NCPD 2.5 HOURS
Nursing Continuing Professional Development

Acute Ischemic Stroke

A review of updated guidelines, nursing assessment, and evidence-based treatment.

ABSTRACT: Stroke, the most common form of cerebrovascular disease, is a leading cause of death and disability throughout the world. There have been no significant advances in the development of effective therapeutics for hemorrhagic stroke, and for ischemic stroke highly effective, evidence-based therapies such as alteplase and mechanical thrombectomy are widely underutilized. Improving outcomes for patients experiencing ischemic stroke requires faster recognition and appropriate intervention within the treatment window (the first 24 hours after symptom onset). This article discusses the pathophysiology underlying the various types of ischemic stroke; the risk factors for ischemic stroke; stroke presentation; and the evidence-based treatments, nursing assessments, and monitoring protocols that are critical to patient recovery.

Keywords: acute ischemic stroke, alteplase, assessment, emergency care, endovascular recanalization therapy, ischemic stroke, mechanical thrombectomy, stroke, thrombolytic therapy

In the United States, approximately 90 people have a stroke every hour, which results in a death about every four minutes.[1] Stroke is the fifth leading cause of death in the United States[2] and the second leading cause of death and disability worldwide, following ischemic heart disease.[3] Stroke mortality rates are higher for those born and living in the southeastern United States, aptly named the "stroke belt," in which residents are 20% to 50% more likely to die of stroke than residents of other parts of the country.[4] (See Figure 1.[5])

TWO MAJOR CATEGORIES OF STROKE

Stroke is broadly divided into two categories: ischemic and hemorrhagic. In the United States, 87% of stroke diagnoses are ischemic; 13% are hemorrhagic.[1]

Hemorrhagic stroke includes both intracerebral hemorrhage, which is abnormal bleeding within the brain or brain parenchyma, and subarachnoid hemorrhage, which is abnormal bleeding within the subarachnoid space. Both intracerebral hemorrhage and subarachnoid hemorrhage can occur spontaneously or result from trauma. Although hemorrhagic stroke is survivable with excellent medical care, the development of evidence-based therapeutics for hemorrhagic stroke has lagged behind the innovations seen in the treatment of ischemic stroke,[6] which are unfortunately significantly underutilized.[7]

Ischemic stroke, which describes a disruption of blood flow to the brain parenchyma that causes brain cells to die from lack of oxygen, may result from large-artery atherosclerosis, small vessel occlusions (SVOs), and cardiac emboli, among other causes.[8]

Globally, ischemic stroke is associated with a slightly lower mortality rate than hemorrhagic stroke, accounting for 2.7 million deaths in 2016, versus the 2.8 million deaths attributed to hemorrhagic stroke that year.[3]

This article focuses on ischemic stroke because its incidence is much higher than that of hemorrhagic stroke and also because the underutilization of evidence-based treatments for ischemic stroke contributes significantly to stroke-related morbidity and mortality. For example, though endovascular thrombectomy has been shown to significantly improve outcomes in patients with large vessel

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occlusions (LVOs), which account for 24% to 46% of acute ischemic strokes, the number of thrombectomies performed annually is well below what would appear to be indicated based on annual LVO incidence.[9] The failure to employ evidence-based treatments for ischemic stroke creates a substantial economic burden for patients, their families, and the community at large. Between 2014 and 2015, annual direct and indirect costs associated with stroke totaled nearly $46 billion in the United States alone.[1] Here we'll discuss the pathophysiology underlying ischemic strokes; stroke presentation; modifiable and nonmodifiable stroke risk factors; evidence-based treatments for acute ischemic strokes; and critical nursing assessments and monitoring protocols that promote patient recovery, the knowledge of which can empower nurses to support underutilized treatments, further reducing the negative impact of ischemic stroke.

