Ischemic Stroke

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- Read the enclosed course.
- Complete the questions at the end of the course.
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Faculty Disclosure
Contributing faculty, Lori L. Alexander, MTPW, ELS, MWC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience
This course is designed for physicians, nurses, and physician assistants in the primary care setting. Neurologists and other healthcare practitioners will also benefit from this course.

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Course Objective

The early identification and management of the risk factors for ischemic stroke can lead to substantial improvement in health and reductions in cost. However, research has documented gaps between healthcare professionals' knowledge and practice with respect to prevention, with data on adherence to evidence-based or guideline-endorsed recommendations demonstrating underuse or ineffective use of all interventions for primary and secondary prevention. The purpose of this course is to provide needed information about the roles of diagnosis and screening, evaluation of individuals with suspected stroke, immediate treatment of stroke, and the elements of effective rehabilitation programs so that healthcare professionals may implement the necessary interventions appropriately.

Learning Objectives

Upon completion of this course, you should be able to:

1. Describe the primary types of cerebrovascular disorders and their causes.
2. Discuss differences in prevalence, morbidity, and mortality according to age, sex, and race/ethnicity.
3. Identify the nonmodifiable and modifiable risk factors for ischemic stroke.
4. Implement primary prevention strategies according to evidence-based guidelines.
5. Discuss the need for education at the community and patient levels.
6. Apply models of predicting risk of ischemic stroke.
7. Select the appropriate tools for screening, diagnosis, and early management of ischemic stroke.
8. Describe the elements of stroke systems of care and a comprehensive stroke center.
9. Discuss evidence-based treatment options for ischemic stroke.
10. Describe the benefits and components of a specialized stroke rehabilitation team.
11. Outline the aspects of patient assessment for stroke rehabilitation.
12. Discuss evidence-based recommendations for secondary prevention of ischemic stroke.

EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Cerebrovascular disease is associated with significant morbidity and mortality in the United States. Stroke occurs in approximately 795,000 individuals each year, of which 610,000 are first-time strokes and 185,000 are recurrent [1]. Stroke is the leading cause of long-term disability in adults; 65% of stroke survivors have some degree of impairment [1; 2]. Approximately 3% of men and 2% of women reported that they were disabled because of stroke [3]. The effect of stroke on mortality is illustrated by the fact that cerebrovascular disease is the third leading cause of death in the United States, with an age-adjusted mortality rate of 37.3 per 100,000 population as of 2016 [1; 3]. This represents a 16.7% decrease in the mortality rate and a 3.7% increase in actual deaths since 2006. It is a substantial healthcare issue, with one of every three deaths being attributed to stroke in 2016 [3]. In addition, the financial cost associated with cerebrovascular disease poses a substantial economic burden, with an estimated direct and indirect cost of $351.2 billion between 2014 and 2015 [3]. Despite the considerable progress being made in the areas of prevention, management, and rehabilitation, it appears that stroke will increasingly cause death and disability in the coming decades as the population ages [4]. By 2030, an additional 3.4 million U.S. adults (3.9% of the population) will have had a stroke, which is a 20.5% increase in prevalence from 2012. Additionally, the total direct medical costs of cerebrovascular disease are projected to increase to approximately $918 billion [1].

The two primary types of stroke are ischemic and hemorrhagic, and ischemic strokes account for the majority (87%) of cerebrovascular disorders [1]. There are several risk factors for ischemic stroke, and predicting risk is an important element in prevention. In predicting risk, consideration should be given not only to comorbidities but also to age, sex, and race/ethnicity, as disparities in prevalence, morbidity, and mortality have been attributed to these patient characteristics [5; 6; 7; 8]. Evidence-based guidelines for primary and secondary prevention have been developed and should be implemented [9; 10].

Among the most important risk factors for ischemic stroke is a transient ischemic attack (TIA); approximately 12% of ischemic strokes are preceded by a TIA [1]. The greatest risk for post-TIA stroke is within the first 48 hours, and the risk continues beyond 48 hours to 3 months [1; 11]. Improved understanding of TIAs among both clinicians and patients is needed. A survey of 200 primary care physicians showed that 88% could not correctly identify the typical symptoms and duration of a TIA, and studies have indicated that half of individuals who have a TIA do not report the event to their primary care clinician [1; 12].

The early identification and management of the risk factors for ischemic stroke can lead to substantial improvement in health and reductions in cost [13]. For example, the incidence of stroke has been reduced by 30% to 40% with the appropriate use of antihypertensive therapy [10]. Yet, research has documented gaps between physicians' knowledge and practice with respect to prevention, with data on adherence to evidence-based or guideline-endorsed recommendations demonstrating underuse or ineffective use of all interventions for primary and secondary prevention [11; 14; 15]. Evidence-based guidelines have also been developed for the early management of stroke and for rehabilitation after stroke and should be followed to provide optimum care [16; 17; 18].

The focus of this course is ischemic stroke, due to its overwhelming prevalence. Advances have been made in tools for the screening and diagnosis of ischemic stroke, and a better understanding of the options for patients at risk is needed. This course explores the role of the physical examination and history, laboratory studies, and imaging techniques in screening and diagnosis. Also discussed are evidence-based guidelines for the prevention and early management of ischemic stroke, as well as emerging treatment options. Because data have shown that outcome is improved by care provided in comprehensive stroke centers and by early rehabilitation, these topics are addressed as well [17; 19; 20; 21]. The importance of a multidisciplinary rehabilitation team, appropriate patient assessment, and an exercise program is emphasized.

OVERVIEW OF CEREBROVASCULAR DISEASE

Although "cerebrovascular disease" is often used interchangeably with the term "stroke," the disease encompasses any neurovascular disorder that exists in the presence or absence of an ictus (e.g., carotid artery stenosis, arteriovenous malformations). Despite advances in understanding the pathophysiology of cerebrovascular diseases, the term "stroke" (also known as cerebrovascular accident or brain attack) is inconsistently defined. Stroke has been classically characterized as an injury to the central nervous system (CNS) by a vascular cause. Because this definition is mainly clinical and not inclusive of advances in science and technology, the American Heart Association (AHA)/American Stroke Association (ASA) convened a writing group to develop an updated definition of stroke. The AHA/ASA recommend that the term "stroke" be broadly used to include a variety of definitions (***Table 1***).

TYPES OF CEREBROVASCULAR DISORDERS

The multiple sources, pathophysiologic mechanisms, and sequelae of stroke are reflected in the diverse types of cerebrovascular disorders. The World Health Organization classifies cerebrovascular diseases under "Diseases of the nervous system" in the 11th revision of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-11), the international standard diagnostic classification for all general epidemiologic purposes and many health management purposes (***Table 2***) [22]. TIAs and traumatic intracranial hemorrhage are also included in the nervous system disease category in the ICD-11; vascular dementia is not. Its exclusion illustrates the heterogeneity of stroke and its sequelae. Vascular dementia, listed as dementia due to cerebrovascular disease, is categorized under "Mental, behavioral, or neurodevelopmental disorders: Neurocognitive disorders."

As noted, the two primary types of stroke are ischemic and hemorrhagic. In the United States, approximately 87% of all strokes are ischemic; 10% are hemorrhagic strokes [1]. An ischemic stroke occurs when any artery that supplies the brain with oxygen becomes stenosed or occluded, resulting in infarction [23]. In the case of hemorrhagic stroke, bleeding occurs below the arachnoid, the location of the brain's blood supply, allowing blood to directly contact and damage brain tissue. Although ischemic stroke is the focus of this course, a brief overview of hemorrhagic strokes will help to provide context and comparison of the clinical features of both types of stroke. In addition, TIAs are discussed here, as they are often a precursor to ischemic stroke.

Hemorrhagic Strokes

Hemorrhagic stroke is associated with a higher risk of fatality than ischemic stroke, and roughly one-third of patients die within 30 days after the event [1; 24]. Hemorrhagic strokes are categorized by the location of the hemorrhage, either intracerebral or subarachnoid, with the former being more common.

Approximately 87% of hemorrhagic strokes are due to intracerebral hemorrhage (ICH), and because of this, the term hemorrhagic stroke often refers to ICH [25]. ICHs are characterized by bleeding directly into the brain parenchyma [25; 26]. Intraventricular hemorrhage describes bleeding that extends into the ventricles [26; 27]. Nontraumatic ICH is categorized as primary (unrelated to congenital or acquired lesions), secondary (caused by a congenital or acquired condition), or spontaneous (unrelated to trauma or surgery) [26].

The signs and symptoms of ICH include headache, vomiting, seizures, depressed consciousness, meningeal irritation, and blood-tainted cerebrospinal fluid. The onset of symptoms may occur within seconds to minutes after the start of an ICH. Individuals with this type of stroke often feel more ill than those with an ischemic stroke.

AHA/ASA DEFINITION OF STROKE	
Injury/Episode	**Definition**
CNS infarction	Brain, spinal cord, or retinal cell death attributable to ischemia, based on: • Pathologic, imaging, or other objective evidence of cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution; or • Clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury based on symptoms persisting ≥24 hours or until death, and other etiologies excluded.
Ischemic stroke	Episode of neurologic dysfunction caused by focal cerebral, spinal, or retinal infarction
Silent CNS infarction	Imaging or neuropathologic evidence of CNS infarction, without history of acute neurologic dysfunction attributable to the lesion
Intracerebral hemorrhage	Focal collection of blood within the brain parenchyma or ventricular system, not caused by trauma
Stroke caused by intracerebral hemorrhage	Rapidly developing clinical signs of neurologic dysfunction attributable to focal collection of blood within brain parenchyma or ventricular system, not caused by trauma
Silent cerebral hemorrhage	Focal collection of chronic blood products within the brain parenchyma, subarachnoid space, or ventricular system on neuroimaging or neuropathologic examination, not caused by trauma and without history of acute neurologic dysfunction attributable to the lesion
Subarachnoid hemorrhage	Bleeding into subarachnoid space
Stroke caused by subarachnoid hemorrhage	Rapidly developing signs of neurologic dysfunction and/or headache because of bleeding into the subarachnoid space, not caused by trauma
Stroke caused by cerebral venous thrombosis	Infarction or hemorrhage in the brain, spinal cord, or retina because of thrombosis of a cerebral venous structure. Symptoms or signs caused by reversible edema without infarction or hemorrhage do not qualify as stroke.
Stroke, not otherwise specified	Episode of acute neurologic dysfunction presumed to be caused by ischemia or hemorrhage, persisting ≥24 hours or until death, but without sufficient evidence to be classified as one of the above
CNS = central nervous system.	
Source: Reprinted with permission from Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013;44(7):2064-2089.	*Table 1*

SELECTED CEREBROVASCULAR DISEASES AS CLASSIFIED BY THE INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS, 11TH REVISION (ICD-11)	
ICD Code	**Disease**
8B00	Intracerebral hemorrhage
8B01	Subarachnoid hemorrhage
8B02	Nontraumatic subdural hemorrhage
8B03	Nontraumatic epidural hemorrhage
8B0Z	Intracranial hemorrhage, unspecified
8B10	Transient ischemic attack
8B11	Cerebral ischemic stroke
8B1Y	Other specified cerebral ischemia
8B1Z	Cerebral ischemia, unspecified
8B20	Stroke, not known if ischemic or hemorrhagic
Source: [22]	*Table 2*

ICH is the least treatable type of stroke [28]. Functional independence is regained within 6 months in approximately 20% of survivors [29]. The morbidity and mortality depend on the volume and location of the hematoma. The 1-year mortality rate varies according to anatomic location, with the highest mortality rate (65%) associated with ICH in the brain stem; the rate is 57% for lobar hemorrhage, 51% for deep hemorrhage, and 42% for cerebellar hemorrhage [30]. Overall, 46% of patients with ICH survive one year and 29% survive five years [31].

As many as 80% of primary ICHs occur after small vessels are compromised by chronic hypertension [32]. Hypertension is associated with ICH originating in the periventricular deep white matter, deep subcortical structures, pons, and cerebellum [33]. In individuals older than 70 years of age, cerebral amyloid angiopathy, a condition that leads to amyloid protein infiltration into the cortical arterioles, is responsible for approximately 20% of ICHs [34]. Other causes of ICH include anticoagulant and antiplatelet use, drug use (e.g., cocaine, phenylpropanolamine), and other bleeding diathesis [28; 35]. Fewer than 15% of all cases of ICH are secondary to congenital vascular abnormalities and malignant brain lesions [26].

Subarachnoid hemorrhages occur less frequently than ICHs. The hallmark of subarachnoid hemorrhage is the immediate onset of a severe headache with signs of meningeal irritation [36]. Individuals may describe this headache as their "worst ever." Nausea, vomiting, neck pain, and photophobia are also classic symptoms, although they are not always present [36]. Neurologic deficits may be acute or may manifest hours to days after the onset of bleeding.

Nontraumatic subarachnoid hemorrhages are subcategorized as aneurysmal or non-aneurysmal [37]. Aneurysmal subarachnoid hemorrhage is associated with higher rates of morbidity and mortality than non-aneurysmal hemorrhage. Among patients who live 3 months after the event, the risk of death is 8.7% within 5 years and 17.9% within 10 years [38]. In contrast, non-aneurysmal subarachnoid hemorrhages are associated with better outcomes and are less likely to cause death [39].

Most nontraumatic subarachnoid hemorrhages involve rupture of an intracranial aneurysm or cerebral arteriovenous malformation. Congenital arteriovenous anomalies are more likely to cause stroke in adolescents and young adults [40]. The incidence of perimesencephalic subarachnoid hemorrhage, a non-aneurysmal type, is increasing. Although the cause remains unknown, increased use of antithrombotic medications may be a factor [41; 42].

TIAs

TIAs are sometimes referred to as "ministrokes" because, like ischemic strokes, they are caused by inadequate cerebral blood flow. TIAs are also called warning strokes, as they often precede an ischemic stroke [43]. The superseded definition of a TIA was "a sudden, focal neurologic deficit that lasts for less than 24 hours, is presumed to be of vascular origin, and is confined to an area of the brain or eye perfused by a specific artery" [44]. The 24-hour time limit was an arbitrary remnant of the time interval used in prospective surveys in the early 1970s [45]. Magnetic resonance imaging (MRI) and computed tomography (CT) have demonstrated that one-third of TIAs, including those that last only minutes, cause infarcts [46].

Because TIA and ischemic stroke are less distinct from one another than once believed, a new TIA definition was proposed, revised, and endorsed in 2009. The proposed definition states that TIA is "a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than 1 hour, and without evidence of acute infarction" [44]. This definition was designed to better reflect the ischemic pathogenesis of TIA, promote its early management, and support the use of diagnostic imaging techniques to ensure that the patient does not have infarction [44]. The definition was endorsed by the 2009 AHA/ASA guideline, with the omission of "typically less than 1 hour" (as infarction

is not necessarily bound by a set period of time) and reads, "Transient ischemic attack (TIA): a transient episode of neurologic dysfunction caused by focal brain, spinal-cord, or retinal ischemia, without acute infarction" [10; 47].

Research shows that a TIA should be considered a dire condition that requires urgent treatment in order to prevent a more potent ischemic stroke; approximately 15% of ischemic strokes are preceded by a TIA [3]. However, there are several challenges to immediate treatment of TIAs [10]:

- A wide majority of the general population and many healthcare professionals believe that TIAs are generally benign.
- Individuals experiencing a TIA often believe they can postpone or forego professional treatment because clinical symptoms usually resolve quickly and without care.
- Due to the 24-hour arbitrary time limit in the previously accepted definition, healthcare professionals often choose to monitor a patient with a TIA rather than provide immediate treatment.

The risk of ischemic stroke is dangerously high in the period following a TIA. Research indicates that one-half of subsequent strokes occur within the first 48 hours, and a meta-analysis showed that approximately 5% of patients who have a TIA will have an ischemic stroke within seven days of that event [11; 43]. The risk of stroke within three months after a TIA is approximately 10% to 20% and is 24% to 29% over the following five years [11]. Early initiation of treatment for TIA and minor stroke with existing therapies has been shown to reduce the risk of early recurrent stroke by 80% [48].

As with any stroke, the symptoms of TIA depend on the affected vascular territory. For instance, involvement of the carotid artery causes disturbances in the ipsilateral eye or brain [49]. Although the most common focal neurologic signs of TIA are sudden-onset unilateral weakness and numbness or tingling in a limb, a TIA can cause any of the following symptoms [49; 50]:

- Numbness of the face, hand, or leg, with or without weakness
- Paralysis
- Slurred speech
- Dizziness
- Double vision
- Hemianopia
- Transient monocular blindness
- Imbalance
- Aphasia
- Confusion
- Head pain

Transient graying or blurring of vision is also common. Occasionally, the line of sight will be shaded. Vertebrobasilar TIAs reflect vestibulocerebellar symptoms such as ataxia, dizziness, vertigo, dysarthria, vision abnormalities (e.g., double vision, hemianopia, bilateral vision loss), and unilateral or bilateral motor and sensory dysfunctions [10].

By the time of evaluation, however, most patients appear asymptomatic because TIAs usually resolve within 5 minutes [51]. A clinician should highly suspect a TIA if the patient says, "I don't know why I'm here. Whatever it was, it is all better now" [52].

TIAs are caused by conditions similar to those leading to ischemic stroke [10]. Among the common causes are atherosclerosis of large vessels, cardioembolism, and atrial fibrillation (AF). Uncommon causes include hypercoagulable states, arterial dissection, sympathomimetic drugs (e.g., cocaine), and arteritis (caused by noninfectious necrotizing vasculitis, drugs, irradiation, or local trauma) [53].

The risk factors for TIA are also similar to those for ischemic stroke and include many modifiable factors, such as hyperhomocysteinemia, hyperlipidemia, smoking, obesity, and diabetes [10]. Risk can be reduced substantially by the treatment of vascular anomalies such as hypertension and AF, two conditions commonly associated with older age. Younger individuals (18 to 45 years of age) who have a TIA or ischemic stroke often have no detectable vascular risk factors [54].

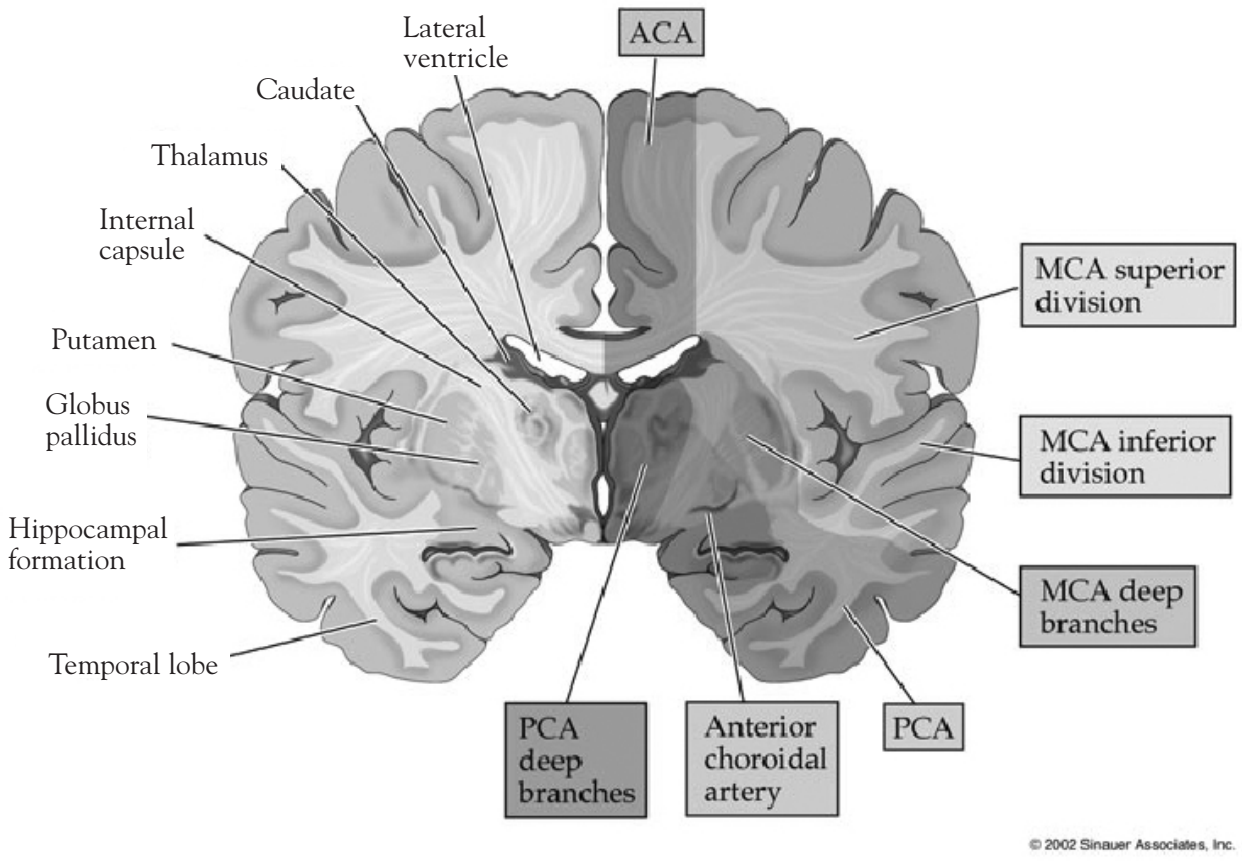
GENERAL REGIONS OF ISCHEMIC STROKE AND CORRESPONDING NEUROLOGIC DEFICITS	
Affected Region	**Common Signs and Potential Sequelae**
Left anterior hemisphere	Aphasia (esp. difficulty reading, writing, calculating) Right limb weakness and sensory loss Right field visual defect
Right anterior hemisphere	Limb motor weakness or loss Left field visual neglect Unable to determine two-point stimuli on left side
Left posterior cerebral artery	Aphasia (esp. difficulty reading, naming objects) Right visual field defect Occasionally, right-sided numbness
Right posterior cerebral artery	Left limb sensory loss Left-sided neglect Left field visual defect
Vertebrobasilar territory (posterior circulation)	Bilateral vision disturbances and nystagmus Dysarthria and dysphagia Ataxia Dizziness, vomiting, headache No cortical deficits (e.g., aphasia, cognitive impairments)
Caudate nucleus, thalamus, frontal lobe (anterior circulation)	Sudden abnormal behavior
Thalamus (posterior circulation)	Numbness, decreased sensation on face, arm, leg on same side
Source: [57; 58; 59]	*Table 3*

Ischemic Strokes

Within minutes of the onset of ischemic stroke, the core of an infarct can begin to form at the least-perfused site. This site is encircled by an area partially altered metabolically and ionically by cytotoxic edema [55]. This area, the ischemic penumbra, is structurally intact and generally salvageable if reperfusion is achieved promptly. Because cerebral function deficits develop rapidly (within minutes to hours) as an ischemic stroke progresses, these brain attacks are a medical emergency. Each minute that passes results in an average loss of 1.9 million neurons and 14 billion synapses; an ischemic brain ages 3.6 years for every hour that passes after the onset of stroke [56]. For this reason, stroke specialists use the mantra, "time is brain." Although irreversible damage occurs, most individuals with stroke have recoverable penumbral tissue for at least three hours following the onset of symptoms [16].

