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Hyperacute Management of Ischemic Stroke

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Abstract

Stroke is a devastating disease and currently the fourth leading cause of death in this country. Acute ischemic stroke is an emergency and requires effective triage, diagnosis, and critical management. The hyperacute management of ischemic stroke begins in the field, with recognition of stroke symptoms by emergency medical systems (EMS) personnel. The EMS is an important component to an effective stroke system of care, which also includes primary stroke centers, routing protocols for acute ischemic stroke, and telemedicine. Following the arrival of a potential stroke patient to the emergency room setting, patients should be stabilized and undergo assessment for potential intravenous alteplase (IV tPA) treatment. Assessments include diagnostic tests, neuroimaging, and standardized stroke evaluations. After these assessments have been performed, IV tPA, the only medication for acute stroke approved by the U.S. Food and Drug Administration, can be considered using a variety of inclusion and exclusion criteria. Previously time restrictions limited the usage of IV tPA to 3 hours, but this time window has now been extended for eligible candidates to 4.5 hours. The administration of IV tPA has specific requirements for monitoring and should be standardized via protocol across hospitals.

Keywords

acute ischemic stroke; stroke systems of care

Stroke is a devastating illness¹ that affects 795,000 people in the United States each year.² Stroke is the second-leading cause of hospital admission among elderly Americans, and results in about \$74 billion of direct and indirect annual costs.² Given the societal and economic burden of this disease, reducing the risk of poor outcome after suffering stroke is largely dependent upon what occurs when each patient is first struck with stroke symptoms. Proper identification of stroke and essential prehospital protocols by emergency medical systems (EMS) personnel followed by appropriate acute management of the ischemic stroke in the emergency room setting can lead to decreased morbidity and mortality for ischemic stroke patients. The success of this course requires a seamless stroke system of care. Another component of this process relies upon the ability for emergency room physicians and neurologists to work together to provide the very best stroke care for each patient.³

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Stroke Systems of Care

The main goal of an effective stroke system of care is to support each stroke patient from prevention to rehabilitation.³ First recommended by the Institute of Medicine of the National Academy of Science in 2001, systems of care were defined to prevent both ineffective and inefficient usage of resources for the treatment and prevention of disease.⁴ Translated into stroke terms, a stroke system of care should allow for the following components: primary and secondary prevention; education; EMS response; hyperacute, acute, and subacute treatment of stroke; rehabilitation; and quality measures with continuous evaluation and feedback. Governmental support for the development of stroke systems of care has also been demonstrated.⁵ General recommendations were published by the American Stroke Association's Task Force on the Development of Stroke Systems in 2005.³ Included in the 2005 recommendations were delineations of a successful stroke system of care, including the need for a standardized approach in all components of the system, and effective collaboration among the different agencies and individuals providing care for stroke patients at different points. Another point emphasized was the need for constant review of protocols to ensure best-care practices, as well as the customized tailoring of each stroke system according to geographical or regional differences.

Primary and Comprehensive Stroke Centers

The Brain Attack Coalition (BAC) first described the elements that would identify hospitals as primary stroke centers (PSCs) in 2000 and updated their recommendations in 2011.^{6,7} The purpose of delineating specific hospitals as PSCs was to ensure that stroke patients were treated according to evidence-based guidelines, including protocols for treatment with intravenous alteplase (IV tPA) and available imaging services. Other components of primary stroke centers included aspects such as available neurosurgical services, laboratory services, community educational outreach, and maintenance of a stroke registry. Additional recommendations added to the revised guidelines in 2011 included early evaluation and treatment by rehabilitation specialists, and specific monitoring protocols for acute stroke patients while in the emergency department.⁷ The Joint Commission (TJC) began to designate hospitals as PSCs based upon the BAC's recommendations in 2003; other organizations, such as state health departments, Det Norske Veritas, and the Healthcare Facilities Accreditation Program soon followed.^{2,7} There are currently more than 900 PSCs certified by TJC, with as many as 250 more designated by other organizations.^{7,8} Admission to PSCs has been associated with improved clinical outcomes for acute stroke patients, including increased usage of thrombolytic therapy, decreased mortality, and reduced institutional care.^{9,10} Also, the longer that a hospital had been certified as a PSC, the more likely it was to administer thrombolysis to acute stroke patients.^{11,12}

Those hospitals not officially certified as stroke PSCs should also be included in collaborating in stroke systems of care. One suggestion is to designate predetermined pathways for transfer of acute stroke patients to certified PSCs. Another way to treat acute stroke in a nondesignated stroke center is to utilize teleneurology services once the patient has arrived in the emergency room (see Teleneurology section below).