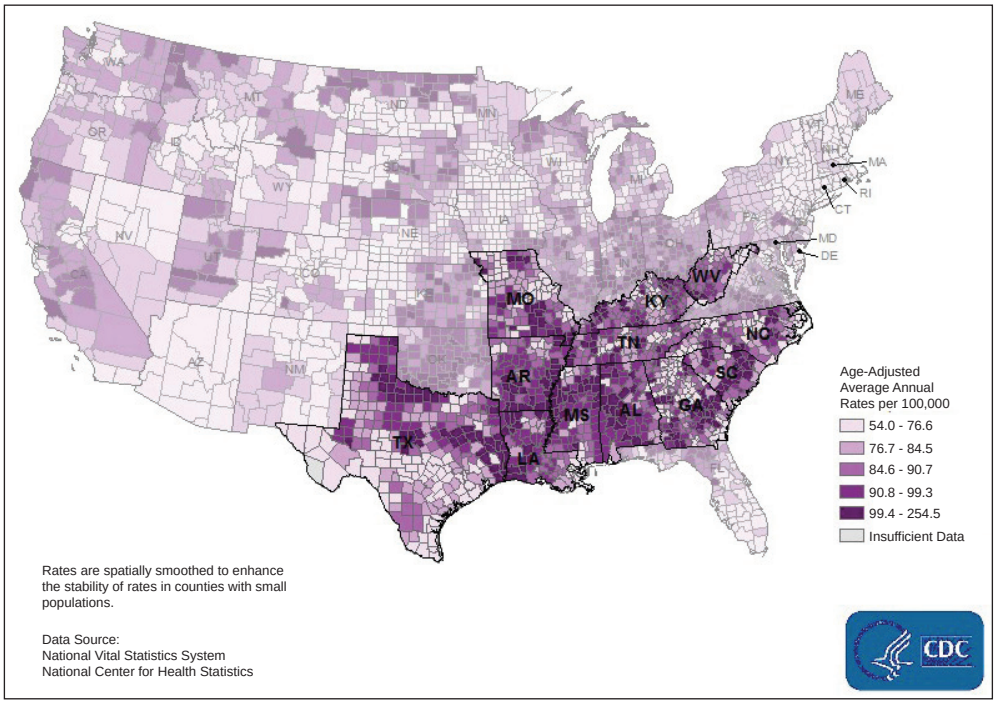

Figure 1. Stroke mortality rates in the United States are highest in the southeastern "stroke belt."[5]

PATHOPHYSIOLOGY OF ISCHEMIC STROKES

The term *ischemic stroke* encompasses several types of pathophysiological changes that can disrupt blood flow to the brain.

Cardioembolic strokes occur when an embolus, which may take the form of a clot, plaque, or pocket of air, travels to and becomes lodged within an artery in the brain. Embolic strokes can affect multiple vessels in different areas. Identifying an embolic stroke is important because reperfusion of the blocked artery or arteries doesn't eliminate the danger. The actual cause of the embolus must be identified and treated to prevent stroke recurrence. Cardioembolic strokes are commonly associated with atrial fibrillation, systolic heart failure, myocardial infarction, prosthetic heart valves, and infective endocarditis.

Embolic stroke of undetermined source (ESUS) is a relatively new term used to characterize cryptogenic strokes, which have an undetermined cause after other known causes of embolic stroke have been ruled out.[10] After vascular risk factors for stroke have been evaluated, etiology may remain unclear because many patients have multiple potential sources of embolism.[11,12] This may complicate the process of determining the most appropriate preventive measures to take (for example, antiplatelet versus anticoagulation therapy) to protect the brain from subsequent potential embolic sources.[12] Previous clinical trials have provided no clear answer as to the best practices for secondary prevention of ESUS.[11]

Thrombotic strokes may result from LVOs and SVOs.[8] LVOs involve one of the major vessels supplying blood flow to the brain, including the extracranial vessels (common carotids, internal carotids, and vertebral arteries), the intracranial arteries of the circle of Willis and its major branches (anterior cerebral artery, middle cerebral artery, and posterior cerebral artery), as well as the two posterior communicating arteries and the anterior communicating artery. LVOs may result from atherosclerosis, arterial dissection, arteritis, vasculitis, vasoconstriction, noninflammatory vasculopathy, moyamoya syndrome, or fibromuscular dysplasia.

In contrast, SVOs arise from penetrating intracerebral arteries that thrombose when endothelial damage, often triggered by hypertension, causes blockages. SVOs, also called lacunar strokes, occur

in deep brain structures such as the basal ganglia, thalami, and pons.

