Initial assessment and management of acute stroke

Author
Jamary Oliveira Filho, MD, MS, PhD

Section Editor
Scott E Kasner, MD

Deputy Editor
John F Dashe, MD, PhD

All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Nov 2015. | **This topic last updated:** Jul 01, 2015.

INTRODUCTION — The subacute and long-term assessment and management of patients who have suffered a stroke includes physical therapy and testing to determine the precise etiology of the event so as to prevent recurrence. The acute management differs. Immediate goals include minimizing brain injury, treating medical complications, and moving toward uncovering the pathophysiologic basis of the patient's symptoms.

Patient assessment and management during the acute phase (first few hours) of an ischemic stroke will be reviewed here. Use of thrombolytic therapy, treatment of patients not eligible for thrombolytic therapy, the clinical diagnosis of various types of stroke, and the subacute and long-term assessment of patients who have had a stroke are discussed separately. (See "Intravenous fibrinolytic (thrombolytic) therapy in acute ischemic stroke: Therapeutic use" and "Reperfusion therapy for acute ischemic stroke" and "Antithrombotic treatment of acute ischemic stroke and transient ischemic attack" and "Clinical diagnosis of stroke subtypes" and "Overview of the evaluation of stroke".)

INITIAL ASSESSMENT — Sudden loss of focal brain function is the core feature of the onset of ischemic stroke. However, patients with conditions other than brain ischemia may present in a similar fashion (table 1). (See "Differential diagnosis of transient ischemic attack and stroke".)

In addition, patients suffering a stroke may present with other serious medical conditions. Thus, the initial evaluation requires a rapid but broad assessment [1].

The goals in the initial phase include:

- Ensuring medical stability, with particular attention to airway, breathing, and circulation
- Quickly reversing any conditions that are contributing to the patient's problem
- Determining if patients with acute ischemic stroke are candidates for thrombolytic therapy (table 2)
- Moving toward uncovering the pathophysiologic basis of the patient's neurologic symptoms

Time is of the essence in the hyperacute evaluation of stroke patients; all tests should lead to a "best guess" of the stroke mechanism, which will eventually guide therapy. The history, physical examination, serum glucose, oxygen saturation, and a noncontrast CT scan are sufficient in most cases (see 'Immediate laboratory studies' below). Other tests are considered based upon individual patient characteristics, but the absence or unavailability of any additional tests need not be a reason to delay therapy if otherwise indicated.

Airway, breathing and circulation — Assessing vital signs and ensuring stabilization of airway, breathing, and circulation is the part of the initial evaluation of all patients with critical illness, including those with stroke [1]. Patients with increased intracranial pressure due to hemorrhage, vertebrobasilar ischemia, or bihemispheric ischemia can present with a decreased respiratory drive or muscular airway obstruction. Hypoventilation, with a resulting increase in carbon dioxide, may lead to cerebral vasodilation, which further elevates intracranial pressure.

Intubation may be necessary to restore adequate ventilation and to protect the airway from aspiration; this is especially important in the presence of vomiting, which occurs commonly with increased intracranial pressure, vertebrobasilar ischemia, and intracranial hemorrhage. Patients with adequate

ventilation should have the oxygen saturation monitored. Patients who are hypoxic should receive supplemental oxygen to maintain oxygen saturation >94 percent [1]. Supplemental oxygen should not routinely be given to nonhypoxic stroke victims [1].

History and physical — Establishing the time of ischemic stroke symptom onset is critical because it is the main determinant of eligibility for treatment with intravenous thrombolysis (table 2). For patients who are unable to provide a reliable onset time, it is defined as the time the patient was last awake and free of stroke symptoms [1]. For patients presenting within the therapeutic window for thrombolysis (less than 4.5 hours from symptom onset), the history needs to be accurate but rapid; contraindications to thrombolytic treatment should also be assessed (table 2). (See "Intravenous fibrinolytic (thrombolytic) therapy in acute ischemic stroke: Therapeutic use", section on 'Patient selection and eligibility'.)

The history and physical examination should be used to distinguish between other disorders in the differential diagnosis of brain ischemia (table 1). As examples, seizures, syncope, migraine, hypoglycemia (see 'Hypoglycemia' below), or drug toxicity can mimic acute ischemia [1]. The most difficult cases involve patients with focal signs and altered level of consciousness. It is important to ask the patient, relative, or any reliable informant whether the patient takes insulin or oral hypoglycemic agents, has a history of epilepsy, drug overdose or abuse, or recent trauma. (See "Differential diagnosis of transient ischemic attack and stroke".)

