The “Golden Hour” of Acute Ischemic Stroke

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A Look at Current Stroke Treatment

What’s Changed in 2000?
“EMS systems should implement a prehospital stroke protocol to evaluate and rapidly identify patients who may benefit from fibrinolytic therapy, similar to the protocol for chest pain patients” (Class IIb).
“Patients who may be candidates for fibrinolytic therapy should be transported to hospitals identified as capable of providing acute stroke care, including 24-hours availability of CT scan and interpretation.” (Class IIb).
“Stroke presenting with 3 hours should be triaged on an emergent basis with urgency similar to acute ST-elevation myocardial infarction.”

Intravenous fibrinolysis for acute ischemic stroke
- Class I
  IV - t-PA within 3 hours of onset
- Class Indeterminate
  IV - t-PA between 3 and 6 hours of onset

Intra-arterial fibrinolysis
- Class IIb
  IA prourokinase within 3 to 6 hours after symptom onset

Source: ASA, Circulation, 2000

What Has Not Changed?
Impact of Stroke
- 3rd leading cause of death in the U.S.
- Leading cause of adult disability
- Over 700,000 new stroke cases per year in U.S. with 150,000 stroke deaths per year
- 85% are ischemic
- Less than 25% of eligible thrombolytic candidates receiving therapy
Acute Stroke - Where are we Today?
Where are we today?
- Public poorly informed
- Response time too slow
- Presentation too late
- Hospitals ill prepared
- Fatalistic

Models for the “Golden Hour”
Trauma
- Golden hour for intervention
- Centralized trauma center system, certified by the ACS

Acute myocardial infarction
- Similar door-drug/groin benchmarks for reperfusion
- Decentralized system

Trauma - Example
Stab wound to the abdomen
- Very rapid EMS activation and transport
- Not exactly a difficult diagnosis
- Lots of communication
- Big teams
- Detailed protocols
- “The Golden Hour”
- What is the mortality and morbidity? - Low
**Acute Myocardial Infarction - Example**

The paradigm has shifted

- Chest pain - patients know to call 911
- Rapid access to EMS
- Pre-hospital identification and call
- Pre-hospital ECG
- Team, protocols, drugs in the ED
- “Door to Drug” in 30 Minutes
- What is the mortality and morbidity? - Low.

**Forces of Change**

- Public expectations
  - Aware of “Draino for the Braino”
  - Nihilistic attitude of stroke changing
- Medical - legal pressures
- Managed care cost concerns
- New treatments of stroke on horizon
- Change in treating physicians' perceptions of “risk”

**Organized Stroke Care Saves Lives**

- 21% reduction in early mortality
- 18% reduction in 12 month mortality
- Decreased length of hospital stay
- Decreased need for institutional care

Source: Jorgenson, Stroke, 1994
Cost Effectiveness for rt-PA in Acute Ischemic Stroke

<table>
<thead>
<tr>
<th></th>
<th>rt-PA</th>
<th>placebo</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS</td>
<td>10.9</td>
<td>12.4</td>
<td>0.02</td>
</tr>
<tr>
<td>Discharge Home</td>
<td>48%</td>
<td>36%</td>
<td>0.002</td>
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</tbody>
</table>

With rt-PA, considering 1,000 eligible patients:

- Hospitalization costs = $1.7 million more
- Rehabilitation costs = $1.4 million less
- Nursing home costs = $4.8 million less
- 564 quality-adjusted life-years saved

Treatment Guidelines & Recommendations - Part I

NIH National Symposium Recommendations

• Door-to-MD: < 10 minutes
• Door-to-Neurologic Expertise: < 15 minutes
• Door-to-CT scan: < 25 minutes
• Door-to-CT Interpretation: < 45 minutes
• Door-to-Drug: (80% compliance) < 60 minutes
• Door-to-Admission: < 3 hours

Notes:
At this National Symposium, experts developed in-hospital time intervals to allow the stroke patient to be treated and evaluated in an expedient manner. These recommendations include:

• Emergency department arrival to initial physician evaluation: 10 minutes
• Emergency department arrival to Stroke Team Notification: 15 minutes
• Emergency department arrival to CT Scan initiation: 25 minutes
• And they recommended that 80% of eligible stroke patients presenting to the emergency department should be treated with tPA within 60 minutes.

