



## **Acute Stroke Care: It's Not Just tPA**

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### **Case Presentation**

A 72-year-old woman with a history of hypertension and diabetes develops sudden onset of slurred speech, left facial droop, left-sided weakness. The family calls 911. An ACLS squad is dispatched and, based on history, physical examination, determines that she is having acute stroke. The squad plan to take the patient to the nearest ED. En route the squad notifies the receiving hospital of a possible stroke patient. Anticipating a 15-20 minute time for transport, the medics ask the medical commander on duty whether they should administer aspirin.

The patient arrives to the ED and is found to have a right gaze preference, left face droop, dysarthria, left arm paresis and mild left side neglect. The BP is 220/120, HR is 100 and the blood glucose is 316 mg%.

The patient appears alert, and is able to slowly respond to simple commands. The patient has a patent airway, no carotid bruits, clear lungs, and a regular cardiac rate and rhythm. An immediate CT without contrast is performed, revealing a large area of hypodensity with mild edema and mass effect.

## **Key Clinical Questions and Learning Points**

### **Should aspirin be administered prehospital or early in the ED course of acute stroke care?**

Although early aspirin administration in stroke has not been studied directly, a recent meta-analysis was done of over 40,000 subjects in nine trials treated with aspirin within 48 hours of acute stroke symptoms. This analysis showed that for every 1,000 patients treated with aspirin, there were seven fewer early recurrent strokes and 13 fewer patients who were dead or dependent at six months when administered aspirin. These improved ischemic stroke and mortality rates came at the expense of approximately two more patients with intracerebral hemorrhage. There was a minor but statistically significant improvement in survival among aspirin-treated patients at 6 months.

Indirect evidence of aspirin's effects can be found in the analysis of the early trials of streptokinase and the phase IV trials of tPA use in the treatment of acute ischemic stroke. Early administration of aspirin in these trials was thought to be associated with an increased incidence of intracerebral hemorrhage when used in combination with a fibrinolytic agent. The current approach, however, suggests that early aspirin administration still is the preferred in acute ischemic stroke, once the CT confirms a non-hemorrhagic infarct and the patient is determined not to be a candidate for thrombolytic therapy with tPA.

### **What early changes might be observed on the cranial CT obtained acutely in Emergency Department patients being treated for acute ischemic stroke?**

Early changes that might be observed on an ED cranial CT include:

- Loss of the insular ribbon
- Loss of a distinct gray-white interface
- Inability to identify sulci
- Acute hypodensity
- Mass effect and midline shift
- Dense MCA sign

**What is the significance of early ischemic changes on the initial CT in acute ischemic stroke?**

At a minimum, early ischemic changes in the distribution of the artery that apparently is causing the acute stroke should cause the clinician to question whether or not the stroke is less than 180 minutes old. As such, observed early ischemic changes may preclude an aggressive approach to the use of tPA.

Early ischemic changes are considered 'minor' if they are well localized and include less than 1/3 of the distribution of the middle cerebral artery. When a more extensive area of hypodensity or edema is observed, it may suggest an increased risk of intracerebral bleeding and death. Although important, this suggested relationship has not been consistently observed across all ischemic stroke studies.

Current recommendations suggest that tPA be excluded when major early ischemic changes are observed, particularly if the changes are observed in an area that is much greater than 1/3 of the CNS supplied by the middle cerebral artery.

**What is the role of IV or subcutaneous heparin in the setting of acute ischemic stroke or in stroke prophylaxis?**

There has only been one study of the IV administration of heparin in acute ischemic stroke. Patients (n=225) were given IV heparin or placebo for 7 days after an acute ischemic stroke. There were no differences in stroke progression or functional activity at 7 days, 3 months or at one year when heparin was administered. Additionally, more patients in the heparin group died within one year than patients in the placebo group.

In one study, there was an observed reduction in the incidence of acute ischemic stroke in patients treated with subcutaneous heparin. However, the incidence of hemorrhagic stroke was also increased with this heparin prophylaxis, such that there was no net benefit to its use. Currently, the AHA and EUSI state:

1. There is no recommendation for general use of Heparin, LMWH or heparinoids after ischemic stroke. (Level I)
2. Full dose heparin for selected indications such as atrial fibrillation, high risk of re-embolism, arterial dissection, or high grade arterial stenosis. (Level IV)
3. Heparin is recommended for DVT prophylaxis only.

