Interventions for Acute Ischemic Stroke

Objectives
1. Discuss the use of IV t-PA and indications for stroke patients
2. Discuss interventions outside of the three hour symptom onset available for stroke patients, including IA t-PA, interventional procedures and surgery

Epidemiology: Stroke in the US
- "800,000 new or recurrent strokes each year
  - One every 40 seconds
    - 85% are ischemic stroke
- Stroke is a leading cause of disability
  - Over 6.8 million >20 years of age have had a stroke
  - Projections show by 2030, an additional 3.4 million will have stroke
- Stroke is the 5th leading cause of death in the US
  - Every 4 minutes someone dies of stroke
- 10% Return to normal
- 48% Weak on one side
- 22% Unable to walk
- 38% Complete or partial dependence
- 15% Aphasic
- 32% Clinically depressed

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The Stroke Belt


Kentucky Stroke Care Disparities
- Culture
- Education
  - Risk factors
  - Warning signs
  - Treatments
- Geography - Remote locations
- Lifestyle choices - Food choices, low activity level, high smoking rates
- Socio-economic status
- Few stroke-care experts

Types of Stroke
- Hemorrhagic 13%
- Ischemic 87%
- Cryptogenic 26%
- Atherosclerotic 37%
- Cardiembolic 17%
- Other 4%
- Leriche 21%


Ischemic 87%
Atherosclerotic 17%
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Ischemic Penumbra:
Hypo-perfused Area of Focal Ischemia That May Be Salvaged by Timely Intervention

- Infarct: <8 mL/100 g/min
- Penumbra: 8-20 mL/100 g/min
- Normal: 50 mL/100 g/min

Core Infarct
Penumbra
Tissue Left to Save

Time Is Brain—Quantified

<table>
<thead>
<tr>
<th>Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke</th>
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<tbody>
<tr>
<td>Neurites Lost</td>
</tr>
<tr>
<td>Per Stroke 1.2 billion</td>
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<tr>
<td>Per Hour 120 million</td>
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<tr>
<td>Per Minute 1.9 million</td>
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<tr>
<td>Per Second 32 000</td>
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Treatment Windows from Time Last Known Well

- Intravenous (IV) ActiVase® (Alteplase) (rt-PA) is FDA approved within 3 hours and recommended by AHA and AAN within 4.5 hours.
- Mechanical thrombectomy is recommended for patients with large vessel occlusion in whom groin puncture can be obtained within 6 hours.
- Multiple randomized controlled trials have shown endovascular thrombectomy to be significantly beneficial in the treatment of Emergent Large Vessel Occlusion (ELVO).
  - The AHA Guidelines recommend utilization of thrombectomy for patients within 6 hours, but stipulate that appropriate candidates may exist far outside that window.
  - Neuro-interventionalists are increasingly using imaging rather than time to determine candidacy for intervention.

Standard of Care: Treatment Windows from Time Last Known Well

- FDA approved
  - IV tPA: 3 Hours
  - IA tPA: 6 Hours
  - Mechanical Retrieval: 12 Hours

Endovascular intervention may be considered beyond 12 hours.

ED Stroke Alert

- Door to first physician contact: 10 minutes (UK 5 minutes)
- Door to initiation of CT Scan: 25 minutes
- Interpretation of CT Scan: 20 minutes after test completion
- Door to EKG, Labs and Chest x-ray result: 45 minutes
- Door to Needle Time: <60 minutes

AHA/ASA Guideline Recommendations

- Target treatment with rt-PA should be within 1 hour of the patient's arrival to the ED (Class I, Level of Evidence A)
**Time is Brain: 2million neurons/minute**

**Emergency Stroke Alert**

- **ABCs**
- History: TIME – last known normal
- Physical Exam: Baseline NIHSS
- Imaging: CT/CTA
  - CT rules out hemorrhage
  - CTA establishes location of occlusion
  - Perfusion

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**Activase Alteplase**

*A Recombinant Tissue Plasminogen Activator (rt-PA, aka t-PA)*

- The only FDA-approved thrombolytic agent for treatment of stroke
  - Approved June 1996
- An enzyme which has the property of fibrin-enhanced conversion of plasminogen to plasmin
- Binds to fibrin in a thrombus and converts the entrapped plasminogen to plasmin
- Initiates local fibrinolysis

“Stroke Clot Buster”

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**Overall Benefits and Risk of IV rt-PA for Stroke**

- Benefit: neurologically normal at 3 months
  - 55% relative increase
  - 12% absolute increase
- Very robust effect: NNT = 8

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Using rt-PA in Routine Clinical Practice

- Rate of ICH at 36 hours: 4%-6.4%
  - No increase in 90-day mortality compared to placebo group

- Overall risk of complications, including ICH increases with protocol violations:
  - Time window violations
  - Poor blood pressure control
  - Using prohibited agents
  - Wrong dose
  - Elevated blood sugar also increases risk