The physical signs, symptoms, and sequelae of ischemic stroke are usually unilateral because of the circulatory anatomy of the brain (***Table 3***). Anterior circulation is composed of the paired internal carotid arteries and vessels that supply blood to the cerebral hemispheres [57]. Each common carotid artery bifurcates into the internal and external carotid arteries. The ophthalmic artery, posterior communicating artery, and anterior choroidal artery are supplied by the internal carotid artery (***Figure 1***). Most importantly, the internal carotid artery provides blood to the middle cerebral artery, the largest intracerebral vessel. The middle cerebral artery provides oxygen to the lateral, frontal, parietal, and temporal lobes and the basal ganglia. It also supplies the anterior cerebral artery, which is responsible for the medial part of the frontal and parietal lobes, most of the corpus callosum, the frontobasal cerebral cortex, deep structures, and the anterior diencephalon. The anterior choroidal artery supplies a portion of the thalamus and the posterior limb of the internal capsule.

CORONAL SECTION OF THE CEREBRUM ILLUSTRATING ARTERIAL TERRITORIES



Source: [60] Reprinted from Blumenfeld H. Neuroanatomy Through Clinical Cases. 2nd ed. Boston, MA: Sinauer Associates, Inc.; 2013, with permission from Sinauer Associates, Inc. *Figure 1*

Posterior circulation is primarily composed of the vertebrobasilar artery, the posterior cerebral artery, which it supplies, and other branching vessels [57]. The posterior cerebral artery provides blood to the occipital and medial temporal lobes, as well as regions of the midbrain, subthalamic nucleus, basal nucleus, thalamus, mesial inferior temporal lobe, and occipitoparietal cortices. The two main segments of the posterior cerebral artery (P1 and P2) are connected by the posterior communicating artery. The Circle of Willis links the anterior and posterior circulation at the base of the brain.

In general, ischemic strokes are categorized according to etiology: thrombotic and embolic [61]. In addition, they are classified into five subtypes according to a system developed by the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) [62].

Thrombotic Stroke

A thrombotic stroke occurs when a thrombus impairs cerebral blood flow by further narrowing or blocking an artery, typically around an atherosclerotic plaque. The stenosed or occluded artery may be a large vessel (e.g., carotid artery systems, vertebral arteries, the Circle of Willis) or a small vessel (e.g., branches of the Circle of Willis, the posterior circulation). Approximately 21% to 27% of ischemic strokes arise from atherosclerotic disease of the large vessels [63; 64]. The cerebral artery branch points, especially those of the internal carotid artery, are the most vulnerable [65]. Small-vessel disease is associated with 21% to 25% of ischemic strokes [63; 64]. Thrombotic strokes caused by small-vessel disease are traditionally associated with lacunar infarcts, small, deep, subcortical lesions of 15 mm or less in diameter

resulting from occlusion of a single penetrating artery [62; 66]. As many as 20% of older individuals who are otherwise healthy have asymptomatic lacunar infarcts unrelated to an ictal event [67]. These silent infarctions were previously believed to be benign with a good long-term prognosis. However, they now have been linked to increased risks of stroke and death and can lead to debilitating cognitive impairments such as vascular dementia [67; 68].

Independent risk factors for lacunar infarcts include hypertension, gender, age, diabetes, smoking, and a history of TIA [67]. Although hypertension is strongly associated with the development of small-vessel occlusion, lacunar infarcts also occur in individuals without hypertension. However, normotensive individuals with lacunar infarcts are typically 85 years of age or older, suggesting that hypertension accelerates the arteriopathy underpinning small-vessel disease. Diabetes is an independent risk factor for lacunar infarcts [69].

Embolic Stroke

An embolic stroke occurs when an embolus (i.e., any circulating clot or particle originating from a distal point) blocks an artery that supplies oxygen to the brain. Stroke registries indicate that 14% to 30% of ischemic strokes are embolic [70; 71; 72; 73; 74]. Emboli include blood clots, fatty deposits, atherosclerotic plaque fragments, and cancerous cells or infectious materials emanating from conditions such as atrial myxoma and endocarditis, respectively. Clinical symptoms of the resulting infarct correspond to the location of the embolus, not its type. The region of the middle cerebral artery is most frequently blocked by emboli [75].

AF is the most common cause of embolic stroke, increasing the risk of embolic stroke fivefold and doubling the risk of death [76; 77]. Patients with valvular thrombi, from endocarditis or prosthetic valves, or mural thrombi from myocardial infarction (MI), AF, severe heart failure, or patent foramen ovale, are at high risk for the development of emboli [78; 79]. MI is associated with a 2% to 3% incidence of embolic stroke, 70% of which occur in the first week after the event [77; 79].

TOAST Classification

The subtype of ischemic stroke influences treatment decisions, prognosis, and risk of recurrent stroke. The TOAST system was designed to facilitate decision making and standardize ischemic stroke research (***Table 4***) [62]. Most strokes are subclassified as a large-artery atherosclerosis (caused by either a thrombus or an embolus), a cardioembolism, or an occlusion of a small vessel (lacuna) [62]. Approximately 4% of individuals with stroke have coexisting large-vessel and small-vessel disease [61; 80]. Other determined causes are rare (approximately 3%), and registries have classified up to 33% of ischemic strokes as being of "undetermined etiology" [81].

MORBIDITY AND MORTALITY

Approximately 16% of men and 14% of women have a stroke by 85 years of age, and stroke is the third leading cause of death in the United States, accounting for more than 840,678 deaths in 2016 [1; 3; 84]. Morbidity associated with stroke is also high, with at least 65% of stroke survivors having some sort of impairment [85]. At three months after a stroke, approximately 20% of survivors depend on long-term care. Between 15% and 30% of stroke survivors are permanently disabled [86]. A six-month follow-up of ischemic stroke survivors (65 years of age and older) demonstrated that [87]:

- 50% had some degree of hemiparesis
- 35% had depressive symptoms
- 30% were unable to walk without some assistance
- 26% were dependent in activities of daily living
- 26% were in a nursing home
- 19% had aphasia

FIVE SUBTYPES OF ISCHEMIC STROKE AS CLASSIFIED BY THE TRIAL OF ORG 10172 IN ACUTE STROKE TREATMENT (TOAST)	
Classification	**Major Characteristics**
Large-artery atherosclerosis (may be an embolus or thrombus)	Greater than 50% stenosis or occlusion of a major brain artery or branch cortical artery Cortical, cerebellar, brain stem, or subcortical infarct >15 mm Cortical or cerebellar dysfunction
Cardioembolism (may be high or medium risk based on evidence of embolism)	Cardiac source of emboli Cortical, cerebellar, brain stem, or subcortical infarct >15 mm Cortical or cerebellar dysfunction
Small-vessel (lacuna) occlusion	Patient presents with lacunar syndrome[a] Subcortical or brain stem infarcts <15 mm may be detected
Other determined cause	May be caused by conditions such as dissection, hypercoagulable states, or sickle cell anemia May have characteristics of any of the other stroke subtypes
Undetermined etiology	May be any of the following: Two or more causes identified Negative evaluation Incomplete evaluation
[a]The five classic lacunar syndromes are pure motor hemiparesis, pure sensory stroke, sensorimotor stroke, ataxic hemiparesis, and clumsy-hand dysarthria.	
Source: [62; 66; 82; 83]	*Table 4*

Fortunately, stroke mortality has been declining since the early 20th century. In the United States, stroke has fallen from the third to the fifth leading cause of death, representing a true mortality decline rather than a repositioning of causes of death [3; 84]. This decline is a result of reduced incidence of stroke and lower case-fatality rates, concurrent with cardiovascular risk factor control interventions (e.g., hypertension control). Other efforts (e.g., diabetes control, smoking cessation programs) likely have also contributed to the decline in stroke mortality. The effects of telemedicine and stroke systems of care require additional study but appear to be significant. The decline has occurred in both women and men, for all racial/ethnic and age groups, and represents a major improvement in public health and a reduction in years of potential life lost [88].

Disparities in Prevalence and Mortality

Age, gender, and race/ethnicity play major roles in the prevalence of stroke and its associated mortality.

Age

Prolonged damage of the aging cardiovascular system by various risk factors for stroke doubles the risk of ischemic stroke for each decade of life after 55 years of age [9]. Thus, clinicians should be sensitive to their patients' modifiable risk factors, most notably hypertension, starting at an early age [1]. As many as 70% of strokes occur in individuals older than 65 years of age, and the average age at the time of ischemic stroke is 71 years in men and 75 years in women [1]. Stroke patients 85 years of age and older comprise 17% of all stroke patients [1].

Clinicians should be particularly aware of silent cerebral infarctions in older individuals, as these infarctions occur more commonly in this population [89].

COMPARISON OF MEDIAN SURVIVAL AFTER A FIRST STROKE ACCORDING TO SEX		
Age	**Median Survival**	
	Women	**Men**
55 to 64 years	7.8 years	13.1 years
65 to 74 years	7.7 years	6.2 years
≥75 years	2.3 years	2.1 years
Source: [97]		*Table 5*

COMPARISON OF PREVALENCE OF SELECT SYMPTOMS IN MEN AND WOMEN		
Symptom on Presentation	**Prevalence**	
	Men	**Women**
Overall nontraditional symptoms	19%	28%
Pain	8%	12%
Altered consciousness	12%	17%
Traditional Symptoms		
Imbalance	20%	15%
Hemiparesis	24%	19%
Source: [102]		*Table 6*

Gender

Women have a higher lifetime risk of stroke than men [90; 91; 92]. According to estimates from the Framingham Heart Study, among people 55 to 75 years of age, the risk of stroke is 1 in 5 for women and 1 in 6 for men [93]. Age-specific stroke incidence rates are substantially lower among women than men, except in those 80 years of age and older, in which the incidence rate in women is approximately equal to or higher than the rate in men [90; 91; 94; 95; 96]. Among individuals 65 years of age and older, the median survival time after a first stroke is typically longer for women than for men. For both men and women, the median survival decreases with age (***Table 5***) [97]. However, the possibility of gender disparities in how health care is provided to individuals who present with stroke symptoms is also being evaluated.

Studies suggest that, compared with men, women are evaluated less frequently following a stroke and that any evaluation is more likely to be delayed [98; 99; 100]. This pattern results from women's presentation with nontraditional symptoms or without traditional symptoms and inappropriate worry by both clinician and patient about treatment-related risks (***Table 6***) [98; 99; 101; 102; 103]. Although studies to evaluate differences in strokes between men and women are in early stages, preliminary results indicate that emergency medical service (EMS) personnel and clinicians need an accurate understanding of symptom presentation patterns for men and women. The prevalence of nontraditional symptoms is higher among women than men; nontraditional stroke symptoms include headache, face and limb pain, nausea, and hiccups as well as symptoms typically believed to be unrelated to neurologic deficits (e.g., chest pain, shortness of breath, palpitations) [102].

RACIAL/ETHNIC VARIATIONS IN PREVALENCE OF STROKE AND HYPERTENSION		
Population	**Stroke Prevalence**	**Hypertension Prevalence**
American Indian/Alaskan Native	5.3%	NA
Non-Hispanic Black	4.1%	55.4%
Non-Hispanic White	2.7%	42.8%
Hispanic or Latino	2.3%	41.1%
Asian/Pacific Islander	1.2%	NA
NA = Not available		
Source: [1]		*Table 7*

Race/Ethnicity

The decline in stroke mortality has reduced, but not eliminated, the racial/ethnic gap in stroke mortality [88]. Racial/ethnic disparities in the incidence of stroke and its related mortality are substantial, and the factors contributing to the disparities are complex and poorly understood [1; 5; 6; 7; 8; 104]. The risk of first-time stroke among black individuals is 1.5 times higher than that for white individuals in the United States, and the incidence of first-ever stroke is increasing among Hispanic Americans compared to whites [1]. The Northern Manhattan Study (NOMAS) showed that the age-adjusted incidence of first ischemic stroke per 100,000 individuals was 191 in the black population, 149 in the Hispanic population, and 88 in the white population [1; 104]. Another study showed that the prevalence of stroke among these three groups also varied according to age [6]. In the black population, the prevalence was 4.8% for individuals 45 to 64 years of age and 10% for individuals 65 years of age and older; the corresponding prevalences were 2.3% and 10% for Hispanic individuals and 2% and 9% for white individuals [6]. Intracranial atherosclerotic strokes were the most common type of strokes among the black and Hispanic populations [1; 104].

According to the AHA 2019 update on statistics for heart disease and stroke, the prevalence of stroke is highest for American Indian/Alaskan Natives and lowest for Asian/Pacific Islanders (***Table 7***) [1]. Data indicate variation among stroke-related mortality rates as well and show that stroke deaths have increased in minority populations while decreasing in the white population. Projections indicate a 20.5% increase in stroke by 2030, with the greatest increase (29%) in Hispanic men [1].

Data from 2016 demonstrated an overall rate of 37.3 deaths per 100,000, with a rate of 51.9 for the black (non-Hispanic) population, 36.1 for the white (non-Hispanic) population, 32.1 for the Hispanic population, 31.0 for the Asian/Pacific Islander population, and 30.7 for the American Indian/Alaskan Native population [1]. Risk factors, such as hypertension, diabetes, and obesity, vary among these populations as well, but increased risks alone cannot completely explain increased prevalence or mortality [9].

MODIFIABLE RISK FACTORS

Several modifiable risk factors for stroke have been well-documented in the literature, and some have been less well-documented (***Table 8***). The well-documented risk factors include many associated with cardiovascular disease as well, and proper management of these factors can reduce both the risk of a first-time stroke and the development of a cardiovascular condition [7; 9]. Clinicians should discuss the potential for stroke associated with risk factors specific to patients and offer strategies to reduce or eliminate them [9]. Four lifestyle factors warrant brief review because of the substantial role the patient has in helping to manage risk: smoking, diet and nutrition, physical inactivity, and obesity and body fat distribution.

MODIFIABLE RISK FACTORS FOR STROKE	
Well-Documented Factors[a]	**Less-Documented Factors[b]**
Hypertension Atrial fibrillation (AF) Diet and nutrition Diabetes Cigarette smoking Dyslipidemia Obesity and body fat distribution Cardiac conditions other than AF Asymptomatic carotid stenosis Sickle cell disease Physical inactivity	Metabolic syndrome Inflammation and infection Migraine Alcohol abuse Hypercoagulability Sleep-disordered breathing Elevated lipoprotein (a) Drug abuse Hyperhomocysteinemia
[a] Listed in descending order of quality of documentation. [b] Information on less-documented risks for stroke can be found in the American Heart Association (AHA) guideline "Primary Prevention of Stroke."	
Source: [9]	*Table 8*

Diet and Nutrition

Increased consumption of fruits and vegetables reduces the risk of stroke in a dose-dependent manner. Risk is reduced 6% for each serving of fruits and vegetables per day [105]. Reducing sodium intake and increasing antioxidants, potassium, and calcium also mitigates the risk of stroke [9; 106; 107]. The AHA/ASA recommend that individuals with stroke residing in long-term care facilities be evaluated for calcium and vitamin D supplementation [21]. The Dietary Approaches to Stop Hypertension (DASH) diet, which is rich in fruits, vegetables, and low-fat dairy products and which limits saturated and total fat intake, has been shown to lower blood pressure and likely reduce the risk of stroke [106; 107].

Cigarette Smoking

Overwhelming evidence shows an undeniable association between cigarette smoking and stroke [9; 108]. Smoking doubles the risk for ischemic stroke and increases the risk of hemorrhagic stroke 2 to 4 times [109]. Studies also indicate that repeated exposure to environmental ("secondhand") smoke almost doubles the risk of stroke [110]. Secondhand smoke exposure is a contributing factor in more than 8,000 stroke deaths each year [111]. Using data from the National Health Interview Survey and death certificate data for 2000 through 2004, the Centers for Disease Control and Prevention estimated that smoking resulted in an annual average of 61,616 stroke deaths among men and 97,681 stroke deaths among women [112].

Individuals who smoke should be prescribed smoking cessation medications and be informed about cessation programs, counseling, and nicotine-replacement products. Epidemiologic studies show that, following smoking cessation, stroke risk decreases over time [9]. Individuals who do not smoke should be encouraged not to start.

Obesity and Body Fat Distribution

One study has found that in the body mass index (BMI) range of 25 to 50 kg/m^2, each 5 kg/m^2 increase in BMI was associated with a 40% increased risk of stroke mortality; in the BMI range of 15 to 25 kg/m^2, there was no relationship between BMI and stroke mortality [113].

Another large epidemiologic study showed that the risk almost doubled for overweight and obese men [114]. A meta-analysis of data from 25 studies involving more than 2.2 million people showed an increased risk of ischemic stroke of 22% in overweight individuals and 64% in obese individuals [115]. Studies have not yet addressed if losing weight reduces this risk [9]. However, it is well-documented that weight loss lowers blood pressure and cholesterol and positively affects other risk factors for stroke. Clinicians should encourage overweight patients to begin a weight-loss program that includes a healthful diet and exercise and provide patients with safe weight-loss strategies, such as those recommended by the AHA [9].

Body fat distribution has proven to be a fairly reliable indicator of stroke risk [116; 117]. While some studies support abdominal adiposity as a significant risk factor for stroke only in men, other research indicates that a high concentration of abdominal fat is a significant risk factor in both men and women, independent of BMI [9]. On the other hand, gynoid adiposity in women appears to be associated with a lower risk for stroke, even for women with a higher BMI [117]. A high hip-to-waist ratio may be a more important risk factor for vascular disease, including stroke, than BMI score alone [118].

Physical Inactivity

A large and generally consistent body of evidence indicates that routine physical activity prevents stroke [9]. A habitually sedentary lifestyle increases an individual's chance of stroke. Physically active men and women generally have a 25% to 30% lower risk of stroke or death than the least active people [119]. Individuals should be strongly encouraged to engage in aerobic exercise at moderate intensity for 150 minutes or more weekly, at vigorous intensity for 75 minutes or more per week, or a combination of both that fulfills these requirements [9]. It should be noted that only moderate-to-vigorous intensity exercise has been found to reduce the incidence of stroke [104].

PREVENTION

PRIMARY PREVENTION

To decrease the incidence of first-time stroke in the United States, primary prevention should focus on individuals at high risk with modifiable risk factors. In areas of the United Kingdom, the incidence of major stroke has been reduced 40% through a reduction in the incidence of risk factors [120]. The AHA has established evidence-based recommendations for primary prevention of stroke and has developed public campaigns and educational materials to help raise awareness of stroke.

Evidence-Based Recommendations

For most individuals with nonmodifiable stroke risks, the probability of stroke can be decreased substantially with rigorous preventive measures and the treatment of modifiable risks [9; 16]. The AHA recommends addressing lifestyle risk factors, as discussed, and medically managing several risk factors, including hypertension, diabetes, AF, other cardiac conditions, dyslipidemia, and asymptomatic carotid stenosis [9].

Hypertension

Hypertension is perhaps the most significant risk factor for stroke, and risk increases as blood pressure increases [9]. Fortunately, the prevalence of hypertension has plateaued over the past decade and remained stable, at 29%, between 2008 and 2017 [121; 122]. Control of hypertension (defined as blood pressure less than 140/90 mm Hg) also has improved, with rates of control increasing from 27.3% in 1988–1994 to 50.1% in 2007–2008 [9]. These improvements are likely attributable to heightened awareness and treatment, with awareness among U.S. residents increasing from 69% in 1988–1994 to 81% in 2007–2008 [9]. Still, more than two-thirds of people 65 years of age and older are hypertensive [123].

The AHA and other professional organizations recommend that all adults 18 years of age and older be screened for high blood pressure [124]. The U.S. Preventive Services Task Force (USPSTF) recommends screening for all adults 18 years of age and older and annual screening for adults 40 years of age and older who are at increased risk for high blood pressure. Increased risk is defined as [124]:

- High-normal blood pressure (130–139/85–89 mm Hg)
- Overweight or obese
- Black race

Individuals 18 to 39 years of age with normal blood pressure (<130/85 mm Hg) who do not have other risk factors should be screened every 3 to 5 years. The USPSTF additionally recommends rescreening with properly measured office blood pressure. If the blood pressure is elevated, the diagnosis should be confirmed with ambulatory blood pressure monitoring [124].

The 2017 Guideline for High Blood Pressure in Adults recommends screening every 2 years for adults with a blood pressure less than 120/80 mm Hg and screening every 3 to 6 months for people with systolic blood pressure of 120 to 129 mm Hg or with diastolic blood pressure greater than 80 mm Hg [125]. The AHA/ASA recommends that women be screened for high blood pressure before taking birth control pills, as the combination increases the risk of stroke [126].

Appropriate management of hypertension may also include dietary changes, other lifestyle modifications, and pharmacologic therapy. Studies have shown that management is possible for the majority of patients, but most will require treatment that includes two or more drugs [9].

Diabetes

The risk for stroke is 2 times higher among individuals with diabetes. In 2014, after adjusting for population age differences, hospitalization rates for stroke were more than three times higher among adults 20 years of age and older with diagnosed diabetes compared with those without diagnosed diabetes [127]. Type 2 diabetes is associated with an increased prevalence of atherogenic risk factors, such as hypertension, obesity, and dyslipidemia. The combination of hyperglycemia and hypertension is thought to increase the risk of stroke [9]. The AHA recommends that the target blood pressure for individuals with diabetes be less than 140/90 mm Hg [9]. Pharmacologic therapy with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) has been shown to be safe and effective in this population [9]. In addition, lipid-lowering statins reduce the risk of first-time strokes in patients with diabetes, irrespective of the baseline lipid levels, pre-existing vascular conditions, and glycemic control [128].

