General

Guideline Title

Diagnosis and initial treatment of ischemic stroke.

Bibliographic Source(s)

Anderson D, Larson D, Bluhm J, Charipar R, Fiscus L, Hanson M, Larson J, Rabinstein A, Wallace G, Zinkel A. Diagnosis and initial treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2012 Jul. 122 p. [238 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2010 Jun. 70 p.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC) and the Institute for Clinical Systems Improvement (ICSI): For a description of what has changed since the previous version of this guidance, refer to Summary of Changes Report -- July 2012 . In addition, ICSI began its transition to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system as a method of assessing the quality of evidence and writing recommendations.

The recommendations for the diagnosis and initial treatment of ischemic stroke are presented in the form of a table with a list of evidence-based recommendations and three algorithms with 38 components, accompanied by detailed annotations. Algorithms are provided in the original guideline document for: Screening (Ambulatory), Emergency Department in a Stroke-Ready Facility [SRF] Treatment, and Stroke Code. Clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Quality of evidence (Low Quality, Moderate Quality, and High Quality) and strength of recommendation (Weak or Strong) definitions are repeated at the end of the "Major Recommendations" field.

Clinical Highlights

- Intravenous (IV) tissue plasminogen activator (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 3 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 computed tomography (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 to 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 prophylaxis
    - Initiate early mobilization
    - Establish fall prevention
    - Perform nutritional status assessment
    - Treat hyperthermia

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 physicians, other medical specialty physicians, emergency medical services, nursing staff in a clinic or urgent care setting or even non-medical triage personnel prior to emergency department (ED) 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.

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
   - 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 ED. 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 launched 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 for the general public has been developed 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 ED itself (ROSIER [Recognition of Stroke in the Emergency Room] scale). These tools are listed in the Implementation Tools and Resource Table in the original guideline document.

   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:

   - 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 phenomenon).

- 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 be distinguished from ischemic stroke by the anatomic distribution of the symptoms and in the case of radiculopathy, by the associated painful symptoms. Bell's palsy, vestibular neuritis 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 CT])
  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 or reactions 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 encyclopedic guide to discerning 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 ED or Physician'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 ED 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. 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," in the original guideline document.

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 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. Applying the new definition requires imaging. The pre-imaging syndrome has been designated "acute neurovascular 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.

6. Possible Ischemic Stroke—Symptoms Onset within 24 Hours?
   If the symptoms resolve completely and then recur, for the purposes of determining whether thrombolysis can 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 ED 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—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).

11. Transport to ED 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 3 hours but less than 24 hours ago should be taken to a stroke-ready ED 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.

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. 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 of Stroke?") or CT
    - Vascular imaging: magnetic resonance angiography (MRA), computed tomography angiography (CTA) or carotid ultrasound (if symptoms suggest ischemia in the carotid distribution)
    - Blood work: complete blood count, electrolytes, blood urea nitrogen (BUN), creatinine, international normalized ratio (INR), activated partial thromboplastin time (aPTT), fasting lipids, fasting glucose, glycosylated hemoglobin (HbA1c), troponins
    - Echocardiogram (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 tPA/See Stroke Code Algorithm
    Patients presenting to the ED soon after the onset of symptoms may be candidates for treatment with IV tPA and will therefore require a rapid evaluation and treatment initiation. (See Appendix A, "Broader Issues," in the original guideline document.) 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 ED will require at least 30 minutes in most cases (CT scan of head, laboratory tests performed and results returned, IV access obtained, neurological exam and history completed, informed consent obtained). The guideline work group has 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 the 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 to 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 to 15 minutes.

Refer to the original guideline document for information on tPA tested in large, randomized, placebo-controlled clinical trials.

21. ED in a SRF Initiates Evaluation for Possible TIA
Patients with a history of clinical TIA should be evaluated promptly. The following diagnostic evaluations should typically be performed. 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 ED 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 ED. 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. (see 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 TIA identifies higher risk of stroke. At this time, an MRA of the carotids and intracranial arteries can be performed if indicated.

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

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

23. High Risk for Stroke?
Recommendation

- A qualified clinician (i.e., trained and experienced in the management of patients with TIAs 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*).

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% to 40% risk of having a stroke in the five years following a clinical TIA. The more salient question is about the short-term risk.

Analysis of the Oxfordshire population-based sample of clinical TIA episodes (n=209) yielded an ABCD score identifying those at high risk of stroke.

