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Health Care Guideline and Order Sets:
Diagnosis and Initial Treatment of Ischemic Stroke

Screening (Ambulatory) Algorithm

**EBR = Evidence-based recommendation included**

**Note:** Not all numbered boxes have annotated content

Text in blue in this algorithm indicates a linked corresponding annotation.

1. Initial contact with patient with complaint of neurological symptoms
2. Immediate evaluation for ischemic stroke
3. Symptoms consistent with new ischemic stroke, TIA or unsure?
   - no → Continue to next step
   - yes → Refer to an emergency department (ED) or clinician's office as appropriate for other conditions

*See Special Considerations

4. Symptoms present now?
   - no → Yes
   - yes → Call 911 and transport to emergency department in a stroke-ready facility

5. TIA symptoms > 24 hrs ago but < 7 days ago?
   - no → Ischemic stroke symptoms present for > 24 hours/symptoms mild and stable
   - yes → Rapid outpatient evaluation or admit to hospital

6. Possible ischemic stroke – symptoms onset within 24 hours?
   - no → Ischemic stroke symptoms present for > 24 hours/symptoms mild and stable
   - yes → See Emergency Department in a Stroke-Ready Facility (SRF) Treatment algorithm

7. Call 911 and transport to emergency department in a stroke-ready facility

8. Ischemic stroke symptoms present for > 24 hours/symptoms mild and stable

9. Clinical TIA – symptoms within 3 hours?
   - yes → See Emergency Department in a Stroke-Ready Facility (SRF) Treatment algorithm
   - no → Rapid outpatient evaluation or admit to hospital

10. TIA symptoms > 3 hours ago, but within last 24 hours?

11. Transport to emergency department in a stroke-ready facility

12. TIA symptoms > 24 hrs ago but < 7 days ago?

13. Rapid outpatient evaluation or admit to hospital
   - Evaluation:
     - Vascular imaging: carotid ultrasound, CTA or MRA
     - Blood work
     - Cardiac rhythm assessment
     - Echocardiogram (if suspect cardioembolic)
     - Case-specific interventions
     - Risk factor assessment and counseling
     - Brain imaging: MRI (preferred) or CT

14. TIA symptoms > 7 days ago

15. Clinic appointment within 1 week

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Emergency Department in a Stroke-Ready Facility (SRF) Treatment Algorithm

16. Patient enters emergency department in a stroke-ready facility (SRF) via:
   - Primary care referral
   - Walk in
   - EMS transport

*See Special Considerations

17. Neurological deficit present at time of evaluation?
   - yes
   - no

18. History suggestive of TIA?
   - yes
   - no

19. Out of guideline

20. ED in a stroke-ready facility (SRF) initiates evaluation for possible TIA:
   - Brain imaging: MRI (preferred) or CT
   - Vascular imaging: carotid ultrasound, CTA or MRA
   - Complete blood count (CBC)
   - Electrolytes, BUN, creatinine, glucose
   - Prothrombin time (INR)
   - Activated partial thromboplastin time (aPTT)
   - Cardiac biomarkers (troponin)
   - Echocardiography
   - Consider Hb A1c if suspect diabetes
   - Case-specific interventions
   - Risk factor assessment and counseling

21. TIA symptoms within 24 hours?
   - yes
   - no

22. High risk for stroke?
   - yes
   - no

23. Definitive management of TIA patient in an inpatient or observational bed with telemetry
   - Inpatient diagnostic evaluation:
     - Brain imaging: MRI (preferred) or CT
     - Vascular imaging: carotid ultrasound, CTA or MRA
     - Blood work
     - EKG
     - Echocardiogram (if suspect cardioembolic)
   - Lab:
     - Fasting lipid profile, fasting glucose
     - Serial cardiac biomarkers (suspect acute coronary syndrome)
     - Consider Hb A1c (if not done in ED)
     - Case-specific interventions
     - Risk factor assessment and counseling

24. Definitive management of TIA patient in an outpatient expedited care TIA clinic or program
   - Outpatient evaluation:
     - Brain imaging: MRI (preferred) or CT
     - Vascular imaging: carotid ultrasound, CTA or MRA
     - Blood work
     - EKG
     - Echocardiogram (if suspect cardioembolic)
   - Lab:
     - Fasting lipid profile, fasting glucose
     - Hb A1c (if not done in ED)
     - Case-specific interventions
     - Risk factor assessment and counseling

25. Clinic evaluation within 1 week

26. TIA symptoms > 7 days ago

27. No
Stroke Code Algorithm

Evaluation (should occur concurrently with intervention)
- Review history and tPA treatment indications and contraindications
- Perform baseline NIHSS stroke scale
- Perform exam with neuro checks (not NIHSS) and vital signs every 15 minutes
- Record weight (estimate if needed)
- Draw blood for lab tests
- Perform EKG
- Perform CT head without contrast (or other equivalent imaging)
- Perform other cardiac assessment as appropriate (telemetry)

Intervention (should occur concurrently with evaluation)
- Educate patient/family
- Treat blood pressure (BP) if greater than 185 systolic or 110 diastolic if patient is otherwise a tPA candidate. If patient is not a tPA candidate by other considerations, treat BP > 220 systolic and 120 diastolic.
- Initiate two IV lines
- Start isotonic IV fluids
- Initiate other systemic management

Patient meets criteria for IV tPA, has no contraindications and symptom onset still less than 4.5 hours?

- yes
  - Initiate IV tPA
  - Refer to appropriate specialist or facility

- no
  - Is patient a candidate for intra-arterial reperfusion treatments?
    - yes
      - Initiate aspirin unless contraindicated
    - no
      - Post-ED medical management

Post-ED medical management (postthrombolysis)
- Admit to ICU or acute stroke care unit/cardiac monitoring
- Perform vital signs with neuro checks (not NIHSS) per protocol
- Treat BP if greater than 180 systolic or 105 diastolic
- Initiate bleeding precautions
- Monitor for CNS hemorrhage
- Initiate antithrombotic therapy 24 hours after tPA

Other post-ED medical management (first 24-48 hours)
- Perform swallow evaluation
- Continue to treat hyperthermia, hyperglycemia or hypoglycemia
- Initiate deep vein thrombosis (DVT) prophylaxis
- Initiate early rehabilitation therapy post-ED medical management (first 24-48 hours)
- Perform nutritional status assessment

EBR = Evidence-based recommendation included
Note: Not all numbered boxes have annotated content

Text in blue in this algorithm indicates a linked corresponding annotation.

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Evidence Grading

Literature Search

A consistent and defined process is used for literature search and review for the development and revision of ICSI guidelines. Literature search terms for the current revision of this document include acute ischemic stroke, transient ischemic attack, ABCD2, hypertension, hyperglycemia, thrombolysis, decompressive craniectomy, imaging, hyperthermia, deep vein thrombosis (or venous thromboembolism) prevention, aspirin, swallow screening, stroke unit, time factors, early treatment, emergency medical services, telemedicine, telestroke, outcomes, quality improvement, guidelines, systematic reviews, randomized trials and meta-analyses published between January 2010 and December 2011 in MedLine and Cochrane databases.

Exclusion criteria: non-human, hemorrhagic stroke, non-English, age less than 18.

GRADE Methodology

Following a review of several evidence rating and recommendation writing systems, ICSI has made a decision to transition to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.

GRADE has advantages over other systems including the current system used by ICSI. Advantages include:

- developed by a widely representative group of international guideline developers;
- explicit and comprehensive criteria for downgrading and upgrading quality of evidence ratings;
- clear separation between quality of evidence and strength of recommendations that includes a transparent process of moving from evidence evaluation to recommendations;
- clear, pragmatic interpretations of strong versus weak recommendations for clinicians, patients and policy-makers;
- explicit acknowledgement of values and preferences; and
- explicit evaluation of the importance of outcomes of alternative management strategies.

In the GRADE process, evidence is gathered related to a specific question. Systematic reviews are utilized first. Further literature is incorporated with randomized control trials or observational studies. The evidence addresses the same population, intervention, comparisons and outcomes. The overall body of evidence for each topic is then given a quality rating.

Once the quality of the evidence has been determined, recommendations are formulated to reflect their strength. The strength of a recommendation is either strong or weak. Only outcomes that are critical are considered the primary factors influencing a recommendation and are used to determine the overall strength of this recommendation. Each recommendation answers a focused health care question.

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## Evidence Grading

<table>
<thead>
<tr>
<th>Category</th>
<th>Quality Definitions</th>
<th>Strong Recommendation</th>
<th>Weak Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Quality Evidence</strong></td>
<td>Further research is very unlikely to change our confidence in the estimate of effect.</td>
<td>The work group is confident that the desirable effects of adhering to this recommendation outweigh the undesirable effects. This is a strong recommendation for or against. This applies to most patients.</td>
<td>The work group recognizes that the evidence, though of high quality, shows a balance between estimates of harms and benefits. The best action will depend on local circumstances, patient values or preferences.</td>
</tr>
<tr>
<td><strong>Medium Quality Evidence</strong></td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
<td>The work group is confident that the benefits outweigh the risks but recognizes that the evidence has limitations. Further evidence may impact this recommendation. This is a recommendation that likely applies to most patients.</td>
<td>The work group recognizes that there is a balance between harms and benefits, based on moderate quality evidence, or that there is uncertainty about the estimates of the harms and benefits of the proposed intervention that may be affected by new evidence. Alternative approaches will likely be better for some patients under some circumstances.</td>
</tr>
<tr>
<td><strong>Low Quality Evidence</strong></td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change. The estimate or any estimate of effect is very uncertain.</td>
<td>The work group feels that the evidence consistently indicates the benefit of this action outweighs the harms. This recommendation might change when higher quality evidence becomes available.</td>
<td>The work group recognizes that there is significant uncertainty about the best estimates of benefits and harms.</td>
</tr>
</tbody>
</table>

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# Recommendations Table

The following table is a list of evidence-based recommendations for the Diagnosis and Initial Treatment of Ischemic Stroke guideline.

Note: Other recommendation language may appear throughout the document as a result of work group consensus but is not included in this evidence-based recommendations table.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Quality of Evidence</th>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>Annotation Number</th>
<th>Relevant References</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA/ minor stroke care</td>
<td>Moderate</td>
<td>Qualified clinician (i.e., trained and experienced in the management of patients with transient ischemic attacks or supported via telemedicine arrangement with such a clinician) should evaluate patients with transient ischemic attack or minor stroke symptoms and initiate case-specific secondary prevention measures urgently on an inpatient or expedited outpatient basis.</td>
<td>Strong</td>
<td>23</td>
<td>Joshi, 2011; Easton, 2009; Luengo-Fernandez, 2009; Rothwell, 2007</td>
</tr>
<tr>
<td>Early hypertension management in tPA candidates and recipients</td>
<td>Low</td>
<td>Clinician should treat patients with ischemic stroke who are tPA candidates to reduce blood pressure below 185/110 prior to administration of tPA. Clinician should treat hypertension in tPA recipients to maintain BP below 180/105 during the first 24 hours.</td>
<td>Strong</td>
<td>31</td>
<td>Sandset, 2011; Robinson, 2010; Ahmed, 2009; Adams, 2007; Castillo, 2004; Willmot, 2004; Leonardi-Bee, 2002; National Institute of Neurological Disorders and Stroke tPA Stroke Study Group (NINDS), 1995</td>
</tr>
<tr>
<td>IV tPA</td>
<td>High</td>
<td>Qualified clinician (i.e., trained and experienced in acute stroke management or supported via telemedicine arrangement by such a clinician) should administer IV tPA to selected and qualifying patients with acute ischemic stroke within 4.5 hours of symptom onset or of time last known to be at their baselines in appropriate care circumstances (i.e., in a “stroke-ready” emergency department or hospital). ICSI or other guidelines for selection and management specifics should be followed.</td>
<td>Strong</td>
<td>33</td>
<td>Carpenter, 2011; Lees, 2010; Lansberg, 2009; Hacke, 2008; Wahlgren, 2007; Clark, 1999; Hacke, 1998; Hacke, 1995; National Institute of Neurological Disorders and Stroke tPA Stroke Study Group (NINDS), 1995</td>
</tr>
<tr>
<td>Intra-arterial thrombolysis</td>
<td>1. Moderate 2. Moderate 3. Moderate</td>
<td>Qualified clinician (i.e., appropriately trained in neurocritical care, neurointerventional procedures or neurosurgery) should consider treating selected and qualifying patients with acute ischemic stroke with intra-arterial thrombolysis under the following circumstances: 1. Arrival within the window for IV tPA &lt; 4.5 hours but contraindication for IV tPA 2. Arrival beyond window for IV tPA &lt; 4.5 hours and within accepted time windows for relevant vascular site and thrombolytic strategy 3. Continued major deficit after IV tPA and evidence for persisting occlusion of a relevant and accessible large artery</td>
<td>Strong</td>
<td>34</td>
<td>Lee, 2010; Meyers, 2009; Penambrak, 2009; Schonevile, 2009 Smith, 2008; Furlan, 1999; del Zoppo, 1998; Wijdicks 1997; Brandt 1996; National Institute of Neurological Disorders and Stroke tPA Stroke Study Group (NINDS), 1995</td>
</tr>
</tbody>
</table>

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### Immediate aspirin for tPA non-recipients and tPA recipients

<table>
<thead>
<tr>
<th>Topic</th>
<th>Quality of Evidence</th>
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<th>Strength of Recommendation</th>
<th>Annotation Number</th>
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</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Clinician must immediately administer 160-325 mg aspirin to patients with acute ischemic stroke not treated by IV tPA by rectum or, if patient passes a bedside swallow screen, by mouth. * For patients treated with IV, tPA aspirin (160-325 mg) should be administered 24 hours after IV tPA.</td>
<td>Strong</td>
<td>35</td>
<td>Sandercock, 2009b</td>
<td></td>
</tr>
</tbody>
</table>

### Early hypertension management in tPA non-recipients

<table>
<thead>
<tr>
<th>Topic</th>
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<th>Strength of Recommendation</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Acutely and during the first 24 hours, clinician may treat extreme hypertension (e.g., systolic &gt; 220 mmHg, diastolic &gt; 120 mmHg or mean arterial blood pressure &gt; 130 mmHg) in patients with acute ischemic stroke not treated with IV tPA. Target for correction of hypertension is a 15% reduction.</td>
<td>Weak</td>
<td>37</td>
<td>Sandset, 2011; Robinson, 2010; Ahmed, 2009; Castillo, 2004; Willmot, 2003; Leonardi-Bee, 2002</td>
<td></td>
</tr>
</tbody>
</table>

### Care setting

<table>
<thead>
<tr>
<th>Topic</th>
<th>Quality of Evidence</th>
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<th>Strength of Recommendation</th>
<th>Annotation Number</th>
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</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Qualified clinicians (i.e., trained and experienced in acute stroke management or supported via telemedicine arrangement by such a clinician) should manage patients with acute ischemic stroke, including diagnosis of mechanism, deployment of case-specific and generic secondary prevention measures, avoidance of complications, initiation of rehabilitative services, provision of patient and family education, in a care setting characterized by interdisciplinarity, experience and expertise with stroke, and availability of rehabilitative services.</td>
<td>Strong</td>
<td>38</td>
<td>Xian, 2011; Smith, 2010; Audebert, 2009; Saposnik, 2009; Terént, 2009; Stroke Unit Trialists Collaboration, 2007</td>
<td></td>
</tr>
</tbody>
</table>

### Swallow screen

<table>
<thead>
<tr>
<th>Topic</th>
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<th>Strength of Recommendation</th>
<th>Annotation Number</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Clinician should perform a swallow screening test as soon as feasible on a patient with acute ischemic stroke and withhold oral intake of fluids, medications or food until/unless the screen is successfully passed.</td>
<td>Strong</td>
<td>38</td>
<td>Schepp, 2011; Lakshminarayan, 2010; Perry, 2001; Oldakson, 1995</td>
<td></td>
</tr>
</tbody>
</table>

### Hyperglycemia

<table>
<thead>
<tr>
<th>Topic</th>
<th>Quality of Evidence</th>
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<th>Annotation Number</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Clinician may treat hyperglycemia (i.e., 180 mg/dL) in patients with ischemic stroke.</td>
<td>Weak</td>
<td>38</td>
<td>Johnson, 2009; Adams, 2007; Gray, 2007</td>
<td></td>
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</tbody>
</table>

### Deep vein thrombosis prophylaxis

<table>
<thead>
<tr>
<th>Topic</th>
<th>Quality of Evidence</th>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>Annotation Number</th>
<th>Relevant References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>Clinician should provide appropriate prophylaxis against deep vein thrombosis in immobilized patients with acute ischemic stroke, weighing risks and benefits of various options by selecting the appropriate prophylaxis such as unfractionated heparin or low-molecular-weight heparin in patients without contraindications.</td>
<td>Strong</td>
<td>38</td>
<td>Lederle, 2011; Qaseem, 2011; Dennis, 2010; Dennis, 2009; Sherman, 2007</td>
<td></td>
</tr>
</tbody>
</table>

### Mobilize patient early

<table>
<thead>
<tr>
<th>Topic</th>
<th>Quality of Evidence</th>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>Annotation Number</th>
<th>Relevant References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>Clinician should mobilize patients with acute ischemic stroke as soon as possible, monitoring for and avoiding postural hypotension.</td>
<td>Strong</td>
<td>38</td>
<td>Cumming, 2011; Craig, 2010; Langhorne, 2010</td>
<td></td>
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<tr>
<td>Topic</td>
<td>Quality of Evidence</td>
<td>Recommendation</td>
<td>Strength of Recommendation</td>
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<td></td>
<td>2. Moderate</td>
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<td></td>
<td>3. High</td>
<td></td>
<td></td>
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<tr>
<td>Hyperthermia</td>
<td>Moderate</td>
<td>Clinician should treat hyperthermia (i.e., temperature &gt; 38°C) with specific measures (e.g., antibiotics targeted to discovered infections) and/or nonspecific measures (e.g., cooling blankets, acetaminophen) in patients with acute ischemic stroke.</td>
<td>Strong</td>
<td>38</td>
<td>Broessner, 2009; Hajat, 2000; Wang, 2000b; Castillo, 1998; Reith, 1996; Azzimondi, 1995; Terént, 1981</td>
</tr>
<tr>
<td>Pre-hospital emergency services</td>
<td>1. Moderate</td>
<td>Policy-makers and relevant public service entities should: 1. Develop and/or support public education programs on recognition of stroke symptoms and signs and importance of calling 911 if recognized in oneself or another person. 2. Encourage use of 911 for facilitating transport of patients with acute ischemic stroke to appropriate facilities. 3. Develop and/or support education of potential health services contacts (doctors’ offices, nurse lines, EMS dispatch) regarding need for rapid triage of patients with possible acute ischemic stroke. 4. Develop and/or support systems to facilitate rapid transport of patients with possible acute ischemic stroke to facilities with appropriate resources and expertise to carry out expedited assessment and treatment. 5. Develop and/or support education programs for EMS personnel emphasizing importance of time, uniform pre-hospital assessment, and hospital pre-notification for patients with possible acute ischemic stroke.</td>
<td>Strong</td>
<td>Appendix A</td>
<td>1. Fussman, 2010; Lecouturier, 2010; Morgenstern, 2003 2. Morris, 1999; Barsan, 1993 3. Buck, 2009; Handschu, 2003; Pericous, 1999 4. Schwamm, 2009a; Schwamm, 2009c 5. Patel, 2011; Kidwell, 2000; Kothari, 1999</td>
</tr>
<tr>
<td></td>
<td>2. Strong</td>
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<td></td>
<td>3. Weak</td>
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<tr>
<td></td>
<td>4. Moderate</td>
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<td></td>
<td>5. Moderate</td>
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Foreword

Introduction

The Greeks' term "apoplexy" and the Anglo-saxons' "stroke" have never been bested in conveying the essential clinical features of this neurologic calamity. Terms, like "cerebrovascular accident" or "cerebral infarction" fall short in capturing the signature suddenness, apparent randomness and gravity. Using the term to connote a clinical syndrome, strokes are most often due to vascular disease. Of vascular causes, focal brain ischemia is most common (80%). Vessel rupture into brain parenchyma (10%) and into the subarachnoid space (10%) comprise the remainder. Whichever the mechanism, personal toll is often high. Mortality of cerebral infarcts is 5-10% during hospitalization, 10-20% by 30 days, 20-30% by a year. Dependency is 50% among survivors.

Bigger picture, stroke is the fourth leading cause of death, recently dropping from third after decades long efforts to reduce incidence by treatment of risk factors. It remains the leading cause of disability among adults. Costs of hospitalizations, other cares and lost wages are simply enormous.

The best medical response to these daunting individual and societal costs is prevention. The work group is charged with recommending the approach when prevention has failed. The net yield is smaller, but the individual saves are rewarding, often inspiring. The guideline is about how to manage stroke due to ischemic brain ischemia/infarction best.

Scope and Target Population

The scope of the following guideline is the 48 hours beginning when a patient age 18 years or older presents to the health care system with symptoms of ischemic stroke or transient ischemic attack. For most stroke patients who are hospitalized, the guideline's temporal scope will expire before discharge. The guideline work group on Diagnosis and Initial Treatment of Ischemic Stroke recognizes that two time frames are critically important in the overall outcome, and fall outside the defined scope. They are the pre-hospital era, i.e., recognition and pre-hospital care, and continuing care of stroke patients after 48 hours, which includes the development of a long-term secondary prevention strategy. The work group recommends the following guidelines from the American Heart Association/American Stroke Association.

A. Regarding pre-hospital care:


B. Regarding continuing care after the initial 48 hours and secondary prevention:

Aims

1. Increase the percentage of patients age 18 years and over presenting in time for IV tPA to be initiated within 3 hours, or up to 4.5 hours for patients meeting selected criteria of stroke onset who are evaluated within 10 minutes of arriving in the emergency department. Under usual circumstances these time-related goals should be achievable for patients presenting to an appropriate treatment setting within 2 hours and 30 minutes, and 4 hours of symptom onset, respectively. *(Annotations #18, 29)*

2. Increase the percentage of patients age 18 years and over at high risk for stroke presenting with TIA symptoms within 24 hours who are admitted to the hospital inpatient or observational unit or undergo identical assessment in an expedited outpatient program. *(Annotation #23)*

3. Increase the percentage of patients age 18 years and over receiving appropriate thrombolytic and appropriate antithrombotic therapy for ischemic stroke (use of tPA and aspirin, other antiplatelet agents or an anticoagulant). *(Annotations #29, 30, 33, 35)*

4. Increase the percentage of tPA non-recipients who have hypertension appropriately managed in the first 24-48 hours of hospitalization or until neurologically stable. *(Annotation #37)*

5. Increase the percentage of stroke patients age 18 years and over who receive stroke unit care during the initial 24-48 hours including prevention and management of complications such as: *(Annotations #31, 37, 38)*
   - dehydration/hypertension/hypotension
   - aspiration
   - hypoglycemia and hyperglycemia
   - deep vein thrombosis
   - immobility
   - falling
   - nutritional status decline
   - hyperthermia

6. Improve patient and family education of patients with ischemic stroke in both the emergency department and the admitting hospital unit. *(Annotation #31)*

Clinical Highlights

- Intravenous tPA continues to be a proven treatment for ischemic stroke when administered within recommended time parameters. *(Annotations #18, 29; Aim #3)*

- Intravenous tPA, if given, should be administered within three hours (4.5 hours in selected patients; see Annotation #18, "Consider IV Tissue Plasminogen Activator [tPA]/See Stroke Code Algorithm") of stroke onset and less than 60 minutes of arrival at the emergency department. *(Annotations #29, 30, 33; Aim #3)*

- Patients presenting with signs and symptoms of transient ischemic attack should be evaluated for risk of immediate future events using the ABCD2 score. *(Annotation #23; Aim #1)*

- Patients presenting with stroke onset who are not candidates for intravenous tPA should promptly be given aspirin, after exclusion of hemorrhage on CT scan. *(Annotation #35; Aim #3)*
• Education regarding early stroke symptoms, risk factors, diagnostic procedures and treatment options should be offered to the patient and family. Informed consent discussions should be documented in the patient chart. *(Annotation #31; Aim #6)*

• Stroke unit care should be provided for prevention and management of complications within the initial 24-48 hours: *(Annotation #38; Aim #5)*
  - manage volume and blood pressure appropriately
  - perform swallow evaluation before oral intake, including medications
  - treat hypoglycemia and hyperglycemia
  - initiate deep vein thrombosis prevention
  - initiate early mobilization
  - establish fall prevention
  - perform nutritional status assessment
  - treat hyperthermia

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**Implementation Recommendation Highlights**

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

• Hospitals should consider developing and implementing critical pathways, standing orders and a stroke process to accomplish rapid evaluation and treatment. The process should expedite the evaluation and treatment of patients who are candidates for intravenous tPA and assure uniform, guideline-driven care for all patients with respect to issues like:
  - diagnosis of mechanism,
  - initiation of appropriate secondary prevention,
  - prevention of complications, and
  - early assessment for and early employment of rehabilitative services.

• A process should be in place for the patient and family that will rapidly orient them to the suspected diagnosis, emergency department process, tests to be performed, tPA treatment and its risks, and other treatment measures to be considered. This could include both face-to-face interactions with the patient and family by the caregiver, and teaching tools in written form.

**System Improvement**

There is evidence that benchmarking can guide and drive quality improvement. Using essentially the same quality indicators as The Joint Commission (TJC) and ICSI, programs like the American Heart Association’s Get With The Guidelines-Stroke *(LaBresh, 2008; Schwamm, 2009b)* and the Paul Coverdell National Acute Stroke Registry *(Stoeckle-Roberts, 2006)* have been shown to improve the quality of stroke care, as well as hard outcomes, like mortality *(Xian, 2011)*.

**Centers for Medicare and Medicaid Services**

The Joint Commission (TJC) Primary Stroke Center Certification

TJC offers certification as Primary Stroke Centers to hospitals that meet specific qualifications. The focus is on the early recognition and management of stroke, and the scope of accreditation includes integrated efforts in public awareness, emergency medical services, emergency department and hospitalization (Alberts, 2011; Alberts, 2000). The link is http://www.jointcommission.org/certification/primary_stroke_centers.aspx (last accessed May 24, 2012).

Beginning in October 2009, all TJC-accredited hospitals are required to submit the eight National Quality Forum-endorsed stroke consensus measures.