For the more complex and severe acute stroke patients, comprehensive stroke centers (CSCs) are hospitals that offer a higher level of intensity of acute stroke diagnosis, treatment, and management than PSCs. Comprehensive stroke centers were first defined by the BAC in 2005.¹³ Examples of CSC requirements include advanced imaging capability, defined by 24/7 magnetic resonance imaging (MRI) and neuroradiology availability; endovascular specialists, with the ability to treat acute ischemic and hemorrhagic strokes, including aneurysmal subarachnoid hemorrhage; and a full intensive care unit staffed by neurointensivists. The TJC began designating hospitals as CSCs in 2012.

Acute Stroke Routing Protocols

One recommendation for an effective stroke system of care was for EMS to transport stroke patients to stroke-ready or “acute stroke-capable” facilities.¹¹ In 2000, counties in Texas and Alabama were the first to begin routing acute stroke patient to stroke-designated facilities. By 2010, there were 16 states, and counties in an additional 3 states, that had routing protocol policies in place.⁸ The implementation of these routing policies drove PSC certification in the state of California.¹⁴ In addition, prehospital triage to PSCs was noted to more than double the acute stroke thrombolysis rate for stroke patients.¹⁵ Logistical considerations for the competent triage of acute stroke patients include the time of last known well, number of PSCs in the area, and patient preference. It is reasonable for patients to be routed to a closer hospital instead of a PSC if routing to a PSC would add more than 15 minutes. Recommendations also include taking all patients within 6 to 8 hours of stroke symptom onset to a PSC or a CSC, if only one hospital in the region is certified; if there are multiple certified centers within equivalent distances, the stroke patient should be transported to the highest level facility (CSC over PSC).¹¹

Prehospital Clinical Management of Acute Ischemic Stroke Patients

The main goal of prehospital management of acute stroke patients is to ensure that patients are assessed appropriately, efficiently, and safely. Because stroke patients often present late to emergency rooms with their stroke symptoms due to a variety of factors, including a lack of recognition of stroke symptoms and a decreased awareness to dial 9-1-1 with stroke symptoms, time is of the essence.¹⁶ Part of a proficient stroke system of care is the use of diagnostic algorithms for EMS activation and response. The purpose of these diagnostic algorithms and protocols is to systematically evaluate each potential acute stroke patient, provide appropriate emergent care to each patient, and transport each patient to the most appropriate hospital.¹⁷ Because EMS providers are the professionals in the field, it is their responsibility to obtain as accurate a patient history as possible, including establishing the last known well time, or time of stroke symptom onset. This information is essential in determining whether an acute stroke patient is a candidate to receive intravenous thrombolysis.

One of the most important protocols for EMS to establish is the type of standardized stroke assessment tool to be used in the field. Such tools include the LAPSS (Los Angeles Prehospital Stroke Screen), the CPSS (Cincinnati Prehospital Stroke Scale) and the FAST score (facial droop, arm drift, speech problem), and have been shown to provide consistency

in accurately identifying potential strokes.^{11,18} In addition, EMS providers should be directed to err on the side of “overtriage” as opposed to “undertriage” to ensure timely and appropriate transport of possible stroke patients.¹⁷ Continued education and training for recognition and treatment of stroke for EMS providers is also crucial, with active collaboration between the EMS, emergency room personnel, and key stakeholders; this emphasis on both community and professional education increases the usage of IV tPA.¹⁹ It is also critical for hospital providers to give feedback to prehospital providers. Another important component of EMS management of acute stroke patients includes the prenotification of hospitals that stroke patients are arriving. Prenotification improves time targets for stroke, including door to imaging and door to needle, and increases the likelihood of receiving IV thrombolysis.^{20–22}

Up to half of stroke patients can arrive at the emergency room outside of EMS activation via personal car or other mode of transportation. In those instances, the protocols dictated by the emergency room personnel will be essential in ensuring proper identification and triage of acute stroke patients.