The elements of the scale from this derivation sample are:

A - for age	Over the age of 60 years	1 point
B - for blood pressure	A systolic greater than 140 mm Hg or diastolic greater than 90 mm Hg	1 point
C - for clinical features	Unilateral weakness	2 points
	Speech disturbance without weakness	1 point
	Other clinical features	0 points
D - for duration of symptoms	Symptoms lasting greater than 60 minutes	2 points
	Symptoms lasting 10-59 minutes	1 point
	Symptoms lasting less than 10 minutes	0 points

The ABCD score was subsequently validated in a second population-based sample of clinical TIA episodes (n=190). The 7-day risks of stroke in the combined derivation and validation samples (n=299) were:

> 0-4 points (73% of combined samples): 0.4% (95% confidence interval [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%)

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 2 days following a clinical TIA. This new score was derived and validated in patients seen in EDs 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 2 days, which is more useful in the outpatient setting. Data from the validation groups included 4,799 patients.

A - for age	60 years or older	1 point
B - for blood pressure	A systolic 140 mmHg or greater or diastolic of 90 mmHg or greater	1 point
C - for clinical features	Unilateral weakness	2 points
	Speech disturbance without weakness	1 point
D - for duration of symptoms	Symptoms lasting greater than 60 minutes	2 points
	Symptoms lasting 10-59 minutes	1 point
	Symptoms lasting less than 10 minutes	0 points
D - Diabetes		1 point

Risk of stroke at 2 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.

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.

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, whereas urgent vascular imaging and EKG monitoring for patients with <4 points on the ABCD2 were advocated by others.

Certain diagnostic entities, if suspected, may require hospitalization for specific management, even with presentation later than 24 to 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.

Refer to the original guideline document for additional information on risk assessment which can help identify patients at high risk of stroke.

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, allows for ready access to fibrinolysis should the patient have an acute stroke, facilitates early carotid revascularization if indicated, and offers 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:

- 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 7 days should be evaluated as soon as possible. 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 and 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

Stroke Code Algorithm Annotations

29. ED in a 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: time is brain. The National Institutes of Health (NIH) recommendation of "door to drug" is within 60 minutes.

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.
- Expedited 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 physician 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.

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 National Institute of Health Stroke Scale (NIHSS)

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

    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," above) 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, nonvascular 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 extensive volume of infarcted tissue.
    - Unlikelihood of stroke mimickers, 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.

    Contraindications for tPA

    The clinical, history, laboratory, and radiological contraindications for thrombolytic therapy (tPA) that are listed below should be considered relative contraindications. Clinical judgment should weigh the patient's risk 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 4)

- Sensory symptoms only
- Ataxia without other deficits
- Dysarthria without other deficit
- Mild motor signs (non-disabling)
- Visual field defect without other deficits

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

- 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 mm Hg are excluded only if the blood pressure exceeds the limits on consecutive measurements, and if aggressive (i.e., beyond boluses of labetalol, nicardipine or doses of nitropaste) treatment is required to lower the blood pressure into an appropriate 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 when 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 3 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 noncompressible site within the last 7 days or lumbar puncture within the last 3 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 having 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

NOTE: The appropriate management of IV tPA in patients taking novel oral anticoagulants, e.g., direct thrombin inhibitors and factor Xa inhibitors, remains unsettled.

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
- 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 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 need 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- to 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 European Cooperative Acute Stroke Study (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 >one third of the MCA 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. The work group encourages 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 (5 to 8 minutes), which is an important feature in this clinical setting.

The NIHSS has been demonstrated in several evaluations to have both validity and reliability.

Refer to the original guideline document for more information on baseline NIHSS.

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

It is the standard of practice to perform a baseline NIHSS neurological assessment, 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 or 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 option.

Level of Consciousness – measures the level of alertness 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 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 the 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 in the original guideline document for 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 needed)

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
- Aspartate aminotransferase (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. 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 should 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 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. 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. 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 this CT 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.

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, 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," below and Appendix C, "tPA for Cerebral Ischemia within Three Hours of Onset – Changes in Outcome Due to Treatment," in the original guideline document). 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*).

Refer to the original guideline document for discussion of supporting evidence and an approach for the management of elevated blood pressure in patients with acute ischemic stroke.

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 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]".)

33. Initiate 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*).

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" (see the original guideline document).

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 1 to 2 minutes and the remainder infused over 1 hour. 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*)

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 3 hours or 4.5 hours in selected patients; see Annotation #18, "Consider IV Tissue Plasminogen Activator [tPA]/See Stroke Code Algorithm," above). 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 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," in the original guideline document.

Middle Cerebral Artery Occlusion

Criteria for consideration of angiographic evaluation for intra-arterial treatment:

- MCA occlusion defined by:
  - Symptom complex consistent with this vascular distribution:
    - Contralateral hemiplegia and face 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 6 hours from onset of symptoms for middle cerebral occlusions beyond 4.5 hours of onset and using intra-arterial tPA.