Among the requirements for TJC certification as a Primary Stroke Center is ongoing process improvement guided by data and benchmarking. The quality indicators chosen by TJC overlap with those developed by the ICSI Diagnosis and Initial Treatment of Ischemic Stroke guideline work group. The TJC quality indicators are:

1. Deep Vein Thrombosis (DVT) Prophylaxis*
2. Discharged on Antithrombotics*
3. Patients with Atrial Fibrillation Receiving Anticoagulation Therapy*
4. Thrombolytic Therapy Administered (in eligible patients)
5. Antithrombotic Therapy by End of Hospital Day Two
6. Discharged on Cholesterol Reducing Medication
7. Dysphagia Screening **
8. Stroke Education
9. Smoking Cessation/Advice Counseling **
10. Assessed for Rehabilitation

* Initial standard stroke measure set.

** Note: indicators for 7 and 9 are not currently (as of 2010) required by The Joint Commission. The remaining eight indicators are required. These eight are also endorsed by the National Quality Forum.

Measures 1, 4, 5, 7, 8 and 10 are similar to or identical to those measures listed in this document and within the scope of the guideline.

The Minnesota Department of Health (MDH)

The MDH has been leading working groups of stakeholders in stroke care across the state of Minnesota in planning a system to support care of acute stroke in all parts of the state. The groups include representatives of hospitals and emergency medical services, as well as primary care and specialty clinicians from large and small, urban and rural hospitals. The care issues include facilitation of reperfusion therapies in selected patients and according to guidelines but also continuing care issues such as those articulated by TJC for primary and comprehensive stroke centers. The role of "stroke-ready" hospitals is under current discussion.

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Related ICSI Scientific Documents

Guidelines
- Antithrombotic Therapy Supplement
- Hypertension Diagnosis and Treatment
- Palliative Care
- Venous Thromboembolism Diagnosis and Treatment
- Venous Thromboembolism Prophylaxis

Protocol
- Prevention of Falls (Acute Care)

Definitions

Clinician – All health care professionals whose practice is based on interaction with and/or treatment of a patient.

Stroke-Ready Facility (SRF) – Acute care facility that has 24/7 on-site qualified clinician availability (with or without telemedicine) and the ability to perform a computed tomographic (CT) scan of the brain within 25 minutes and administer intravenous (IV) tPA to eligible stroke patients within 60 minutes of arrival. Certified primary and comprehensive stroke centers are by definition stroke-ready facilities. For other hospitals or ERs, stroke readiness is defined by ability to give IV tPA. Protocols are also in place to transfer appropriate patients to primary or comprehensive stroke centers. Note: SRF could be a freestanding ED without inpatient services.

tPA – Tissue plasminogen activator. At present, alteplase is the only FDA-approved plasminogen activator for ischemic stroke.

Special Considerations

Screening (Ambulatory) Algorithm, Step #1
Patient’s complaint of neurological symptoms and initial contact may be made with any of these: primary care clinician, emergency medical services, registered nurse via telephone referral, non-medical evaluation (triage, etc.). ICSI work group assumes this to be the entry point to the Diagnosis and Initial Treatment of Ischemic Stroke guideline.

Screening (Ambulatory) Algorithm, Step #4
Stroke-ready facility is a term the ICSI work group employs in place of the formerly used "emergency department." The term identifies a facility’s capability to administer IV tPA.

Emergency Department in a Stroke-Ready Facility (SRF) Treatment Algorithm, Step #18
Time frame to initiate tPA was extended in recent years from three hours to 4.5 hours in selected patients with additional cautions applied:
- Patient age older than 80 years
- Patient taking oral anticoagulants regardless of INR
- NIHSS score > 25 or large infarct on CT
- Patient with history of both stroke and diabetes
Emergency Department in a Stroke-Ready Facility (SRF) Treatment Algorithm, Step #21

The following studies are usually necessary for the initial diagnosis and definitive management of patients with TIA. Some of the workup is typically performed in an emergency room and the remainder after admission to an inpatient unit, observation unit or outpatient TIA clinic. Where the tests will be obtained may differ depending on the case, the facility and other factors. Duplication of testing should be avoided, if possible. The complete and definitive management of a TIA case typically requires:

- Brain imaging: MRI (preferred) or CT
- Vascular imaging: MRA, CTA, or carotid ultrasound (if symptoms suggest carotid distribution)
- Blood work: complete blood count, electrolytes, BUN, creatinine, INR, aPTT, fasting lipids, fasting glucose, HbA1c, troponins
- EKG and cardiac rhythm monitoring
- Echocardiography (if suspect cardioembolism)
- Case-specific interventions
- Risk factor assessment and counseling

Algorithm steps #21, 24 and 26 have similar elements. Some of the elements will be completed in the ED, step #21.

- Step #21 is about early assessment.
- Steps #24 and 26 are about definitive TIA assessment.
- Sometimes most or all is done in the emergency department, i.e., step #21 setting.
- Sometimes a disposition is made early to admit and most of the tests are done in the inpatient or observation unit, i.e., step #24 or 26.

Emergency Department in a Stroke-Ready Facility (SRF) Treatment Algorithm, Step #23

Indicators of high risk in TIA patients include:

- Patient age older than 60 years
- Blood pressure > 140/90
- Diabetes history
- Motor deficit during TIA
- Speech deficit during TIA
- Longer duration of TIA
- Acute lesion on diffusion weighted MRI or CT

Emergency Department in a Stroke-Ready Facility (SRF) Treatment Algorithm, Step #24

See special considerations for Step #21 (above).

Emergency Department in a Stroke-Ready Facility (SRF) Treatment Algorithm, Step #26

See special considerations for Step #21 (above).

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Stroke Code Algorithm, Step #29

Stroke-ready facility should have developed and implemented critical pathways, standing orders and stroke code processes to expedite management of acute ischemic stroke. Development of a stroke system should enable access to best care for all.

Stroke Code Algorithm, Step #32

Time frame to initiate tPA was extended in recent years from three hours to 4.5 hours in selected patients with additional cautions applied to the following groups:

- Patient age older than 80 years
- Patient taking oral anticoagulants regardless of INR
- NIHSS score > 25 or large infarct on CT
- Patient with history of stroke and diabetes

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Screening (Ambulatory) Algorithm Annotations

1. **Initial Contact with Patient with Complaint of Neurological Symptoms**

   Contact may occur with one of several medical system personnel, including primary care clinicians, other medical specialty clinicians, emergency medical services, nursing staff in a clinic or urgent care setting or even non-medical triage personnel prior to emergency department evaluation. This contact may be by phone or in person. Potential staff contacts should be educated in the importance of stroke symptom recognition and the appropriate triage. Time is of the essence in the setting of acute cerebral ischemia. Processes should be in place at all points along a continuum to expedite recognition, transport, assessment and definitive reperfusion.

   Public awareness messages in the future should focus on the possibility of urgent treatment (tPA) for ischemic stroke in addition to stroke warning signs and risk factors (Kleindorfer, 2009).

2. **Immediate Evaluation for Ischemic Stroke**

   Critical information includes detail as to the location, severity, duration of symptoms and any aggravating or relieving factors. Symptoms that are commonly associated with ischemic stroke or transient ischemic attack (TIA) include:

   * sudden numbness or weakness of the face, arm or leg – especially on one side of the body;
   * sudden mental confusion, trouble speaking or understanding;
   * sudden trouble walking, dizziness, loss of balance or coordination;
   * sudden trouble seeing in one or both eyes; and
   * sudden severe headache with no known cause.

   * List from American Stroke Association for public education

   Recognition of stroke is a challenging first step in a race against time to save the brain. Recognition starts with the patient, family or bystanders and must continue with emergency medical personnel and in the emergency department. Tools to facilitate recognition have been developed for these settings. For the public, two scales have been disseminated. The American Stroke Association, American Academy of Neurology and American College of Emergency Physicians have recently completed a public awareness campaign entitled "Give Me 5," emphasizing that stroke typically presents as problems of walking, talking, reaching, seeing and/or feeling. Another scale has been developed for the general public by the National Stroke Association. It is entitled "FAST," emphasizing the importance of changes in the appearance of one's Face, difficulty in raising Arms, abnormality of quality of Speech, and the imperative to intervene in a Timely manner to get help.

   Scales have also been developed for emergency medical services (Cincinnati and Los Angeles scales) and for the emergency department itself (ROSIER [Recognition of Stroke in the Emergency Room] scale) (Nor, 2005; Kidwell, 2000; Kothari, 1999). These tools are listed in the Implementation Tools and Resource Table.

   Symptoms of ischemic stroke can also, of course, be represented in atypical ways.
Clinical diagnoses with neurologic symptoms that may imitate or superficially resemble ischemic stroke or TIA include the following (Adams, 2007):

- **Migraine**
  Neurologic symptoms experienced with migraine tend to have a more gradual onset and slower development. Headache is typically but not always present in migraine but may also be a feature of ischemic stroke. The two problems may be indistinguishable.

- **Seizures**
  Although seizures are typically manifested by a "positive" phenomenon (jerking of a limb) rather than loss of neurologic function (weakness or paralysis of a limb), symptoms and signs during the ictus or in the postictal state may be similar to ischemic stroke (e.g., confusion or speech arrest during the ictus as in a complex partial seizure, postictal confusion, postictal paralysis, and other sensory or visual phenomena).

- **Syncope**
- **Transient global amnesia (TGA)**
  TGA is characterized by a sudden onset anterograde and retrograde memory disturbance without other neurologic symptoms. If the patient experiences symptoms of transient global amnesia, it would be inappropriate to assume the diagnosis without a complete neurologic assessment.

- **Peripheral nerve disorders**
  Mononeuropathy and radiculopathy can often be distinguished from ischemic stroke by the anatomic distribution of the symptoms, and in the case of radiculopathy, by associated painful symptoms. Bell's palsy, vestibular neuronitis and extraocular muscle imbalance due to cranial neuropathy may also imitate ischemic stroke; a complete history and neurologic examination are required to accurately differentiate from ischemic stroke.

- **Intracranial hemorrhage (cannot be distinguished reliably from ischemia without brain imaging)**
- **Other intracranial masses, e.g., tumor, abscess (often differentiated by computed tomography)**
  The mode of onset and early course tend to be more gradual in development, but mimicry of stroke is not uncommon.

- **Psychogenic presentation**
  Psychogenic conditions such as anxiety, panic disorder, or conversion reactions must be considered in some cases.

- **Metabolic disorders**
  Hypoglycemia is the most common metabolic disorder producing neurologic symptoms that imitate stroke.

This discussion is not meant to be a detailed or encyclopedic guide to distinguishing between ischemic stroke and other diagnoses. If there is any uncertainty as to symptom causation, the evaluation should proceed as though ischemic stroke or TIA is confirmed so as not to delay appropriate emergency treatment if indicated.
4. **Refer to an Emergency Department (ED) or Clinician's Office as Appropriate for Other Conditions**

Some conditions in the differential diagnosis of ischemic stroke outlined in Annotation #2, "Immediate Evaluation for Ischemic Stroke," may warrant emergency department evaluation because of the urgency of the alternative problem itself or the inability of the contact person to distinguish the other condition from ischemic stroke (Adams, 2007). In these uncertain cases, the contact person should continue on to the Screening (Ambulatory) algorithm, box #5, "Symptoms Present Now?"

Best outcome depends on getting patients with acute ischemic stroke as quickly as possible to settings where they can receive timely, necessary and optimal care. See Appendix A, "Broader Issues."

5. **Symptoms Present Now?**

This annotation focuses on whether symptoms suggestive of cerebral ischemia are present or have resolved at the time of initial contact. If ischemic symptoms have resolved and were present for less than 24 hours, the situation is clinically defined as a transient ischemic attack (TIA).

A few years ago, a new definition of TIA was proposed: TIA is a transient episode of neurologic dysfunction caused by focal brain, spinal cord or retinal ischemia without acute infarction (Easton, 2009). Applying the new definition requires imaging. The pre-imaging syndrome has been designated "acute neuro-vascular syndrome." The work group will use "clinical TIA" in this document, corresponding to the older, pre-2009 definition of TIA, in lieu of acute neurovascular syndrome (Easton, 2009).

6. **Possible Ischemic Stroke – Symptoms Onset within 24 Hours?**

If the symptoms resolve completely and then recur, for the purposes of determining whether thrombolysis may be considered for stroke, the time of onset would be the last time the patient was normal (just prior to the recurrence of symptoms.) Patients may be unable to give this information if they have an aphasia or mental confusion. Family members or other witnesses may need to give this information. If the patient was sleeping and awakened with the problem, the time of onset would be the moment the patient was last known to be normal just before falling asleep.

7. **Ischemic Stroke Symptoms Present for > 24 Hours/Symptoms Mild and Stable**

Patients with stable mild deficits present longer than 24 hours may be transported to the emergency department for evaluation and treatment by means other than 911. As a rule, they should be admitted to the hospital or to an observation unit to assure thorough and expeditious evaluation and treatment. Outpatient evaluation and treatment is an acceptable alternative if they can be accomplished as quickly as if done inpatient and if all goals of inpatient assessment (diagnosis of mechanism, initiation of appropriate secondary prevention, prevention of complications, early assessment for and deployment of rehabilitative services) can be successfully addressed. It should be appreciated that recurrence risk is high in the initial hours and days following a minor stroke, similar to the case of TIA (see below); hence, expeditious assessment and mechanism-specific treatment are warranted.
9. **Clinical Transient Ischemic Attack (TIA) – Symptoms within Three Hours?**

Patients presenting with history of clinical TIA within three hours of symptom onset should be triaged like patients with stroke, i.e., call 911 (Adams, 2007).

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11. **Transport to Emergency Department in a Stroke-Ready Facility (SRF)**

A stroke-ready facility is defined as an acute care facility that has 24/7 on-site qualified clinician availability (with or without telemedicine) and the ability to perform a CT scan of the brain within 25 minutes and administer IV tPA to eligible stroke patients within 60 minutes of arrival. Certified primary and comprehensive stroke centers are by definition stroke-ready facilities. For hospitals or ERs, stroke readiness is defined by ability to give IV tPA. Protocols are also in place to transfer appropriate patients to primary or comprehensive stroke centers. Note: SRF could be a freestanding ED without inpatient services.

Patients whose transient symptoms occurred more than three hours but less than 24 hours ago should be taken to a stroke-ready emergency department expeditiously; use of 911 is at the clinician's discretion. As an alternative to admission to a hospital or observation unit, the patient may be assessed in a specialized clinic or other program in which the evaluation can be carried out as quickly and treatment initiated as definitively as if the patient were admitted to the hospital. The work group otherwise recommends that the clinician strongly consider hospitalization or observation unit stay for clinical TIA patients who appear within 24 hours of the event to expedite workup and possibly administer tPA if the deficit recurs.

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13. **Rapid Outpatient Evaluation or Admit to Hospital**

Patients whose transient symptoms occurred more than 24 hours but less than one week ago should receive rapid outpatient evaluation (TIA clinic or other program) or be admitted to the hospital as soon as possible (Johnston, 2006). In addition to a risk factor assessment for stroke, the patient should be diagnostically evaluated including:

- Brain imaging: magnetic resonance imaging (MRI) (preferred because diffusion-weighted sequences may identify patients at particularly high risk of early major recurrence – see Annotation #23, "High Risk for Stroke?") or computed tomography (CT)
- Vascular imaging: MRA, CTA or carotid ultrasound (if symptoms suggest ischemia in the carotid distribution)
- Blood work: complete blood count, electrolytes, BUN, creatinine, INR, aPTT, fasting lipids, fasting glucose, HbA1c, troponins
- EKG and cardiac rhythm monitoring
- Echocardiography (if suspect cardioembolism)
- Case-specific interventions
- Risk factor assessment and counseling
Emergency Department in a Stroke-Ready Facility (SRF)

Treatment Algorithm Annotations

18. Consider IV Tissue Plasminogen Activator (tPA)/See Stroke Code Algorithm

Patients presenting to the emergency department soon after the onset of symptoms may be candidates for treatment with intravenous (IV) tissue plasminogen activator (tPA) and will therefore require a rapid evaluation and treatment initiation (Albers, 2004). (See Appendix A, "Broader Issues.") Although the time window from onset of symptoms to treatment can be up to 3 hours, i.e., 180 minutes (or 4.5 hours, i.e., 270 minutes in selected patients), the evaluation in the emergency department will require at least 30 minutes in most cases (CT scan of head, laboratory tests performed and results have returned, IV access obtained, neurological exam and history completed, informed consent obtained) (Adams, 2007). We have therefore chosen 150 minutes or 240 minutes in selected patients, as a practical cutoff time for this triage decision.

There are important exceptions to this time limitation guideline for triage of patients into the "stroke code" process. In certain instances, the time required for evaluation may be shorter, and "stroke code" may be feasible for patients presenting as late as 165 or 170 minutes (255-260 minutes in selected patients) after onset. One example would be the patient who is already in the hospital and has undergone the appropriate laboratory evaluation, has an IV access in place, and much of the history is already known. In that case, a brief neurologic exam and rapid evaluation with CT may be the only items required prior to treatment and could theoretically be performed in 10-15 minutes.

Initial Thrombolytic Trials

Thrombolytic therapy for ischemic stroke using intravenous tPA (alteplase) has now been tested in several large, randomized, placebo-controlled clinical trials. The National Institute of Neurological Disorders and Stroke (NINDS) stroke trial (actually two trials: one with a 24-hour and the other with a 90-day outcome measure) compared placebo with tPA at a dose of 0.9 mg/kg initial bolus given within three hours of symptom onset in 624 patients (National Institute of Neurological Disorders and Stroke tPA Study Group, 1995). The time of stroke onset was strictly defined, blood pressure was maintained within a specified range, and other anticoagulant and antiplatelet drugs were avoided within the first 24 hours after treatment. The prespecified threshold for a clinically important difference at 24 hours was not met. However, at three months and one year (Kwiatkowski, 1999), there were significantly increased percentage of patients (11-13%) with favorable outcomes in the tPA group, compared with controls. Results were consistent across all four of the standard outcome measures that were assessed. Treatment with tPA resulted in an increased risk of symptomatic intra-cerebral hemorrhage (6.4% tPA treated vs. 0.6% in the placebo group, p < 0.001). Mortality was lower at three months in those treated with tPA (17% vs. 21% in placebo treated), but the difference did not reach statistical significance. On the basis of the favorable results from these combined trials, the Food and Drug Administration approved tPA for use in the United States in 1996. Alteplase is currently the only FDA-approved thrombolytic agent for use in ischemic stroke.

The European Cooperative Acute Stroke Study (ECASS) performed concurrent with the NINDS trial also compared intravenous tPA to placebo in a randomized, placebo-controlled trial in 620 patients. However, the study design was different in a number of respects, including longer time window to treatment (six hours), higher dose of tPA (1.1 mg/kg), and lack of strict blood pressure control (Hacke, 1995). Over 80% of the patients were treated between three and six hours after symptoms began. The intention-to-treat analysis did not demonstrate significant improvement in the primary outcome measure (combination of Barthel Index and modified Rankin Scale at three months). However, there was a high rate of major protocol violation (109 patients). In a secondary analysis including only the target population (i.e., excluding those with protocol violations), there was a significant difference in favor of tPA treatment, but the margin was of questionable clinical significance.
In 1998, a third large tPA study was completed. The protocol of ECASS II was nearly identical to that of the original ECASS study except that the tPA dose was lowered to 0.9 mg/kg (Hacke, 1998). A total of 800 patients were enrolled, and approximately 80% were treated three to six hours after stroke onset. The results indicated that there was no significant difference in neurological function between tPA and placebo patients. There was a trend in favor of treatment that did not reach statistical significance.

The Thrombolytic Therapy in Acute Ischemic Stroke Study (ATLANTIS) sponsored by Genentech also used a longer time window, but was similar in other respects to the NINDS tPA trial (Clark, 2000). Only 15% of patients were enrolled within three hours. Although a significantly higher percentage of tPA-treated patients showed early improvement at 24 hours measured with the National Institutes of Health Stroke Scale (NIHSS), these findings were reversed at one month, with the placebo group having a statistically higher percentage of patients showing improvement on this scale. Symptomatic intracerebral hemorrhage was significantly increased compared to placebo (11% vs. 0%), with the greatest risk of hemorrhage in patients treated between five and six hours.

Three similar large-scale clinical trials comparing intravenous streptokinase to placebo in a randomized trial design were performed concurrent with the NINDS tPA and ECASS studies (Australian Streptokinase Trial [ASK], 1996; Donnan, 1996; Multicenter Acute Stroke Trial [MAST], 1996; Multicenter Acute Stroke Trial [MAST], 1995). All three studies were terminated before completion because of safety concerns with excessive rates of intracerebral hemorrhagic complications and higher mortality in the treated groups.

These early studies support use of intravenous tPA at a dose of 0.9 mg/kg with appropriate precautions and treatment beginning within three hours of symptom onset (Ingall, 2004). Following FDA approval of tPA for stroke, several reports of community experience with this treatment appeared in the literature (Charipar, 2008; Buchan, 2000; Hanson, 2000; Katzan, 2000; Wang, 2000a; Tanne, 1999; Chiu, 1998). Although clinical results for the most part have been concordant with those in the NINDS study, some reports document an increase in intracerebral hemorrhagic complications among patients whose treatment deviated from the NINDS protocol, supporting the importance of following the NINDS tPA study protocol.

The significance of early time to treatment was further emphasized by a secondary analysis of the NINDS tPA study population showing gradual decline in measured efficacy even within the three-hour time window (Marler, 2000). American Heart Association (AHA) consensus guidelines for the use of tPA have been published, and treating clinicians are encouraged to evaluate patients for this treatment and initiate treatment with urgency (Adams, 2007). Another analysis using pooled data from the early tPA and later randomized trials suggested efficacy might be achieved even after the three-hour window (ATLANTIS, ECASS, and NINDS tPA Study Group Investigators, 2004).

More Recent Thrombolytic Trials

ECASS III (Hacke, 2008) was a multicenter trial conducted in Europe to evaluate intravenous recombinant tPA (alteplase) versus placebo administered between 3 and 4.5 hours after onset of ischemic stroke symptoms. A total of 821 patients were enrolled, nearly one-third more than in the NINDS trial that led to the adoption of tPA for the treatment of acute ischemic stroke within the first three hours after symptom onset. Arms were acceptably well balanced, although initial stroke severity and previous history of stroke were greater in the placebo group.

Treatment with tPA was associated with a significant improvement in the rate of favorable functional outcome as defined by a modified Rankin score of 0 or 1 (i.e., mild or no deficits). These rates were 52% for the tPA group and 45% for the placebo group (OR 1.34; 95% CI 1.02-1.76) in the intention-to-treat analysis. The benefit was more pronounced when only patients treated with tPA according to the protocol were analyzed (OR 1.47; 95% CI 1.10-1.97), and it was also present when a global outcome measure that included the NIHSS, the Barthel index, the Glasgow Outcome scale, as well as the modified Rankin Scale was used as the endpoint. Overall, the chances to regain full independence were 28% higher among patients treated with tPA, and 14 patients had to be treated for one additional patient to achieve a favorable outcome.

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Mortality was not significantly different between the groups, but slightly higher in the placebo arm. The rate of symptomatic intracranial hemorrhage as defined by the NINDS criteria was 7.9% in the tPA group (versus 6.4% in the NINDS trial). Furthermore, only 2.4% of patients were thought to have worsened because of intracranial hemorrhage in the active treatment group.

The positive results of ECASS III are similar to those predicted by a pooled analysis of previous tPA trials (ATLANTIS, 2004). Yet, some have expressed skepticism, pointing out the discrepancy with previous negative results of ATLANTIS, a U.S. trial evaluating intravenous tPA versus placebo most within five hours of stroke onset (Clark, 1999). ECASS III was different from the NINDS and ATLANTIS trials. The main difference with NINDS was the lower stroke severity of enrolled patients, which explains the much higher rate of complete or near complete recovery at 90 days in ECASS III (modified Rankin 0-1; 52% in ECASS III vs. 39% in NINDS in the tPA arm; and 45% in ECASS III vs. 26% in NINDS in the placebo arm). The main difference with ATLANTIS was the shorter time from symptom onset to treatment in ECASS III (76% treated with tPA after 4 hours in ATLANTIS vs. 37% in ECASS III).

While attention to detail and critical analysis of the data are essential before applying trial results to change clinical practice, the results of ECASS III provide high-quality evidence supporting the use of intravenous tPA in acute stroke patients up to 4.5 hours after symptom onset. However, extending the therapeutic window for intravenous thrombolysis should not invite complacency. It is very clear that thrombolytic treatment should be started as soon as possible. Thrombolysis is most effective when initiated within 90 minutes of symptom onset (Lees, 2010; ATLANTIS, 2004; Marler, 2000), and any delay decreases the benefit. Also, it is prudent to be selective when extending the window to 4.5 hours. The criteria used for patient selection in ECASS III should be replicated when considering thrombolytic treatment between 3 and 4.5 hours after symptom onset in clinical practice. Age greater than 80, combined history of previous stroke and diabetes mellitus, use of anticoagulation regardless of INR and very high initial stroke severity (NIHSS > 25 or radiological evidence of infarction involving more than one-third of the middle cerebral artery territory) were exclusion criteria in ECASS III. These characteristics should be considered cautions in individuals whose treatment with IV tPA cannot be initiated until the 3-4.5 hour interval.

Additional analysis of the ECASS III population confirmed the value of thrombolysis between 3 and 4.5 hours in all subgroups studied, although benefit was lower in patients > 65 years, and these patients also had higher risk of hemorrhage (Bluhmki, 2009). A separate analysis of the trial results concluded that one in six patients had a better outcome and 1 in 35 patients had a worse outcome after treatment with intravenous thrombolysis between 3 and 4.5 hours after symptom onset (Saver, 2009).

Meta-analyses of efficacy of IV tPA as a function of time from onset to treatment and including ECASS III data have narrowed the confidence intervals in support of efficacy extending to 4.5 hours (Carpenter, 2011; Lees, 2010; Lansberg, 2009).

Based on the results of the ECASS III trial, the Stroke Council of the American Heart Association and the American Stroke Association recommended the administration of intravenous rtPA to eligible stroke patients presenting between 3 and 4.5 hours after stroke onset (del Zoppo, 2009). Extending the treatment window for intravenous tPA to 4.5 hours has not been approved by the Food and Drug Administration. The work group recognizes that policies about written as opposed to oral informed consent vary among institutions, especially for use of treatments that are not FDA approved. The work group recommends that clinicians be aware of and follow relevant policies where they practice.
21. ED in a Stroke-Ready Facility (SRF) Initiates Evaluation for Possible TIA

Patients with a history of clinical TIA should be evaluated promptly (Adams, 2007). The following diagnostic evaluations should typically be performed (Calvet, 2007; Coutts, 2005; Albers, 2002; Johnston, 2002). The speed and venue of the assessment described below will depend on the currency of the symptoms and the clinician's assessment of risk of early recurrence of clinical TIA or the development of stroke. The ICSI work group recommends that patients presenting less than 24 hours since initial clinical TIA with high risk symptoms (see Annotation #23, "High Risk for Stroke?") generally not leave the emergency department until the following are completed or scheduled within the next few hours on an inpatient basis.

