th>THrace</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Key inclusion criteria</strong></td>
<td>NIHSS &gt; 2, age ≥ 18, moderate/good collaterals (CTA)</td>
<td>NIHSS &gt; 5, ASPECTS &gt; 5</td>
<td>Eligible for IV-tPA &lt; 4.5 hours from stroke onset, ischemic core &lt; 70 cm³, mismatch</td>
<td>Eligible for IV-tPA &lt; 4.5 hours from stroke onset, age 18-80, NIHSS &gt; 29, ASPECTS &gt; 6</td>
<td>Eligible for IV-tPA &lt; 4.5 hours from stroke onset, age 18-80, NIHSS &gt; 6, ASPECTS ≥ 7</td>
<td>Eligible for IV-tPA &lt; 4.5 hours from stroke onset, age 18-80, NIHSS &gt; 10, ASPECTS ≥ 7</td>
<td></td>
</tr>
<tr>
<td><strong>Interventional arm</strong></td>
<td>Intra-arterial therapy</td>
<td>Intra-arterial therapy</td>
<td>Endovascular thrombectomy with Solitaire FR stentriever</td>
<td>Endovascular thrombectomy with Solitaire FR stentriever</td>
<td>Endovascular thrombectomy with Penumbra aspiration system</td>
<td>Endovascular mechanical thrombectomy</td>
<td></td>
</tr>
<tr>
<td><strong>Control arm</strong></td>
<td>Best medical management (+/- IV-tPA)</td>
<td>Best medical management (+/- IV-tPA)</td>
<td>IV-tPA only</td>
<td>IV-tPA only</td>
<td>Best medical management (+/- IV-tPA)</td>
<td>IV-tPA only</td>
<td></td>
</tr>
<tr>
<td><strong>Time window for intervention</strong></td>
<td>&lt; 6 hours from onset</td>
<td>&lt; 12 hours from onset</td>
<td>&lt; 6 hours from onset</td>
<td>&lt; 6 hours from onset</td>
<td>&lt; 8 hours from onset</td>
<td>&lt; 4.5 hours from onset</td>
<td>&lt; 5 hours from onset</td>
</tr>
<tr>
<td><strong>Number of patients</strong></td>
<td>500 (l. 233, C. 267)</td>
<td>315 (l. 165, C. 150)</td>
<td>70 (l. 98, C. 98)</td>
<td>206 (l. 103, C. 103)</td>
<td>108 (l. 54, C. 54)</td>
<td>365 (l. 190, C. 195)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean/median age (year)</strong></td>
<td>l. 65.8, C. 65.7</td>
<td>l. 71, C. 70</td>
<td>l. 68.6, C. 70.2</td>
<td>l. 66.3, C. 65.0</td>
<td>l. 65.7, C. 67.2</td>
<td>NR</td>
<td>l. 62, C. 62</td>
</tr>
<tr>
<td><strong>Median NIHSS</strong></td>
<td>l. 17, C. 18</td>
<td>l. 16, C. 17</td>
<td>l. 17, C. 17</td>
<td>l. 17, C. 17</td>
<td>l. 17, C. 17</td>
<td>NR</td>
<td>l. 17, C. 17</td>
</tr>
<tr>
<td><strong>Median ASPECTS</strong></td>
<td>l. 9, C. 9</td>
<td>l. 9, C. 9</td>
<td>NR</td>
<td>l. 9, C. 9</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td><strong>Received IV-tPA</strong></td>
<td>l. 87.1%, C. 90.6%</td>
<td>l. 72.7%, C. 78.7%</td>
<td>l. 100%, C. 100%</td>
<td>l. 100%, C. 100%</td>
<td>l. 100%, C. 100%</td>
<td>l. 100%, C. 100%</td>
<td>l. 100%, C. 100%</td>
</tr>
<tr>
<td><strong>Median time from stroke onset to groin puncture (minute)</strong></td>
<td>290</td>
<td>241</td>
<td>210</td>
<td>224</td>
<td>269</td>
<td>226</td>
<td>255</td>
</tr>
<tr>
<td><strong>Intervention with stentriever device</strong></td>
<td>81.5%</td>
<td>86.1%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Improvement in mRS 0-2 at 90 days</strong></td>
<td>(l. 32.6%, C. 19.1%)</td>
<td>(l. 30.0%, C. 29.3%)</td>
<td>(l. 71.4%, C. 40.0%)</td>
<td>(l. 60.2%, C. 35.5%)</td>
<td>(l. 43.7%, C. 28.2%)</td>
<td>(l. 38.0%, C. 30.4%)</td>
<td>(l. 54.2%, C. 42.1%)</td>
</tr>
<tr>
<td><strong>Decrease in mortality at 90 days</strong></td>
<td>1.1%</td>
<td>8.6*</td>
<td>11.4%</td>
<td>3.2%</td>
<td>2.9%</td>
<td>11.9%</td>
<td>0.6%</td>
</tr>
<tr>
<td><strong>TICI grade 2b/3 recanalization</strong></td>
<td>58.70%</td>
<td>72.40%</td>
<td>86.20%</td>
<td>88.00%</td>
<td>65.70%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Symptomatic ICH</strong></td>
<td>l. 7.7%, C. 6.4%</td>
<td>l. 3.6%, C. 2.7%</td>
<td>l. 0%, C. 5.7%</td>
<td>l. 0%, C. 3.1%</td>
<td>l. 1.9%, C. 1.9%</td>
<td>l. 10.9%, C. 11.3%</td>
<td>NR</td>
</tr>
</tbody>
</table>
endovascular therapy extends to 24 hours in select patients