Transient ischemic attacks (TIAs) occur when blood flow to the brain is temporarily interrupted, causing a brief period of neurologic dysfunction. Sometimes referred to as a "ministroke," TIAs produce many of the signs and symptoms of stroke, but blood flow returns spontaneously after a brief period of deprivation, causing no permanent damage. Clinicians should advise patients diagnosed with a TIA to receive prompt medical follow-up and information about managing stroke risk factors from their primary care provider or a neurologist. A 2007 systematic review and meta-analysis of 11 studies reporting on the risk of stroke after a TIA found that the pooled risk of stroke was 8% at 30 days and 9.2% at 90 days following a TIA.[13]

RISK FACTORS FOR ISCHEMIC STROKE

Knowing the risk factors for ischemic stroke can speed the identification of stroke and is key to preventive patient teaching that can mitigate disability.

Nonmodifiable risk factors include advanced age and female sex. Risk of stroke increases with age, and women have a greater number of strokes than men, but this is often attributed to women's longer life span. Some racial and ethnic characteristics are also associated with increased stroke risk: Native Americans, Alaska Natives, and Black Americans have a higher prevalence of stroke than those identified as White,[14] but the reason for this isn't clear. Differences could be due to modifiable risk factors, lack of access to health care, or language disparities. Genetics, which influences such conditions as hypertension, may also play a role.

Modifiable risk factors. More than 90% of the world's stroke burden is attributable to such modifiable behavioral and metabolic factors as poor diet, insufficient physical activity, current smoking, alcohol consumption, hypercholesterolemia, diabetes mellitus, and hypertension,[15,16] with hypertension being significantly undertreated and unrecognized.[17]

Atrial fibrillation, which is associated with both hypertension and hypercholesterolemia, increases the lifetime risk of stroke fivefold to sixfold.[18]

Overweight and obesity, which are associated with numerous other modifiable stroke risk factors, increase the risk of ischemic stroke by 22% and 64%, respectively,[19] underscoring the integral role of dietary modifications and the American Heart Association (AHA)/American College of Cardiology recommendation that adults engage in moderate to vigorous aerobic physical activity for 40 minutes three to four days per week.[20]

Potentially modifiable risk factors for ischemic stroke include depression, trouble sleeping, and lower household income.[21]

TIME TO TREATMENT

An estimated 1.9 million neurons die each minute after an LVO occurs, and for every hour in which treatment is delayed, the brain loses as many neurons as it would in 3.6 years of normal aging.[22] Quick and informed identification of strokes by nurses can prompt appropriate medical treatment that significantly improves patient function.

Factors influencing time to treatment. For many people, stroke care starts when they call 911, or activate emergency medical services (EMS). Stroke alert activation by EMS may improve patient outcome by reducing time to hospital presentation, evaluation, and appropriate treatment.[23] Data collected from 10 New Jersey hospitals showed that of the patients who presented to the hospital with stroke symptoms, time from symptom onset to hospital arrival was within 90 minutes for 32%, within three hours for 46%, and within six hours for 61%, with older patients and those who had more severe symptoms arriving earlier than younger patients and those with less severe symptoms.[24] Patients transported by ambulance arrived sooner than those who transported themselves.

THE INITIAL NURSING ASSESSMENT

The first nursing encounter with the patient can both speed the identification of stroke and help to determine the most appropriate lifesaving therapies. In addition to assessing patient risk factors, signs, and symptoms, thereby facilitating early stroke recognition, the nurse can, through conversations with the patient or family members, establish the last time the patient was functioning normally. This information is essential to determining the stroke therapeutics for which the patient may qualify, which may include transfer to a certified stroke center capable of performing either surgical thrombectomy or mechanical thrombectomy, also known as endovascular recanalization therapy (ERT). Not all certified stroke centers, however, are certified for ERT.[25]

Differentiating strokes from stroke mimics. Nonstroke disease processes that may present like a stroke are often called *stroke mimics*. They represent 7%[26] to 31%[27] of stroke presentations and may receive antithrombotic treatment because the benefit of treating a stroke outweighs the low risk of a hemorrhagic event in treating a stroke mimic.[28] A 2017 observational cohort study found that of 674 patients presenting with stroke symptoms, 48 were ultimately diagnosed with a stroke mimic after IV thrombolysis treatment, which did not lead to hemorrhagic complications in these patients, all of whom had favorable outcomes.[26] Common stroke mimics include the following[27]:

- migraine with aura
- migraine variants

- toxic or metabolic encephalopathies, including hypoglycemia
- seizure
- presyncope
- syncope

Whereas loss of function, weakness, numbness, or visual loss are more commonly symptoms of acute ischemic stroke, stroke mimics are often associated with overactivity of the central nervous system and symptoms such as auras, bright or flashing lights, paresthesia, or rhythmic clonic movements.