Atrial Fibrillation

AF is associated with a fourfold to fivefold increased risk of ischemic stroke, and approximately 60,000 strokes occur among the 2.3 million individuals with AF annually [9]. According to the AHA/ASA, women older than 75 years of age should be screened for AF risk due to its link to greater stroke risk [126]. The AHA recommends that individuals with AF who have valvular heart disease (particularly individuals who have mechanical heart valves) should receive anticoagulant therapy [9]. Antithrombotic therapy with adjusted-dose warfarin or aspirin is approved for stroke prevention in individuals with nonvalvular AF based on their calculated risk of stroke and estimated risk of bleeding. The individual's preferences and access to high-quality anticoagulation monitoring should be considered. Warfarin therapy to maintain an international normalized ratio (INR) of 2.0 to 3.0 (target: 2.5) is strongly recommended for high-risk

individuals (those with more than a 4% annual risk of stroke) with AF and no significant contraindications to oral anticoagulants [9; 129]. Despite the effectiveness of such treatments, anticoagulant therapy continues to remain underprescribed due to overestimation of the associated risks of warfarin (e.g., intracranial, extracranial hemorrhage) and underestimation of stroke risk [129]. Some physicians err on the side of caution and aim for an INR greater than the recommended target, with a corresponding reduction in therapeutic effectiveness.

Other Cardiac Conditions

The management of valvular heart disease, unstable angina, chronic stable angina, acute MI, and other cardiac conditions is a critical factor in stroke prevention. Strategies to prevent postoperative neurologic injury and stroke in patients undergoing surgical revascularization for atherosclerotic heart disease can be found in the American College of Cardiology coronary artery bypass graft surgery guidelines, which are approved by the AHA [9; 130]. The AHA states that it is "reasonable" to use warfarin for patients who have had ST-elevation MI and left ventricular dysfunction with extensive regional wall-motion abnormalities [9].

Dyslipidemia

The AHA recommends that statin therapy be prescribed for individuals with known coronary heart disease or high-risk hypertension (e.g., patients with diabetes), including those with normal low-density lipoprotein (LDL) cholesterol levels [9]. In addition, these individuals should be encouraged at every interaction to exercise, eat a healthful diet, and quit smoking. Niacin, bile acid sequestrants, ezetimibe, or fibric acid derivatives may also be considered for individuals with known coronary heart disease and low levels of high-density lipoprotein cholesterol, such as people in whom target cholesterol levels cannot be achieved with statins or people who cannot tolerate statin therapy; however, their effectiveness in decreasing stroke risk has not been established [9].

Asymptomatic Carotid Stenosis

Individuals with asymptomatic carotid artery stenosis should be screened for other modifiable risk factors, and any risk factors identified should be controlled as soon as possible. Antiplatelet therapy with aspirin is recommended, unless contraindicated [9]. Preventive carotid endarterectomy performed by a skilled surgeon is an option for patients when it is determined that the morbidity/mortality risk is less than 3% to 6%; however, the reduction in stroke risk is modest at best [9; 10]. Comorbidities and life expectancy should be considered when determining if surgery is appropriate. In addition, thorough discussion with the patient and his or her family/caregivers is a necessity. Topics should include the possibility of surgery-related death, the risks and benefits associated with the procedure, and the patient's preferences. For patients with a high surgical risk, carotid angioplasty/stenting may be considered. However, the periprocedural and overall 1-year event rates in some studies have dampened the AHA's enthusiasm for the stenting option [9; 10].

The U.S. Preventive Services Task Force (USPSTF) recommends against screening for asymptomatic carotid artery stenosis in the general adult population. The USPSTF concludes that for individuals with asymptomatic carotid artery stenosis there is moderate certainty that the benefits of screening do not outweigh the harms.

(https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/carotid-artery-stenosis-screening. Last accessed March 11, 2020.)

Strength of Recommendation/Level of Evidence: D (The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.)

Depressive Symptoms

After publication of the AHA guidelines, the findings of a large study showed that depressive symptoms are an independent risk factor for stroke, especially for patients younger than 65 years of age [131]. Clinicians may consider managing depressive symptoms and mood disorders as aggressively as hypertension or diabetes, because mood disorders appear to increase risk for all types of stroke [132].

PUBLIC HEALTH CAMPAIGNS

Although public knowledge regarding the warning signs and risks of stroke has improved, the majority of the general public is still unaware that early treatment can prevent severe disability and death [133; 134]. Estimates vary widely, however; the International Stroke Trial found that only 4% of patients with acute ischemic stroke arrive at the emergency department (ED) within 3 hours after the onset of symptoms, and a separate study found that 21% to 25% of individuals with acute ischemic stroke arrive at an ED within the same timeframe [135; 136]. Of these individuals, 2% to 4% receive thrombolytic treatment [137; 138]. It has been estimated that if all individuals called for emergency help at the onset of symptoms, as many as 29% could realistically receive treatment within 3 hours [137]. In addition, if all patients arrived at the ED within 1 hour after known symptom onset and received optimal treatment, the projected rate of thrombolysis would be 57%.

To improve the rate of early arrival in the ED, public education campaigns designed to help individuals recognize a stroke and seek early treatment often use the "five sudden warning signs" devised by the Brain Attack Coalition, or "FAST," a mnemonic device created by study investigators on the basis of the Cincinnati Prehospital Stroke Scale [139; 140]. The AHA and the National Stroke Association and other organizations use FAST. Early signs and symptoms that comprise the five sudden warning signs include [140; 141]:

- Numbness or weakness of the face, arm, or leg (especially on one side)
- Trouble seeing from one or both eyes
- Severe headache
- Dizziness, difficulties with walking, and loss of balance and coordination
- Confusion and trouble speaking or understanding

FAST was designed to focus on fewer common signs of stroke onset (face numbness, arm numbness, and slurred speech) and to include an action component (time) for lay persons who may have trouble recalling the warning signs and the appropriate action. A retrospective study exploring the capacity of the FAST campaign to facilitate the recognition of stroke suggests that it leads to the identification of approximately 89% of individuals who have a stroke or TIA [140]. The most common stroke symptoms were related to the face, arm, and speech/language. The same study found that a modified version of FAST (with removal of the word "numbness") decreased the number of TIAs identified and targeted ischemic stroke more readily than hemorrhagic stroke. Ultimately, it is unknown whether the general public is more likely to remember FAST or the five sudden warning signs.

In 1989, the United States Department of Health and Human Services Public Affairs launched a National Health Observance to help stimulate awareness of the risk factors, prevention, and early treatment of stroke. For more than 25 years, May has been recognized as National Stroke Awareness Month, with special campaigns to heighten awareness of stroke among the general public. Resources to aid community campaigns can be obtained from the American Stroke Association at https://www.stroke.org/en/about-the-american-stroke-association/american-stroke-month/community-resources-english.

PATIENT EDUCATION

Patient education should be presented in several forms and focus on modifiable risk factors, patients' needs, lifestyle, and life stage. Healthcare professionals can be most effective in reducing the risk of stroke when they demonstrate an interest in a patient's lifestyle and psychologic status. For instance, if a patient depends on his or her spouse or companion for meals, optimum benefits will result from educating the spouse/companion about healthy diet practices. Clinicians should also consider cultural needs when addressing prevention strategies.

When a patient/caretaker does not speak the same language as the clinician, a professional interpreter should be consulted to ensure accurate communication. A systematic review of the literature has shown that the use of professional interpreters provides better clinical care than the use of informal interpreters, with the former improving the quality of care for patients with limited English language skills to a level equal to that for patients with no language barriers [142]. Use of professional interpreters has been associated with improvements in communication (errors and comprehension), utilization, clinical outcomes, and satisfaction with care [142]. Individuals with limited English language skills have indicated a preference for professional interpreters rather than family members [143].

Whether the education involves stroke prevention, stroke recognition, care after stroke, coping with the effects of stroke, or palliative care, written materials are as important as verbal communication. Several organizations supply general or specialized educational resources, and many also provide patients and family/caregivers with psychosocial, financial, and assisted-living information or aid (***Table 9***). Clinicians should attempt to obtain materials written in languages appropriate for their patient population and, if appropriate, that target patients in high-risk racial/ethnic populations, especially American Indian/Alaskan native and black individuals.

ORGANIZATIONS PROVIDING PATIENT EDUCATION RESOURCES ON STROKE

American Heart Association
(800) AHA-USA-1 (242-8721)
https://www.heart.org

American Stroke Association
(a division of the American Heart Association)
(800) AHA-USA-1 (242-8721)
https://www.stroke.org

Brain Aneurysm Foundation
(888) BRAIN02 (272-4602)
https://bafound.org

Brain Attack Coalition
(301) 496-5751
https://www.brainattackcoalition.org

Centers for Disease Control and Prevention
https://www.cdc.gov/stroke

Internet Stroke Center
(214) 648-3111
http://www.strokecenter.org

BrightFocus Foundation
(800) 437-2423
https://www.brightfocus.org

Hazel K. Goddess Fund for Stroke Research in Women
http://www.thegoddessfund.org

National Aphasia Association
https://www.aphasia.org

Source: Compiled by Author *Table 9*

PREDICTING RISK

When determining the appropriate degree of risk management, information regarding an individual's risk of first stroke is valuable. The goals of risk assessment tools include [9]:

- Identifying patients who are unaware of their elevated risk
- Assessing the total risk of multiple factors
- Discerning the utility of modifications and treatments
- Projecting a quantitative risk in order to select appropriate treatments or stratification in clinical trials
- Guiding appropriate use of diagnostic tests

The numerous nonmodifiable and modifiable factors that contribute to the risk of stroke have been discussed. Although many of these are independent risk factors, their interactions can affect predictions and management decisions in unexpected ways. No simple, validated stroke risk-assessment tool is currently available [9]. Although risk-assessment tools may have some utility, it is unknown if they improve primary prevention, especially when applied across subgroups according to age, gender, and race/ethnicity [9; 144].

Because TIA is a substantial risk factor for a subsequent stroke, clinicians in many EDs are stratifying such patients by degree of risk with use of the ABCD or ABCD2 assessments [145; 146]. The ABCD clinical tool is designed to predict 7-day risk of stroke through assessment of age (1 point for patients 60 years of age or older), blood pressure (1 point for a blood pressure greater than 140/90 mm Hg), clinical features (2 points for unilateral weakness with or without speech impairment or 1 point for speech impairment without weakness), and duration (1 point for 10 to 59 minutes, 2 points for greater than 59 minutes) [147]. The "2" designation in ABCD2 was added to represent the presence or absence of diabetes. The effectiveness of these screening tools is lessened by the fact that some individuals do not seek emergency care for a TIA or do not report a TIA to their clinician. However, the ABCD2 assessment has been shown to identify 21% of individuals with a high 2-day risk of having an ischemic stroke [145]. Individuals with high-risk TIA require the same intensity of evaluation and stroke prevention as individuals with ischemic stroke. Scores that predict future stroke risk should be used in conjunction with other diagnostic studies (e.g., imaging) and laboratory tests. The use of ED diagnostic protocols and observation units can reduce length of stay while improving patient treatment and reducing stroke rate [148; 149].

EARLY MANAGEMENT

Because the temporal window for effective stroke treatment is short, it is imperative that evaluation and diagnosis are performed promptly and accurately. Use of EMS by persons with stroke is associated with earlier ED arrival, faster ED evaluation, more rapid treatment, and more eligible patients receiving treatment. However, only 60% of all patients with stroke use EMS. In particular, male, black, and Hispanic patients are less likely to use EMS [150].The AHA/ASA has established several evidence-based recommendations for the diagnosis and early management of adult-onset ischemic stroke [16]. These recommendations address the evaluation of the individual before he or she arrives at an ED, diagnosis in the ED, the history and physical examination, laboratory tests, carotid ultrasonography, cerebral angiography, and imaging studies.

PREHOSPITAL EVALUATION

The single most important factor influencing the treatment of stroke within 3 hours after the onset of symptoms is the rapid triage and transportation provided by EMS [151]. Public health leaders and medical professionals should design and implement education programs that emphasize the need to rapidly seek emergency care when a stroke is suspected. These programs should be racially/ethnically, age, and sex/gender diverse and should target the public, healthcare providers, and hospital and EMS personnel to increase use of the EMS system, decrease stroke onset to ED arrival times, and increase the timely use of appropriate treatment [16].

Stroke assessment should begin with the EMS dispatcher [16]. When stroke or TIA is suspected, the dispatcher should notify the appropriate EMS provider and coordinate with an appropriate acute stroke treatment facility (***Table 10***). Regardless of the degree of the neurologic deficits, an individual with suspected stroke or TIA should be dispatched and triaged as if he or she were a serious trauma patient [16]. If possible, the individual should be taken to a designated stroke center [16; 19].

"STROKE CHAIN OF SURVIVAL" FROM THE 2013 AMERICAN HEART ASSOCIATION GUIDELINES
Detection: Recognize stroke signs and symptoms
Dispatch: Call 911 and priority emergency medical services dispatch
Delivery: Prompt pre-hospital notification and transport to hospital
Door: Immediate emergency department triage
Data: Emergency department evaluation, prompt laboratory studies, and computed tomography
Decision: Diagnosis and decision about appropriate therapy
Drug/Device: Administration of appropriate drugs or other interventions
Disposition: Timely admission to stroke unit, intensive care unit, or transfer
Source: [152] *Table 10*

After the individual's airway, breathing, and circulation have been assessed and stabilized, the EMS personnel should initiate a prehospital evaluation [16; 153]. If the individual exhibits common signs of stroke and/or a stroke is indicated by a validated prehospital examination tool (e.g., Los Angeles Prehospital Stroke Screen, Cincinnati Prehospital Stroke Scale), EMS providers should notify the ED that an individual with suspected stroke is in transport [16; 153; 154]. Any information about coexisting conditions and, most importantly, time of symptom onset should be provided in advance. A blood glucose level should also be determined, as symptoms of hypoglycemia may mimic those of a stroke [16].

Prehospital evaluation expedites the physician's evaluation of the patient on arrival in the ED. If possible, a witness (preferably a close family member or companion) should be transported with the patient to assist with patient history, symptom onset, and contact information. If no witness was present, a family member should be contacted to go to the hospital and should be informed that he or she may need to provide consent for the patient's treatment. History obtained by EMS providers should include [16]:

- Information about recent events (e.g., stroke, MI, trauma, surgery, bleeding)
- Comorbid diseases (e.g., hypertension, diabetes)
- Use of medications (e.g., anticoagulants, insulin, antihypertensives)

The patient's medication containers should be transported to the ED as well, especially if medications include anticoagulant, antiplatelet, or antihypertensive drugs. Because 60% of individuals with suspected stroke do not use EMS for initial medical care access, ED staff should be alert to signs of stroke among individuals waiting to be seen in the ED [16; 150].

DIAGNOSIS IN THE ED

Organization of the ED's stroke team and assessment protocol is paramount to maximize the likelihood of early and successful management [16]. The acute stroke team should include physicians, nurses, and laboratory/radiology personnel. After the patient has been triaged and stabilized, the inaugural ED evaluation (history and physical examination), laboratory studies, and CT imaging should be performed concurrently. The multimodal approach has three goals [16]:

- Rapid and careful identification of people with stroke for treatment purposes
- Determination of the underlying cause of the stroke for secondary prevention
- Detection of stroke-mimicking conditions that may require immediate care

IMMEDIATE DIAGNOSTIC STUDIES TO EVALUATE PATIENTS WITH SUSPECTED ISCHEMIC STROKE, AS RECOMMENDED BY THE AMERICAN HEART ASSOCIATION	
Population	**Diagnostic Test**
All patients	Cerebral computed tomography or magnetic resonance imaging (without contrast medium)
	Blood glucose
	Serum electrolytes/renal function tests
	Markers of cardiac ischemia
	Complete blood count, including platelet count
	Prothrombin time/international normalized ratio (INR)
	Activated partial thromboplastin time
	Oxygen saturation
	Electrocardiography
Selected patients	Hepatic function tests
	Toxicology screen
	Blood alcohol level
	Pregnancy test
	Arterial blood gas tests (if hypoxia is suspected)
	Chest radiography (if lung disease is suspected)
	Lumbar puncture (only if stroke is suspected to be secondary to an infectious disease)
	Electroencephalography (if seizures are suspected)

Source: [155] Reprinted from Christensen H, Fogh Christensen A, Boysen G. Abnormalities on ECG and telemetry predict stroke outcome at 3 months. J Neurol Sci. 2005;234:99-103. With permission from Elsevier. *Table 11*

Within 1 hour of the patient's arrival, the evaluation (including a neurologic examination) and treatment decision should be completed. The AHA recommends that all patients receive a standardized battery of tests and procedures, with alternative tests performed only if a particular condition is suspected or the patient's history is incomplete (***Table 11***) [16]. Generally, diagnostic tests should be limited to save time. In addition, all diagnostic tests for stroke should be available 24 hours a day, 7 days a week.

PHYSICAL EXAMINATION AND HISTORY

In addition to time of onset, other crucial historical data that should be obtained include [16]:

- Information about atherosclerotic and cardiac disease risk factors
- Prior and current drug abuse and history of migraine, seizure, infection, trauma, or pregnancy
- Eligibility for treatment of ischemic stroke

If a patient presents with classic signs of stroke and has one or more cardiovascular risk factors, the diagnosis of stroke can be straightforward.

However, identifying more unusual cases may be a challenge. If fever and a cardiac murmur are present, the cause of the stroke may be infective endocarditis [156; 157]. Giant cell arteritis may be the cause if the patient is 50 years of age or older, has a headache, and has an elevated erythrocyte sedimentation rate. The presence of ptosis and miosis contralateral to the deficit may suggest carotid artery dissection [156; 157]. If the symptoms were maximal at their onset, a subarachnoid hemorrhage or embolic stroke should be suspected [158]. In up to 40% of patients with subarachnoid hemorrhage, a severe headache (sometimes called a thunderclap or sentinel headache) that may abate within minutes or hours is the only symptom [158]. Cerebral CT should be immediately performed in any patient with a suspected subarachnoid hemorrhage [36].

The general physical examination should involve assessment of the head, neck, heart, lungs, abdomen, skin, and extremities, as well as the cardiovascular, respiratory, and gastrointestinal systems [16]. Pulse oximetry and body temperature are also important evaluations. When performing the head and neck examination, the clinician should look for physical signs of trauma or seizure activity (e.g., contusions, tongue lacerations) or heart failure (jugular venous distention). Thrombolytic treatment is inadvisable for a seizure in the absence of acute ischemia detected by imaging [21].

When examining the patient's neck, carotid bruits may be heard. Although these sounds may suggest atherosclerosis, they are not sufficient for diagnosing carotid stenosis [159]. Because the prevalence of asymptomatic carotid bruits increases with advancing age, it is not a reliable clinical marker of stroke risk in individuals older than 65 years of age [160].

The cardiac examination may demonstrate contributing factors or comorbidities, such as myocardial ischemia, valvular conditions, arrhythmias, or aortic dissection (a rare cause of ischemic stroke). The diagnostic evaluation should include electrocardiography (ECG), because cardiovascular conditions such as AF and MI are prevalent among individuals with stroke [16; 155]. The findings of studies have suggested that the value of chest x-ray as part of the diagnostic workup is debatable, and the 2019 AHA/ASA guideline recommends a chest x-ray only if lung disease is suspected [16]. Although cardiac monitoring in patients with stroke has not been evaluated, the AHA/ASA recommend its use in the first 24 hours to monitor for AF or MI, either of which can lead to stroke or be a dangerous coexisting condition [16].

Blood pressure sustained at or above 180/120 mm Hg may signal hypertensive encephalopathy [123; 161]. Examination of the respiratory system and the abdomen may lead to the detection of additional conditions. The state of the skin and extremities may indicate systemic conditions, including coagulopathies, platelet disorders, or liver dysfunction [16]. An irregular pulse may be indicative of AF.

If only historical information and/or physical examination are relied on, up to 19% of stroke mimics are mistaken for stroke. Yet, a patient's history and examination may also identify a condition masquerading as a stroke (***Table 12***) [16; 162]. The use of MRI or CT with laboratory studies enhances the accuracy of diagnosis, but detecting mimics with imaging techniques is a challenge if the patient has a history of stroke [16].

Another important component of the physical examination is assessment with the National Institutes of Health Stroke Scale (NIHSS). Although initially devised as a research tool to quantify neurologic deficits, this tool is now widely used to measure the severity of a stroke, devise an effective treatment plan that establishes a priority for patient safety, identify the potentially occluded vessel, and predict patient outcome [16; 164]. The NIHSS is standardized, reliable, and fast and facilitates communication among healthcare professionals.

COMMON NONCEREBROVASCULAR CONDITIONS THAT MIMIC STROKE	
Stroke Mimic	**Differential Symptoms**
Brain tumor	Gradual progression of symptoms
Drug overdose	Altered mental status without focal findings
Conversion disorder	Neurologic findings in a nonvascular distribution Inconsistent examination Other psychiatric disorders
Hypertensive encephalopathy	Headache Delirium Significant hypertension Cortical blindness Cerebral edema Seizure
Hypoglycemia	History of diabetes Low blood glucose level Decreased level of consciousness
Migraine with aura (complicated migraine)	History of similar events Preceding aura Headache Hemiplegia that outlasts the headache
Seizures/postictal paresis	Paresis History of seizures Witnessed seizure activity
Drug toxicity	History of lithium, phenytoin, or carbamazepine use
Source: [162; 163]	*Table 12*

Any trained healthcare professional can use the scale at the bedside in 5 to 8 minutes. In addition, results are based only on patient evaluation; a history or information from others is not necessary. It is recommended that the scale be used to assess the patient during the ED evaluation and during treatment with recombinant tissue plasminogen activator (rt-PA) or other therapies and that it be repeated often in the first 24 hours. Further information about the NIHSS and a copy of the scale can be obtained from the National Institute of Neurological Disorders and Stroke [165].

LABORATORY TESTS

For all patients with suspected stroke, the battery of diagnostic tests should be carried out concurrently with laboratory tests, including blood glucose level (to rule out hypoglycemia as a stroke mimic), complete blood count (with platelet count), serum electrolyte levels, renal function studies, and cardiac ischemia biomarkers [16]. Determination of prothrombin time and partial thromboplastin time are of particular importance when considering thrombolysis. Generally, waiting for the results of a diagnostic test should not be a reason to delay thrombolytic therapy [16]. The risk of increased neurologic damage and death caused by ischemic stroke outweighs that of a secondary hemorrhage except when a bleeding or blood disorder is suspected, the patient was given warfarin or heparin, or the patient takes anticoagulant drugs.

