Hyperacute Stroke: Time Is Brain

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Disclosures

- Honorarium
  - Bard
  - Neurooptics
- American Association of Neuroscience Nurses President
- Medical Advisory Board
  - Brain Trauma Foundation
  - Neurooptics
Hyperacute Stroke:
Time is Brain

- Systems of Care

- USA
Patient with abnormal vital functions in need of acute resuscitation

Transport to nearest hospital for stabilization of vital signs

Once vital functions stabilized, transfer to nearest CSC (or PSC if long distances)

Patient with acute onset of stroke symptoms within 6-8 hours

Transport patient to closest PSC or CSC if <15-20 minutes transport time

If PSC and/or CSC >15-20 minutes away, go to closest ASRH

Patient with acute stroke and seen initially at an ASRH

ASRH might use telemedicine to help evaluate the patient and to make transfer recommendations

Transfer to nearest PSC or CSC based on stroke type, patient's medical condition, treatment options

Interactions Within Stroke Systems of Care: A Policy Statement From the American Heart Association/American Stroke Association


on behalf of the American Heart Association Advocacy Coordinating Committee

Stroke. 2013;44:2961-2984; originally published online August 29, 2013;
doi: 10.1161/STR.0b013e3182a6d2b2
Hyperacute Stroke: Time is Brain

• Systems of Care

• Canada

Optimally, in Canada, all acute stroke patients should be initially managed in centres providing either advanced or comprehensive stroke services.

Advanced and comprehensive centres not only provide access to acute thrombolysis, they also have active stroke teams that can be mobilized in a timely manner to rapidly assess, diagnose and implement management strategies to reduce the risk of stroke recurrence or poor outcomes.
Hyperacute Stroke Care Systems of Care

Figure 2.1: Canadian Stroke Best Practices Continuum of Care

- Public Awareness
- Prevention: Primary & Secondary
- Hyperacute Stroke Management
- Acute Stroke Management
- Rehabilitation
- Community Re-integration
Time Is Brain
Hyperacute Stroke

**Time is Brain**

- **Two women - Ages 75 & 39**
  - 
  - R arm/leg hemiplegia, aphasia, R facial droop

- **Transported to Stroke Center**

- **Triage to Acute Stroke Beds in ED**

- **Time of Symptom Onset**
  - 75 year old 25 minutes PTA
  - 39 year old last seen normal 4 hours PTA

- **Team Response – Stroke Alert**
• **Ischemia**
  - Size varies on vessel distribution/collateral flow

• **Immediate Rapid Actions:**
  - Airway – Breathing: O2 for SpO2 < 94%
  - Circulation: ECG, BP assessment & IV/Labs (√BG)
  - D (Neuro): NIHSS or Canadian Neurological Scale (CNS), Neuro Exam & Neuro MD
  - Expedited Tx to Radiology
    - CT non-contrast (complete by 25 min)
    - Decision point for tPA
    - Additional Studies: CTA and diffusion/perfusion
Hyperacute Stroke

** TIME IS BRAIN **

- Monitoring - General
  - Oxygenation: SpO2
  - ECG
  - Vital Signs: BP - Tx dependent on plan
    - No tPA > 220/120  tPA > 185/110
- Monitoring - Neuro
- Stroke Scale & Neuro Clinical Exam
- Pupils – Pupillometry

**Parameter** | **Normal** | **Abnormal**
--- | --- | ---
Pupil Size | Equal | > 1mm difference
NPI | ➤ 3 - 5 | < 3 or NPI difference of > .7 between L & R
Constrictio n Velocity | >0.81 mm/sec | <0.80 mm/sec
**TIME is BRAIN**

**Medical Management**
- R/O Stroke Mimics
- Establish diagnosis of acute ischemic stroke
- Tx decisions
  - Do Nothing
  - IV tPA: 3 to 4.5 h
  - Interventional: within 6-8 h
    - Thrombectomy devices
    - Off-label use of tPA IA

**Clinical Policy: Use of Intravenous tPA for the Management of Acute Ischemic Stroke in the Emergency Department**

**CRITICAL QUESTIONS**
1. Is IV tPA safe and effective for acute ischemic stroke patients if given within 3 hours of symptom onset?
2. Is IV tPA safe and effective for acute ischemic stroke patients treated between 3 to 4.5 hours after symptom onset?