Usage of Telemedicine for Acute Stroke

First coined in 1999, the term “telestroke” was seen as a way to enhance emergency treatment of stroke, including evaluation of neuroimaging and streamlined transfer for potential endovascular therapy.²³ Telemedicine, or telestroke, allows for acute stroke patients to be rapidly assessed for stroke by specialists, and if applicable, to be evaluated for IV thrombolysis. Teleradiology, or the viewing of radiology images remotely by specialists, is widespread.²⁴ However, by using video technology to connect acute stroke patients with neurology specialists, telestroke allows for swift clinical assessment and supportive decision making 24 hours a day, especially in a setting where a specialist may not be readily available, such as in rural areas without nearby PSCs. Since its inception, many “hub-and-spoke” telestroke systems have arisen. The model of “hub-and-spoke” refers to a central institution that is a PSC or CSC (hub), with contracted relationships with outlying hospitals (spoke), whereby stroke neurologists at the hub supervise the evaluation and management of acute stroke patients at spokes via teleconsultation (telephone or video consult). If patients are deemed IV tPA candidates, tPA is initiated at the outside spoke hospital, and the patient is transferred to the hub hospital (“drip and ship”). Neurologists who perform telestroke consultations must have access to neuroimaging, in addition to other clinical information and technological tools, such as webcams, headphones, and an Internet connection. Telestroke is safe and feasible and clinical outcomes between hospitals utilizing telestroke and PSCs, including mortality, are similar.^{25,26} Telestroke networks were also cost effective when compared with usual care in a cost-effectiveness analysis.²⁷ Preliminary studies looking at the feasibility of using telemedicine technologies from inside the EMS vehicles to hasten triage are on the horizon.²⁸

Acute Stroke Patient Arrival at Emergency Room

Once a suspected acute ischemic stroke patient arrives in the emergency room, regardless of whether there is EMS prenotification, a certain sequence of events must occur in a timely

fashion. Each potential stroke patient should be treated with the utmost priority and urgency, given the limited time window of stroke therapeutics. The National Institutes of Neurological Disorders and Stroke (NINDS) convened a consensus panel to describe the “stroke chain of survival” to identify the key events occurring after a stroke patient is admitted to the emergency room and goal times. The key events and target times are as follows: door to physician, 10 minutes; door to stroke team, 15 minutes; door to computed tomography (CT) initiation 25 minutes; door to CT interpretation, 45 minutes; door to IV tPA, 60 minutes; and door to stroke unit admission, 3 hours.²⁹ The presence of an acute stroke team, primed and prepared for the arrival of any stroke patients, has been recommended as part of a multidisciplinary stroke system of care.³ Acute stroke teams greatly improve the flow of the events within the emergency room, coordinating the sequence of events from patient arrival to patient transfer to the stroke unit for monitoring. Once a patient has been triaged as a potential acute stroke patient, or when patients have been predetermined to be potential stroke patients by EMS, acute stroke teams must be notified (or prenotified) so that acute stroke pathways and protocols can be followed and stroke treatments can be considered efficiently.³⁰ If a telestroke system is in place, the stroke team should be notified of potential stroke patients so as to facilitate video evaluation.

The basics are as in the field: assessment of airway, breathing, and circulation (the ABCs). Blood glucose is drawn in the field by EMS and should be corrected as appropriate. The patient should be monitored with blood pressure, heart rate, and oxygen saturation checks with frequent cycling. After the essential and basic assessment has been made, rapid neurological assessment and diagnostic testing must follow. Rapid neurological assessment of the acute stroke patient includes three key components: history, including time that the patient was last known to be normal, or last known well time; physical exam, including vital signs and auscultation of the chest for the cardiac and lung exam; and neurologic examination utilizing a formal scale, such as the NIH Stroke Scale (NIHSS).

