Acute Ischemic Stroke for Hospitalists

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Disclosures: none
Objectives

1. Outline the management of acute stroke including treatment time points
2. Outline the workup of acute stroke.
3. Describe secondary prevention strategies for acute stroke
Overview

• **Acute Ischemic Stroke**
  • Hyperacute therapy
    ○ tPA
    ○ Endovascular therapy
  • **Stroke Hospitalization/Workup**
    ○ Management
    ○ Workup
  • **Secondary Prevention**
    ○ Antiplatelets
    ○ (Afib/DOACs)
    ○ (PFO)
Stroke Subtypes

- Normal
- Ischemic Stroke 87%
- Intracerebral Hemorrhage 10%
- Subarachnoid Hemorrhage 3%
Current Literature: 
Hyper Acute Therapies for Acute Ischemic Stroke

IV tPA (recombinant tissue-type plasminogen activator)
- **0 – 3 hours**: NINDS trial, 1995
- **3-4.5 hours**: ECASS3, 2007
- **(>4.5 hours)** there is some early evidence: WAKE-UP, 2018; EXTEND, 2019

Endovascular Mechanical Thrombectomy
- **0 – 6 hours**: MR CLEAN, REVASCAT, SWIFT PRIME, EXTEND-IA, ESCAPE, 2015
- **6-18/24 hours**: DAWN/DEFUSE3, 2017-2018
Acute Stroke Treatment Timeline of studies

NINDS 0-3 h TPA 1995

2008 ECASSIII 3-4.5 h TPA

6 RCTs 0-6 h EVT 2015

WAKE-UP/EXTEND 4.5-9 h TPA 2018/19

2017/18 DAWN DEFUSE3 6-18/24h EVT
IV tPA
NNT = 7
0-3 h window
<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability, despite symptoms; able to perform all usual duties and activities</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability; unable to perform all previous activities but able to look after own affairs without assistance</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability; requires some help, but able to walk without assistance</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability; bedridden, incontinent, and requires constant nursing care and attention</td>
</tr>
<tr>
<td>6</td>
<td>Death</td>
</tr>
</tbody>
</table>
Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke

Werner Hacke, M.D., Markku Kaste, M.D., Erich Bluhmki, Ph.D., Miroslav Brozman, M.D., Antoni Dávalos, M.D., Donata Guidetti, M.D., Vincent Larrue, M.D., Kennedy R. Lees, M.D., Zakaria Medeghri, M.D., Thomas Machts, M.D., Dietmar Schröder, M.D., Rüdiger von Kummer, M.D., Nils Wahlgren, M.D., and Danilo Toni, M.D., for the ECASS Investigators

IV tPA
NNT=14
in 3-4.5h window
MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke

Poll:

A 75 yo man woke up with left hemiplegia. Last seen normal was 12 hours ago. Noncontrast head CT is normal. CTA shows no large vessel occlusion. Is he a candidate for TPA?

a. Yes
b. No
c. Need more information
EVT
NNT = 2.6
0-6 h window

(Includes MR CLEAN, REVASCAT, SWIFT-PRIME, EXTEND-IA, ESCAPE)
ORIGINAL ARTICLE

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct


ORIGINAL ARTICLE

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

DEFUSE 3 and DAWN Trials

NNT = 2.8
**Perfusion:**

**Green:** Delayed arrival of contrast of more than 6 seconds likely to progress to infarction if reperfusion does not occur.

**Pink:** Cerebral blood flow of <30%, likely to be irreversibly injured.

**Mismatch Volume:** Potentially salvageable tissue.

**Mismatch Ratio**
Current Literature: Hyper Acute Therapies for Acute Ischemic Stroke

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• (>4.5 hours there is some early evidence: WAKE-UP, 2018: EXTEND, 2019)

Endovascular Mechanical Thrombectomy
• 0 – 6 hours: MR CLEAN, REVASCAT, SWIFT PRIME, EXTEND-IA, ESCAPE, 2015 (second-generation stent retriever device for proximal thrombus up to 6 hours after LKW)
• 6-18/24 hours: DAWN/DEFUSE3, 2017-2018 (select patients with large territory still at risk, benefit from EVT up to 18/24h)
Poll:

A 40 yo man admitted to a tertiary care hospital with aspiration pneumonia after an overdose develops acute onset of hemiparesis and aphasia witnessed by the nurse. Head CT is normal. CTA shows left M1 occlusion. Last known well 4 hours ago. In addition to permissive hypertension and maintenance of normothermia and normoglycemia what is the best management strategy?

a. IV tPA
b. IV tPA and endovascular mechanical thrombectomy
c. Supportive care only
Poll:

75 yo woman with DM2, HTN presents with aphasia and R sided weakness. Last known well was 20 hours ago, CTA shows left M1 occlusion, CT perfusion shows a large mismatch, with a small core and large territory at risk for infarct. Is the patient a candidate for mechanical thrombectomy?

