Treating Ischemic Stroke as an Emergency

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The success of treatment with tissue plasminogen activator serves as an impetus to approach stroke as a medical emergency; diagnosis and treatment must be accurate and prompt. The initial evaluation should be straightforward and aimed at confirming ischemic stroke as the cause of the patient's acute neurologic impairments. Until the usefulness of diagnostic tests to demonstrate an arterial occlusion is established in emergent management, their application before treatment should not be mandated. Most individuals with acute ischemic stroke will receive their initial, key treatment in a community setting. Thus, strategies for emergent treatment should aim at management of patients whose strokes are diagnosed and first treated by emergency treatment and primary care physicians with the collaboration of neurologists.

Ischemic stroke is the most common acute neurologic illness and a leading cause of death, disability, and human suffering. Financially, it also is an expensive disease. Stroke costs the US economy more than $40 billion per year. Thus, successful management of ischemic stroke has vast public health implications. In the past, ischemic stroke was approached with nihilism by both the public and health care providers. This negative attitude is being abandoned in response to a revolution in the management of stroke. Stroke now is being treated as the life-threatening disease it is. Several factors underpin modern management. The interval from onset until treatment is critical. Ischemic stroke usually is caused by thromboembolic occlusion of an artery supplying a portion of the brain, and improving perfusion will be fundamental for success. The spectrums of neurologic impairments and causes of stroke are broad; as a result, the prognosis of patients varies considerably. Besides treating the stroke itself, management includes measures to prevent or control medical or neurologic complications, rehabilitation, and therapies to prevent recurrent stroke. Management also is influenced by the patient's condition and his/her wishes. Most patients with acute ischemic stroke will not be treated initially by neurologists or stroke care specialists. Because of limited availability of acute stroke care units, most patients are admitted to community hospitals that do not have special expertise in the treatment of cerebrovascular disease.

The primary goal of modern treatment of acute ischemic stroke is to limit or reverse the brain injury so that the patient can recover as much as possible. A sustained improvement in neurologic outcome is the measure to judge responses to treatment. Ischemic stroke is a complex vascular and metabolic process that evolves over minutes to hours. The concept of the ischemic penumbra emphasizes that although a core of infarcted tissue might not be salvageable with any intervention, an area of dysfunctional, ischemic brain might be rescued if a therapy is prescribed promptly. Experimental studies amply demonstrate that the interval from onset of ischemia until initiation of treatment is critical for success for any therapy. The window for effective treatment may be only a few hours. The maximum interval is not known but an intervention prescribed more than 24 hours after onset of symptoms is not likely to be of much benefit.
Starting treatment as soon as possible is and will continue to be a driving force in emergent stroke care.

The push to start treatment quickly is the basis of efforts to increase public and professional awareness of stroke, which is summarized in the term brain attack. Delays in recognition, transport, evaluation, and treatment must be overcome to meet the short time windows required for current emergent care. The public’s knowledge about the presentations of stroke and the best responses to their appearance is limited. A concerted public education campaign is needed; in particular, high-risk patients and their family members, neighbors, friends, and coworkers should be instructed on the common symptoms of stroke. The message to the public also should emphasize that stroke is treatable but that time is critical. The educational program for acute ischemic stroke (brain attack) can be modeled on that used for acute myocardial ischemia (heart attack). Neurologists should lead these educational efforts in their communities.

Emergency medical services (EMS) should give acute stroke the same priority as acute heart disease. Educational programs on the importance of stroke care are needed for all components of EMS systems, including dispatchers and rescue squads. Evaluation in the field by EMS personnel should be prompt and transportation to a hospital should be speedy. The first assessments should include relevant medical history, measurement of vital signs, and a brief neurologic examination. If a paramedic is in attendance, blood work and an electrocardiogram can be obtained and an intravenous line can be placed. A protocol that coordinates care between the EMS and hospital can expedite transfer. The rescue squad should inform the hospital that a patient with a possible stroke is being transported to the emergency department. The patient should go to a hospital that has the ability to emergently perform computed tomography on a 24-hour per day and a 7-day per week basis. Such a requirement might mean bypassing the closest hospital because it does not have imaging facilities.