Diagnosing an intracerebral hemorrhage (ICH) or subarachnoid hemorrhage (SAH) as soon as possible can be lifesaving [2,3]. The history may be helpful in this regard. The presence of onset headache and vomiting favor the diagnosis of ICH or SAH compared with a thromboembolic stroke (figure 1), while the abrupt onset of impaired cerebral function without focal symptoms favors the diagnosis of SAH. Another important element of the history concerns the whether the patient takes anticoagulant drugs. Even with these clues, diagnosing intracranial hemorrhage on clinical grounds is very imprecise, so early triage of the patient to CT or MRI scan is critical. However, it is important to assess and stabilize vital physiologic functions **before** sending the patient for an imaging study.

The physical examination should include careful evaluation of the neck and retroorbital regions for vascular bruits, and palpation of pulses in the neck, arms, and legs to assess for their absence, asymmetry, or irregular rate. The heart should be auscultated for murmurs (see "Auscultation of cardiac murmurs in adults"). The lungs should be assessed for abnormal breath sounds, bronchospasm, fluid overload, or stridor.

The skin should be examined for signs of endocarditis, cholesterol emboli, purpura, ecchymoses, or evidence of recent surgery or other invasive procedures, particularly if reliable history is not forthcoming. The funduscopic examination may be helpful if there are cholesterol emboli or papilledema. The head should be examined for signs of trauma. A tongue laceration may suggest a seizure.

In cases where there is a report or suspicion of a fall, the neck should be immobilized until evaluated radiographically for evidence of serious trauma. Examination of the extremities is important to look for evidence of systemic arterial emboli, distal ischemic, cellulitis, and deep vein thrombosis; the latter should raise the possibility that the patient is receiving anticoagulant treatment.

Neurologic evaluation — Ischemia in different vascular territories presents with specific syndromes, some of which provide a clue to the underlying stroke pathophysiology (table 3). The history should focus upon the time of symptom onset, the course of symptoms over time, possible embolic sources, items in the differential diagnosis, and concomitant diseases. (See "Clinical diagnosis of stroke subtypes".)

The neurologic examination should attempt to confirm the findings from the history and provide a quantifiable examination for further assessment over time. Many scales are available that provide a structured, quantifiable neurologic examination. One of the most widely used and validated scales is the National Institutes of Health Stroke Scale (NIHSS), composed of 11 items (table 4) adding up to a total score of 0 to 42 (calculator 1); NIHSS scores ≥20 indicate a severe stroke [4].

The three most predictive examination findings for the diagnosis of acute stroke are facial paresis, arm drift/weakness, and abnormal speech (a combination of dysarthria and language items derived from the NIHSS) [5,6]. The NIHSS score on admission has been correlated to stroke outcome (table 5) [7,8], and its use is recommended for all patients with suspected stroke [9].

Immediate laboratory studies — Urgent brain imaging with CT or MRI is mandatory in all patients with sudden neurologic deterioration or acute stroke. (See 'Neuroimaging' below.)

All patients with suspected stroke should have the following studies urgently as part of the acute stroke evaluation [1,2]:

- Noncontrast brain CT or brain MRI
- Serum glucose
- Oxygen saturation

Other immediate tests for the evaluation of ischemic and hemorrhagic stroke include the following [1,2]:

- Electrocardiogram
- Complete blood count including platelets
- Cardiac enzymes and troponin
- Serum electrolytes, urea nitrogen, creatinine
- Prothrombin time and international normalized ratio (INR)
- Activated partial thromboplastin time

However, fibrinolytic therapy for acute ischemic stroke (see 'Acute therapy' below) should not be delayed while awaiting the results of hematologic studies unless the patient has received anticoagulants or there is suspicion of a bleeding abnormality or thrombocytopenia.