a. Yes
b. No
Management and Hospitalization of Stroke Patients

Management:
• Permissive HTN
• Normothermia
• Normoglycemia

Hospitalization:
• Workup for Etiology
• Determine the best secondary prevention (based on etiology)
• Additional testing: 30 day ATM, hypercoag testing
Workup

- Brain imaging (MRI preferred, HCT if not possible, TIA definition)
- Vessel imaging (CTA vs MRA head/neck, carotid/TCD)
- EKG, telemetry 48 h
- Cardiac Imaging (TTE, +/- bubble study, TEE)
- Stroke labs: fasting lipid panel (goal LDL <70), HgA1C
Advanced Evaluation

- Vessels
  - Catheter angioplasty
  - Transcranial Doppler monitoring for emboli
  - Vasculitis tests

- Cardiac — rhythm
  - Prolonged (2–4 wk) outpatient cardiac telemetry

- Hematologic testing
  - Arterial hypercoagulability tests (all patients)
  - Venous hypercoagulability tests (if right-to-left shunt)

Stroke considered to be cryptogenic after advanced evaluation

Specialized Evaluation

- Genetic testing
  - Mitochondrial disease
  - CADASIL, Fabry's disease, other genetic causes

- Vessels
  - Detailed autoimmune evaluation
  - CSF examination
  - Brain biopsy

- Cardiac — structure
  - Cardiac CT
  - Cardiac MRI

- Cardiac — rhythm
  - Prolonged (1–3 yr) outpatient loop recording

- Hematologic testing
  - Workup for occult cancer
Poll:

A 52 yo man with no prior medications is treated with tPA for a ischemic stroke secondary to large vessel atherosclerosis and is ready for discharge. He was started on aspirin and Plavix during the admission. What antiplatelet agent(s) should he be discharged on?

a. Aspirin 81 mg daily
b. Aspirin 325 mg daily
c. Aspirin 81 mg daily and clopidogrel 75 mg daily indefinitely
d. Aspirin 81 mg indefinitely and clopidogrel 75 mg for three months
e. Clopidogrel 75 mg daily indefinitely
Antiplatelet Agents

- Aspirin 81 mg
- Clopidogrel 75 mg
- Aspirin 25mg + dipyridamole 200 mg BID
- Cilostazol 100 mg BID
- Ticagrelor 90mg BID
Antiplatelet Failure

Limited data on antiplatelet choice after a stroke or TIA in patients already on aspirin.

Meta analysis in 2017 suggests patients do benefit from either switching agents, or a short course of dual antiplatelet therapy.

HR 0.7 (CI 0.54 – 0.92)

Dual Antiplatelet Therapy

The duration of dual antiplatelet therapy depends on the indication:

1) ASA + Plavix for 3 weeks after minor stroke or TIA

2) ASA + Plavix for 3 months for large artery atherosclerosis
CHANCE Trial

First large, randomized trial of dual antiplatelet therapy after TIA or minor stroke

Plavix for 90 days + plus Aspirin for 21 days vs Aspirin alone

Strokes occurred in 11.7% of the ASA group vs 8.2% in dual therapy (HR 0.68, CI 0.57 – 0.81, P <0.001)

No difference in hemorrhage

But... study done in China. Applicable to US population?

CHANCE Trial

Probability of Survival Free of Stroke.

Hazard ratio, 0.68 (95% CI, 0.57–0.81)
P<0.001

POINT Trial
Aspirin + Plavix for 3 months after minor stroke or TIA reduces early recurrent stroke.

HR 0.75, CI 0.59 – 0.95, p=0.02
Most recurrent strokes occurred in the first week
Increased risk of bleeding, HR 2.3, but occurred later in the study

POINT: Aspirin + Plavix for 3 weeks after minor stroke or TIA reduces early recurrent stroke.
POINT: Risk of hemorrhage increases after 30 days

Antiplatelets for Large Artery Atherosclerosis

**SAMMPRIS**: Trial of aggressive medical therapy vs stenting in intracranial atherosclerosis → significantly favored medical therapy

ASA 325 + Clopidogrel 75 x **90 days**, high dose statin, aggressive blood pressure control, diabetic treatment, diet & exercise

Adding Cilostazol for Long Term DAPT

ASA 81 mg OR clopidogrel 75 mg + cilostazol 100 mg BID

HR of 0.49 (CI 0.31–0.76), p=0.001 compared to monotherapy

No increase in bleeding complications

SUMMARY

Dual antiplatelet for 21-30 days for minor stroke or TIA is reasonable

Dual antiplatelet for 90 days for large artery atherosclerosis

Can consider cilostazol if dual antiplatelet necessary for > 90 days
Additional discussion

Timing of starting anticoagulation
Role of heparin drip
Cardiac monitoring, ATM, ILR
PFO discussion
References