Basilar Artery Occlusion

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

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.

Refer to the original guideline document for newer approaches to mechanical reperfusion techniques, emerging technologies, and for information on studies investigating intra-arterial thrombolysis in patients with middle cerebral artery and basilar artery occlusion.

35. Initiate Aspirin Unless Contraindicated
    Recommendation

- Clinician must immediately administer 160 to 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*). Note: For patients treated with IV tPA, aspirin (160 to 325 mg) should be administered 24 hours after IV tPA.
  Note: In patients receiving IV tPA, the National Institute of Neurological Disorders and Stroke tPA Stroke Study Group (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)."

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 to 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.

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 nonfatal stroke - 9 fewer per 1,000 treated ($p=0.001$)
- Death or dependency at discharge or 6 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 aspirin 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).

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.

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. 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. There may be subgroups that benefit, but further studies of this problem are required for confirmation. 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 to be common clinical practice.

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 ED
- Management of hypo- and hyperglycemia
- Prevention of deep vein thrombosis in immobilized patients
- Treatment of temperature elevation

36. Post-ED Medical Management (Postthrombolysis)
    - Admit to intensive care unit or acute stroke care unit/cardiac monitoring.
    - Perform vital signs and neurologic checks (not full NIHSS) every 15 minutes for 2 hours, then every 30 minutes for 6 hours, then every 60 minutes for 16 hours for a total of 24 hours (recommend use of an abbreviated NIHSS for neurologic checks). (See Appendix B, "Non-NIHSS Neuro Check," in the original guideline document.)
    - Treat blood pressure if greater than 180/105 (see Table 3 in Annotation #31 in the original guideline document).
        - 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 neurologic 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 cross match 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*).

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 to 125 cc per hour or 2 to 3 L/day should be initiated to avoid dehydration. 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.

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. Dehydration with hemoconcentration may also increase the risk of thrombus formation and recurrent embolization in cardiogenic stroke. 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

In the absence of unambiguous data, consensus-based guidelines recommend measures described in Table 3, "Approach to Elevated Blood Pressure in Acute Ischemic Stroke" (see the original guideline document), 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. 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.

38. Other Post-ED Medical Management (First 24 to 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*).

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 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." The stroke unit concept remains alive and healthy at the time of publication of this ICSI guideline.

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*).

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."

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 mimicker 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*).

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.

Initiate Deep Vein Thrombosis (DVT) Prophylaxis

Recommendation

- Clinician should provide appropriate prophylaxis against DVT 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*).

The evidence to support the prophylaxis for 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% to 50%), and prophylaxis with parenteral anticoagulant decreases the incidence (10% to 20%). The risk of pulmonary embolism appears to be decreased as well, although numbers have been small and statistical significance not achieved.

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 (VTE) 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.

Low-molecular-weight heparin is renally cleared. For patients with a creatinine clearance (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.

All patients should receive patient education that includes signs and symptoms of VTE and therapy options, and encouraged to ambulate early and perform flexion/extension exercises. 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. Interestingly, below-the-knee stockings were found to be inferior to thigh-length graduated elastic compression stockings, suggesting that the former may predispose to DVT. Intermittent pneumatic compression should be considered for patients at high risk for VTE who have contraindications to pharmacologic prophylaxis.

See the NGC summaries of the ICSI guidelines Antithrombotic Therapy Supplement and Venous Thromboembolism Prophylaxis.

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*).

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 DVT, 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. 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. Poor nutritional status in patients admitted for stroke is associated with increased morbidity and mortality. However, a trial did not find benefit in administering nutritional supplementation.

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

2. Surgical decompression of large cerebellar infarcts
3. Hemicraniectomy for malignant middle cerebral infarction in patients age <60 years

(*Strong Recommendation, 1. Moderate Quality Evidence, 2. Moderate Quality Evidence, 3. High Quality Evidence*)

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 infractions, 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 3 and 5 days after stroke onset, marked early swelling (in the first 24 to 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 MCA territory and large areas of hypoperfusion on perfusion scans (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. 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. Mannitol 20% is usually administered as a bolus of 1 to 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 4 to 6 hours. In patients with established signs of herniation, a rescue dose of 23.4% of saline solution (30 cc) may be useful.

Hyperventilation should be avoided except for mild to moderate hyperventilation (target pCO_2 30 to 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*).

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.

In human studies, early hyperthermia in acute stroke is associated with increased risk of poor outcome, higher mortality and increased infarct volume. 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 4 to 6 hours, not to exceed 4 to 6 grams in 24 hours) and regular monitoring of temperature status (every 4 hours). A recent phase III trial of this approach in patients with 96.8 to 102.2°F (36 to 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 to 102.2°F (36 to 39°C) range. 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. However, the role of hypothermia in ischemic stroke therapy has yet to be established.