CAROTID ULTRASONOGRAPHY

Carotid ultrasonography is a noninvasive vascular imaging technique used to measure arterial blood flow and determine the site and degree of stenosis/occlusion of cerebral vasculature. In particular, transcranial Doppler ultrasonography, which can be performed at the bedside, serves multiple purposes in the cerebrovascular setting. Its most common uses are to assess a patient's primary and secondary stroke prevention needs and to monitor a patient's progress during the early post-acute stroke phase [10; 16; 166]. Additional uses of transcranial Doppler ultrasonography in patients with stroke include [16; 166; 167]:

- Detection of intracranial and extracranial vascular disorders
- Assessment of recurrent stroke risk (e.g., microemboli detection)
- Identification of candidates for intensive prophylactic interventions (e.g., carotid endarterectomy, angioplasty/stenting)
- Intraoperative monitoring of carotid endarterectomy
- Detection of right-to-left shunts
- Identification of subclavian steal syndrome
- Measurement of a post-subarachnoid hemorrhage vasospasm
- Assessment of recanalization (spontaneous or thrombolytically induced)
- Prognosis of patients with stroke (performed during post-acute phase)

Despite the usefulness of this technique, its performance is highly operator-dependent [166]. Considerable anatomic and physiologic knowledge of the cerebral vasculature is required, as vessel images are not produced, and skill and experience are prerequisites for data interpretation. Data acquisition and interpretation tend to be time-consuming and may delay treatment [166; 168]. While these reasons suggest that vascular imaging is not practical for the diagnosis of ischemic stroke in most cases, it may be useful in some. A recommendation in the 2019 AHA/ASA guidelines states that noninvasive imaging of the cervical carotid arteries should be routinely performed within 24 hours of admission in patients with nondisabling acute ischemic stroke in the carotid territory who are candidates for carotid endarterectomy [16]. Additionally, intracranial vessel imaging is recommended to guide selection of appropriate secondary stroke prevention treatments [16].

CEREBRAL ANGIOGRAPHY

Conventional catheter angiography is invasive, uses ionic radiation, and requires a nephrotoxic contrast medium [169]. It is particularly valuable for the detection of pathologic vascular disorders that lead to cerebral hemorrhage or ischemia, including aneurysm, vasculitis, arteriovenous malformation, atherosclerosis, and arterial dissection [10; 16]. Digital subtraction angiography (DSA), a type of catheter angiography, remains the standard criterion of conventional angiography for detection of many types of cerebrovascular lesions and diseases [170; 171; 172; 173; 174]. Its sensitivity and specificity equal or exceed those of noninvasive techniques; however, it can cause serious complications, such as stroke or death [16].

Unlike catheter angiography, magnetic resonance angiography (MRA) is not an x-ray. This technique creates a map of blood flow, not a true image of the vasculature anatomy. Noninvasive time-of-flight MRA is performed without contrast medium, whereas phase-contrast MRA is performed with contrast medium and is minimally invasive (catheter insertion into a blood vessel is unnecessary). Although MRA provides a high-resolution image of many vessels, it cannot reliably resolve distal or branch occlusions of the intracranial vasculature [16]. Another major disadvantage of MRA is that it overestimates the degree and length of high-grade stenosis by signaling loss of flow when blood flow is turbulent, in-plane, or slow [175]. Although MRA continues to advance technologically, in large part through the improvement of contrast media, high-grade stenosis is still overestimated using this technique when compared with DSA [176].

MRA is helpful for detecting less common causes of ischemic stroke or TIAs (e.g., arterial dissection, venous thrombosis) [172]. The 2019 AHA/ASA guideline recommends the use of MRA with diffusion-weighted MRI (DW-MRI) for selecting candidates for mechanical thrombectomy between 6 and 24 hours after last known well time [16]. DW-MRI is sensitive to acute cellular injury in cerebral ischemia and can be used to assess ischemic lesions in the first few hours [177].

Computed tomography angiography (CTA) provides a means to rapidly and noninvasively screen intracranial and extracranial vasculature for stenoses and occlusions. Preliminary data suggest that CTA effectively detects large-vessel intracranial occlusions when compared with ultrasound and DSA; however, because it provides a static image of vascular anatomy, it is inferior to DSA for demonstrating flow rates and direction [16; 178]. Although CTA is fast and can be adapted to conventional CT, contrast medium is required and patients are exposed to additional radiation [16]. The 2019 AHA/ASA guideline recommends the use of CTA with computed tomographic perfusion (CTP) or MRA for selecting candidates for mechanical thrombectomy between 6 and 24 hours after last known well time [16].

Transcranial Doppler (TCD) ultrasonography has been used to detect intracranial vessel abnormalities and to evaluate occlusions and stenoses in intracranial vessels. It is less accurate than CTA or MRA for steno-occlusive disease but can detect microembolic signals that indicate extracranial or cardiac sources of embolism [152]. TCD has been shown to predict and enhance outcomes with intravenous rt-PA [179].

Because the time between the onset of stroke and treatment should be limited, catheter angiography is not recommended by the AHA for the diagnosis of a suspected stroke [152]. In the case of a stroke, the utility of the imaging tool increases after a diagnosis has been made. As with transcranial Doppler ultrasonography, cerebral angiography is particularly useful for confirming the diagnosis, monitoring the progression of thrombolytic therapy, and assisting with the prognosis, particularly during the first 72 hours after a stroke [152].

IMAGING STUDIES

High diagnostic accuracy of stroke and treatment decisions is optimized by the use of imaging tools such as CT and MRI. Collectively, these neuroimaging options provide detailed information that influences stroke treatment decisions, including infarct age, severity, and distribution; intracranial vascular status; cerebral hemodynamics; estimated reversibility of ischemic damage; and hemorrhage type and distribution [16]. For instance, a widespread distribution of early infarction or edema increases hemorrhagic transformation risk following thrombolytic therapy. CT without contrast medium is readily sensitive to these conditions [16].

For prompt and accurate diagnosis, the use of noncontrast CT or DW-MRI is recommended for suspected stroke [16]. Although noncontrast CT is less expensive, faster, and more widely available, DW-MRI more readily detects small cortical, small subcortical, and posterior fossa infarcts and distinguishes chronic ischemia from acute ischemia. MRI is also sensitive to subclinical satellite ischemic lesions that characterize the pathophysiology of the stroke [152; 180]. As stated, DW-MRI can detect acute ischemic changes within minutes after the onset of stroke; CT may not detect ischemic stroke until up to 1 hour after the event [16]. However, not all patients with suspected stroke may benefit from MRI. Contraindications for MRI include claustrophobia, pacemakers, and metal implants.

If a patient is eligible for rt-PA, the AHA/ASA recommend that treatment be initiated as quickly as possible and not delayed for additional multimodal imaging (e.g., CT, MRI). Multimodal CT and MRI are not necessary when the diagnosis of ischemic stroke is very likely and their performance may delay time-sensitive administration of rt-PA. In cases of substantial diagnostic uncertainty, advanced imaging may be beneficial [16].

Although CT and MRI are increasingly available in EDs, the AHA/ASA state that noncontrast computed tomography (NCCT) is sufficient to identify contraindications to fibrinolysis and to ensure that patients with ischemic stroke receive timely intravenous fibrinolytic therapy. The AHA recommends that NCCT be obtained within 25 minutes after the patient's arrival in the ED [152].

TREATMENT

Because strokes are highly heterogeneous, are associated with multiple medical complications, and are time-critical, their effective management depends on organized and comprehensive care. Such treatment is optimally provided in comprehensive stroke centers and stroke systems of care. In 2007, the AHA/ASA published evidence-based guidelines to provide recommendations for treatment. These guidelines were updated in 2013 and again in 2019 [16; 152].

STROKE SYSTEMS OF CARE AND COMPREHENSIVE STROKE CENTERS

Comprehensive stroke centers are designed to accommodate the needs of patients with complicated forms of stroke, intracranial hemorrhages, and subarachnoid hemorrhages, as well as patients in need of aggressive intervention measures and intensive care [19]. In general, primary and comprehensive stroke centers have been shown to be associated with better adherence to evidence-based guidelines and with an increased use of intravenous rt-PA [181]. Nationally, only 2% to 3% of individuals with stroke are treated with rt-PA, but the rate is typically greater than 10% at primary and comprehensive stroke care centers [19; 138]. Overall care may also be improved at comprehensive stroke centers [181; 182]. A formal certification process for comprehensive stroke centers has been established by the Joint Commission and the ASA. The Joint Commission has been certifying primary stroke centers since 2004, and it began providing certification for comprehensive stroke centers in 2014 [16]. Because patients are more likely to receive thrombolytic therapy at primary and comprehensive stroke centers, many states have enacted policies mandating the direct routing of individuals with suspected stroke (with onset of symptoms less than 3 hours previously) to either of these types of facilities. As of 2015, 1,505 of the 4,640 general hospitals and emergency rooms in the United States have been certified as primary stroke centers [183]. Seventy-four percent of the primary stroke centers have been certified by the Joint Commission and the AHA/ASA, 20% have been certified by state organizations, and 6% have been certified by other organizations. The highest proportion of primary stroke center certifications has occurred in the Northeastern United States [183]. Telemedicine for stroke (also called telestroke) and air transport are being increasingly used to serve individuals in rural areas that lack local stroke expertise [16; 182].

Stroke centers are commonly part of a comprehensive support network known as a stroke system of care [16]. The system seeks ways to coordinate the highest quality of stroke prevention, community education, EMS, acute care, and post-acute care. Without a system of care, these components often operate less effectively and in isolation. Implementation of a stroke system of care in underserved regions could substantially improve treatment statistics statewide or nationwide; for example, one study showed that the additional resources at as few as six target hospitals in the western part of North Carolina would increase patient access to stroke care by 61.5% throughout the state [184].

Guidelines for establishing a stroke system of care were developed by an ASA Task Force [20]. Because of the multidisciplinary aspects of a stroke system, Task Force members were experts in areas of stroke prevention, EMS, acute stroke care, rehabilitation, and healthcare policy. Overall, the recommendations promote the communication and collaboration of patients, clinicians, facilities, and agencies. General ASA recommendations for stroke systems of care are [20]:

- Support local/regional educational initiatives designed to increase stroke awareness among the general population, with enriched targeting of populations at increased risk of stroke and poor post-stroke outcomes.
- Design/implement innovative behavioral interventions that address barriers to healthy behaviors and prevention adherence.
- Design/implement public education programs that are repetitive, designed to reach diverse populations, and focused on stroke systems and the need to urgently seek emergency care (by calling 911).
- Develop triage protocols that ensure all patients with known or suspected stroke are rapidly identified and assessed with validated stroke screening instrument.
- All stroke center certification systems should meet or exceed the standards set by nationally certified stroke centers and should work regionally in an integrated way to provide and share best practices.
- Adopt approaches to secondary prevention that address all major modifiable risk factors and are consistent with national guidelines for patients with a history or suspected history of stroke or TIA.
- Standardize postacute care and discharge. Trained stroke nurses, nurse practitioners, social workers, community health workers, and others play a critical role in this process.
- Advance the use of technology and patient-reported outcomes to facilitate improvements in stroke care transitions.
- Enact federal-level policies that standardize the organization of stroke care throughout the continuum.

EVIDENCE-BASED GUIDELINES

Thrombolytic therapy with rt-PA is the only treatment approved by the U.S. Food and Drug Administration (FDA) for ischemic stroke [16]. Anticoagulant and antiplatelet agents are also used, but their appropriateness is a source of debate and ongoing research. Intra-arterial rt-PA may be beneficial for select patients; however, the drug is not FDA approved for this use [18]. Mechanical thrombectomy is a consideration as both a primary reperfusion strategy and in conjunction with pharmacologic fibrinolysis [16].

The AHA/ASA recommendations for the treatment of ischemic stroke are based on an exhaustive review of available studies and emphasize the importance of early management [16; 18]. Since publication of the 2013 guidelines, substantial new high-quality evidence on the clinical efficacy of endovascular treatments has become available. This new evidence is the basis of the AHA/ASA 2015 focused update to the 2013 guidelines and is included, where appropriate, in the recommendations that follow [18].

Recombinant Tissue Plasminogen Activator (rt-PA)

The intravenous administration of rt-PA has been FDA-approved for the treatment of stroke since 1996. Rapid administration of rt-PA to appropriate patients remains the mainstay of early treatment of acute ischemic stroke [18]. Treatment with rt-PA is highly effective if administered within 3 hours. The earlier treatment is initiated, the higher the probability of a full recovery. Treatment within 90 minutes has been associated with a higher rate of favorable outcome at 3 months compared with treatment administered within 180 minutes [185].

For patients who meet national and international eligibility guidelines, intravenous rt-PA improves functional outcomes at 3 to 6 months when given within 4.5 hours after ischemic stroke onset and should be administered [18]. However, the therapeutic window may extend to 6 hours [186; 187]. Studies to determine the threshold of rt-PA benefits are ongoing. The AHA/ASA recommend that health systems set a goal of increasing their percentage of stroke patients treated within 60 minutes of presenting to hospital (i.e., door-to-needle time of 60 minutes) to at least 80% [152].

EVIDENCE-BASED PRACTICE RECOMMENDATION

With a goal to improve functional outcomes, the American College of Emergency Physicians recommends that intravenous tPA should be offered and may be given to selected patients with acute ischemic stroke within three hours after symptom onset at institutions where systems are in place to safely administer the medication. The increased risk of symptomatic intracerebral hemorrhage should be considered when deciding whether to administer tPA.

(https://www.acep.org/globalassets/new-pdfs/clinical-policies/tpa-for-stroke_new.pdf. Last accessed March 11, 2020.)

Strength of Recommendation: B (Recommendation based on moderate clinical certainty)

The AHA/ASA have changed some of their recommendations regarding rt-PA treatment since their 2013 guidelines (***Table 13***) [16]. Administration of rt-PA is not recommended for patients who have a systolic blood pressure greater than 185 mm Hg or a diastolic blood pressure greater than 110 mm Hg [16].

Between 31% and 50% of patients treated with rt-PA have a 4-point or greater improvement on the NIHSS by 3 months after the stroke [152]. These clinical improvements do not recede for at least 1 year after the stroke. In general, the best response to rt-PA has been found for patients who are younger than 75 years of age, with a baseline NIHSS score of less than 20, and no history of diabetes or pre-existing disability [152].

The most common serious medical complication of rt-PA is secondary brain hemorrhage, which occurs in 6% of patients [188]. Yet, the risk does not outweigh the benefits of rt-PA. Three months following rt-PA therapy, approximately 30% of patients are neurologically normal or near normal; 30% have mild-to-moderate neurologic deficits; 20% have moderate-to-severe deficits; and 20% have died [189]. Other dangerous complications of rt-PA, although rare, are angioedema, anaphylaxis, systemic hemorrhage, and, if rt-PA is administered soon after an acute MI, myocardial rupture [16; 190].

Anticoagulants

The AHA/ASA Task Force reviewed and discussed several studies addressing the use of heparin or low-molecular-weight heparin (LMWH) as an adjunct to a thrombolytic agent in the treatment of stroke [16]. In general, the Task Force concluded that early administration of heparin or LMWH is inadvisable partly due to the increased risk of bleeding complications, especially the hemorrhagic transformation of ischemic strokes. Additionally, early administration has not been shown to prevent recurrent stroke, lessen the risk of neurologic worsening, or improve patient outcome [16].

Antiplatelets

Although no new data regarding antiplatelet treatment have emerged since the 2003 version of the AHA/ASA guideline for ischemic stroke management, the AHA/ASA recommendations for antiplatelet therapy have changed (***Table 14***) [16]. Data combined from two large clinical trials suggest that administration of aspirin (325 mg) within 48 hours after the onset of stroke slightly reduces mortality and morbidity by preventing early recurrent stroke in some patients [191; 192].

AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION RECOMMENDATIONS FOR THROMBOLYTIC THERAPY
Class I Recommendations
In patients eligible for IV rt-PA, benefit of therapy is time dependent; treatment should be initiated as quickly as possible (*Class I, Level of Evidence A*).
Intravenous rt-PA (0.9 mg/kg, maximum dose 90 mg) is recommended for selected patients who may be treated within 3 hours of onset of ischemic stroke (*Class I, Level of Evidence A*). Physicians should review the criteria outlined in the AHA/ASA guidelines to determine the eligibility of patients.
Intravenous rt-PA (0.9 mg/kg, maximum dose 90 mg) is recommended for administration to eligible patients who can be treated in the time period of 3 to 4.5 hours after stroke onset (*Class I, Level of Evidence B*). Physicians should review the criteria outlined in the AHA guidelines to determine the eligibility of patients.
Intravenous rt-PA is recommended for eligible patients with mild but disabling stroke systems who may be treated within 3 hours of onset of stroke symptoms (*Class I, Level of Evidence B*).
Intravenous rt-PA is reasonable in patients whose blood pressure can be lowered safely (to less than 185/110 mm Hg) with antihypertensive agents, with the physician assessing the stability of the blood pressure before starting intravenous rt-PA. Blood pressure should be maintained at <180/105 mm Hg for at least the first 24 hours (*Class I, Level of Evidence B*).
In addition to bleeding complications, physicians should be aware of the potential side effect of angioedema that may cause partial airway obstruction (*Class I, Level of Evidence B*).
Class II Recommendations
Intravenous rt-PA (0.9 mg/kg, maximum dose 90 mg) administered within 4.5 hours of stroke symptom recognition may be beneficial in patients who awake with stroke symptoms or have unclear time of onset >4.5 hours (*Class II, Level of Evidence B*).
Intravenous rt-PA may be beneficial for adults presenting with acute ischemic stroke with known sickle cell disease (*Class IIa, Level of Evidence B*).
Intravenous rt-PA may be beneficial in patients with a hyperdense MCA sign (*Class IIa, Level of Evidence B*).
Intravenous rt-PA administration should not be delayed while waiting for hematologic or coagulation testing, if no abnormal test results are expected (*Class IIa, Level of Evidence B*).
Administration of IV rt-PA is reasonable in otherwise eligible patients who have previously had a small number (1 to 10) of CMBs demonstrated on MRI (*Class IIa, Level of Evidence B*).
In otherwise eligible patients who have previously had a high burden of CMBs (>10) demonstrated on MRI, treatment with IV rt-PA may be associated with an increased risk of sICH, and the benefits of treatment are uncertain. Treatment may be reasonable if there is the potential for substantial benefit (*Class IIb, Level of Evidence B*).
The risk of antithrombotic therapy (other than intravenous aspirin) within the first 24 hours after treatment with IV rt-PA (with or without mechanical thrombectomy) is uncertain. Use might be considered in the presence of concomitant conditions for which such treatment given in the absence of IV rt-PA is known to provide substantial benefit or withholding such treatment is known to cause substantial risk (*Class IIb, Level of Evidence B*).
It may be reasonable to choose tenecteplase (single IV bolus of 0.25 mg/kg, maximum 25 mg) over IV rt-PA in patients without contraindications for IV fibrinolysis who also are eligible to undergo mechanical thrombectomy (*Class IIb, Level of Evidence B*).
Tenecteplase (0.4 mg/kg single IV bolus) might be considered as an alternative to IV rt-PA in patients with minor neurologic impairment and no major intracranial occlusion (*Class IIb, Level of Evidence B*).
Intravenous rt-PA may be reasonable for patients who can be treated within 3 to 4.5 hours of stroke symptom of onset (*Class IIb, Level of Evidence B*).
The usefulness of IV administration of the glycoprotein IIb/IIIa inhibitors tirofiban and eptifibatide coadministered with intravenous rt-PA is not well established (*Class IIb, Level of Evidence B*).

Table 13 continues on next page.

AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION RECOMMENDATIONS FOR THROMBOLYTIC THERAPY *(Continued)*
Class III Recommendations
Intravenous rt-PA is not recommended for patients who could be treated within 3 hours of stroke symptom onset (*Class III, Level of Evidence B)*. This applies to otherwise eligible patients with mild nondisabling stroke symptoms (NIHSS score 0–5).
Do not administer abciximab concurrently with IV rt-PA (*Class III, Level of Evidence B*).
Do not administer IV aspirin within 90 minutes of initiation of IV rt-PA (*Class III, Level of Evidence B*).
Intravenous rt-PA is not indicated for nonvascular conditions (*Class III, Level of Evidence B*). Clinicians should be aware that hypoglycemia and hyperglycemia may mimic acute stroke and should determine blood glucose levels prior to initiation of IV rt-PA.
Do not administer IV rt-PA to patients who have received a full treatment dose of LMWH within the previous 24 hours (*Class III, Level of Evidence B*).
Intravenous rt-PA is not recommended for patients who could be treated within 3 to 4.5 hours of stroke symptom onset (*Class III, Level of Evidence C*). Applies to otherwise eligible patients with mild nondisabling stroke symptoms (NIHSS score 0–5).
Do not delay treatment with IV rt-PA to monitor improvement (*Class III, Level of Evidence C*).
MCA=middle cerebral artery; CMB=cerebral microbleed; MRI=magnetic resonance imaging; sICH=symptomatic intracerebral hemorrhage.
Source: [16] *Table 13*

AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION RECOMMENDATIONS REGARDING ANTIPLATELET TREATMENT FOR ISCHEMIC STROKE
Class I Recommendations
The oral administration of aspirin (initial dose is 325 mg) within 24 to 48 hours after stroke onset is recommended for treatment of most patients (*Class I, Level of Evidence A*). For patients treated with IV rt-PA, aspirin administration is generally delayed 24 hours.
In patients presenting with minor noncardioembolic ischemic stroke (NIHSS score ≤3) who did not receive IV rt-PA, treatment with dual antiplatelet therapy (aspirin/clopidogrel) started within 24 hours after symptom onset and continued for 21 days is effective in reducing recurrent ischemic stroke for a period of up to 90 days from symptom onset (*Class I, Level of Evidence A*).
Class II Recommendations
The efficacy of intravenous tirofiban and eptifibatide is not well established (*Class IIb, Level of Evidence B*). Further trials are necessary to clarify the safety and efficacy of this intervention.
Class III Recommendations
Ticagrelor is not recommended over aspirin for treatment of patients with minor stroke (*Class III, Level of Evidence B*). Ticagrelor may be a reasonable alternative in stroke patients with a contraindication to aspirin.
The administration of abciximab as medical treatment for acute ischemic stroke is potentially harmful and should not be performed (*Class III, Level of Evidence B*).
Aspirin is not recommended as a substitute for other acute interventions for treatment of stroke, including the intravenous administration of rt-PA (*Class III, Level of Evidence B*).
Source: [16] *Table 14*

The findings of these trials do not suggest the use of aspirin within 24 hours of thrombolytic administration or as a substitute for thrombolytic therapy. A 2014 Cochrane review confirmed the results of these trials [193]. A review that summarized the results of nine randomized controlled trials also confirmed these findings and demonstrated increased odds of complete recovery [194]. Other oral antiplatelet therapies (e.g., ticagrelor, clopidogrel, dipyridamole) are being studied in the setting of acute ischemic stroke [195].