Stroke mimics like seizures or migraines tend to spread gradually from one body part to another. Todd paralysis, which is associated with seizures in the postictal period, is characterized by a temporary motor deficit that often lasts for several hours.

Neurologic assessment should include symptom presentation, exacerbating and alleviating factors, potential emotional triggers at symptom onset, fluctuating weakness, and monocular or binocular vision loss.

THE INTRODUCTION OF ALTEPLASE FOR ISCHEMIC STROKE

Differentiating ischemic from hemorrhagic stroke was of little importance prior to 1996, because treatment options were limited for both.[29] The 1996 approval by the U.S. Food and Drug Administration (FDA) of the tissue plasminogen activator (t-PA) alteplase (Activase) as a treatment for acute ischemic stroke changed this.[30] Alteplase is now considered the preferred treatment for patients with all types of ischemic stroke who meet diagnostic and treatment criteria and have no contraindications.

The benefits of timely treatment. Every 15-minute reduction in treatment delay following symptom onset decreases poststroke disability by approximately one month.[31] Patients treated with alteplase had 30% more favorable outcomes than those given placebo as measured by the Barthel Index, modified Rankin Scale (mRS), Glasgow Outcome Scale, and the National Institutes of Health Stroke Scale (NIHSS).[32] Furthermore, patients treated for stroke with t-PA were more likely to be discharged to home without the need for postacute rehabilitation.[33] Unfortunately, the rate of treatment with IV alteplase remains low, with only an estimated 3.4% to 5.2% of U.S. patients with ischemic stroke receiving the treatment.[7] This underutilization has been attributed to the narrow treatment window, delays in activating EMS, insufficient hospital infrastructure and processes, and patient contraindications.[7]

UPDATED AHA/ASA GUIDELINES

The 2019 update to the 2018 AHA and American Stroke Association (ASA) guidelines for the early management of acute ischemic stroke revised some of the performance standards for clarity and added some new recommendations.[28] For example, the earlier guidelines proposed that initial stat computed tomography (CT) of the head to rule out intracranial hemorrhage be completed before alteplase is administered within 4.5 hours of symptom onset. The 2019 update continues to emphasize the importance of the 4.5-hour treatment window but clarifies that noncontrast CT (NCCT) or magnetic resonance imaging (MRI) may be used to rule out intracranial hemorrhage. In addition, it notes that computed tomographic angiography (CTA) with computed tomographic perfusion (CTP) or MR angiography (MRA) with diffusion-weighted MRI with or without MR perfusion is recommended for certain patients and may be useful in selecting candidates for mechanical thrombectomy between six and 24 hours after they were last known to be well.[28] (For the 2019 AHA/ASA update, go to www.ahajournals.org/doi/10.1161/STR.0000000000000211.)

Patients presenting to the ED with suspected stroke should receive emergency brain imaging on arrival, before any specific therapy is initiated.[28] Door to needle time with administration of alteplase in less than 60 minutes is the current standard.[28] These are AHA/ASA class I recommendations, suggesting strong data supporting beneficial outcomes.

MECHANICAL THROMBECTOMY OF LVOs

A total of 60% to 80% of people with LVO anterior circulation strokes die within 90 days of stroke onset or fail to regain function despite alteplase treatment.[34] AHA/ASA treatment guidelines recommend mechanical thrombectomy using a stent retriever for adults with an internal carotid artery or middle cerebral artery LVO if they have a prestroke mRS score of 0 to 1, an NIHSS score of 6 or greater, and an Alberta Stroke Program Early CT Score (ASPECTS) of 6 or greater, and if treatment can be started within six hours of symptom onset.[28]

Support for ERT. Multiple studies conducted from 1995 through 2019 show improved functional outcomes and less disability in patients with ischemic stroke who received ERT at various intervals following symptom onset, ranging from three to 24 hours.[32, 34-43] The two factors with the greatest influence on functional outcome are volume of the ischemic core and time to reperfusion.[42]

The likelihood of a good outcome decreases with ischemic core volumes greater than 100 mL and with every hour in which treatment is delayed.[42] ERT involves advancing a stent retriever or an aspiration catheter through the blood vessels under the guidance of a cerebral angiogram in order to remove the clot either mechanically or chemically. ERT is preferably done in anterior circulation strokes that are easier to access with the catheter used.