- Brain imaging: MRI (preferred) or CT
- Vascular imaging: MRA, CTA, or carotid ultrasound (if symptoms suggest carotid distribution)
- Blood work: complete blood count, electrolytes, BUN, creatinine, INR, aPTT, fasting lipids, fasting glucose, HbA1c, troponins
- EKG and cardiac rhythm monitoring
- Echocardiography (if suspect cardioembolism)
- Case-specific interventions
- Risk factor assessment and counseling

Sometimes most or all these evaluations are done in the emergency department. Other times, a disposition is made early to admit, and most of the tests are done in the inpatient or observation unit, for complete TIA evaluation and to institute case-specific management. (Annotations #24 or #26)

Brain Imaging

If the patient is not having symptoms at the time of presentation, an MRI with a diffusion-weighted sequence (DW-MRI) is preferred, if available. Restricted proton diffusion in the setting of a clinical transient ischemic attack identifies higher risk of stroke (Purroy, 2004). At this time, an MRA of the carotids and intracranial arteries can also be performed if indicated.

If MRI is not available, a CT of the head is indicated and, if feasible, a CTA of the head and neck can also be performed if indicated.

(Latchaw, 2009; Boulanger, 2007; Douglas, 2003)

Another approach for patients with symptoms referable to a carotid territory would be CT of the brain followed by carotid ultrasound as vascular imaging.

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23. High Risk for Stroke?

Recommendation:

- A qualified clinician (i.e., trained and experienced in the management of patients with transient ischemic attacks or supported via telemedicine arrangement with such a clinician) should evaluate patients with TIA or minor stroke symptoms and initiate case-specific secondary prevention measures urgently on an inpatient or expedited outpatient basis (Strong Recommendation, Moderate Quality Evidence) (Joshi, 2011; Easton, 2009; Luengo-Fernandez, 2009; Rothwell, 2007).
The risk of a stroke following a TIA is highest in the first week – nearly 10%. Observational studies have shown that outpatient follow-up in urgent (within 48 hours) TIA clinics is associated with lower rates of stroke and stroke-related hospitalizations. Outpatient management of TIA patients may be safe and more cost effective than hospitalization, depending on the availability of urgent TIA clinics. Most agree that patients with a TIA should either be hospitalized (at least outpatient observation) or evaluated in an outpatient setting by a neurologist or other stroke expert in an expedited manner. Local protocols should be based on availability of resources.

The major issue in dealing with clinical TIA patients is making the best decisions about the speed of workup, the appropriate evaluation to guide preventive therapy, and the most efficacious therapies to avert stroke. To make the best decisions, the clinician must know what the early risk of stroke is for the given patient, whether speed of workup and treatment matter, and, if so, what treatments should be deployed. Information about these points is just becoming available. That a clinical TIA is a risk factor for stroke is not new news. The traditional wisdom is that a patient has a 30-40% risk of having a stroke in the five years following a clinical TIA. The more salient question is about the short-term risk.

Several studies have identified factors in patients presenting with clinical TIAs that predict subsequent ischemic stroke. Older studies using a clinical definition of TIA (the neurologic syndrome prior to completion of imaging) examined factors predisposing to ischemic stroke within a time frame of months or years after the clinical TIA, but provide limited information about acute risk. Examples of risk factors identified in these older studies include advanced age, presenting with more than four clinical TIAs in the two weeks prior to the index clinical TIA, and the comorbidities of hypertension, myocardial infarction, cardiac arrhythmia, and diabetes mellitus (Friday, 1997; Streifler, 1995; Hankey, 1992; Kernan, 1991; Dennis, 1990). The presentation of transient monocular blindness or amaurosis fugax generally confers a more benign prognosis (Evans, 1994; Wilterdink, 1992; Dennis, 1989). Brown, et al., proposed an algorithm for triage and evaluation of patients with clinical TIA and minor ischemic stroke, citing these data to estimate specific risk (Flemming, 2004; Brown, 1994).

Data from recent studies also using a clinical definition of TIA are more relevant to the issue at hand in the emergency department, i.e., the risk over the next few days and weeks. A cohort study described the early (one-week and three-month) risk of ischemic stroke, cardiovascular events, and death in 1,707 patients presenting with a diagnosis of clinical TIA to emergency departments within the Kaiser Permanente system in northern California (Johnston, 2000). Fifteen percent of the patients were admitted for further monitoring, and the rest were discharged from the emergency department. The risk of stroke or admission for other cardiovascular events (myocardial infarction, unstable angina, cardiac arrhythmia, congestive heart failure) were reported as follows:

<table>
<thead>
<tr>
<th>Event</th>
<th>Seven Days</th>
<th>Three Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>6%*</td>
<td>10.5%+</td>
</tr>
<tr>
<td>Clinical TIA</td>
<td></td>
<td>13%+</td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td></td>
<td>2.7%+</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td>2.6%</td>
</tr>
</tbody>
</table>

* Over half occurred within two days.
+ Taken in total, 26.2% of clinical TIA patients returned to the hospital within three months with another cerebrovascular or cardiovascular event.

In multivariate analysis, five factors independently predicted higher risk:

- Age greater than 60 years
- Diabetes mellitus
- Clinical TIA lasting longer than 10 minutes
• Clinical TIA including motor weakness as a symptom
• Clinical TIA including abnormal speech as a symptom

The features comprise a risk stratification scheme known as the "California Score."

The same issue of early risk was examined in the population-based Oxford Vascular Study (Coull, 2004). The short-term fate of 87 consecutive Oxfordshire residents with clinical TIA or minor stroke was examined. Risk of stroke was 8% at one week, 11.5% at one month and 17.3% at three months. The risks were slightly higher after minor stroke (11.5%, 15% and 18.5%, respectively) at the three time intervals.

Another study examined patients with carotid stenosis randomized to medical therapy after first clinical TIA in the North American Symptomatic Carotid Endarterectomy Trial. The study found stroke risk of 5.5% at two days and 20.1% at 90 days following the qualifying clinical TIA, emphasizing that early risk is substantial after clinical TIA in this setting (Eliasziw, 2004). The study also showed that because of occurrence of stroke early after TIA, benefit of carotid endarterectomy in such patients drops significantly as time to the procedure exceeds two weeks from the ischemic event, arguing that speed of assessment and treatment are all-important (Rothwell, 2004).

Giles, in a meta-analysis of studies of stroke risk by day two and seven post-clinical TIA, reported that variability among reports of rates of stroke may relate to the setting in which the patients are seen for evaluation and whether treatments are offered (Giles, 2007).

From these studies it is clear that in general clinical TIA is a potent short-term risk factor for stroke. From the Kaiser Permanente study, it is also suggested that risk is heterogeneous, i.e., some patients are at higher risk than others. If true, it might then be possible to identify those at highest short-term risk prospectively and reliably. They could be triaged to an expedited management track.

Confirmatory information has since accumulated. Analysis of the Oxfordshire population-based sample of clinical TIA episodes (n=209) yielded an "ABCD" score identifying those at high risk of stroke (Rothwell, 2005).

**Table 1.**

The elements of the scale from this derivation sample are as shown:

<table>
<thead>
<tr>
<th>A – for age</th>
<th>Over the age of 60 years</th>
<th>1 point</th>
</tr>
</thead>
<tbody>
<tr>
<td>B – for blood pressure</td>
<td>A systolic greater than 140 mmHg or diastolic greater than 90 mmHg</td>
<td>1 point</td>
</tr>
<tr>
<td>C – for clinical features</td>
<td>Unilateral weakness</td>
<td>2 points</td>
</tr>
<tr>
<td></td>
<td>Speech disturbance without weakness</td>
<td>1 point</td>
</tr>
<tr>
<td></td>
<td>Other clinical features</td>
<td>0 points</td>
</tr>
<tr>
<td>D – for duration of symptoms</td>
<td>Symptoms lasting greater than 60 minutes</td>
<td>2 points</td>
</tr>
<tr>
<td></td>
<td>Symptoms lasting 10-59 minutes</td>
<td>1 point</td>
</tr>
<tr>
<td></td>
<td>Symptoms lasting less than 10 minutes</td>
<td>0 points</td>
</tr>
</tbody>
</table>

(Rothwell, 2005)

The ABCD score was subsequently validated in a second population-based sample of clinical TIA episodes (n=190). The seven-day risks of stroke in the combined derivation and validation samples (n=299) were:

- 0-4 points (73% of combined samples): 0.4% (95% CI 0-1.1%)
- 5 points (18% of combined samples): 12.1% (4.2-20.0%)
- 6 points (9% of combined samples): 31.4% (16.0-46.8%)
Note the similarity of the ABCD score features, derived and validated in Great Britain, to those of the California Score described above. The next challenge was to demonstrate the generalizability of these approaches, i.e., to show the reliability of the prediction models in all patient groups and settings.

The ABCD scheme was applied in additional cohorts. One (Cucchiara, 2006) found the scheme not as sensitive for high risk as originally reported, but the study used a different outcome set than the original report. Another (Tsivgoulis, 2006) found the scheme very reliable in identifying high-risk patients. Both cohorts were already hospitalized patients under care of neurologists. It might be argued that a more relevant setting to study the validity of the scheme would be in a community-based sample of patients seen by non-neurologists in an emergency room. Finally, a retrospective analysis (Bray, 2007) concluded that the ABCD score was highly predictive in identifying patients with clinical TIA at a high short-term risk of stroke.

More recently, the groups from Kaiser Permanente (California Score) and Oxford (ABCD score) together, validated the two similar prognostic scores in four independent groups of patients and generated a new unified score (the ABCD2 Score) to predict the risk of stroke in the two days following a clinical TIA (Johnston, 2007). This new score was derived and validated in patients seen in emergency departments and outpatient clinics and is a more accurate predictor than either of the two previous scores (California Score and ABCD Score). Also, the score predicted the risk of stroke within two days, which is more useful in the outpatient setting. Data from the validation groups included 4,799 patients.

Table 2.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>A – for age</td>
<td>60 years or older</td>
</tr>
<tr>
<td>B – for blood pressure</td>
<td>A systolic 140 mmHg or greater or diastolic of 90 mmHg or greater</td>
</tr>
<tr>
<td>C – for clinical features</td>
<td>Unilateral weakness, Speech disturbance without weakness</td>
</tr>
<tr>
<td>D – for duration of symptoms</td>
<td>Symptoms lasting greater than 60 minutes, Symptoms lasting 10-59 minutes, Symptoms lasting less than 10 minutes</td>
</tr>
<tr>
<td>D – Diabetes</td>
<td>Diabetes</td>
</tr>
</tbody>
</table>

Risk of stroke at two days:

- Low risk (0-3 points): 1.0%
- Moderate risk (4-5 points): 4.1%
- High risk (6-7 points): 8.1%

Based on these results, the authors suggest admitting patients who present with a clinical TIA and have an ABCD2 score of 4 or greater.

A recent systematic review and pooled analysis of 20 cohort validation studies (9,808 patients) compared the ABCD and ABCD2 TIA scoring schemes. It demonstrated independent validation of the ABCD scoring system with no increase in accuracy for ABCD2 over ABCD. With the exception of retrospective data extractions, both systems showed good predictive value for stroke within seven days (Giles, 2010).

Another approach has used imaging to stratify early risk (Purroy, 2004). Detection of ischemic infarct by diffusion-weighted MRI confers risk similar to an ABCD2 score of four or greater. Clinical scoring schemes...
and imaging are both independently predictive of increased early risk, and a combined scheme has been proposed (Giles, 2010). Initial evaluation for possible TIA includes:

- Complete blood count
- Electrolytes, BUN, creatinine, glucose
- Prothrombin time (INR)
- aPTT (activated partial thromboplastin time)
- Cardiac biomarkers (troponin)
- Electrocardiogram
- Fasting lipid profile
- Consider HbA1C if suspecting diabetes
- Vascular imaging: carotid ultrasound, CTA, MRA
- Risk factor assessment and counseling

These reports highlighted the frequent early occurrence of stroke and other cardiovascular events, and the validity of risk stratification schemes. The next question is whether hospitalization or expedited outpatient management mitigates high risk.

Other work has suggested that deployment of streamlined systems that address clinical TIAs very quickly (e.g., within 48 hours) with definitive diagnostic testing and initiation of secondary prevention are associated with reduced the rates of early stroke (EXPRESS, SOS-TIA). These studies used historic cohorts as controls, randomization of rapid vs. slow assessment being ethically impossible. The EXPRESS Trial (Rothwell, 2007), for example, compared stroke rate at 90 days in clinical TIA patients treated in an expedited process with that of an historical control group in the same medical system. The expedited process reduced time from clinical TIA to initial assessment by stroke specialists from 3 days to less than 1 day, and the time to initiation of secondary prevention from 20 days to 1 day. The 90-day stroke risk fell from 10.3% to 2.1%. The expedited care systems that have been examined include outpatient assessments as in the EXPRESS and SOS-TIA trials (Lavallee, 2007), as well as in hospital protocols (FASTER) (Kennedy, 2007; Rothwell, 2007). Interestingly, these studies did not use stratification to select patients at higher risk. Even so, they demonstrated value in expedited evaluation. Uncertain at this point is what role stratification should play. It is also not clear which interventions lead to the difference in patient outcomes seen with the expedited systems.

Based on what is known and acknowledging the continuing areas of uncertainty, the work group recommends that patients seen within 24 hours of initial clinical TIA be admitted to a hospital (inpatient or observation status) or triaged to a program of expedited outpatient assessment. The clinical or imaging factors outlined above that predict high risk of recurrence might theoretically influence decision-making in this patient group. Caveats have already appeared in results of validation studies of the ABCD2 scale in other patient groups. While its validity has been confirmed in principle, the ABCD2 scale's sensitivity has been shown to be imperfect in these studies. Sensitivity improved if glucose > 120 mg/dL and history of hypertension were included in a new scale in one experience (Fothergill, 2009), whereas urgent vascular imaging and EKG monitoring for patients with < 4 points on the ABCD2 were advocated by others (Amarenco, 2009; Ois, 2008).

Certain diagnostic entities, if suspected, may require hospitalization for specific management, even with presentation later than 24-48 hours from clinical TIA occurrence or lower ABCD2 score (e.g., carotid or vertebral artery dissection, carotid stenosis, specific coagulopathy or arteriopathy, cerebral venous thrombosis). Not settled is whether the assessment of those at low risk by these schemes can be safely pursued.
at a more leisurely pace or foregone altogether. At present, the work group is not prepared to recommend that patients be selected for hospitalization or expedited outpatient assessment based solely on the ABCD2 scheme. It recognizes that it may be being used in that way in some hospitals in the region and encourages that the effectiveness of the approach be monitored in those hospitals.

In summary, the work group recommends consideration of hospitalization or observation unit stay for patients with first clinical TIA within the past 24 hours to facilitate early deployment of lytic therapy, if necessary, and to expedite institution of definitive secondary prevention. For others, the risk stratification data described above might also justify hospitalization rather than expedited ambulatory management. Whatever the strategy, speed is critical. Patients managed in the outpatient setting should be fully educated about the need to return immediately if symptoms recur, to allow use of lytic therapy.

(Goldstein, 2006; Johnston, 2006; Purroy, 2004)

24. Definitive Management of TIA Patient in an Inpatient or Observational Bed with Telemetry

Patients with clinical TIA symptoms within 24 hours and at high risk for stroke (see Annotation #23, "High Risk for Stroke?") should be admitted to a monitored unit (ideally telemetry) for observation and further evaluations. Triaging patients to an inpatient or observation unit status may expedite diagnostic evaluation, allow for ready access to fibrinolysis should the patient have an acute stroke, facilitates early carotid revascularization if indicated, and offer greater opportunity for risk factor modification for secondary stroke prevention (the effect of the "teachable moment" of a hospital stay). Again, expedited outpatient programs may be equivalent (see Annotation #26, "Definitive Management of a TIA Patient in an Outpatient Expedited Care TIA Clinic or Program").

The following diagnostic evaluations should be performed for inpatients (Latchaw, 2009; Adams, 2007; Douglas, 2003; Albers, 2002; Johnston, 2000):

- Brain imaging: MRI (preferred) or CT
- Vascular imaging: MRA, CTA, or carotid ultrasound (if symptoms suggest carotid distribution)
- Blood work: complete blood count, electrolytes, BUN, creatinine, INR, aPTT, fasting lipids, fasting glucose, HbA1c, troponins
- EKG and cardiac rhythm monitoring
- Echocardiography (if suspect cardioembolism)
- Case-specific interventions
- Risk factor assessment and counseling

26. Definitive Management of TIA Patient in an Outpatient Expedited Care TIA Clinic or Program

Patients with clinical TIA symptoms that occurred more than 24 hours ago but within the last seven days should be evaluated as soon as possible (Albers 2002; Johnston, 2002). Some organizations have developed TIA clinics for the rapid evaluation of patients in the outpatient setting. Patients who cannot be evaluated rapidly as an outpatient should be admitted to the hospital or observation unit. The following diagnostic evaluations should be performed within 48 hours:

- Brain imaging: MRI (preferred) or CT
Stroke Code Algorithm Annotations

29. Emergency Department in a Stroke-Ready Facility (SRF) Admits Patient and Begins Stroke Code

The goal of the stroke code is to rapidly administer tPA in appropriately screened candidates. The onset of symptoms to treatment (onset to needle) time can be up to 180 minutes (or 270 minutes in selected patients); see Annotation #18, "Consider IV Tissue Plasminogen Activator [tPA]/See Stroke Code Algorithm." Available evidence indicates that reperfusion treatment is more effective in relation to how quickly it is given (Lees, 2010; ATLANTIS, 2004; Marler, 2000): time is brain. NIH recommendation of "door to drug" is within 60 minutes (Adams, 2007).

The work group uses the term "stroke code" to refer to a process in the emergency department for the rapid evaluation and treatment of patients who have presented in a time frame qualifying them for thrombolytic therapy. This process may take many forms. It might include a formal hospital-based "stroke team" that is called to the emergency department whenever a possible candidate for tPA has presented, or it may include the emergency department staff who have been trained in the rapid evaluation and treatment of stroke patients. Whatever model is used, the stroke code concept should also be implemented in planning a rapid response to inpatient stroke. The goals of stroke code are the following:

- Rapid triage of patients as soon as they arrive in the emergency department
- Immediate phlebotomy for appropriate blood tests, followed by CT scan or other equivalent imaging
  The NIH recommendation for the timing of "door to initiation of CT scan" for thrombolytic candidates is within 25 minutes.
- Expeditied first clinician contact for history and exam
- The NIH recommendation for timing of "door to first clinician contact" for thrombolytic candidates is within 10 minutes of arrival
- Rapid access to the best neurologic and radiologic expertise for evaluation of the patient and interpretation of the CT scan prior to treatment
  This may include a neurologist and neuroradiologist physically present at the time of treatment. Alternatively, it may be a primary care clinician with expertise in stroke diagnosis and administration of tPA and a general radiologist with expertise in reviewing head CT scans. Teleradiography and telemedicine may be used to provide expertise in one or both roles.
  The NIH recommendation for interpretation of CT scan after completion is within 20 minutes.
- Timely administration of tPA in appropriately screened candidates
  The NIH recommendation for "door to drug" time for IV thrombolytic treatment is within 60 minutes (Adams, 2007; Bock, 1999).
Although the recommended door to drug time goal is 60 minutes, the ICSI work group challenges emergency departments and hospitals to streamline their processes further. Time is brain. In the same spirit, the work group recommends that patients arriving within 30 minutes of the end of the time window, i.e., 150 minutes or 240 minutes in selected patients, be managed as candidates for IV tPA. A 30-minute or even shorter door to needle time can sometimes be safely achieved.

30. Evaluation (Should Occur Concurrently with Intervention)

Review History and tPA Treatment Indications and Contraindications, and Baseline NIHSS

Take a focused patient history, including a review of indications and contraindications for treatment with tPA (Adams, 2007).

Indications for tPA

- Acute onset of focal neurological symptoms, consistent with ischemic stroke in patients 18 years of age and older
- Clearly defined onset of stroke less than 3 hours (4.5 hours in selected patients; see Annotation #18, "Consider IV Tissue Plasminogen Activator [tPA]/See Stroke Code Algorithm") prior to planned start of treatment
  
  If the patient awakens with symptoms, onset is defined as the time when the patient was last known to be at his/her baseline neurological status prior to sleep onset.
- CT scan showing no evidence of intracranial hemorrhage, non-vascular lesions (e.g., brain tumor, abscess) or signs of advanced cerebral infarction such as sulcal effacement, hemispheric swelling or large areas of low attenuation consistent with an extensive volume of infarcted tissue
- Unlikelihood of stroke mimics, e.g., postictal state
- A patient with a seizure at the time of onset of stroke may be eligible for treatment as long as the clinician believes that residual deficit is secondary to stroke and not a postictal phenomenon (Adams, 2007).

Contraindications for tPA

The clinical history, laboratory and radiological contraindications for thrombolytic therapy (tPA) that are listed below should be considered relative contraindications. Clinical judgement should weigh the patient's risks compared with the benefits of thrombolytic therapy.

Clinical contraindications

- Clearly defined onset of stroke greater than 3 hours (4.5 hours in selected patients; see Annotation #18, "Consider IV Tissue Plasminogen Activator [tPA]/See Stroke Code Algorithm") prior to projected start of treatment
- If the patient awakens with symptoms, onset is defined as the time of the last known baseline neurological status prior to falling asleep.
- Rapidly improving symptoms
- Mild stroke symptoms/signs (NIHSS less than four)
  - Sensory symptoms only
  - Ataxia without other deficits
  - Dysarthria without other deficits
- Mild motor signs (non-disabling)
- Visual field defect without other deficits

On the other hand, some deficits measured at one to three on the scale may be very disabling and warrant use of tPA, e.g., moderate isolated aphasia in an individual using language in his/her profession, such as a journalist. Hence clinical judgment may override.

- Obtunded or comatose state in the setting of middle cerebral artery (MCA) stroke
- Clinical presentation suggestive of subarachnoid hemorrhage, regardless of CT result
- Hypertension – systolic blood pressure (SBP) greater than 185 mmHg or diastolic blood pressure (DBP) greater than 110 mmHg

Patients with a systolic blood pressure greater than 185 mmHg or diastolic blood pressure greater than 110 mmHg are excluded only if the blood pressure exceeds the limits on consecutive measurements, and if aggressive (i.e., beyond boluses of labetolol, nicardipine or doses of nitropaste) treatment is required to lower the blood pressure into range.

Throughout this guideline, the work group frequently refers to blood pressure limits that are represented as systolic/diastolic. These ranges are intended to establish the blood pressure limits as excessively elevated if either the systolic level OR the diastolic level is above the threshold.

**History contraindications**

- Minor ischemic stroke within the last month
- Major ischemic stroke or head trauma within the last three months
- History of intracerebral or subarachnoid hemorrhage if recurrence risk is substantial
- Untreated cerebral aneurysm, arteriovenous malformation (AVM) or brain tumor
- Gastrointestinal or genitourinary hemorrhage within the last 21 days
- Arterial puncture at a non-compressible site within the last seven days or lumbar puncture within the last three days
- Major surgery or trauma within the last 14 days
- Clinical presentation suggestive of acute myocardial infarction (MI) or post-MI pericarditis
- Patient taking oral anticoagulants and INR greater than 1.7
- Patient receiving heparin within the last 48 hours and has an elevated aPTT
- Patient receiving low-molecular-weight heparin within the last 24 hours
- Pregnant, or possibly pregnant, female
- Known hereditary or acquired hemorrhagic diathesis or unsupported coagulation factor deficiency

**Laboratory contraindications**

Glucose should always be measured prior to giving tPA; other parameters should be checked before treatment if there is reason to believe they may be abnormal (e.g., INR and aPTT should be checked if patient has been exposed recently to warfarin or heparin, or if there is history of liver disease).

- Glucose less than 50 or greater than 400 mg/dL
- Platelet count less than 100,000 mm$^3$

**NOTE:** The appropriate management of IV tPA in patients taking novel oral anticoagulants, e.g., direct thrombin inhibitors and factor Xa inhibitors, remains unsettled.
• INR greater than 1.7
• Elevated aPTT unless on basis of a lupus anticoagulant
• Positive pregnancy test

Radiology contraindications
• Intracranial hemorrhage
• Large area of low attenuation consistent with an infarcted brain

Changes of this type apparent in a potential tPA candidate by reported symptom onset time suggest that actual onset of the infarct was earlier than the symptom history indicated. Recheck patient history and time of symptom onset.

• Intracranial tumor, aneurysm, arteriovenous malformation (AVM) or other space-occupying lesion

History or imaging discovery of an unruptured aneurysm or arteriovenous malformation are among the relative contraindications that clinicians often do not heed if there is clinical confidence that hemorrhage is not the mechanism of a patient's symptoms.

Once indications and contraindications have been reviewed, a patient-specific informed consent discussion should ensue with the patient and/or his/her surrogate (see also Annotation #31, "Intervention [Should Occur Concurrently with Evaluation]"). Following the discussion, the patient should be appropriately managed and reasons tPA was or was not given documented.

As documented earlier in this guideline, eligibility for treatment in the 3-4.5 hour time window is similar to eligibility for patients treated within 3 hours with additional cautions or relative contraindications because certain subgroups were not included in the pivotal ECASS III trial; hence, the positive trial results cannot be applied to them. These cautions are:

• Patients older than 80 years
• Patients taking oral anticoagulants regardless of INR
• NIH stroke scale > 25 or early CT signs involving > 1/3 of the middle cerebral artery territory
• Patients with a history of both stroke and diabetes

Baseline NIHSS

A history and neurological examination must be performed to assess whether the presentation is consistent with a stroke diagnosis. Once a diagnosis of stroke is strongly suspected, use of the NIHSS by clinicians and nursing staff is encouraged, as the scale provides a uniform and quantitative method of evaluation to facilitate comparison between examiners' observations during the early hours of the stroke care (Adams, 2007). We encourage use of the NIHSS as an initial evaluation tool and after treatment to assess for change.

The NIHSS is a quantitative measure of neurologic deficit in stroke patients that covers the key aspects of the neurological exam, including level of consciousness and orientation, eye movements, visual fields, facial weakness, motor strength in limbs, coordination, sensation, language and comprehension of language, articulation, and neglect. It can be performed in rapid fashion (five to eight minutes), which is an important feature in this clinical setting (Adams, 2007; Brott, 1992).