History, the first component, is essential in determining whether a patient is eligible to receive IV tPA, and may weigh into the decision to attempt endovascular intervention. The first piece of history that is essential to obtain is history of last known well time. The reason that most patients, nearly 77%, do not qualify for IV tPA is because they present out of the eligible time window.³¹ The last known well time is obtained through a combination of patient memory or individuals who may have been with the patient, including family, coworkers, or other witnesses; the EMS run sheet is also useful if the patient arrives via emergency services. Key clues may also be determined through cellphone records, shopping receipts, or elements of the story that signal when stroke symptoms may have started (e.g., the time of a television broadcast). Patients may also wake up with stroke symptoms, and their last known well time could conceivably have been the night before. The second part of history that is necessary to acquire is any significant elements that could direct a practitioner to suspect a stroke mimic, such as seizure, trauma, drug abuse, or migraine. In a cohort of 512 patients treated with IV tPA, 21% were later found to be stroke mimics; however, the mimics treated with IV tPA had no symptomatic hemorrhages.³² The third part of history needed is stroke or cardiac history, and pertinent medications, especially anticoagulants.

Physical exam is the second component of rapid neurologic assessment. Aside from repeated vital sign assessments, the chest should be auscultated for arrhythmias and rales. Clues in the physical exam for an alternate explanation for the patient's presentation, such as evidence of seizure activity denoted by blood in the mouth and tongue biting, trauma, or infection (stigmata of endocarditis), may be present.

Brief and focused neurologic exam is the third component of assessment, and should include a formal standardized scale, such as the NIHSS or Canadian Neurological Scale. These formalized scales help assess the magnitude of neurologic injury, provide indication of localization, and predict early prognosis for outcome.^{33,34} In addition, repeating this formal scale at later points during the stroke patient's journey in the acute setting can swiftly detect clinical improvement or worsening and play an important role in medical decision making. The NIHSS has components ranging from level of consciousness to motor function to language, and ranges in score from 0 (no focal deficits) to 42 (maximal deficits).

Diagnostic Testing for Stroke Patients in the Emergency Setting

Diagnostic testing for the acute stroke patient in the emergency room includes laboratory testing, an electrocardiogram, chest imaging, and neuroimaging. For most patients, a finger-stick glucose test, and neuroimaging to rule out hemorrhage are the only diagnostic test assessments necessary prior to initiating IV thrombolysis. Though recommended, the remainder of the tests does not have to be reported prior to IV tPA except in special circumstances.²⁹

Aside from blood glucose, laboratory diagnostic tests should not delay administration of IV tPA except in certain situations. Hematologic laboratory tests, including complete blood count with platelet count, prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (aPTT), should be checked prior to thrombolysis in instances of patients with history of liver disease or of taking anticoagulants, as they may be abnormal and limit stroke treatment. When it is uncertain whether patients are taking anticoagulant medications, it may also be prudent to wait until these tests are back before initiating thrombolysis. However, in most individuals with no prior history of anticoagulant use or suspected hematologic or hepatic abnormalities it may be safe to proceed with thrombolysis before these test results return.³⁵ Of note, if tPA treatment is initiated and platelet count is found to be less than 100,000 or INR is noted to be > 1.7 , then the tPA should be discontinued. Given the advent of direct thrombin inhibitors and direct factor Xa inhibitors, including dabigatran, rivaroxaban, and apixaban, one could consider more obscure tests, such as the ecarin clotting time (ECT) or the thrombin time (TT), though they may not be helpful or available in a timely fashion.²⁹ Other laboratory tests to consider include cardiac markers and electrolyte studies, including kidney function studies, though again these tests should not delay thrombolysis if appropriate. Troponin is frequently elevated in acute stroke patients, reportedly as high as 34%; these patients are 3 times as likely to have concomitant electrocardiogram (ECG) changes suggestive of myocardial infarction and should be closely monitored.³⁶ Kidney function studies, especially the creatinine or the glomerular filtration rate, are useful if the patient is deemed a candidate for any endovascular intervention that may require intravenous contrast, or further diagnostic

testing requiring contrast (either MRI or CT). Urine or blood toxicological screens for sympathomimetic drugs, such as cocaine and methamphetamines, may identify stroke etiology.

