Care of the Ischemic Stroke Patient: from ER to wards

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Disclosures

- none
Outline

- Epidemiology
- Intravenous thrombolytic
- Thrombectomy
- Stroke management
- Post-stroke complications

Stroke Epidemiology

- 795,000 strokes are estimated to occur in the United States annually
  - 610,000 of these are first or new strokes
- 87% of these are ischemic strokes
- 130,000 Americans die from stroke annually
- Cost is estimated to be $36.6 billion annually
- In 2009, 34% of people hospitalized were younger than 65
Stroke Epidemiology

stroke is 5th leading cause of death.
However, public knowledge of stroke remains poor.
Fewer than half of 911 calls for stroke were made within 1 hour of symptom onset and fewer than half of those callers thought stroke was cause of their symptoms.
Outline

- Epidemiology
- Intravenous thrombolytic
- Thrombectomy
- Stroke management
- Post-stroke complications

NIH-recommended Emergency Department response times
The “golden hour” for evaluating and treating acute stroke

door-to-needle ≤60 min

Relationship between duration and degree of cerebral blood flow (CBF) reduction

Potential to reverse neurologic impairment with thrombolytic reperfusion

References:
Patient Evaluation: Focused history

- Single most important historical information is time last known well
- Never ask: When or what time did this start?
- Rather, ask: How you were last well?
- Very important to have collateral information from friends/family

Patient Evaluation: Focused history

- Felt fine the night before
- Went to bed at 11pm
- Awoke at 7AM
- At 830AM, wife noticed words were slurred and he was weak on his right side
- Time last known well is…
- 11pm
Patient Evaluation: Focused history

- Felt fine the night before
- Went to bed at 11pm
- Awoke at 7AM
- At 7:15 AM, son spoke to patient before leaving for work
- At 8:30 AM, wife noticed words were slurred and he was weak on his left side
- Time last known well is...
- 7:15 AM

Acute stroke: ED evaluation

- **Check/Secure Airway/Breathing/Circulation**
- Physician exam, including neuro exam
- **ED Nurse:** GCS, limb strength, facial droop q 2 hrs for ICU patient; q 4 hrs for med-surg/telemetry patient. *IV tPA patient, see IV tPA flowsheet*
- **2 IV Lines:** IV normal saline 125cc/hr for hydration and BP, if tolerated
- **O2:** 4 liters per nasal cannula or ventilator to keep O2 sat >92%
- **Continued pulse ox**
- **Stat portable chest x-ray**
- **12 lead EKG**
- **Bedside glucose STAT**
- ** Labs:** CBC w/diff & platelets, Comprehensive metabolic panel, PT/INR & PTT, Alcohol/drug screen
  - **Target Door to Lab result ≤ 45 mins.**

- Non-contrast head CT with ACLS transport
- **ED nurses to bring IV tPA to CT if Last Known well < 4.5 hours.**
- **Target Door to CT ≤ 10 minutes of arrival to the ED**
- **Neuro eval by Neurology/NRSIG including NIHSS/swallow eval**
- **Neuro:** includes PO mask, can’t Stroke Team clears patient for swallowing
Stroke mimickers

<table>
<thead>
<tr>
<th>Table 6. Features of Clinical Situations Mimicking Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychogenic</strong></td>
</tr>
<tr>
<td><strong>Seizures</strong></td>
</tr>
<tr>
<td><strong>Hypoglycemia</strong></td>
</tr>
<tr>
<td><strong>Migraine with aura (complicated migraine)</strong></td>
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<tr>
<td><strong>Hypertensive encephalopathy</strong></td>
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<tr>
<td><strong>Wernicke's encephalopathy</strong></td>
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<tr>
<td><strong>CNS abscess</strong></td>
</tr>
<tr>
<td><strong>CNS tumor</strong></td>
</tr>
<tr>
<td><strong>Drug toxicity</strong></td>
</tr>
</tbody>
</table>

