

## *Hospital Peer Review*

**June 2010**

*Hospital Peer Review is a monthly newsletter sponsored by the Rural Healthcare Quality Network to alert Critical Access Hospitals regarding findings from the Peer Review Program. Summarized are a few of the key findings and best practices that would be helpful for other critical access hospitals to be knowledgeable about. This newsletter is edited by Myron Bloom, Medical Director and he can be reached at [drmbloom@msn.com](mailto:drmbloom@msn.com).*

### **Treating Code Stroke**

There are basically two types of stroke, hemorrhagic and ischemic; and this paper will address the later. Up until recently, the cut off time for attempting reperfusion by intravenous thrombolysis was considered to be 180 minutes from the time of ischemic stroke onset. However, after the European Cooperative Acute Stroke Study (ECASS) III study, the rt-PA treatment window has been expanded to 4.5 hours (270 min). **Nevertheless, the maximum benefit and safety is greatest with the shortest interval from onset to rt-PA treatment, so expeditious evaluation and treatment optimizes outcome. Therefore, time sensitive goals are in order.**

The time of onset of symptoms should be explicitly solicited and recorded. It is defined as the last time the patient was known to be “normal” (or at previous pre-stroke baseline). If the symptoms seem to stutter, resolving completely and then reoccur, for the purposes of determining whether thrombolysis can be considered, the time of onset would be the last time the patient was “normal.” If the patient was sleeping and awoke with the symptoms, the time of onset would be when the patient was last known to be “normal,” just before falling asleep.

#### **Key Treatment Time Targets for “CODE STROKE”**

- The "door to first physician contact" goal is within 10 minutes.
- The "door to initiation of CT scan" goal is 25 minutes.
- The "door to drug" goal for thrombolytic treatment is within 60 minutes.

The general clinical flow is as follows:

- ABC's: supplemental oxygen and protect the airway and patient (NPO, head up, rails up, no aspirin until CT interpretation).
- Perform problem focused H&P with baseline NIHSS. The NIHSS is a rapid numerical scoring of deficits in key aspects of the neurological exam including: level of consciousness and orientation, eye movements, visual fields, facial weakness, motor strength, coordination, sensation, language and comprehension, articulation, and neglect.

The NIHSS will give the clinician insight into location of the causative vascular event and prognosis; and can be performed in five to eight minutes.

- Draw blood for lab tests: Glucose (also get finger stick for immediate value), complete blood count (CBC) with platelet count, PT/INR (if patient is on warfarin or liver disease), electrolytes, blood urea nitrogen (BUN), creatinine.
- Perform ECG and possibly monitor rhythm.
- Perform non-contrast head CT to exclude hemorrhage. (Timely MRI is an alternative) expecting interpretation within 20 minutes.
- Review rt-PA indications/contraindications and document as to whether patient is eligible (a checklist is strongly advised; a seizure at the time of onset of stroke does not necessarily contraindicate rt-PA if neurologic findings are secondary to stroke and not a postictal residual.)
- Monitor VS with abbreviated neurologic exam (level of consciousness, orientation, speech and understanding, motor function) every 15 minutes.
- Document change in condition and clinical decision making about why rt-PA was or was not given (a signed patient consent is generally advised).
- If rt-PA is administered, initiate bleeding precautions:
  - Avoid anticoagulant, antiplatelet, or non-steroidal anti-inflammatory agents for the first 24 hours.
  - Avoid placement of central venous access or arterial puncture for the first 24 hours.
  - Placement of an indwelling bladder catheter should be avoided during drug infusion and for at least 30 minutes after infusion ends.
  - Insertion of a nasogastric tube should be avoided, if possible, during the first 24 hours.
  - Monitor for central nervous system (CNS) hemorrhage. If there are any signs of CNS hemorrhage (e.g., neurological deterioration, development of severe headache, sudden severe elevation of BP, or new nausea or vomiting) or signs of major systemic hemorrhage, institute the following measures:
    - ✓ Discontinue infusion of thrombolytic drug.
    - ✓ Obtain hemoglobin, hematocrit, partial thromboplastin time, prothrombin time/INR, platelet count, fibrinogen (also type and cross match if transfusions will be needed).
    - ✓ Obtain emergent head CT without contrast if CNS hemorrhage suspected.
    - ✓ If head CT is positive, get neurosurgical consultation.
- Patients presenting with ischemic stroke who are not candidates for intravenous rt-PA should promptly be given aspirin, after exclusion of hemorrhage on CT scan (clopidogrel if aspirin intolerant).