Both validity and reliability of the NIHSS have been demonstrated in several evaluations as follows:

• Content validity
  - The items contained in the NIHSS were selected on the basis of expert opinion and literature review, thus satisfying the requirements for content validity (Boysen, 1992).
Concurrent criterion validity
- The NIHSS correlates with lesion volume on CT scan (Brott, 1989).
- The NIHSS correlates with other measures of neurological outcome (Duncan, 1992).

Construct validity
- Factor analysis reported by Lyden et al. defined two constructs relating to right and left hemisphere function confirming construct validity of this scale (i.e., it is measuring what it was designed to measure). Also demonstrated is that the scale functions identically in both tPA-treated and placebo-treated patients. That is, the scale result is not affected by the treatment. Instead, it truly reflects clinical outcome, i.e., whether the patient is better or not. This dimension of validity remains consistent in both tPA-treated and placebo patients over time after ischemic stroke treatment (Lyden, 1999).

Predictive validity
- The NIHSS predicts three-month outcome (Adams, 1999; Muir, 1996).

Interrater and intrarater reliability
- The NIHSS has been shown to be a reproducible measure, comparing both different examiners and repeated evaluations by the same examiner. Reliability has been demonstrated for neurologists, other clinicians and nursing caregivers (Dewey, 1999; Goldstein, 1997; Goldstein, 1989). Although the NIHSS was originally designed as a research tool, it has proven to be an excellent measure of neurologic status and can be an important tool for the standardization and communication of clinical information between nurse caregivers and between nurse caregivers and other clinicians (Spilker, 1997).

Perform Vital Signs Every 15 Minutes with Neurological Checks (not NIHSS)

It is the standard of practice to perform a baseline NIHSS neurological assessment (Adams, 2007), whereas for subsequent frequent neuro checks, a less-extensive, but stroke-relevant, tool is appropriate for several reasons. Performing a full NIHSS assessment every 15 minutes is often not feasible and may not be a good use of time. There is not evidence showing that performing a full NIHSS assessment every 15 minutes improves patient outcomes is necessary for early detection of changes in patient condition. Unfortunately, the ICSI work group is not aware of validated and standard non-NIHSS neurological assessment.

The work group has gathered the abbreviated neurological assessments used by several organizations and proposes the following non-NIHSS neuro check as an unvalidated option.

Level of Consciousness – measures the level of alertness and cognition of the patient
- Is the patient alert, alert with stimulation or requires repeated stimulation to remain alert, or comatose?
- Is the patient able to correctly state or mouth his/her name and age?
- Is the patient able to correctly follow simple commands of opening and closing his/her eyes?

Motor Functions – measures motor functions and patient's ability to follow commands
- Is the patient able to lift and hold his/her arm in extension?
- Is the patient able to lift and hold his/her leg in extension?

Language Skills – detects and provides impression of severity of aphasia and dysarthria in response to asking patients to answer a question, describe an item, or read several sentences

See Appendix B for an example of a non-NIHSS neuro check form.
The ICSI work group encourages organizations to assess and report upon the use of non-NIHSS assessment tools to grow the evidence in this area.

**Record Weight** (estimate if necessary)

**Draw Blood for Lab Tests**

Necessary/critical laboratory tests (results must be available before treatment in all cases):

- Glucose

Recommended laboratory tests (results must be available before treatment if physical exam and/or patient history indicates the possibility of abnormal results):

- Complete blood count (CBC) with platelet count
- Electrolytes, BUN, creatinine
- PT/INR, aPTT – **must be available** if patient on warfarin or heparin, respectively, or at risk for other coagulopathy
- Pregnancy test – **must be available** if possibility patient is pregnant

Others to consider:

- Troponin
- AST

These tests are used to evaluate for dehydration, metabolic disorders that might influence neurologic status (especially hypoglycemia and hyperglycemia), hematologic disorders such as polycythemia that may affect cerebral perfusion, or coagulopathies that could affect the treatment decision (Adams, 2007). Prior to administration of tPA, the glucose level should be reviewed. If the patient is known to be on warfarin or has received heparin within the last 24 hours, the prothrombin time and partial thromboplastin time must be reviewed prior to treatment. A urine or serum pregnancy test should be obtained in women of childbearing potential if there is substantial reason to believe the patient may be pregnant.

**Perform Electrocardiography (EKG)**

An EKG should be performed for the purpose of screening for concomitant cardiac disease, either acute or chronic, that may impact immediate treatment decisions. It is not an absolute requirement prior to treatment with IV tPA.

**Perform CT Head without Contrast (or Equivalent Imaging)**

A CT scan without contrast must be performed prior to treatment with tPA, primarily for the purpose of excluding hemorrhage. Early signs of infarct should also be sought as this finding confers greater risk of symptomatic intracerebral hemorrhage with tPA treatment (Adams, 2007). It has been recently shown that MRI scans of the brain with diffusion- and susceptibility-weighted (gradient echo) sequences are much more sensitive than CT in detecting new infarction and chronic hemorrhage, and of equal sensitivity for acute hemorrhage (Latchaw, 2009; Chalela, 2007; Fiebach, 2004). Consequently, when it is possible to perform MRI as quickly as CT with equally expert and timely interpretation, MRI is an option in this situation. Whichever is used, it is recommended that the greatest level of radiologic expertise possible be obtained for interpretation, with the caveat that the reading should not create excessive delays in the evaluation and treatment process. A procedure for rapid teleradiography readings should be in place if needed to provide this expertise quickly.

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31. Intervention (Should Occur Concurrently with Evaluation)

Educate Patient and Family

A process should be in place for educating the patient and family to the suspected diagnosis, emergency department (ED) process, tests to be performed, tPA treatment and its risks, and other treatment measures to be considered. This could include face-to-face interaction by the caregiver with the patient and family, as well as teaching tools in written form (see Annotation #33, "Initiate IV tPA," and Appendix C, "tPA for Cerebral Ischemia within Three Hours of Onset – Changes in Outcome Due to Treatment"). Education should be documented in the medical record.

Treatment of Hypotension and Dehydration

Dehydration is common among patients admitted with acute ischemic stroke. Hypotension is not; most patients are hypertensive. These issues are discussed more fully in Annotation #37, "Post-ED Medical Management of Volume and Blood Pressure (Not a Thrombolysis Candidate)."

Treatment of Hypertension If Blood Pressure Greater than 185 Systolic or 110 Diastolic (tPA Candidates)

Recommendation:

- Clinician should treat patients with ischemic stroke who are tPA candidates to reduce blood pressure below 185/110 prior to administration of tPA.

Clinician should treat hypertension in tPA recipients to maintain BP below 180/105 during the first 24 hours (Strong Recommendation, Low Quality Evidence) (Sandset, 2011; Robinson, 2010; Ahmed, 2009; Adams, 2007; Castillo, 2004; Willmot, 2003; Leonardi-Bee, 2002; National Institute of Neurological Disorders and Stroke tPA Study Group [NINDS], 1995).

The strength of the recommendations mirrors that for IV tPA in selected patients and following the protocol of the NINDS tPA trial. It is indirectly supported by less favorable results in thrombolytic trials in which blood pressure was not treated as aggressively and by phase IV reports in which higher rates of hemorrhage occurred when NINDS guidelines were not followed.

Patients with a systolic blood pressure (BP) greater than 185 mmHg or diastolic blood pressure greater than 110 mmHg are excluded from IV tPA and by extension from IA chemical or mechanical thrombolysis (see Annotation #34, "Is Patient a Candidate for Intra-Arterial Reperfusion Treatments?") only if the blood pressure remains elevated on consecutive measurements (Adams, 2007), and if aggressive treatment is required to lower the blood pressure into an appropriate range (e.g., if more than a few doses of any medication is required or if nitroprusside drip is required).

In patients who have received reperfusion therapy, blood pressure should be maintained below 180/105 during the first 24 hours after treatment (see Table 3, "Approach to Elevated Blood Pressure in Acute Ischemic Stroke"). These policies are defined in the NINDS trial’s protocol for use of IV tPA for ischemic stroke in the 0-3 hour time window. Evidence supporting them for general application in the aftermath of reperfusion therapies is not based on randomized trials in which blood pressure was the independent variable. The therapists are supported indirectly in that reported experiences in which blood pressure and other parameters were not maintained according to the protocol are associated with a higher rate of adverse outcomes, such as intracranial bleeding and mortality (Katzan, 2000). For more information on treating blood pressure post-stroke, see Annotation #37, "Post-ED Medical Management of Volume and Blood Pressure (Not a Thrombolysis Candidate)." Blood pressure in tPA non-recipients is treated more liberally; see
Annotation #37, "Post-ED Medical Management of Volume and Blood Pressure (Not a Thrombolysis Candidate)" (Katzan, 2000).

### Table 3.

#### Approach to Elevated Blood Pressure in Acute Ischemic Stroke

<table>
<thead>
<tr>
<th>Blood Pressure Level mm/Hg</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP &lt; 220 or diastolic &lt; 120</td>
<td>Observe unless other end-organ involvement, e.g., aortic dissection, acute myocardial infarction, pulmonary edema, hypertensive encephalopathy. Treat other symptoms of stroke such as headache, pain, agitation, nausea and vomiting. Treat other acute complications of stroke including hypoxia, increased intracranial pressure, seizures or hypoglycemia.</td>
</tr>
<tr>
<td>Systolic BP &gt; 220 or diastolic BP &gt; 120</td>
<td>- Labetalol 10-20 mg IV over 2 minutes. May repeat or double every 10 minutes (maximum dose 300 mg in 24 hours), or - Nicardipine 5 mg/hour IV infusion as initial dose; titrate to desired effect by increasing 2.5 mg/hour every 5 minutes to maximum of 15 mg/hour. *Aim for 15% reduction of BP.</td>
</tr>
<tr>
<td>Diastolic BP &gt; 140</td>
<td>Nitroprusside 0.5 mcg/kg/minute IV infusion as initial dose with continuous BP monitoring (maximum dose of 10 mcg/kg/minute). *Aim for 10-15% reduction of BP.</td>
</tr>
</tbody>
</table>

#### B. Eligible for Thrombolytic Therapy

**Pretreatment**

<table>
<thead>
<tr>
<th>Blood Pressure Level mmHg</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP &gt; 185 or diastolic BP &gt; 110</td>
<td>- Labetalol 10-20 mg IV over 2 minutes. May repeat x 1; or - Nitroglycerin ointment USP 2% 1-2 inches; titrate to effect or - Nicardipine infusion @ 5 mg/hour, titrate up by 2.5 mg/hour at 5-15 minute intervals; maximum dose 15 mg/hour; when desired BP attained, reduce to 3 mg/hour. * If BP does not decline and remains &gt; 185/110, DO NOT administer tPA.</td>
</tr>
</tbody>
</table>

**During and After Treatment with rtPA**

<table>
<thead>
<tr>
<th>Blood Pressure Level mmHg</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP 180-230/105-120 mmHg</td>
<td>- Labetalol 10-20 mg IV over 2 minutes, may repeat every 10-20 minutes (maximum dose 300 mg in 24 hours); or - Labetalol 10 mg IV followed by an infusion at 2-8 mg/minute (maximum dose 300 mg in 24 hours).</td>
</tr>
<tr>
<td>BP &gt; 230/121-140 mmHg</td>
<td>- Labetalol 10-20 mg IV over 2 minutes, may repeat every 10-20 minutes (maximum dose 300 mg in 24 hours); or - Labetalol 10 mg IV followed by an infusion at 2-8 mg/minute (maximum dose 300 mg in 24 hours); or - Nicardipine infusion 5 mg/hour, titrate to desired effect, may increase 2.5 mg/hour every 5-15 minutes; maximum dose of 15 mg/hour. - If BP not controlled, consider nitroprusside infusion 0.5 mcg/kg/minute (maximum dose of 10 mcg/kg/minute).</td>
</tr>
</tbody>
</table>

**Initiate Two Intravenous Lines**

Two IV lines should be started so that tPA may have a dedicated line.

**Start Intravenous Fluids**

See Annotation #37, "Post-ED Medical Management of Volume and Blood Pressure (Not a Thrombolysis Candidate)."

**Other Systemic Management**

Based on the patient's presentation, other ED management may be required to control hyperthermia, hypothermia, hyperglycemia, hypoglycemia, hypotension, hypovolemia and/or hypoxia. (For additional information, please see Annotation #38, "Other Post-ED Medical Management [First 24-48 Hours]").

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**33. Initiate IV tPA**

**Recommendation:**

- Qualified clinician (i.e., trained and experienced in acute stroke management or supported via telemedicine arrangement by such a clinician) should administer IV tPA to selected and qualifying patients with acute ischemic stroke within 4.5 hours of symptom onset or of time last known to be at their baselines in appropriate care circumstances (i.e., in a "stroke-ready" emergency department or hospital). ICSI or other guidelines for selection and management specifics should be followed (Strong Recommendation, High Quality Evidence) (Carpenter, 2011; Lees, 2010; Lansberg, 2009; Hacke, 2008; Wahlgren, 2007; Clark, 1999; Hacke, 1998; Hacke, 1995; National Institute of Neurological Disorders and Stroke tPA Stroke Study Group (NINDS), 1995).

See Annotation #18, "Consider IV Tissue Plasminogen Activator (tPA)/See Stroke Code Algorithm."

Stakes are high, impact of treatment is substantial, and evidence is strong for treatment of appropriately selected patients. In recommending IV tPA, the work group placed high value on optimizing neurologic function.

The work group recommends using a decision support tool with patient and families, such as that in Appendix C, "tPA for Cerebral Ischemia within Three Hours of Onset – Changes in Outcome Due to Treatment." This pictorial tool shows that for 100 patients with acute stroke treated with IV tPA within three hours of symptom onset, 13 more patients will be normal or near normal (modified Rankin score of 0-1), 19 additional patients will be improved, three patients will be worse, and one patient will be severely disabled or die compared with those treated with placebo. The number needed to treat to improve one patient is three. The number needed to treat to cause harm to one patient is 100. It is available on the Internet at http://www.heart.org/idc/groups/heart-public/@wcm/@hcm/@gwtg/documents/downloadable/ucm_310119.pdf (last accessed 5/24/2012). The work group is not aware of a similar tool for the 3-4.5 hour time frame.

If the patient/family selects tPA, treatment consists of tPA 0.9 mg/kg intravenously to a maximum dose of 90 mg. Ten percent of this dose should be given as a bolus over one to two minutes and the remainder infused over one hour (Adams, 2007). This dosing may be based upon actual or estimated weight.
34. Is Patient a Candidate for Intra-Arterial Reperfusion Treatments?

Recommendation:

- Qualified clinician (i.e., appropriately trained in neurocritical care, neurointerventional procedures or neurosurgery) should consider treating selected and qualifying patients with acute ischemic stroke with intra-arterial thrombolysis under the following circumstances:
  
  1. Arrival within the window for IV tPA < 4.5 hours but contraindication for IV tPA
  2. Arrival beyond window for IV tPA < 4.5 hours and within accepted time windows for relevant vascular site and thrombolytic strategy
  3. Continued major deficit after IV tPA and evidence for persisting occlusion of a relevant and accessible large artery

(Strong Recommendation, Moderate Quality Evidence) (Lee, 2010; Meyers, 2009; Penumbra 2009; Schonewille, 2009; Smith, 2008; Furlan, 1999; del Zoppo, 1998; Wijdicks, 1997; Brandt, 1996; National Institute of Neurological Disorders and Stroke tPA Stroke Study Group [NINDS], 1995)

The stakes are high in most patients for whom intra-arterial chemical thrombolysis with tPA is considered, with high NIHSS score and large vessel occlusion being typical. Evidence of substantial efficacy with intra-arterial therapy exists; however, the evidence has limitations. The strongest supporting evidence was collected using a thrombolytic agent that is no longer available rather than with tPA. Trials of the various circumstances in which intra-arterial chemical thrombolysis is currently used – e.g., in those ineligible for IV tPA, in IV tPA unresponsive cases – in those who cannot be treated until the 4.5-6 hour interval post onset, have not been individually studied and reported. The procedural risks are high. The treatment is invasive and costly. It is available in only a few centers; hence, broad accessibility to such treatments will depend on local triage arrangements or development of a system of acute stroke care. Despite the limitations of evidence, the ICSI work group members' recommendation is strong in view of the likelihood of a poor outcome without intervention.

Consider If Intra-Arterial (IA) Recanalization Candidate

Intra-arterial (IA) thrombolytic therapy may be a treatment option for selected patients presenting in an early time frame but beyond the time window for IV tPA, i.e., the three-hour (or 4.5 hours in selected patients; see Annotation #18, "Consider IV Tissue Plasminogen Activator [tPA]/See Stroke Code Algorithm") (Adams, 2007). It is emphasized that there is no evidence that IA tPA has greater efficacy in any time frame in which IV tPA has been shown to be effective, i.e., within 4.5 hours of symptom onset. Trials are under way to determine whether sequential IV and IA tPA provides benefit compared with IV tPA alone in selected patients.

The availability of the IA option will be institution dependent, and patients must be highly selected. If considering this treatment option for a patient, a clinician must explain to the patient and family that IA therapy is beyond standard of usual care and has substantial risk. Despite the limitations of available study data, in cases of more severe presentation with middle cerebral or basilar artery occlusion, IA thrombolytic treatment may be appropriate because the prognosis without treatment is poor.

If the patient is an appropriate candidate for this treatment, consideration should be given to immediate transfer to an institution offering this intervention. If an endovascular interventionist skilled in this technique is available elsewhere, the patient should be mobilized quickly. See also Appendix A, "Broader Issues."
Middle cerebral artery occlusion

Criteria for consideration of angiographic evaluation for IA treatment:

- Middle cerebral artery (MCA) occlusion defined by:
  - Symptom complex consistent with this vascular distribution:
    - Contralateral hemiplegia and facial weakness
    - Contralateral hemisensory loss
    - Aphasia if ischemia is on left, "neglect" if on right
    - Commonly, contralateral homonymous visual field deficit, reduced level of arousal, eye deviation toward side of brain ischemia (away from side of weakness)
  - MCA "clot sign" on baseline pretreatment CT scan with appropriate clinical presentation
  - CT angiogram, MRA or transcranial Doppler (TCD) demonstration of the occlusion with appropriate clinical presentation

Current practice is that treatment begins less than six hours from onset of symptoms for middle cerebral occlusions beyond 4.5 hours of onset and using intra-arterial tPA.

In the case of middle cerebral artery occlusion, the estimated degree of benefit may seem to be less dramatic than that with basilar occlusion, but the supporting studies offer a superior level of evidence. In the first of two PROACT studies (Prolyse in Acute Cerebral Thromboembolism Study), an improved rate of recanalization was established for intra-arterial recombinant pro-urokinase (r-proUK) plus IV heparin when compared with intra-arterial infusion of placebo plus IV heparin (57.7% versus 14.3%, 2p=0.017) (del Zoppo, 1998). This was a small phase II trial (n=40, 26 received r-proUK and 14 received placebo). Clinical efficacy was not a primary endpoint and was not established in this study. In PROACT II, intra-arterial r-proUK plus IV heparin (n=121) was compared to IV heparin alone (n=59) (Furlan, 1999) in patients with stroke onset within six hours (almost all treated after three hours since onset) and middle cerebral artery (MCA) occlusion. Significant clinical benefit with treatment was established, showing a 15% absolute increase in the percentage of patients with good outcome at three months (primary outcome measure was modified Rankin score of 2 or less). The complication of symptomatic intracerebral hemorrhage was higher than that seen in the NINDS IV tPA trial (10.2% vs. 6.4%, respectively) (National Institute of Neurological Disorders and Stroke tPA Stroke Study Group, 1995). However, the pretreatment severity of stroke in PROACT II was also higher than that in the NINDS study, probably accounting for this excess of hemorrhagic complications.

Despite these promising results, r-proUK was not approved by the FDA for the indication of ischemic stroke, and r-proUK has never been available in the U.S. for any indication. The results of PROACT II, however, have served as a proof of principle for the efficacy of an intra-arterial lytic approach to proximal MCA (M1 or M2 segment) occlusion in the three- to six-hour time frame. It should be recalled that the available lytic agent, tPA, has not been examined in a similar comparison by randomized trial of the intra-arterial route. In summary, intra-arterial tPA thrombolysis is recommended for treatment within six hours of onset of middle cerebral artery occlusion. It should not preclude IV tPA in patients who otherwise qualify (Meyers, 2009).

Basilar artery occlusion

- Basilar artery (BA) occlusion defined by the following.
  - Symptom complex consistent with this vascular distribution:
    - Quadriparesis, sometimes with posturing
    - Bulbar dysfunction (dysarthria, dysphagia, dysphonia)
• Typically dysconjugate eye movement deficits
• Commonly, depressed level of arousal, respiratory abnormalities
  - Hyperdense "clot sign" in basilar artery on baseline non-contrast CT scan with appropriate clinical presentation
  - CT angiogram, MRA or transcranial Doppler (TCD) demonstration of the occlusion with appropriate clinical presentation

The occurrence of acute basilar artery occlusion with bilateral brainstem symptoms is typically a catastrophic neurological event portending a poor prognosis if reperfusion does not occur, with estimations of over 75% mortality and severe disability in survivors (Caplan, 1983; Archer, 1977; Kubik, 1946). Several investigators have reported their results in series of treated patients with basilar thrombosis using intra-arterial urokinase or tPA, showing recanalization rates between 40 and 78% and good outcome by various measures in 20 to 50% (Gonner, 1998; Cross, 1997; Wijdicks, 1997; Becker, 1996; Brandt, 1996; Zeumer, 1993; Hacke, 1988). These are dramatic results when compared to the natural history of this disease as reported in the literature.

Current practice is that treatment with intra-arterial chemical thrombolysis begins more than 4.5 hours but less than 12 hours from onset of symptoms.

There are no randomized, controlled trials of cases of basilar occlusion comparing intravenous tPA to intra-arterial thrombolysis within 3 or 4.5 hours of symptom onset or comparing intra-arterial therapy to placebo controls in any time window, but the limited number of patients presenting with this specific entity would make such trials a difficult undertaking. In patients presenting within a three-hour time window (4.5 hours in select patients; see Annotation #18, "Consider IV Tissue Plasminogen Activator [tPA]/See Stroke Code Algorithm"), the work group suggests that IV tPA be administered. Subsequent intra-arterial treatment may be considered in some centers.

A systematic review identified five qualifying randomized IA chemical thrombolysis vs. no treatment trials in MCA or BA occlusions for which clinical outcome data were available. All five had extended time windows for intervention. The meta-analysis demonstrated improved rates of independence and cure (no residual deficit or residual deficit having no effect on life), with statistically significant odds ratios of 2.05 and 2.14, respectively, in favor of intervention (Lee, 2010).

Other approaches to acute reperfusion are under study. One has been to combine the speed of intravenous therapy with the superior recanalization effect of intra-arterial administration. The Emergency Management of Stroke (EMS) Bridging Trial was a small study (n=35) comparing combined use of intravenous and intra-arterial tPA in patients presenting within the three-hour time window (Lewandowski, 1999). This study demonstrated the feasibility of the combined intravenous/intra-arterial approach showing better recanalization rates when compared to intra-arterial treatment alone. The study was too small to adequately assess efficacy and safety. A larger study (n=80) by the Interventional Management of Stroke (IMS) Investigators compared efficacy and safety of the approach using matched historical controls from the NINDS IV tPA trial (IMS Study Investigators, 2004). Efficacy of the intra-arterial approach was slightly greater and safety similar to the historical IV-tPA-treated patients. A randomized trial of combined therapy vs. IV tPA alone was ongoing into early 2012. According to the NINDS Web site, however, recruitment was stopped in the spring based on futility. There were no safety concerns.

Mechanical reperfusion techniques

Another approach uses mechanical rather than chemical clot removal. The three devices created specifically for mechanical reperfusion in the setting of acute thromboembolic occlusion are the MERCI (mechanical embolus removal in cerebral ischemia) catheter, a corkscrew-shaped retrieval device; the Penumbra system, which relies on clot suctioning and mechanical disruption through separation; and the Solitaire device, a removable stent with mesh-like walls that entrap thrombus material. The MERCI and Multi-MERCI trials
showed that recanalization could be safely achieved in up to 70% patients presenting within eight hours after occlusion of a proximal artery, e.g., internal carotid, MCA, BA, vertebral artery (Smith, 2008; Gobin, 2004). Recanalization rates exceeding 80% have been reported with the penumbral system in patients with similar characteristics in a single study funded by Penumbra, Inc. (Penumbra Pivotal Stroke Trial Investigators, The, 2009). In a recent head-to-head comparison of the Solitaire device vs. the Merci device, the former showed greater efficacy in recanalization, as well as better clinical outcomes. The results have been reported orally but not yet in a peer-reviewed publication. The FDA has approved all three of these devices for treatment of patients with intracranial large artery thromboembolic occlusion and acute ischemic stroke. The utility of these devices in improving clinical outcomes remains unclear (Meyers, 2009).

To summarize and conclude, at this point in time, there are no studies comparing intravenous to intra-arterial therapy within the three-hour or 4.5-hour windows. Intravenous treatment with tPA is proven effective in these time frames. Intra-arterial thrombolysis with the agents currently available for use has theoretic advantages in certain stroke types (demonstrated large vessel occlusion of the internal carotid, middle cerebral or basilar arteries), but its superiority in improving clinical outcomes remains unproved. Also, there are logistic challenges deploying intra-arterial catheter techniques that may delay the time to intervention, thus limiting the benefit for these patients. For these reasons, treatment within the 4.5-hour time window with intra-arterial instead of intravenous thrombolysis cannot be recommended for these large vessel occlusion cases. Centers with expertise in use of intra-arterial tPA or mechanical clot removal are encouraged to continue utilizing intra-arterial techniques in appropriate candidates presenting beyond the 4.5-hour time window. Accepted but not evidence-based time frames for intra-arterial tPA are 4.5 to 6 hours for MCA occlusion – M1 or M2 segment – and 4.5 to 12 hours for BA occlusion. For intra-arterial mechanical clot removal corresponding time frames are 4.5 to 8 hours for MCA occlusion and 4.5 to 12 hours for BA occlusion. The ICSI work group encourages interventionists to collect outcome data and report their experience to the medical community. Even more desirable, these same centers should participate in randomized, controlled trials so that the efficacy of these approaches can be fully established and their roles in the acute ischemic stroke treatment armamentarium clarified for all.