**IV TPA**

- Approved by FDA in 1996
- This was on basis of NINDS rtPA Stroke Trial in which 624 patients with ischemic strokes were treated with placebo or IV TPA.
- In Part 1, end point was neurological improvement at 24 hours
- In Part 2 (pivotal efficacy trial), end point was favorable outcome
- Treatment was associated with an increase in odds of a favorable outcome (OR 1.9)
  - In a subgroup analysis, OR was 2.11 when treatment was within 90 minutes (1.69 when treatment was 90-180 min)
IV TPA

- Major risk is intracerebral hemorrhage.
- Occurred in 6.4% of patients and 0.6% of patients in placebo group.
- However, mortality was similar at 3 months and at 1 year.
- These results have been replicated in the ECASS I/II and ATLANTIS A/B trials.

Broderick, Stroke 1997
IV TPA: ICH risk factors

- High stroke scale
- Blood Pressure/hypertension
- Hyperglycemia
- Age (in some studies)

Blood pressure (BP) management for patients eligible for Activase* (t-PA): pretreatment

AHA/ASA 2007 Guidelines for the Early Management of Adults With Ischemic Stroke

Indication that patient is eligible for Activase (t-PA)

If SBP >185 mm Hg or DBP >110 mm Hg

- Labetalol 10–20 mg IV over 1–2 min; may repeat x1;
- or-
- Nitropaste 1–2 inches;
- or-
- Nicardipine infusion, 5 mg/h; titrate up by 2.5 mg/h at intervals of 5–15 min (maximum dose 15 mg/h); when desired BP is attained, reduce to 3 mg/h

If BP does not decline and remains >185/110 mm Hg, do not administer Activase (t-PA)

AHA/ASA=American Heart Association/American Stroke Association.

DBP=diastolic blood pressure.

Absolute Contraindications

- Acute ICH
- History of ICH*
- BP > 185/110*
- Head trauma/stroke <3 months
- Thrombocytopenia/coagulopathy
- NOAC use

Relative Contraindications

- Advanced age
- Mild, improving symptoms
- Severe stroke
- Recent major surgery
- Recent GI hemorrhage
IV TPA: so what about 3-4.5 hours?

- ECASS III evaluated TPA in this window.
- Patients were randomized to tPA or placebo
- Had same inclusion/exclusion criteria as prior trials with the additional exclusion criteria of: age > 80, NIHSS > 25, taking oral anticoagulants, and combination of stroke and diabetes.
- OR of 1.28 of having a favorable outcome in the treatment group
- Mortality did not differ in the 2 groups
- Concluded that tPA can be safely given and can improve outcomes up to 4.5 hours in selected patients

IV TPA: so what about 3-4.5 hours?

- The European Medicines Agency expanded approval for IV tPA to 4.5 hours but FDA has not.
- However, this is recommended by AHA/ASA
Post-tPA care

- ICU admission
- Careful blood pressure monitoring: Goal <180/105
- No aspirin
- No anti-coagulation
- Monitor for swelling/edema

Outline

- Epidemiology
- Intravenous thrombolytic
- Mechanical Thrombectomy
- Stroke management
- Post-stroke complications
Pre-2015

• MERCI (2005)
• MULTI MERCI (2008)
• PENUMBRA (2009)
• IMS III (2013)
• SYNTHESIS (2013)
• MR RESCUE (2013)

Post-2015

• MR CLEAN (2014)
• EXTEND-IA (2015)
• ESCAPE (2015)
• SWIFT-PRIME (2015)
• REVASCAT (2016)
MR CLEAN

• Multicenter randomized clinical trial
• First positive trial demonstrating benefit with thrombectomy
• Study conducted across 16 centers in the Netherlands