Definitions:

Quality of Evidence and Strength of Recommendations

Category	Quality Definitions	Strong Recommendation	Weak Recommendation
High Quality Evidence	Further research is very unlikely to change the work group's confidence in the estimate of effect.	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.	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.
Medium Quality Evidence	Further research is likely to have an important impact on the work group's confidence in the estimate of effect and may change the estimate.	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.	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.
Low Quality Evidence	Further research is very likely to have an important impact on the work group's confidence in the estimate of effect and is likely to change. The estimate or any estimate of effect is very uncertain.	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.	The work group recognizes that there is significant uncertainty about the best estimates of benefits and harms.

Clinical Algorithm(s)

The following detailed and annotated clinical algorithms are provided in the original guideline document :

- Screening (Ambulatory)
- Emergency Department in a Stroke-Ready Facility (SRF) Treatment
- Stroke Code

Scope

Disease/Condition(s)

- Ischemic stroke
- Transient ischemic attack (TIA)

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Cardiology

Critical Care

Emergency Medicine

Family Practice

Internal Medicine

Neurology

Radiology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Emergency Medical Technicians/Paramedics

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

- To increase the percentage of patients age 18 and over presenting in time for intravenous (IV) tissue plasminogen activator (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
- To increase the percentage of patients age 18 years and over at high risk for stroke presenting with transient ischemic attack (TIA) symptoms within 24 hours who are admitted to the hospital inpatient or observational unit or undergo identical assessment in an expedited outpatient program
- To increase the percentage of patients age 18 years and over receiving appropriate thrombolytic and antithrombotic therapy for ischemic stroke (use of tPA and aspirin, other antiplatelet agents or an anticoagulant)
- To increase the percentage of tPA non-recipients who have hypertension appropriately managed in the first 24 to 48 hours of hospitalization

or until neurologically stable

- To increase the percentage of stroke patients age 18 years and over who receive stroke unit care during the initial 24 to 48 hours including prevention and management of complications such as:
  - Dehydration/hypertension/hypotension
  - Aspiration
  - Hypoglycemia and hyperglycemia
  - Deep vein thrombosis
  - Immobility
  - Falling
  - Nutritional status decline
  - Hyperthermia
- To improve patient and family education of patients with ischemic stroke in both the emergency department and the admitting hospital unit

Target Population

Patients age 18 years or older with symptoms of ischemic stroke or transient ischemic attack

Interventions and Practices Considered

Diagnosis/Evaluation/Screening

1. Emergency department (ED) or clinic evaluation, as appropriate
2. History and physical examination, including neurologic examination (use of National Institutes of Health Stroke Scale [NIHSS]), risk assessment using ABCD and ABCD2 scores, and establishing time of symptom onset
3. Screening for tissue plasminogen activator (tPA) treatment indications and contraindications
4. Diagnostic testing, such as laboratory testing (e.g., complete blood count, electrolytes, blood urea nitrogen, creatinine, glucose, prothrombin time/international normalized ratio [INR], activated partial thromboplastin time [aPTT], hemoglobin A1c, fasting lipid profile, troponin, aspartate aminotransferase [AST], urine or serum pregnancy testing), electrocardiogram, echocardiogram, brain and vascular imaging (e.g., computed tomography [CT] of the head without contrast, CT angiography of head and neck, magnetic resonance imaging [MRI], diffusion-weighted MRI, magnetic resonance angiography [MRA], CT or carotid ultrasound), cardiac monitoring
5. Other cardiac assessment (telemetry) as appropriate
6. Considering if intra-arterial recanalization is appropriate

Management/Treatment

1. Education of patient/family regarding diagnosis, ED process, tests, treatment and risks
2. Blood pressure management
3. Intravenous (IV) isotonic fluids
4. tPA
5. Aspirin or other antithrombotics
6. Post ED management
   - Hospital care in intensive care unit or acute stroke unit/cardiac monitoring
   - Physical examinations, including vital signs and neurologic checks
   - Hypertension management
   - Bleeding precautions
   - Monitoring for complications of therapy
   - Treatment of hyperthermia or hypo-/hyperglycemia
   - Continued IV fluids
   - Deep vein thrombosis prophylaxis with low dose heparin, low-molecular-weight heparin (e.g., enoxaparin) or heparinoids; intermittent pneumatic compression
   - Swallow evaluation
   - Assessment for risk of falls and implementation of falls mitigation strategies
   - Early rehabilitation
   - Nutritional status assessment