Ticagrelor is a reversible, short-acting P2Y12 agonist. The Acute Stroke or Transient Ischemic Attack Treated With Aspirin or Ticagrelor and Patient Outcomes (SOCRATES) trial tested the efficacy of ticagrelor (18-mg loading dose, then 90 mg twice daily) to aspirin in 13,199 patients with acute ischemic stroke or high-risk TIA [196]. The primary outcome (i.e., time to stroke occurrence, MI, or death within 90 days) occurred in 6.7% of patients treated with ticagrelor versus 7.5% treated with aspirin. Ischemic stroke occurred in 5.8% in the ticagrelor arm versus 6.7% in the aspirin arm. There were no differences in major bleeding, intracranial hemorrhage, or fatal bleeding. A subgroup analysis of the SOCRATES trial found that ticagrelor was effective at preventing the primary outcome in patients with a background history of aspirin use [197]. Ticagrelor versus placebo was the subject of the THALES (Acute Stroke or Transient Ischemic Attack Treated with Ticagrelor and ASA for Prevention of Stroke and Death) trial, which was completed in December 2019. As of 2020, the results have not yet been published [198].

EVIDENCE-BASED PRACTICE RECOMMENDATION

In patients with acute ischemic stroke or transient ischemic attack, the American College of Chest Physicians recommends early (within 48 hours) aspirin therapy at a dose of 160–325 mg.

(https://journal.chestnet.org/issue/S0012-3692(12)X6003-3. Last accessed March 11, 2020.)

Strength of Recommendation/Level of Evidence: 1A (Strong recommendation, high-quality evidence)

Several trials have examined the efficacy of clopidogrel plus low-dose aspirin [199; 200; 201; 202; 203; 204]. While the data from two of these trials suggest a benefit from dual antiplatelet therapy (i.e., clopidogrel/aspirin), the results of the other trials suggest a lack of benefit and possibly harm in the longer term. The combination dipyridamole plus aspirin for ischemic stroke management has been studied in several trials involving more than 17,000 patients [205; 206; 207; 208; 209; 210]. The combination was found to be an acceptable antiplatelet therapy for patients with ischemic stroke or TIA and probably superior to aspirin alone. However, twice-daily dosing and headache cause many patients to discontinue the regimen [207; 208; 209; 210].

The efficacy of intravenous glycoprotein IIb/IIIa receptor blockers (GP IIb/IIIa inhibitors), such as abciximab, in combination with other interventions or alone is under investigation. Preliminary results from the Abciximab in Emergent Stroke Treatment Trial (AbESTT) indicate that intravenous GP IIb/IIIa inhibitors may accelerate spontaneous recanalization, improve microvascular patency, and offer an adequate safety profile [211; 212]. However, a systematic review of GP IIb/IIIa inhibitors as well as results of the AbESTT-II (a phase III trial of abciximab) did not demonstrate either safety or efficacy of the drug for treatment of acute ischemic stroke and found an increased rate of symptomatic or fatal intracranial hemorrhage, with no reduction in death or disability in survivors [213; 214]. The 2019 AHA/ASA guideline contains both revised and new recommendations regarding the use of IV GP IIb/IIIa inhibitors, including abciximab (***Table 14***) [16].

Angioplasty and Stenting

Although emergent angioplasty and stenting are high-risk procedures, progressing strokes, which occur when patients' moderate neurologic deficits deteriorate significantly within 72 hours after onset, are associated with very poor outcomes and high mortality rates [215]. Therefore, some case studies suggest that emergency angioplasty followed by immediate or delayed stenting is appropriate for

patients with a progressing stroke caused by carotid artery occlusion or stenosis, respectively [216; 217]. However, the safety and efficacy of emergency carotid artery stenting are not established, and the procedure remains controversial [218; 219].

Angioplasty and stenting may be appropriate for patients with acute stroke secondary to carotid artery dissection [220; 221]. In one study, emergency angioplasty and stenting of the internal carotid artery performed in conjunction with intra-arterial thrombolysis was associated with more favorable outcomes than pharmacologic treatment alone in patients with acute carotid artery occlusion and secondary artery-to-artery embolism to the middle cerebral artery [222]. In a larger study by the same group of investigators, treatment with urokinase followed by angioplasty and stenting increased recanalization [223]. Another study found that angioplasty and stenting of the proximal occlusion and stent-based thrombectomy of the intracranial occlusion may be feasible, effective, and safe in selected patients with acute internal carotid artery occlusion and concomitant major vessel embolic stroke [221].

The AHA/ASA assert that the use of angioplasty and intra-arterial thrombolytics in the emergency management of stroke should be limited to comprehensive stroke centers, which have the resources and physician expertise to perform them safely, and in the setting of clinical trials [18].

In addition to use in emergent angioplasty and stenting, mechanical thrombectomy is both a primary reperfusion strategy and an adjunct to pharmacologic fibrinolysis for achieving recanalization in patients with acute ischemic stroke [16]. Mechanical treatments include the use of catheters during angiography to directly deliver either a clot-disrupting or retrieval device to an artery-occluding thromboembolus [224].

The primary advantage of mechanical devices is their ability to remove a clot in a matter of minutes, compared with pharmacologic thrombolytics (even those delivered intra-arterially) that may take as long as two hours to dissolve the clot [225; 226].

A second advantage is that newer devices (e.g., retrievable stents) have shown higher recanalization rates and better outcomes than those seen with older devices (e.g., the Merci Retriever) [224]. The primary disadvantage of endovascular therapy is the delay in initiation of treatment because of the time required to mobilize the interventional team and, in many cases, the need to transfer the patient to another hospital [227; 228]. In the absence of sufficient trial data, it had been uncertain whether endovascular therapy, with or without the previous use of intravenous rt-PA, would be more effective than intravenous rt-PA alone [229]. However, newer trials (i.e., MR CLEAN, EXTEND-IA, ESCAPE, and SWIFT-PRIME) have demonstrated the efficacy of endovascular therapy using the newer, retrievable stents [230; 231; 232].

In addition to reviewing the results of these four trials, the AHA/ASA also reviewed the results of the REVASCAT trial [18; 233]. Of the five stent retriever trials, MR CLEAN, ESCAPE, and SWIFT-PRIME permitted use of salvage intra-arterial fibrinolytic drugs, whereas EXTEND-IA and REVASCAT did not [18]. Every or nearly every patient in the trials first received intravenous rt-PA. All five studies enrolled participants 18 years of age and older. Four of the trials used NIHSS scores (>2, >5, and 8–29) as eligibility criteria, and the fifth trial enrolled patients with a similar distribution of NIHSS scores. Four of the five trials used a prestroke function eligibility criterion. All five trials required baseline nonenhanced CT or MRI and used different strategies of an imaging-based selection criterion in addition to nonenhanced CT or MRI. The overwhelming majority of patients in the trials had ICA or proximal MCA (M1) occlusion. All five trials allowed the inclusion of patients with proximal cervical carotid stenosis, and all but one trial (SWIFT-PRIME) allowed the inclusion of patients with complete atherosclerotic cervical carotid occlusion. General anesthesia and conscious sedation were the two most frequently used anesthetic approaches for patients with acute ischemic stroke receiving endovascular therapy. None of the trials established the usefulness of mechanical thrombectomy devices other than stent retrievers [18].

AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION RECOMMENDATIONS REGARDING ENDOVASCULAR INTERVENTIONS FOR ISCHEMIC STROKE

Class I Recommendations

Eligible patients should receive intravenous rt-PA even if endovascular treatments are being considered (*Class I, Level of Evidence A*).

Patients should receive endovascular therapy with a stent receiver if they meet all the following criteria (*Class I, Level of Evidence A*):

- Prestroke mRS score 0 to 1
- Acute ischemic stroke receiving intravenous rt-PA within 4.5 hours of onset according to guidelines from medical societies
- Causative occlusion of the internal carotid artery or proximal MCA (M1)
- Age ≥18 years
- NIHSS score of ≥6
- ASPECTS of ≥6
- Treatment can be initiated (groin puncture) within 6 hours of symptom onset

As with intravenous rt-PA, reduced time from symptom onset to reperfusion with endovascular therapies is highly associated with better clinical outcomes. To ensure benefit, reperfusion to TICI grade 2b/3 should be achieved as early as possible and within 6 hours of stroke onset (*Class I, Level of Evidence B*).

Use of stent retrievers is indicated in preference to the MERCI device (*Class I, Level of Evidence A*).

The technical goal of the thrombectomy procedure should be a TICI 2b/3 angiographic result to maximize the probability of a good functional clinical outcome (*Class I, Level of Evidence A*).

Initial treatment with intra-arterial fibrinolysis is beneficial for carefully selected patients with major ischemic strokes of less than 6 hours' duration caused by occlusions of the MCA (*Class I, Level of Evidence B*). However, these data derive from clinical trials that no longer reflect current practice, including use of fibrinolytic drugs that are not available. A clinically beneficial dose of intra-arterial rt-PA is not established, and rt-PA does not have FDA approval for intra-arterial use. As a consequence, endovascular therapy with stent retrievers is recommended over intra-arterial fibrinolysis of first-line therapy (*Class I, Level of Evidence E*).

Class II Recommendations

When treatment is initiated beyond 6 hours from symptom onset, the effectiveness of endovascular therapy is uncertain for patients with acute ischemic stroke who have causative occlusion of the internal carotid artery or proximal MCA (*Class IIb, Level of Evidence C*). Additional randomized trial data are needed.

In carefully selected patients with anterior circulation occlusion who have contraindications to intravenous rt-PA, endovascular therapy with stent retrievers completed within 6 hours of stroke onset is reasonable (*Class IIa, Level of Evidence C*). There are inadequate data at this time to determine the clinical efficacy of endovascular therapy with stent retrievers for patients whose contraindications are time-based or nontime based (e.g., prior stroke, serious head trauma, hemorrhagic coagulopathy, or receiving anticoagulant medications).

Although the benefits are uncertain, use of endovascular therapy with stent retrievers may be reasonable for carefully selected patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the M2 or M3 portion of the MCAs, anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries (*Class IIb, Level of Evidence C*).

Although the benefits are not established in this age group, endovascular therapy with stent retrievers may be reasonable for some patients <18 years of age with acute ischemic stroke who have demonstrated large vessel occlusion in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset (*Class IIb, Level of Evidence C*).

Although the benefits are uncertain, use of endovascular therapy with stent retrievers may be reasonable for patients with acute ischemic stroke in whom treatment can be initiated within 6 hours of symptom onset and who have prestrike mRS score of >1, ASPECTS <6, or NIHSS score <6 and causative occlusion of the internal carotid artery or proximal MCA (M1) (*Class IIb, Level of Evidence B*).

The use of mechanical thrombectomy devices other than stent retrievers may be reasonable in some circumstances (*Class IIb, Level of Evidence B*).

The use of a proximal balloon guide catheter or a large bore distal access catheter rather than a cervical guide catheter alone in conjunction with stent retrievers may be beneficial (*Class IIa, Level of Evidence C*). Future studies should examine which systems provide the highest recanalization rates with the lowest risk for nontarget embolization.

Use of salvage technical adjuncts, including intra-arterial fibrinolysis, may be reasonable to achieve these angiographic results, if completed within 6 hours of symptom onset (*Class IIb, Level of Evidence B*).

Angioplasty and stenting of proximal cervical atherosclerotic stenosis or complete occlusion at the time of thrombectomy may be considered, but the usefulness is unknown (*Class IIb, Level of Evidence C*). Future randomized studies are needed.

Intra-arterial fibrinolysis initiated within 6 hours of stroke onset in carefully selected patients who have contraindications to the use of intravenous rt-PA might be considered, but the consequences are unknown (*Class IIb, Level of Evidence C*).

It might be reasonable to favor conscious sedation over general anesthesia during endovascular therapy for acute ischemic stroke. However, the ultimate selection of anesthetic technique during endovascular therapy for acute ischemic stroke should be individualized based on patient risk factors, tolerance of the procedure, and other clinical characteristics. Randomized trial data are needed (*Class IIb, Level of Evidence C*).

Table 15 continues on next page.

AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION RECOMMENDATIONS REGARDING ENDOVASCULAR INTERVENTIONS FOR ISCHEMIC STROKE (*Continued*)
Class III Recommendations
Observing patients after intravenous rt-PA to assess for clinical response before pursuing endovascular therapy is not required to achieve beneficial outcomes and is not recommended (*Class III, Level of Evidence B*).
Source: [18] *Table 15*

RECOMMENDATIONS RATING SCHEME	
Class/Level	**Definition**
Classification of Interventions	
I	Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful, effective, and beneficial
IIa	Conditions for which there is evidence for and/or general agreement that the procedure or treatment may be useful, effective, and beneficial
IIb	Usefulness/efficacy is less well established by evidence or opinion
III	Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful
Level of Evidence	
A	Data derived from high-quality multiple randomized clinical trials or meta-analyses of high-quality randomized clinical trials
B	Data derived from a single randomized trial or nonrandomized studies
C	Randomized or nonrandomized observational or registry studies of limited design or execution or meta-analyses of such studies
E	Consensus opinion of experts

The AHA/ASA analysis of and conclusions about these five stent retriever trials form the basis of their 2015 focused update to the guidelines on the management of patients with acute ischemic stroke (***Table 15***) [18].

Carotid Endarterectomy

In the setting of acute ischemic stroke, justification for emergent (within the first 24 hours) or early revascularization with carotid endarterectomy (CEA) is based on reports of increased risk of recurrent stroke in patients undergoing medical therapy while awaiting revascularization. Some studies have found that CEA is most beneficial when performed within 2 weeks of the last cerebrovascular symptom and that the benefits decline rapidly after 3 weeks [194; 234]. However, the risk associated with emergency CEA is believed to be high, for several reasons, particularly in patients with an unstable neurologic status [235]. First, embolic and hemodynamic injuries can occur [236]. Second, detection of an arterial lesion and mobilization of an operating room staff is time-intensive. Lastly, hyperperfusion, which occurs in 0.3% to 1.2% of patients who have CEA, can lead to brain edema and hemorrhagic transformation [236]. Other complications may also develop.

For some patients, however, the benefit of CEA may outweigh the risk. For instance, patients with acute ischemic stroke who have already had previous CEA may be successfully treated with surgical revascularization. Some studies indicate that early CEA may also be appropriate for patients with small, nondisabling stroke in whom the goal is to reduce ongoing thromboembolism or flow-limiting ischemia [235; 237; 238; 239; 240; 241]. Results of other small studies have suggested that administration of an anticoagulant and delaying surgery until after the patient is stabilized is a better option [242]. Due to the limited and conflicting data, high perceived risk, and unestablished usefulness, the AHA/ASA have a Class II, Level of Evidence B recommendation regarding the use of carotid endarterectomy for treatment of acute ischemic stroke [16].

REHABILITATION

More than two-thirds of stroke survivors receive rehabilitation services after hospitalization, yet only a minority receive thrombolytic therapy and many have residual functional deficits, despite the development of designated stroke centers and improvements in stroke recognition and care delivery [21]. Effective stroke rehabilitation is likely to continue to be an essential component of the continuum of stroke care for the foreseeable future. Thus, in 2016 the AHA/ASA published a guideline for stroke rehabilitation and recovery [21]. This guideline spans the entire course of rehabilitation, from the early actions taken in the acute care hospital through the patient's reintegration into the community. The guideline uses the framework (rating scheme) established by the AHA concerning classes and levels of evidence [21].

The likelihood of functional independence and survival is enhanced by organized multidisciplinary rehabilitation; five more patients for every 100 treated are able to live independently with such rehabilitation [243]. Early initiation of rehabilitation is a particularly strong predictor of improved outcome [21; 244].

Rehabilitation in an inpatient stroke unit has been associated with better outcomes than rehabilitation in a general healthcare facility, with improved quality of life, survival, and functional status at 5 years [17; 21; 245; 246; 247; 248; 249]. Yet the decision to refer a stroke patient to a particular setting after discharge is dictated by a complex set of demographic, clinical, and nonclinical factors that are also inevitably related to patient outcomes [21]. Variations in outcomes for inpatient stroke rehabilitation have been found among racial/ethnic populations [21; 250; 251; 252; 253; 254]. Black individuals have less functional improvement at discharge compared with white individuals and are more likely to be discharged to home despite worse functional independence measure (FIM) scores [255]. Asian individuals have functional improvements similar to those for white individuals but have less improvement at 3 months after discharge [255]. These disparities point to the need for focused attention on appropriate rehabilitation services for minority populations.

MULTIDISCIPLINARY REHABILITATION TEAM

Because the effects of stroke are multifaceted and unique to each patient, multidisciplinary and organized services play an important role in patient recovery [21; 246]. Post-acute stroke care settings include specialized inpatient rehabilitation hospitals, stroke rehabilitation units in acute care hospitals, outpatient therapy clinics, long-term care facilities, and patients' homes. The findings of a systematic review showed that, of these settings, an inpatient specialized stroke unit is best for providing care due to the presence of skilled nursing services, physician care, and variety of therapies [256]. However, the rehabilitation needs of some patients with mild or no disabilities may be addressed effectively in an outpatient facility (e.g., all-day care at a hospital) or in their homes [21; 257]. For select patients, early discharge to a community setting for ongoing rehabilitation may provide outcomes similar to those achieved in an inpatient rehabilitation unit. This "early supported discharge" model links inpatient care with community-based rehabilitation services and allows some patients to return home sooner [21]. In some cases, recovery may occur without the need for rehabilitation services.

For inpatient and outpatient rehabilitative intervention, the multidisciplinary teams typically consist of several or all of the following: physicians, physical therapists, occupational therapists, kinesiotherapists, speech and language pathologists, social workers, recreational therapists, and nurses [21]. Nursing care for patients in the post-acute phase is particularly intensive. Patients who are triaged to inpatient facilities receive great benefit from 24-hour care by nurses who specialize in stroke care [257; 258].

AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION RECOMMENDATIONS FOR THE ORGANIZATION OF POST-STROKE REHABILITATION CARE (LEVELS OF CARE)
Class I Recommendations
Organized, coordinated, interprofessional care is recommended for stroke patients who are candidates for postacute rehabilitation (*Class I, Level of Evidence A*).
Stroke survivors who qualify for and have access to inpatient rehabilitation facility (IRF) care should receive treatment in an IRF in preference to a skilled nursing facility (SNF) (*Class I, Level of Evidence B*).
Organized community-based and coordinated interprofessional rehabilitation care is recommended in the outpatient or home-based settings (*Class I, Level of Evidence C*).
Class II Recommendations
Early supported discharge services may be reasonable for people with mild-to-moderate disability (*Class IIb, Level of Evidence B*).
Source: [21] *Table 16*

AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION RECOMMENDATIONS FOR REHABILITATION IN THE INPATIENT HOSPITAL SETTING
Class I Recommendations
Early rehabilitation for hospitalized stroke patients should be provided in environments with organized, interprofessional stroke care (*Class I, Level of Evidence A*).
Stroke survivors should receive rehabilitation at an intensity commensurate with anticipated benefit and tolerance (*Class I, Level of Evidence B*).
Class III Recommendations
High-dose, very early mobilization within 24 hours of stroke onset can reduce the odds of a favorable outcome at 3 months and is not recommended (*Class III, Level of Evidence A*).
Source: [21] *Table 17*

Depending on the patient's and family's/caregivers' specific needs, a clinical psychologist, psychiatrist, dietitian, and other healthcare professionals may join a patient's stroke rehabilitation team [21; 258]. However, a team's exact composition is less important in maximizing a patient's outcome than is early intervention and the use of a coordinated, interdisciplinary approach. Without communication and coordination, isolated efforts to rehabilitate the stroke survivor are unlikely to achieve their full potential [21].

The AHA/ASA recommendations for the organization of post-stroke rehabilitation care and interventions specific to the inpatient hospital setting are summarized in ***Table 16*** and ***Table 17*** [21].

Stroke is an acute and harrowing event, and the emotions and deficits that follow are usually overwhelming to the patient and the patient's family. The multidisciplinary rehabilitation team should therefore develop a treatment strategy to help individual patients based on a consensus model that incorporates family members and caregivers. Securing the family's/caregivers' active involvement early in the rehabilitation process optimizes the patient's chances for recovery and community reintegration [21; 259]. After the rehabilitation team has formulated a plan of action for the patient, a team liaison should present its recommendations to the patient and family/caregivers through open discussions [260]. Providing patients and families/caregivers with both interactive and written materials is equally important [260]. Information to be presented should include:

- Preferred setting and environment based on the patient's projected recovery
- Treatment options, including suggested rehabilitation programs, estimated length of stay, frequency of therapy, and discharge criteria
- Information regarding the patient's prognosis and the anticipated recovery process

Once rehabilitation has commenced, involving the patient's family/caregivers in the rehabilitation sessions and training them to assist the patient with functional activities may aid patient recuperation [21; 261]. During rehabilitation, at least one or two informal meetings per week should be held with family/caregivers to reassess their concerns about the process [262].

Social and Family Caregiver Support

As stated, the stroke survivor's family members and caregivers are integral to the post-stroke treatment plan [21]. However, 12% to 55% of caregivers suffer from emotional distress, most commonly depression [21; 263; 264]. Untreated depression is associated with a lower quality of life for both the caregiver and the stroke survivor [21; 265]. A growing body of research is focused on treatment strategies to benefit both the caregiver and the stroke survivor and on educational programs that target issues such as supportive problem solving, physical care needs, financial and domestic assistance, respite, reassurance, and counseling [21; 266; 267; 268; 269; 270].

PATIENT ASSESSMENT

For individuals who have had a stroke and are medically stable, rehabilitation assessment, prevention of medical complications, and secondary prevention become the focal points [10; 16; 21]. To begin, the rehabilitation team's systematic evaluation of the patient addresses various issues, including the need for rehabilitation services; the risk of complications; physical functioning, cognition, and communication; and psychosocial conditions [21]. Next, the team works with the patient and family to implement a rehabilitation plan that includes a detailed exercise program and general as well as tailored strategies for secondary prevention [10]. Throughout, the team should strive to foster a climate of familial support [21].

Need for Rehabilitation Services

When a patient is medically stabilized, a rehabilitation physician is consulted to assess the patient's rehabilitative needs and recommend the proper rehabilitation setting (***Table 18***) [17]. Additionally, the patient's complete medical history is provided to the rehabilitation physician. If indicated, other rehabilitation specialists may perform specialized or more intensive assessments. Overall, rehabilitation assessments should be [21]:

- Multidisciplinary, to account for the heterogeneous effects of stroke.
- Well-coordinated and prompt, so patients can begin a rehabilitation program as soon as possible.
- Well-documented, to provide the patient's rehabilitation team with accurate and detailed information.
- Conducted using formal standardized, validated measures.