The following laboratory studies are appropriate in selected patients [1-3]:

- Liver function tests
- Toxicology screen
- Blood alcohol level
- Pregnancy test in women of child-bearing potential
- Arterial blood gas if hypoxia is suspected
- Chest radiograph if lung disease is suspected
- Lumbar puncture if subarachnoid hemorrhage is suspected and head CT scan is negative for blood; note that lumbar puncture will preclude administration of tPA, though tPA should not be given if there is suspicion for subarachnoid hemorrhage as the cause of the symptoms
- Electroencephalogram if seizures are suspected
- Thrombin time and or ecarin clotting time if known or suspected that the patient is taking direct thrombin inhibitor or direct factor Xa inhibitor

In addition to these tests, we suggest obtaining a finger stick for faster glucose measurement if the patient is diabetic, taking insulin or oral hypoglycemic agents, or if there is clinical suspicion for hypoglycemia. Chest radiography, urinalysis and blood cultures are indicated if fever is present. We also suggest blood for type and cross match in case fresh frozen plasma is needed to reverse a coagulopathy if ICH is present. (See "Spontaneous intracerebral hemorrhage: Pathogenesis, clinical features, and diagnosis".)

In order to limit medication dosage errors, particularly with the use of alteplase, an accurate body weight should be obtained early during the urgent evaluation [10].

Neuroimaging — In the evaluation of the acute stroke patient, imaging studies are necessary to exclude hemorrhage as a cause of the deficit, and they are useful to assess the degree of brain injury

and to identify the vascular lesion responsible for the ischemic deficit. Some advanced CT and MRI technologies are able to distinguish between brain tissue that is irreversibly infarcted and that which is potentially salvageable, thereby allowing better selection of patients who are likely to benefit from therapy. This topic is discussed separately. (See "Neuroimaging of acute ischemic stroke".)

Cardiac studies — Electrocardiography (ECG) is important for detecting signs of concomitant acute cardiac ischemia. This test is particularly important in the setting of stroke, as patients with ischemic stroke frequently harbor coronary artery disease but may not be able to report chest pain.

Stroke alone can be associated with ECG changes. The sympathetic response to stroke can lead to demand-induced myocardial ischemia. In large strokes, especially subarachnoid hemorrhage, there are centrally mediated changes in the ECG.

The ECG and cardiac monitoring are important for the detection of chronic or intermittent arrhythmias that predispose to embolic events (eg, atrial fibrillation) and for detecting indirect evidence of atrial/ventricular enlargement that may predispose to thrombus formation. Current guidelines recommend cardiac monitoring for at least the first 24 hours after the onset of ischemic stroke to look for atrial fibrillation (AF) or atrial flutter [1]. However, paroxysmal AF, if transient, infrequent, and largely asymptomatic, may be undetected on standard cardiac monitoring such as continuous telemetry and 24 or 48-hour Holter monitors. Extended cardiac event monitoring for patients with ischemic stroke or TIA who present with sinus rhythm can significantly increase the detection of occult AF. Such monitoring may reduce in the risk of recurrent ischemic stroke by prompting the appropriate use of long-term anticoagulation. The optimal monitoring method – continuous telemetry, ambulatory electrocardiography, serial electrocardiography, transtelephonic ECG monitoring, or implantable loop recorders – is uncertain, though longer durations of monitoring are likely to obtain the highest diagnostic yield. (See "Overview of the evaluation of stroke", section on 'Monitoring for occult atrial fibrillation' and "Stroke in patients with atrial fibrillation", section on 'Long-term therapy'.)

Transthoracic and transesophageal echocardiography adequately detect cardiogenic and aortic sources for cerebral embolism (see "Echocardiography in detection of cardiac and aortic sources of systemic embolism"). However, their use can be postponed until after the acute treatment phase, when the patient is in a more stable clinical condition. Exceptions include patients with a moderate or high suspicion of endocarditis, where echocardiography may provide confirmation of the diagnosis. (See "Clinical manifestations and diagnosis of infective endocarditis", section on 'Echocardiography' and "Overview of the evaluation of stroke", section on 'Cardiac evaluation'.)

STROKE MANAGEMENT ISSUES — In addition to stabilization of airway, breathing, and circulation, and rapid neurologic evaluation discussed above, early key management issues that often arise in acute stroke include blood pressure control (see 'Blood pressure management' below), fluid management, treatment of abnormal blood glucose levels (see 'Hypoglycemia' below and 'Hyperglycemia' below), swallowing assessment (see 'Swallowing assessment' below), and treatment of fever and infection (see 'Fever' below). Care in a dedicated stroke unit (see 'Stroke unit care' below) is associated with better outcomes.