- Early treatment of ischemic brain edema

Major Outcomes Considered

- Risk of stroke
- Validity and reliability of stroke assessment instruments
- Early stroke recurrence
- Stroke progression
- Mortality due to stroke
- Disability due to stroke

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

A consistent and defined process is used for literature search and review for the development and revision of Institute for Clinical Systems Improvement (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.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence and Strength of Recommendations

Category	Quality Definitions	Strong Recommendation	Weak Recommendation
High Quality Evidence	Further research is very unlikely to change the work group's confidence in the estimate of effect.	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.	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.
Medium	Further research is likely to	The work group is confident that	The work group recognizes that there is a balance

Quality Category Evidence	Quality Definitions	Strong Recommendation	Weak Recommendation
	have an important impact on the work group's confidence in the estimate of effect and may change the estimate.	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.	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.
Low Quality Evidence	Further research is very likely to have an important impact on the work group's confidence in the estimate of effect and is likely to change. The estimate or any estimate of effect is very uncertain.	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.	The work group recognizes that there is significant uncertainty about the best estimates of benefits and harms.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Guideline Development Process

A work group consisting of 6 to 12 members that includes physicians, nurses, pharmacists, other healthcare professionals relevant to the topic, and an Institute for Clinical Systems Improvement (ICSI) staff facilitator develops each document. Ordinarily, one of the physicians will be the leader. Most work group members are recruited from ICSI member organizations, but if there is expertise not represented by ICSI members, 1 or 2 work group members may be recruited from medical groups, hospitals or other organizations that are not members of ICSI.

The work group will meet for 7 to 8 three-hour meetings to develop the guideline. A literature search and review is performed and the work group members, under the coordination of the ICSI staff facilitator, develop the algorithm and write the annotations and literature citations.

Once the final draft copy of the guideline is developed, the guideline goes to the ICSI members for critical review.

Rating Scheme for the Strength of the Recommendations

See the "Rating Scheme for the Strength of the Evidence" field.

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Critical Review Process

The purpose of Critical Review is to provide an opportunity for the clinicians in the member groups to review the science behind the recommendations and focus on the content of the guideline. Critical review also provides an opportunity for clinicians in each group to come to consensus on feedback they wish to give the work group and to consider changes needed across systems in their organization to implement the guideline.

All member organizations are expected to respond to critical review guidelines. Critical review of guidelines is a criterion for continued membership within the Institute for Clinical Systems Improvement (ICSI).

After the critical review period, the guideline work group reconvenes to review the comments and make changes as appropriate. The work group prepares a written response to all comments.

Approval

Each guideline, order set, and protocol is approved by the appropriate steering committee. There is one steering committee each for Respiratory, Cardiovascular, Women's Health, and Preventive Services. The Committee for Evidence-based Practice approves guidelines, order sets, and protocols not associated with a particular category. The steering committees review and approve each guideline based on the following:

- Member comments have been addressed reasonably.
- There is consensus among all ICSI member organizations on the content of the document.
- Within the knowledge of the reviewer, the scientific recommendations within the document are current.
- When evidence for a particular recommendation in the guideline has not been well established, the work group identifies consensus statements that were developed based on community standard of practice and work group expert opinion.
- Either a critical review has been carried out, or to the extent of the knowledge of the reviewer, the changes proposed are sufficiently familiar and sufficiently agreed upon by the users that a new round of critical review is not needed.

Once the guideline, order set, or protocol has been approved, it is posted on the ICSI Web site and released to members for use. Guidelines, order sets, and protocols are reviewed regularly and revised, if warranted.

Revision Process of Existing Guidelines

ICSI scientific documents are revised every 12 to 36 months as indicated by changes in clinical practice and literature. ICSI checks with every work group 6 months before the schedule revision to determine if there have been changes in the literature significant enough to cause the document to be revised earlier or later than scheduled.

ICSI staff working with the work group to identify any pertinent clinical trials, meta-analysis, systematic reviews, or regulatory statements and other professional guidelines conduct a literature search. The work group will meet for 1-2 three-hour meetings to review the literature, respond to member organization comments, and revise the document as appropriate.

A second review by members is indicated if there are changes or additions to the document that would be unfamiliar or unacceptable to member organizations. If a review by members is not needed, the document goes to the appropriate steering committee for approval according to the criteria outlined above.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate screening and referral for patients presenting with neurological symptoms
- Rapid evaluation and treatment of patients who are candidates for thrombolytic therapy
- Improved management of ischemic stroke
- Effective prevention of stroke progression/recurrence
- Decreased mortality and morbidity associated with ischemic stroke

Potential Harms

- *Adverse effects of thrombolytic drugs* can include signs of central nervous system hemorrhage (e.g., neurological deterioration, development of severe headache, sudden severe elevation of blood pressure, or new nausea or vomiting) or signs of major systemic hemorrhage.
- *Management of hypertension*: 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. 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. In conclusion, the theoretical adverse effects of inadvertent overtreatment are substantial.
- The evidence to support *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.