**Emerging technologies**

Several groups have reported use of imaging to support decisions about reperfusion therapies (Albers, 2006; Furlan, 2006; Hacke, 2005). MR and CT technologies provide information about the status of the vascular supply and parenchyma of acutely ischemic brain. Vascular studies (MRA, CTA) demonstrate presence and location of occlusive thrombus, as well as collateral channels. This knowledge enables the offending thrombus to be targeted more precisely and may expand reperfusion options to include intra-arterial chemical or mechanical means. Special CT and MR imaging protocols measure cerebral transit time, blood flow, blood volume and in the case of MR, presence or absence of cytotoxic edema characteristic of infarcting or infarcted brain by detecting restricted proton diffusion. From these parenchymal data, presence and extent of penumbra vs. infarct can be inferred.

It has been argued that information available from these technologies may be of equal or greater importance as time elapsed since symptom onset in deciding whether and how to undertake a reperfusion therapy. The hypothetical ideal reperfusion scenario is when a vascular occlusion is identified and the parenchymal signature is that of penumbra with little or no infarct. On theoretical grounds, treating in such a scenario might be defended even if the time limit were exceeded. A small randomized trial recently supported this idea by showing that intravenous tPA may be beneficial beyond three hours compared with placebo in patients with perfusion-diffusion "mismatch" (i.e., a larger volume of brain with reduced flow than that of already infarcted tissue) using perfusion- and diffusion-weighted MRI (Davis, 2008). Interestingly, patients without mismatch improved as much as those with mismatch in this underpowered study. Analysis of the same patients examining clinical-diffusion mismatch (i.e., deficit more severe than expected considering area of restricted proton diffusion) also found that mismatch did not predict efficacy of IV tPA in a prolonged time window (Ebinger, 2009). The science has been made more difficult because of the complexity of the technology,
lack of standardized metrics, and variability among patients in important factors such as robustness of collaterals (Miteff, 2009). Also, the role of mismatch detection in selecting patients has been confused in recent studies that are simultaneously examining other issues, such as newer chemical thrombolytic agents along with the efficacy of imaging in selecting patients for recanalization therapy (Hacke, 2009; Parsons, 2009).

A systematic review identified five trials in which IV chemical thrombolytic agents were compared with placebo in patients presenting in an extended time window and having mismatch. Mismatch was defined by either MRI or CT. Clinical and radiologic outcomes were examined. The meta-analysis found a relationship between recanalization and improved clinical outcome but no relationship between administration of a thrombolytic agent and clinical outcome. The review did not address the practical question of whether identification of mismatch was useful because subjects having no mismatch were excluded from the trials. At present, management based on mismatch is not evidence based (Mishra, 2010).

Management protocols using such approaches are being assessed in several hospitals in this region. Their use to supersede time-based reperfusion policies must still be considered outside of standard care. In conclusion, the accuracy and usefulness of such studies have not been established (Latchaw, 2009).

**35. Initiate Aspirin Unless Contraindicated**

**Recommendation:**

- Clinician must immediately administer 160-325 mg aspirin to patients with acute ischemic stroke not treated by IV tPA by rectum or, if patient passes a bedside swallow screen, by mouth *(Strong Recommendation, High Quality Evidence)* (Sandercock, 2009b). Note: For patients treated with IV tPA, aspirin (160-325 mg) should be administered 24 hours after IV tPA.

Note: In patients receiving IV tPA, the NINDS protocol discourages administration of any antithrombotic agent, including aspirin, within the 24 hours following administration of IV tPA. The ICSI work group recommends that the NINDS protocol be followed. To our knowledge, there is no direct evidence, i.e., randomized trials in which aspirin use is the dependent variable, supporting this policy. It is supported indirectly by the overall results of the NINDS trial showing efficacy of tPA and acceptable safety. See also Annotation #36, "Post-ED Medical Management (Postthrombolysis)."

This recommendation is based on a Cochrane review with data from over 40,000 patients that showed that aspirin (160-300 mg) started within 48 hours of the onset of ischemic stroke symptoms was beneficial in preventing recurrent strokes. Although there was a small risk of bleeding, this risk was more than offset by the reduction in recurrent stroke. There is also a small benefit from aspirin in reducing the odds of pulmonary embolism in stroke patients.

**Aspirin**

Exceptions to prompt aspirin-dosing approach would be justified in those with contraindications to aspirin therapy (e.g., aspirin allergy, gastrointestinal hemorrhage). For patients with an aspirin allergy, 75 mg of clopidogrel may be reasonable. Intravenous or oral loading with 150-600 mg of clopidogrel establishes antiplatelet effect more rapidly; however, efficacy in this setting is unproven.
Although the benefits of aspirin therapy for long-term preventive therapy for stroke are well established, the use of aspirin to improve outcome in the acute treatment setting has also been demonstrated. Large randomized controlled trials have identified a small but measurable benefit with use of aspirin started within the first 48 hours following ischemic stroke onset (Bath, 2001b; Chinese Acute Stroke Trial Collaborative Group, 1997; International Stroke Trial Collaborative Group, 1997; Sandercock, 1993).

The studies together demonstrate benefit of small magnitude, but with statistical significance in the following outcome measures:

- Early recurrent ischemic stroke – 7 fewer per 1,000 treated (p< 0.0001)
- Death from any cause – 4 fewer per 1,000 treated (p=0.05)
- Death or early recurrence of non-fatal stroke – 9 fewer per 1,000 treated (p=0.001)
- Death or dependency at discharge or six months – 13 fewer per 1,000 treated (p=0.007)

Also, the measured hazard appears to be small and statistically insignificant:

- Hemorrhagic stroke or transformation – 2 more per 1,000 in ASA treated (p=0.06)

**Considerations with Heparin Use**

In contrast, to the proof of efficacy for aspirin, results from the International Stroke Trial (IST) provide powerful evidence against the routine use of any heparin regimen as intensive as the moderate-dose subcutaneous regimen studied in this very large clinical trial (unfractionated heparin – 12,500 units subcutaneous twice daily) (International Stroke Trial Collaborative Group, 1997).

The concept that anticoagulation improves outcome of stroke by reducing initial deficit, preventing progression, and avoiding early recurrence has been refuted by several large trials at this point. Even the traditionally accepted, favorite targets of the bygone era, i.e., vertebrobasilar distribution ischemia and ischemic stroke in the setting of atrial fibrillation, analyzed separately, were not benefitted by heparin in the IST. Similarly, the weight of available data regarding use of full-dose low-molecular-weight heparin or heparinoid for the acute treatment of stroke does not support their routine use for limiting disability or decreasing mortality in this setting (Sandercock, 2009b; Bath, 2001b; Publications Committee for the Trial of ORG 10172 in Acute Ischemic Stroke, 1998).

In summary, the routine use of acute anticoagulation treatment with unfractionated heparin, low-molecular-weight heparin, or heparinoid in acute ischemic stroke is not supported by the available evidence (International Stroke Trial Collaborative Group, 1997). This treatment does not appear to improve clinical outcome from the index stroke. Also, use of full-dose IV anticoagulant en route to oral anticoagulation with warfarin has not been shown to be superior to use of oral aspirin (Berge, 2000). There may be subgroups that benefit, but further studies of this problem are required for confirmation (Sandercock, 2009b). It remains to be seen whether anticoagulation to improve outcome of the index stroke will be restudied using the new oral anticoagulants.

Despite these discouraging results, the use of continuous heparin infusion in acute stroke has continued clinical practice (Albers, 2004; Coull, 2002; Diener, 2001; Berge, 2000). Given these data, if the decision is made to use full-dose continuous heparin infusion for a specific indication (e.g., large vessel atherothrombosis or dissection), clinicians are strongly encouraged to discuss with their patients the lack of proof for this therapy and to detail the potential hazards.

**Heparin use for venous thromboembolism (VTE) prophylaxis**

Refer to Annotation #38, "Other Post-ED Medical Management (First 24-48 Hours)," which addresses:

- Admission to stroke unit care
- Performance of swallow screen if not done in the emergency department
36. Post-ED Medical Management (Postthrombolysis)

- Admit to intensive care unit or acute stroke care unit/cardiac monitoring.

- Perform vital signs and neurological checks (not full NIHSS National Institutes of Health Stroke Scale) every 15 minutes for two hours, then every 30 minutes for six hours, then every 60 minutes for 16 hours for a total of 24 hours (recommend use of an abbreviated NIHSS for neurological checks). (See Appendix B, "Non-NIHSS Neuro Check.")

- Treat blood pressure (BP) if greater than 180/105 (see Table 3 in Annotation #31, "Intervention [Should Occur Concurrently with Evaluation].")
  - First 24 hours: Treat if systolic blood pressure greater than 180 mmHg or diastolic blood pressure greater than 105 mmHg.
  - Monitor BP and any corresponding neurological changes in the emergency department and first few days of hospitalization.

- Initiate bleeding precautions:
  - Avoid placement of central venous access or arterial puncture for the first 24 hours.
  - Avoid placement of an indwelling bladder catheter during drug infusion and for at least 30 minutes after infusion ends.
  - Avoid insertion of a nasogastric tube, if possible, during the first 24 hours.
  - Avoid use of anticoagulant, antiplatelet, or non-steroidal anti-inflammatory agents for the first 24 hours.
  - Monitor for central nervous system (CNS) hemorrhage.

- If any signs of CNS hemorrhage (e.g., neurological deterioration, development of severe headache, sudden severe elevation of BP, or new nausea or vomiting) or signs of major systemic hemorrhage, institute the following measures:
  - Discontinue infusion of thrombolytic drug.
  - Obtain hemoglobin, hematocrit, partial thromboplastin time, prothrombin time/INR, platelet count, fibrinogen (also type and crossmatch if transfusions will be needed).
  - Obtain surgical consultation if necessary.
  - Obtain emergent CT head without contrast if CNS hemorrhage suspected.

- Initiate antithrombotic therapy 24 hours after tPA administration (antiplatelet agent or anticoagulant as appropriate). See also Annotation #35, "Initiate Aspirin Unless Contraindicated."
37. Post-ED Medical Management of Volume and Blood Pressure (Not a Thrombolysis Candidate)

**Recommendation:**

- Acutely and during the first 24 hours, clinician may treat extreme hypertension (e.g. systolic > 220 mmHg, diastolic > 120 mmHg or mean arterial blood pressure > 130 mmHg) in patients with acute ischemic stroke not treated with IV tPA. Target for correction of hypertension is a 15% reduction (Weak Recommendation, Low Quality Evidence) (Sandset, 2011; Robinson, 2010; Ahmed, 2009; Castillo, 2004; Willmot, 2003; Leonardi-Bee, 2002).

Treatment of extreme hypertension in patients in the acute stroke phase is widely accepted based on consensus guidelines showing poor outcomes at the far end of the hypertension spectrum (e.g., systolic > 220 mmHg, diastolic > 120 mmHg or mean arterial blood pressure > 130 mmHg). There is no definitive information available yet on the effect of altering blood pressure on outcome during the acute stroke phase. Until there is more information available, a recommendation to treat the extreme and monitor and treat where necessary in the less extreme is warranted.

**Management of Dehydration/Hypotension**

Treatment with a 0.9% normal saline at a rate of 75-125 cc per hour or 2-3 L/day should be initiated to avoid dehydration (Adams, 2007). The rate should be adjusted for febrile patients. IV fluids are particularly important, of course, for patients in whom oral intake is prevented or limited by swallowing problems. Dehydration is common on admission in stroke patients. Deciding if a patient is dry in the setting of the reflex hypertension of acute cerebral is not straightforward, and checking for orthostatic changes in pulse rate or blood pressure is not encouraged in the hyperacute setting. Hypotension relative to the brain's needs may exist, even when blood pressure is conventionally normal. Signals that volume may be low include fluctuating deficit, particularly when correlated with lower pressure, even though the change may be small. A fluid bolus, e.g., 500 cc of normal saline, is warranted if there are questions.

Disturbances related to blood rheology may be a factor in limiting cerebral blood flow in the setting of ischemic stroke. Interventions to affect blood viscosity by lowering hematocrit to increase blood flow have been studied, with some suggestion that they might be useful therapeutically (Wade, 1983; Thomas, 1977). Results have been mixed in studies of hemodilution techniques that decrease blood viscosity utilizing phlebotomy and volume expansion with dextran or pentastarch. Although small clinical trials were promising, when it was subjected to more rigorous study with large controlled trials, this treatment was unsuccessful (Italian Acute Stroke Study Group, 1988; Scandinavian Stroke Study Group, 1987). Proponents of this treatment have argued that results would be improved with earlier time-to-treatment, a more individualized approach with treatment decisions, or a more aggressive hypervolemic hemodilution approach. Additional large-scale trials have, however, not been undertaken. Use of a hypervolemic approach in order to further raise cardiac output by volume expansion was complicated in some cases by cerebral edema and increased mortality, raising questions regarding the safety of this treatment (Hemodilution in Stroke Study Group, 1989). Therefore, hemodilution therapy is not recommended since clinical benefit has not been established. The possibility of risk due to the development of cerebral edema has been suggested, and there is a risk of heart failure.

In conclusion, in the general medical management of patients with stroke, it is important to administer adequate fluids to avoid the development of dehydration and to treat it when present since dehydration with relative hypotension and hemoconcentration may impair cerebral blood flow (Thomas, 1977). Dehydration with hemoconcentration may also increase the risk of thrombus formation and recurrent embolization in cardiogenic stroke (Arboix, 1998; Yasaka, 1993; Yasaka, 1990). Therefore, it is suggested that isotonic...
intravenous fluids be administered to not only those admitted with dehydration or at risk for dehydration due to problems with swallowing, but to all stroke patients. Hypotonic fluids should be avoided because they promote brain swelling.

Management of Hypertension

A full understanding of this issue requires understanding of the physiology. Cerebral blood flow (CBF) is regulated by the relationship between cerebral perfusion pressure (CPP) and cerebrovascular resistance (CVR) (CBF=CPP/CVR). CPP represents the difference between arterial blood pressure forcing the blood into the cerebral circulation and the venous back pressure. Under normal circumstances, the venous back pressure is negligible and CPP is equal to arterial blood pressure. Normally, changes in blood pressure (or CPP) over a wide range have little effect on CBF. This phenomenon, termed autoregulation, is mediated via changes in the CVR. An increase in CPP (or arterial blood pressure) produces vasoconstriction and a decrease produces vasodilation. This autoregulation keeps the cerebral blood flow at a steady level over a range of 60-150 mmHg mean arterial pressure. In individuals with chronic hypertension, the range for autoregulation is shifted upwards so that they may be more tolerant of higher blood pressure and less tolerant of lower blood pressure (decreased cerebral blood flow).

Acute ischemic stroke will cause a change in autoregulation in the ischemic zone by two mechanisms. First, when an artery is occluded, a central core of severe ischemia is produced. This is surrounded by a zone with less reduction in blood flow termed the penumbra where perfusion is maintained by collateral circulation. The blood vessels in the penumbra are maximally dilated, and for that reason blood flow through them may be completely dependent on blood pressure.

Second, during the acute period, the phenomenon of autoregulation even outside of the penumbra can be impaired in patients both with and without persistent arterial occlusion, changing the autoregulation curve so that maintenance of blood flow is completely dependent on the blood pressure.

These abnormalities in autoregulation may persist for days or weeks. There is evidence to suggest that there is slow improvement in disordered autoregulation in the acute period. But early on, lowering the blood pressure may reduce blood flow to critical levels in the ischemic region, potentially extending the area of infarct. This is supported by data from both animal and human studies (Christensen, 2002; Powers, 1993).

Although the potential dangers of lowering arterial blood pressure in patients with acute ischemic stroke are accepted theory influencing practice, documentation of actual risk is based on a few published case reports (Grossman, 1996; Lavin, 1986; Britton, 1980). In conclusion, the theoretical adverse effects of inadvertent overtreatment are substantial.

There are rational but also theoretic arguments for reducing elevated blood pressure in the setting of acute ischemic stroke. Lowering the pressure may reduce edema, blood-brain barrier disruption, and conversion to hemorrhagic infarction. Beginning treatment in the acute setting would be a head start in an important pillar of secondary prevention.

Observational studies and reviews not examining deliberate interventions have suggested a U-shaped relationship between blood pressure and various outcomes with poorer outcomes at very low and very high blood pressures and best outcomes around systolic BP 150 mmHg (Ahmed, 2009; Castillo, 2004; Willmot, 2003; Leonard-Bee, 2002), providing grounds for the current consensus-based guidelines to treat BP if it falls outside of arbitrarily derived thresholds established according to thrombolysis status (see Table 3, "Approach to Elevated Blood Pressure in Acute Ischemic Stroke") (Adams, 2007). To be anticipated is more research to gather evidence about what the thresholds should actually be.

A systematic review of RCTs examining whether deliberately altering blood pressure affected outcome in acute stroke identified 12 trials and 1,153 participants with either acute ischemic stroke or primary intracerebral hemorrhage. It found insufficient evidence to evaluate the outcome of altering blood pressure during the acute stroke phase (Geeganage, 2008).
Several recent randomized trials have not clarified matters, unfortunately. A placebo controlled trial in patients with stroke due to ischemia or hemorrhage assessed safety and outcome efficacy of early BP reduction. Subjects were not on BP medications before the trial and had early post-stroke systolic blood pressure > 160 mmHg. Goal was reduction to 145-155 mmHg or by 15%. The trial was stopped when its funding ran out. It was underpowered to detect efficacy but suggested that mild BP reduction within 36 hours with labetolol or lisinopril was safe (Potter, 2009). Another randomized controlled study on the effects of antihypertensive treatment after stroke examined continuing or stopping antihypertensive medications 24 to 48 hours after onset for a period of two weeks. The study excluded patients with dysphagia and consisted mostly of patients with mild stroke. The study was underpowered to address the efficacy of continuing or stopping antihypertensive medication after acute stroke. It showed no obvious harm in continuing compared to stopping (Robinson, 2010). Another RCT tested starting candesartan vs. placebo for seven days to lower blood pressure in patients with acute stroke onset < 30 hours and a systolic blood pressure of > 140 mmHg. The study, also underpowered, concluded treatment with candesartan was associated with a non-significant increased risk of poor functional outcome at six months compared to placebo. These authors concluded that there is no place for routine blood pressure lowering in the acute stroke phase (Sandset, 2011). Specific parameters remain uncertain.

In the absence of unambiguous data, consensus-based guidelines recommend the following measures (Table 3) for treatment of BP in patients with acute ischemic stroke (AIS).

The information in Table 3 was compiled from manufacturer package inserts and is current as of April 13, 2012. For the most up-to-date medication and prescribing information, consult with your pharmacy or consider the following sources: http://www.epocrates.com, http://www.micromedex.com, http://www.uptodate.com and http://www.pdr.net.

In patients who are on an antihypertensive medication program at the time of the ischemic stroke, these medications are often withheld or halved for the initial 24 hours and reinstated after 24 hours, assuming that oral or tube administration is possible and hypotension is not present (Adams, 2007). Many potential reasons for deviating from this general principle exist. For example, suspension of a beta-blocker in a patient with coronary heart disease may be dangerous, and discontinuation of clonidine may cause rebound hypertension. Recent studies that might bear on the issue have been underpowered to show efficacy in either stopping or starting blood pressure medications during the acute stroke phase (Sandset, 2011; Robinson, 2010; Potter, 2009).

### 38. Other Post-ED Medical Management (First 24-48 Hours)

**Recommendation:**

- Qualified clinicians (i.e., trained and experienced in acute stroke management or supported via telemedicine arrangement by such a clinician) should manage patients with acute ischemic stroke, including diagnosis of mechanism, deployment of case-specific and generic secondary prevention measures, avoidance of complications, initiation of rehabilitative services, provision of patient and family education, in a care setting characterized by interdisciplinarity, experience and expertise with stroke, and availability of rehabilitative services *(Strong Recommendation, High Quality Evidence)* (Xian, 2011; Smith, 2010; Audebert, 2009; Saposnik, 2009; Terént, 2009; Stroke Unit Trialists' Collaboration, 2007).
The reported impact (e.g., number needed to treat for benefit) of optimizing a care setting is substantial, rivaling that of IV tPA. The recommendation then is strong. Supporting evidence appears consistent although not unambiguous. The ambiguity around evidence stems from the plurality of models that have been described, as well as the multiple components involved in the concept. The components broadly include elements such as clinician training and orientation, care processes, organization, and a host of linked procedures, e.g. swallowing protocols, early mobilization and rehabilitation, and patient education. The contributions of individual elements to overall benefit remain uncertain. As a result, implementation of this complex "treatment" is not as straightforward as with other, simpler interventions.

Stroke unit care was the first intervention shown to reduce death, institutionalization, and dependency in individuals entering hospital with acute ischemic or hemorrhagic stroke. The concept dates back at least 30 years, well preceding the other current evidence-based interventions for ischemic stroke, i.e., IV tPA for ischemic stroke (1995), early deployment of aspirin to prevent recurrence of ischemic stroke (1997), and use of decompressive hemicraniectomy for malignant ischemic edema (2009). The stroke unit concept was truly international with reported experiences and randomized trials from many countries, including the U.S. In the 1990s the ad hoc "Stroke Unit Trialists' Collaboration" performed meta-analyses of trial data showing that stroke unit care reduced unfavorable outcomes (death, institutionalization, dependency) by about 20% compared with other care settings. While the concept is well established, a concise definition of stroke unit as an intervention has remained imprecise, presumably because it is a care setting and philosophy rather than a pill or procedure.

The most recent Cochrane review defines stroke unit as organized inpatient care for stroke patients in hospital under a multidisciplinary team that specializes in stroke management. Core characteristics invariably included are "1. Multidisciplinary staffing – that is medical, nursing and therapy staff (usually including physiotherapy, occupational therapy, speech therapy, social work), and 2. Coordinated multidisciplinary team care incorporating meetings at least once per week" (Stroke Unit Trialists' Collaboration, 2009). The stroke unit concept remains alive and healthy at the time of publication of this ICSI guideline.

The Cochrane systematic review, including 31 completed qualifying trials, supports the previously reported ~20% reduction in death, institutionalization and dependency associated with stroke unit care compared with standard care. Improvement in patient outcomes has been found in randomized trials of stroke unit models emphasizing early management through protocol development and clinician education (Middleton, 2011; Audebert, 2009; Audebert, 2006). To this point, no demographic (e.g., age, gender) or clinical (e.g., severity, stroke mechanism, comorbidity) features have identified groups that do not benefit from such care (Smith, 2010; Stroke Unit Trialists' Collaboration, 2009; Saposnik, 2009; Terént, 2009). It has been shown that providing elements of stroke unit (expertise in stroke, multidisciplinarity, early rehabilitative services, clinician education) improves outcome (Audebert, 2009; Audebert, 2006).

The Certified Primary Stroke Center (PSC) concept championed by the Brain Attack Coalition is engrafted upon the older stroke unit concept, retaining the principles of interdisciplinarity, early rehabilitation, early mobilization, ongoing education of staff, and others. The newer principles defining PSCs are coordination of care processes to facilitate deployment of time-sensitive treatments, uniformity of care processes, and quality improvement, including audit and feedback. Emerging data suggest that primary stroke centers do improve survival after ischemic ischemic stroke (Xian, 2011).
Perform Swallow Evaluation

Recommendation:

- Clinician should perform a swallow screening test as soon as feasible on a patient with acute ischemic stroke and withhold oral intake of fluids, medications or food until/unless the screen is successfully passed (*Strong Recommendation, Low Quality Evidence*) *(Schepp, 2011; Lakshminarayan, 2010; Perry, 2001; Odderson, 1995)*.  

Pneumonia is a common and serious complication of acute stroke. Swallow studies have been shown to identify patients at higher risk of aspiration pneumonia. The work group acknowledges that there is no consensus on the best tool to use as a swallowing screen and large studies have not been performed demonstrating decreased rates of pneumonia through the use of a swallow screen. However, the low risk to the patient of performing the intervention of swallow screen, combined with the high morbidity caused by aspiration pneumonia, led the work group to strongly recommend the implementation of a swallow screen for all patients with acute stroke and withholding of oral intake until the screen is successfully passed. It was noted by the work group that this swallow screen should in no way delay the administration of aspirin for patients with acute stroke and that rectal aspirin should be used for those patients who are not able to pass a swallow screen in the acute setting.

Clinicians are encouraged to see the ICSI recommendation for swallow screens prior to administering aspirin, in Annotation #35, "Initiate Aspirin Unless Contraindicated."

Pneumonia is a common finding among patients with acute stroke, its incidence ranging from 6 to 32% *(Perry, 2001)*, and it is associated with stroke-related dysphagia symptoms. Implementation of a coordinated swallow evaluation on all acute stroke patients has been shown to significantly decrease the incidence of pneumonia among patients with acute stroke *(Odderson, 1995)*. Adherence with use of a dysphagia screening tool for patients with acute stroke has been shown to be variable with up to 25% of patients not screened *(Lakshminarayan, 2010)*. When implemented, failing a dysphagia screen has been found to be a predictor of post-stroke pneumonia *(Lakshminarayan, 2010)*. Lack of standardized, high-quality tools has hampered implementation, and a review found only four of 35 protocols met basic quality criteria *(Schepp, 2011)*. Those four protocols included the Barnes Jewish Hospital Stroke Dysphagia Screen, the modified Mann Assessment of Swallowing Ability, The Emergency Physician Swallowing Screen and Toronto Bedside Swallowing Screen Test. Lack of consensus around the best tools to use has also led The Joint Commission to retire the dysphagia screen measure as a performance indicator for certification as a Primary Stroke Center.

Treat Hyperglycemia or Hypoglycemia

Detecting and treating hypoglycemia is a leading priority in managing patients presenting with stroke syndrome. Indeed, the stroke may be cured by giving glucose, since hypoglycemia is a famous stroke mimicer by producing asymmetric neurologic deficits. An evidence-based threshold for giving a bolus of glucose is not established. Consensus of the ICSI work group is to err on side of treating at higher rather than lower threshold, and most would treat below 70 mg/dL. Despite meager proper evidence, the recommendation is strong.

**Recommendation:**

- Clinician may treat hyperglycemia (i.e., 180 mg/dL) in patients with ischemic stroke *(Weak Recommendation, Low Quality Evidence)* *(Johnson, 2009; Adams, 2007; Gray, 2007)*.
Hyperglycemic control, although deemed important to treat, based on expert opinion, has not been adequately studied in the presence of the acute stroke phase. While the ICSI work group recommends that controlling high blood sugar is important, a tight regimen of glucose control has not yet shown improved clinical outcomes.