Imaging studies for ERT differentiate irreversible damage (the core of the infarct, located at the cen-

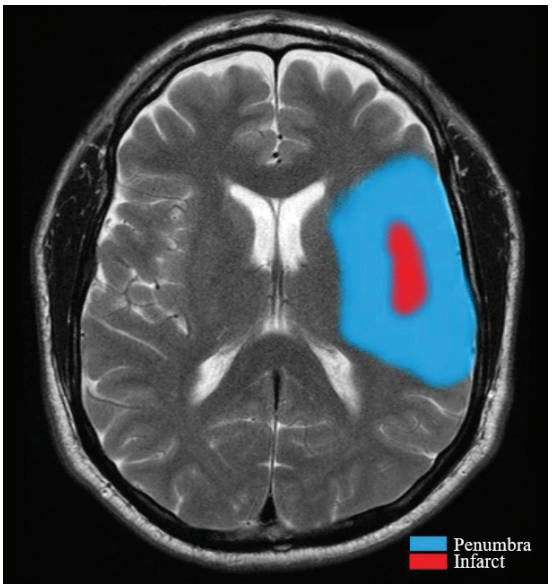

Figure 2. The penumbra (shown here in blue) is the area surrounding the infarcted core tissue (in red). If the stroke continues to evolve, the penumbra may become infarcted or irreversibly damaged. Image courtesy of the University of Texas Southwestern Medical Center, Dallas.

ter of injury where the clot or blockage occurs) from reversible damage (the penumbra, which is the area surrounding the core). Because the penumbra may become infarcted or irreversibly damaged if the stroke continues to evolve, it is the area to be saved with ERT.[44] (See Figure 2.) CT scans of cerebral blood flow or CTP studies and diffusion-weighted MRI or MR perfusion studies can be used with software that can calculate the volume of the infarct core and penumbra.[44] Favorable outcomes have been seen with infarct core volumes less than 70 mL,[45] though the SELECT (Selection for Endovascular Treatment in Acute Ischemic Stroke) trial found that ERT delivered more than 12 hours after the patient was last known to be well was unlikely to result in functional independence if ischemic core volumes exceeded 50 mL.[42] The likelihood of good outcomes decreases with an increase in both infarct core volumes and time to treatment.[42]

The mismatch ratio compares the volumes of the infarct core and the penumbra.[35] Endovascular thrombectomy has been found to be associated with good outcomes when the ASPECTS is 6 or greater and CTP is favorable, meaning that the following criteria have been met[46]:

- core, as estimated by cerebral blood flow, less than 30%
- volume, less than 70 mL
- mismatch volume, greater than 10 mL
- mismatch ratio, greater than 1.2

The ASPECTS measures early ischemic changes in the middle cerebral artery, allowing an estimate of ERT efficacy.[47] This score is calculated by providers with the use of computers at some facilities. (See Figure 3.[48]) Although for ERT, the current AHA/ASA guidelines recommend an ASPECTS of 6 or greater based on brain imaging by NCCT, CTA, MRI, or MRA,[28] a multicenter, pooled analysis of seven institutional prospective stroke registries found that an ASPECTS ranging from 0 to 5 supports LVO treatment with ERT.[48] Applying the ASPECTS to patients with LVOs has proven effective in predicting the probability of functional independence after ERT.

ASSESSING PATIENTS DURING ERT

Patients undergoing ERT benefit from specialized nursing care in acute stroke units and ICUs. They require frequent neurologic examinations and the NIHSS administered and the trend evaluated at regular intervals. In conjunction with neuroimaging (CT and MRI), posttreatment scales are used to assess the degree of reperfusion achieved through ERT.