Berkhemer, NEJM, 2015

MR CLEAN: inclusion criteria and methods

• Age > 18 with acute ischemic stroke caused by intracranial occlusion within the anterior circulation including distal ICA, M1 or M2, A1 or A2 seen on CTA or MRA
• Initiation of treatment had to be <6 hours from onset
• NIHSS > 2
• Patients randomized to intervention vs standard therapy
• Primary outcome was mRS at 90 days. Secondary outcome included NIHSS at 1, 5-7 days.
MR CLEAN: results

Berkhemer, *NEJM*, 2015
Positive thrombectomy trials

- MR CLEAN (2014)
- EXTEND-IA (2015) – smallest trial, relied on CT perfusion
- ESCAPE (2015) – used delayed CTA, fastest recanalization
- SWIFT-PRIME (2015) – highest recanalization rate
- REVASCAT (2016)
Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

- HERMES collaboration
- Pooled data from 5 trials

Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

<table>
<thead>
<tr>
<th>Intervention population</th>
<th>Control population</th>
<th>Risk difference (%)</th>
<th>Rate ratio (95% CI)</th>
<th>Odds ratio (95% CI)</th>
<th>Adjusted rate ratio (95% CI)</th>
<th>Adjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic intracranial haemorrhage</td>
<td>4.4% (28/634)</td>
<td>5.3% (28/533)</td>
<td>0.1</td>
<td>1.06 (0.63-1.80); p=0.82</td>
<td>1.07 (0.62-1.83); p=0.81</td>
<td>1.07 (0.62-1.84); p=0.81</td>
</tr>
<tr>
<td>Parenchymal haematoma type 2</td>
<td>5.1% (32/639)</td>
<td>5.3% (44/826)</td>
<td>-0.2</td>
<td>0.99 (0.60-1.63); p=0.97</td>
<td>0.99 (0.60-1.63); p=0.97</td>
<td>1.04 (0.64-1.69); p=0.88</td>
</tr>
<tr>
<td>Mortality</td>
<td>25.3% (57/226)</td>
<td>18.9% (226/646)</td>
<td>-3.6</td>
<td>0.82 (0.63-1.07); p=0.15</td>
<td>0.87 (0.64-1.16); p=0.32</td>
<td>0.82 (0.62-1.08); p=0.15</td>
</tr>
</tbody>
</table>

Data show the proportion of patients with outcome (n/N), unless otherwise stated.

Table 4: Safety outcomes at 90 days

Thrombectomy beyond 6 hours: Dawn of a New Era

- Prospective, randomized open-label trial assessing thrombectomy versus standard therapy
- Patients with ICA or MCA occlusion with mismatch
- Thrombectomy occurred 6-24 hours
- Primary end point included mRS score and rate of functional independence
- Trial terminated early due to superiority of thrombectomy

DAWN trial

<table>
<thead>
<tr>
<th>Variables</th>
<th>Thrombectomy Group (n=63)</th>
<th>Control Group (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>65.3 (12.2)</td>
<td>71.6 (15.1)</td>
</tr>
<tr>
<td>Age older—ms (yr)</td>
<td>24 (20)</td>
<td>24 (20)</td>
</tr>
<tr>
<td>Male sex—ms (%)</td>
<td>31 (49)</td>
<td>33 (52)</td>
</tr>
<tr>
<td>Area of the occlusion—ms (%)</td>
<td>61 (24)</td>
<td>54 (24)</td>
</tr>
<tr>
<td>Intracranial location—ms (%)</td>
<td>29 (47)</td>
<td>21 (32)</td>
</tr>
<tr>
<td>Hypertension—ms (%)</td>
<td>40 (63)</td>
<td>72 (90)</td>
</tr>
<tr>
<td>Previous ischemic stroke or transient ischemic stroke—ms (%)</td>
<td>13 (21)</td>
<td>11 (17)</td>
</tr>
<tr>
<td>NIHSS score</td>
<td>7.3 (1.6)</td>
<td>8.7 (1.6)</td>
</tr>
<tr>
<td>Median</td>
<td>7.0 (1.9)</td>
<td>8.9 (1.9)</td>
</tr>
<tr>
<td>Infract volume—ml</td>
<td>100 (61)</td>
<td>100 (61)</td>
</tr>
<tr>
<td>Infract volume—interquantile range</td>
<td>100 (61)</td>
<td>100 (61)</td>
</tr>
<tr>
<td>Time to awakening—ms (%)</td>
<td>25.5 (9.7)</td>
<td>22.9 (10.1)</td>
</tr>
<tr>
<td>Time to intervention—ms (%)</td>
<td>22.9 (10.1)</td>
<td>24.7 (11.4)</td>
</tr>
<tr>
<td>Time to last image of middle cerebral artery—ms (%)</td>
<td>31 (15)</td>
<td>31 (15)</td>
</tr>
<tr>
<td>Length of treatment—ms (%)</td>
<td>24.7 (11.4)</td>
<td>24.7 (11.4)</td>
</tr>
</tbody>
</table>