Contraindications

Contraindications

Relative Contraindications for Tissue Plasminogen Activator (tPA)

Clinical Contraindications

- Clearly defined onset of stroke greater than 3 hours (4.5 hours in selected patients) 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 (National Institutes of Health Stroke Scale less than 4): sensory symptoms only, ataxia without other deficits, dysarthria without other deficits, mild motor signs (non-disabling), and visual field defect without other deficits (note: deficits measured at one to three on the scale may be very disabling and warrant use of tPA, e.g., moderate isolated aphasia in a professional using language in his/her profession, such as a journalist; hence clinical judgment may override guidelines)
- Obtunded or comatose state in the setting of middle cerebral artery (MCA) stroke
- Clinical presentation suggestive of subarachnoid hemorrhage regardless of computed tomography result
- Hypertension—systolic blood pressure (SBP) greater than 185 mm Hg or diastolic blood pressure (DBP) greater than 110 mm Hg. Patients with a systolic blood pressure greater than 185 mm Hg or diastolic blood pressure greater than 110 mm Hg are excluded only if the blood pressure exceeds the limits on consecutive measurements, and if aggressive treatment (i.e., beyond boluses of labetalol, nicardipine or doses of nitropaste) is required to lower the blood pressure into an appropriate range.

History Contraindications

- Minor ischemic stroke within the last month
- Major ischemic stroke or head trauma within the last 3 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 noncompressible site within the last 7 days or lumbar puncture within the last 3 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 international normalized ratio (INR) greater than 1.7
- Patient receiving heparin within the last 48 hours and having an elevated activated partial thromboplastin time (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 less than 50 or greater than 400 mg/dL
- Platelet count less than 100,000/mm^3
- 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 symptoms of the infarct was earlier than the symptom history first indicated; recheck patient history and time of symptom onset)
- Intracranial tumor, aneurysm, arteriovenous malformation or other space-occupying lesion

Contraindications to Aspirin (ASA) Therapy

- Aspirin allergy
- Gastrointestinal hemorrhage

Qualifying Statements

Qualifying Statements

- The information contained in this Institute for Clinical Systems Improvement (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.
- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition.
- The guideline work group 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 guidelines from the American Heart Association/American Stroke Association.
- Hyperthermia. In human studies, early hyperthermia in acute stroke is associated with increased risk of poor outcome, high mortality, and increased infarct volume. 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.
- Hyperglycemia. 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 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.
- Heparin. 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. This treatment does not appear to improve clinical outcome from the index stroke. There may be subgroups that benefit, but further studies of this problem are required for confirmation.

Implementation of the Guideline

Description of Implementation Strategy

Once a guideline is approved for general implementation, a medical group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they form a guideline action group.

In the action groups, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

Detailed measurement strategies are presented in the original guideline document to help close the gap between clinical practice and the guideline recommendations. Summaries of the measures are provided in the National Quality Measures Clearinghouse (NQMC).

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 tissue plasminogen activator (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
    - 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 as well as 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 for Accreditation of Healthcare Organizations (TJC) and Institute for Clinical Systems Improvement (ICSI), programs like the American Heart Association's Get with The Guidelines-Stroke and the Paul Coverdell National Acute Stroke Registry have been shown to improve the quality of stroke care, as well as hard outcomes, like mortality.

Centers for Medicare and Medicaid Services (CMS)

Beginning in 2010, hospitals submitting Medicare claims for stroke must notify CMS whether they participate in a database registry for stroke care. For further information on the CMS Final FY 2010 Rule, refer to http://www.cms.gov .

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. The link is http://www.jointcommission.org/certification/primary_stroke_centers.aspx .

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

Refer to the original guideline document for information regarding the requirements for TJC certification.

Implementation Tools

Chart Documentation/Checklists/Forms

Clinical Algorithm

Quality Measures

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Related NQMC Measures

Diagnosis and treatment of ischemic stroke: percentage of patients initially presenting with acute symptoms of ischemic stroke 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.

Diagnosis and treatment of ischemic stroke: percentage of patients admitted to the hospital, observation unit or expedited outpatient TIA clinic with documentation of clinical TIA symptoms within the last 24 hours.

Diagnosis and treatment of ischemic stroke: percentage of eligible patients with ischemic stroke treated with tPA.

Diagnosis and treatment of ischemic stroke: 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.

Diagnosis and treatment of ischemic stroke: percentage of eligible patients receiving tPA according to guideline.