### **Absolute Clinical Contraindications**

- Onset of stroke greater than 4.5 hours prior to initiating rt-PA
- Rapidly improving symptoms
- Mild stroke symptoms/signs (NIHSS less than 4):
  - Sensory symptoms only
  - Ataxia without other deficits
  - Dysarthria without other deficit
  - Mild motor signs (non-disabling)
  - Visual field defect without other deficit
- Intracranial neoplasm, arteriovenous malformation or aneurysm
- Clinical presentation suggestive of subarachnoid hemorrhage regardless of CT result
- Hypertension - systolic blood pressure (SBP) greater than 185 mm Hg **OR** diastolic blood pressure (DBP) greater than 110 mm Hg on consecutive measurements despite treatment (IV labetalol, nicardipine, or nitroglycerine recommended)

### **Other Contraindication Considerations**

- In the setting of middle cerebral artery stroke, an obtunded or comatose state, or CT showing early changes of recent major infarction such as edema, sulcal effacement, mass effect may be a contraindication (higher risk of hemorrhagic transformation).
- Minor ischemic stroke within the last month
- Major ischemic stroke or head trauma within the last three months
- History of intracerebral or subarachnoid hemorrhage
- Gastrointestinal or genitourinary hemorrhage within the last 21 days
- Arterial puncture at a non-compressible site within the last seven days or lumbar puncture within the last three days
- Major surgery, major trauma, or CPR within the last 14 days
- Clinical presentation suggestive of acute myocardial infarction (MI) or post-MI pericarditis
- Patient with liver disease or taking oral anticoagulants and international normalized ratio (INR) greater than 1.7
- Patient receiving heparin within the last 48 hours and having an elevated activated partial thromboplastin time (aPTT)
- Patient receiving low-molecular-weight heparin within the last 24 hours
- Platelet count <100,000 mm<sup>3</sup> or Fibrinogen <120mg/ml
- Known hereditary or acquired hemorrhagic diathesis
- Pregnant, or delivery within 14 days

The combination of history and physical findings has anatomical implications. Limited motor or sensory abnormalities perhaps with a stuttering onset, without alteration of level of consciousness, language, or cognition implies subcortical small vessel disease (lacunar infarction); whereas suddenly maximal, mixed sensory-motor, level of consciousness and cognitive dysfunction represents large vessel disease, carrying a much worse prognosis and a neuro ICU candidacy. Simply broken down, cortical stroke affecting the leg is an Anterior Cerebral Artery hit; face and arm symptoms are Middle Cerebral Artery; and homonymous Hemianopsia is Posterior Cerebral Artery. Intra-arterial thrombolytic therapy may be a treatment option for selected patients with Middle Cerebral or Basilar Artery occlusion presenting within 6 and 12 hours, respectively.

Middle Cerebral Artery occlusion has the following symptom complex:

- Reduced level of consciousness
- Contralateral hemiplegia and face weakness
- Contralateral hemisensory loss
- Aphasia if ischemia is on the left, "neglect" if on the right
- Contralateral homonymous visual field deficit, eye deviation toward side of brain ischemia (away from the side of weakness)

Basilar artery occlusion defined by the following:

- Symptom complex consistent with this vascular distribution:
  - Quadriparesis, sometimes with posturing bulbar dysfunction (dysarthria, dysphagia, dysphonia)
  - Typically dysconjugate eye movement deficits
  - Commonly, depressed level of arousal, respiratory abnormalities

The National Institutes of Health Stroke Scale (NIHSS) score and a classification methodology for stroke type (large-artery atherosclerosis, cardioembolic, small-artery occlusion) were compared for patient outcomes at 7 days and 3 months. The NIHSS was more predictive of prognosis. The likelihood of an excellent outcome at 3 months was about 20% for patients with an NIHSS score above 15 and 65% for those with a score of 4 to 6. Every point increase on the NIHSS decreased the likelihood of an excellent neurologic outcome at 3 months by 17%. These findings were independent of stroke type, although small artery lacunar strokes had better outcomes than other types.<sup>1</sup>

Many physicians have questioned the validity of the results from the National Institute of Neurological Disorders and Stroke (NINDS) Recombinant Tissue Plasminogen Activator Stroke Study because any imbalance in baseline stroke severity between the rt-PA and placebo groups might account for the better outcomes in the rt-PA group, as well as other factors known to affect stroke outcome (age, blood pressure at admission, diabetes, hospital resources and consultant availability, and initial computed tomography findings). To address these concerns, investigators from the NINDS study group performed a post hoc multivariate subgroup analysis for all subgroups, finding patients treated with rt-PA were more likely to have a favorable outcome than

were those who were not treated (adjusted odds ratio, >1) and mortality rates at 90 days did not differ significantly.<sup>2</sup>

The National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study group conducted a post hoc analysis of NINDS data for outcomes and incidence of symptomatic intracerebral hemorrhage in groups of patients with minor stroke defined as either:

- 1) pretreatment NIHSS score of 0 or 1 for each NIHSS item except level of consciousness, which was required to be 0; or
- 2) presumed small-vessel occlusion and lacunar-like infarct; or
- 3) motor deficits without deficits in language or consciousness or other signs of large-territory ischemia; or
- 4) lowest quartile of NIHSS scores ( $\leq 9$ ), excluding patients with aphasia, extinction, or neglect; and
- 5) NIHSS score  $\leq 9$ .