Nogueira, NEJM, 2018
DAWN trial

- Rate of stroke-related death or symptomatic intracerebral hemorrhage did not differ
- Outcome were better in patients who were carefully selected based on imaging criteria with thrombectomy at 6-24 hours compared to standard medical therapy
- For every 2 patients who underwent thrombectomy, 1 additional patients had less disability
Thrombectomy beyond 6 hours: DEFUSE 3

- Randomized, open-label trial assessing endovascular therapy versus standard medical therapy
- Patients underwent intervention between 6 and 16 hours
- Patients were eligible if stroke volume was less than 70mL with an occlusion of ICA or MCA
- Primary outcome was mRS score

DEFUSE 3

Table 1: Baseline Characteristics of the Patients and Features of Thrombectomy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Endovascular Therapy (N=85)</th>
<th>Medical Therapy (N=86)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR) — yr</td>
<td>70 (60-79)</td>
<td>71 (60-80)</td>
</tr>
<tr>
<td>Female sex — no. (%)</td>
<td>46 (55)</td>
<td>46 (51)</td>
</tr>
<tr>
<td>Median NIHSS score (IQR)</td>
<td>16 (10-20)</td>
<td>16 (12-21)</td>
</tr>
<tr>
<td>Stroke onset witnessed — no. (%)</td>
<td>31 (36)</td>
<td>35 (39)</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms present on awakening</td>
<td>49 (58)</td>
<td>47 (54)</td>
</tr>
<tr>
<td>Symptoms began during waistwashing</td>
<td>12 (14)</td>
<td>13 (14)</td>
</tr>
<tr>
<td>Treatment with intravenous tPA — no. (%)</td>
<td>10 (12)</td>
<td>8 (9)</td>
</tr>
<tr>
<td>Imaging characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qualifying imaging — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT perfusion imaging</td>
<td>69 (75)</td>
<td>66 (71)</td>
</tr>
<tr>
<td>Diffusion and perfusion MRI</td>
<td>22 (26)</td>
<td>26 (29)</td>
</tr>
<tr>
<td>Median volume of ischemic core (IQR) — ml</td>
<td>9.4 (3.1-33.8)</td>
<td>10.1 (3.1-24.3)</td>
</tr>
<tr>
<td>Median volume of perfusion lesion (IQR) — ml</td>
<td>114.7 (73.3-164.3)</td>
<td>116.1 (73.4-158.2)</td>
</tr>
<tr>
<td>Occlusion site on baseline CTA or MRA — no. (%)</td>
<td>32 (38)</td>
<td>36 (42)</td>
</tr>
<tr>
<td>Internal carotid artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle cerebral artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median AASPECTS on baseline CT (IQR)</td>
<td>6 (2-8)</td>
<td>8 (7-9)</td>
</tr>
<tr>
<td>Process measures — from time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median time from stroke onset to qualifying imaging (IQR)</td>
<td>10:29 (8:00–11:40)</td>
<td>9:35 (7:59-12:20)</td>
</tr>
<tr>
<td>Median time from stroke onset to randomization (IQR)</td>
<td>10:53 (8:44-12:21)</td>
<td>10:44 (8:42-13:04)</td>
</tr>
<tr>
<td>Median time from qualifying imaging to femoral puncture (IQR)</td>
<td>0:39 (0:19–1:27)</td>
<td>NA</td>
</tr>
<tr>
<td>Median time from femoral puncture to reperfusion (IQR)</td>
<td>0:18 (0:16–0:33)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Albers, NEJM, 2018
Figure 2. Scores on the Modified Rankin Scale at 90 Days.