- Risk of ICH can be reduced by closely following the rt-PA protocol

It is important to utilize a rt-PA Checklist as approved at your facility

Indications for IV rt-PA

- Diagnosis of ischemic stroke causing measurable neurological deficit
- Computed tomography (CT) rules out hemorrhage or non-stroke cause of deficit
- 18 years old or older
- Time to treatment less than 3 hours of confirmed time Last Known Well, or 4.5 hours with additional considerations

Contraindications

- Current intracranial hemorrhage
- Suspicion of subarachnoid hemorrhage
- Intra-axial intracranial neoplasm
- History of intracranial/intraspinal surgery within 3 months
- Severe head trauma within 3 months
- Gastrointestinal malignancy or active internal bleeding within 21 days
- Bleeding diathesis
  - Platelets less than 100,000/mm³
  - International Normalized Ratio (INR) greater than 1.7
  - Activated partial thromboplastin time greater than 40 seconds
- Warfarin use with INR greater than 1.7
- Bleeding diathesis
- Low molecular weight heparin within 24 hours (prophylactic and treatment doses)
- Direct thrombin inhibitors or direct factor Xa inhibitors (less than taken within 48 hours of discontinuation of appropriate screening tests)
- Sustained/uncontrolled BP more than 185/110 mmHg (refractory to antihypertensives)
- Acute bacterial endocarditis

Warnings/Use Clinical Judgment

- History of intracranial hemorrhage
- History of ischemic stroke within 3 months (considerations: size, location & timing of prior stroke)
- Extensive regions of hypodensity or hypodensity on initial CT
- Unruptured/unsecured AVM
- Major surgery within 14 days
- Major trauma within 14 days
- Arterial puncture of noncompressible vessel within 7 days
- History of gastrointestinal or genitourinary hemorrhage
- Malperfusion with life expectancy less than one year
- History of bleeding diathesis
- Hemorrhagic ophthalmic condition
- Acute pericarditis
- History of myocardial infarction involving left anterior myocardium within 3 months
- Left sided heart thrombus
- Pregnancy

Additional Warning for 3–4.5 hour Window

- 3 hour window contraindications and warnings continue to apply, PLUS:
  - NIH Stroke Scale (NIHSS) greater than 25
    - benefit is uncertain due to lack of evidence
    - these may be candidates for thrombectomy
10 Easy Steps for Reconstitution

**rt-PA Kit:**
- Activase Vial
- Vial of Sterile Water (USP)
- Transfer device

**Other Items Needed:**
- Alcohol swabs
- 2 Syringes
  1. Bolus
  2. Discarded Activase
- Large bore needles

1. Remove caps from each vial
2. Swab the top of each vial with alcohol wipe. Keep vial upright.
3. Remove transfer device from wrapper & remove the cap from one end.
4. Insert piercing pin vertically into the center of the stopper of the sterile water. 2 minutes.
5. Turn Activase vial up-side-down & pierce device in the center.
6. Invert and allow sterile water to flow into Activase vial.
rt-PA Dose

0.9 mg/kg (Maximum total dose of 90 mg)

All excess rt-PA needs to be removed from vial prior to dose preparation to prevent excess infusion

10% of the total calculated dose administered as an initial IV bolus over 1 minute
drip the remainder over 60 minutes

IV normal saline flush infused at the same rate immediately following rt-PA administration, in order to clear the line and infuse entire calculated dose

IV rt-PA Considerations: New Anticoagulants

- Dabigatran (Pradaxa)
- Rivaroxaban (Xarelto)
- Apixaban (Eliquis)
- Edoxaban (Savaysa)

Consensus Statement:
- Last dose within 48 hours = Contraindication to IV rt-PA
- Or presence of therapeutic effect on appropriate screening tests = Contraindication to IV rt-PA

If reason to suspect abnormal platelet counts or coagulation studies:
- aPTT for heparin; PT/INR for warfarin; Anti-factor Xa for LMWH; direct thrombin assay for dabigatran and direct factor Xa assays for rivaroxaban, edoxaban, & apixaban
**IV rt-PA Considerations: BP Management**

- IV rt-PA is recommended in patients whose blood pressure can be lowered safely (to <185/110 mm Hg) with antihypertensive agents, with the physician assessing the stability of the blood pressure before starting IV rt-PA
  - (C-I, L-B)
- If medications are given to lower blood pressure, the clinician should be sure that the blood pressure is stabilized at the lower level before beginning treatment with IV rt-PA and maintained below 180/105 mm Hg for at least the first 24 hours after IV rt-PA treatment
  - (C-I, L-B)

*Class, Level of Evidence*

**IV rt-PA Considerations: Labs**

- Given the extremely low risk of unsuspected abnormal platelet counts or coagulation studies in a population, it is reasonable that urgent IV rt-PA treatment not be delayed while waiting for hematologic or coagulation testing if there is no reason to suspect an abnormal test
  - (C-IIa, L-B)

