Assessment and Treatment of Acute Stroke

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Treatment of Acute Stroke

- Perspective
- Diagnosis of Stroke
- Assessment of Stroke Victim
- Treatment of Acute Ischemic Stroke with IV tPA
- Stroke treatments beyond the 3 hour time window are now available

Stroke is common.

- 1 person suffers a stroke every 53 seconds
- 4.5 million living American stroke victims
- 1 person dies from stroke every 3.3 minutes (436/day) and 250,000 people die each year
- 750,000 new and recurrent stroke victims each year in US

Who does stroke affect?

- Stroke risk doubles each 10 years after age 55
- 30% stroke victims younger than age 55
- More common in men
- Women more likely to die from stroke than men
  1. 1 in 6 women die from stroke
  2. 1 in 25 women die from breast cancer

Stroke is devastating

- #1 cause of disability and #3 cause of death in the US
- 7-30% mortality in first 30 days following stroke
- 4.5 Million living American stroke victims:
  - 50% hemiparetic
  - 30% unable to walk without assistance
  - 26% dependent in ADLs (grooming, eating, bathing)
  - 26% institutionalized in nursing home
  - 19% aphasic

People Fear Stroke the Greatest

- Many elderly would rather die than be alive and severely disabled.
- 45%-69% of stroke patients considered stroke to be a worse outcome than death.
- >80% of elderly population without stroke considered death preferable to severe disability.

Stroke Treatment in the U.S.

• Alteplase/tPA is the only drug approved by FDA for treatment of acute stroke
• tPA has been available in U.S. since 1996
• Only 3-4% of stroke patients receive t-PA for their acute stroke

Reasons more stroke patients aren’t treated with tPA

• People don’t recognize their symptoms as stroke symptoms
• Don’t know that a treatment is available with a 3 hour time-window of opportunity to receive treatment
• Most physicians don’t have experience with the use of tPA for stroke
• Many hospitals are not organized to deliver tPA treatment for stroke

Diagnosis of Stroke

• Stroke apoplexy -“struck suddenly with violence” (Greek)
• Stroke is a unique clinical syndrome characterized by a sudden loss of neurologic function attributable to a vascular territory of the brain (i.e., MCA stroke, basilar artery stroke)
• TIA or transient ischemic attack is when symptoms resolve in < 1 hour (N Engl J Med 2002;347:1713)

What is stroke?

• Stroke apoplexy -“struck suddenly with violence” (Greek)
• Stroke is a unique clinical syndrome characterized by a sudden loss of neurologic function attributable to a vascular territory of the brain (i.e., MCA stroke, basilar artery stroke)
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Symptoms of Stroke

• Sudden numbness or weakness of the face, arm or leg especially on one side of the body
• Sudden loss of vision in one or both eyes
• Sudden confusion, trouble speaking or understanding
• Sudden trouble walking, loss of balance or coordination especially with dizziness

Types of Stroke

85% Ischemic
15% Hemorrhagic
Ischemic Stroke
Sudden occlusion by clot
Permanent damage

Hemorrhagic Stroke

Acute Ischemic Stroke:
Pathophysiology

Stroke symptoms are due to arterial occlusion
- Arterial occlusion is seen in 80-90% on angiograms within 6-24 hrs from symptom onset
- 80% of acute strokes are in MCA territory
- 50-70% are embolic (cardiogenic, artery-to-artery)

Majority of stroke due to embolism

An interactive graphic will be inserted here during the presentation

Many sources of emboli

Intracranial Atherosclerosis
Carotid Plaque with Atherosclerotic Emboli
Aortic Arch Plaque
Cardiogenic Emboli
Penetrating Artery Disease
Flow Reducing Carotid Stenoses
Atrial Fibrillation
Valve Disease
Left Ventricular Thrombus
**Stroke Syndromes**

- Left Middle Cerebral Artery (MCA) Syndrome
- Right MCA Syndrome
- Posterior Circulation Strokes
- Lacunar Syndromes

**MCA Territory Stroke**

- Language loss (aphasia)
- Right hemiparesis
- Right hemisensory loss
- Right visual field cut
- Left gaze preference