Diagnosis and treatment of ischemic stroke: 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.

Diagnosis and treatment of ischemic stroke: percentage of patients with stroke symptoms who undergo a CT scan within 25 minutes of arrival in the emergency department.

Diagnosis and treatment of ischemic stroke: percentage of tPA non-recipients who have hypertension appropriately managed in the first 48 hours of hospitalization or until neurologically stable.

Diagnosis and treatment of ischemic stroke: percentage of patients who receive appropriate intervention for hypoglycemia and hyperglycemia.

Diagnosis and treatment of ischemic stroke: percentage of patients who receive appropriate intervention for hyperthermia.

Diagnosis and treatment of ischemic stroke: percentage of patients with dehydration who receive IV fluids.

Diagnosis and treatment of ischemic stroke: percentage of patients with ischemic stroke with paralysis or other reason for immobility receiving appropriate prevention for VTE (subcutaneous heparin or pneumatic compression device).

Diagnosis and treatment of ischemic stroke: percentage of ischemic stroke patients who are assessed with a swallow screening test before receiving food, fluids or medications by mouth.

Diagnosis and treatment of ischemic stroke: percentage of patients mobilized from bed within 24 hours of admission.

Diagnosis and treatment of ischemic stroke: percentage of patients presenting in the emergency department with ischemic stroke for whom patient/family education is documented in the medical record.

Diagnosis and treatment of ischemic stroke: percentage of patients admitted to a hospital unit with ischemic stroke for whom patient/family

education is documented in the medical record.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Patient-centeredness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

Anderson D, Larson D, Bluhm J, Charipar R, Fiscus L, Hanson M, Larson J, Rabinstein A, Wallace G, Zinkel A. Diagnosis and initial treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2012 Jul. 122 p. [238 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2001 Oct (revised 2012 Jul)

Guideline Developer(s)

Institute for Clinical Systems Improvement - Nonprofit Organization

Guideline Developer Comment

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers; Allina Medical Clinic; Aspen Medical Group; Baldwin Area Medical Center; Brown Clinic; Center for Diagnostic Imaging/Medical Scanning Consultants; CentraCare; Central Lakes Medical Clinic; Chippewa County – Montevideo Hospital & Clinic; Cuyuna Regional Medical Center; Essentia Health; Fairview Health Services; Family HealthServices Minnesota; Family Practice Medical Center; Fergus Falls Medical Clinic; Gillette Children's Specialty Healthcare; Grand Itasca Clinic and Hospital; Hamm Clinic; HealthEast Care System; HealthPartners Central Minnesota Clinics; HealthPartners Medical Group & Regions Hospital; Hennepin County Medical Center; Hennepin Faculty Associates; Howard Young Medical Center; Hudson Physicians; Hutchinson Area Health Care; Hutchinson Medical Center; Integrity Health Network; Lake Region Healthcare Corporation; Lakeview Clinic; Mankato Clinic; MAPS Medical Pain Clinics; Marshfield Clinic; Mayo Clinic; Mercy Hospital and Health Care Center; Midwest Spine Institute; Minnesota Association of Community Health Centers; Minnesota Gastroenterology; Multicare Associates; New Richmond Clinic; North

Central Heart Institute; North Clinic; North Memorial Health Care; Northwest Family Physicians; Obstetrics and Gynecology Specialists; Olmsted Medical Center; Park Nicollet Health Services; Planned Parenthood Minnesota, North Dakota, South Dakota; Quello Clinic; Raiter Clinic; Rice Memorial Hospital; Ridgeview Medical Center; River Falls Medical Clinic; Riverwood Healthcare Center; South Lake Pediatrics; Southside Community Health Services; Stillwater Medical Group; University of Minnesota Physicians; Winona Health

ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; e-mail: icsi.info@icsi.org; Web site: www.icsi.org.

Source(s) of Funding

The Institute for Clinical Systems Improvement's (ICSI's) work is funded by the annual dues of the member medical groups and five sponsoring health plans in Minnesota and Wisconsin.