Patients in the endovascular therapy group received endovascular therapy plus standard medical therapy. Patients in the medical-therapy group received standard medical therapy alone. Scores on the modified Rankin scale range from 0 to 6, with 0 indicating no symptoms, 1 no clinically significant disability, 2 slight disability, 3 moderate disability, 4 moderately severe disability, 5 severe disability, and 6 death. There was a significant difference favoring the endovascular-therapy group over the medical-therapy group in the overall distribution of scores (unadjusted common odds ratio, 2.77; 95% CI, 1.63 to 4.70; P < 0.001).

Nogueira, NEJM, 2018

Table 3. Clinical and Imaging Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Endovascular Therapy (N=90)</th>
<th>Medical Therapy (N=90)</th>
<th>Odds Ratio or Risk Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary efficacy outcome: median score on modified Rankin scale at 90 days (NRI)</td>
<td>3 (2-4)</td>
<td>4 (2-6)</td>
<td>2.77 (1.50-4.90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Secondary efficacy outcome: functional independence at 90 days — no. (%)</td>
<td>41 (45)</td>
<td>15 (17)</td>
<td>2.67 (1.60-4.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Safety outcomes — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death at 90 days</td>
<td>13 (14)</td>
<td>23 (26)</td>
<td>0.56 (0.30-1.02)</td>
<td>0.05</td>
</tr>
<tr>
<td>Symptomatic intracranial hemorrhage</td>
<td>6 (7)</td>
<td>4 (4)</td>
<td>1.47 (0.64-3.35)</td>
<td>0.27</td>
</tr>
<tr>
<td>Early neurologic deterioration</td>
<td>8 (9)</td>
<td>1 (1)</td>
<td>0.31 (0.10-1.09)</td>
<td>0.04</td>
</tr>
<tr>
<td>Parenchymal hematoma type 2</td>
<td>8 (9)</td>
<td>3 (3)</td>
<td>2.61 (0.73-14.65)</td>
<td>0.21</td>
</tr>
<tr>
<td>Imaging outcomes**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median initial volume at 24 hr (mL)</td>
<td>15 (18-82)</td>
<td>41 (25-106)</td>
<td>—</td>
<td>0.19</td>
</tr>
<tr>
<td>Median infarct growth at 24 hr (mL)</td>
<td>23 (10-75)</td>
<td>33 (18-75)</td>
<td>—</td>
<td>0.04</td>
</tr>
<tr>
<td>Reperfusion &gt;90% at 24 hr — no./total no. (%)</td>
<td>59/75 (79%)</td>
<td>12/67 (18%)</td>
<td>4.39 (2.68-7.43)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Complete recanalization at 24 hr — no./total no. (%)</td>
<td>65/81 (75%)</td>
<td>19/77 (18%)</td>
<td>4.31 (2.65-7.02)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TICI score of 2 or 3 — no./total no. (%)</td>
<td>69/91 (76%)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Nogueira, NEJM, 2018
Case #1 – Patient KN

- 64 year woman with history of hypertension presents to ED with acute left sided weakness
- Witnessed onset of symptoms by husband 45 minutes prior to arrival while eating breakfast at a restaurant
- Normal finger stick BP 149/76
- R gaze preference, L field cut, L sided plegia, left sided neglect
- NIHSS 17
- CT negative
Patient KN