**Patient Management Recommendations**

*Level A recommendations.* In order to improve functional outcomes, IV tPA should be offered to acute ischemic stroke patients who meet National Institute of Neurological Disorders and Stroke (NINDS) inclusion/exclusion criteria and can be treated within 3 hours after symptom onset.*

*Level B recommendations.* In order to improve functional outcomes, IV tPA should be considered in acute ischemic stroke patients who meet European Cooperative Acute Stroke Study (ECASS) III inclusion/exclusion criteria and can be treated between 3 to 4.5 hours after symptom onset.*

*The effectiveness of tPA has been less well established in institutions without the systems in place to safely administer the medication.*

*Note:* Within any time window, once the decision is made to administer IV tPA, the patient should be treated as rapidly as possible. As of this writing, tPA for acute ischemic stroke in the 3- to 4.5-hour window is not FDA approved.

Acute Thrombolytic Therapy

4th Edition
2012-2013 UPDATE
May 23, 2013

All patients with disabling acute ischemic stroke who can be treated within 4.5 hours of symptom onset should be evaluated without delay by a physician with stroke expertise (either on-site or by telemedicine/telestroke consultation) to determine their eligibility for treatment with intravenous tissue plasminogen activator (tPA) (Alteplase) [Evidence Level A].

3.4.1: Intravenous Thrombolysis

i. Eligible patients are those who can receive intravenous tPA within 4.5 hours of the onset of stroke symptoms in accordance with criteria adapted from National Institute of Neurological Disorders and Stroke (NINDS) tPA Stroke Study and the European Cooperative Acute Stroke Study (ECASS III) [Evidence Level A]. Refer to Box 3.4 for inclusion and exclusion criteria for tPA eligibility.

ii. All eligible patients should receive intravenous tPA as soon as possible after hospital arrival, with a target door-to-needle time of less than 60 minutes [Evidence Level C].

iii. Administration of tPA should follow the American Stroke Association guidelines using a dose of 0.9 mg/kg to a maximum of 90 mg total dose, with 10 percent (0.09 mg/kg) given as intravenous bolus over one minute and the remaining 90 percent (0.81 mg/kg) given as an intravenous infusion over 60 minutes [Evidence Level A].
Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke


METHODS

We randomly assigned eligible patients who had received intravenous t-PA within 3 hours after symptom onset to receive additional endovascular therapy or intravenous t-PA alone, in a 2:1 ratio. The primary outcome measure was a modified Rankin scale score of 2 or less (indicating functional independence) at 90 days (scores range from 0 to 6, with higher scores indicating greater disability).
Background: Endovascular therapy is increasingly used after administration of IV tPA for patients with moderate-to-severe acute ischemic stroke, but whether a combined approach is more effective than IV tPA alone is uncertain.

Conclusion: Trial showed similar safety outcomes and NO SIGNIFICANT difference in functional independence with endovascular therapy after IV tPA, as compared with IV tPA alone.

Closer look at evidence: the more severe stroke group (NIHSS 20+) DID have a > benefit with endovascular therapy approach (7% functional outcome) over the IV tPA alone group.
3.4.2: Endovascular Therapies for Acute Ischemic Stroke Treatment

i. Endovascular therapies for acute ischemic stroke treatment, including intra-arterial delivery of thrombolytic drug and/or endovascular mechanical thrombectomy by device or by aspiration, are being investigated as additions to acute stroke thrombolysis. **However, IV thrombolysis remains the standard of care for hyperacute ischemic stroke treatment for appropriate patients [Evidence Level A].**

a. Endovascular therapies for acute ischemic stroke should ideally be reserved for investigational use in the context of randomized controlled trials [Evidence Level C].

b. Endovascular therapy is a possible therapeutic addition to intravenous thrombolysis in highly selected circumstances. Emergency consultation with stroke experts and interventional radiology experts is relevant for this kind of decision-making [Evidence Level C].

ii. Endovascular mechanical thrombectomy alone, without intravenous or intra-arterial tPA, is a possible therapeutic option for patients who do not qualify for tPA thrombolysis due to increased systemic bleeding risks [Evidence Level C].