Stroke Chain of Survival & Recovery

Detection: Early recognition
Dispatch: Early EMS activation
Delivery: Transport & management
Door: ED triage
Data: ED evaluation & management
Decision: Specific therapies
Drug: Thrombolytic & future agents
Dispatch & Delivery: Transport & Management

- ABC’s
- Stroke recognition
- Establish time of onset / his
- Perform neurological evaluation
- Check glucose
- Early hospital notification
- Rapid transport

Cincinnati Pre-Hospital Stroke Scale

Facial Droop

- Normal: Both sides of face move equally
- Abnormal: One side of face does not move at all

Arm Drift

- Normal: Both arms move equally or not at all
- Abnormal: One arm drifts compared to the other

Speech

- Normal: Patient uses correct words without slurring
- Abnormal: Slurred or inappropriate words or mute

NIH Stroke Scale

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Level of Consciousness</td>
<td>0 – 3</td>
</tr>
<tr>
<td>1b</td>
<td>LOC Questions</td>
<td>0 – 2</td>
</tr>
<tr>
<td>1c</td>
<td>LOC Commands</td>
<td>0 – 2</td>
</tr>
<tr>
<td>2</td>
<td>Best Gaze</td>
<td>0 – 2</td>
</tr>
<tr>
<td>3</td>
<td>Best Visual</td>
<td>0 – 3</td>
</tr>
<tr>
<td>4</td>
<td>Facial Palsy</td>
<td>0 – 3</td>
</tr>
<tr>
<td>5</td>
<td>Motor Arm Left</td>
<td>0 – 4</td>
</tr>
<tr>
<td>6</td>
<td>Motor Arm Right</td>
<td>0 – 4</td>
</tr>
<tr>
<td>7</td>
<td>Motor Leg Left</td>
<td>0 – 4</td>
</tr>
<tr>
<td>8</td>
<td>Motor Leg Right</td>
<td>0 – 4</td>
</tr>
<tr>
<td>9</td>
<td>Limb Ataxia</td>
<td>0 – 2</td>
</tr>
<tr>
<td>10</td>
<td>Sensory</td>
<td>0 – 2</td>
</tr>
<tr>
<td>11</td>
<td>Neglect</td>
<td>0 – 2</td>
</tr>
<tr>
<td>12</td>
<td>Dysarthria</td>
<td>0 – 2</td>
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<tr>
<td>13</td>
<td>Best Language</td>
<td>0 – 3</td>
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Preparation
Know your stroke team before you need them

- Check glucose
- Two large IV lines
- Oxygen as needed
- Cardiac monitor
- Continuous pulse-ox
- Stat non-contrast CT scan
- ECG
- CXR
- Get rt-PA
  > Prepare to mix
  > Have pharmacy alerted
- Discuss options with patient and family
- Contact primary care provider

American Heart Association Recommendations
Oxygen

- Use to correct hypoxia
- Suggestion that supernormal levels may hurt
  > one year survival 69% 3L NC vs 73% control

Glucose

- Maintain euglycemia
- Treat glucose > 300 mg/dl with insulin

Source: Rønning, Stroke 1999

True Time of Onset
How normal were they?

- What are they like at baseline?
- Who saw them last?
- Clearly no symptoms?

