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Learning Objectives

- Identify the key barriers that prevent acute ischemic stroke patients from reperfusion to determine workable solutions allowing for care within recommended timeframes
- Adhere to current treatment guidelines and indications/contraindications when determining effective treatment plans for patients presenting with signs of acute ischemic stroke
- Adopt technologies and other collaborative measures that link hospitals in rural areas with certified stroke centers and specialists to increase the expertise and quality of stroke care

Improving Stroke Outcomes

- Current guidelines for the management of patients with acute ischemic stroke published by the AHA/ASA include specific recommendations for the administration of IV rt-PA
- Despite its effectiveness in improving neurological outcomes, many patients with ischemic stroke are not treated with rt-PA, because they arrive late or because of delays in assessment/administration of IV rt-PA
- Earlier administration of IV rt-PA after the onset of stroke symptoms is associated with greater functional recovery
- One of the potential approaches to increase treatment opportunities and improve stroke outcomes is to provide this treatment in a more timely fashion after patient arrival (reduce the door to needle time for IV rt-PA)

But First, a History Lesson: What We Learned from STEMI – “Time is Muscle”

The Need for Speed in STEMI

• 1.4 million Americans will suffer a heart attack annually
• Approximately 400,000 of those will experience STEMI
• Time is muscle. The outcome of STEMI events depends greatly on the care patients receive and the timeframe in which they receive it. The American Heart Association wants to ensure that healthcare systems are able to deliver prompt and appropriate care to STEMI patients during the critical “golden hour” following their heart attack
STEMI: Time is Muscle

Barriers to Timely Reperfusion in STEMI

- The patient
  - Failure to promptly recognize symptoms
  - Hesitation to seek medical attention
- Time to transport
  - Mandated delivery to the closest hospital, regardless of PCI capabilities
  - Long transport in rural areas
- Decision process on arrival
  - Clot-busting drugs vs PCI
  - Off hours
  - Transfer to PCI facility
- Time to implement treatment strategy
  - Procedural factors
  - Team assembly

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Management of Acute Stroke

Introduction

With rapid, aggressive prehospital stroke care, at-risk patients can be appropriately managed and quickly assessed for fibrinolytic therapy that may significantly improve their outcomes.

AHA/ASA Guideline Recommendations

• Intravenous rt-PA is recommended for selected patients who may be treated within 3 hours of onset of ischemic stroke (Class I Recommendation, Level of Evidence A)

• Patients who are eligible for treatment with rt-PA within 3 hours of onset of stroke should be treated as recommended in the 2007 Guidelines

• Although a longer time window for treatment with rt-PA has been tested formally, delays in evaluation and initiation of therapy should be avoided, because the opportunity for improvement is greater with earlier treatment

• rt-PA should be administered to eligible patients who can be treated in the time period of 3 to 4.5 hours after stroke (Class I Recommendation, Level of Evidence B)


Improving Stroke Outcomes

• Current guidelines for the management of patients with acute ischemic stroke published by the AHA/ASA include specific recommendations for the administration of intravenous rt-PA

• Despite its effectiveness in improving neurological outcomes, many patients with ischemic stroke are not treated with rt-PA, because they arrive late or because of delays in assessment/administration of intravenous rt-PA

• Earlier administration of intravenous rt-PA after the onset of stroke symptoms is directly associated with greater functional recovery

• One of the potential approaches to increase treatment opportunities and improve stroke outcomes is to provide this treatment in a more timely fashion after patient arrival (reduce the door-to-needle time for intravenous rt-PA)

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Seven-step Stroke Chain of Survival and Recovery

Before Hospital Arrival
- Detection
- Dispatch
- Delivery

After Hospital Arrival
- Door
- Data
- Decision
- Drug


Prehospital Care

- Stroke education
- Call 911
- Prehospital assessment tools
- Field management
- Rapid transport to stroke center
- Prehospital notification
- The Bottom Line: Focus on limiting delays and recognize that interhospital transfers of acute stroke patients for higher-level care are increasingly common
Before Hospital Arrival

- Early treatment of stroke depends on the victim, family members, or other bystanders detecting the event.
- The Emergency Medical Service (EMS) system must be notified as soon as a stroke is detected, and EMS dispatchers must prioritize stroke calls.
- Acute stroke is a signal for EMS responders to "load and go" and to establish the time of stroke onset as "zero time."
- The victim must be rapidly transported to the receiving facility, with pre-arrival notification of the receiving facility.