Establish Treatment Plan

- 75 yr female: NIHSS 24 ...
  - 85 minutes since onset & 60 minutes since arrival
  - CT negative for hemorrhage or edema
  - IV tPA ordered and given
- 39 yr female: NIHSS 26
  - 4 ½ hours since last seen normal
  - Does not quality for IV tPA
  - CT demonstrates possible carotid arterial dissection
**TIME IS BRAIN**

**Individualize Care**

- **75 yr old – IV tPA**
  - BP 181/84 - Labetalol 10 mg IV prior to IV tPA bolus
  - 1330: BP 154/84
  - 1335: NIHSS 24 - tPA 5 mg IVP
  - 1340: tPA IV drip started 45 mg over 60 minutes
  - 1342: BP 196/82
  - 1344: Labetalol 10 mg IV
  - 1350: To Neuro ICU for close monitoring of VS/Neuro

**Individualize Care**

- **39 year old – Interventional**
  - CT / CTA Left Terminus ICA/MCA occlusion and L ICA Dissection
  - Cerebral angio confirms dissection
  - Interventional Plan: attempt to cross to LMCA via RICA-ACA path to reopen L MCA
  - L MCA occlusion
  - Diminutive Dissected L ICA
  - L MCA occlusion Unable to reopen
**TIME IS BRAIN**

- Individualize Care
  - 39 year old – Interventional
    - Pupillometer changes indicative of worsening edema
      - NPI worsening with left pupil
    - Sedation while on table making it difficult to ascertain changes in LOC
    - Neurosurgery called

<table>
<thead>
<tr>
<th>Pupillometer Readings</th>
<th>On arrival</th>
<th>1 hour after arrival</th>
<th>3 hours after arrival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Size</td>
<td>3.2mm</td>
<td>3.3mm</td>
<td>3.3mm</td>
</tr>
<tr>
<td>NPI</td>
<td>4.4</td>
<td>4.0</td>
<td>4.3</td>
</tr>
<tr>
<td>CV</td>
<td>-1.54</td>
<td>-1.43</td>
<td>-1.45</td>
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<td>5.2mm</td>
</tr>
<tr>
<td>NPI</td>
<td>4.3</td>
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<td>2.5</td>
</tr>
<tr>
<td>CV</td>
<td>-1.45</td>
<td>-1.28</td>
<td>-0.45</td>
</tr>
</tbody>
</table>

Clock set to 1:00
**Sequence of Care**

- Post IV tPA - 75 yr old
  - A-B-C:
    - SpO2 97% on RA
    - BP controlled 138/70
  - D: Neuro SS improved
    - Monitoring q 15 min x 8, q 30 x 6 hr then hourly x 24 hours
    - NIHSS ↓ 5 within 6 hours
    - Moving R arm/leg
    - Still has speech issues
    - NPO with order for swallow evaluation

**Sequence of Care**

- Surgery for 39 yr old
  - Decompressive Hemi-Craniecotomy
  - ICP/PbtO2 catheters
  - Dissection and placement of Superficial Temporal artery over L parietal area
  - Post –Op to Neuro ICU
  - Begin Mild Hypothermia
### Hyperacute Stroke

