Current Standards for Treatment of Stroke: Management of Acute Ischemic Stroke

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Current Standards for Treatment of Stroke

Management of Acute Ischemic Stroke

Dr. John Castaldo, MD
Professor and Chief of Neurology
Acute Ischemic Stroke

- How big and how bad a problem is it?
- How good are the treatment options?
  - Why don’t we use them more often?
- What are the risks of good therapies?
  - Who should receive these therapies?
- How should we move forward to obtain best practice for our communities?
# Cerebrovascular Disease: Pathogenesis

## Ischemic Stroke (83%)
- Atherothrombotic Cerebrovascular Disease (30%)
- Cardio embolic (30%)
- Lacunar (25%) (small vessel disease)
- Other (vasculitis, dissection, hypercoagulable, Etc. (10%)
- Cryptogenic (5%)

## Hemorrhagic Stroke (17%)
- Intracerebral Hemorrhage (70%)
- Subarachnoid Hemorrhage (30%)

**Image(s) have been omitted**
How Big and How Bad a Problem is Acute Ischemic Stroke?
Stroke is Very Big and Very Bad

- Happens a lot
- Kills many
- Disables most
- Costs a ton
- Happens fast

- Window of RX small
- 800,000/year
- 1 every 3 minutes
- Leading US cause
- $50,000,000,000/year
- 2 million neurons
- 14 billion synapses
- 7.5 miles of axons/min
- Under 4.5 hours/onset
How Good are the Treatment Options?
Preventive and Acute Intervention Therapies Work Well (But ....)

- Antihypertensive RX
- Blood glucose control
- Afib anticoagulation
- Antiplatelet Rx
- Anti hyperlipidemia Rx
- Life Style Change
- Smoking Cessation
- tPA

- Costs
- Commitment
- Time
- Effort
- Reimbursement
- Compliance
- Culture
- Not fun
Why Don’t More AIS Patients Receive Early Restorative Treatment?
Patients Arrive Late

- Mean 155 minutes
- Mean 380 minutes
- 40%
- 66%
- 5%
- Only 25%

- If using 911
- If first call PCP
- Arrive within 90 min
- Arrive within 4 hrs
- Actually get tPA
- Know stroke signs
Stroke Specialists are Rare

- Neurologists / USA
- Vascular boarded
- Hospitals USA
- Total Beds
- JC Primary Stroke Centers
- BAC Comprehensive
- Telestroke spoke.hub
- tPA administration
- 13,400
- 345
- 5795
- 944,000
- 800
- 200 anticipated
- Vascular neuro only
- Rare by ED physician
Tissue Plasminogen Activator (tPA)

Image(s) have been omitted
How Safe and How Effective is tPA Anyway?
How good is tPA in Stroke?

- Roughly 50% of patients who receive tPA within time window leave hospital with minimal disability (ranking 0-1)
- Roughly 85% of patients who don’t receive tPA are disabled, 15% are dead
Comparison 90 Day Outcomes tPA Treated
LVH to NINDS Study
Modified Rankin Scale @ 90 Days

LVH IV tPA
N=209
(5/00-12/08)

NINDS tPA
N=309

- 0%
- 20%
- 40%
- 60%
- 80%
- 100%

Percentage of Patients

- Minimal/No Disability (0-1)
- Moderate (2-3)
- Severe 4-5
- Death (6)

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IV tPA - Is Safe and It Works

- If
  - Pt recognizes signs
  - Pt calls 911
  - Arrives at a PCS
  - Stroke team in place
  - Neurologist on scene

- But
  - Few do
  - Many call PCP
  - Ambulance don’t divert
  - 24/7 hard to muster
Using tPA in Routine Clinical Practice

- Overall only about 3%-4% of stroke patients receive tPA—mostly due to time delays
- Efficacy similar to NINDS trial at most centers
- Rate of ICH: 4%-6%
- Risk of ICH increases with protocol violations
  - Time > 4.5 hours
  - Poor blood pressure control
  - INR > 1.7
  - Recent prior stroke
  - Wrong dose
    - 0.9 mg/kg
    - Maximum dose: 90 mg
  - Elevated age and blood sugar also increases risk
Time is Brain: Benefits of IV tPA Diminish Rapidly

3 hr
Influence of Interval Response to tPA: Odds Ratio for Favorable Outcomes

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Odds Ratio</th>
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<td>&lt;90</td>
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<tr>
<td>91–180</td>
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<tr>
<td>181–270</td>
<td>1.40</td>
</tr>
<tr>
<td>&gt;270</td>
<td>1.15</td>
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</table>
Acute Carotid Stroke
Post Stent and tPA ICA Stenosis
Who Should Receive tPA?
Questions to Ask Before Initiating Thrombolytic Therapy