Most observational studies document either increased mortality or decreased functional outcome, or both, with higher glucose levels. Some have speculated that early hyperglycemia in the setting of acute stroke is simply a marker of physiologic stress and an epiphenomenon in those who have suffered severe stroke (Bruno, 1999; Jorgensen, 1994; Kiers, 1992; Woo, 1990). Others have documented that it is an independent predictor of poor outcome and propose that it has a causative role (Lindsberg, 2004; Baird, 2003; Parson, 2002). Despite the extensive body of literature describing this relationship, a definitive clinical trial of managing hyperglycemia in ischemic stroke patients to improve outcome is still lacking. A randomized pilot study on glucose regulation in acute stroke patients showed the safety and feasibility of using tight glucose control with insulin infusion. The study was not designed or powered to assess efficacy. The author documented the findings as critically important to support the design of future trials (Johnson, 2009). Another study assessed a continuous infusion of insulin, glucose and potassium in the setting of acute ischemic stroke (Gray, 2007). The trial was discontinued due to low enrollment. Significant but modest reductions in glucose level, as well as blood pressure, were seen in those randomized to active treatment. When stopped, it showed no benefit by the primary (mortality) or secondary (death or disability) endpoints. The study was underpowered and had other limitations, making its negative results not definitive. It remains unclear whether early hyperglycemia in the setting of acute stroke is a marker of physiologic stress or an independent predictor of poor outcome. Usual management of hyperglycemia (glucose levels greater than 180 mg/dL) with gentle dosing of subcutaneous insulin, avoiding hypoglycemia, in a timely manner during acute ischemia would seem prudent until ongoing clinical trials address the appropriateness of more aggressive treatment measures (Adams, 2007).

**Initiate Deep Vein Thrombosis (DVT) Prophylaxis**

**Recommendation:**

- Clinician should provide appropriate prophylaxis against deep vein thrombosis in immobilized patients with acute ischemic stroke, weighing risks and benefits of various options.

Select the appropriate prophylaxis, such as unfractionated heparin or low-molecular-weight heparin in patients without contraindications (Strong Recommendation, Moderate Quality Evidence) (Lederle, 2011; Qaseem, 2011; Dennis, 2010; Dennis, 2009; Sherman, 2007).

The evidence to support the prophylaxis for deep vein thrombosis (DVT) in all patients with ischemic stroke in the acute phase is lacking. While a risk for DVT is high and prophylaxis may decrease the incidence, the risk for bleeding and bleeding events may outweigh outcome benefits. Clinicians should weigh the risks and benefits of starting injectable anticoagulants in ischemic stroke patients in the acute stroke phase and proceed with caution.

One may consider DVT prophylaxis in any patient admitted to the hospital with lower extremity weakness related to an ischemic stroke. The risk of DVT is high (25-50%), and prophylaxis with parenteral anticoagulant decreases the incidence (10-20%). The risk of pulmonary embolism (PE) appears to be decreased, as well, although numbers have been small and statistical significance not achieved (Counsell, 2001).
The PREVAIL Trial compared the low-molecular-weight enoxaparin (40 mg/day) with unfractionated heparin (5,000 units twice daily) for 10 days after stroke preventing walking. There was a 43% reduction in the incidence of venous thromboembolism in the enoxaparin group (10%), compared with the unfractionated heparin group (18%). Overall bleeding rates were similar. Based on this trial, low-molecular-weight heparin is superior to unfractionated heparin in prevention of venous thromboembolism after stroke with inability to ambulate (Sherman, 2007).

Low-molecular-weight heparin is renally cleared. For patients with a CrCl less than 30 mL/min, use unfractionated heparin. The patient should be monitored for the possible development of heparin-induced thrombocytopenia (HIT) and bleeding. Obtain a platelet count and hemoglobin every other day, beginning on the second day of heparin therapy.

Systematic review of multiple randomized controlled trials show prophylaxis for venous thromboembolism with heparin or low-molecular-weight heparin may decrease pulmonary embolism in medical patients and patients with stroke combined. However, review also shows an increased risk for bleeding and major bleeding events, and had no statistically significant effect on mortality (Lederle, 2011). Clinicians may choose to use heparin (for patient with CrCl < 30 ml/min) or low-molecular-weight heparin (LMWH) for venous thromboembolism prevention in patients with stroke based on the assessment of risk for thromboembolism and risk of bleed (Qaseem, 2011).

All patients should receive patient education that includes signs and symptoms of venous thromboembolism (VTE) and therapy options, and encouraged to ambulate early and perform flexion/extension exercises (Geerts, 2004). Thigh-length graduated elastic compression stockings have been shown in a randomized trial not to be effective in reducing risk of deep vein thrombosis after stroke (Clots Trials Collaboration, The, 2009). Interestingly, the same trialists found below-the-knee stockings to be inferior to thigh-length graduated elastic compression stockings, suggesting that the former may predispose to deep vein thrombosis (Clots Trials Collaboration, The, 2010). Intermittent pneumatic compression should be considered for patients at high risk for VTE who have contraindications to pharmacologic prophylaxis.

See the ICSI Antithrombotic Therapy Supplement and ICSI Venous Thromboembolism Prophylaxis guideline.

**Initiate Rehabilitation Early**

**Recommendation:**

- Clinician should mobilize patients with acute ischemic stroke as soon as possible, monitoring for and avoiding postural hypotension (Strong Recommendation, Moderate Quality Evidence) (Cumming, 2011; Craig, 2010; Langhorne, 2010).

The work group recommends early mobilization in the first 24 hours following an acute stroke, though it is currently unclear if the benefit is derived from the early mobilization or the increased duration of therapy received when patients with acute stroke are mobilized early. Early mobilization of patients with acute stroke appears to improve functional outcomes based on two randomized controlled trials. This intervention poses little to no harm to the patient, but does require increased availability of physical therapists in the hospital setting.

Early mobilization within 24 hours of admission, in the form of early initiation of appropriate rehabilitation swivels or other nursing intervention, is advocated for the purpose of preventing complications related to immobility, including deep vein thrombosis, contractures, joint disorders, and pressure sores/decubitus ulcers. Randomized controlled trials have demonstrated improved functional outcomes with mobilization in the first 24 hours following an acute stroke (Cumming, 2011; Craig, 2010; Langhorne, 2010). These studies were both confounded by the duration of therapy for the intervention group receiving approximately 100 more minutes of therapy compared to the control group.
Assess Risk of Falls

- Stroke patients have a high risk of falling. A falls assessment is recommended for a patient admitted to the hospital for acute stroke.
- Implement falls mitigation strategies.

Perform Nutritional Status Assessment

Assessment of the patient's baseline nutritional status and the implementation of treatments to correct any major nutritional problems are recommended (Adams, 2007). Poor nutritional status in patients admitted for stroke is associated with increased morbidity and mortality (Food Trial Collaboration, 2003). However, a trial did not find benefit in administering nutritional supplementation (Food Trial Collaboration, 2005).

Treatments for Complications of Ischemic Brain Edema

Recommendation:

- Qualified specialists (i.e., appropriately trained clinicians in neurocritical care, neurointerventional procedures or neurosurgery) should treat selected and qualifying ischemic stroke patients showing evidence of increased intracranial pressure with appropriate surgical intervention:
  1. Ventricular drainage for hydrocephalus (Adams, 2007)
  2. Surgical decompression of large cerebellar infarcts (Adams, 2007; Hornig, 1994)
  3. Hemicraniectomy for malignant middle cerebral infarction in patients age < 60 years (Hofmeijer, 2009; Vahedi, 2007a; Vahedi, 2007b)


Ventricular drainage for hydrocephalus and suboccipital craniectomy for large cerebellar infarcts can be life-saving procedures compatible with excellent functional recovery. Evidence supporting these treatments consists merely of case series. There is extensive experience demonstrating their value, and it is extremely unlikely that more studies will be conducted in the future. Decompressive hemicraniectomy for patients ≤ 60 years with massive hemispheric brain infarctions, however, is supported by randomized controlled trial data. The decision to opt into such surgery must stem from the patient's and family's values, especially considering the risk of disability post-hemicraniectomy. This surgery decreases mortality and improves the chances of recovery of functional independence. However, patients and families should be informed that moderate or severe neurological sequelae are likely despite surgery. A shared decision-making process should be pursued when discussing the intervention, and patient values must be carefully considered. At present, this surgical intervention has no proven value for patients older than 60 years.

Although ischemic brain swelling typically peaks between three and five days after stroke onset, marked early swelling (in the first 24-48 hours) causing mass effect and tissue shift can occur in the most severe cases ("malignant" ischemic brain edema). Low attenuation changes exceeding two-thirds of the middle cerebral artery territory and large areas of hypoperfusion on perfusion scans (computed tomography [CT] perfusion or magnetic resonance perfusion) on initial radiological evaluation are associated with high risk of developing malignant brain edema. Patients with these features should be strictly monitored with serial neurological examinations, ideally in a stroke unit. Repeating CT scan of the brain to evaluate for progression of regional mass effect is indicated if the patient develops any signs of neurological deterioration. The value of serial CT scans of the brain in the absence of clinical changes remains to be established.
Decompressive hemicraniectomy with durotomy improves survival and functional outcome (Vahedy, 2007b). The optimal timing of the procedure is not well established, but most experts recommend early intervention. Improvement in functional outcome has been shown only for patients 60 years old or younger.

Osmotherapy (mannitol 20% or hypertonic saline) may be used to treat ischemic brain edema, but there is very limited data supporting its value (Bardutzky, 2007). Mannitol 20% is usually administered as a bolus of 1-2 g/kg of body weight, followed by repeated boluses as needed for neurological decline or scheduled doses of 0.25 to 0.5 g/kg every four to six hours. In patients with established signs of herniation, a rescue dose of 23.4% of saline solution (30 cc) may be useful (Koenig, 2008).

Hyperventilation should be avoided except for mild to moderate hyperventilation (target pCO₂ 30-34 mmHg) for brief periods of time because of the risk of exacerbating ischemia by causing vasoconstriction.

**Treat Hyperthermia**

**Recommendation:**

- Clinician should treat hyperthermia (i.e., temperature > 38°C) with specific measures (e.g., antibiotics targeted to discovered infections) and/or non-specific measures (e.g., cooling blankets, acetaminophen) in patients with acute ischemic stroke (Strong Recommendation, Low Quality Evidence) (Broessner, 2009; Hajat, 2000; Wang, 2000b; Castillo, 1998; Reith, 1996; Azzimondi, 1995; Terént 1981).

While evidence is low quality, the recommendation is strong because of observational information that fever is associated with poor outcome. Treating fever will never be subjected to a clinical trial with a control group deprived of treatment because it would be unethical. The work group prioritizes concrete and persuasive experience of vulnerability of injured brain over the lack of trial data. At this time there is insufficient evidence to make a recommendation about temperature reduction in normothermic patients.

The acutely injured brain, whether due to trauma or ischemia, is inordinately susceptible to the damaging effects of brain temperature elevation. This fact is well supported by both animal and human studies (Ginsberg, 1998; Terént, 1981).

In human studies, early hyperthermia in acute stroke is associated with increased risk of poor outcome, higher mortality and increased infarct volume (Azzimondi, 1995; Castillo, 1998; Hajat, 2000; Reith, 1996). The causality and the relationship of temperature elevation to these poor outcomes are not fully understood. Whether intervention with cooling methods will result in improved outcomes is unknown.

Interventions for patients with temperatures of greater than 99.5°F (37.5°C) include appropriate dosing of acetaminophen (1 gram orally or 650 mg rectally every four to six hours, not to exceed 4 grams in 24 hours) and regular monitoring of temperature status (every four hours). A recent phase III trial of this approach in patients with 96.8-102.2°F (36-39°C) failed to identify benefit in primary analysis and does not support routine use of acetaminophen for cooling in normothermic patients, although possible benefit was shown post hoc in those with mild to moderate temperature elevation in the 96.8-102.2°F (37-39°C) range (den Hertog, 2009). For those patients with extreme hyperthermia, greater than 103°F (39.4°C), aggressive interventions, including cooling blankets and ice packs, are encouraged. Causes for temperature elevation should be sought and treated.

Mild hypothermia is an established neuroprotectant in the laboratory model. At the clinical level, mild hypothermia has shown benefits in patients who have experienced a cardiac arrest (Oommen, 2011). However, the role of hypothermia in ischemic stroke therapy has yet to be established (Hemmen, 2010).
The Aims and Measures section is intended to provide guideline users with a menu of measures for multiple purposes, which may include the following:

- Population health improvement measures
- Quality improvement measures for delivery systems
- Measures from regulatory organizations such as The Joint Commission
- Measures that are currently required for public reporting
- Measures that are part of Center for Medicare Services Physician Quality Reporting initiative
- Other measures from local and national organizations aimed at measuring population health and improvement of care delivery

This section provides resources, strategies and measurement for use in closing the gap between current clinical practice and the recommendations set forth in the guideline.

The subdivisions of this section are:

- Aims and Measures
- Implementation Recommendations
- Implementation Tools and Resources
- Implementation Tools and Resources Table
Aims and Measures

1. Increase the percentage of patients age 18 years and over presenting in time for IV tPA to be initiated within three hours, or up to 4.5 hours for patients meeting selected criteria of stroke onset who are evaluated within 10 minutes of arriving in the emergency department. Under usual circumstances, these time-related goals should be achievable for patients presenting to an appropriate treatment setting within 2 hours and 30 minutes, and 4 hours of symptom onset, respectively.

Measure for accomplishing this aim:

a. Percentage of patients presenting within three hours, or up to 4.5 hours for patients meeting selected criteria of stroke onset who are evaluated by a clinician within 10 minutes of arriving in the emergency department.

2. Increase the percentage of patients age 18 years and over at high risk for stroke presenting with TIA symptoms within 24 hours who are admitted to the hospital inpatient or observational unit or undergo identical assessment in an expedited outpatient program.

Measure for accomplishing this aim:

a. Percentage of patients with first TIA in the preceding 24 hours who are admitted to the inpatient service, observational unit or expedited outpatient TIA clinic.

3. Increase the percentage of patients age 18 years and over receiving appropriate thrombolytic and appropriate antithrombotic therapy for ischemic stroke (tPA and aspirin, other antiplatelet agents, or an anticoagulant).

Measures for accomplishing this aim:

a. Percentage of eligible patients with ischemic stroke treated with tPA.

b. Percentage of patients who are not candidates for tPA treatment who receive aspirin within 24 hours of hospitalization, after a negative head CT, unless contraindicated.

c. Percentage of eligible patients receiving tPA according to guideline. (Refer to Annotations #30 and 33)

d. Percentage of patients with stroke symptoms who are candidates for tPA with a "door to drug" time (time of arrival to time of drug administration) of less than 60 minutes.

e. Percentage of patients with stroke symptoms who undergo a computed tomography scan within 25 minutes of arrival in the emergency department.

4. Increase the percentage of tPA non-recipients who have hypertension appropriately managed in the first 48 hours of hospitalization or until neurologically stable.

Measure for accomplishing this aim:

a. Percentage of tPA non-recipients who have hypertension appropriately managed in the first 48 hours of hospitalization or until neurologically stable.

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5. Increase the percentage of stroke patients age 18 years and over who receive appropriate medical management within the initial 24-48 hours of diagnosis for prevention of complications such as:
   - Dehydration
   - Aspiration
   - Hypoglycemia and hyperglycemia
   - Deep vein thrombosis
   - Immobility
   - Falling
   - Nutritional status decline
   - Hyperthermia

Measures for accomplishing this aim:

a. Percentage of ischemic stroke patients with hyper- or hypoglycemia who receive appropriate intervention.

b. Percentage of ischemic stroke patients with hyperthermia who receive appropriate intervention.

c. Percentage of ischemic stroke patients with dehydration who receive intravenous fluids.

d. Percentage of ischemic stroke patients with paralysis or other reason for immobility who receive appropriate prevention for venous thromboembolism (subcutaneous heparin or pneumatic compression device).

e. Percentage of ischemic stroke patients who are assessed with a swallow screening test before receiving food, fluids or medications by mouth.

f. Percentage of ischemic stroke patients mobilized from bed within 24 hours of admission.

6. Improve patient and family education of patients with ischemic stroke in both the emergency department and the admitting hospital unit.

Measures for accomplishing this aim:

a. Percentage of patients presenting in the emergency department with ischemic stroke for whom patient/family education is documented in the medical record.

b. Percentage of patients admitted to a hospital unit with ischemic stroke for whom patient/family education is documented in the medical record.
Measurement Specification

Measurement #1a
Percentage of patients presenting within three hours, or up to 4.5 hours for patients meeting selected criteria of stroke onset who are evaluated by a clinician within 10 minutes of arriving in the emergency department.

Population Definition
Adults patients age 18 years and older initially presenting with acute symptoms of ischemic stroke.

Data of Interest
- # of patients evaluated by a clinician within 10 minutes of arriving in the emergency department
- # of patients presenting within three hours, or up to 4.5 hours for patients meeting selected criteria of stroke onset

Numerator/Denominator Definitions
Numerator: Number of patients evaluated by a clinician within 10 minutes of arriving in the emergency department.
Denominator: Number of patients presenting within three hours, or up to 4.5 hours for patients meeting selected criteria of stroke onset.

Method/Source of Data Collection
Review medical records for patients meeting criteria under Population Definition who presented within three hours, or up to 4.5 hours for patients meeting selected criteria of stroke onset and determine whether they were evaluated by a clinician within 10 minutes of arriving in the emergency department.

Time Frame Pertaining to Data Collection
Monthly.

Notes
This is a process measure, and improvement is noted as an increase in the rate.

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Measurement #2a

Percentage of patients with documentation of clinical TIA symptoms admitted within the last 24 hours to the hospital, observation unit or expedited outpatient TIA clinic.

Population Definition

Patients age 18 years and older initially presenting with TIA.

Data of Interest

\[
\frac{\text{# of patients with documentation of clinical TIA symptoms within the last 24 hours}}{\text{# of patients admitted to the hospital, observation unit or expedited outpatient TIA clinic}}
\]

Numerator/Denominator Definitions

Numerator: Number of patients with documentation of clinical TIA symptoms within the last 24 hours.

Denominator: Number of patients admitted to the hospital, observation unit or expedited outpatient TIA clinic.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition who were admitted to the hospital, observation unit or expedited outpatient TIA clinic.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.
Measurement #3a

Percentage of eligible patients with ischemic stroke treated with tPA.

Population Definition

Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke who are eligible for tPA.

Data of Interest

\[
\frac{\text{# of patients treated with tPA}}{\text{# of patients eligible for tPA}}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who were treated with tPA.

Denominator: Number of patients eligible for tPA treatment.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients treated with tPA.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

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Measurement #3b

Percentage of patients who are not candidates for tPA treatment who receive aspirin within 24 hours of hospitalization, after a negative head CT, unless contraindicated.

Population Definition

Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke who are not eligible for tPA.

Data of Interest

\[
\text{# of patients treated with aspirin within 24 hours of hospitalization, after a negative head CT, unless contraindicated} \div \text{# of patients not eligible for tPA}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who were treated with aspirin within 24 hours of hospitalization, after a negative head CT, unless contraindicated.

Denominator: Number of patients not eligible for tPA treatment.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients treated with aspirin within 24 hours of hospitalization, after a negative head CT, unless contraindicated.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

Return to Table of Contents
Measurement #3c

Percentage of eligible patients receiving tPA according to guideline. (Refer to Annotations #29 and 30.)

Population Definition

Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke who are eligible for tPA.

Data of Interest

\[
\frac{\text{# of patients treated with tPA according to guideline}}{\text{# of patients eligible for tPA and treated with tPA}}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who were treated with tPA according to guideline.
Denominator: Number of patients eligible for tPA treatment and treated with tPA.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients treated with tPA according to guideline.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.
Measurement #3d

Percentage of patients with stroke symptoms who are candidates for tPA with a "door to drug" time (time of arrival to time of drug administration) of less than 60 minutes.

Population Definition

Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke who are eligible for tPA.

Data of Interest

\[
\frac{\text{# of patients treated with tPA with a "door to drug" time of less than 60 minutes}}{\text{# of patients eligible for tPA and treated with tPA}}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who were treated with tPA with a "door to drug" time of less than 60 minutes.

Denominator: Number of patients eligible for tPA treatment and treated with tPA.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients treated with tPA and "door to drug" time of less than 60 minutes.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.
Measurement #3e
Percentage of patients with stroke symptoms who undergo a computed tomography scan within 25 minutes of arrival in the emergency department.

Population Definition
Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke.

Data of Interest
\[
\frac{\text{# of patients with CT scan within 25 minutes of arrival in the emergency department}}{\text{# of patients with stroke symptoms}}
\]

Numerator/Denominator Definitions
Numerator: Number of patients who had a CT scan within 25 minutes of arrival in the emergency department.
Denominator: Number of patients presenting with acute symptoms of ischemic stroke.

Method/Source of Data Collection
Review medical records for patients meeting criteria under Population Definition and determine the number of patients who had CT scan within 25 minutes of arrival in the emergency department.

Time Frame Pertaining to Data Collection
Monthly.

Notes
This is a process measure, and improvement is noted as an increase in the rate.
Measurement #4a

Percentage of tPA non-recipients who have hypertension appropriately managed in the first 48 hours of hospitalization or until neurologically stable.

Population Definition

Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke and not receiving tPA for their symptoms.

Data of Interest

\[
\text{Number of patients who have hypertension managed in the first 48 hours of hospitalization or until neurologically stable} \\
\div \text{Number of patients who are non-tPA recipients}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who have hypertension managed in the first 48 hours of hospitalization or until neurologically stable. Refer to guideline for detailed description of appropriate management.

Denominator: Number of patients presenting with acute symptoms of ischemic stroke who are non-tPA recipients.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients who had hypertension managed in the first 48 hours of hospitalization or until neurologically stable.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.
Measurement #5a

Percentage of patients who receive appropriate intervention for hypoglycemia and hyperglycemia.

Population Definition

Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke.

Data of Interest

\[
\text{# of patients who have appropriate intervention for hypoglycemia and hyperglycemia} / \text{# of patients who present with acute symptoms of ischemic stroke, and hypoglycemia and hyperglycemia}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who have appropriate intervention for hypoglycemia and hyperglycemia. Refer to guideline for detailed description of appropriate management.

Denominator: Number of patients presenting with acute symptoms of ischemic stroke.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients who have appropriate intervention for hypoglycemia and hyperglycemia.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.
**Measurement #5b**

Percentage of patients who receive appropriate intervention for hyperthermia.

**Population Definition**

Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke.

**Data of Interest**

\[ \frac{\text{# of patients who have appropriate intervention for hyperthermia}}{\text{# of patients who present with acute symptoms of ischemic stroke}} \]

**Numerator/Denominator Definitions**

Numerator: Number of patients who have appropriate intervention for hyperthermia. Refer to guideline for detailed description of appropriate management.

Denominator: Number of patients presenting with acute symptoms of ischemic stroke.

**Method/Source of Data Collection**

Review medical records for patients meeting criteria under Population Definition and determine the number of patients who have appropriate intervention for hyperthermia.

**Time Frame Pertaining to Data Collection**

Monthly.

**Notes**

This is a process measure, and improvement is noted as an increase in the rate.

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Measurement #5c
Percentage of patients with dehydration who receive intravenous fluids.

Population Definition
Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke.

Data of Interest
\[
\text{# of patients who receive IV fluids} \over \text{# of patients who present with acute symptoms of ischemic stroke and dehydration}
\]

Numerator/Denominator Definitions
Numerator: Number of patients who receive IV fluids.
Denominator: Number of patients presenting with acute symptoms of ischemic stroke and dehydration.

Method/Source of Data Collection
Review medical records for patients meeting criteria under Population Definition and determine the number of patients who receive IV fluids.

Time Frame Pertaining to Data Collection
Monthly.

Notes
This is a process measure, and improvement is noted as an increase in the rate.

Return to Table of Contents
Measurement #5d

Percentage of patients with ischemic stroke with paralysis or other reason for immobility receiving appropriate prevention for venous thromboembolism (subcutaneous heparin or pneumatic compression device).

Population Definition

Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke.

Data of Interest

\[
\frac{\text{# of patients who have appropriate prevention for VTE}}{\text{# of patients who present with acute symptoms of ischemic stroke and paralysis or other reason for immobility}}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who have appropriate prevention for VTE such as subcutaneous heparin or pneumatic compression device.

Denominator: Number of patients presenting with acute symptoms of ischemic stroke and paralysis or other reason for immobility.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients who have appropriate prevention for VTE.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

Return to Table of Contents
Measurement #5e

Percentage of ischemic stroke patients who are assessed with a swallow screening test before receiving food, fluids or medications by mouth.

Population Definition

Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke.

Data of Interest

\[
\frac{\text{# of patients who receive an early swallow evaluation}}{\text{# of patients who present with acute ischemic stroke}}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who were screened for dysphagia before taking any food, fluids or medication (including aspirin) by mouth.

Denominator: Number of all patients presenting with symptoms of acute ischemic stroke.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients who have an early swallow evaluation.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

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Measurement #5f

Percentage of patients mobilized from bed within 24 hours of admission.

Population Definition

Patients age 18 years and older initially presenting with acute ischemic stroke.

Data of Interest

\[
\frac{\# \text{ of patients who are mobilized from bed within 24 hours of admission}}{\# \text{ of patients who present with acute symptoms of ischemic stroke}}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who are mobilized from bed within 24 hours of admission.
Denominator: Number of patients presenting with symptoms of ischemic stroke.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients were mobilized from bed within 48 hours of admission.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

Return to Table of Contents
Measurement #6a

Percentage of patients presenting in the emergency department with ischemic stroke for whom patient/family education is documented in the medical record.

Population Definition

Patients age 18 years and older initially presenting with acute ischemic stroke and presenting in the emergency department.

Data of Interest

\[
\frac{\text{# of patients who have education documentation}}{\text{# of patients with acute symptoms of acute ischemic stroke}}
\]

Numerator/Denominator Definitions

Numerator: Number of patients who have education documentation.

Denominator: Number of patients presenting with symptoms of acute ischemic stroke.

Method/Source of Data Collection

Review medical records for patients meeting criteria under Population Definition and determine the number of patients who had education documentation.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

Return to Table of Contents
Measurement #6b
Percentage of patients admitted to a hospital unit with ischemic stroke for whom patient/family education is documented in the medical record.

Population Definition
Patients age 18 years and older initially presenting with acute symptoms of ischemic stroke and admitted to a hospital unit with ischemic stroke.

Data of Interest
\[
\frac{\text{# of patients who have education documentation}}{\text{# of patients with acute symptoms of acute ischemic stroke}}
\]

Numerator/Denominator Definitions
Numerator: Number of patients who have education documentation.
Denominator: Number of patients presenting with symptoms of acute ischemic stroke.

Method/Source of Data Collection
Review medical records for patients meeting criteria under Population Definition and determine the number of patients who had education documentation.

Time Frame Pertaining to Data Collection
Monthly.

Notes
This is a process measure, and improvement is noted as an increase in the rate.