#### Science of Hypothermia

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krieger et al</td>
<td>Stroke 2001; 32: 1847-1854</td>
<td>COOLAID study; 10 pts with NIHSS&gt;8 tx with hypothermia to 32 C for 12-72 hrs (9 pts concurrent controls); Hypo safe and feasible</td>
</tr>
<tr>
<td>Schwab et al</td>
<td>Stroke 2001 ; 32: 2033-2035</td>
<td>50 pts with MCA occlusion cooled x 24-72 hrs. Mod hypo feasible but with side effects. Most deaths occurred during rewarming due to Inc ICP. Pts require longer rewarming period.</td>
</tr>
<tr>
<td>Georgiadis et al</td>
<td>Stroke 2001; 32: 2550-2553</td>
<td>Induction/maintenance with endovascular device feasible (6 pts); safety remains to be evaluated</td>
</tr>
<tr>
<td>Thorsten et al</td>
<td>Stroke 2001; 32: 2833-2835</td>
<td>13 pts cooled to 33 and slowly rewarmed ; inc temp causes inc ICP; slowed rewarmed feasible</td>
</tr>
<tr>
<td>COOL AID Pilot</td>
<td>Stroke 2001; 32: 2833-2835</td>
<td></td>
</tr>
<tr>
<td>De Georgia et al</td>
<td>Neurology 2004; 63: 312-317</td>
<td>40 pts (18 pts cooled to 33 C with endovascular) x 24 hrs; Cooling feasible; clinical outcomes similar</td>
</tr>
<tr>
<td>Lyden et al</td>
<td>J Cerebrovas Dis 2005; 14: 107-114</td>
<td>Endovascular cooling to 33C in AIS pts 12-24h with controlled rewarmed over 12h; Awake stroke pts: Can be done needs further study</td>
</tr>
<tr>
<td>Hemmen et al</td>
<td>Stroke 2010; 41: 2265-2270</td>
<td>Pts IVtPA + hypothermia x 24 hrs at 33 C wth 12h rewarmed; 59 pts enrolled with 28 pts Hypo &amp; 30 Normo; Endovascular hypo can be combined with IV tPA in awake pts (↑ pneumonia). No diff</td>
</tr>
</tbody>
</table>
**TIME IS BRAIN**

**Brain Priorities: 75yo tPA**
- Maintain BP within target limits to enhance flow but reduce risk of bleeding
- Close neurologic monitoring for changes in neuro status
  - Stroke Scale
  - Pupils with pupillometry
    - WNL
  - Clinical Exam improving

**Brain Priorities: 39 yo**
- Reduce ICP
- Provide collateral flow
  - Increase BP to enhance collateral flow
  - Promote STA angiogenesis
- Institute mild hypothermia x 72 hours to
  - Limit ischemic damage to left hemisphere
  - Buy time until STA angiogenesis
TIME IS BRAIN

- Rest, Restore and Revascularize

- 39 year old case
  - Intubated & Sedated (Versed/Fentanyl)
  - Hypothermia instituted to target of 33.5°C
  - BP ↑ 160 - 180 mm Hg Target

Rewarm @ 0.05°C/hr
Hyperacute Stroke

• **Avoid Complications – Advanced Care**

**IV tPA**
- Aspiration precautions/swallow eval with nutrition supplements
- Avoid fever: induced normothermia
- Remove foley catheter to reduce UTI
- DVT prophylaxis and early mobility
- Glycemic control – avoid hypoglycemia and hyperglycemia

**ICP Management/Hypothermia**
- **ICP**
  - Drain CSF
  - Maintain MAP/CPP
  - Sedation/analgesia
  - Mannitol/hypertonic saline
  - PaCO2 35-40 mm Hg
- **Hypothermia**
  - Avoid shivering
  - Reduce complications i.e., pneumonia, infection, bleeding
  - Manage ICP during rewarm
- **System:** DVT prophylaxis, Glycemic control, Nutrition etc
TIME IS BRAIN

• Interdisciplinary Teamwork & Improve Outcomes

• Interventions based on assessments
  • PT/OT/ST
  • Dietitian
  • Pharmacy
  • Respiratory Therapy
  • Case Management

• Improve Processes & Outcomes
TIME IS BRAIN

• Interdisciplinary Teamwork & Improve Outcomes
  • Interventions based on assessments

• Improve Processes & Outcomes
  • Analyze care processes & patient responses to improve systems of care
  • Learn from each patient!
TIME IS BRAIN:

Improve Processes & Outcomes

- Definitions: Stroke November 2013

Table 2. Annotations to the Definition of the Door-to-Needle Time

Start (the door)
- For patients admitted through the emergency department: the moment the patient first enters the door of the first facility.
- For patients already in the hospital at the time of symptom onset: the moment the neurologist was first consulted.