The modified Thrombolysis in Cerebral Infarction score characterizes the percentage and quality of reperfusion achieved through ERT in one of five categories[49]:

- Grade 0/1–no or minimal reperfusion
- Grade 2a–partial filling, less than 50% of territory
- Grade 2b–partial filling, 50% or more of territory
- Grade 2c–near complete perfusion except slow flow or few distal cortical emboli
- Grade 3–complete perfusion

Grades 2c and 3 are best predictors of early neurologic improvement and functional independence following ERT.[49, 50]

NURSING CONSIDERATIONS DURING THROMBOLYTIC TREATMENT

Nurses caring for patients with presumed stroke must know how to prepare patients for administration of thrombolytic medications. Consider urinary catheter insertion before thrombolysis. Throughout thrombolytic therapy, it will be necessary to monitor vital signs; establish large-bore IV access; obtain blood samples to assess glucose level, prothrombin time, partial thromboplastin time, and international normalized ratio; perform a complete blood count with platelets; monitor electrocardiograms; and in women of childbearing age, check beta human chorionic gonadotropin values.

Although alteplase is currently the only FDA-approved medication for acute stroke,[51] tenecteplase (TNKase), a genetically modified variant of alteplase,[52] has shown promise for increasing widespread treatment of acute ischemic stroke.[51, 52]

Tenecteplase is a fibrinolytic, which, like alteplase, acts on fibrin-bound plasminogen within a thrombus.