- Complete recovery post-procedure.
- NIHSS 0
- Discharged to home hospital day #3 with event monitor
- Paroxysmal atrial fibrillation identified
- Anticoagulation started
Patient #2 - JH

- 78 year old woman presenting with left sided weakness upon waking up
- She had history of atrial fibrillation and was taken off Coumadin but taken off due to recent subdural hematoma
- Last known normal was last night
- NIHSS 16

Patient JH

[CT scan images]
Outline

- Epidemiology
- Intravenous thrombolytics
- Thrombectomy
- **Stroke management**
- Post-stroke complications

Stroke work-up

- MRI
- CT angiogram
- Aspirin
- Statin
- Cholesterol level
- Diabetes screen
- Echocardiogram
- Swallow screen
- Dvt prophylaxis
- Rehab evaluation
- Telemetry monitoring
- Blood pressure management

*Off hand, I'd say you're suffering from an arrow through your head, but just to play it safe, I'm ordering a bunch of tests.*
### Imaging

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Brain Imaging</th>
<th>COR</th>
<th>LOE</th>
<th>New, Revised, or Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Routine use of brain MRI in all patients with AIS is not cost-effective and</td>
<td>Iib</td>
<td>C-ED</td>
<td>New recommendation.</td>
</tr>
<tr>
<td></td>
<td>is not recommended for initial diagnosis or to plan subsequent treatment.</td>
<td></td>
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</tr>
<tr>
<td>2.</td>
<td>In some patients with AIS, the use of MRI might be considered to provide</td>
<td>Iib</td>
<td>C-ED</td>
<td>New recommendation.</td>
</tr>
<tr>
<td></td>
<td>additional information for initial diagnosis or to plan subsequent treatment,</td>
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<tr>
<td></td>
<td>although the effect on outcomes is uncertain.</td>
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<tr>
<td>3.</td>
<td>In patients with AIS, routine noninvasive imaging by means of CTA or MRA of</td>
<td>Iib</td>
<td>C-ED</td>
<td>New recommendation.</td>
</tr>
<tr>
<td></td>
<td>the intracranial vasculature to determine the presence of intracranial</td>
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<tr>
<td></td>
<td>arterial stenosis or occlusion is not recommended to plan secondary</td>
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<tr>
<td></td>
<td>preventive treatment.</td>
<td></td>
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<tr>
<td>4.</td>
<td>Routine use of echoangiography in all patients with AIS to plan</td>
<td>Iib</td>
<td>B-NR</td>
<td>New recommendation.</td>
</tr>
<tr>
<td></td>
<td>subsequent secondary preventive treatment is of limited value and is not</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>recommended.</td>
<td></td>
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</tr>
<tr>
<td>5.</td>
<td>In selected patients with AIS, echoangiography to provide additional</td>
<td>Iib</td>
<td>B-R</td>
<td>New recommendation.</td>
</tr>
<tr>
<td></td>
<td>information to plan subsequent secondary preventive treatment may be</td>
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<tr>
<td></td>
<td>reasonable.</td>
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</tbody>
</table>

Powers, *Stroke*, 2018
Cholesterol

Powers, Stroke, 2018

PCSK9 antibody: future standard therapy?

• Proprotein convertase subtilisin-kexin type 9
• PCSK9 bind to LDL receptors and promotes its degradation
• PCSK9 inhibitors allow LDL receptors to remove LDL
• Two agents: alirocumab, evolocumab
• Cost $200 vs $14,000
2013 AHA guideline

Stone, et al. 2013
Types of statin therapy

Table 5. High-, Moderate-, and Low-Intensity Statin Therapy (Used in the RCTs Reviewed by the Expert Panel)*