In turn, the hospital should have an acute stroke care protocol to meet ambitious but feasible goals to rapidly assess and treat patients. The availability of a treatment of proven efficacy for improving outcomes of individuals with ischemic stroke (tissue plasminogen activator) but which must be given within 3 hours of onset of stroke highlights the importance of these efforts. The protocol should include a list of physicians, nurses, laboratory and radiology personnel, and pharmacists who will be members of an acute stroke care team. In institutions that do not have continuous coverage by stroke specialists or neurologists, primary care or emergency medicine physicians likely will be the leaders of this team. The protocol should outline steps in emergent evaluation that focus on confirming ischemic stroke as the likely cause of the neurologic impairments and detecting acute medical or neurologic complications. The emergent diagnostic studies for assessment of a patient with a suspected acute ischemic stroke should include the following: computed tomography of the brain without contrast; electrocardiogram; chest x-ray film; complete blood cell count and platelet count; prothrombin time and activated partial thromboplastin time; blood chemistry studies, including serum electrolytes and blood glucose level; arterial blood gases, if hypoxia is suspected clinically; and cervical spine x-ray films, if the patient is unconscious and no medical history is available about the onset of neurologic impairments. In addition, the protocol should include components for general emergent management and the initiation of treatments of the stroke, including deciding whether a patient might be treated with tissue plasminogen activator (Table). The published guidelines for care of acute stroke can be used as the templates for writing these protocols.

Intravenous administration of tissue plasminogen activator has engendered controversy. Intravenous thrombolysis is not a cure-all but, at present, it is the only therapy of proven efficacy for management of individuals with acute ischemic stroke. While intra-arterial administration of thrombolytic drugs has theoretical advantages, its superiority over intravenous thrombolysis is not proved. Although the results of some studies are promising, neither antithrombotic drugs nor neuromodulator drugs are established as effective in improving outcomes after stroke. Until other therapies or treatment strategies are of proven value in improving neurologic outcome after ischemic stroke, the goal of emergent management should be aimed at treatment with intravenous tissue plasminogen activator.

The short time window for effective and safe treatment with tissue plasminogen activator has implications for all physicians, including neurologists. Initial management likely will occur in an emergency department. Most emergency departments are staffed by emergency medicine specialists or primary care physicians and in many hospitals neurologists are not readily available. Many patients cannot reach large tertiary medical centers with stroke specialists within 3 hours; in particular, patients in rural areas likely cannot be transported to a major hospital quickly enough to be treated with tissue plasminogen activator. Thus, a strategy to provide emergent care, including the use of tissue plasminogen activator, must be developed for a community setting. Hachinski advised that 3 criteria must be in place for the successful use of thrombolytic drugs: (1) availability of a physician with expertise in the diagnosis and management of stroke, (2) accessibility to modern brain imaging studies, and (3) capability to handle potential complications of treatment, especially brain hemorrhage. One could argue that these requirements are needed for treatment of individuals with stroke, regardless of the use of tissue plasminogen activator. To expedite care of individuals with stroke, neurologists should be readily available for consultations in emergency departments. Pending increased involvement of neurologists in emergency management, guidelines for acute ischemic stroke should be written with the primary audience being physicians who are not neurologists. Strategies that permit rapid access to a neurologist for individuals located in remote places should be explored; potential approaches include telemedicine or air evacuation. A possible scenario would be for the patient to be treated with tissue plasminogen activator in a community hospital with the advice of a neurologist via telemedicine followed by air evacuation to a tertiary medical center for subsequent treatment.
Besides being a life-threatening neurologic disease, ischemic stroke is a symptom of an underlying vascular disease that leads to thromboembolic occlusion of an artery supplying a portion of the brain. The cause of stroke affects the patient’s prognosis; people with strokes secondary to occlusion of a penetrating brain artery (lacunes) generally have a better prognosis than those with occlusions of a major extracranial or intracranial vessel. Determination of the most likely cause of stroke has implications on plans to prevent recurrent stroke; for example, anticoagulants are prescribed to most individuals with cardioembolic stroke while antiplatelet aggregating drugs are given to most patients with stroke secondary to extracranial or intracranial atherosclerosis. Still, the diagnosis of cause of stroke can be difficult; physicians, including neurologists who have special expertise in stroke, often disagree. Even diagnosis of a lacunar stroke can be difficult. A lacunar syndrome may not be due to a lacunar infarction and the misdiagnosis could hamper the use of potentially effective treatment. In addition, etiologic diagnoses made in an emergency department often change in subsequent days. Unfortu-
nately, an accurate diagnosis of subtype of ischemic stroke often requires the use of ancillary tests (ie, transesophageal echocardiography, carotid duplex, or arteriography) that may not be available at a community hospital. In addition, the reliability, sensitivity, and specificity of these tests when performed in an emergency setting are not known. Such information is critical because of the potential for incorrect treatment if an ancillary test gives either false-positive or false-negative information. Even if these tests are available in a community hospital, the time required to mobilize personnel and other resources to perform the test endangers the opportunity for treatment with tissue plasminogen activator. Considerable research is needed to test the assumption that the diagnosis of subtype of stroke is needed before starting emergent treatment. Data from clinical trials give limited support for the urgency of making an “accurate” stroke subtype diagnosis. In particular, the American trial of tissue plasminogen activator did not note differences in responses to thrombolytic therapy among people with disparate subtypes. Until available evidence shows that the diagnosis of stroke subtype critically affects acute management, ancillary diagnostic tests to determine the likely cause of stroke should not be mandated before emergent treatment. At present, data do not support, in general, a recommendation to tailor acute management of stroke based on the presumed cause.