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Implementation Recommendations

Prior to implementation, it is important to consider current organizational infrastructure that address the following:

- System and process design
- Training and education
- Culture and the need to shift values, beliefs and behaviors of the organization.

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline:

- Hospitals should consider developing and implementing critical pathways, standing orders and a stroke process to accomplish rapid evaluation and treatment. The process should expedite the evaluation and treatment of patients who are candidates for intravenous tPA and assure uniform, guideline-driven care for all patients with respect to issues like:
  - diagnosis of mechanism,
  - initiation of appropriate secondary prevention,
  - prevention of complications, and
  - early assessment for and early employment of rehabilitative services.

- A process should be in place for the patient and family that will rapidly orient them to the suspected diagnosis, emergency department process, tests to be performed, tPA treatment and its risks, and other treatment measures to be considered. This could include both face-to-face interactions with the patient and family by the caregiver, and teaching tools in written form.

System Improvement

There is evidence that benchmarking can guide and drive quality improvement. Using essentially the same quality indicators as The Joint Commission (TJC) and ICSI, programs like the American Heart Association’s Get With The Guidelines-Stroke (LaBresh, 2008; Schwamm, 2009b) and the Paul Coverdell National Acute Stroke Registry (Stoeckle-Roberts, 2006) have been shown to improve the quality of stroke care, as well as hard outcomes, like mortality (Xian, 2011).

Centers for Medicare and Medicaid Services


The Joint Commission (TJC) Primary Stroke Center Certification

TJC offers certification as Primary Stroke Centers to hospitals that meet specific qualifications. The focus is on the early recognition and management of stroke, and the scope of accreditation includes integrated efforts in public awareness, emergency medical services, emergency department and hospitalization (Alberts, 2011; Alberts, 2000). The link is http://www.jointcommission.org/certification/primary_stroke_centers.aspx (last accessed May 24, 2012).

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Beginning in October 2009, all TJC-accredited hospitals are required to submit the eight National Quality Forum-endorsed stroke consensus measures.

Among the requirements for TJC certification as a Primary Stroke Center is ongoing process improvement guided by data and benchmarking. The quality indicators chosen by TJC overlap with those developed by the ICSI Diagnosis and Initial Treatment of Ischemic Stroke guideline work group. The TJC quality indicators are:

1. Deep Vein Thrombosis (DVT) Prophylaxis*
2. Discharged on Antithrombotics*
3. Patients with Atrial Fibrillation Receiving Anticoagulation Therapy*
4. Thrombolytic Therapy Administered (in eligible patients)
5. Antithrombotic Therapy by End of Hospital Day Two
6. Discharged on Cholesterol Reducing Medication
7. Dysphagia Screening **
8. Stroke Education
9. Smoking Cessation/Advice Counseling **
10. Assessed for Rehabilitation

* Initial standard stroke measure set.

** Note: indicators for 7 and 9 are not currently (as of 2010) required by The Joint Commission. The remaining eight indicators are required. These eight are also endorsed by the National Quality Forum.

Measures 1, 4, 5, 7, 8 and 10 are similar to or identical to those measures listed in this document and within the scope of the guideline.

The Minnesota Department of Health (MDH)

The MDH has been leading working groups of stakeholders in stroke care across the state of Minnesota in planning a system to support care of acute stroke in all parts of the state. The groups include representatives of hospitals and emergency medical services, as well as primary care and specialty clinicians from large and small, urban and rural hospitals. The care issues include facilitation of reperfusion therapies in selected patients and according to guidelines but also continuing care issues such as those articulated by TJC for primary and comprehensive stroke centers. The role of "stroke-ready" hospitals is under current discussion.
Implementation Tools and Resources

Criteria for Selecting Resources

The following tools and resources specific to the topic of the guideline were selected by the work group. Each item was reviewed thoroughly by at least one work group member. It is expected that users of these tools will establish the proper copyright prior to their use. The types of criteria the work group used are:

- The content supports the clinical and the implementation recommendations.
- Where possible, the content is supported by evidence-based research.
- The author, source and revision dates for the content is included where possible.
- The content is clear about potential biases and when appropriate conflicts of interests and/or disclaimers are noted where appropriate.

Resources Available to ICSI Members Only

ICSI has knowledge resources that are only available to ICSI members (these are indicated with an asterisk in the far left-hand column of the Resources Table). In addition to the resources listed in the table, ICSI members have access to a broad range of materials including tool kits on Continuous Quality Improvement processes and Rapid Cycling that can be helpful. To obtain copies of these or other Resources, go to the Education and Quality Improvement page on the ICSI Web site. To access these materials on the Web site, you must be logged in as an ICSI member.

The resources in the table on the next page that are not reserved for ICSI members are available to the public free-of-charge unless otherwise indicated.

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### Implementation Tools and Resources Table

<table>
<thead>
<tr>
<th>Author/Organization</th>
<th>Title/Description</th>
<th>Audience</th>
<th>Web Sites/Order Information</th>
</tr>
</thead>
</table>
| American Association of Neuroscience Nurses (AANN) | * Professional association's Web site  
* Patient education resources                                                               | Health Care Clinicians            | [http://www.aann.org](http://www.aann.org)                                                  |
| ASA (American Stroke Association)          | * Comprehensive Web site  
* Patient education resources                                                                                                                     | Health Care Clinicians; Patients and Families | [http://www.strokeassociation.org/STROKEORG](http://www.strokeassociation.org/STROKEORG) |
| Association of Black Cardiologists         | * Patient education resources  
* Mission to eliminate cardiovascular disparities through education, research and advocacy                                                                | Health Care Clinicians; Patients and Families | [http://www.abcardio.org](http://www.abcardio.org)                                          |
| The Brain Attack Coalition                 | * Contains tools for health care professionals developing systems to enable the rapid diagnosis and treatment of acute stroke  
* Patient education resources                                                                | Health Care Clinicians; Patients and Families | [http://www.stroke-site.org/](http://www.stroke-site.org/)                                |
| Demaerschalk                              | This article offers a practical presentation of how telemedicine can be set up for stroke. Helpful information for those considering entry to telestroke arrangements. | Health Care Clinicians            | [Mayo Clinic Proc. 2009;84(1):53-64 Stroke Telemedicine](http://stroke.ahajournals.org/content/40/5/1793.full.pdf) |
| GLRSN (Great Lakes Regional Stroke Network) | * Comprehensive Web site  
* Patient education resources                                                                                                                     | Health Care Clinicians; Patients and Families | [http://tigger.uic.edu/depts/glstrknet/](http://tigger.uic.edu/depts/glstrknet/)           |
| Gropen                                    | A report from a cutting-edge consortium that prioritizes system and policy changes to implement stroke systems of care. Recommendations for multi-state regional collaboratives to decrease rural/urban disparities through uniform stroke care systems. | Health Care Clinicians            | [http://stroke.ahajournals.org/content/40/5/1793.full.pdf](http://stroke.ahajournals.org/content/40/5/1793.full.pdf) |
| Institute for Clinical Systems Improvement | Shared Decision-Making (SDM) model is available to ICSI members. A quality improvement pilot study was launched in 2010 tracing the rates of SDM by clinical groups adopting the Collaborative Conversations™ model. | Health Care Clinicians            | [http://www.icsi.org/health_care_redesign_/shared_decision-making/](http://www.icsi.org/health_care_redesign_/shared_decision-making/) |

* Available to ICSI members only.
# Implementation Tools and Resources Table

<table>
<thead>
<tr>
<th>*</th>
<th>Author/Organization</th>
<th>Title/Description</th>
<th>Audience</th>
<th>Web Sites/Order Information</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minnesota Stroke Association</td>
<td>• Patient education resources</td>
<td>Patients and Families</td>
<td><a href="http://www.strokemn.org/">http://www.strokemn.org/</a></td>
</tr>
<tr>
<td></td>
<td>NSA (National Stroke Association)</td>
<td>• Comprehensive Web site</td>
<td>Health Care Clinicians; Patients and Families</td>
<td><a href="http://www.stroke.org">http://www.stroke.org</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Patient education resources</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Links to survivor/caregiver products and services and additional related Web sites</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NINDS (National Institute of Neurological Disorders and Stroke)</td>
<td>• Links to clinical trials</td>
<td>Health Care Clinicians; Patients and Families</td>
<td><a href="http://www.ninds.nih.gov/">http://www.ninds.nih.gov/</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Contains entire discussion and guidelines for system change to address stroke treatment</td>
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<tr>
<td></td>
<td>Web MD</td>
<td>Site for medical information for general public</td>
<td>Patients and Families</td>
<td><a href="http://webmd.com/stroke/default.htm">http://webmd.com/stroke/default.htm</a></td>
</tr>
</tbody>
</table>

* Available to ICSI members only.

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ICSI Order Sets utilize two types of boxes for orders. One is the open box that clinicians will need to check for the order to be carried out. The second box is a pre-checked box; orders that have strong evidence and/or are standard of care and require documentation if the clinician decides to "uncheck" the order.

Organizations are recognizing the benefit of using pre-checked boxes for other orders to promote efficiency. Organizations are encouraged, through a consensus process, to identify those orders to utilize pre-checked boxes to increase efficiency, reduce calls to clinicians, and to reduce barriers for nursing and other professionals to provide care that is within their scope.

Throughout the order set you will note annotation numbers. These annotation numbers correspond with the guideline itself and provide associated discussion and evidence when available.

It is assumed that clinicians will supplement this information from standard pharmaceutical sources to inform their decisions for individual patients.

Order sets are available in MS Word format at http://www.icsi.org.

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Order Set – Admission for Ischemic Stroke for Patients not Receiving tPA

This order set pertains to those admission orders from ER or direct admit to the hospital for patients 18 years or older who present with symptoms of recent neurologic dysfunction suggestive of brain ischemia. These orders exclude patients with TIA, hemorrhagic stroke or ischemic stroke receiving thrombolytic therapy.

Patient Information (Two are required.)

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Last Name:</td>
<td>_________________________</td>
</tr>
<tr>
<td>First Name:</td>
<td>_________________________</td>
</tr>
<tr>
<td>Date of Birth:</td>
<td>__ / __ / ______</td>
</tr>
<tr>
<td>Patient’s age:</td>
<td>______</td>
</tr>
<tr>
<td>ID #:</td>
<td>_________________________</td>
</tr>
</tbody>
</table>

Admitting Data

Admit to:
- □ ICU bed
- □ Step down: □ with telemetry □ without telemetry
- □ Stroke/neurology: □ with telemetry □ without telemetry
- □ Other ________________________________

Attending physician: ________________________________

Primary physician: ________________________________
- □ Contact primary care physician

Notify stroke nurse clinicians ________________________________
- □ Notify stroke research team if that patient is eligible for stroke research

Diagnosis

Admitting Dx:
- □ Acute ischemic infarct
- □ Other ________________________________

Secondary Dx: ________________________________

Patient excluded from thrombolytic therapy (tPA) due to:
- □ Time from onset contraindications
- □ Clinical contraindications
- □ Patient history contraindications
- □ Laboratory contraindications
- □ Radiologic contraindications
- □ Other ________________________________

Condition
- □ Stable   □ Unstable   □ Other ________________________________

Code Status
- □ Full code
- □ DNR/DNI
- □ Unknown

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Vitals

☑ Telemetry/monitor for first 24 hours:
  ■ Notify physician if EKG or telemetry is suspicious for atrial fibrillation

☐ Telemetry/monitor for 48 hours
  ■ Notify physician if EKG or telemetry is suspicious for atrial fibrillation

☑ Vital signs (BP, heart rate and O2 sat) and non-NIHSS neuro check:
  ☑ every hour for 4 hours then
  ☑ every 4 hours while awake (if stable)

☐ Notify physician for antihypertensives required for blood pressure greater than 220 mmHg systolic or
  120 mmHg diastolic

☐ Notify physician for antihypertensives required for blood pressure greater than _______ mmHg systolic or
  mean arterial pressure greater than _______ mmHg after the first 24 hours.

☐ Notify physician if blood pressure is less than _______ mmHg or systolic _______ mmHg diastolic

☐ Orthostatic blood pressure check and heart rate before patient is mobilized from bed (lying, sitting, and standing
  if patient is able to stand)

☐ Weight on admission and then every day

☐ Input/output for 24 hours or ______

☐ Temperature every 4 hours for 48 hours while awake

☐ Temp every shift after 48 hours while awake if temp is normal

☐ Notify physician if temp greater than 101.3°F (38.5°C)

☐ Fall risk assessment

Activity

☐ Bed rest for _______ hours with turns every _______ hours

☐ In chair twice daily beginning as soon as no fluctuating neurologic status

☐ Up with assistance

☐ Up ad lib

Allergies/Adverse Drug Reactions

☐ None

☐ Yes, Name: __________________________ Type of reaction: __________________________
  __________________________ Type of reaction: __________________________
  __________________________ Type of reaction: __________________________

Nursing Orders

☑ Keep patient with nothing by mouth until/unless patient passes nursing bedside swallowing evaluation

☑ Bedside glucose test now (if not done in ER)

☑ O₂ saturation monitor until O₂ saturations remains stable. Check with vitals
  ☑ Oxygen 2 liters per minute by nasal cannula if O₂ saturations less than 94%. Titrate O₂ to maintain
    saturation greater than or equal to 94%
  ☑ Notify physician if O₂ saturation is less than 91%

☐ Cough and deep breath every hour while awake

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Incentive spirometer every _______ hours while awake

☐ Straight catheter  ☐ Every shift if no void  ☐ 300 cc by bladder scan  
☐ Notify physician if 2 consecutive straight catheterizations needed for no void

☐ Bedside glucose checks every 4 hours for 24 hours  
☐ Notify physician if glucose greater than 180 mg/dL AND no sliding scale ordered

☐ Bedside glucose checks 4 times a day after 24 hours, e.g., ac and hs. Discontinue glucose checks if glucose stable and less than 150 mg/dL

☐ Nursing bedside swallowing evaluation – contact speech therapy for formal evaluation if fail any of the below:  
- More than one swallow to empty mouth  
- Wet voice after swallow  
- Drooling  
- Cough on water

☐ Soft care mattress (if nursing assessment identifies risk of skin breakdown)  
☐ Fall alert (if nursing assessment identifies risk of falling)  
☐ Heel protection (if nursing assessment identifies risk of skin breakdown)

Diet (If patient fails bedside swallow screen, keep patient with nothing by mouth until speech therapy formal evaluation)  
☐ Nothing by mouth  
Diet as recommended by speech therapist

IVs (Avoid use of dextrose 5% in water, especially if hyperglycemic and avoid hypotonic solutions)  
☐ Establish IV saline lock with flush every 12 hours  
☐ 0.9% NaCl in water at __________ mL/hour  
☐ __________ mL/hour at _________ mL/hour

☐ Dextrose 25 mL every 15 minutes as needed to maintain glucose level above 70 mg/dL

Sedative/Symptom Medication (Note: No oral medications until/unless patient passes a bedside swallow screen)  
☐ Acetaminophen 650 mg maximum cumulative 4 grams per 24 hours ☐ by mouth or ☐ rectal suppository every four hours as needed if  
☐ Temperature greater than 99.5°F (37.5°C) OR ☐ pain  
☐ Sedative ____________________________ _________ mg by mouth at bedtime as needed

☐ Bowel care:  
☐ Docusate sodium 100 mg by mouth every 12 hours as scheduled for constipation  
☐ Magnesium hydroxide (Milk of Magnesia®) __________ 30 mL (30-60 mL) by mouth daily as needed for constipation (maximum dose 60 mL per 24 hours)  
☐ Bisacodyl 10 mg suppository. Repeat in 1 hour if inadequate results as needed for constipation  
☐ Fleets enema as needed for constipation

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Medications

Pharmacologic VTE Prophylaxis (Aspirin is not recommended as monotherapy for VTE prophylaxis.)

☐ Dalteparin 5,000 units subcutaneous every 24 hours beginning at admission (Use low-dose unfractionated heparin for creatinine clearance [CRCL] less than 30 mL/min.)

Initiate the following if dalteparin ordered:
- Platelet count and hemoglobin every other day beginning on day two
- **Discontinue** dalteparin if platelet count drops 50% or more from baseline value and **notify physician**
- Initiate patient education
- **Notify physician** if bleeding occurs

☐ Enoxaparin 40 mg subcutaneous every 24 hours beginning at admission (Use unfractionated heparin for CRCL less than 30 mL/min.)

Initiate the following if enoxaparin ordered:
- Platelet count and hemoglobin every other day beginning day two
- **Discontinue** enoxaparin if platelet count drops 50% or more from baseline value and **notify physician**
- Initiate patient education
- **Notify physician** if bleeding occurs

☐ Unfractionated heparin 5,000 units subcutaneous every 8 hours beginning at admission.

Initiate the following if unfractionated heparin ordered:
- Platelet count and hemoglobin every other day beginning day two
- **Discontinue** unfractionated heparin if platelet count drops 50% or more from baseline value and **notify physician**
- Initiate patient education
- **Notify physician** if bleeding occurs

☐ (Alternative pharmacologic VTE prophylaxis program)

Mechanical VTE Prophylaxis

☐ Pneumatic compression:
  - Knee-high
  - Thigh-high
  - Foot boots

Early Secondary Stroke Prevention (Document contraindications if not given. Withhold ibuprofen for 30 minutes after aspirin administration.)

☐ Aspirin ______ mg (160-325 mg) **immediately**  ☐ By mouth  ☐ Coated  ☐ Buffered  ☐ Rectal suppository

☐ Aspirin ______ mg (160-325 mg) daily by mouth  ☐ Coated  ☐ Buffered  ☐ Rectal suppository

☐ ________________ mg by mouth every ________

Acute Post Stroke Hypertension Management (Consider IV regimen if swallow is questionable.)

BP less than 220/120 mmHg
  - Observe with vitals.

BP systolic greater than 220 OR diastolic greater than 120 mmHg or mean arterial pressure greater than 130 mmHg for the first 24 to 48 hours
  - Labetalol 10-20 mg IV over 2 minutes. May repeat or double every 10 minutes to achieve 10-15% reduction in blood pressure (maximum dose 300 mg per 24 hours).
  - Nicardipine 5 mg/hour IV infusion initial dose; titrate up 2.5 mg/hour every 5 min. to 15 mg/hour. to achieve 15% reduction in blood pressure (maximum 15 mg/hour).

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BP diastolic greater than 140 mmHg
☐ Labetalol __________ mg (100-200 mg) by mouth initially and ________ mg every two hours as needed to maintain BP less than ________ mmHg (max. 800 mg per 24 hours)

☐ Labetalol 10 mg IV over 2 minutes. May repeat with 40-80 mg IV every 10-20 minutes as needed to maintain BP less than ________ mmHg (maximum cumulative dose 300 mg per 24 hours)

☐ Nitroprusside 0.5 mcg/kg/minute IV infusion initial dose with continuous BP monitoring. **Notify physician if** blood pressure not controlled with medication

☐ _____________________________ ________ mg every ________ hours as needed to maintain BP at ________ mmHg

☐ **Notify physician if** systolic BP greater than 220 or diastolic BP greater than 120 (MAP greater than 130) with medication.

☐ **Notify physician if** systolic BP greater than ________ or diastolic BP greater than ________ (MAP greater than ________) with medication.

### Management of Prehospital Hypertension Medication Program
*(Note: No oral medications until/unless patient passes a bedside swallow screen)*

☐ Hold all prehospital antihypertensive drugs first 24 hours

☐ Give half doses of prehospital antihypertensive drugs first 24 hours, i.e.,

☐ Give full doses of prehospital antihypertensive drugs first 24 hours, i.e.,

☐ Other program for prehospital antihypertensive drugs first 24 hours, i.e.,

☐ Give full doses of prehospital antihypertensive agents after 24 hours

☐ Ask physician for orders after 24 hours

*Return to Table of Contents*
Management of Other Prehospital Medications Program (Note: No oral medications until/unless patient passes a bedside swallow screen)

☐ Hold all prehospital medications first 24 hours

☐ Other program for prehospital medications first 24 hours, i.e.,

☐ Give full doses of prehospital medications after 24 hours
☐ Ask physician for orders after 24 hours

GI Prophylaxis
☐ __________________________ mg every ________ by mouth □ IV

Laboratory/Diagnostics: (those not performed in ED or office)
☐ CBC with platelet count □ STAT □ Next routine draw (Refer to unit’s protocol.)

☐ Electrolytes, glucose, BUN, creatinine □ STAT □ Next routine draw (Refer to unit’s protocol.)

☐ ALT □ AST □ GGT □ Alk phosphatase □ CPK (Liver and muscle enzymes are important in preparation for statin medication initiation.)

☐ PT/INR □ STAT □ Next routine draw (Refer to unit’s protocol.)
☐ PTT □ STAT □ Next routine draw (Refer to unit’s protocol.)

☑ Fasting cholesterol, triglyceride, HDL, LDL

☐ Electrocardiogram

☐ CT of head without enhancement

☐ CT angiogram: □ Head □ Neck

☐ Magnetic resonance imaging of head (per protocol)

☐ Magnetic resonance angiography: □ Head □ Neck

☐ Carotid doppler ultrasound
  Indication: ________________________________

☐ Transesophageal echocardiogram □ With bubble on day ________ (if suspicion of cardioembolic source when patient is stable for study and not vulnerable with hypotension and/or sedation)

☐ Transthoracic echocardiogram □ With bubble on day ________
  ________________________________

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Other

Rehabilitation (*Therapies will be discontinued by the specific services when unnecessary. Therapies will be advanced to twice daily as appropriate.*)

- Physical therapy
- Occupational therapy
- Speech therapy
- Smoking cessation (*for current users*)

Consults

- Neurology: reason ________________________________
- Hospitalist: reason ________________________________
- Neurosurgery: reason ________________________________
- Cardiology: reason ________________________________
- Physical medicine and rehabilitation: reason ________________________________
- Chaplaincy for advanced directive OR Other _________
- Nutrition: reason ________________________________
- Other: ________________________________

Discharge Planning

- Social service consult for assistance in discharge planning
- Financial counselor consult

Authorized Prescriber Signature: ________________________________

Printed Name: ________________________________

Date/Time of Orders: _____/_____/____  _____:_______

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Order Set – Admission for Ischemic Stroke for Patients Receiving tPA

This order set pertains to those admission orders from ED or direct admit to the hospital for patients 18 years or older who present with symptoms of recent neurologic dysfunction suggestive of brain ischemia who are candidates for tPA. These orders exclude patients with TIA, hemorrhagic stroke, or ischemic stroke not meeting the criteria for tPA administration.

Legend:
☐ Open boxes are orders that a clinician will need to order by checking the box.
☐ Pre-checked boxes are those orders with strong supporting evidence and/or regulatory requirements that require documentation if not done.

Patient Information (Two are required.)

<table>
<thead>
<tr>
<th>Last Name:</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name:</td>
</tr>
<tr>
<td>Date of Birth: <em>/<strong>/</strong></em>__</td>
</tr>
<tr>
<td>Patient’s Age:</td>
</tr>
<tr>
<td>ID #:</td>
</tr>
</tbody>
</table>

Admitting Data

Admit to:
☐ ICU bed
☐ Step down: ☐ With telemetry
☐ Stroke/neurology: ☐ With telemetry
☐ Other ____________________________

Attending physician: ____________________________

Primary physician: ____________________________
☐ Contact primary care physician

Notify stroke nurse clinicians ____________________________
☐ Notify stroke research team if eligible for stroke research

Diagnosis

Admitting Dx:
☐ Acute ischemic infarct treated with IV tPA
☐ Other ____________________________

Secondary Dx: ____________________________

Patient excluded from thrombolytic therapy (tPA) due to:
☐ Time from onset contraindications
☐ Clinical contraindications
☐ Patient history contraindications
☐ Laboratory contraindications
☐ Radiologic contraindications
☐ Other

(If patient does not meet criteria for thrombolytic therapy, stop order set here. Initiate admission for ischemic stroke for patients NOT receiving tPA order set.)