An ECG, in conjunction with the cardiac markers, should be performed to evaluate baseline cardiac status. Besides being useful for assessing for baseline arrhythmias that can predispose to stroke, such as atrial fibrillation, ECG can also indicate evidence of cardiac damage due to myocardial ischemia, which can occur in conjunction with acute ischemic stroke. If abnormal, the studies can also indicate whether continued monitoring with serial ECGs or cardiac markers should be pursued to evaluate change over time. Continuous cardiac telemetry or Holter monitoring should also be utilized for at least the first 24 hours after stroke.²⁹

Chest radiograph is more controversial, as newer evidence suggests there may be decreased utility in obtaining before thrombolysis. One study showed 3.8% of chest radiographs obtained in the acute stroke code setting showed potentially significant findings that could impact acute stroke care.³⁷ It is generally recommended that chest radiographs should be performed while the stroke patient is in the emergency room, but should not delay thrombolysis unless there is a strong suspicion for aortic dissection.²⁹

Initial brain imaging is typically noncontrast-enhanced CT, although some institutions have a dedicated MRI scanner available emergently for stroke codes. However, CT is considered satisfactory for the identification of parenchymal hemorrhage or other imaging findings (such as tumor) that would be considered an exclusionary reason to halt thrombolytic therapy. Computed tomography findings performed in the acute phase can also indicate location of stroke or help to predict clinical outcome. Hyperdense middle cerebral artery (MCA) clot typically represents occlusion and hyperdensity within the sylvian fissure, or the MCA “dot” sign, has been associated with M2 or M3 clot.^{38,39} Early CT findings, such as diffuse swelling or cerebral sulci effacement, have been associated with more severe strokes, but not with increased risk of adverse clinical outcomes due to thrombolysis.⁴⁰ However, frank hypodensity involving more than a third of the MCA territory should pre-empt the administration of IV tPA.²⁹

If utilizing MRI, the most sensitive and specific sequence is the diffusion-weighted imaging (DWI) sequence, which can detect even small and posterior acute ischemic lesions within minutes of symptom onset.⁴¹ In addition, the gradient echo or susceptibility weighted imaging sequences are able to detect hemorrhage, both acute and chronic, including microbleeds. There is some controversy as to whether microbleeds indicate an increased risk of hemorrhage after thrombolytic therapy and more studies are needed.^{42,43}

Regardless of modality, the target time from patient arrival to neuroimaging is within 25 minutes.²⁹ When comparing CT with MRI, the benefit of CT is the shorter time of acquiring images, the greater availability of CT to more patients (without the restrictions of MRI use in patients with metal or stent exclusions), decreased expense, and the ability of practitioners to see whether areas of hemorrhage or other exclusionary findings for IV thrombolysis are present. However, MRI provides greater precision of ischemic stroke diagnosis and higher

degree of sensitivity, especially in the posterior fossa. Perfusion imaging, both CT and MRI, has become more popular especially in the setting of patient selection for further acute reperfusion therapies, but is not available in most institutions and is not necessary to proceed with IV thrombolytic therapy.²⁹

Basic Supportive Care

Supportive care in the acute stroke setting includes supine positioning if the patient is nonhypoxic and tolerates lying flat.⁴⁴ However, in those patients who are at aspiration risk or are thought to have elevated intracranial pressures, 15 to 30 degrees is the acceptable elevation for the head of bed.⁴⁵ Supplemental oxygen, if the patient is hypoxic, should be administered using the least invasive method and endotracheal intubation should be executed in the event of airway compromise or decreased level of consciousness.²⁹ Hyperthermia is associated with increased mortality and worse clinical outcomes, though there is no evidence that acetaminophen to prevent fever is effective in improving outcome.^{46,47} Therapeutic hypothermia, though promising in experimental models, has not yet been proven to be beneficial or harmful in the setting of acute ischemic stroke and more clinical trials have been proposed.⁴⁸ Hyperglycemia is associated with poor stroke outcomes, and thus the glucose levels should be carefully monitored with a goal ideal blood glucose between 140 to 180 mg/dL.²⁹ Euvolemic patients should receive maintenance IV fluids, though patients with renal or heart failure should be treated cautiously. Hypovolemic patients should have their depletion treated with IV saline.²⁹

Elevated blood pressure is often seen in the setting of acute ischemic stroke, and even higher blood pressure may be seen in those patients with a past medical history of hypertension.²⁹ However, the ideal blood pressure range during acute stroke likely differs between patients and includes consideration of medical history, clinical scenario, and ischemic stroke subtype. Current recommendations state that within the first 24 hours of a stroke the blood pressure should not be treated unless it is > 220/120 mm Hg, unless other urgent considerations are present.^{29,49} For patients considered for thrombolytic therapy, the blood pressure must be < 185/110 mm Hg prior to treatment. Once IV tPA has been given, the blood pressure must be maintained at or below 180/105 mm Hg. If blood pressure must be lowered before IV tPA can be given, having a hospital protocol with prespecified medications in place is recommended. Current recommendations to lower the blood pressure before administering IV tPA include using IV labetalol, given in pushes, or IV nicardipine, in the form of a drip.²⁹