Caplan has articulated the importance of demonstrating an arterial occlusion before making decisions about acute treatment. To test this assumption, trials are testing the value of intra-arterial thrombolytic therapy in treatment of patients with arteriographically confirmed occlusions of extracranial or intracranial arteries. While results are promising, intra-arterial thrombolytic therapy has not been shown convincingly to be either safer or more effective than intravenous therapy. The requirement for visualization of an arterial occlusion by arteriography before treatment greatly limits the use of the therapy; a minority of patients can be treated because only a limited number of hospitals have the required personnel and sophisticated interventional capabilities. In addition, withholding treatment with a therapy of proven value (intravenous tissue plasminogen activator) while marshaling the resources to give intra-arterial thrombolytic therapy is problematic, particularly when intra-arterial therapy is not established as superior to intravenous therapy. Considerable research is needed to test the hypothesis that knowledge of the vascular anatomy underlying stroke is necessary before starting emergent treatment. Until such evidence is available, examination of the vascular anatomy before treatment should not be mandated.

Physicians know that the clinical severity of stroke strongly predicts outcomes and affects decisions about treatment. The National Institutes of Health Stroke Scale (NIHSS) is a widely used and accepted system to numerically rate the severity of a patient’s stroke. The aggregate score of the NIHSS strongly correlates with outcomes. Patients with very mild deficits (low NIHSS score) generally have a favorable prognosis regardless of treatment; these patients might not need to be treated with tissue plasminogen activator or any other acute intervention. Conversely, patients with multilobar infarctions have high NIHSS scores; these patients usually have

**Algorithm for Decisions About Administration of Tissue Plasminogen Activator for Treatment of Acute Ischemic Stroke**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the interval from the onset of neurologic symptoms?</td>
<td>If symptoms &gt; 3 h, not eligible for treatment</td>
</tr>
<tr>
<td></td>
<td>If stroke occurred during sleep (&gt;3 h) or if onset is uncertain, not</td>
</tr>
<tr>
<td></td>
<td>eligible for treatment</td>
</tr>
<tr>
<td>Can the patient’s symptoms be attributed to an illness other than</td>
<td>yes</td>
</tr>
<tr>
<td>ischemic stroke?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>if in particular, screen for</td>
</tr>
<tr>
<td></td>
<td>Hypoglycemia</td>
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<tr>
<td></td>
<td>Seizures with a postictal paralysis</td>
</tr>
<tr>
<td></td>
<td>Craniofacial trauma</td>
</tr>
<tr>
<td></td>
<td>Any recent events that could increase the risk of bleeding</td>
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<tr>
<td></td>
<td>complications and that could contraindicate treatment with tissue</td>
</tr>
<tr>
<td></td>
<td>plasminogen activator?</td>
</tr>
<tr>
<td></td>
<td>In particular, ask about</td>
</tr>
<tr>
<td></td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td></td>
<td>Ischemic stroke</td>
</tr>
<tr>
<td></td>
<td>Craniofacial trauma</td>
</tr>
<tr>
<td></td>
<td>Bleeding</td>
</tr>
<tr>
<td></td>
<td>Surgery</td>
</tr>
<tr>
<td>Is the patient being treated with warfarin or heparin?</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>The use of these medications leading to a prolongation of the</td>
</tr>
<tr>
<td></td>
<td>prothrombin time or activated partial thromboplastin time</td>
</tr>
<tr>
<td></td>
<td>precludes treatment with tissue plasminogen activator</td>
</tr>
<tr>
<td>Is the patient’s blood pressure &gt; 185 mm Hg systolic or &gt; 110 mm Hg</td>
<td>yes</td>
</tr>
<tr>
<td>diastolic?</td>
<td>An elevated blood pressure precludes treatment with tissue plasminogen activator for most cases because the blood pressure cannot be stabilized within the 3-hour time window</td>
</tr>
<tr>
<td>How severe are the neurologic impairments using the National Institutes</td>
<td>yes</td>
</tr>
<tr>
<td>of Health Stroke Scale?</td>
<td>Patients with minimal neurologic impairments may not be treated</td>
</tr>
<tr>
<td></td>
<td>with tissue plasminogen activator because their</td>
</tr>
<tr>
<td></td>
<td>prognosis usually is good. Conversely, caution should be</td>
</tr>
<tr>
<td></td>
<td>exercised in giving tissue plasminogen activator to patients</td>
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<tr>
<td></td>
<td>with severe strokes because of the risk of intracranial bleeding</td>
</tr>
<tr>
<td>Does computed tomography demonstrate findings of a major infarction?</td>
<td>yes</td>
</tr>
<tr>
<td>Early computed tomographic findings of a multilobar infarction</td>
<td>yes</td>
</tr>
<tr>
<td>preclude treatment with tissue plasminogen activator</td>
<td>yes</td>
</tr>
</tbody>
</table>