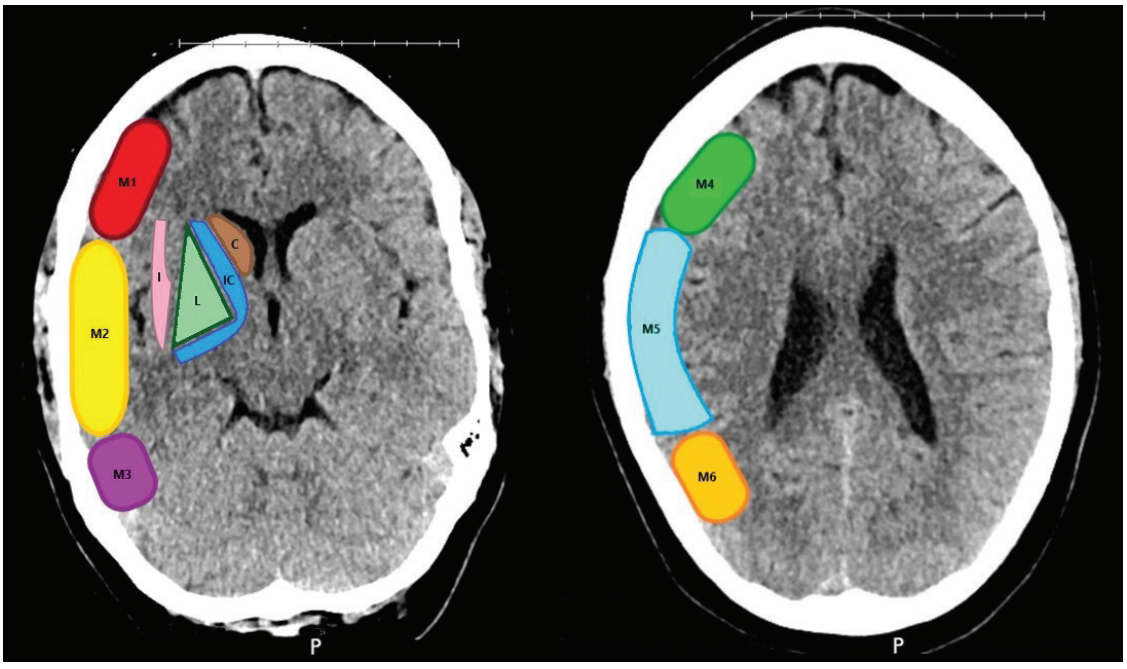

Figure 3. ASPECTS is a 10-point quantitative topographic score, based on regions of the MCA as shown in a noncontrast CT scan of the brain. The 10 colored areas represent the 10 regions on which ASPECTS is based: M1, anterior MCA cortex; M2, MCA cortex lateral to the insular ribbon; M3, posterior MCA cortex; M4, anterior MCA superior territory; M5, lateral MCA superior territory; M6, posterior MCA superior territory; I, insular ribbon; L, lentiform nucleus; IC, internal capsule; and C, caudate. The score is calculated by subtracting one point for evidence of ischemia detected in any of these 10 regions. In a normal brain, in which none of these areas was affected by ischemia, the ASPECTS would be 10. If every colored area shown above revealed evidence of ischemia, the ASPECTS would be 0. Scores ranging from 0 to 5 support LVO treatment with ERT.[48] ASPECTS = Alberta Stroke Program Early CT Score; CT = computed tomography; ERT = endovascular recanalization therapy; LVO = large vessel occlusion; MCA = middle cerebral artery. Image courtesy of the University of Texas Southwestern Medical Center, Dallas.

It has a longer plasma half-life than alteplase and is not deactivated by the enzyme plasminogen activator inhibitor 1. It can be administered as a single IV bolus of 30 to 50 mg (0.53 mg/kg of body weight) over five to 10 seconds, unlike the 90-minute accelerated infusion regimen required for alteplase.[53]

Bedside nurses in the United States may soon be infusing tenecteplase instead of alteplase for ischemic stroke therapy. Tenecteplase is substantially less expensive than alteplase, has a less complicated dosing regimen, and because of its extended half-life and greater fibrin specificity, does not require the long infusion times alteplase does.[51]

REDUCING RISK OF COMPLICATIONS AFTER ISCHEMIC STROKE

With frequent nursing assessment, complications of ischemic stroke can be identified early so that appropriate risk-reducing measures may be taken.

Cerebral edema is a leading cause of death and decline in patients with supratentorial LVOs. These large-core LVOs can produce severe cerebral edema resulting in compression of the brain. Edema may begin to develop within the first two days, with symptoms worsening after three to five days.[54] Symptoms of cerebral edema include headache, dizziness, nausea, vomiting, weakness, sedation, lethargy, anisocoria (difference in pupil size), sensory changes, respiratory depression, diplopia, and seizures. Interventions to reduce intracranial pressure may include elevating the head of the bed, administering osmotic diuretics and sedatives, emergent intubation, hyperventilation, and hypothermic therapy.[55] In severe cases, decompressive hemicraniectomy may reduce risk of death.[55] Nursing care associated with these treatments includes frequent neurologic assessments, patient preparation for stat CT scans of the head, monitoring results of laboratory tests, ensuring that the patient maintains neutral head and body positioning, and preparing the patient and family members for possible interventions.

Secondary stroke. To prevent secondary stroke, venous thromboembolism prophylaxis with intermit-

tent pneumatic compression devices is often used, as well as aspirin and hydration unless otherwise contraindicated. The benefit of heparin or low-molecular-weight heparin prophylaxis is not well established but is a class IIb recommendation in the AHA/ASA guidelines, having shown reductions in symptomatic pulmonary embolism and asymptomatic deep vein thrombosis following ischemic stroke.[28]

For nondisabling, minor strokes, a clinical review by Mendelson and Prabhakaran concluded that dual antiplatelet therapy, such as aspirin with clopidogrel, started within 24 hours after ischemic stroke is beneficial when continued for three weeks, and was shown to reduce the secondary risk of stroke at 90 days when compared with aspirin therapy alone.[56] However, patients with such complicating factors as atrial fibrillation, severe internal carotid artery stenosis, and other factors for which dual antiplatelet therapy is already indicated were not included in the trials.

Depression. In the absence of any contraindications, screening and treatment for depression should be initiated following ischemic stroke and are class I AHA/ASA guideline recommendations.[28]

Smoking cessation intervention and nicotine replacement therapy are also class I recommendations.[28]

STROKE: A GROWING PROBLEM

The number of Americans ages 65 and older is projected to nearly double from 52 million in 2018 to 95 million by 2060.[57] Since risk of stroke increases with age, this demographic trend potentially increases the number of Americans who will present with signs and symptoms of stroke in EDs; ICUs; acute stroke units; and postsurgical, cardiac, and geriatric units. Nurses are the first line of defense for the population at risk for stroke. Knowing how to assess and care for patients with presumed stroke can significantly help improve patient outcomes. ▼

For 30 additional nursing continuing professional development activities on the topic of stroke, go to www.nursingcenter.com.

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