After Hospital Arrival

- ABCs of critical care (Airway, Breathing, and Circulation)
- Rapid Emergency Department triage
- Rapid neurological stroke assessment focusing on:
  - Level of consciousness; type, location, severity of stroke
- Emergency diagnostic studies
  - CT scan should be obtained and read within 45 minutes of arrival
  - Withhold fibrinolytics until CT has ruled out brain hemorrhage

ACUTE ISCHEMIC STROKE: OVERCOMING BARRIERS FOR OPTIMAL MANAGEMENT

Thrombolytic Therapy Checklist

Eligibility Criteria

- >18 years of age with ischemic stroke <3 hours
- Stroke deficit assessment
  - Deficit found to be potentially disabling
    - Severity quantified with NIH stroke scale (0-42 scale)
    - (stroke scale training available at: www.asatrainingcampus.org)
- Coagulation status
  - No evidence of coagulopathy, if tested: INR <1.8 and normal
  - PTT if taking warfarin, INR <1.8
  - Platelets >100,000
- Blood Pressure SBP <185 mm Hg, DBP <110 mm Hg
- Glucose >50 mg/dL


Thrombolytic Checklist

Contraindications

- Evidence of intracranial hemorrhage on pretreatment CT
- Clinical presentation suggestive of subarachnoid hemorrhage
- Active internal bleeding
- Within 3 months, any intracranial surgery, serious head trauma, or previous stroke
- On repeated measurements, SBP greater than 185 mm Hg or DBP greater than 110 mm Hg at the time treatment is to begin
- History of intracranial hemorrhage
- Known arteriovenous malformation, or aneurysm

AHA/ASA Guideline Recommendations

• Emergency Departments should establish standard operating procedures and protocols to triage stroke patients expeditiously (Class I, Level of Evidence B)

• Standard procedures and protocols should be established for benchmarking time to evaluate and treat eligible stroke patients with rt-PA expeditiously (Class I, Level of Evidence B)

• Target treatment with rt-PA should be within 1 hour of the patient’s arrival in the ED (Class I, Level of Evidence A)

Fibrinolytic Therapy for Ischemic Stroke

• Intravenous rt-PA represents the first FDA-approved therapy for acute ischemic stroke

• In the NINDS trial, patients treated with rt-PA within 3 hours of onset of symptoms were at least 30% more likely to have minimal or no disability at 3 months compared with placebo

• But careful patient selection and strict adherence to treatment protocol is essential
Fibrinolytic Therapy for Ischemic Stroke

• However, there were 10-fold increases in the risk of fatal intracranial hemorrhage in the treated group (3% vs 0.3%) and the frequency of all symptomatic hemorrhage (6.4% vs 0.6%)

• This increase in symptomatic hemorrhage did not lead to an overall increase in mortality in the treated group

What is Telestroke?

• Evaluation, diagnosis, and treatment of stroke patients using telemedicine
• Multiple technology platforms
  – Mobile (Robotic, Cart)
  – Fixed high-quality videoconferencing
Acute TeleStroke: Provider-to-Provider Link


NINDS-recommended Stroke Evaluation Targets for Potential Fibrinolytic Candidates*

<table>
<thead>
<tr>
<th>Time Target</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door to doctor</td>
<td>10 minutes</td>
</tr>
<tr>
<td>Door to CT† completion</td>
<td>25 minutes</td>
</tr>
<tr>
<td>Door to CT read</td>
<td>45 minutes</td>
</tr>
<tr>
<td>Door to treatment</td>
<td>60 minutes</td>
</tr>
<tr>
<td>Access to neurological expertise‡</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Access to neurosurgical expertise‡</td>
<td>2 hours</td>
</tr>
<tr>
<td>Admit to monitored bed</td>
<td>3 hours</td>
</tr>
</tbody>
</table>

*Target times will not be achieved in all cases, but they represent a reasonable goal  
†CT indicates computed tomography  
‡By phone or in person

Summary
Pre-hospital UNACCEPTABLE Actions

• Failure to recognize signs and symptoms of stroke/TIA
• Failure to attempt to determine symptom onset
  – Delay in transport
  – Transporting a potential stroke patient to an ED not capable of treating acute ischemic stroke with fibrinolytic therapy


Number Needed to Treat to Benefit from Intravenous rt-PA Across Full Range of Functional Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal/Near Normal</td>
<td>8.3</td>
</tr>
<tr>
<td>Improved</td>
<td>3.1</td>
</tr>
</tbody>
</table>