Times of reference

- Television
- The time the basketball game started
### Stroke Risk Factors

**Modifiable risk factors**
- High blood pressure
- Cigarette smoking
- Transient ischemic attacks
- Heart disease
- Diabetes mellitus
- Hypercoagulopathy
- Carotid stenosis
- Other

**Non-modifiable risk factors**
- Age
- Gender
- Race
- Prior stroke
- Heredity
Treatment Guidelines & Recommendations - Part II

Early CT Changes in Ischemic Stroke

- Loss of insular ribbon
- Loss of gray-white interface
- Loss of sulci
- Acute hypo density
- Mass effect
- Dense MCA sign

Differential Diagnosis

- Intracerebral hemorrhage
- Hypoglycemia / Hyperglycemia
- Seizure
- Migraine headache
- Hypertensive crisis
- Epidural / Subdural
- Meningitis / Encephalitis / Brain abscess
- Tumor

What are the Options?

No thrombolytics

- Nothing
- Aspirin
- Heparin

Intravenous rt-PA

Other

- Intra-arterial thrombolytics
- Low dose IV rt-PA followed by IA rt-PA
- Investigation procedure

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Treatment Based on CT Findings

<table>
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<tr>
<th>CT Findings</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td>None</td>
<td>Treat</td>
</tr>
<tr>
<td>Subtle &lt; 1/3 MCA</td>
<td>Treat</td>
</tr>
<tr>
<td>Subtle &gt; 1/3 MCA</td>
<td>Probably treat</td>
</tr>
<tr>
<td>Hypodensity &lt; 1/3 MCA</td>
<td>Probably treat</td>
</tr>
<tr>
<td>Hypodensity &gt; 1/3 MCA</td>
<td>Don’t treat</td>
</tr>
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Exclusions to Thrombolytics

- Stroke or head trauma in 3 mos
- Major surgery within 14 days
- Any history of intracranial hemorrhage
- SBP > 185 mm Hg
- DBP > 110 mm Hg
- Rapidly improving or minor symptoms
- Symptoms suggestive of subarachnoid hemorrhage
- Glucose < 50 or > 400 mg/dl
- GI hemorrhage within 21 days
- Urinary tract hemorrhage within 21 days
- Arterial puncture at non-compressible site past 7 days
- Seizures at the onset of stroke
- Patients taking oral anticoagulants
- Heparin within 48 hours AND an elevated PTT
- PT >15 / INR >1.4
- Platelet count <100 X 10/L

“Patients were also excluded if aggressive measures were required to lower the blood pressure to within specified limits”

Pretreatment BP Treatment

“Gentle” management if thrombolytic candidate:

- SBP > 180 mm Hg
- DBP > 110 mm Hg

Choices:

- Labetalol 10 - 20 mg IV
- Enalapril 1.25 mg IV
- Nitropaste 1” to chest wall

No nipride or nitroglycerin gtts
Treatment Considerations: Who Will Benefit from rt-PA?

- Patient age and past medical history (diabetes)
- Time from onset
- Blood pressure
- Stroke severity
- Stroke subtype
- CT findings

Factors Associated with Increased Risk of ICH

- Treatment initiated > 3 hours
- Increased thrombolytic dose
- Elevated blood pressure
- NIHSS > 20 *
- Acute hypodensity or mass effect *

* Even though increased r/o ICH, still with benefit vs. placebo
Treatment Guidelines & Recommendations - Part III

Symptomatic Hemorrhages by NIH Stroke Scale in NINDS Trial

Percentage of Patients that Developed Symptomatic Hemorrhages

[Bar chart showing percentage of patients with symptomatic hemorrhages based on edema or mass effect seen on initial CT.

Edema or Mass Effect Seen on Initial CT
Source: Broderick, Stroke 1997]

Percentage of rt-PA Patients with Symptomatic ICH

[Bar chart showing percentage of rt-PA patients with symptomatic ICH based on baseline NIH Stroke Scale score.