Guideline Committee

Cardiovascular Steering Committee

Composition of Group That Authored the Guideline

Work Group Members: David Anderson, MD (*Work Group Co-Leader*) (University of Minnesota Physicians and Hennepin County Medical Center) (Neurology); David Larson, MD (*Work Group Co-Leader*) (Ridgeview Medical Center) (Emergency Medicine); Gail Wallace, NP (Essentia Health) (Nursing); Lynne Fiscus, MD, MPH (Fairview Health Services) (Internal Medicine and Pediatrics); Andrew Zinkel, MD (Marshfield Clinic) (Emergency Medicine); Ron Charipar, MD (Marshfield Clinic) (Internal Medicine and Pediatrics); Alejandro Rabinstein, MD (Mayo Clinic) (Neurology); Jeff Larson, PharmD (Park Nicollet Health Services) (Pharmacy); Myounghee Hanson (Institute for Clinical Systems Improvement) (Facilitator); Jim Bluhm, MPH (Institute for Clinical Systems Improvement) (Team Director)

Financial Disclosures/Conflicts of Interest

Disclosure of Potential Conflicts of Interest

David Anderson, MD (Work Group Leader)
Professor, Neurology Department, Neurology, University of Minnesota Physicians and Hennepin County Medical Center
National, Regional, Local Committee Affiliations: NNINDS NHLBI as an event adjudicator for two clinical trials: SAMMPRIS (Stenting Versus Aggressive Medical Management for Preventing Recurrent Stroke), and AIM-HIGH (Atherothrombosis Intervention in Metabolic Syndrome with Low HDL Cholesterol/High Triglyceride and Impact on Global Health Outcomes)
Guideline-Related Activities: None
Research Grants: None
Financial/Non-Financial Conflicts of Interest: MN Acute Stroke Systems Council, MDH and member of MN Time Critical Care Committee, MDH

Ron Charipar, MD (Work Group Member)
Professor, Internal Medicine, Marshfield Clinic
National, Regional, Local Committee Affiliations: None
Guideline-Related Activities: None
Research Grants: None
Financial/Non-Financial Conflicts of Interest: None

Lynne Fiscus, MD, MPH (Work Group Member)
Internal Medicine and Pediatrics Department, Fairview Health Services
National, Regional, Local Committee Affiliations: None
Guideline-Related Activities: None
Research Grants: None
Financial/Non-Financial Conflicts of Interest: None

David Larson, MD, FACEP (Work Group Member)
Medical Director, Ridgeview Emergency Department, Ridgeview Medical Center
National, Regional, Local Committee Affiliations: None
Guideline-Related Activities: None
Research Grants: None
Financial/Non-Financial Conflicts of Interest: Clinical Advisory Panel Leader, TogetherMD, LLC, MN Acute Stroke Systems Council, MDH and member of MN Time Critical Care Committee, MDH

Jeff Larson, PharmD (Work Group Member)
Staff Pharmacist, Pharmacy, Park Nicollet Health Services
National, Regional, Local Committee Affiliations: None
Guideline-Related Activities: None
Research Grants: None
Financial/Non-Financial Conflicts of Interest: None

Alejandro Rabinstein, MD (Work Group Member)
Professor, Neurology, Mayo Clinic
National, Regional, Local Committee Affiliations: None
Guideline-Related Activities: None
Research Grants: Cardionet, MCOT use for an investigator-initiated project
Financial/Non-Financial Conflicts of Interest: Member of the Data Safety Monitoring Board for the PREVAIL study by ARTITECH (now Boston Scientific)

Gail Wallace, NP (Work Group Member)
Neurology Nurse Practitioner, Nursing, Essentia Health East Region
National, Regional, Local Committee Affiliations: None
Guideline-Related Activities: None
Research Grants: None
Financial/Non-Financial Conflicts of Interest: None

Andrew Zinkel, MD (Work Group Member)
Section Head and Medical Director of Quality, Department of Emergency Medicine, HealthPartners Medical Group and Regions Hospital
National, Regional, Local Committee Affiliations: None
Guideline-Related Activities: None
Research Grants: None
Financial/Non-Financial Conflicts of Interest: Clinical Advisory Panel Leader, TogetherMD, LL

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2010 Jun. 70 p.

Guideline Availability

Electronic copies: Available from the Institute for Clinical Systems Improvement (ICSI) Web site .

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org ; e-mail: icsi.info@icsi.org.

Availability of Companion Documents

The following are available:

- Diagnosis and initial treatment of ischemic stroke. Executive summary. Bloomington (MN): Institute for Clinical Systems Improvement; 2012 Jul. Electronic copies: Available from the Institute for Clinical Systems Improvement (ICSI) Web site.
- Health care order set: admission for ischemic stroke for patient not receiving tPA. Bloomington (MN): Institute for Clinical Systems Improvement; 2012 Jul. 7 p. Electronic copies: Available from the ICSI Web site.
- Health care order set: admission for ischemic stroke for patient receiving tPA. Bloomington (MN): Institute for Clinical Systems Improvement; 2012 Jul. 7 p. Electronic copies: Available from the ICSI Web site.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

Additionally, the Non-National Institute of Health Stroke Scale (NIHSS) Neuro Check form is available in the appendices of the original guideline document.

Patient Resources

None available

NGC Status

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