For every 100 patients treated with t-PA, 32 benefit, 3 harmed

Saver JL. Stroke. 2007;38:2279-2283.
ACUTE ISCHEMIC STROKE: OVERCOMING BARRIERS FOR OPTIMAL MANAGEMENT

Time Trend in the Proportion of Patients with Door-to-Needle Times within 60 Minutes: Before and after Initiation of Target: Stroke

(Fonarow GC et al. 2012 Intern Stroke Conf. San Diego, CA. 2/14/14. P<0.0001 for comparison of the two slopes)

Clinical Outcomes Before and After Initiation of Target: Stroke

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pre-target: Stroke (n=27,319)</th>
<th>Post-target: Stroke (n=43,850)</th>
<th>Difference Pre and Post</th>
<th>PValue</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital Mortality</td>
<td>9.93%</td>
<td>8.25%</td>
<td>-1.68%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Discharge Home</td>
<td>37.6%</td>
<td>42.7%</td>
<td>+5.1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ambulatory Status Independent</td>
<td>42.2%</td>
<td>45.4%</td>
<td>+3.2%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Symptomatic ICH</td>
<td>5.68%</td>
<td>4.68%</td>
<td>-1.00%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any t-PA Complications</td>
<td>6.68%</td>
<td>5.50%</td>
<td>-1.18%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Target: Stroke – Results of the Initiative

- The proportion of patients with DTN times <60 minutes increased from 29.6% immediately prior to the start of Target Stroke in Quarter 4 of 2009 to 53.3% in Quarter 3 of 2013 ($P<0.0001$)
- The median Door-to-Needle time was 74 minutes in Quarter 4 of 2009 immediately prior to initiation of Target: Stroke and declined to 59 minutes by Quarter 3 of 2013 ($P<0.0001$)
- In 2009, prior to initiation of Target: Stroke, 15.6% of hospitals had DTN times <60 minutes in 50% or more of rt-PA treated stroke patients, whereas in 2013, this benchmark was being met by 46.6% of participating hospitals ($P<0.0001$)


Target: Stroke Initiative: Conclusions

- The timeliness of rt-PA administration improved substantially in GWTG – Stroke Hospitals after initiation of the multidimensional AHA/ASA Target: Stroke quality initiative
- The proportion of patients with DTN times <60 minutes increased from 29.6% to 53.3%; there was also a more than 4-fold increase in annual rate of improvement in patients with DTN times <60 min
- More rapid perfusion therapy in acute ischemic stroke is not only feasible, but can be achieved with actual reductions in complications and improved outcomes

Conclusion

• Now, fibrinolytic and other emerging therapies offer practitioners the opportunity to limit neurological insult and improve outcomes in stroke patients

• However, there is considerable variability among various institutions in their ability to promptly initiate lytic treatment in eligible acute stroke victims
## ACUTE ISCHEMIC STROKE
Overcoming Barriers for Optimal Management

### I. A Report Card on Barriers to Timely Intravenous rtPA Treatment
A Clinical Tool for Stroke Champions

### TIME OF SYMPTOM ONSET TO TIME OF HOSPITAL ARRIVAL

<table>
<thead>
<tr>
<th>Event</th>
<th>Time Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom onset to 911 call</td>
<td>___ &lt; 5 min, ___ 5-15 min, ___ 15-30 min, ___ 30-60 min, ___ &gt; 60 min</td>
</tr>
<tr>
<td>911 call to EMS arrival</td>
<td>___ &lt; 5 min, ___ 5-15 min, ___ 15-30 min, ___ 30-60 min, ___ &gt; 60 min</td>
</tr>
<tr>
<td>EMS arrival to departure</td>
<td>___ &lt; 5 min, ___ 5-10 min, ___ 10-15 min, ___ 14-30 min, ___ &gt; 30 min</td>
</tr>
<tr>
<td>Hospital notification by EMS during transfer?</td>
<td>___ yes, ___ I don’t know, ___ no</td>
</tr>
<tr>
<td>EMS arrival to ED department (door)</td>
<td>___ &lt; 5 min, ___ 5-15 min, ___ 15-30 min, ___ 30-60 min, ___ &gt; 60 min</td>
</tr>
</tbody>
</table>