*Class, Level of Evidence*

**IV rt-PA Consideration: Consent**

- IV rt-PA in suspected stroke patient is considered emergent treatment. A separate consent is **NOT** required, unless required by your organization
  - (C-I, L-C)
- Required documentation includes that “risks, benefits and alternatives” were explained and verbal or written consent obtained *(when possible)*

*Class, Level of Evidence*
During and 24 hours After IV rt-PA

- Avoid:
  - Blood pressure elevations more than SBP 180 and DBP 105
  - Anticoagulants, antiplatelets, antithrombotics, thrombolytics
  - Invasive procedures, invasive lines, catheters or tubes
    - unless deemed medically imperative
  - Mobilization
    - safety is maximized when on bedrest precautions

Keep NPO until infusion complete & no side effects are observed, and until dysphagia screen or evaluation passed after infusion

Monitoring During and After IV t-PA

- "Enhanced neurological check"/abbreviated NIHSS and vital signs:
  - Every 15 minutes for 2 hours, then every 30 minutes for 6 hours, every 1 hour for 16 hours, every 2 hours for 24 hours, every 4 hours for 24 hours, after the initial 72 hours: every 8 hours and prn until discharge

- NIHSS:
  - Baseline at arrival, just prior to bolus, repeat at 30 minutes (half way through infusion), at 60 minutes (end of infusion)
    - Expert Consensus Recommendation: then every 2 hours for 48 hours, every 4 hours for 24 hours, after initial 72 hours: every 12 hours and prn with any neurological decline until discharge

Monitoring During and After IV t-PA

- Bleeding
  - Intracranial bleeding
  - Internal bleeding
    - Intracranial and retroperitoneal sites
    - GI, GU or respiratory tracts
  - Superficial bleeding

- Orolingual Angioedema
  - Angioedema is a rare (1-2%), but potentially serious complication
    - especially experienced by those on ACE inhibitors
    - Orolingual angioedema can be asymmetric and can occur contralateral to the ischemia
    - Can be treated with epinephrine, antihistamines and corticosteroids
Management of Hemorrhage After rt-PA

If bleeding is clinically suspected:

- Sudden headache, deterioration in mental status, hypotension, etc.
  - Discontinue rt-PA infusion immediately
  - Emergent CT scan of head and/or body where hemorrhage suspected
  - STAT Prothrombin Time (PT), Partial Thromboplastin Time (PTT), platelet, fibrinogen, type/cross
  - Prepare 6-8 units of cryoprecipitate
  - Prepare 6-8 units of platelets

Management of Hemorrhage After rt-PA

If hemorrhage present:

- Administer cryoprecipitate or platelets as needed
- STAT neurosurgical consultation if intracranial hemorrhage present
- Consider STAT surgical consultation if extracranial hemorrhage present
- Consider second CT scan of hemorrhage to assess progression

Additional Interventions

- HOB 30 degrees
- Cardiac monitoring
- Aspiration/fall/seizure precautions
- Continual assessment and treatment of:
  - ABC's
  - Enhanced Neurological Check
  - NIHSS
  - Vital Signs
  - Normothermia
  - Dysphagia
  - 0.9% saline at 50-100 cc/hour (no D5W)
  - O2 per nasal cannula to keep Sats > 94%
30-50% of strokes are large vessel occlusions

What Constitutes Large Vessel?

Vessels:
- ICA
- A1
- M1
- M2
- Basilar
- Vertebral

New Designation: ELVO

• Stroke process due to occlusion of ‘large’ vessel

• ANALOGY:
  - STEMI = ST Elevation Myocardial Infarction
  - ELVO = Emergent Large Vessel Occlusion
ELVO Trials

- MR-CLEAN
- EXTEND-IA
- SWIFT PRIME
- ESCAPE

Halted early for efficacy

Intra-arterial (IA) rt-PA

- Angiograph catheter
- 6 hours
  - Not FDA approved
  - Is given based on clinical trial data
- 20-30% recanalization rate
**Mechanical Thrombectomy**
- Merci Retrieval System®
- Penumbra Retrieval Device
- Solitaire™ FR
- Trevo®

**12 Hours with ELVO**

**Stroke Transfer Protocol**
Emergent Large Vessel Occlusion (ELVO)

- **Clinical Signs of Stroke**
- Non-contrast Head CT & TIA Available
- Intracerebral Hemorrhage or Subarachnoid Hemorrhage
- No Hemorrhage
- Ischemic Stroke Protocol (including IV tPA as appropriate) if there is ELVO or CTA or MRI is positive
- Continue Stroke Protocol and Consult CSC

**Extracranial Angioplasty and Stenting**

- Usually for prevention
- **Acute Ischemic Stroke:**
  - Etiology of stroke is cessation of flow in the extracranial carotid or vertebral artery
    - Atherosclerosis
    - Dissection
  - Catheter access to intracranial thrombus is impeded by extracranial stenosis or occlusion
Decompressive Hemicraniectomy

- Usually large volume or posterior fossa infarctions
- Can reduce mortality from 80% to ~20%

References