**Left MCA Syndrome**

- Language loss (aphasia)
- Right hemiparesis
- Right hemisensory loss
- Right visual field cut
- Left gaze preference

**Right MCA Syndrome**

- Left hemi-neglect (visual, spatial)
- Left hemiparesis
- Left hemisensory loss
- Left visual field cut
- Neglect of deficits “anasgnosia”

**Posterior Circulation Ischemia**

- Ataxia or Gait unsteadiness
- Dysarthria, diplopia, or dysphagia
- Nausea/Vomiting
- Vertigo
- Crossed motor/sensory
- Fluctuating consciousness
Lacunar Stroke

- Pure Motor Hemiparesis
- Pure Sensory Loss
- Ataxia-hemiparesis
- Clumsy-hand-Dysarthria

Lacunar Stroke Syndromes

Stroke Mimics

- Hypoglycemia
- Hypergycemia
- Seizure
- Subdural Hematoma
- Migraine

Altered conscious
Prior history of:
Diabetes
Seizure disorder
Trauma

Prehospital Stroke Screen

Pre-hospital Stroke Care

Pre-hospital Stroke Screening Form
State-Wide Prehospital Stroke Screen

- FAST or Cincinatti Stroke Screen
- Face-Facial Droop
- Arm- Arm drift or focal weakness
- Speech- language or clarity of speech loss
- Time

Facial Droop

Arm Drift

Speech

- Ask patient to repeat a phrase "Montana is big sky country", "The sky is blue"...

Acute Management

- Vitals and ABCs
- Place O₂, labs, EKG, foley, second IV, weight
- Quick History
  - Is this a stroke? Onset? prior symptoms? prior stroke? on coumadin?
- Quick Exam
  - Severity, NIHSS, Localization
- To head CT

Acute Management: Vitals

- Airway - secure?
- Breathing - O₂ Sat, CHF?
- Circulation - BP too high or too low? A-Fib?
Acute Management:

- Symptom onset or time last seen normal
- Correlate times (alarms, work, drive time TV)
- Corroborate with witness
- Prodromal or previous symptoms/TIAs
- Exclude stroke mimics (seizure, trauma, hypoglycemia, orthostasis)

Modified NIH Stroke Scale

- Quantified neurologic exam
- Points added for each deficit (max=31)
  - Hi score = severe deficits or big stroke
- Predicts:
  1. Outcome
  2. Success from thrombolysis
  3. Disposition

Blood Pressure Management in Acute Ischemic Stroke

No thrombolytics

BP > 220/120 MAP > 130 requires

- Labetalol 10-30 mg IV q 10-15min
- Enalapril 0.625-1.25 mg IV q 6-8hrs
- Nitroprusside 0.5-1.0 µg/kg/min cont. IV
- Nicardipine 2.5-15 mg/hr continuous IV

BP > 185/110

- Nitropaste 1-2 inches
- Labetalol 10-30 mg IV q 10-15min
- Enalapril 0.625-1.25 mg IV q 6-8hrs (watch for angioedema)

CT Evaluation in Acute Stroke

Normal Late Ischemia Hemorrhagic

Treatment of Acute Ischemic Stroke
Acute Ischemic Stroke Treatment:
IV Thrombolysis

Stroke Treatment in the U.S.

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- tPA has been available in U.S. since 1996
- Only 3-4% of stroke patients receive t-PA for their acute stroke

IV Alteplase (tPA) for Acute Ischemic Stroke

- Approved in the US in 1996 after publication of NINDS trials
- Approved in:
  - Canada 1999
  - Germany 2000
  - Europe 2002
  - South America
- Endorsed by:

IV Alteplase (tPA) for acute ischemic stroke

- 6 trials, 2776 patients, 300 hospitals, 18 countries
- ~30 communities reporting experience in >1000 patients

Acute stroke care in the US: results from 4 pilot prototypes of the Paul Coverdell National Acute Stroke Registry.
Stroke 2005;36(8):1820

- CDC sponsored pilot stroke registry
- Michigan, Ohio, Mass., Georgia
- 98 hospitals
- October 2001-November 2002