**What is the optimal BP after ischemic or hemorrhagic stroke?**  
**Does BP management change when fibrinolytic therapy is considered?**  
**Which antihypertensive is most appropriate?**

There are no controlled studies to guide the management of blood pressure after stroke. In general, the concept of “permissive hypertension” has been the overriding consensus and practice. In general, the target BP in patients with prior hypertension is 180 / 100-105 mmHg and the target BP in previously normotonic patients is 160-180 / 90-100 mmHg. These BPs correspond to mean arterial pressures of approximately 120-125 mmHg and 110-115, respectively. It is important to note that 1) the BP considered to be the upper limit of acceptable in the NINDS clinical trial was approximately 180/110 and 2) hypotension and drastic reductions in BP must be avoided in order to prevent catastrophic reductions in cerebral blood flow.

It is not clear that any one antihypertensive agent acutely is preferred over another. In the setting of cardiac ischemia, nitrates can be used to address both the potential cardiac complications and the hypertension associated with the acute stroke. When patients are hypertensive and tachycardic, IV labetalol can be used. Regardless of what agent is used, it is important to both recheck the BP manually after the patient has been stabilized, and to utilize antihypertensives judiciously in order to avoid relative hypotension.

**Is high blood glucose adaptation to the stress of stroke and thus desirable or is it detrimental after stroke?**

Hyperglycemia is present in 25 to 50% of stroke patients. Hyperglycemia (defined as blood glucose of as low as 125 mg %) has been associated with worse outcome in the setting of acute ischemic stroke. Glucose elevation increases the potential for cerebral edema and hemorrhagic transformation of ischemic strokes. Accordingly, current recommendations include the treatment of glucose levels > 300 mg% with insulin. However, studies are underway that are attempting to determine if more intensive glucose management may improve the outcome of acute ischemic stroke patients.

**What are the indications for immediate neurosurgical evaluation in patients with intracerebral hemorrhage?**

Neurosurgical evaluation is required in patients with:

1. Large clots in the frontal, temporal or occipital regions with progressive clinical deterioration.
2. Deep basal ganglia clot in the non-dominant hemisphere with progressive deficit.
3. Acute cerebellar hematoma larger than 3cm, indicating the need for operative intervention.

**What are summary pearls regarding the adjuncts in the ED management of acute ischemic stroke patients?**

- In general, aspirin should be avoided until after CT confirmation that the stroke is non-hemorrhagic, and that tPA is not indicated for the patient.
- BP management should be guided by the need to avoid both marked hypertension and hypotension.
- Early ischemic changes on CT assist in decision-making by suggesting the appropriateness of tPA use, based on the likely stroke onset time and the size of the involved cerebral cortex.
- Heparin has no role (other than DVT prophylaxis) in acute ischemic stroke.
- Glucose management should attempt to reduce hyperglycemia patients to a normal glucose level.
- Transfer ischemic stroke patients when perfusion imaging, interventional neuroradiology, or neurosurgical consultation are required.

## **Patient Case Outcome**

### **Emergency Department Course**

The patient's blood pressure remained elevated, but was reduced to an acceptable of 180/106 after the administration of 20 mg IV labetalol. Seven units of subcutaneous regular insulin were given, and a repeat Accucheck at two hours was 135 mg%. The patient's bed was elevated to 30%, but no further treatment for elevated ICP was required. The patient remained clinically stable without any further deterioration in mental or neurological status. Aspirin at a dose of 162 mg was provided once the CT demonstrated the absence of a hemorrhagic stroke and 24 hours after t-PA administration. Other than subcutaneous unfractionated heparin for DVT prophylaxis, no other antithrombotic therapy was provided in the ED.

### **Hospital Course and Patient Outcome**

The patient underwent MRI with perfusion-diffusion studies. The images showed an area of injury on diffusion substantially smaller than the area of ischemia on perfusion scan. Cerebral angiography with microangiographic administration of tPA was performed. The patient tolerated the procedure well and was discharged home with physical therapy on day 7 with partial resolution of the initial stroke deficits.