Fluids — Intravascular volume depletion is frequent in the setting of acute stroke, particularly in older adult patients [11], and may worsen cerebral blood flow. For most patients with acute stroke and volume depletion, isotonic saline without dextrose is the agent of choice for intravascular fluid repletion and maintenance fluid therapy [12]. In general, it is best to avoid excess free water (eg, as in ½ isotonic saline) because hypotonic fluids may exacerbate cerebral edema in acute stroke and are less useful than isotonic solutions for replacing intravascular volume. In addition, it is best to avoid fluids containing glucose, which may exacerbate hyperglycemia. However, fluid management must be individualized on the basis of cardiovascular status, electrolyte disturbances, and other conditions that may perturb fluid balance. (See "Maintenance and replacement fluid therapy in adults".)

In particular, hyponatremia following subarachnoid hemorrhage may be due to inappropriate secretion of antidiuretic hormone (SIADH) or rarely, to cerebral salt-wasting; these are physiologically distinct and are treated differently, as discussed separately. (See "Treatment of aneurysmal subarachnoid hemorrhage", section on 'Hyponatremia'.)

Hypoglycemia — Hypoglycemia can cause focal neurologic deficits mimicking stroke, and severe hypoglycemia alone can cause neuronal injury. It is important to check the blood sugar and rapidly correct low serum glucose (<60 mg/dL or 3.3 mmol/L) at the first opportunity. Normoglycemia is the desired goal while avoiding marked elevation of serum glucose [1].

Hyperglycemia — Hyperglycemia, generally defined as a blood glucose level >126 mg/dL (>7.0 mmol/L), is common in patients with acute stroke and is associated with poor functional outcome [13-17]. In a series of 59 patients with acute ischemic stroke, admission hyperglycemia was present in 32 percent of patients without diabetes and 81 percent of patients with diabetes [18]. Stress hyperglycemia may be the most common cause [15], although newly diagnosed diabetes is also important [16].

Hyperglycemia may augment brain injury by several mechanisms including increased tissue acidosis from anaerobic metabolism, free radical generation, and increased blood brain barrier permeability. Several lines of evidence point to the deleterious effects of elevated glucose in acute stroke [19]:

- Hyperglycemia worsens ischemic damage in animal models of stroke
- Glucose reduction decreases ischemic damage in experimental models
- Acute hyperglycemia is associated with reduced salvage of penumbral tissue and greater final infarct size by neuroimaging [20]
- Hyperglycemia is associated with reduced benefit from recanalization with thrombolytic therapy and higher odds for symptomatic intracerebral hemorrhage [21]

In light of these observations, it is reasonable to treat severe hyperglycemia in the setting of acute stroke. The American Heart Association/American Stroke Association guidelines for acute ischemic stroke recommend treatment for hyperglycemia to achieve serum glucose concentrations in the range of 140 to 180 mg/dL (7.8 to 10 mmol/L) [1]. The European Stroke Initiative guidelines recommend treatment for glucose >180 mg/dL (>10 mmol/L) [22].

An ongoing National Institute of Neurological Disorders and Stroke (NINDS)-funded multicenter randomized trial (SHINE) is evaluating whether tight control of glucose with intravenous insulin improves outcome in patients with acute ischemic stroke [23,24]. However, the currently available evidence suggests that it does not. A 2014 systematic review identified 11 controlled trials involving nearly over 1500 adults with acute ischemic stroke who were randomly assigned to either intensively monitored insulin infusion therapy or to usual care [25]. There was no difference between the treatment and control groups for the combined outcome of death or dependency, and no difference between groups for the outcome of final neurologic deficit. In addition, the intervention group had a higher rate of symptomatic hypoglycemia.

Swallowing assessment — Dysphagia is common after stroke and is a major risk factor for developing aspiration pneumonia. It is important to assess swallowing function prior to administering oral medications or food. Thus, prevention of aspiration in patients with acute stroke includes initial nulla per os (NPO) status until swallowing function is evaluated. (See "Medical complications of stroke", section on 'Dysphagia and aspiration'.)

Head and body position — During the acute phase of stroke, the position of the patient and the head of bed should be individualized with respect to the risk of elevated intracranial pressure and aspiration, and the presence of comorbid cardiopulmonary disease. However, available data are limited, and no randomized trials have addressed these issues.