The NIHSS is a strong prognosticator of functional outcome, rendering it a valuable tool for determining rehabilitation needs [271; 272]. It is the most widely used global assessment of impairment in the United States. It is a good predictor of short- and long-term morbidity and mortality and has been found to be sensitive to change in numerous studies [21]. Multiple assessments with the scale provide the rehabilitation team with a sense of the patient's recovery trajectory as he or she enters the rehabilitation stage.

AREAS OF SPECIAL INTEREST FOR PURPOSES OF REHABILITATION ASSESSMENT
Risk factors for stroke recurrence
Medical comorbidities
Swallowing
Skin assessment and risk for pressure ulcers
Bowel and bladder function
Risk of deep vein thrombosis
Pain
Mobility, with respect to the patient's needs for assistance in movement
Safety awareness
Motor function
Cognition and communication status
Psychologic status
History of previous antiplatelet or anticoagulation use, especially at the time of the stroke
Psychosocial status
Source: [17] *Table 18*

The NIHSS provides detailed information in addition to an overall stroke severity score. A score of less than 5 indicates minor or no functional disability, whereas a score of more than 16 suggests severe disability and an increased probability of death [273]. With the advent of stroke treatment, patients with a score of 5 to 15 are likely to benefit from rehabilitation without the need for a nursing facility [274]. Patients with a score of more than 15 may improve with rehabilitation; however, these patients will likely require long-term care. More than one-half of survivors with a baseline score greater than 20 are initially sent to some form of rehabilitation facility rather than directly discharged to a nursing facility or home [274].

Because the type of stroke affects the usefulness of the NIHSS, its results should be qualified by medical history, examination, and brain imaging data [275]. Specifically, the scale is better suited for predicting functional outcomes at 3 and 6 months after stroke for patients with subcortical lesions than for patients with cortical lesions [21; 276; 277]. Additionally, the reliability of the scale in predicting depressive symptoms and cognitive dysfunctions depends on the hemisphere affected [21; 277]. Because the NIHSS does not include evaluation of weakness of the distal part of the upper extremity, which is common in patients with stroke, a finger extension evaluation should be conducted in addition to the scale [278; 279]. The presence of finger extension or partial shoulder abduction within 72 hours after stroke onset can help predict the patient's functional recovery at six months [280; 281].

Although new measurement tools are being developed, they are difficult to evaluate with the traditional criteria (e.g., validity, reliability) normally used in evidence-based reviews [21]. The AHA/ASA recommendations for the assessment of rehabilitation needs (***Table 19***) are based on traditional measurement models, such as the FIM [21].

Soon after patient assessment, family/caregivers should be educated about and referred to community resources [21; 282]. If it is recommended that the patient be discharged from an acute care facility to a nursing facility or the patient's home, relevant contact and background information for nursing home facilities, assisted-living services, social support groups, and stroke-related organizations should be provided to facilitate familial decision-making. Viable options should be presented to the family, especially information about long-term care placement if a severely disabled patient is not a candidate for rehabilitation [21].

AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION RECOMMENDATIONS FOR DISABILITY ASSESSMENT AND REHABILITATION NEEDS
Class I Recommendations
It is recommended that all individuals with stroke be provided a formal assessment of their ADLs and IADLs, communication abilities, and functional mobility before discharge from acute care hospitalization and the findings be incorporated into the care transition and the discharge planning process (*Class I, Level of Evidence B*).
It is recommended that all individuals with stroke discharged to independent community living from postacute rehabilitation or SNFs receive ADL and IADL assessment directly related to their discharge living setting (*Class I, Level of Evidence B*).
A functional assessment by a clinician with expertise in rehabilitation is recommended for patients with an acute stroke with residual functional deficits (*Class I, Level of Evidence C*).
Determination of postacute rehabilitation needs should be based on assessments of residual neurologic deficits; activity limitations; cognitive, communicative, and psychologic status; swallowing ability; determination of previous functional ability and medical comorbidities; level of family/caregiver support; capacity of family/caregiver to meet the care needs of the stroke survivor; likelihood of returning to community living; and ability to participate in rehabilitation (*Class I, Level of Evidence C*).
Class II Recommendations
It is reasonable that individuals with stroke discharged from acute and postacute hospitals/centers receive formal follow-up on their ADL and IADL status, communication abilities, and functional mobility within 30 days of discharge (*Class IIa, Level of Evidence B*).
The routine administration of standardized measures can be useful to document the severity of stroke and resulting disability, starting in the acute phase and progressing over the course of recovery and rehabilitation (*Class IIa, Level of Evidence C*).
A standardized measure of balance and gait speed (for those who can walk) may be considered for planning postacute rehabilitation care and for safety counseling with the patient and family (*Class IIb, Level of Evidence B*).
ADLs = activities of daily living, IADLs = instrumental activities of daily living (tasks involving more complex domestic, community, and leisure activities), SNF = skilled nursing facility.
Source: [21] *Table 19*

If the family/caregivers will be taking care of the patient at a private residence (with or without professional assistance), it is essential to foster discussions about the needs of the patient, challenges the patient and family/caregivers may face, and the benefits of social support programs for the patient and family/caregivers. Whenever possible, written materials should be provided, and they should be in the primary language of the family. Among the important topics to discuss and provide education about include [21]:

- Secondary prevention and medication administration specifics
- Nutrition and hydration
- Symptoms of complications
- Specifics regarding assistance with activities of daily living (e.g., transfers, positioning, bathing, toileting, dressing, and grooming)
- Swallowing difficulties
- Feeding tube use
- Bladder catheter care
- Signs of mood disorders
- Strategies to improve cognitive skills and communication
- Exercises (range of motion)

Education about and referral to appropriate community resources can help to support the needs and priorities of the patient and the family or caregiver [21]. A systematic review and meta-analysis demonstrated that functional outcomes (i.e., motor, cognitive, and psychosocial function) can be improved or, at a minimum, maintained in stroke survivors when community interventions are available [21; 283; 284].

The patient's psychosocial status will influence his or her willingness and approach to participating in a rehabilitation program. A psychosocial assessment enables the rehabilitation team to incorporate family/caregivers more effectively into the rehabilitation process [285]. In addition, how the team manages the patient's care may be contingent on the patient's life circumstances and personality profile. Some patients and their caregivers fail to discuss psychosocial issues with their providers [21; 264]. Cultural differences may also play a part in a patient's willingness to discuss these issues [21]. Areas of emphasis for the psychosocial assessment should include:

- Medical history
- Coping style
- Therapeutic style and recovery expectations
- Demographic information
- Response to treatment
- Substance use and abuse
- Psychiatric/psychologic evaluation
- Emotional and mental status and history
- Education and employment
- Spiritual and cultural beliefs
- Family/caregiver relationship
- Preferred activities

When designing and implementing the patient's treatment plan, the rehabilitation team should also take into account the residual effects of any difficulties the patient may have had before the stroke, such as drug or alcohol addiction; stress from recent life events, such as divorce, a loved one's death, or retirement; or clinical depression [21]. Individual patients will vary in how well they respond to challenging and demanding therapeutic approaches. After a patient's unique needs and circumstances are determined, relevant specialists will be incorporated into the team. All members of the rehabilitation team should be sensitive to the patient's psychosocial needs.

Risk of Complications

Medical complications related to illness, being bedridden, or lack of proper care/attention can prolong hospitalization, impede rehabilitation, increase disability, or result in death. Living in an inappropriate post-stroke environment also substantially increases a patient's risk for complications. Complications may develop in as many as 85% of hospitalized patients who have had a stroke [286]. Thus, medical examinations before and during a patient's rehabilitation program should assess the most common risks of complications: skin breakdown, deep vein thrombosis (DVT), swallowing dysfunction, bowel and bladder incontinence, falls, and pain [21].

Skin Breakdown and Contractures

Pressure ulcers are a commonly encountered complication in hospital and long-term care facilities, occurring in approximately 10% and 25% of patients in those settings, respectively [286]. According to the National Pressure Ulcer Advisory Panel, a pressure ulcer is a "localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear" [287; 288]. Although ulcers typically occur proximal to osseous prominences (e.g., the sacrum, hips, ankles), skin breakdown at the ears is also common in certain settings [289; 290]. Most pressure ulcers are

associated with deep tissue injury [291]. Regular assessment of skin and the use of objective risk scales (e.g., the Braden scale) may help prevent skin injury and should be followed by regular skin inspection with documentation [21; 292]. Risk factors for pressure ulcers include [286]:

- Immobility
- Poor hygiene
- Urinary incontinence and other sources of moisture
- Diabetes and other causes of poor circulation
- Peripheral vascular disease
- Lower body mass index
- Localized infection or trauma
- Edema
- Poor hydration and/or nutrition

Conditions secondary to pressure ulcers include pain, localized infection, cellulitis, osteomyelitis, sepsis, and even death [293; 294]. However, not all pressure ulcers, even those that are severe, will elicit a pain sensation [295].

Ulcers can be prevented or minimized with several measures, including proper positioning, turning, and transferring techniques; good hygiene; proper nutrition and hydration; and the use of barrier sprays, special mattresses, and protective dressings [21; 292]. Good pain management may be necessary to perform correct positioning and frequent turning. Patients should be monitored daily for skin breakdown [21]. Any sign of a pressure ulcer warrants daily treatment [21].

Following stroke with hemiparesis, contracture on the affected side will develop in approximately 60% of patients within the first year, with wrist contractures occurring most commonly in patients who do not recover functional hand use [21; 296; 297]. Contractures are painful and can make self-care difficult. Many clinicians recommend daily stretching of the affected limb(s); families and patients should be taught proper stretching technique [21]. The effectiveness of resting hand splints is not well established [21]. Contractures of the ankle/foot can affect gait quality and patient safety. Ankle-foot orthosis and the nighttime use of a resting ankle splint may be beneficial in preventing ankle contracture [21].

Deep Vein Thrombosis

DVT affects only 2% of patients with stroke; yet, its prevention is critical [286]. The American Academy of Family Physicians recommends that DVT risk be calculated with use of the Well's DVT prediction model, and the results of this model will dictate subsequent DVT testing (***Table 20***) [298; 299]. For patients with symptoms in both legs, the more symptomatic leg should be tested. A score of 3 or more on the Well's test indicates a high clinical probability of DVT; the probability is intermediate for a score of 1 or 2.

The D-dimer test alone is not recommended to rule out DVT in patients who have had a stroke. Patients with intermediate-to-high risk for DVT should be screened with use of ultrasonography. This imaging modality may not detect DVT in the calf, however, and repeat ultrasonography or venography should be used when DVT in the calf is suspected. Contrast venography was previously the most definitive test for the diagnosis of DVT, but today, Doppler ultrasound is the diagnostic study of choice [299].

Measures such as early mobilization and anticoagulation therapy are recommended to decrease the incidence of DVT after stroke. A patient's risk can be substantially reduced by 50-foot walks daily (with assistance, if necessary), administration of subcutaneous, low-dose unfractionated heparin (5,000 units twice a day, unless contraindicated), and the use of graduated compression stockings (GCS) as an adjunct to medication [300]. GCS and intermittent pneumatic compression may be considered for prevention of post-stroke DVT, but their routine prophylactic use requires further study. The benefit of treatment should be weighed against the increased risk of skin complications [21; 301; 302].

WELL'S PREDICTION RULE FOR DIAGNOSING DEEP VENOUS THROMBOSIS: CLINICAL EVALUATION TABLE FOR PREDICTING PRETEST PROBABILITY OF DEEP VEIN THROMBOSIS	
Clinical Characteristic	**Score**
Active cancer (treatment ongoing, within previous 6 months, or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden >3 days or major surgery in previous 12 weeks requiring general or regional anesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling 3 cm larger than asymptomatic side (measured 10 cm below tibial tuberosity)	1
Pitting edema confined to the symptomatic leg	1
Collateral superficial veins (nonvaricose)	1
Alternative diagnosis at least as likely as venous thrombosis	-2
Source: [299]	*Table 20*

Swallowing Dysfunction

Based on instrumental testing results, dysphagia may develop in 42% to 78% of patients within three days after stroke [21; 303]. This disorder is strongly linked to the development of malnutrition and pneumonia if not identified early and managed properly [21; 303; 304]. The AHA/ASA guidelines include a Class I recommendation for early dysphagia screening in patients with acute stroke [21]. Patients with dysphagia often have problems with aspiration, which can cause serious consequences if the stroke has suppressed cough sensations [21]. Although cerebral and cortical strokes can cause dysphagia, swallowing is most severely compromised by brain stem strokes [303].

The speech and language pathologist on the rehabilitation team should perform a brief swallow assessment on all patients with stroke before oral intake of food and fluids [21; 305]. A dysfunctional swallow should be further examined using a complete bedside swallow examination. If bedside swallow screenings indicate an affected swallow, or if the patient has a high risk for aspiration and/or dysphagia, performing a videofluoroscopy swallowing study or fiberoptic endoscopic examination is recommended [21; 305; 306]. The grade of dysphagia correlates with dysarthria, aphasia, low functional independence, and level of cognitive functioning [306]. The speech and language pathologist may best identify the specific physiologic problem and recommend the necessary management and interventions for treatment. A Cochrane review assessing the effectiveness of a variety of interventions (e.g., acupuncture, neuromuscular electrical stimulation, physical stimulation) on functional outcome found that behavioral interventions and acupuncture reduced dysphagia, and pharyngeal electrical stimulation reduced pharyngeal transit time. However, the authors concluded that data are insufficient to determine the effect of these and other interventions (e.g., nutritional/fluid supplementation) on functional outcome and death. [304]. Authors of another review found that acupuncture may be effective for treatment of post-stroke dysphagia, but concluded that the reported benefits should be verified with further studies [307].

Bladder and Bowel Dysfunction

Upon admission to community-based facilities, approximately 50% of stroke survivors have urinary incontinence and 30% have fecal incontinence [308; 309]. Almost all patients with fecal incontinence (98%) also suffer from urinary incontinence. Urinary and fecal incontinence can lead to patient discomfort, skin breakdown, and sepsis. Fecal incontinence, in particular, reduces patient and family morale.

Large infarcts, aphasia, cognitive impairment, functional disability, lesions in the frontal cortex or frontoparietal lobes, and advanced age are associated with post-stroke urinary dysfunction [310]. Medications such as diuretics, alpha-adrenoreceptor blockers, and anticholinergic drugs can cause or exacerbate this complication [311; 312]. Hyper-reflexia and hyporeflexia are the most common mechanisms of urinary incontinence in stroke survivors [313]. Detrusor sphincter dyssynergia, a cause of incomplete bladder voiding, is uncommon because its pathogenesis involves lesions between the brain stem and spine [312]. When assessing bladder function in patients with acute stroke, it is important to evaluate urinary retention with use of a bladder scanner or an in-and-out catheterization; urinary frequency, volume, and control; and the presence of dysuria. Patients who have urinary incontinence may benefit from bladder-training regimens and scheduled voiding [311; 314].

Fecal incontinence can be due to neurogenic impairments or leakage around a fecal impaction (overflow incontinence) [315]. If the underlying cause of fecal incontinence is neurogenic, the signs and symptoms would likely include reduced rectal sensation and tone, inability to voluntarily contract the rectal sphincter, and stool in the rectal vault [315]. A diagnosis of constipation with overflow incontinence is more likely if the patient has rectal sensation and tone.

Risk factors for impaction and constipation include immobility, inactivity, dehydration, some medications, mood disorders, and cognitive deficits [316; 317]. Multivariate analysis has shown that advanced age and diabetes are risk factors for fecal incontinence [317]. Patients with persistent constipation or fecal incontinence may benefit from bowel-management programs and psychosocial support [318]. Because of the risk of skin breakdown, the social stigma, and the burden of care associated with bowel and bladder incontinence, management is an essential component of the rehabilitation process [21].

Falls

Within 12 weeks after a stroke, approximately 25% of patients will fall [286]. Up to 70% of individuals with a stroke fall during the first six months after discharge from the hospital or rehabilitation facility [21; 319]. Individuals with stroke are also at risk of repeated falls that include injury [21; 320]. One study found that most falls occur at home in the first 3 months following post-stroke risk assessment [320]. Falls are a common complication for several reasons, including [315; 321; 322]:

- Unfamiliar environment and physical state
- Pain, fatigue, poor balance, and muscle weakness
- Incontinence
- Frequent positioning, turning, and transferring, especially in rehabilitative settings
- Cognitive impairments, mood disorders (including depressive symptoms), visual impairments, spatial neglect, and any other condition that can decrease a patient's safety awareness

The Berg Balance Scale may be the most appropriate screen for patients who are likely to fall [21; 323; 324]. This scale tests 14 specific functional movements of daily living of increasing difficulty [325]. The 56-point maximum score indicates adequate balance and low risk of a fall. A score of less than 45 is associated with a proclivity for falling [323; 325]. The score at 2 months post-stroke is useful for informing a patient's risk of falls, but it does not account for the multifactorial nature of the problem and should not preclude risk management provided in conjunction with exercise interventions, such as rehabilitation that targets gait coordination, to improve mobility [320; 326]. If the patient is able to walk, the Stops Walking When Talking test may further help to identify the risk for a fall [323]. With this test, the examiner initiates a conversation with the patient while walking; if the patient stops walking to respond, the risk of a fall is increased [327]. St. Thomas' Risk Assessment Tool in Falling Elderly Inpatients (known as STRATIFY), a tool used commonly in the rehabilitation setting, has been shown to be a poor predictor of the risk for fall when screening patients with stroke [328].

In addition to the physical consequences associated with falls, there are also psychologic and social consequences. Impairments in balance, gait, motor control, perception, and vision contribute to a heightened fear of falling in the stroke survivor, with 30% to 80% reporting various levels of fear associated with falling and mobility [21]. This fear can cascade into reduced levels of physical activity and deconditioning, resulting in greater physical decline, loss of ability to perform activities of daily living, loss of independence, social isolation, and depression. Education in fall prevention, including balance training, is an essential component of the rehabilitation process [21].

Pain

Pain is one of the most frequently experienced complications. Almost one-half of all stroke survivors experience chronic pain, 65% of whom have shoulder pain [286]. Whether chronic or periodic, pain can delay functional recovery by masking motor function improvement, diminishing a patient's motivation or willingness to perform rehabilitative tasks, or limiting the patient's movement or requiring the use of a cane or wheelchair for ambulation [17]. Pain most often results from joint immobilization and the fixation of tendons and ligaments in one position [85]. In some patients, however, stroke-induced sensorimotor pathway damage leads to the sensation of pain in an affected extremity or side of the body. The most common pain syndrome of this type is central post-stroke pain, which affects 8% of patients, or at least 56,000 stroke patients in the United States each year [21; 329; 330]. Four percent of patients with central post-stroke pain experience it as shoulder pain. Central post-stroke pain can be difficult to manage, even with medications. Only amitriptyline and lamotrigine have been shown to be effective in placebo-controlled studies [331].

The AHA/ASA recommend patient and family education (i.e., range of motion, positioning) about shoulder pain and care following stroke [21]. A clinical assessment of the pain that includes musculoskeletal evaluation, evaluation of spasticity, identification of any subluxation, and testing for regional sensory changes is also recommended. Ultrasound may be considered for diagnosis of shoulder soft tissue injury [21]. Botulinum toxin injection or a trial or neuromodulating pain medications may be useful to reduce severe hypertonicity in hemiplegic shoulder muscles. Positioning and the use of supportive devices may help reduce pain [21].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The evidence from randomized controlled trials so far does not confirm or refute that electrical stimulation around the shoulder after stroke influences reports of pain, but there do appear to be benefits for passive humeral lateral rotation.

(https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD001698/full. Last accessed March 11, 2020.)

Level of Evidence: Meta-Analysis

Use of diagnostic criteria for central post-stroke pain can be helpful [21]. Additionally, initial medical examinations should thoroughly document suspected etiology of any pain, its location and characteristics (e.g., burning, tingling, stabbing, dull), its duration and intensity, and what aggravates or relieves the pain. Any pain that interferes with the rehabilitation process should be identified and treated accordingly. There is limited evidence on the efficacy of proposed treatments for central post-stroke pain. Combined pharmacotherapy (e.g., amitriptyline, lamotrigine) and therapeutic exercise may be reasonable. Few nonpharmacologic options exist [21].

Functional Outcome

Approximately 45% of stroke survivors have residual neurologic deficits that impair mobility, which is one of the most devastating sequelae of stroke [21; 87]. At 6 months, about half of ischemic stroke survivors who are 65 years of age or older have hemiparesis, nearly one-third require assistance with walking, and more than one-quarter need assistance with activities of daily living [87]. Although functional outcome primarily depends on the patient's post-stroke neurologic damage and compensatory capacity, the multidisciplinary rehabilitation team plays a major role in recovery [246]. The team's coordinated and customized efforts can help many stroke survivors adopt an active and social lifestyle. To tailor services to a patient's needs, the team should assess his or her functional abilities during the immediate post-acute stroke phase before hospital discharge. Assessment relies on a physical examination and a systematic battery of tests that measure a patient's ability to complete activities of daily living and that screens for cognitive/communication skills as well as visual/spatial neglect disorders [21]. Knowledge of the patient's preferred activities is also helpful.

Several functions/activities are typically measured to assess comprehensive functional status initially and during the rehabilitation process (***Table 21***). Although many measurement tools can be used to objectively record a patient's comprehensive functional acuity, the most widely used and trusted instrument in the stroke rehabilitation setting is the FIM [332; 333]. Throughout the rehabilitation process, FIM-supported systematic screening can help the rehabilitation team to [21; 332]:

- Identify functional, cognitive, and visual/spatial deficits not previously detected
- Set realistic functional goals and document progression toward these goals
- Deduce discharge or extended care plans
- Ensure patients' safety as they perform functional tasks and teach proper mechanics to reduce their risk of injury with continued performance

As stated, loss of mobility is a devastating post-stroke outcome and restoration of gait-related activities (e.g., rising to stand, sitting down, climbing stairs) is often one of the primary goals of rehabilitation. Additionally, many patients will require assistive devices, adaptive equipment, and other items to maximize independent functioning after stroke [21].