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poor outcomes regardless of treatment with tissue plasminogen activator, and the risk of hemorrhagic complications is higher in this group. The NIHSS is a useful way to quantify the patient’s neurologic signs and because the NIHSS score influences decisions about acute treatment, neurologists should lead efforts to teach physicians about the nuances of performing and scoring this scale. Goldstein and Samsa showed that non-neurologists can effectively use the NIHSS in assessment of patients with stroke.

Decisions about acute treatment also are affected by the results of brain imaging studies. Current guidelines for the use of tissue plasminogen activator recommend not treating patients who have computed tomographic evidence of a multifocal stroke. Fortunately, the aggregate NIHSS score correlates with the size of stroke found by brain imaging. Thus, the computed tomographic findings will be most critical among people with major deficits (high NIHSS score). Other brain imaging studies, such as perfusion and diffusion magnetic resonance imaging, might improve selection of patients for treatment. However, some clinicians have cautioned against the overdependence on such ancillary diagnostic tests. The value of these studies in a clinical setting has not been ascertained and the superiority of these tests over the clinical findings, such as the NIHSS score, or the results of computed tomography need to be determined. Until data are available that prove the usefulness of ancillary brain imaging studies in the selection of patients to treat, these tests should not be required before starting emergent treatment of ischemic stroke.

The patient’s general health has a major impact on management of acute ischemic stroke. Severe comorbid medical or neurologic diseases affect prognosis and decisions about treatment. For example, a patient who is disabled because of dementia, heart disease, or arthritis likely will not be nondisabled after management of stroke. The wishes of the patient and his/her family also should be considered. Stroke affects a large number of elderly individuals who fear the disease more because of the potential for the loss of independence than for the potential for death. They may not wish aggressive therapies that might prolong their illness or result in chronic, severe disability. Similarly, families might not wish therapies that they consider to be excessive.

At present, intravenous use of tissue plasminogen activator is the only treatment that is known to be effective in emergent management of patients with acute ischemic stroke. The strategy used by the National Institutes of Neurological Disorders and Stroke tissue plasminogen activator investigators proved to be successful; patients within 3 hours of stroke can benefit from treatment if a similar approach is used. Intravenous thrombolysis has limitations. It cannot be given with impunity; bleeding complications occur, especially among individuals with severe strokes. Patients must receive the medication within 3 hours and, thus, a minority of patients can be treated.

Intravenous thrombolysis is the first, not the final, treatment that will be shown to be effective in improving neurologic outcome after ischemic stroke. Still, the success of tissue plasminogen activator means that attitudes toward stroke must be changed—patients can be treated and their outcomes improved. Neurologists should be in the forefront of efforts to treat stroke as a medical emergency and to develop specialized stroke care facilities in their communities. However, the critical part of care of most individuals with stroke will not be in specialized stroke centers, and neurologists should not demand that all patients with acute stroke be evaluated and treated only at tertiary-level, specialized centers. Such a requirement could undermine the public’s and medical community’s support for emergent stroke care. Rather, neurologists should strive to collaborate with primary care and emergency medicine physicians in increasing the availability of stroke therapies.

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