Emergency Department Management of Acute Ischemic Stroke

R. Jason Thurman, MD
Associate Professor of Emergency Medicine and Neurosurgery
Associate Director, Vanderbilt Stroke Center
Vanderbilt University, Nashville, TN
Acute Ischemic Stroke
The “Eight D’s” of ED management

- Prehospital Management
  - Detection
  - Dispatch
  - Delivery

- Emergency Department Management
  - Door
  - Data
  - Decision

- Emergent Therapeutic Options
  - Drug
  - Device
Prehospital Care: General Principles

- Successful stroke treatment is built on the principle of “time=brain.”
- Patients that arrive to the hospital outside of their therapeutic window have no effective emergent treatment options.
- Public education efforts are needed to advance awareness of the signs and symptoms of stroke.
- The public must understand that stroke=911!
Prehospital Management: EMS Care

**SUMMARY**

- Identify the possibility of an ongoing stroke.
- Establish a concrete time of onset if at all possible—use all available resources.
- Complete prehospital assessment including CPHSS, Blood Glucose Check.
- Notify appropriate receiving hospital as soon as possible.
- Run emergency traffic if onset within 6 hours.
Emergency Department Management: *Door*

- Successful triage must include a dependable method of recognition of stroke symptoms, especially in non EMS patients!
- On arrival, the acute stroke patient is placed in a high acuity area and given the same triage priority as an unstable patient.
- Once the airway, breathing, and circulation are assessed, the most appropriate first step in management is-
Emergency Department Management: *Door*

- Vitals, IV access, and **confirmation of blood glucose** are performed immediately.
- An accurate focused history and physical exam are quickly performed by the ED team.
- Time of symptom onset is a critical component of the history.
The Rapid ED Neurologic Exam

- Rapid focused neurological exam identifies deficits- should include 6 essential components of neurological function (Mental Status, Cranial Nerves, Motor Exam, Sensory Exam, Reflexes, Coordination)

- The NIH Stroke Scale may be used as a tool for rapid neurological assessment and quantification of neurological deficits
Emergency Department Management: *Door*

- The Head CT Scan serves as a critical fork in the road for stroke care.
- Emergency Department personnel must streamline acute stroke patients into the head CT scanner as soon as possible and all unnecessary delays must be avoided!
  - Multimodal CT imaging may influence decision making, when available (more later!)
NINDS Time Targets

- Door to doctor: 10 minutes
- Door to CT completion: 25 minutes
- Door to CT interpretation: 45 minutes
- Door to decision/treatment: 60 minutes

HOW?
Emergency Department Management: *Decision*

- Once head CT scan is interpreted, the ED/Stroke Team must come to a decision with the patient and his or her family.

- The decision of whether or not to treat with thrombolytic therapy is a difficult multifaceted one and should be made only after careful consideration and conversation have occurred.
NINDS Trial Design

- Two part double-blinded study with 624 acute stroke patients randomized to IV t-PA or placebo

- Favorable outcome defined as normal or near normal at 90 days using four outcome measures: NIHSS, Glasgow Outcome Scale, Modified Rankin Scale, Barthel Index

- Primary analysis based on global synthesis of the four measures of favorable outcome
NINDS Trial

- NINDS Trial analysis concluded that there was a statistically significant difference in favorable outcome for t-PA treated patients.

- Much controversy followed in the wake of the NINDS Trial.

- FDA approval for the use of IV t-PA for acute ischemic stroke followed closely behind the publication of the study.

- Many criticisms followed as well.
NINDS Validation

- In response to criticisms, the NINDS released its data set from the 1995 Trial for independent review.
- 2003: Independent Panel performs review addressing major criticisms and validates NINDS Trial analysis.
- Statistically significant clinical benefit confirmed (Odds Ratio For Favorable Outcome=2.1, 95% CI= 1.5-2.9)

*Stroke* (2004;35:2418-2424)
Association of Outcome with Early Stroke Treatment: Pooled Analysis of ATLANTIS, ECASS, and NINDS rt-PA Stroke Trials