Paul Coverdell Registry Experience

- 6867 Acute strokes; 4280 ischemic
- 60% age >70; 55% women
- 23% presented <3 hours
- 7.6% presented <1 hour
Paul Coverdell Registry Experience
Stroke 2005;36(8):1820

177 (4.5%) patients treated with IV+/-IA118 (4.1%) treated with IV alone 10-20% treated < 60 min from door 60-77% treated 1-2 hrs from door Symptomatic ICH 5 (4.1%)

Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST)
Lancet 2007; 360: 275-82

SITS-MOST design
Lancet 2007; 360: 275-82

- 6483 patients received 0.9 mg/kg IV tPA <3 hrs
- 285 Centers; 14 countries; 3.5 yrs
- Prospective, open, monitored observational registry

SITS-MOST results
Lancet 2007; 360: 275-82

- Mean Age 68
- Baseline NIHSS 12; 40% NIHSS >15
- 10.6% Tx’d <90 min; 66% 120-180 min
- Median of 12 patients treated per hospital
- 50% of centers were new to treatment with tPA (at least 5 treated patient before enrollment)

SITS-MOST results
Lancet 2007; 360: 275-82

- Symptomatic ICH 4.6%
- Complete Recovery 39% at 90d
- Median NIHSS fell from 12 to 4 at discharge or 7 days
- Overall Mortality 11%
- Mortality related to treatment 1.5%

IV Alteplase (tPA) for acute ischemic stroke

- Consistent results in academic and community hospitals
- 30-45% chance of recovery to complete independence
- 3.5-6% risk of symptomatic ICH
- No increase in mortality (17% t-PA vs 21% placebo)
“Time is Brain”
NINDS/NSA recommended time guideline for evaluation and treatment of stroke victims

<table>
<thead>
<tr>
<th></th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door to physician</td>
<td>10 min</td>
</tr>
<tr>
<td>Door to neurologic expertise*</td>
<td>15 min</td>
</tr>
<tr>
<td>Door to CT completion</td>
<td>25 min</td>
</tr>
<tr>
<td>Door to CT interpretation</td>
<td>45 min</td>
</tr>
<tr>
<td>Door to thrombolysis</td>
<td>60 min</td>
</tr>
<tr>
<td>Door to neurosurgical care</td>
<td>2 hours</td>
</tr>
<tr>
<td>Door to monitored bed</td>
<td>3 hours</td>
</tr>
</tbody>
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* by phone if not personally available

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IV tPA

**Inclusion**
- Onset/last seen normal ≤ 3 hours
- Ischemic stroke with measurable deficit (NIHSS>4)
- Age 18 years

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**Exclusions**
- CT with any hemorrhage
- BP >185/110 at time of treatment
- Rapidly improving symptoms
- Clinical history suggestive of subarachnoid hemorrhage (even when CT normal)
- INR >1.5 or receiving heparin with elevated PTT
- Platelets < 100K
- Glucose < 50 or 400

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Administering IV t-PA

- BPs every 15 minutes
- Serial neurologic exams
- 2 IVs and foley
- Maximum dose 90mg
- Total dose = 0.9 mg/kg
  1. 10% bolus/1 min
  2. 90% continuous/60 minutes

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Post-thrombolysis monitoring

- BPs every 15 min
- Serial neurologic exams
- No heparin, aspirin or other antithrombotics x24 hrs
- Avoiding unnecessary blood draws or transports x24 hrs
- Head CT for any worsening or new onset severe nausea/vomiting/headache
IV tPA: What to expect

**Benefit**
- Improvement may be seen as early as 1-2 hours after initiation
- 30-40% chance of significant improvement or return to being independent
- More severe stroke symptoms can expect lesser chances of improvement

**Risk**
- 4-6% chance of having serious bleeding into brain
- Does not increase risk of death

Common Protocol Violations

- Blood pressure not controlled <185/110
- Time of onset not accurately determined
- Treated >3 hours due to delay in ED
- Use of heparin with tPA

Extended Stroke Treatment Window

- IV t-PA 3 to 4.5 hours
- Mechanical Thrombectomy
  - MERCI catheter
  - Penumbra catheter