Intravenous Fibrinolysis Therapy for Acute Stroke

Intravenous tPA was first approved by the U.S. Food and Drug Administration (FDA) to treat acute ischemic stroke in 1996, based upon the large NINDS trials which showed that patients had a 4 point improvement on the NIHSS or complete neurologic recovery at 24 hours; follow-up studies later showed favorable outcomes at 3 months and again at 1 year.^{50,51} Initially, IV tPA was approved for stroke symptoms that had occurred within 3 hours. The investigators found that shorter onset time to treatment was associated with better outcomes.⁵² One study found that reducing time to treatment by even 15 minutes could lower the odds of in-hospital mortality by 5%.⁵³

The most common reason patients are ineligible for IV tPA is arrival outside the therapeutic window. Multiple clinical trials have explored extending the 3-hour time window for IV tPA administration, including the European Cooperative Acute Stroke Study (ECASS) 1 and 2 and the Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke (ATLANTIS) study A and B. Pooled data from these studies suggested a possible benefit for stroke patients out to 4.5 hours.^{54,55} There was no net benefit of treating stroke patients in the 4.5-to 6-hour window.⁵⁴ Because of these pooled findings, the ECASS 3 trial randomized patients presenting within 3 to 4.5 hours (median treatment interval was ~ 4 hours) to receive either IV tPA or placebo. In addition to the NINDS exclusions, ECASS 3 excluded patients over 80, patients with severe strokes (NIHSS score > 25), patients with a history of both diabetes mellitus and prior stroke, and patients taking any oral anticoagulants despite normal hematologic tests. Results from ECASS 3 revealed that those who received IV tPA had improved functional outcomes, and mortality was similar, between those who had received IV tPA and those who had received placebo.⁵⁶ The Safe Implementation of Thrombolysis in Stroke-International Stroke Treatment Registry 3-to-4.5-Hour Study subsequently compared patients who had received IV tPA before 3 hours and patients who had received IV tPA between 3 and 4.5 hours and found similar rates of symptomatic intracerebral hemorrhage and mortality between the two groups.⁵⁷ In 2009 the American Heart Association released a science advisory stating that the 4.5-hour expanded time treatment window for IV tPA should be considered for selected patients.⁵⁸ The FDA, however, declined to approve tPA in the 3- to 4.5-hour window.

Administering IV tPA

The inclusion and exclusion criteria that must be addressed with each potential tPA candidate are found in Table 1. The classic 3-hour inclusion criteria for receiving IV tPA include measurable neurologic deficit likely attributed to ischemic stroke, onset of symptoms occurring less than 3 hours before treatment, and age greater than or equal to 18 years old. The 3-hour exclusion criteria include multiple clinical scenarios, including prior stroke in the previous 3 months; history of previous intracranial hemorrhage; active internal bleeding; and intracranial neoplasm, arteriovenous malformation, or aneurysm.²⁹ Use of direct thrombin inhibitors and direct factor Xa inhibitors should also be considered an exclusion criteria. Extending therapy to the 4.5-hour window is limited by the aforementioned ECASS 3 criteria.⁵⁸

The total dosage of IV tPA is 0.9 mg/kg, with a maximum dose of 90 mg. A bolus dose of 10% should be slowly injected over 1 minute, with the remaining 90% given over a 1-hour infusion. Vitals and neurologic assessments should be checked every 15 minutes for at least 2 hours, with blood pressure medications (labetalol or nicardipine) given as needed if the blood pressure exceeds 180/105. After 2 hours, the blood pressure should be monitored and assessments should be performed every 30 minutes for 6 hours, then every hour for 16 hours until a full 24-hour period has been reached.²⁹ During that time, the patient should be admitted to the intensive care or stroke unit for monitoring, and placement of nasogastric tubes or bladder catheters should be avoided unless necessary. After 24 hours, the patient should receive a follow-up imaging study, CT or MRI, to assess for hemorrhage. During

those 24 hours, if the patient suffers a neurologic deterioration, imaging should be immediately obtained to assess for symptomatic hemorrhage.