A number of reports suggest that cerebral perfusion pressure or intracranial large artery flow velocity is maximal when patients are in the horizontal position [26,27]. As an example, in a study involving 20 patients with moderately severe ischemic stroke in the middle cerebral artery (MCA) territory, mean flow velocity in the MCA measured by transcranial Doppler increased by an average of 20 percent when the head-of-bed elevation decreased from 30 to 0 degrees, and by an average of 12 percent when head-of-bed elevation decreased from 30 to 15 degrees [27]. Thus, a supine position is preferred for nonhypoxic patients with acute ischemic stroke who are able to tolerate lying flat [1].

Furthermore, some patients with acute ischemic stroke may develop increased ischemic symptoms upon standing, sitting, or elevating the head of the bed, due to reduction in flow through stenotic vessels or collateral pathways [28,29].

While elevated intracranial pressure may be exacerbated with flat head-of-bed positioning [26], significant aggravation of elevated intracranial pressure or clinical deterioration due to progressive cerebral edema is unlikely in the first 24 hours after ischemic stroke onset [30-34]. Thus, the head of bed may be kept flat even for patients with large cerebral ischemic infarction who are within 24 hours of onset, since this position may improve cerebral blood flow and help to preserve the ischemic penumbra. However, patients with intracerebral hemorrhage should be maintained at 30 degrees in bed, as should patients who are deteriorating beyond 24 hours from stroke onset with large ischemic infarction This issue is discussed separately for patients with intracerebral hemorrhage. (See "Spontaneous intracerebral hemorrhage: Treatment and prognosis", section on 'Intracranial pressure'.)

Flat head positioning may not be tolerated well in some patients with cardiac and pulmonary disease (eg, heart failure). Such patients may need head elevation to improve oxygenation [35,36].

Given these data, the head of bed position should be individualized for each patient [37].

- We recommend keeping the head in neutral alignment with the body and elevating the head of the bed to 30 degrees for patients in the acute phase of stroke who are at risk for any of the following problems:
  - Elevated intracranial pressure (ie, intracerebral hemorrhage, clinical deterioration >24 hours from stroke onset in patients with large ischemic infarction)
  - Aspiration (eg, those with dysphagia and/or diminished consciousness)
  - Cardiopulmonary decompensation or oxygen desaturation (eg, those with chronic cardiac and pulmonary disease)
- We suggest keeping the head of bed flat (0 to 15 degree head-of-bed position) for patients in the acute phase (first 24 hours) of ischemic stroke who are not at risk for elevated intracranial pressure, aspiration, or worsening cardiopulmonary status.

Keeping the patient flat is a temporary measure that should be discontinued in most patients after 24 to 48 hours. National guidelines favor early mobilization because it lessens the likelihood of major complications such as pneumonia, deep vein thrombosis, pulmonary embolism, and pressure sores after stroke [1]. Exceptions may include those who exhibit neurologic deterioration upon assuming more upright postures. For this reason, close observation is recommended when patient position is altered [1], as during the transition from lying to sitting and standing. In addition, there is a potential increased risk of aspiration if a flat position is maintained for a prolonged period [38].

Earlier mobilization of patients with acute stroke may be harmful. The multicenter randomized AVERT trial, with over 2000 patients, evaluated a protocol of very early mobilization, which was started within 24 hours of stroke onset and consisted of frequent out-of-bed activity including sitting, standing, and walking. Compared with usual care, very early mobilization and early rehabilitative therapies reduced the odds of a favorable outcome at three months [39].

Fever — Fever has special significance in patients presenting with acute neurologic deterioration. Both problems may occur in patients with a primary central nervous system infection such as meningitis, subdural empyema, brain abscess, and infective endocarditis. These conditions need to be excluded as the etiology of fever. In addition, common etiologies of fever including aspiration pneumonia and urinary tract infection should also be excluded.