Condition
☐ Stable
☐ Unstable
☐ Other ____________________________

Code Status
☐ Full code
☐ DNR/DNI
☐ Unknown

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Vitals

☑️ Telemetry/monitor for 24 hours
   ☑️ Notify physician if ECG or telemetry is suspicious for atrial fibrillation

☐ Telemetry/monitor for ________ hours
   ☐ Notify physician if ECG or telemetry is suspicious for atrial fibrillation
☑️ Baseline NIHSS check (if not performed in ED)
☑️ Vital signs (blood pressure, pulse, O₂ saturation):
   ☑️ every 15 minutes for 2 hours then
   ☑️ every 30 minutes for 6 hours then
   ☑️ every 60 minutes for 24 hours

☐ Neuro checks with non-NIHSS neuro check:
   ☑️ every 15 minutes for 2 hours then
   ☑️ every 30 minutes for 6 hours then
   ☑️ every 60 minutes for 24 hours

☑️ Notify physician for antihypertensives required for blood pressure greater than 180 mmHg systolic or 105 mmHg diastolic during the first 24 hours after admission
☐ Notify physician for antihypertensives required for blood pressure greater than ________ mmHg systolic or mean arterial pressure greater than ________ mmHg after the first 24 hours
☐ Notify physician if blood pressure is less than ________ mmHg or systolic ________ mmHg diastolic
☑️ Temperature every 4 hours for 48 hours while awake

☐ Temp every shift after 48 hours while awake if temp is normal

☐ Notify physician if temp greater than 101.3°F (38.5°C)

☐ Weight on admission and then every day

☐ Input/output every shift for 24 hours or every ________ hours

☐ Orthostatic blood pressure and heart rate check before a patient is mobilized from bed (lying, sitting, and standing if patient is able to stand)

Activity

☐ Bed rest for ________ hours with turns every ________ hours
☐ In chair every 12 hours on day two if neurologically stable
☐ Up with assistance

Allergies/Adverse Drug Reactions

☐ None
☐ Yes, Name: __________________________ Type of reaction: __________________________
                                __________________________ Type of reaction: __________________________
                                __________________________ Type of reaction: __________________________

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Nursing Orders

☑ Keep patient with nothing by mouth until nursing bedside swallowing evaluation

☐ Bedside glucose test now (if not done in ED)

☑ O2 saturation monitor until O2 saturation remains stable. Check with vitals

☑ Oxygen two liters per minute by nasal cannula if O2 saturation less than 94%. Titrate O2 to maintain saturation greater than or equal to 94%

☑ Notify physician if O2 saturation is less than 91%

☑ Initiate bleeding precautions including the following interventions:
  - Pressure dress all puncture sites and monitor for bleeding
  - Avoid placement of central venous access or arterial puncture for first 24 hours
  - Avoid placement of bladder catheter during tPA infusion and for at least 30 minutes after infusion ends
  - Avoid placement of nasogastric tube (if possible) for first 24 hours
  - Avoid administration of anticoagulation, antiplatelet or anti-inflammatory medication for the first 24 hours

☐ Notify physician if patient needs any of the above interventions

☑ Initiate monitoring for angioedema during infusion:
  - Tongue swelling
  - Difficulty breathing
  - Swelling of eyes or lips

☐ Initiate monitoring for CNS hemorrhage indications:
  - Neurologic deterioration
  - Development of severe headache
  - Sudden severe elevation of BP
  - New onset of nausea or vomiting

☐ Notify physician if signs of possible CNS hemorrhage present. Discontinue infusion of thrombolytic drug. Obtain the following if signs of CNS hemorrhage are present (STAT):
  - Hemoglobin
  - Hematocrit
  - Platelet count
  - aPTT
  - PT/INR
  - Fibrinogen
  - Type and screen _______ units
  - Type and cross match _______ units (if needed)
  - Prepare _______ units fresh frozen plasma
  - Prepare _______ units cryoprecipitate
  - Surgical consult (if necessary)
  - Emergent CT head without contrast. Indication _______

☐ Cough and deep breath every hour while awake

☐ Incentive spirometer every _______ hour(s) while awake

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☐ Straight cath (*Wait at least 30 minutes after thrombolytic drug ends.*)
  ☐ every shift if no void
  ☐ 300 cc by bladder scan
  ☐ **Notify physician** if two consecutive straight caths needed for no void

☐ Bedside glucose checks every 4 hours for 24 hours
  ☐ Initiate insulin management protocol if glucose greater than 150 mg/dL

☐ Nursing bedside swallowing evaluation – contact speech therapy for formal evaluation if fail any of the below:
  - More than one swallow to empty mouth
  - Wet voice after swallow
  - Drooling
  - Cough on water
  - Nursing documentation of bedside swallow evaluation in chart

☐ Soft care mattress *(if nursing assessment identifies risk of skin breakdown)*
☐ Fall alert *(if nursing assessment identifies risk of falling)*

☐ Heel protection *(if nursing assessment identifies risk of skin breakdown)*

☐ Head of bed at ______ degrees for ______ hours

**Diet** *(Keep patient with nothing by mouth if patient fails swallowing evaluation until speech therapy formal evaluation.)*
  ☐ Nothing by mouth
  ☐ Other (specify) ______

**IVs** *(Avoid use of dextrose 5% in water, especially if hyperglycemic. Avoid hypotonic solutions.)*
  ☐ Establish two large bore IV lines if thrombolytic therapy planned
  ☐ Establish IV saline lock with flush every shift
  ☐ 0.9% NaCl in water at ______ mL/hour
  ☐____________________ ____________ mL/hour

**Sedative/Symptom Medication**
  ☐ 50% dextrose 25 mL every 15 minutes as needed to maintain glucose level above 70 mg/dL
  ☐ Acetaminophen 650 mg ☐ By mouth or ☐ Rectal suppository every 4 hours as needed if temperature greater than 99.5°F (37.5°C) *(maximum dose 4 grams per 24 hours)*

  ☐ Pain
    ☐ Sedative ____________________ ________ mg by mouth at bedtime as needed

  ☐ Bowel care:
    ☐ Docusate sodium 100 mg by mouth every 12 hours daily as scheduled
    ☐ Magnesium hydroxide (Milk of Magnesia®) ________ 30 mL by mouth daily as needed for constipation *(maximum dose 60 mL per 24 hours)*
    ☐ Bisacodyl 10 mg suppository. Repeat in 1 hour if inadequate results as needed for constipation

*Return to Table of Contents*
Medications

Thrombolytic Therapy (tPA)

- tPA 0.9 mg/kg IV infusion over 1 hour with an initial bolus dose (10% of total dose) over 1-2 minutes (maximum dose 90 mg)

Pharmacologic VTE Prophylaxis – Do not initiate in the first 24 hours after tPA administration

(Aspirin is not recommended as monotherapy for VTE prophylaxis.)

- Dalteparin 5,000 units subcutaneous every 24 hours beginning 24 hours after tPA administration (Use unfractionated heparin for creatinine clearance less than 30 mL/minute)
  - Initiate the following if dalteparin ordered:
    - Platelet count and hemoglobin every other day, beginning day two
    - Discontinue dalteparin if platelet count drops 50% or more from baseline value, and notify physician
    - Initiate patient education
    - Notify physician if bleeding occurs

- Enoxaparin 40 mg subcutaneous every 24 hours, beginning 24 hours after tPA administration (Use unfractionated heparin for creatinine clearance less than 30 mL/minute)
  - Initiate the following if enoxaparin ordered:
    - Platelet count and hemoglobin every other day, beginning day two
    - Discontinue enoxaparin if platelet count drops 50% or more from baseline value, and notify physician
    - Initiate patient education
    - Notify physician if bleeding occurs

- Unfractionated heparin 5,000 units subcutaneous every 8 hours, beginning 24 hours after tPA administration
  - Initiate the following if unfractionated heparin ordered:
    - Platelet count and hemoglobin every other day, beginning day two
    - Discontinue unfractionated heparin if platelet count drops 50% or more from baseline value, and notify physician
    - Initiate patient education
    - Notify physician if bleeding occurs

Mechanical VTE Prophylaxis

- Pneumatic compression:
  - Knee-high
  - Thigh-high
  - Foot boots

Early Secondary Stroke Prevention – Do not initiate in the first 24 hours after tPA administration

(Document contraindications if not given. withheld NSAIDs for 30 minutes after aspirin administration.)

- Aspirin ______ mg (160-325 mg) daily by mouth
  - Coated
  - Buffered
  - Rectal suppository starting 24 hours after tPA administration
  - _________________ mg by mouth every __________

Return to Table of Contents
Hypertension Management for the first 24 hours *(Consider IV regimen if swallow is questionable.)*

**Pre-tPA:**
BP systolic greater than 185 (pre-tPA treatment) OR diastolic 110 mmHg (BP threshold before tPA treatment can be given)

- Labetalol 10-20 mg IV over 2 minutes. May repeat 1x
  - OR
  - Nitroglycerin ointment 2% USP 1-2 inches, titrate to effect
  - OR
  - Nicardipine infusion 5 mg/hour, titrate up by 2.5 mg/hour at 5 to 15 minute intervals, maximum dose 15 mg/hour; when desired blood pressure attained, reduce to 3 mg/hour

*If blood pressure does not decline and remains greater than 185/110 mmHg, do not administer tPA.*

**Post-tPA**
BP less than 180/105 mmHg
- Observation and vitals

BP systolic 180-230 mmHg (post tPA treatment) or diastolic 105-120 mmHg
- Labetalol 10 mg IV over 2 minutes, may repeat every 10-20 minutes. Maximum dose of 300 mg in 24 hours
  - OR
  - Labetalol 10 mg IV followed by an infusion at 2 to 8 mg/minute. Maximum dose 300 mg in 24 hours

BP systolic greater than 230 mmHg or diastolic 121-140 mmHg
- Labetalol 10-20 mg IV over 2 minutes, may repeat every 10 to 20 minutes, maximum cumulative dose of 300 mg in 24 hours
  - OR
  - Labetalol 10 mg IV followed by an infusion at 2 to 8 mg/minute
  - OR
  - Nicardipine infusion 5 mg/hour titrate up to desired effect by increasing 2.5 mg/hour every 5 minutes to a maximum dose of 15 mg/hour

*If blood pressure is not controlled, consider sodium nitroprusside 0.5 mcg/kg/minute.*

☑ Notify physician if systolic BP greater than 180 or diastolic BP greater than 105 with medication.
☑ Notify physician if systolic BP greater than ________ or diastolic BP greater than ________ *(MAP greater than ____)* with medication.

**GI Prophylaxis**
- ____________________________ mg every ________ by □ mouth □ IV

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Laboratory/Diagnostics: (those not performed in ED or office)
- CBC with platelet count  □ STAT  □ Next routine draw (Refer to unit’s protocol.)
- Electrolytes, glucose, BUN, creatinine  □ STAT  □ Next routine draw (Refer to unit’s protocol.)
- ALT □ AST □ GGT □ Alk phosphatase □ CPK (Liver and muscle enzymes are important in preparation for statin medication initiation.)
- PT/INR □ STAT □ Next routine draw (Refer to unit’s protocol.)
- aPTT □ STAT □ Next routine draw (Refer to unit’s protocol.)
- Fasting cholesterol, triglyceride, HDL, LDL
- Electrocardiogram
- CT of head without enhancement
- CT angiography: head and neck
- Magnetic resonance imaging of head (per protocol)
- Magnetic resonance angiography: □ Head □ Neck
- Carotid Doppler ultrasound
- Transesophageal echocardiogram □ With bubble study on day ______ (if suspicion of cardioembolic source when patient is stable for study)
- Transthoracic echocardiogram □ With bubble study on day ______
- ________________________________

Other
Rehabilitation (Therapies will be discontinued by the specific services when unnecessary. Therapies will be advanced to twice daily as appropriate.)
- Physical therapy
- Occupational therapy
- Speech therapy
- Smoking cessation (for current users)

Consults
- Neurology: reason ____________________________________________
- Hospitalist: reason ____________________________________________
- Neurosurgery: reason __________________________________________
- Cardiology: reason ____________________________________________
- Physical medicine and rehabilitation: reason ________________________________
- Chaplaincy for advanced directive OR Other: ________________________________
- Nutrition: reason ________________________________________________
- Other: _________________________________________________________

Discharge Planning
- Social service consult for assistance in discharge planning
- Financial counselor consult

Authorized Prescriber Signature: ________________________________

Printed Name: ________________________________________________

Date/Time of Orders: _____ / _____ / _____   _____:_____
The subdivisions of this section are:

• References
• Appendices
References


Links are provided for those new references added to this edition (author name is highlighted in blue).
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Silliman SL, Quinn B, Huggett V, Merino JG. Use of a field-to-stroke center helicopter transport program to extend thrombolytic therapy to rural residents. *Stroke* 2003;34:729-33. (Reference)


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Appendix A – Broader Issues

Recommendation:

Policy-makers and relevant public service entities should:

1. develop and/or support public education programs on recognition of stroke symptoms and signs and importance of calling 911 if recognized in oneself or another person (Fussman, 2010; LeCouturier, 2010; Morgenstern, 2002);

2. encourage use of 911 for facilitating transport of patients with acute ischemic stroke to appropriate facilities (Morris, 1999; Barsan, 1993);

3. develop and/or support education of potential health services contacts (doctors' offices, nurse lines, EMS dispatch) regarding need for rapid triage of patients with possible acute ischemic stroke (Buck, 2009; Handschu, 2003; Porteous, 1999);

4. develop and/or support systems to facilitate rapid transport of patients with possible acute ischemic stroke to facilities with appropriate resources and expertise to carry out expedited assessment and treatment (Schwamm, 2009a; Schwamm, 2009c); and

5. develop and/or support education programs for EMS personnel emphasizing importance of time, uniform pre-hospital assessment, and hospital pre-notification for patients with possible acute ischemic stroke (Patel, 2011; Kidwell, 2000; Kothari, 1999).

(Strong Recommendation, Evidence Quality:

1. Public education – Low Quality Evidence

2. 911 – Moderate Quality Evidence

3. Rapid triage – Low Quality Evidence

4. Systems of care – Moderate Quality Evidence

5. EMS training – Moderate Quality Evidence)

The ICSI work group's recommendation is strong for the above linked pre-hospital priorities. The strength is based on ample evidence that efficacy of reperfusion depends strongly and inversely on time from onset of symptoms to treatment, as well as evidence that there is much progress to be made in all steps of the continuum, from recognition to arrival at an appropriate care destination. Evidence for efficacy of interventions at each of the steps, however, varies from low to moderate. Evidence of efficacy of public education measures to increase recognition of stroke symptoms and importance of calling 911 is weak to moderate. Efficacy of using 911 rather than other means of transport is moderate. Evidence of efficacy of training potential first health care contacts and EMS dispatchers on stroke symptoms and optimal triage strategies is weak. Evidence of value of stroke systems of care is moderate. Evidence of efficacy of training EMS personnel in stroke recognition, support and hospital pre-notification is moderate. The work group recommends that research aimed at defining best practices continue.

Excellence in the care of hospitalized stroke patients as in those with other problems is patient centered, safe, effective, timely, efficient and equitable. For a patient with acute ischemic stroke, timeliness is of paramount importance, and the clock is running before the patient passes through the doors of the emergency room. In fact, in reperfusion cases, the greatest share of onset to treatment time is spent in the pre-hospital segment. Since time is brain, pre-hospital issues cannot be ignored.

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Public Awareness

The earliest link is recognition of stroke symptoms or signs by patient or witness and awareness that the situation is a medical emergency. Obstacles in recognition are the diversity and variability of stroke manifestations and the minimization of their significance and import, which is a typical component of the stroke's effects. Public awareness of the importance of speed is growing. While awareness is growing naturally with time, proof of efficacy beyond secular effects is lacking for various public awareness campaigns studied to date. Current recommendations to make such campaigns more effective include focusing on groups at highest risk and increasing emphasis on the need for speed.

Dispatch and EMS

Calling 911 speeds arrival of stroke patients to appropriate care compared with other means of transport. Important in optimal triage and transport are informed dispatch and trained EMS services with protocols to guide initial assessment, care, transport destinations and pre-emergency room notification.

Stroke Systems of Care

Two advances in ischemic stroke care – IV tPA and coordinated inpatient care processes (often considered together as "stroke unit care") – are known to improve outcomes. The urgency, complexity and potential risks of the former and training required for the latter challenge the resources of emergency rooms and hospitals that may care for only a few ischemic stroke patients each year. A national survey showed that 64% of all United States hospitals had not administered IV tPA for stroke during the two-year sampling interval (2005-07), and 40% of Americans live in counties in which no hospitals have substantial experience with IV tPA administration (Kleindorfer, 2009). At the same time, many hospitals with large volumes of such patients have developed stroke programs driven by local competition and supported by quality improvement programs offered through The Joint Commission (TJC), the American Heart Association, National Stroke Association, CDC and others.

In contrast to those who arrive at hospitals with fully developed stroke programs, stroke patients in most remote/rural areas in our state and region until relatively recently did not have access to advantages of informed, urgently deployed reperfusion techniques (especially IV tPA but also intra-arterial chemical and mechanical reperfusion therapies for selected cases) and stroke unit care during their hospitalizations. It is likely that outcomes are impacted by low rates of IV tPA use, suboptimal patient selection for IV tPA, and hospital processes that are not guideline based. In fact, one might calculate from number-needed-to-treat metrics that many poor outcomes each year in Minnesota might result from disparities in care based on geography.

Ad hoc systems have been developed in Minnesota and elsewhere to eliminate the disparities in care resulting from geographic exigencies (Switzer, 2009; Hoody, 2008; Switzer, 2008; Vaishnav, 2008; Frey, 2005; Silverman, 2005; Wang, 2004; Rymer, 2003; Silliman, 2003; Wang, 2003; Wang, 2000b). Typically the systems that have evolved provide support for remote/rural emergency rooms and hospitals by neurologists or other stroke experts who are physically located elsewhere, usually at a urban hospital with a stroke program. The focus to date has been administration of IV tPA or other reperfusion treatments as soon as possible, i.e., pre-hospital admission. A single urban hospital with stroke program (a "hub") may provide support for several remote/rural emergency rooms and hospitals ("spokes"). Several models of support have evolved. In some models, the stroke cases are transferred to the hub or hospital with a stroke program. Models include:

- Field to comprehensive stroke center transport – For example, a ground ambulance or helicopter is deployed by regional EMS to a farmhouse, and the patient is transport to a stroke center without intermediate hospitalization, i.e., "spokeless." This model has not proliferated beyond a few areas.
"Trip to drip" – A stroke expert or team of experts travels quickly to the remote/rural emergency room or hospital to provide or supervise acute care. This model is limited by distances and availability of mobile stroke experts/teams.

"Ship and drip" – The stroke patient is transferred prior to initiation of reperfusion therapies from remote/rural emergency room or hospital to a stroke center.

"Drip and ship" – After assessment of eligibility with input of supportive expert, IV tPA is started at the remote/rural hospital, and the patient is immediately transported to the stroke center.

"Drip and keep" – IV tPA is given with support as above, and the patient remains at remote/rural hospital for acute hospitalization.

There is considerable latitude for individual variation within these models. For example, the formality of expectations between the hub and spoke varies from casual (e.g., a phone call to a hospital neurology consulting line) to explicit, including expectation for 24/7 availability of a stroke expert on the hub side and for formal training, ongoing education, joint protocol development, and joint post-stroke care planning on the spoke side. The form of communication from hub to spoke varies from simple phone call to phone call/teleradiography to telemedicine/teleradiography.

Literature supports the feasibility and safety of administering IV tPA in all of these models. There is level I evidence showing that compared with phone call alone, video telemedicine avoids protocol deviations in administration of IV tPA (Meyer, 2008). The trial was not powered to analyze actual outcomes.

Working relationships between individual stroke centers and remote/rural hospitals and emergency rooms will necessarily and appropriately be customized according to the unique circumstances and goals of the entities. It seems prudent, however, that these evolving relationships be guided by basic principles. The work group makes the following recommendations:

- Agreements between hub and spokes should be formal, as opposed to ad hoc.
- Hub should provide 24/7 availability of support for reperfusion therapies by one or several of the following:
  - telephone +/- teleradiography
  - video telemedicine +/- teleradiography
- Protocols defining care processes between hub and spoke should be jointly developed and support the agreed-upon model, e.g., 3, 4 or 5.
- Initial and ongoing education of spoke personnel relevant for the care model should be provided.
- Initial and ongoing training of spoke personnel (e.g., NIHSS performance and interpretation, conducting an informed consent discussion regarding IV tPA) relevant to the care model should be provided.
- There should be joint planning for stroke unit care at hub (models 3 and 4) or spoke (model 5) and case follow-up. Planning for optimal care of non-reperfusion cases should also be provided.

(Schwamm, 2009a; Schwamm, 2009c)

The Minnesota Department of Health is working with hospitals, clinicians, EMS and other stakeholders to support development of uniform practices and standards of care for patients with acute ischemic stroke across all regions of the state. Proposed is a system in which Minnesota's rural Critical Access Hospitals will be designated as "stroke-ready" if their emergency rooms are able to administer IV tPA, typically with availability of stroke expertise from a larger stroke program hospital via telemedicine. Providing stroke
unit care during hospitalization for acute ischemic stroke in hospitals with low volume is another challenge currently under discussion.

**Nongeographic Disparities in Care**

As discussed above, Minnesota's substantial geographic disparities are being addressed by a broad planning effort to develop a system of care. Other disparities not based on geography are also reported; they include gender, economic and ethnic inequalities in acute stroke care.

Disparities in stroke care are described in many studies. The disparities may be based on race/ethnicity, gender, socioeconomic status, educational level or other characteristics (Cruz-Flores, 2011). Disparities are evident in awareness of stroke symptoms and signs, and the importance of speed. Concerns about expense and distrust of the health system may be elements. There is also an unequal burden of risk among race/ethnic groups with differing rates of hypertension, diabetes and metabolic syndrome. Even after controlling for these factors, risk of stroke is higher in some groups, e.g., younger Hispanics. Access to care varies among race/ethnicity and socioeconomic groups. With minorities based on race/ethnicity constituting 28% of the population and expected to reach nearly 40% by 2030, the importance and societal impact of existing disparities will grow unless corrected. Disparities are multifactorial and addressing them effectively will require concerted effort on many fronts.

**Conclusion**

Given the significant national morbidity and mortality caused by strokes, the ICSI work group recognizes that only incremental progress will be made by optimizing the care for the individual patient. Public health strategies are needed to effectively increase public awareness of stroke symptoms, to coordinate care between primary and tertiary stroke centers, to improve communication of risk and benefit of therapies, and to address disparities in outcomes among differing racial and ethnic groups.

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## Appendix B – Non-NIHSS Neuro Check

**Function & Measurement Format**

<table>
<thead>
<tr>
<th>Level of Consciousness:</th>
<th>Scores:</th>
</tr>
</thead>
<tbody>
<tr>
<td>0=Alert</td>
<td></td>
</tr>
<tr>
<td>1=Not alert, but arousable with minimum</td>
<td></td>
</tr>
<tr>
<td>stimulation</td>
<td></td>
</tr>
<tr>
<td>2=Not alert, requires repeated stimulation</td>
<td></td>
</tr>
<tr>
<td>to attend</td>
<td></td>
</tr>
<tr>
<td>3=Coma</td>
<td></td>
</tr>
</tbody>
</table>

**LOC Questions: Ask Patient the Month and His/Her Age**

| 0=Answers both correctly                     |         |
| 1=Obeys one correctly                        |         |
| 2=Both incorrect                             |         |

**LOC Commands: Ask Patient to Open and Close Eyes**

| 0=Opens both correctly                       |         |
| 1=Obeys one correctly                        |         |
| 2=Both incorrect                             |         |

**Motor Functions: Arms**

| 0=Normal extension arms 90° or 45° for 10  |         |
|   seconds without drift                      |         |
| 1=Drift                                     |         |
| 2=Some effort against gravity               |         |
| 3=No effort against gravity                 |         |
| 4=No movement                               |         |
| 9=Untestable – Joint fused or limb amputated|         |
|   (Do not include this in total score)      |         |

**Motor Functions: Legs**

| 0=Normal – hold leg 30° position for 5     |         |
|   seconds                                  |         |
| 1=Drift                                    |         |
| 2=Some effort against gravity              |         |
| 3=No effort against gravity                |         |
| 4=No movement                              |         |
| 9=Untestable – Joint fused or limb amputated|         |

**Best Language**

| 0=No aphasia                                |         |
| 1=Mild to moderate                          |         |
| 2=Severe aphasia                            |         |
| 3=Mute                                      |         |

**Dysarthria**

| 0=Normal articulation                       |         |
| 1=Mild to moderate slurring of words        |         |
| 2=Near unintelligible or unable to speak    |         |
| 3=Mute                                      |         |

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Appendix C – tPA for Cerebral Ischemia within Three Hours of Onset – Changes in Outcome Due to Treatment

A decision matrix figure illustrates the benefits and risks of IV tPA administered within the 3-hour window based upon data from the two NINDS-TPA trials.

ICSI has long had a policy of transparency in declaring potential conflicting and competing interests of all individuals who participate in the development, revision and approval of ICSI guidelines and protocols.

In 2010, the ICSI Conflict of Interest Review Committee was established by the Board of Directors to review all disclosures and make recommendations to the board when steps should be taken to mitigate potential conflicts of interest, including recommendations regarding removal of work group members. This committee has adopted the Institute of Medicine Conflict of Interest standards as outlined in the report, Clinical Practice Guidelines We Can Trust (2011).

Where there are work group members with identified potential conflicts, these are disclosed and discussed at the initial work group meeting. These members are expected to recuse themselves from related discussions or authorship of related recommendations, as directed by the Conflict of Interest committee or requested by the work group.

The complete ICSI policy regarding Conflicts of Interest is available at http://bit.ly/ICSICOI.

Funding Source

The Institute for Clinical Systems Improvement provided the funding for this guideline revision. ICSI is a not-for-profit, quality improvement organization based in Bloomington, Minnesota. ICSI's work is funded by the annual dues of the member medical groups and five sponsoring health plans in Minnesota and Wisconsin. Individuals on the work group are not paid by ICSI but are supported by their medical group for this work.

ICSI facilitates and coordinates the guideline development and revision process. ICSI, member medical groups and sponsoring health plans review and provide feedback but do not have editorial control over the work group. All recommendations are based on the work group's independent evaluation of the evidence.

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All ICSI documents are available for review during the revision process by member medical groups and sponsors. In addition, all members commit to reviewing specific documents each year. This comprehensive review provides information to the work group for such issues as content update, improving clarity of recommendations, implementation suggestions and more. The specific reviewer comments and the work group responses are available to ICSI members at http://bit.ly/Stroke0712.

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Acknowledgements

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During this revision, the following groups reviewed this document. The work group would like to thank them for their comments and feedback.

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Released in July 2012 for Tenth Edition.
The next scheduled revision will occur within 24 months.

Document History

- 2012 implemented the GRADE methodology to identify and evaluate recommendations.

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ICSI Document Development and Revision Process

Overview

Since 1993, the Institute for Clinical Systems Improvement (ICSI) has developed more than 60 evidence-based health care documents that support best practices for the prevention, diagnosis, treatment or management of a given symptom, disease or condition for patients.

Audience and Intended Use

The information contained in this ICSI Health Care Guideline is intended primarily for health professionals and other expert audiences.

This ICSI Health Care Guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients and families are urged to consult a health care professional regarding their own situation and any specific medical questions they may have. In addition, they should seek assistance from a health care professional in interpreting this ICSI Health Care Guideline and applying it in their individual case.

This ICSI Health Care Guideline is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition.

Document Development and Revision Process

The development process is based on a number of long-proven approaches and is continually being revised based on changing community standards. The ICSI staff, in consultation with the work group and a medical librarian, conduct a literature search to identify systematic reviews, randomized clinical trials, meta-analysis, other guidelines, regulatory statements and other pertinent literature. This literature is evaluated based on the GRADE methodology by work group members. When needed, an outside methodologist is consulted.

The work group uses this information to develop or revise clinical flows and algorithms, write recommendations, and identify gaps in the literature. The work group gives consideration to the importance of many issues as they develop the guideline. These considerations include the systems of care in our community and how resources vary, the balance between benefits and harms of interventions, patient and community values, the autonomy of clinicians and patients and more. All decisions made by the work group are done using a consensus process.

ICSI's medical group members and sponsors review each guideline as part of the revision process. They provide comment on the scientific content, recommendations, implementation strategies and barriers to implementation. This feedback is used by and responded to by the work group as part of their revision work. Final review and approval of the guideline is done by ICSI's Committee on Evidence-Based Practice. This committee is made up of practicing clinicians and nurses, drawn from ICSI member medical groups.

Implementation Recommendations and Measures

These are provided to assist medical groups and others to implement the recommendations in the guidelines. Where possible, implementation strategies are included that have been formally evaluated and tested. Measures are included that may be used for quality improvement as well as for outcome reporting. When available, regulatory or publicly reported measures are included.

Document Revision Cycle

Scientific documents are revised every 12-24 months as indicated by changes in clinical practice and literature. ICSI staff monitors major peer-reviewed journals every month for the guidelines for which they are responsible. Work group members are also asked to provide any pertinent literature through check-ins with the work group midcycle and annually to determine if there have been changes in the evidence significant enough to warrant document revision earlier than scheduled. This process complements the exhaustive literature search that is done on the subject prior to development of the first version of a guideline.

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