**Total time from symptom onset to hospital arrival = _______**  (target < 120 min)

### TIME FROM HOSPITAL ARRIVAL TO TIME OF rtPA ADMINISTRATION

<table>
<thead>
<tr>
<th>Event</th>
<th>Time Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door to doctor</td>
<td>___ &lt; 5 min, ___ 5-10 min, ___ 10-15 min, ___ 15-25 min, ___ &gt; 25 min (target &lt; 10 min)</td>
</tr>
<tr>
<td>Door to completion of ED physician work-up</td>
<td>___ &lt; 5 min, ___ 5-10 min, ___ 10-15 min, ___ 15-25 min, ___ &gt; 25 min (target &lt; 15 min)</td>
</tr>
<tr>
<td>Door to neurology consult</td>
<td>___ &lt; 10 min, ___ 10-15 min, ___ 15-25 min, ___ 25-45 min, ___ &gt; 45 min (target &lt; 25 min)</td>
</tr>
<tr>
<td>Door to CT scan and interpretation</td>
<td>___ &lt; 15 min, ___ 15-30 min, ___ 30-45 min, ___ 45-60 min, ___ &gt; 60 min (target &lt; 45 min)</td>
</tr>
</tbody>
</table>

**Total time from door to treatment = _______**  (target < 60 min)

**Total time from symptom onset to treatment = _______**  (target < 180 min)
II. Inclusion and Exclusion Criteria for Use of Intravenous Recombinant Tissue Plasminogen Activator (rtPA)*

**INCLUSION CRITERIA**
- Diagnosis of ischemic stroke causing measurable neurological deficit
- Onset of symptoms < 3 (< 4.5) hours before beginning treatment
- Aged ≥ 18 years

**EXCLUSION CRITERIA**
- Severe stroke (NIHSS > 25)
- Significant head trauma or prior stroke in previous 3 months
- History of both diabetes and prior ischemic stroke
- Symptoms suggest subarachnoid hemorrhage
- Arterial puncture at noncompressible site in previous 7 days
- History of previous intracranial hemorrhage
- Intracranial neoplasm, arteriovenous malformation, or aneurysm
- Recent intracranial or intraspinal surgery
- Elevated blood pressure (systolic > 185 mm Hg or diastolic > 110 mm Hg)
- Active internal bleeding
- Predisposition for acute bleeding
- Platelet count < 100,000/mm³
- Heparin within 48 hours, and aPTT greater than the upper limit of normal

- Current use of anticoagulant with INR > 1.7 or PT > 15 seconds
- Current use of direct thrombin inhibitors or direct factor Xa inhibitors
- Blood glucose concentration < 50 mg/dL (2.7 mmol/L)
- CT demonstrates multilobar infarction (hypodensity > 1/3 cerebral hemisphere)
- Aged > 80 years

**RELATIVE EXCLUSION CRITERIA**
- Only minor or rapidly improving stroke symptoms (clearing spontaneously)
- Pregnancy
- Seizure at onset with postictal residual neurological impairments
- Major surgery or serious trauma (within previous 14 days)
- Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days)
- Recent acute myocardial infarction (within previous 3 months)

*This checklist includes some indications and contraindications for administration of intravenous rtPA for acute ischemic stroke. A physician with expertise in acute stroke care may modify this list.

** Recent experience suggests that under some circumstances, with careful consideration and weighing of risk to benefit, patients may receive fibrinolytic therapy despite 1 or more relative contraindications.


III. Immediate Diagnostic Studies for Evaluation of All Patients with Suspected Acute Ischemic Stroke

- Noncontrast brain CT or brain MRI
- Blood glucose
- Oxygen saturation
- Serum electrolytes/renal function tests*
- Complete blood count, including platelet count*
- Markers of cardiac ischemia*
- Prothrombin time/INR*
- Activated partial thromboplastin time*
- ECG*

* Although it is desirable to know the results of these tests before giving intravenous recombinant tissue-type plasminogen activator, fibrinolytic therapy should not be delayed while awaiting the results unless:

- There is clinical suspicion of a bleeding abnormality or thrombocytopenia
- The patient has received heparin or warfarin
- The patient has received direct thrombin inhibitors or direct factor Xa inhibitors


IV. A Tool for Patient Education

**WHAT YOUR PATIENTS NEED TO KNOW TO IDENTIFY SIGNS OF ACUTE STROKE:**
- SUDDEN numbness or weakness of face, arm, or leg – especially on one side of the body
- SUDDEN confusion
- SUDDEN trouble speaking or understanding
- SUDDEN trouble seeing in one or both eyes
- SUDDEN trouble walking, dizziness, loss of balance or coordination
- SUDDEN severe headache with no known cause

**IF YOUR PATIENTS SUSPECT AN ACUTE EVENT IN THEMSELVES, FAMILY, OR FRIENDS:**

- **CALL 911 IMMEDIATELY**

This reference tool is a companion to “ACUTE ISCHEMIC STROKE: Overcoming Barriers for Optimal Management,” a CME-certified program jointly sponsored by the American College of Emergency Physicians and Rockpointe.

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