- Did the stroke start within the last 3 hours?
- Any recent illness associated with bleeding risk?
- Is patient taking anticoagulants?
- Are the baseline coagulation tests normal?
- Any medical contraindication for treatment?
- Any neurologic contraindication for treatment?
- What are the findings on CT?
- Are patient and family aware of risks for bleeding?
- What is the blood pressure?
ACCP 2008 Recommendations: Thrombolytic Therapy in AIS

- For eligible patients, we recommend IV tPA 0.9 mg/kg (maximum of 90 mg), provided that treatment is initiated within 3 hours of clearly defined symptom onset (Grade 1A)

- For patients with extensive (greater than 1/3 of the MCA territory) and clearly identifiable hypo density on CT, we recommend against thrombolytic therapy (Grade 1B)
Treatment of Hypertension During and Following Administration of IV tPA

- **SBP 180–230 mm Hg or DBP 105–120 mm Hg**
  - Labetalol—10 mg IV over 1–2 min
    - Repeat every 10–20 min; maximum dose 300 mg; or
  - Labetalol—10 mg IV followed by infusion 2–8 mg/min

- **SBP >230 mm Hg or DBP 121–140 mm Hg**
  - Labetalol as above; or
  - Nicardipine—IV infusion at 5 mg/hr
    - Titrate up to desired effect by 2.5 mg/hr every 5 min; maximum rate 15 mg/hr

- **DBP >140 mm Hg**
  - Nitroprusside infusion 0.5 µg/kg/min; titrate to desired effect
Goals of Antihypertensive Treatment
(in search of the Goldilocks BP)

- Too high is bad and may cause bleeding
- Too low may decompensate collaterals and extend infarct size
- Lowering too fast is worse than not lowering blood pressure at all (unless considering tPA)
- In general target 140-180/90-105
- Start with Nicardipene for best results
What Does Best Practice for AIS Look Like in the Age of tPA?
AIS Treatment: Other Options

- IA administration
- Mechanical thrombolysis
- IA and IV administration
- New thrombolytic agents
- Combination with other antithrombotic agents
- Combination with neuroprotective agents
Thrombolysis: IV or IA Approach?

- An IA approach to recanalization allows for titrated and potentially more effective recanalization vs. IV alone.

- But takes longer and time is brain.

- Requires Neuro Interventionalist with experience.

- Delays or eliminates window for IV tPA which may be fleeting.

- Complications.
90-Day Modified Rankin Score
Revascularized vs. Unrevascularized

<table>
<thead>
<tr>
<th></th>
<th>mRS 0-2</th>
<th>mRS 3-5</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recan</td>
<td>53%</td>
<td>16%</td>
<td>31%</td>
</tr>
<tr>
<td>Non-Recan</td>
<td>6%</td>
<td>32%</td>
<td>62%</td>
</tr>
</tbody>
</table>
Antiplatelet Therapy

- ACCP 2008 Guidelines for Use of Antiplatelet Therapy in Ischemic Stroke
  - In patients not eligible for thrombolytic therapy, early Aspirin therapy (160–325 mg/day) is recommended (Grade 1A)
  - Delay Aspirin for at least 24 hours after tPA
  - Aspirin can be used safely in combination with low doses of subcutaneous Heparin
Early Anticoagulation

- Urgent anticoagulation is not recommended
  - Does more harm than good in all studies

- Should not be given at all unless imaging has excluded hemorrhage

- Requires slow initial administration and continuous monitoring of anticoagulation and adjustments in dose
Case Presentation (BM)

- 36yo man found down in a pile of mulch
- LVH ED 30 minutes out from discovery
- Stroke Alert: Flaccid quadriplegia, sluggish pupils, absent gag, respiratory arrest
- Toes Up going bilaterally
BM
Found down unresponsive
Distal Basilar Artery Occlusion
Distal Basilar Artery Occlusion
Interventional Catheter Clot Penetration of Basilar Clot
Basilar Clot Extracted with Penumbra Device:

Image(s) have been omitted
Basilar Occlusion After TPA and Reopro
Re-cannalization after tPA Cath in SCA
Basilar Artery: Final Intervventional Results
MRI Day 2 Stroke Alert
Outcome

- NIHSS 0
- Walking the hospital floor unaware of any neurological deficits
- Discharged home
TCD Bubble Study with Valsalva (BM)
On Follow-up

- TEE showed small PFO
- TCD showed aggressive bubble emboli
- Randomized to RESPECT
- Amplatzer device deployed
- Patient has remained free of neurological deficits for 2 years
In a typical acute ischemic stroke, every minute the brain loses

- 1.9 million neurons
- 14 billion synapses
- 7.5 miles myelinated fibers

-- Saver, Stroke 2006
Rapid diagnosis and treatment is crucial to outcome: Time is Brain!

Different strategies are necessary for different time windows for IV and IA tPA

Neuroimaging is opening better understanding of tissue at risk/therapeutic outcome with aggressive therapy

Early Risk Factor Modification and Stroke Unit improves outcomes substantially