Other Considerations for IV tPA

There are multiple relative exclusion criteria to receiving IV tPA, including pregnancy, mild or rapidly improved stroke symptoms, seizure with postictal neurologic deficits, major surgery or serious trauma within 14 days, recent myocardial infarction within the previous 3 months, and recent gastrointestinal or urinary tract hemorrhage within 21 days. In these circumstances, the practitioner must weigh the risks and benefits with patients and families to determine whether to proceed with thrombolytic therapy. These relative exclusions are controversial. For instance, a substantial number of patients with mild or improving stroke symptoms not treated with IV tPA have poor stroke outcomes⁵⁹ and whether this subset of patients should receive tPA is unclear.

Complications of IV tPA

Symptomatic hemorrhage is the most feared complication of IV tPA. The original NINDS tPA trial reported a 6.4% symptomatic intracranial hemorrhage rate.⁵⁰ Despite this, patients treated with tPA as a group still had better outcomes than the placebo group.⁶⁰ Hemorrhage risk is directly proportional to the degree of IV tPA protocol deviation.^{29,61}

Orolingual angioedema, or swelling of the lips, tongue, or oropharynx, are typically transient symptoms, occurring up to 5.1% of patients who receive IV tPA for stroke.⁶² Patients with strokes in the frontal or insular cortex or on an angiotensin-converting enzyme inhibitor are more likely to have an angioedema reaction. Treatment with diphenhydramine, steroids (typically methylprednisolone), and ranitidine intravenously is generally effective.²⁹

Endovascular Interventions for Acute Stroke

A patient eligible for IV tPA should undergo thrombolysis promptly. Endovascular intervention remains a consideration in many situations, including persistent severe deficits, proximal occlusion, and clinical symptomatology consistent with a large vessel occlusion, the patient, if not at a CSC, should be transferred to a CSC expediently. Several devices are effective in recanalizing occluded vessels, such as the Merci (Concentric Medical, Fremont, CA), the Penumbra System (Penumbra, Inc., Alameda, CA), the Solitaire FR (ev3 Endovascular, Inc., Plymouth, MN), and the Trevo thrombectomy device (Stryker, Kalamazoo, MI).²⁹ However, rigorous trials and long-term outcome studies have not yet demonstrated these devices or procedures to be superior to IV thrombolysis.²⁹

Conclusions

Acute ischemic stroke is an emergency. The effective treatment of acute stroke requires speed and cooperation among stakeholders, including EMS, emergency room physicians, and neurologists.

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Table 1

Intravenous alteplase (IV tPA) criteria for 3- and 4.5-hour time window (adapted from the 2013 American Heart Association/American Stroke Association guidelines on management of acute ischemic stroke²⁹)

Inclusion criteria	
Measurable neurologic deficit from acute ischemic stroke	
Age ≥ 18	
Exclusion criteria	
3-h IV tPA	4.5-h tPA
Previous 3 months	All of 3-hour IV tPA exclusion criteria PLUS
Prior stroke	Age > 80 years old
Significant head trauma	NIH Stroke Scale score > 25
Myocardial infarction	Oral anticoagulant usage regardless of INR
Suspected subarachnoid hemorrhage	Past medical history of both stroke and diabetes
Any prior history of intracranial:	
Tumor	
Arteriovenous malformation	
Aneurysm	
Hemorrhage	
Abnormal laboratory results	
Platelets < 100,000	
INR > 1.7 (with current anticoagulant usage)	
PT > 15 seconds	
Glucose < 50	
Heparin administration in past 48 h, abnormal PTT	
Active internal bleeding	
Recent intracranial or intraspinal surgery	
Arterial puncture at noncompressible site within 7 days	
Direct thrombin inhibitor or direct factor Xa inhibitor usage	
Relative contraindications:	
Pregnancy	
Seizure at onset of symptoms	
Major surgery or trauma within past 2 weeks	
Mild or rapidly improving stroke symptoms	

Abbreviations: INR, international normalized ratio; PT, prothrombin time; PTT, partial thromboplastin time.