Of the 624 patients in the NINDS trials, 177 (99 in the treated group and 78 in the placebo group) had NIHSS scores  $\leq 9$ . The subgroup analysis of low NIHSS score patients found those treated with rt-PA were more likely to have favorable outcomes and less likely to have bad outcomes (modified Rankin scale >2) than those not treated. In patients with a NIHSS score of 9 or less, the incidence of symptomatic intracerebral hemorrhage was 3%, which was lower than the incidence reported in the original study for the overall treated cohort (6.4%). The authors of this study concluded that the data would support rt-PA treatment for minor stroke.<sup>3</sup>

The European Cooperative Acute Stroke Study (ECASS) III was a manufacturer-sponsored, double-blind, placebo-controlled trial of the efficacy of rt-PA in 821 patients at 130 sites in 19 European countries with acute stroke symptoms persisting for 3.0 to 4.5 hours. The primary endpoint was disability at day 90 as assessed by the modified Rankin scale, classifying outcomes as favorable (no symptoms or symptoms without disability) or unfavorable (slight disability or worse). The median time to treatment was about 4 hours. At 90 days, the percentage of patients with a favorable outcome was higher in the rt-PA group than in the placebo group (52.4% vs. 45.2%; odds ratio, 1.34;  $P=0.04$ ). Compared with the placebo group, the rt-PA group had slightly fewer deaths (7.7% vs. 8.4%; OR, 0.90;  $P=0.68$ ), but more intracranial hemorrhages (27.0% vs. 17.6%; OR, 1.73;  $P=0.001$ ) and symptomatic intracranial hemorrhage (2.4% vs. 0.2%;  $P=0.008$ ).<sup>4</sup>

Researchers conducted an updated analysis of pooled data from eight trials involving 3,670 patients (median age: 68; age range: 19–101) randomized to receive rt-PA or placebo within 360 minutes of onset of stroke symptoms. In multivariate logistic regression analysis, the odds of a favorable 3-month outcome were found to be inversely related to time of symptoms onset to rt-PA treatment, with no benefit after 270 minutes. Adjusted odds of favorable 3-month outcomes were 2.55 for 0–90 minutes, 1.64 for 91–180 minutes, 1.34 for 181–270 minutes, and 1.22 for 271–360 minutes. Adjusted odds of mortality increased from 0.78 for 0–90 minutes to 1.49 for 271–360 minutes. The probability of a favorable outcome decreases by a factor of about two for every 90-minute delay in treatment after stroke onset and after 4.5 hours (270 min) rt-PA

treatment increases mortality. Large parenchymal bleeds occurred in 5.2% of rt-PA patients independent of the time-to-treatment interval compared to only 1% of controls.<sup>5</sup>

Because neurologists are often unavailable in emergency departments when patients present with stroke, researchers reported on their use of the telephone to direct rt-PA administration to 53 patients at 43 hospitals as far as 277 miles away from the researchers' stroke center. The symptomatic ICH rate in this group was low (1 of 53 patients), and their outcomes were equivalent to those of 73 patients treated in-house at the neurologist's facility.<sup>6</sup>

The NIHSS is a useful tool but has its limitations. For instance, it assigns mutism and global aphasia a NIHSS score of 3, which is the same score that would be given to a patient with mild facial weakness, mild dysarthria, and mild upper-extremity drift. Therefore, neurologic (and preferably telemedicine video) consultation is especially advisable for rt-PA consideration in both higher and lower NIHSS scores.

Researchers reviewed the characteristics of 33 malpractice actions involving use of rt-PA (1<sup>st</sup> approved for acute stroke by the FDA in 1996) identified by a review of seven legal databases. Harm to the patient was alleged to have resulted from failure to treat with rt-PA in 29 cases and from administration of RT-PA in only 3. Emergency physicians were defendants in 19 cases, twelve cases had results favorable to the plaintiff, 10 involved failure to treat with rt-PA while 2 involved claims of injury resulting from rt-PA treatment. Most cases are decided in favor of the defendant but failure to treat with rt-PA was the most common cause of legal action in acute stroke cases.<sup>7</sup>

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### Sources:

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<sup>2</sup> Kwiatkowski T, Libman R, Tilley BC, et al. The impact of imbalances in baseline stroke severity on outcome in the National Institute of Neurological Disorders and Stroke Recombinant Tissue Plasminogen Activator Stroke Study. *Ann Emerg Med*. April 2005;45(4):377-384.

<sup>3</sup> National Institute of Neurological Disorders Stroke rt-PA Stroke Study Group. Recombinant tissue plasminogen activator for minor strokes: The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study experience. *Ann Emerg Med*. September 2005;46(3):243-252.

<sup>4</sup> Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med*. September, 25, 2008;359(13):1317-1329.

<sup>5</sup> Lees KR, Bluhmki E, von Kummer R, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet*. May 15, 2010;375(9727):1695-1703.

<sup>6</sup> Frey JL, Jahnke HK, Goslar PW, et al. t-PA by telephone: Extending the benefits of a comprehensive stroke center. *Neurology*. January 11, 2005;64:154-156.

<sup>7</sup> Liang BA and Zivin JA. Empirical characteristics of litigation involving tissue plasminogen activator and ischemic stroke. *Ann Emerg Med*. August 2008;52(2):160-164.