Fever may contribute to brain injury in patients with an acute stroke. This concept has been demonstrated in animal models in which ischemic injury is increased in the presence of elevated temperature. Hyperthermia may act via several mechanisms to worsen cerebral ischemia [40]:

- Enhanced release of neurotransmitters
- Exaggerated oxygen radical production
- More extensive blood-brain barrier breakdown
- Increased numbers of potentially damaging ischemic depolarizations in the focal ischemic penumbra
- Impaired recovery of energy metabolism and enhanced inhibition of protein kinases
- Worsening of cytoskeletal proteolysis

Fever is associated with unfavorable outcomes in human studies of stroke [41-44]. One meta-analysis analyzed fever and outcome in patients with neurologic injury, including hemorrhagic and/or ischemic stroke [41]. Fever was significantly associated with increased mortality rates, greater disability, more dependence, worse functional outcome, greater severity, and longer intensive care unit and hospital stays. These results were consistent for overall pooled data and for subgroups limited to studies of patients with hemorrhagic, ischemic, or all stroke types. A subsequent meta-analysis found that fever within 24 hours of hospital admission in patients with ischemic stroke was associated with a two-fold increase in the odds of mortality at one month after stroke onset [44].

Treatment — The source of fever should be investigated and treated, and antipyretics should be used to lower temperature in febrile patients with acute stroke [1,2]. We suggest maintaining normothermia for at least the first several days after an acute stroke [40]. However, the clinical utility of this approach has not been established.

- The Paracetamol (Acetaminophen) In Stroke (PAIS) trial evaluated 1400 adults no later than 12 hours after symptom onset of acute ischemic stroke or intracerebral hemorrhage [45]. Included patients had a body temperature of 36ºC to 39ºC. Compared with placebo, paracetamol (acetaminophen) 1 g six times daily for three days did not improve outcome [45]. However, a post-hoc subgroup analysis of 661 patients with a baseline body temperature of 37ºC to 39ºC suggested benefit for paracetamol.

- In a systematic review and meta-analysis of five small randomized controlled trials with a total of 293 patients, there was no benefit for pharmacologic temperature reduction for acute stroke [46]. All the trials enrolled patients within 24 hours of stroke onset, and the duration of treatment ranged from 24 hours to five days. With addition of results from the PAIS trial, the updated meta-analysis found no difference between active treatment and control for a favorable outcome (odds ratio 1.1, 95% CI 0.9-1.3) [45].

Larger trials are needed to determine if pharmacologic temperature reduction improves outcome from acute stroke, particularly for patients with temperature of ≥37ºC, though it seems unlikely that acetaminophen will be effective by itself.

Induced hypothermia is not currently recommended for patients with ischemic stroke [1], outside of clinical trials. An NINDS-funded randomized trial (ICTuS2/3) evaluating the combination of hypothermia and thrombolysis versus thrombolysis alone is currently underway [47].

Stroke unit care — Mounting evidence suggests that patients with acute stroke have better outcomes when admitted to a hospital unit that is specialized for the care of patients with all types of acute stroke,

including ischemic, intracerebral hemorrhage, and subarachnoid hemorrhage [48-51]. The precise components of an acute stroke unit vary between centers and countries, but generally include a hospital ward with dedicated telemetry beds that is continuously staffed by a team of physicians, nurses and other personnel who specialize in stroke care, emphasizing expertise in vascular neurology and neurosurgery [52,53]. Additional components include prompt availability of neuroimaging (eg, CT, MRI, various types of angiography, ultrasound, transcranial Doppler) and cardiac imaging. Implementation of stroke protocols and disease-performance measures may contribute to improved outcomes and decreased risk of stroke-related complications, as shown in some reports [54,55].

Current national guidelines support stroke unit care, when available, for patients with suspected acute stroke [1,56].

BLOOD PRESSURE MANAGEMENT — The approach to blood pressure management in acute ischemic stroke is inherently different from the approach in acute hemorrhagic stroke. Likewise, there are important differences between the blood pressure management in the acute and chronic phases of stroke.

The management of blood pressure in acute phase of stroke is reviewed in the sections that follow. The management of blood pressure after the acute phase of stroke is discussed separately. (See "Antihypertensive therapy to prevent recurrent stroke or transient ischemic attack".)

Acute ischemic stroke — In patients with ischemic stroke, the perfusion pressure distal to the obstructed vessel is low, and the distal vessels are dilated. Blood flow in these dilated vessels is thought to be dependent upon the systemic blood pressure.