Baseline NIH Stroke Scale Score
Source: Broderick, Stroke 1997]
rt-PA Dosing

- 0.9 mg/kg (max = 90 mg)
- 10% bolus (over 1 minute)
- Remainder as a 1 hour infusion
- Have rt-PA in the Emergency Department

Intra-arterial Thrombolytic Efficacy vs. Time of Delivery

![Graph showing Intra-arterial Thrombolytic Efficacy vs. Time of Delivery](image)

Time from onset (hours)
Source: Ernst, Stroke, 2000

Stroke Treatment - Aspirin

- Two important trials:
  - International Stroke Trial (IST)
  - Chinese Acute Stroke Trial (CAST)
- Combined analysis (n=40,090)
- Death / nonfatal strokes reduced 11%
- Don’t forget to check swallowing

Stroke Treatment - Heparinoids

- Two important trials:
  - International Stroke Trial (IST)
  - TOAST (Trial of ORG 10172)
- Decreased recurrent ischemic strokes
- Increased hemorrhagic events
- No net stroke benefit

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Post-Treatment Guidelines & Recommendations

Post Treatment Care - Antihypertensive Therapy

- **SBP 180 - 230 or DBP 105-120 mm Hg**
  - Labetalol 10 mg IV, may repeat / double to 150 mg max
  - Labetalol drip 2-8 mg / min

- **SBP > 230 or DBP 121 - 140 mm Hg**
  - Above

- **DBP > 140 mm Hg**
  - Sodium nitroprusside
  - Sodium nitroprusside (0.5 ug/kg per minute)

May consider enalapril in patients with CHF, asthma, abnormal cardiac conduction
Check with current guidelines

ICH Contingency Plan

- Stat CT
- STAT labs
  - (fibrinogen, CBC, PT/PTT)
- Type and screen
- Fresh frozen plasma
- Neurosurgical consult

Management of Seizures

Prophylactic anticonvulsant medication not recommended

Recurrent seizures require treatment

- Diazepam 5 mg over 2 minutes
- Lorazepam 1-4 mg over 2–10 minutes
- Follow benzodiazepines with longer acting anticonvulsant (phenytoin, phenobarbital, etc.)

Pneumonia After Stroke

- One third of stroke patients develop a pneumonia within 1 month
- 3rd leading cause of death in the first month
- Estimated cost per event $10,000 and a 7 day length of stay
- Laryngeal cough reflex cough tests can identify patients at risk.
Rehabilitation
Early rehabilitation is key for recovery
Early mobilization also prevents:

- Deep venous thromboses and pulmonary emboli
- Decubitus ulcers
- Contractures
- Malnutrition
- Pneumonias
- UTI

What do you need to treat?

- Preplanning and preparation
- Multidisciplinary approach
- Know the mechanics
- Know the risks
- Coordinated post-treatment care
Case Study

History, Timeline, and Initial CT Findings
A 61 year old male, with acute aphasia, right facial droop, and right sided weakness.

12:30  Sudden onset while working in yard.
12:45  Family calls 911.
13:05  Advanced squad evaluates neurologic deficits and glucose.
13:15  Squad notifies receiving hospital of possible stroke patient.
13:30  ED arrival. Initial evaluation by E.D. physician.
13:45  Stroke Team arrives. NIHSS 18.
14:00  CT scan performed.
14:15  Discuss with family and PMD.
14:20  Labs back: gluc 97. BP remains 150/70's.
14:20  CT reading back. (See below.) No hemorrhage or early signs of ischemia.
14:25  Checklist done. No exclusion criteria met.
14:30  Decision time.
14:35  IV rt-PA given. 0.9 mg/kg total
   • 10% bolus - 9 mg
   • 90% over 1 hr - 81 mg
15:45  Patient goes to ICU. Report personally given to ICU staff.
15:50  Pathway actions begin (HOB, BP parameters, aspiration precautions).

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24 Hour Follow-up
A 61 year old male, with acute stroke, treated with rt-PA.
Repeat NIHSS = 3:

- VF intact
- No gaze palsy
- Mild facial palsy
- Mild right arm drift
- Mild dysarthria

Repeat CT shows areas of infarct:
Carotid U/S shows 60-80% stenosis left ICA

- Speech recommends swallowing II diet and daily checks
- Physical therapy pending
- CEA performed day 3
- Patient discharged to home on day 7 near pre-stroke baseline.
References