Stop (the needle)
- The moment the intravenous bolus with rt-PA is administered provided that this is followed immediately by administration of the continuous infusion.

rt-PA indicates recombinant tissue plasminogen activator.

Table 3. Annotations to the Proportion of the Patients With Stroke Treated With IVT or Thrombolysis Rate

<table>
<thead>
<tr>
<th>Numerator</th>
<th>Denominator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients treated with IVT.</td>
<td>Patients admitted to the hospital for ischemic stroke that presented within 4.5 h from symptom onset.</td>
</tr>
</tbody>
</table>

IVT indicates intravenous thrombolysis.

With this article, which is endorsed by an international panel of leading stroke specialists (see Appendix in the online-only Data Supplement), we propose recommendations for performance measures for IVT. Further work on this issue might be a useful task for organizations such as the European Stroke Organization or the American Stroke Association.

Stroke. 2013;44:3249-3253

Comments and Opinions

Door-to-Needle Time and the Proportion of Patients Receiving Intravenous Thrombolysis in Acute Ischemic Stroke: Uniform Interpretation and Reporting

Nyika D. Kruyt, Paul J. Nederkoorn, Martin Dennis, Didier Leys, Peter A. Ringleb, Anthony G. Rudd, Marinus Vermeulen, Jan Stam, Werner Hacke and Yvo B. Roos
Improve Processes & Outcomes Metrics for CSC by AHA 2011

Metric 1: Percentage of patients who have an ischemic stroke or who have a TIA with a deficit at the time of the initial admitting note or neurology consultation noted and documented.

Metric 2: Percentage of ischemic intravenous thrombolysis who receive it within the appropriate time window.

Metric 3: Percentage of patients who are treated for acute ischemic stroke with intravenous thrombolysis whose treatment is started ≤60 minutes after arrival.

Metric 4: Median time from arrival to start of multimodal CT or MR brain and vascular imaging (MRA/MRA or CT/CTA) for ischemic stroke patients arriving within 6 hours of the time that they were last known to be at baseline, if 1 of these studies is ordered.

Metric 5: Percentage of ischemic stroke patients seen within 6 hours of last known to be at baseline who underwent endovascular recanalization therapy or was considered and deemed ineligible. A reason should be documented if an endovascular procedure was not performed.

Metric 6: Median time from arrival to start of treatment for acute ischemic stroke patients undergoing an endovascular intervention.

27 Metrics: Measuring the Advanced Care for Stroke Patients

DOI: 10.1161/STR.0b013e318208eb99

(Stroke, 2011;42:00-00.)
TIME IS BRAIN

Next Steps

- Prepare pt/family or caregiver for Tx or D/C
- Secondary Stroke Prevention

Nuances of Stroke Care

- Seek to maximize team effectiveness in Stroke Systems of Care
**TIME IS BRAIN - Two Women**

- **75 yr old**
  - Transferred to Floor on Day 3
  - Transferred to ARU on Day 5
  - Discharged home on Day 10
    - FIM score of 104
    - Min assist for lower body dressing
    - Mod assist on Bath
    - Some visual field deficit
    - Classified as modified independent
- **3 Months**
  - Living at home with minimal assistance

- **39 yr old**
  - Day 12: Extubated
  - Day 24: GCS 4-6-4
    - Motor exam
      - Left arm/leg 5/5
      - R arm 2/5 R leg 5/5
    - Speech
      - Wernicke’s intact
      - States a complete sentence the day of transfer
  - Walks at side of bed
  - Tx Kaiser
  - Rehab & Home

*SIX Months Later*
Minimize the Impact of Hyperacute Stroke

Maximizes the Outcomes