In general, major rehabilitation goals are for patients to regain safe ambulation in their homes and community and to regain the ability to perform activities of daily living with minimal or no assistance. Thus, patients should be reassessed for

ACTIVITIES MEASURED TO ASSESS COMPREHENSIVE FUNCTIONAL STATUS INITIALLY AND DURING THE REHABILITATION PROCESS
Activities of daily living
Aerobic capacity and endurance
Balance
Bladder and bowel management
Circulatory response to position changes and other functional tasks
Communication and social cognition
Gait
Joint integrity and mobility
Locomotion
Mobility
Motor function (agility, coordination, dexterity)
Muscle performance (activation, endurance, power, strength)
Pain response to functional tasks
Posture
Range of motion
Reflex integrity
Self-care ability
Sexual activity
Upper extremity activity/function
Use of assistive and adaptive devices
Visual and spatial neglect
Source: [21; 332] *Table 21*

daily tasks that are appropriate to their expected level of dependency [21]. If a return to independent community or home living is possible, domestic functioning should be evaluated [17; 334]. Skills needed to stay home alone include preparing a meal, using safety precautions, properly taking medications, and obtaining emergency services. Patients who may resume driving should be assessed thoroughly for driving-related physical, cognitive, and behavioral functions [21]. Driving is an instrumental activity of daily living for many individuals due to its impact on their ability to participate in activities outside the home. Between one- and two-thirds of post-stroke survivors resume driving after one year, but because it is a highly complex activity requiring skills in cognition, perception, and emotional and motor control, the ability to drive is often affected by stroke. The AHA/ASA recommend that [21]:

- Individuals who appear to be ready to return to driving, as demonstrated by successful performance on fitness-to-drive tests, should have an on-the-road test administered by an authorized person and should be referred to a driver rehabilitation program for training if the test is failed.
- It is reasonable to assess individuals for cognitive, perception, physical, and motor abilities to determine readiness to return to driving. This may be achieved with a driving simulation.

Cognition and Communication

Healthy cognition and communication are considered to be essential parts of an individual's well-being. However, stroke frequently has an adverse effect on cognitive and communicative abilities.

Cognition

Calculation, executive functioning (the integration of multiple and complex processes), and visual perception/construction are the cognitive arenas most often affected during the first several weeks after a stroke [335; 336]. Up to 88% of patients with a cerebellar stroke have cognitive deficits, such as impairments in abstract thought, attention, control, memory, planning, and speech [337]. In many cases, patients with stroke-associated right brain damage have anosognosia, a condition in which patients are rendered unaware of their contralateral sensory and motor neurologic deficits (hemiplegia, hemianesthesia, and hemianopia) [338]. Although many survivors regain some or all cognitive skills soon following a stroke, up to 38% remain cognitively impaired at 3 months [339]. Recovery rates may be as high as 80% within 6 months for stroke survivors, with visual perception and visual memory showing the most improvement and language and abstract reasoning showing the least [340; 341]. At 1 and 3 years after a stroke, cognitive impairment is one of the factors most strongly linked with poor physical and mental health status [342]. Cognitive status is an important determinant of post-stroke success. The AHA/ASA recommend that all stroke patients be screened for cognitive deficits before being discharged to home [21].

Stroke-induced damage to the brain's cognition centers is second only to Alzheimer disease as the leading cause of dementia. Stroke-associated dementia manifests with the following symptoms [343]:

- Memory loss, especially short-term memory
- Attention deficits and difficulty following instructions
- Difficulty planning/organizing tasks or solving problems
- Confusion
- Poor judgment
- Behavioral changes, including inappropriate emotions and extreme mood fluctuations
- Mood disturbances and depression

Areas of cognitive and arousal ability that should be assessed before and during rehabilitation are learning and memory, attention, visual/spatial neglect and impairments, executive functioning, and apraxia (loss of the ability to execute skilled movements despite having the desire and the physical ability to perform them) [21]. In addition to its use in assessing functional ability, the FIM is effective as an initial screen of cognitive and functional communication deficits [344]. Because stroke-related cognition deficits are independently associated with left hemispheric stroke, visual field defect, and urinary incontinence, the presence of any of these conditions should heighten awareness of the possibility of the presence of the others [339].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The National Guideline Centre recommends that patients should be screened for cognitive deficits after stroke. Where a cognitive deficit is identified, carry out a detailed assessment using valid, reliable, and responsive tools before designing a treatment program.

(https://www.nice.org.uk/guidance/CG162. Last accessed March 11, 2020.)

Level of Evidence: Expert Opinion/Consensus Statement

Visual and spatial dysfunctions may be particularly difficult to identify during the initial post-stroke examination because multiple neuroanatomic systems can be affected to varying degrees. When a standard medical examination does not include the brief, systematic screening for visual and spatial neglects, more than 60% of these dysfunctions remain undiagnosed. However, the use of the FIM may increase their early identification [344]. Patients with neglect deficits are unknowingly inattentive to specific body parts and/or spaces in

CHARACTERISTICS OF EXPRESSIVE AND RECEPTIVE APHASIA
Patients with expressive aphasia may: • Use single words or short phrases • Omit smaller words like "the," "of," or "and" (the patient's message may sound like a telegram) • Say words out of sequence • Switch sounds or first letters of words (e.g., dishwasher becomes a "wish dasher") • Invent words • Create meaningless sentences by fluently stringing nonsense words and real words together
Patients with receptive aphasia may: • Require a significant amount of extra time to understand verbal communication, especially if the speech is fast • Have difficulty following radio or television news • Interpret figurative speech (e.g., "It's raining cats and dogs.") literally
Patients frequently have global aphasia, with various combinations of expressive and receptive difficulties.
Source: [347] *Table 22*

the external environment. For instance, patients may brush half of their teeth or only eat food on half of their tray. Unilateral neglect is present in almost 50% of patients with right hemispheric stroke [345]. Patients with unilateral neglect are also unaware of limbs contralateral to the site of the brain lesion(s). Neglect disorders are strongly associated with poor functional outcomes and safety issues. Patients with neglect are prone to falls and injuries as well as burns to the affected limbs [322]. Addressing visual and spatial deficits as early as possible in the rehabilitation process using multiple functional adaptation techniques (e.g., visual scanning, external cues) and patient/caregiver education may decrease a patient's risk for injury [21].

Communication

As with cognitive difficulties, communication problems strain relationships between stroke survivors and their social system, impede rehabilitation, and lead to poor quality of life. Common communication-related stroke sequelae are aphasia, dysarthria, and apraxia of speech (motor speech disorder in which the muscles required for speech are less coordinated). Patients with communication disorders may also have dysphagia. How these disorders are manifested as well as their severity depends on the location and degree of the stroke. Interventions for apraxia of speech should be individually tailored and may include behavioral techniques and strategies that target [21]:

- Physiologic support for speech, including respiration, phonation, articulation, and resonance
- Global aspects of speech production (e.g., loudness, rate, prosody)

Augmentative and alternative communication devices and modalities should be used to supplement speech [21].

Aphasia affects one-third of stroke survivors and is one of the most common stroke-associated communication deficits [21; 346].

The three types of aphasia are expressive, receptive, and global (***Table 22***) [347]. Patients with expressive aphasia have difficulties using words and sentences, whereas patients with receptive aphasia struggle to understand what others are communicating to them. Global aphasia is a combination of these two types. Aphasia is typically related to lesions on the left side of the brain, as the language center is located within this hemisphere in most individuals [348]. In many cases, aphasia (mild aphasia in particular) can be an elusive diagnosis because patients may [347]:

MEASURES EVALUATED TO ASSESS COGNITION AND COMMUNICATION SKILLS	
Category	**Skills to Evaluate**
Speech	Fluency, vocal quality, clarity, loudness Strength and coordination of muscles needed for speaking Understanding Use of semantics and syntax Understanding and answering of different types of questions Understanding facts and inferences within extended speech Ability to follow instructions that increase progressively in length and complexity Language sample of an extended story, written and spoken
Expression	Chaining a sequence of events together Describe the "plot" in an action picture Message coherency Word recall Use of complete sentences, telegraphic sentences or phrases, or single words
Social communication	Ability to interpret jokes and sarcasm, as well as absurdities in stories or pictures Ability to initiate conversation, take turns speaking and listening during a discussion, and express thoughts clearly Ability to clarify or restate a message that is initially misunderstood by a conversation partner
Reading and writing	Reading and writing of letters, words, phrases, sentences, and paragraphs
Other	Swallowing (as needed) Ability to use an augmentative or alternative communication aid, if necessary
Source: [349]	*Table 23*

- Be able to carry on normal conversations in many settings
- Have trouble understanding only when sentences are long or complex
- Have trouble finding the words to express an idea or may say, "the word is right on the tip of my tongue"

A variety of treatment approaches for aphasia have been developed, but no conclusions can yet be made about the effectiveness of one treatment over another [21].

An additional challenge in assessment is that members of the rehabilitation team typically do not have a clear sense of the patient's communication skills before the stroke. Lastly, reading and writing skills are usually more affected than oral communication.

Well-trained and organized rehabilitation teams can use alternative methods of communicating to mitigate the effects of cognitive and communication disorders. Ideally, these problems should be recognized and managed early. However, arriving at a diagnosis can be challenging. The speech and language pathologist on the rehabilitation team is best suited to evaluate the patient for cognitive/communication disorders. In some cases, problems are initially undetected or develop after the evaluation. Training the rehabilitation team to recognize symptoms of cognitive and communication deficits early (especially those that are subtle) and report findings to the speech and language pathologist can serve as a "safety net" for patients [21]. For proper diagnosis, the speech and language pathologist should also seek the help of the patient's family to gain an understanding of the patient's cognition and communication history.

Through interviews, conversation, structured observations and other formal tests, the speech and language pathologist comprehensively evaluates the individual's cognition and communication skills in the areas of speech, expression, social communication, and reading/writing (***Table 23***) [21; 349].

If necessary, the speech and language pathologist formulates remediation strategies to accelerate the patient's recovery of affected communication skills, development of compensatory techniques, or use of residual skills [21; 349]. In many cases, patients with stroke-induced attention deficits, visual neglect, memory deficits, executive function deficits, and problem-solving difficulties can be retrained or taught compensation techniques [350]. Strategies to enhance communication with the patient should be taught to the rehabilitation team as well as the family/caregivers [21]. Any interventions should be individually tailored and designed to target the overt communication deficit as well as any deficits that accompany or underlie the communication deficit, including attention, memory, and executive functions. The use of drugs to improve cognitive impairments is not well established [21].

Psychologic Status

Following a stroke, it is understandable that patients and their families experience intense emotions. In many cases, the staff's kindness and helpfulness, familial support, and the passage of time allow patients and their families to deal with the grief and other feelings precipitated by the stroke without medication or psychologic therapy. However, approximately 33% of patients experience post-stroke depression, and other mood disorders also manifest in stroke survivors [1; 351; 352]. In general, psychologic conditions can have a significant impact on the success of rehabilitation. Thus, all patients should be thoroughly evaluated for psychologic disorders as early as possible and on an ongoing basis [21].

Detecting post-stroke depression can be particularly challenging, as symptoms often appear to be typical post-stroke symptoms or are subtle. Patients may experience fatigue, sleeping difficulties, loss of appetite, tearfulness, and feelings of hopelessness. They may refuse to participate in therapy [21]. Additionally, cognitive deficits may prevent the patient from recognizing or having the ability to communicate depressive symptoms. Patients with an acquired flat affect may "sound sad" or indifferent to their situation without having post-stroke depression. Although several screening tools for depression in the older population are available (***Table 24***), a single, universally accepted evaluation tool for post-stroke depression has not been developed. Because little research in this area is available and the condition is underdiagnosed by nonpsychiatric physicians, the diagnosis of post-stroke depression should be based on information from multiple sources, including medical evaluation, patient self-report, observation of patient behavior, patient history, and staff reports of changes in behavior and motivation.

The accompaniment of post-stroke depression with other psychologic disorders is not uncommon [21]. Therefore, the medical evaluation should also screen for other categories of psychiatric symptoms [21]. Generalized anxiety disorder, which affects 20% of survivors, often coexists with post-stroke depression [356]. Generalized anxiety disorder delays the recovery of the ability to carry out activities of daily living and negatively affects social functioning [21]. Additionally, up to 15% of stroke survivors have pseudobulbar affect, characterized by uncontrollable laughing/crying [21].

Both post-stroke depression and pseudobulbar affect respond well to selective serotonin reuptake inhibitors [357]. Although these drugs carry some risk, they are safe in most patients who have had a stroke. However, these medications should not be administered prophylactically [358; 359]. Although studies are limited, the use of cognitive-behavioral therapy techniques and brief supportive therapy in conjunction with medication may be beneficial to those with post-stroke depression and other neuropsychiatric sequelae of stroke [21].

SCREENING TOOLS FOR DEPRESSION			
Evaluation Instrument	**Time Required**	**Benefits**	**Disadvantages**
Beck Depression Inventory (BDI)	10 minutes	Widely used Easily administered Norms available Good for somatic symptoms	Less useful in elderly and in patients with aphasia or neglect High rate of false-positive results Somatic items may not be due to depression
Center for Epidemiologic Studies Depression (CES-D) Scale	<15 minutes	Easily administered Useful in older individuals Effective for screening in stroke population	Not appropriate for patients with aphasia
Geriatric Depression Scale (GDS)	10 minutes	Easy to use with older or cognitively impaired individuals, as well as with individuals with visual or physical problems or low motivation	High rates of false-negative results in minor depression
Hamilton Depression Scale	<30 minutes	Observer rated Frequently used for patients who have had a stroke	Multiple versions compromise interobserver reliability
Folstein Mini-Mental State Examination	10 minutes	Widely used for screening	Several functions with summed score May misclassify patients with aphasia
Patient Health Questionnaire-2 (PHQ-2)	15 minutes	Widely used for screening Easily administered	Poor specificity in detecting major depression
Source: [353; 354; 355]			*Table 24*

EXERCISE PROGRAM

Physical inactivity that typically occurs following a stroke can exacerbate muscle weakness (through atrophy and changes in muscle fibers), fatigue, cardiovascular and metabolic deconditioning, and poor balance [360; 361]. These complications have been shown to slow physical and social recovery and hinder brain activation over time [362]. Comprehensive fitness training may offset these effects (***Table 25***) [360; 363; 364]. Moreover, exercise programs can benefit a stroke survivor by reducing recurrent stroke and cardiovascular risks; reducing the risk and severity of post-stroke osteoporosis, preventing injuries and falls; increasing fitness, strength, flexibility, and functional activities; and promoting socialization [21; 360; 365]. However, exercise is not without risks. Training programs should be tailored to the patient's capabilities and conditions to promote safety and reduce musculoskeletal injuries [366; 367]. For some patients, stroke severity and coexisting conditions may render exercise inadvisable. For instance, silent coronary artery disease, especially in sedentary patients, increases the chance of exercise-induced cardiac death. Because up to 75% of stroke survivors have cardiac comorbidities, the AHA suggests that the medical evaluation for an exercise program should include a graded exercise test with ECG monitoring [360]. Thorough screening, customized exercise program design, monitoring, and patient education should be performed during rehabilitation to maximize benefits and safety.

SUMMARY OF EXERCISE PROGRAM RECOMMENDATIONS FOR STROKE SURVIVORS		
Mode of Exercise	**Major Goals**	**Intensity, Frequency, Duration**[a]
Hospitalization and early convalescence		
Low-level walking, self-care activities Intermittent sitting, standing Seated activities Range of motion activities and motor challenges	Increase independence in activities of daily living Increase walking speed/efficiency Improve tolerance for prolonged physical activity Reduce risk of cardiovascular disease Reduce motor impairment; improve cognition Prevent deconditioning, pneumonia, orthostatic intolerance, and depression	Approximately 10 to 20 beats per minute increases in resting heart rate; rating of perceived exertion (RPE) ≤11 (6–20 scale) Frequency, duration as tolerated, using interval or work-rest approach
Inpatient/outpatient exercise therapy or "rehabilitation"		
Large-muscle activities (e.g., walking, graded walking, stationary cycle/arm ergometry, functional activities seated exercises), if appropriate	Increase walking speed, efficiency Improve functional capacity and independence in activities of daily living Reduce motor impairment Improve cognition Improve vascular health and induce other cardioprotective benefits	40% to 70% peak oxygen uptake; 40% to 70% heart rate reserve; 55% to 80% maximal heart rate; RPE 11–14 (6–20 scale) 3 to 5 days/week 20 to 60 min/session (or multiple 10-min sessions) Complement with pedometers to increase lifestyle physical activity
Strength/endurance (e.g., circuit training, weight machines, free weights, isometric exercise)	Increase independence in activities of daily living Increase muscle strength and endurance Reduce cardiac demands during lifting/carrying objects by increasing muscular strength	1–3 sets of 10–15 repetitions of 8–10 exercises involving the major muscle groups 2 to 3 days/week, with resistance gradually increased over time as tolerance permits
Flexibility/stretching	Increase range of motion (ROM) of involved extremities Prevent contractures Decrease risk of injury Increase activities of daily living	2 to 3 days/week (Before or after aerobic or strength training) Hold each stretch for 10 to 30 seconds
Neuromuscular (coordination and balance activities)	Improve level of safety during activities of daily living Improve balance, skill reacquisition, quality of life, mobility Decrease fear of falling	Use as complement to aerobic, muscular strength/endurance training, and stretching activities 2 to 3 days/week (Consider performing on same day as strength activities)
[a]Recommended intensity, frequency, and duration of exercise depend on each individual patient's level of fitness. Intermittent training sessions may be indicated during the initial weeks of rehabilitation.		
Source: [360] Reprinted from Billinger SA, et al. Physical activity and exercise recommendations for stroke survivors: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(8):2532-2553. With permission from Lippincott Williams & Wilkins.©American Heart Association. *Table 25*		

As with any rehabilitation program, the degree of a patient's cognitive and communicative deficits can affect an exercise program's success. The Neurobehavioral Cognitive Status Examination is a brief screening tool that provides a rapid and sensitive measure of the patient's cognitive function. However, it, and other brief mental status scales, cannot adequately assess executive skills and other higher-level cognitive functions [21]. Personalized, tailored counseling interventions have demonstrated mixed results in improving adherence to an exercise program, whereas physical activity counseling has resulted in greater physical activity at 9 and 52 weeks post-stroke [360]. The crucial elements of a successful physical activity counseling intervention have not been identified definitively [360]. Barriers that may need to be addressed include lack of familial support, depression, fatigue, social integration, and cultural issues [360].

The consequences of inactivity may be most noticeable in patients with hemiparesis or other gait deficits. More than 50% of stroke survivors require rehabilitation to regain a functional level of ambulation [368]. Effects of neural damage underlying gait impairment, spasticity, and poor muscle performance are significantly compounded by muscle weakness, a lack of fatigue resistance, and the increased energy demands of rehabilitation [360]. Patients with mild-to-moderate conditions can benefit from treadmill training with partial body weight support [360]. As the patient walks on a treadmill, his or her body weight is supported by harnesses to facilitate walking at a comfortable speed. This training augments conventional gait rehabilitation therapies by increasing gait speed, muscle performance, and fatigue resistance; however, its effect on long-term walking outcomes requires further study [368; 369].

Incorporation of progressive resistance training increases the generalizability of the fitness program and may improve the ability to carry out activities of daily living [370]. Although there are no accepted guidelines, the AHA suggests more repetitions with reduced loads (10 to 15 repetitions rather than 8 to 12), similar to programs recommended for patients recovering from MI [360]. Additionally, at least one set of at least 8 to 10 exercises should involve the major muscle groups (arms, shoulders, chest, abdomen, back, hips, and legs).

As technology continues to advance, rehabilitation programs may become enhanced with new ways to engage stroke survivors in exercise [21]. A study of virtual reality training sessions was shown to improve arm and hand movement skills in two patients with chronic hemiparesis [371]. The approach was also able to provide individualized, progressive practice based on the patient's level of movement ability and rate of improvement [371]. Other studies have found virtual reality rehabilitation to be an equally effective and potentially motivating alternative and/or supplement to conventional training in post-stroke care [372; 373].

Nerve stimulation therapy has also been proposed as a means to improve motor deficits and physical activity capacity. In 2021, the FDA approved a vagus nerve stimulation system intended to treat moderate-to-severe upper extremity motor deficits associated with chronic ischemic stroke [397]. The device may be incorporated into a comprehensive rehabilitation program for these patients.

TRANSITIONS IN CARE AND REHABILITATION CONTINUITY

The transition from inpatient care to home after a stroke can be difficult for both patients and caregivers. Ongoing rehabilitation, profound or permanent disability, or discharge to a long-term care facility affects not only the transition in care but also the continuity of that care. To ensure medical and rehabilitation continuity for the patient through the rehabilitation process and into the home or community, the AHA/ASA recommend individualized discharge planning in the transition from hospital to home that includes comprehensive assessment of activities of daily living, instrumental activities of daily living, and mobility assessments and discussion of sexual issues (e.g., safety, changes in libido), recreational and leisure activities,

and return to work ability and timeline, where appropriate [21]. Patients for whom the discharge living setting is evaluated should be considered candidates for community- or home-based rehabilitation when feasible. Providers should consider alternative methods of communication and support (e.g., telephone, visits, telehealth, online support), particularly for patients who reside in rural settings [21].

Rehabilitation services provided in the community can improve cardiovascular health, decrease the risk of cardiovascular events, and increase short-term survival rates for stroke survivors [21]. Among the benefits associated with community- and home-based rehabilitation programs are reduced costs, decreased length of stay in hospitals or institutional settings, increased opportunities for involvement by patient and family/caregiver, and less stress for family/caregiver. Patient satisfaction also is generally higher.

SECONDARY PREVENTION: EVIDENCE-BASED RECOMMENDATIONS

In the United States, approximately 23% of stroke incidences are recurrent [1]. Due to the high risk of recurrent stroke and its consequences, secondary ischemic stroke prevention tends to follow a risk-stratified model of disease management [374]. Treatment of at-risk patients' conditions is typically aggressive, as inadequate management can have serious implications.

A patient's risk for a recurrent stroke is highest during the first year; 14% of survivors have a recurrent stroke within 1 year after the initial cerebrovascular event, suggesting that secondary prevention is time-critical and should be initiated during the rehabilitation process [375]. After the first year, the chance of recurrent stroke decreases to 4% per year [374]. Because TIA is an important determinant of stroke, the AHA secondary prevention guidelines for patients with TIA tend to be as aggressive as those established for ischemic stroke [10]. The guidelines focus on controlling several important modifiable risk factors.

CONTROLLING RISK FACTORS

A major component of secondary prevention is the treatment of modifiable risk factors and the underlying cause of the stroke. For patients who have had an ischemic event, the results of large studies have suggested that addressing hypertension, diabetes, smoking, alcohol consumption, and physical activity can reduce the risk of recurrent stroke [109].