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL-C, on average, by approximately 20%</td>
<td>daily dose lowers LDL-C, on average, by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL-C, on average, by &lt;30%</td>
</tr>
<tr>
<td>Atorvastatin (40)-80 mg</td>
<td>Atorvastatin 10 (20) mg</td>
<td>Simvastatin 10 mg</td>
</tr>
<tr>
<td>Rosuvastatin 20 (40) mg</td>
<td>Rosuvastatin 10 mg</td>
<td>Prazavastatin 10-20 mg</td>
</tr>
<tr>
<td></td>
<td>Simvastatin 20-40 mg</td>
<td>Lovastatin 20 mg</td>
</tr>
<tr>
<td></td>
<td>Pravastatin 40 (60) mg</td>
<td>Fluvastatin XL 80 mg</td>
</tr>
<tr>
<td></td>
<td>Lovastatin 40 mg</td>
<td>Fluvastatin 40 mg BID</td>
</tr>
<tr>
<td></td>
<td>Fluvastatin 40 mg</td>
<td>Fluvastatin 5-4 mg</td>
</tr>
</tbody>
</table>

Stone, et al. 2013

Swallow screen

4.6. Dysphagia Screening

1. Dysphagia screening before the patient begins eating, drinking, or receiving oral medications is reasonable to identify patients at increased risk for aspiration.

Dysphagia, a common (37%-78%) complication of acute stroke, is a risk factor for aspiration pneumonia and is associated with higher mortality and worse patient outcomes. The evidence review committee completed a systematic review to determine whether dysphagia screening, compared with no screening or usual care, decreased outcomes of pneumonia, death, or dependency. There were insufficient data to determine whether implementation of a dysphagia screening protocol reduces the risk of death or dependency. However, insufficient evidence does not mean that dysphagia screening is ineffective. Joud et al determined that patients who failed dysphagia screening were older, had a higher rate of multiple comorbidities (including prior stroke and dementia), more often came from a long-term care facility, more often presented with weakness and speech deficits, had a lower level of consciousness, and had a higher stroke severity. Patients who failed dysphagia screening were more likely to develop pneumonia (13.1% versus 1.9%), to have more severe disability (52.4% versus 18.0%), and to be discharged to a long-term care institution (14.0% versus 4.3%). Early dysphagia screening is reasonable to identify patients at higher risk for adverse outcomes.

Powers, Stroke, 2018
Dvt prophylaxis

- Recommendation based on a meta-analysis of 5 trials
- Anticoagulation was not associated with any significant effect on mortality or functional status
- Lower rates of PE and DVT (most were asymptomatic)
- Higher rate of ICH and extracranial hemorrhage
CLOTS study

- Clots in Legs or stockings after stroke
- Enrolled ~2900 patients
- Randomized to pneumatic compression
- DVT occurred in 122 patients in treatment group versus 174 (OR 0.65, p=0.001)
- In treatment group, also an improvement in survival

Outline

- Epidemiology
- Intravenous thrombolytic
- Thrombectomy
- Stroke management
- Post-stroke complications
Stroke Complications

- Infection
- DVT
- Hemorrhage
- Re-stroke
- Cerebral/malignant edema

Cerebral edema

Michinaga, IJMS, 2015
Malignant edema

- Defined as edema severe enough to cause increased intracranial pressure and lead to herniation and death
- Predictors include:
  - Younger age
  - Carotid occlusion
  - History of hypertension

Treatment

- Intubation/hyperventilation
- Sedation
- Head elevation
- Mannitol
- Hypertonic saline
- Decompressive craniectomy
Patient RR

• 46 year man with large L MCA syndrome
• Was not a candidate for tpa or thrombectomy

