Clinical Controversies: Management of Acute Ischemic Stroke 2011
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Case 1

- A 58 year-old woman with no past medical history presented to the ED after the sudden onset of aphasia and right sided weakness.
- Exam shows a mild expressive aphasia, R face and arm weakness as well as L gaze deviation.
- Her symptoms began at 3 p.m., it is now 6:45 p.m.

What treatment should you initiate?

A. IV t-PA
B. IV heparin
C. Antiplatelets
D. Mechanical Embolectomy
E. Intra-arterial t-PA

The 2011 Acute Stroke Timeline

- Time of onset= last time seen normal
  - 0-4.5 Hours  IV-tPA
  - 0-6 Hours  IA-tPA
  - 0-8 Hours  Mechanical Embolectomy
  - Greater than 8 hours  Anticoagulants or Antiplatelets

The speaker has no disclosures.
Intravenous t-PA: Proven, Approved

- Pivotal IV t-PA NINDS trial (0-3 hours)
  - 30% increase in minimal or no disability at 90 days, not the Lazarus effect
  - Symptomatic hemorrhage risk increased 0.6 to 6.4%, half were serious and fatal
  - No change in mortality
  - Multiple recent studies confirm this result in diverse settings
  - THE EARLIER THE BETTER!!

Intravenous t-PA: Proven, Approved

- Ischemic stroke with significant disability
  - No bleed on non-contrast head CT
  - Blood Pressure: below 185/110
  - Remember contraindications: most are relative
    - Low plts <100k, high INR>1.7
    - Seizure at onset
    - Hypoglycemia

Intravenous t-PA: 3-4.5 hours

- ECASS III trial (9/08)
  - 821 pts randomized to t-PA vs placebo
  - Median time: 3h 59min
  - Favorable outcome: 52% vs 45%, p=0.04
  - Symptomatic ICH: 2.4% vs 0.2%, p=0.008
  - No mortality difference

Additional ECASS III Exclusions: 3-4.5 hours

- 1. Age >80
- 2. NIHSS >25
- 3. Combination of previous stroke and diabetes
- 4. Oral anticoagulant treatment (field may move this direction with newer agents anyway)
t-PA 3-4.5 Hour: European Experience

- 2376 patients treated between 3-4.5 hrs, around 20,000 treated within 3 hours
- By the end of 2009, this represented 22% of all t-PA treated patients
- Door to needle time DID NOT increase with the additional window
- At 3 months in 60% of those treated from 3-4.5 hours were functionally independent


We gave t-PA but it’s NOT actually a stroke!

- Previously thought to be a bad idea
- Common mimics: seizure, complicated migraine, conversion disorder
- In a total of 70 patients treated with t-PA with a stroke mimic…
  - Zero instances of sICH
  - 87% had no deficit on discharge

Chernyshev OY et al: Neurology 74:1340, 2010

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Intraarterial t-PA: Proven, Unapproved

- Similar to cardiac lysis vs. urgent cath
- PROACT I/II studies: pro-urokinase
  - Effective up to 6 hours after onset
  - Recent studies with IA t-PA with similar results
Mechanical Embolectomy: Unproven, Approved

- Use up to 8 hours
  - Maybe longer with basilar artery thrombosis
- Useful if t-PA contraindicated
  - High INR
  - Endocarditis
  - Recent Cath
  - Recent Surgery

Future Directions

- Perfusion-Based Time Window
- Ultrasound-enhanced thrombolysis
  - With IV t-PA in 4.5 hour window
- More Neuroprotectant trials: ALIAS, Fast-MAG
- Drip and Ship
- Combination Approaches

Do Stroke Centers Actually Make a Difference?

- Observational study using NY ischemic stroke data from 2005-2006 (n=30,947)
- 49% admitted to a designated stroke center
- Admission to a stroke center associated with a lower 30d (and 1d, 7d, 365d) all-cause mortality and greater use of thrombolysis
- No differences in mortality for GIB or AMI

Xian Y et al: JAMA 305:373, 2011
Case 2

- A 62 year-old man with a history of HTN, DM, smoking presents with 14 hours of right-sided weakness.
- The patient is on ASA 81mg daily

Workup is negative for source:
What treatment should you initiate?

A. IV t-PA  
B. Coumadin  
C. Increase ASA to 325 mg daily  
D. Clopidogrel (Plavix)  
E. ASA+ER Dipyridimole (Aggrenox)

Approach to Stroke Treatment

Acute Stroke Therapy?

- No

Anticoagulants?

- No

Antiplatelets

Shrinking Indications for Anticoagulation in Stroke

1. Atrial Fibrillation
2. Some other cardioembolic sources
   - Thrombus seen in heart
   - ?EF<35
   - ?PFO with associated Atrial Septal Aneurysm
3. Vertebral dissection
   - 2009: Questionable in carotid dissection
4. Rare hypercoagulable states: APLA
Bridging Heparin

- Absolutely no data at all
- Retrospective review of 204 patients
  - Bridging increased hemorrhage rate with no improvement in secondary prevention
- If you are going to do it
  - Never, never bolus
  - Careful not to make patient supratherapeutic

Hallevi H et al: Arch Neurol 2008

Summarizing 20 years of stroke data...

- Almost never use warfarin
- Use heparin even less (basically never)
- Plavix and Aggrenox are equivalent and each better than aspirin
  - (2010: cilostazol as well we guess…)
- Almost never use combinations of antiplatelet medications

Other Acute Stroke Management

- Statins for (almost) all
  - SPARCL (NEJM 8/06), 80mg atorvastatin in stroke and TIA if LDL>100
- High glucose and fever are bad

Permissive Hypertension

- National Guidelines
  - To at least 220/120: Morbidity increases if lower in the acute setting
  - After IV tPA: less than 185 systolic for 24 hours
- Randomized trial of 2020 patients with acute stroke: candesartan vs placebo for 7d
  - Lower pressures with candesartan
  - No benefit to treatment
  - Higher risk of poor functional outcome with candesartan

Permissive Hypertension

• When to stop remains controversial
• Situations where more important
  – Large Vessel Occlusion
  – Fluctuating Symptoms
• We begin a medicine before discharge (~72h) and aim for normotension over a matter of weeks
  – Choose thiazides and ACEI first