Hypertension

The results of meta-analyses have indicated that lowering blood pressure reduces the risk of stroke 30% to 40% [376; 377]. The findings of longitudinal studies suggest that treatment with antihypertensive medications in hypertensive and normotensive patients reduces the incidence of recurrent strokes, MI, and other vascular events [378]. In particular, diuretics or diuretics combined with ACE inhibitors (e.g., ramipril, perindopril) most significantly reduce the risk of recurrent ischemic stroke [10; 378]. However, lifestyle modifications that include weight loss; increased intake of fruits, vegetables, and low-fat dairy products; habitual aerobic physical activity; and limited alcohol consumption are crucial components of controlling blood pressure [123]. Although most studies address the prevention of additional ischemic strokes, hypertension management has also been shown to reduce the risk of recurrent hemorrhagic stroke and is included in guideline recommendations published by the AHA/ASA [10; 378].

AHA Recommendations

- Initiation of blood pressure therapy is indicated for previously untreated patients with ischemic stroke or TIA who, after the first several days, have an established blood pressure ≥140/90 mm Hg. Initiation of therapy for patients with blood pressure <140/90 mm Hg is of uncertain benefit.

- Resumption of blood pressure therapy is indicated for previously treated patients with known hypertension for both prevention of recurrent stroke and prevention of other vascular events in those who have had an ischemic stroke or TIA and are beyond the first several days.
- Goals for target blood pressure level or reduction from pretreatment baseline are uncertain and should be individualized, but it is reasonable to achieve a systolic pressure <140 mm Hg. For patients with a recent lacunar stroke, it might be reasonable to target an systolic pressure of <130 mm Hg.
- The choice of specific drugs and targets should be individualized on the basis of pharmacologic properties, mechanism of action, and consideration of specific patient characteristics for which specific agents are probably indicated (e.g., extracranial cerebrovascular occlusive disease, renal impairment, cardiac disease, diabetes).
- The optimal drug regimen to achieve the recommended level of reductions is uncertain because direct comparisons between regimens are limited.
- Lifestyle modifications are an integral part of a patient's antihypertensive therapy.

Diabetes

Diabetes is a well-documented independent risk factor for recurrent stroke [379; 380]. Aggressive control of hypertension in diabetic patients, with a lower target of 130/80 mm Hg, has been shown to reduce the risk of stroke as well as other cardiovascular events [123]. Including ACE inhibitors in the treatment regimen of patients with diabetes effectively lowers blood pressure, slows the progression of renal disease, and reduces albuminuria [10; 381].

AHA Recommendations

- After a TIA or ischemic stroke, all patients should probably be screened for diabetes with testing of fasting plasma glucose, glycated hemoglobin (HbA1c), or an oral glucose tolerance test. Choice of test and timing should be guided by clinical judgment and recognition that acute illness may temporarily perturb measures of plasma glucose. In general, HbA1c may be more accurate than other screening tests in the immediate postevent period.
- Use of existing guidelines for glycemic control and blood pressure targets for patients with diabetes is recommended for patients who have had a stroke or TIA.

Cigarette Smoking

Smoking doubles the risk of stroke [382]. Its cessation eliminates the elevated risk after 5 years and reduces the overall risk of stroke-related hospitalization [10; 382; 383]. Exposure to secondhand smoke also appears to increase the risk of stroke [10; 384]. The most effective combination of therapies for smoking cessation is nicotine replacement, social support, and counseling [10; 385].

AHA Recommendations

- All patients with TIA or stroke who smoke should be strongly urged to quit and to avoid passive smoke. The use of smoking cessation programs and nicotine-replacement therapy should be considered.
- It is reasonable to advise patients after ischemic stroke or TIA to avoid environmental (passive) tobacco smoke.

Alcohol Consumption

The results of a meta-analysis suggest that the risk of stroke is increased 69% for individuals who have more than five drinks (with one drink defined as 12 ounces of beer, 4 ounces of wine, or 1.5 ounces of liquor) per day compared with nondrinkers [386].

AHA Recommendations

- Patients with ischemic stroke or TIA who drink heavily should be strongly encouraged to reduce or eliminate their alcohol consumption to lessen risk factors that increase the likelihood of recurrent stroke.
- Light-to-moderate amounts of alcohol consumption (up to 2 drinks per day for men; up to 1 drink per day for nonpregnant women) may be reasonable; however, nondrinkers should not be counseled to start drinking.

Physical Activity

Habitual exercise clearly prevents stroke [365]. In addition, a sedentary lifestyle impedes functional recovery and places patients at a higher risk for stroke recurrence.

AHA Recommendations

- After successful screening and completion of formal stroke rehabilitation, an individually tailored exercise program is indicated to enhance cardiorespiratory fitness and reduce risk of stroke recurrence.
- At least three to four sessions per week, 40 minutes per session, of moderate-to-vigorous-intensity aerobic physical exercise is reasonable to reduce stroke risk factors in eligible patients. Moderate-intensity exercise is sufficient to break a sweat or noticeably raise heart rate (e.g., walking briskly); vigorous-intensity exercise includes activities such as jogging.
- Patients who are able and willing to initiate increased physical activity should be referred to a comprehensive, behaviorally oriented program.
- Consider supervision by a healthcare professional (e.g., physical therapist) on initiation of an exercise regimen for individuals with disability after ischemic stroke.

MANAGING DISEASE

For patients who have large-artery atherosclerosis, the specific underlying condition should be managed. Similarly, identification and treatment of cardioembolic stroke sources (e.g., AF, cardiomyopathy, acute MI and left ventricular thrombus, valvular heart diseases) is recommended. Patients with ischemic stroke and a high-risk source of cardioembolism generally benefit from anticoagulant therapy.

Extracranial Carotid Artery Disease

Carotid artery revascularization is recommended by the AHA for certain patients with stenosis greater than 50% [10]. However, surgery is not beneficial for patients with stenosis of less than 50%.

AHA Recommendations

- Carotid endarterectomy (CEA) is recommended for all patients who had a recent TIA or an ischemic stroke within the past 6 months and ipsilateral severe (70% to 99%) carotid artery stenosis if the morbidity/mortality risk is less than 6%.
- CEA is recommended for certain patients (based on age, gender, and comorbidities) who had a recent TIA or an ischemic stroke within the past 6 months and ipsilateral severe (50% to 69%) carotid artery stenosis if the morbidity/mortality risk is less than 6%. CEA is not recommended when the degree of stenosis is <50%.

- When CEA is indicated for patients with TIA or stroke, surgery within 2 weeks is reasonable rather than delaying surgery if there are no contraindications to early revascularization.
- Carotid artery stenting (CAS) is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is found to be reduced by more than 70% on noninvasive imaging or more than 50% on catheter angiography or noninvasive imaging with corroboration and the anticipated rate of periprocedural stroke or death is less than 6%.
- It is reasonable to consider patient age in choosing between CAS and CEA. For patients older than 70 years of age, CEA may be associated with improved outcome compared with CAS, particularly when arterial anatomy is unfavorable for endovascular intervention. For younger patients, CAS is equivalent to CEA in terms of risk for periprocedural complications (e.g., stroke, MI, death) and long-term risk for ipsilateral stroke.
- CAS may be considered for patients with symptomatic severe stenosis (greater than 70%) if the stenosis is difficult to access surgically, medical conditions are present that greatly increase the risk for surgery, or other specific circumstances exist (such as radiation-induced stenosis or restenosis after CEA). In this setting, CAS is reasonable when performed by operators with established periprocedural stroke and mortality rates of less than 6%, similar to those observed in trials of CEA and CAS.
- For patients with recurrent or progressive ischemic symptoms ipsilateral to a stenosis or occlusion of a distal carotid artery, or occlusion of a midcervical carotid artery after institution of optimal medical therapy, the usefulness of extracranial to intracranial bypass is considered investigational.
- Optimal medical therapy, which should include antiplatelet therapy, statin therapy, and risk factor modification, is recommended for all patients with carotid artery stenosis and a TIA or stroke.

Intracranial Atherosclerosis

The rate of stroke recurrence for patients with symptomatic intracranial atherosclerosis is approximately 9% [10]. The findings of retrospective studies have suggested that the greatest rate of recurrence is found among patients with this condition who do not have a response to antithrombotic therapy [387]. Although the results of some studies have indicated that angioplasty or stenting should be considered for such patients, the usefulness of these surgical interventions is unknown and considered investigational [10].

AHA Recommendations

With regard to patients with stroke or TIA due to 50% to 99% stenosis of a major intracranial artery:

- Aspirin 325 mg per day is recommended in preference to warfarin.
- The data are insufficient to make a recommendation regarding the usefulness of clopidogrel alone, the combination of aspirin and dipyridamole, or cilostazol alone.
- Long-term maintenance of blood pressure <140/90 mm Hg and high-intensity statin therapy are recommended.

- Angioplasty and/or stent placement is not recommended, given the low rate of stroke with medical management and the inherent periprocedural risk of endovascular treatment.
- Extracranial-intracranial bypass surgery is not recommended.

With regard to patients with stroke or TIA due to 70% to 99% stenosis of a major intracranial artery, the addition of clopidogrel 75 mg/d to aspirin for 90 days might be reasonable.

Atrial Fibrillation

The anticoagulant warfarin has a narrow therapeutic margin and numerous food and drug interactions, and these factors (which necessitate frequent INR testing and dose adjustment), combined with the associated significant bleeding risks, have led to the underutilization of this drug despite having been shown to prevent recurrent stroke substantially in patients with ischemic stroke or TIA and AF and despite the adoption of performance measures and guidelines advocating its use in these patients [10; 388; 389]. Easy-to-use alternative therapies are required and include dabigatran, rivaroxaban, and apixaban [390; 391; 392]. Significant adverse effects (i.e., serious, sometimes fatal bleeding, acute coronary events) have been associated with some of these agents, making their use inappropriate for some patients [393; 394]. However, a 2011 focused update on dabigatran published by the American College of Cardiology, the AHA, and the Heart Rhythm Society recommends this agent as a useful alternative to warfarin for select patients [395].

Between 35% to 45% of patients with stroke and AF have coexisting conditions that may have caused the stroke [396]. In many cases, both the AF and the other condition (usually stenosis) will require treatment [10].

AHA Recommendations

- For patients who have experienced an acute ischemic stroke or TIA with no other apparent cause, prolonged rhythm monitoring (for approximately 30 days) for AF is reasonable within 6 months of the index event.
- For patients with ischemic stroke or TIA with paroxysmal (intermittent), persistent, or permanent AF, anticoagulation with a vitamin K antagonist (VKA) (target INR: 2.5; range: 2.0 to 3.0) is recommended.
- VKA therapy, apixaban, and dabigatran are all indicated for the prevention of recurrent stroke in patients with nonvalvular AF, whether paroxysmal or permanent. The selection of an antithrombotic agent should be individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including renal function and time in INR therapeutic range if the patient has been taking VKA therapy.
- Rivoroxaban is reasonable for the prevention of recurrent stroke in patients with nonvalvular AF.
- The combination of oral anticoagulation (i.e., warfarin or one of the newer agents) with antiplatelet therapy is not recommended for all patients after ischemic stroke or TIA but is reasonable in patients with clinically apparent CAD, particularly an acute coronary syndrome or stent placement.
- For patients unable to take oral anticoagulants, aspirin alone (75 mg to 100 mg per day) is recommended. The combination of clopidogrel plus aspirin, compared with aspirin therapy alone, might be reasonable.

- For most patients with a stroke or TIA in the setting of AF, it is reasonable to initiate oral anticoagulation within 14 days after the onset of neurologic symptoms. In the presence of high risk for hemorrhagic conversion (i.e., large infarct, hemorrhagic transformation, uncontrolled hypertension, hemorrhage tendency), it is reasonable to delay initiation of oral anticoagulation beyond 14 days.
- For patients with AF at high risk for stroke (i.e., stroke or TIA within 3 months; Cardiac failure, Hypertension, Age, Diabetes, Stroke system [CHADS2] score of 5 or 6; mechanical or rheumatic valve disease) who require temporary interruption of oral anticoagulation, bridging therapy with a LMWH administered subcutaneously is reasonable.

Noncardioembolic Strokes and TIA

The use of certain antiplatelet therapies rather than oral anticoagulation for noncardioembolic ischemic strokes and TIAs has been shown to reduce the overall risk of recurrent stroke and decrease the incidence of fatal recurrent strokes [10]. Clopidogrel is appropriate for patients who are allergic to aspirin or for patients in whom dipyridamole-associated headaches occur.

AHA Recommendation

Aspirin (50 mg to 325 mg per day) monotherapy, the combination of aspirin 25 mg and extended-release dipyridamole 200 mg twice daily, or clopidogrel 75 mg monotherapy are all acceptable options for initial therapy. The selection of an antiplatelet agent should be individualized on the basis of patient risk factor profiles, cost, tolerance, and other clinical characteristics.

CASE STUDY

Patient M is an active woman, 70 years of age, who lost consciousness and collapsed at home. Her daughter, who was visiting her at the time, did not witness the collapse but found her mother on the floor, awake, confused, and slightly short of breath. The daughter estimated that she called EMS within 5 minutes after the collapse, and EMS responded within 10 minutes. EMS evaluated Patient M, drew blood for a glucose level, and determined that she may have had a stroke. They notified the nearest designated comprehensive stroke center that they would be arriving with the patient within 15 minutes. Patient M's daughter accompanied her.

The triage and transportation of an individual with suspected stroke should be similar to that for an individual with serious trauma, and treatment is recommended within 3 hours after the onset of stroke. Because of the limited time available for assessment and diagnosis before optimal treatment, the EMS dispatcher should notify EMS personnel immediately and coordinate transport of the individual to the closest emergency facility, preferably one that is a designated primary (or comprehensive) stroke care center.

On presentation in the emergency department, Patient M is immediately triaged. Because Patient M is still somewhat confused, her daughter is asked to provide information on the patient's history. The daughter reports that her mother had had an episode of sudden-onset numbness and tingling in the right limb, with slight confusion and slurred speech, 3 days previously. The episode lasted only 5 minutes, and Patient M had not called her primary care physician. Additional information provided by the daughter indicates that Patient M has been treated for hypertension for 10 years but notes that she is often not compliant with her antihypertensive medicine, a diuretic. The patient has never smoked, drinks occasionally, and is of normal weight.

Patient M has two significant risk factors for stroke; one is a long history of hypertension. More than two-thirds of individuals older than 65 years of age are hypertensive, and it is important for individuals with hypertension to have regular blood pressure screening and to maintain a blood pressure of less than 140/90 mm Hg. Antihypertension therapy has been found to reduce the incidence of stroke by 30% to 40%. Patient M's noncompliance with her antihypertension medicine likely includes her among the 65% of known hypertensive individuals in whom blood pressure is not controlled.

Patient M's previous episode of numbness, confusion, and slurred speech appears to be evidence of a TIA, another substantial risk factor for stroke. Research has shown that approximately 5% of patients will have an ischemic stroke within 7 days after a TIA. In addition, the risk of stroke within 7 days is doubled for patients with TIAs who did not seek treatment. As is the case for many individuals who have a TIA, Patient M did not seek medical attention because the clinical symptoms resolved quickly. However, research findings indicate that urgent treatment should be provided for TIAs, as early treatment for TIA and minor stroke has been shown to reduce the risk of early recurrent stroke by 80%.

On physical examination, Patient M's blood pressure is 150/95 mm Hg. She has pain in her left arm and a slight headache. There are slight carotid bruits on the right. She is assessed with use of the NIHSS and found to have left hemiparesis and left visual/spatial neglect. The results of laboratory tests, including a complete blood count, prothrombin time, serum electrolyte levels, cardiac biomarkers, and renal function studies, are all within normal limits. CT of the brain indicates a thrombus in a branch of the right internal carotid artery, with approximately 50% occlusion due to atherosclerosis. There is an area of infarction in the right anterior hemisphere. There is no evidence of a subarachnoid hemorrhage. The diagnosis is made 2 hours after Patient M's arrival in the emergency department. She is treated with intravenous rt-PA at a dose of 0.9 mg/kg, and aspirin antiplatelet therapy is started at an initial dose of 325 mg, 24 hours after thrombolytic therapy, and a maintenance dose of 75 mg per day.

Many of the patient's symptoms, including her loss of consciousness, shortness of breath, pain, and headache, are nontraditional symptoms of stroke. Studies have demonstrated that nontraditional symptoms are more prevalent among women, often leading to a delay in the evaluation for stroke. EMS personnel and clinicians should be aware of the potential for nontraditional symptoms in women and carry out a diagnostic evaluation addressing a suspicion of stroke.

Patient M is eligible for thrombolytic therapy with rt-PA according to evidence-based guidelines developed by the AHA/ASA: her blood pressure is lower than 185/110 mm Hg, the onset of symptoms is less than 3 hours prior to the start of treatment, and the laboratory values are within normal limits. Antiplatelet therapy with aspirin 325 mg daily (versus anticoagulant therapy with warfarin) is recommended for treatment of patients with stroke or TIA due to intracranial atherosclerosis with 50% to 99% occlusion. Antiplatelet therapy is not recommended as an adjunctive therapy within 24 hours of thrombolytic therapy.

When Patient M's condition is stabilized, her primary care physician and consultant neurologist provide a referral for stroke rehabilitation, and a multidisciplinary rehabilitation team is formed to assess her rehabilitative needs, recommend the proper rehabilitation setting, and develop a treatment strategy tailored to her specific needs that includes daily antiplatelet therapy. Patient M is again assessed with the NIHSS, and the score is 12. The patient's cognitive and communication skills are intact on evaluation with the FIM, with the exception of the previously documented left visual/spatial neglect. The assessment also includes evaluation of the patient's risk for complications.

Because of her spatial neglect, she is screened with the Berg Balance Scale and the Stops Walking When Talking test. The score on the Berg Balance Scale is 43, and Patient M does stop walking to engage in conversation. Psychosocial assessment includes screening with the Center for Epidemiologic Studies Depression (CES-D) Scale, as well as review of the medical history and conversations with the patient and her children; no signs of depression are present.

Patient M's score of 12 on the NIHSS falls within the range (6 to 15) that indicates she is likely to benefit from rehabilitation. Evaluating a stroke survivor's risk of complications is an important component of the overall assessment, and among the most common complications are falls, deep vein thrombosis, pressure ulcers, swallowing dysfunction, bladder and bowel dysfunction, and depressive symptoms. In assessing the risk of complications, the Berg Balance Scale appears to be the most appropriate screen for patients who are likely to fall, and a score of less than 45 is associated with a likelihood of falling. The risk of a fall is also increased when a patient stops walking to talk, as Patient M did, during the Stops Talking When Walking test.

Screening for signs of depression is also essential, as depression affects approximately 33% of stroke survivors. Signs of depression are subtle and may be vague. Several screening tools are available, but there is no universally accepted tool for use in the post-stroke setting. The CES-D was chosen in this case because it is easy to administer, is useful in older individuals, and has been found to be effective for screening in the stroke population, except for individuals who have aphasia. The diagnosis of depression in stroke survivors should be based on sources in addition to a formal screening tool, such as a medical evaluation, patient self-report, observation of patient behavior, patient history, and staff reports of changes in behavior and motivation.

The rehabilitation team discusses the results of the assessment with Patient M's daughter and son, both of whom live about 45 minutes away from the patient. Together, the team and the family members explore options to determine the best approach to rehabilitation. A decision is made for Patient M to be discharged to an inpatient stroke unit, and a rehabilitation program is developed. The nurse on the team discusses the program with Patient M and her children and explains the course of rehabilitation and the expectations. Rehabilitation will focus on an exercise program consisting of aerobic exercise, strength training, stretching, and coordination and balance activities.

Early initiation of rehabilitation is a particularly strong predictor of improved outcome, and rehabilitation in a stroke unit has been associated with improved quality of life, survival, and functional status at 5 years compared with a general healthcare facility. No studies have demonstrated the superiority of one rehabilitation setting over another, and the inpatient setting was chosen primarily to ensure consistent care, given how far away Patient M's children live, and the limited support she otherwise has for healthcare needs. Decisions about the setting and program for rehabilitation should be shared with family members, and family and other caregivers should be provided with educational resources about the rehabilitation process.

The exercise program developed for Patient M is designed to help her regain the ability to independently carry out activities of daily living safely and to regain a functional level of ambulation. The benefits of an exercise program include increasing fitness, strength, and flexibility; improving function; preventing injuries and falls; and reducing the risk of recurrent stroke.

Patient M gradually resumes the ability to function independently, and after more than 2 weeks in the stroke rehabilitation unit, the score on the NIHSS has improved to 5. Before she is discharged to her home, the rehabilitation team provides instructions for exercises to continue at home and recommends moderate physical activity as a secondary prevention measure. The team also educates Patient M about the importance of maintaining a normal blood pressure through use of her antihypertension medication and lifestyle modifications. At a follow-up visit with her primary care clinician at 3 months, Patient M's blood pressure is 135/80 mm Hg, and she reports that she has been compliant with her antihypertension medicine and antiplatelet therapy and is functioning well at home.

CONCLUSION

Ischemic stroke remains a significant contributor to morbidity and mortality in the United States. Stroke is associated with several modifiable risk factors, such as smoking, diet, physical inactivity, and obesity, and clinicians should encourage their patients to adopt healthy lifestyle habits, especially patients who are at highest risk. In addition, primary prevention of stroke involves the appropriate management of many medical conditions, such as hypertension, diabetes, dyslipidemia, and AF.

Early diagnosis and appropriate immediate treatment are key to recovery of neurologic function and survival after stroke, making it imperative for both healthcare professionals and the general public to recognize the symptoms of stroke and TIAs, a substantial risk factor for stroke. Clinicians, as well as EMS staff and ED staff, should be skilled in identifying possible stroke-related symptoms, especially noting that women are more apt to have nontraditional symptoms of both TIAs and stroke. Efforts to educate the public about the importance of seeking medical care for TIAs and about the warning signs of stroke are also essential.

Several evidence-based guidelines are available for the primary and secondary prevention of ischemic stroke, as well as for early management and rehabilitation. Adherence to these guidelines will help to reduce the prevalence of stroke and to decrease the morbidity and mortality for individuals who have stroke. Thrombolytic therapy with rt-PA is the cornerstone of treatment for ischemic stroke, and the AHA now recommends beginning antiplatelet therapy with aspirin 24 to 48 hours after the onset of stroke. Other antiplatelet agents, as well as anticoagulant therapy, are not recommended on the basis of the evidence to date.

Outcomes after stroke are improved when care is provided in a comprehensive stroke center and when rehabilitative care is provided by a multidisciplinary team. Effective rehabilitation begins with a systematic evaluation of the patient to determine the need for specific rehabilitation services, the risk of complications, the patient's physical functioning and level of cognition and communication, and the patient's psychosocial status. This evaluation allows for the development of a rehabilitation program that addresses an individual patient's specific needs, with tailored strategies for secondary prevention. When all available resources are utilized, prevention and appropriate treatment of stroke will result.

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