Post-OR
Decompressive craniectomy

Alexander, BMJ, 2016

<table>
<thead>
<tr>
<th>Name, publication year and reference number</th>
<th>Duration from symptoms onset to treatment</th>
<th>Age (years)</th>
<th>Indication</th>
<th>n treatment</th>
<th>n control</th>
<th>% females</th>
<th>Rate of timing of termination</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESTROY II 2014, Germany, Jüller</td>
<td>Within 48 hours after the onset of symptoms</td>
<td>65</td>
<td>RSD</td>
<td>130</td>
<td>130</td>
<td>50</td>
<td>47/62, 50%</td>
</tr>
<tr>
<td>DESTROY I 2007, Germany, Jüller</td>
<td>&gt; 12 to &lt;24 hours</td>
<td>18-65 years</td>
<td>28</td>
<td>171/160</td>
<td>171/160</td>
<td>33</td>
<td>1.5/16, 53%</td>
</tr>
<tr>
<td>DECIMAL 2007, France, Yahveli</td>
<td>Within 24 hours</td>
<td>18-55 years</td>
<td>44</td>
<td>20/18</td>
<td>20/18</td>
<td>31</td>
<td>Anticipated sample size 800 patients, sequential analysis planned, stopped after 38th patient due to slow enrollment, large difference in mortality between the two groups, and planned meta-analysis with ongoing European trials.</td>
</tr>
<tr>
<td>HAMLET 2006, Netherlands, Holtegger</td>
<td>Within 4 days</td>
<td>18-69 years</td>
<td>24/24</td>
<td>30/32</td>
<td>30/32</td>
<td>41</td>
<td>Planned sample size 112, stopped early apparently because of large significant effect.</td>
</tr>
<tr>
<td>HAACOPTER 2016, China, Frank</td>
<td>Within 4 days</td>
<td>18-75 years</td>
<td>54</td>
<td>41/10</td>
<td>41/10</td>
<td>38</td>
<td>Planned sample size 75 patients, trial stopped after 20 patients randomized because of judgement that we had achieved our aim for the pilot study without further details.</td>
</tr>
<tr>
<td>Decompressive Haemorrhagectomy 2012, China, Zhao</td>
<td>Within 48 hours</td>
<td>18-90 years</td>
<td>64</td>
<td>24/23</td>
<td>24/23</td>
<td>28</td>
<td>Planned sample size 81 patients, trial stopped after 45 patients recruited because of large significant effect.</td>
</tr>
</tbody>
</table>

Decompressive craniectomy

Alexander, BMJ, 2016

<table>
<thead>
<tr>
<th>mRS ≤ 2</th>
<th>mRS ≤ 4</th>
<th>mRS ≤ 5</th>
<th>mRS &gt; 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=24</td>
<td>n=17</td>
<td>n=122</td>
<td>n=120</td>
</tr>
</tbody>
</table>

| Number per mRS category 
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Best medical</td>
</tr>
<tr>
<td>n=41</td>
</tr>
<tr>
<td>n=38</td>
</tr>
<tr>
<td>n=50</td>
</tr>
</tbody>
</table>

| Number per mRS category 
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical treatment</td>
</tr>
<tr>
<td>n=41</td>
</tr>
<tr>
<td>n=38</td>
</tr>
<tr>
<td>n=50</td>
</tr>
</tbody>
</table>

Legend:
- mRS: modified Rankin Scale
- mRS: modified Barthel Index
- mRS: modified Lovett Scale
- mRS: modified Fugl-Meyer Scale
- mRS: modified Bobath Scale
- mRS: modified Berg Balance Scale
- mRS: modified Tardieu Scale
- mRS: modified Fugl-Meyer Scale"
Controversy: should age matter?

• Hemicraniection clearly results in improved survival
• However, this is potentially offset by a higher rate of severe disability
• Lot of debate about potential age restrictions (first trial excluded patients over age of 60)

When is it the right time?

• Edema thought to peak ~3-5 days
• Question remains when to take patients to OR
• Two general options: Take high risk patients early or wait until there is objective signs of edema
• General consensus to monitor closely and operate
Summary

• Stroke remains a significant burden and leading cause of disability
• Intravenous thrombolytic remains first line therapy for majority of ischemic strokes
• Mechanical thrombectomy can be beneficial in carefully selected patients up to 24 hours from last known well
• Stroke work-up should be guided by type of stroke
• Several complications are possible after acute stroke including cerebral edema in large hemispheric stroke

References