Pooled Analysis of ATLANTIS, ECASS and NINDS IV tPA Trials


European Cooperative Acute Stroke Study (ECASS 3)

NEJM 2008;359:1317-29

- 130 sites 19 European Countries
- 821 patients randomized to Alteplase (418) or placebo (408) from 2003-2007
- 0.9mg/kg IV t-PA total (10%/1 min;90%/1 hour)
ECASS-3 Main Inclusion Criteria

- Acute ischemic stroke
- Age, 18 to 80 years
- Onset of stroke symptoms 3 to 4.5 hours before initiation of study-drug administration
- Stroke symptoms present for at least 30 minutes with no significant improvement before treatment

ECASS-3 Main Exclusion Criteria

- Intracranial hemorrhage
- Time of symptom onset unknown
- Symptoms rapidly improving or only minor before start of infusion
- Severe stroke as assessed clinically (e.g., NIHSS score >25) or by appropriate imaging techniques
- Seizure at the onset of stroke
- Stroke or serious head trauma within the previous 3 months
- Combination of previous stroke and diabetes mellitus
- Administration of heparin within the 48 hours preceding the onset of stroke
- Other major disorders associated with an increased risk of bleeding
- Platelet count of less than 100,000 per cubic millimeter
- Systolic pressure greater than 185 mm Hg or diastolic pressure greater than 110 mm Hg, or aggressive treatment (intravenous medication) necessary to reduce blood pressure to these limits
- Blood glucose less than 50 mg per deciliter or greater than 400 mg per deciliter
- Symptoms suggestive of subarachnoid hemorrhage, even if CT scan was normal
- Oral anticoagulant treatment
- Major surgery or severe trauma within the previous 3 months
- Other major disorders associated with an increased risk of bleeding

European Cooperative Acute Stroke Study (ECASS 3)

- Treatment with IV t-PA associated with a 1.42 odds of independent outcome (mRS 0, 1) at 90 days
- Intracranial hemorrhage greater in t-PA treated (27%) vs. placebo (17%)
- Symptomatic: t-PA (2.4%) vs. placebo (0.3%)
- Mortality: t-PA (7.7%) vs. placebo (8.4%)

0-3 hrs vs. 3-4.5 hrs IV-tPA

<table>
<thead>
<tr>
<th></th>
<th>NIHSS</th>
<th>Favorable Outcome (Odds Ratio)</th>
<th>Symptomatic ICH</th>
<th>Mortality (vs. placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NINDS 0-90 min</td>
<td>14</td>
<td>2.81</td>
<td>6.4</td>
<td>17% vs 21%</td>
</tr>
<tr>
<td>NINDS 90-180 min</td>
<td>1.55</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECASS 3 median 3.59 min</td>
<td>9</td>
<td>1.34</td>
<td>7.9</td>
<td>7.7% vs 8.4%</td>
</tr>
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AHA/ASA Science Advisory

- rtPA should be administered to eligible patients who can be treated in the time period of 3 to 4.5 hours after stroke (Class I Recommendation, Level of Evidence B).
- The eligibility criteria for treatment in this time period are similar to those for persons treated at earlier time periods, with any one of the following additional exclusion criteria: Patients older than 80 years, those taking oral anticoagulants (regardless of INR), those with a baseline National Institutes of Health Stroke Scale score >25, or those with both a history of stroke and diabetes.
Mechanical Embolectomy for Acute Ischemic Stroke

- Onset to treatment up to 8 hours
- Used when clot seen on CT/MR Angiography
- Typically used >3 hours after onset or when IV tPA unsuccessful
- Achieves higher rate of recanalization than IV t-PA
- Performed by experienced interventional neuro/radiologist at limited number of stroke centers

Intra-arterial clot retrieval

Concentric's MERCI clot retrieval device

Penumbra Aspiration Catheter

Summary

- Stroke is a devastating illness
- Treatment is available but time-dependent
- Treatment can now be extended to patients up to 4.5 hrs with iv-tPA and 8 hours with mechanical therapies.
- Alliances with larger stroke centers are critical for small facilities without stroke experience to apply new therapies