The ATLANTIS, ECASS, and NINDS Study Group Investigators

Methods

- Original individual patient data were pooled from 6 randomized controlled trials
- 2775 Patients
- Over 300 Hospitals
- 18 Countries
- Median age 68 years
- Median Baseline NIHSSS 11
Results

- Median onset-to-time treatment = 243 minutes
- Of the 928 (33%) treated within 3 hours, one-third were from studies other than NINDS
- Symptomatic ICH rate = 5.9%
- Adjusted Odds Ratios for Favorable Outcome:
Results

- Median onset-to-time treatment = 243 minutes
- Of the 928 (33%) treated within 3 hours, one-third were from studies other than NINDS
- Symptomatic ICH rate = 5.9%
- Adjusted Odds Ratios for Favorable Outcome:

<table>
<thead>
<tr>
<th>TIME</th>
<th>ODDS RATIO</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-90</td>
<td>2.8</td>
<td>1.8-4.5</td>
</tr>
<tr>
<td>91-180</td>
<td>1.6</td>
<td>1.1-2.2</td>
</tr>
<tr>
<td>181-270</td>
<td>1.4</td>
<td>1.1-1.9</td>
</tr>
<tr>
<td>271-360</td>
<td>1.2</td>
<td>0.9-1.5</td>
</tr>
</tbody>
</table>
Additional Safety Data: Graham GD. *Stroke* 2003

- 2003 Meta-analysis of 15 studies (n=2639)
- Median NIHSS=14
- Studies excluded:
  - n<15
  - Treatment window >3 hours
  - Unreported symptomatic ICH rates
  - Special population limitations
- Overall symptomatic ICH rate=5.2%
Emergency Department Management: *Decision*

- First, review the history and be certain that time of onset is concrete.
- If there is any doubt, thrombolytic therapy is contraindicated.
- The window for FDA Approved IV t-PA treatment is 3 hours from symptom onset.***
Emergency Department Management: *Decision*

Secondly, the differential diagnosis of acute ischemic stroke should be reviewed.

- Hypoglycemia
- Hyperglycemia
- Complicated Migraine
- Todd’s Paralysis
- Intracranial Hemorrhage
- Hypertensive Encephalopathy
- Trauma
- Neoplasm/Mass lesion
- Encephalitis/Meningitis
- Hyponatremia
- Uremia
- Toxicological
- Psychiatric
- Bell’s Palsy
- Arterial Dissection
Thrombolytic Therapy for Acute Ischemic Stroke: Indications

- Acute Ischemic Stroke within 3 hours of symptom onset*** (More soon)
- Age greater than 18 years old
Thrombolytics for Ischemic Stroke: Contraindications

- Evidence of ICH
- Suspicion of SAH
- Recent stroke, intracranial surgery, or serious CHI within 3 months.
- Major surgery or severe trauma within 14 days
- History of ICH
- Intracranial neoplasm, AVM, or aneurysm
- Noncomressible arterial puncture or LP within 7 days
- Major symptoms improving or minor stroke symptoms (NIHSS<4???)
- Uncontrolled HTN at time of treatment***
- Seizure at stroke onset
- Active internal bleeding
- INR >1.7, PT>15 sec, Platelet Ct. <100,000
- Heparinization within 48 hours preceding stroke and elevated aPTT at presentation
Thrombolytics for Ischemic Stroke: Contraindications

- Evidence of ICH
- Suspicion of SAH
- Recent stroke, intracranial surgery, or serious CHI within 3 months.
- Major surgery or severe trauma within 14 days
- History of ICH
- Intracranial neoplasm, AVM, or aneurysm
- Noncompressible arterial puncture or LP within 7 days

- Major symptoms improving or minor stroke symptoms (NIHSS<4???)
- Uncontrolled HTN at time of treatment***
- Seizure at stroke onset
- Active internal bleeding
- INR >1.7, PT>15 sec, Platelet Ct. <100,000
- Heparinization within 48 hours preceding stroke and elevated aPTT at presentation
Emergency Department Management: *Decision*

Once the working diagnosis of acute ischemic stroke is confirmed and inclusion/exclusion criteria have been reviewed, careful discussion with the patient and family takes place. Several important points are emphasized...
NINDS Trial Reported Benefit