6 - 24 hours (median 12.5)

35% increase in functional independence

20% absolute reduction in death/severe disability
AHA guidelines 2018 & 2019 adopt new standard of care

<table>
<thead>
<tr>
<th>3.7. Mechanical Thrombectomy (Continued)</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>8. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.</td>
<td>IIa</td>
<td>B-R</td>
</tr>
</tbody>
</table>
extending window with IV thrombolysis

**WAKE-UP**
IV tPA vs. placebo >4.5 hrs with MRI imaging (DWI-FLAIR) mismatch. ARR 11.5%.

**EXTEND**
IV tPA vs. placebo 4.5-9 hours (from sleep midpoint) with perfusion imaging mismatch. ARR 5.9% . ended early.

**E-CASS 4**
IV tPA vs. placebo 4.5-9 hours with perfusion imaging mismatch. No difference. ended early.

**TIMELESS**
IV tenecteplase (TNK) vs. placebo 0-24 hours with perfusion imaging mismatch

**TEMPO-2**
IV TNK vs. placebo 0-12 hours with perfusion imaging mismatch

**TWIST**
IV TNK vs. placebo <4.5 hours from “wake-up” stroke with noncom CT head
extended window for IV tPA not standard

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is recommended for selected patients who can be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 8 to determine patient eligibility.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>2. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is also recommended for selected patients who can be treated within 3 and 4.5 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 8 to determine patient eligibility.</td>
<td>I</td>
<td>B-R</td>
</tr>
<tr>
<td>3. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 minute) administered within 4.5 hours of stroke symptom recognition can be beneficial in patients with AIS who awake with stroke symptoms or have unclear time of onset &gt; 4.5 hours from last known well or at baseline state and who have a DW-MRI lesion smaller than one-third of the middle cerebral artery (MCA) territory and no visible signal change on FLAIR.</td>
<td>IIa</td>
<td>B-R</td>
</tr>
</tbody>
</table>
step 2
empower all to recognize stroke & call 911

BE FAST

Know the signs of stroke
Stroke is a medical emergency.
For any sign of stroke CALL 911! Every minute counts.
Learn the physical symptoms to swiftly identify stroke
and save your life or the lives of loved ones.

Face
Does the face look uneven?

Balance
Sudden loss of balance.

Arms
Does one arm drift down?
Ask them to raise both arms.

Eyes
Sudden loss of vision in one or both eyes.

Speech
Does their speech sound strange? Ask them to repeat a phrase.

Time
Time is brain.
Every second brain cells die during a stroke.
extended window did even better than the traditional 6 hour window

<table>
<thead>
<tr>
<th></th>
<th>HERMES Early Window &lt;6h</th>
<th>DAWN + DEFUSE 3 Late Window 6-24h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endovascular</td>
<td>46%</td>
<td>47%</td>
</tr>
<tr>
<td>Control</td>
<td>27%</td>
<td>15%</td>
</tr>
<tr>
<td>ARR / NNT</td>
<td>19% / 5</td>
<td>32% / 3</td>
</tr>
</tbody>
</table>
different rates of ischemic core growth
step 3
ensure system of care is ready for rapid triage and treatment

- Stroke patient in the field
- Emergency room door arrival

- 0-4.5 hrs
  - Non-contrast CT
  - Ischemic stroke?
  - IV alteplase?

- 4.5-24 hrs
  - Multimodal CT
  - LVO?
  - EVT?

- NIHSS ≥ 6
  - EVT?
TIME IS BRAIN HAS EVOLVED...
TIME EVERY BRAIN PRECISELY
WITH TISSUE PERFUSION

penumbra

SLASH STROKE DISABILITY AND DEATH