- With IV-tPA treatment, there is a 30% greater chance of improved clinical outcome.
NINDS Trial Symptomatic ICH Rate t-PA Treatment vs. Non-Treatment

**Graham et al: 5.2% Symptomatic ICH Rate**
NINDS Trial 30 Day Mortality

t-PA Treatment vs. Non-Treatment

30 Day Mortality

Treatment Group
Non-Treatment Group

17% 21%
Individual Patient’s Risk/Benefit Profile Reviewed

- Worse outcome regardless of treatment associated with:
  - Diabetes Mellitus
  - Advanced Age
  - Uncontrolled Hypertension
  - Higher NIHSS scores
  - CT findings of edema, hypodensity, or dense MCA

- Increased risk of hemorrhage associated with:
  - Significant findings on head CT scan
  - Treatment beyond 3 hour window
  - NIHSS>20
  - Post treatment elevations in blood pressure
Emergency Department Management: *Drug*

- The total dose of IV-tPA is 0.9mg/kg (90mg max)
- 10% of total dose is given IVP over 1-2 min
- 90% remaining dose is given as IV infusion over one hour
- Excess IV-tPA from vials is discarded to avoid accidental overdose.
Post-Treatment Considerations

- After IV-tPA is given, the patient is admitted to an ICU/Stroke Unit setting with skilled nursing available.
- If such a setting is unavailable, immediate transfer should be considered.
- Neurologic exams are performed every 30 minutes X six hrs. then every hr. X 16 hrs.
- Blood pressure is closely monitored and treated aggressively to maintain strict parameters.
Post Treatment Considerations

- The stroke team’s worst scenario: the post treatment headache...
Post Treatment Considerations

- If post treatment hemorrhage is suspected
  - Immediate discontinuation of rt-PA
  - Emergent Head CT
  - Obtain blood for PT, PTT, Fibrinogen, T&C
  - Prepare platelets, cryoprecipitate
  - Consider Factor VIIa
  - Obtain appropriate surgical consultation.
ED Management: Critical Actions

- Triage the patient with appropriate urgency
- Obtain fingerstick blood glucose
- Activate Stroke Team in timely fashion
- Emergently obtain CT imaging
- Set the stage for treatment decisions
As we speak, multiple new therapies are under investigation.

One very promising new therapy currently in some use is intra-arterial thrombolytic treatment.

Skilled interventional neuroradiologists use a tiny catheter to identify obstructing lesions and deliver thrombolytics at the site of the clot.

This is practice is widely employed, but not yet FDA approved.
The Future

- Ultrasound aided thrombolysis
- New mechanical techniques and new toys for the angiography suite are constantly being developed.
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 Medeghi, M.D., Thomas Machnig, M.D., Dietmar Schneider, M.D., Rüdiger von Kummer, M.D., Nils Wahlgren, M.D., and Danilo Toni, M.D., for the ECASS Investigators*
Additional Considerations

- Age > 80 years
- History of prior stroke and diabetes
- Any anticoagulant use prior to presentation
- NIHSS > 25
- CT findings involving >1/3 MCA territory
At the Frontier: Multimodal Imaging
CT Angiography/CT Perfusion Studies
Clinical Implications???

- Opens opportunities for patients previously excluded under standard protocols.
- Potential to increase likelihood of appropriate treatment selection.
- Potential to increase patient safety by identifying patients more likely to hemorrhage.
- Ongoing studies will determine if the promise of these modalities will be fulfilled.
The Future

- Widespread educational efforts are needed at the public, prehospital, and hospital level.
- Well designed code stroke protocols and guidelines must be established at the prehospital, ED, and inpatient arenas.
- Well integrated stroke teams are needed with cooperation between the departments of Neurology, Radiology, Neurosurgery, Nursing, and Emergency Medicine.
Summary

- BE PREPARED!
- Triage the Patient with Urgency
- Rule out Hypoglycemia and get CT quickly
- Come to a decision with patient and family
- Administer thrombolytics early!
- Admit the patient to appropriate care unit
- Educate the public, your hospital, and your Emergency Department team!
- Consider “the future” today…