The arterial blood pressure is usually elevated in patients with an acute stroke. This may be due to chronic hypertension, an acute sympathetic response, or to other stroke-mediated mechanisms [57]. In many cases, however, the acutely elevated blood pressure is necessary to maintain brain perfusion in borderline ischemic areas [58]. A neuroimaging study with CT or MRI is critical to help guide blood pressure therapy in stroke patients.

The observation that the blood pressure frequently rises spontaneously following cerebral ischemia is consistent with this protective hypothesis, although a stress response to the acute event and to hospitalization may also contribute [59]. The hypertensive effect is transient, as blood pressure falls by as much as 20/10 mmHg within 10 days.

An analysis from the International Stroke Trial of 17,398 patients with an ischemic stroke noted a U-shaped relationship between baseline systolic blood pressure and outcomes [60]. Elevated systolic blood pressure was associated with an increased risk of recurrent ischemic stroke (50 percent greater risk of recurrence with a systolic blood pressure of >200 mmHg versus 130 mmHg), while low blood pressure (particularly <120 mmHg) was associated with an excess number of deaths from coronary heart disease.

A subsequent analysis of 1004 patients with acute ischemic stroke from Okinawa also found a U-shaped relationship between admission blood pressure and death within 30 days after stroke onset [61]. The U-shaped relationship was shifted toward higher pressure in patients who had previous hypertension compared with those who did not have previous hypertension. This finding mirrors the shift seen in cerebral autoregulation that occurs in longstanding hypertension [62].

Interventions — The long-term benefit from antihypertensive therapy does not mean that a reduction in blood pressure will be beneficial during initial management of an acute ischemic stroke [63]. Lowering the systemic blood pressure in patients with acute ischemic stroke has been associated with clinical deterioration. Observational studies from several different groups have found an adverse effect of reducing blood pressure in the first 24 hours after stroke onset [64-66]. Odds ratios [OR] of poor outcome were similar in the first two studies: OR 1.9 per 10 percent systolic blood pressure reduction (95% CI 1.02-3.52) in a Brazilian study [64] and OR 3.8 for a greater than 25 percent diastolic blood

pressure reduction (95% CI 1.2-12.1) in an Austrian study [65]. In a Spanish study, a fall in systolic blood pressure >20 mmHg in the first day was the most important variable associated with neurologic deterioration and poor outcome [66]. Considered together, these data support current blood pressure recommendations in acute ischemic stroke outlined below. (See 'Blood pressure goals ischemic stroke' below.)

Occasional patients even benefit from pharmacologic increases in blood pressure [67]. In a number of small studies, a subset of patients were treated with the pressor agent phenylephrine, and a systolic blood pressure threshold was identified below which ischemic deficits worsened and above which deficits improved [68,69]. A separate group found improved aphasic deficits as blood pressure was increased pharmacologically, concomitant with improved perfusion on MR perfusion study [70]. Others have treated a small number of patients with norepinephrine to improve cerebral perfusion and concluded that the technique is safe and feasible, even in those patients who also received intravenous thrombolysis [71].

On the other hand, severe increases in blood pressure can cause hypertensive encephalopathy, a condition that can mimic stroke. In this case, lowering the blood pressure is the indicated treatment. (See "Moderate to severe hypertensive retinopathy and hypertensive encephalopathy in adults".)

There are no good data from randomized controlled trials to guide blood pressure management in the hyperacute phase of ischemic stroke (ie, the first 12 hours) when the ischemic penumbra may be at risk of irreversible damage if cerebral blood flow is reduced by lowering the blood pressure [72]. The most relevant trials (eg, CATIS [73], SCAST [74], COSSACS [75], and ENOS [76]) enrolled patients as long as 30 to 48 hours after stroke onset, and are therefore less informative regarding the impact of blood pressure treatment in the first hours of ischemic stroke. In addition, many of these trials and others, including the meta-analyses discussed below, enrolled patients with intracerebral hemorrhage, a group that might be expected to benefit from early blood pressure lowering. Keeping these limitations in mind, some of the randomized trial data suggest that initiating blood pressure reduction in acute stroke or merely continuing prestroke blood pressure medications can be harmful:

- A 2014 meta-analysis, evaluating 13 trials (but not ENOS) with over 13,000 patients, found that blood pressure reduction started within seven days of acute stroke led to an increased risk of mortality within 30 days (relative risk 1.34, 95% CI 1.02-1.74) although it had no effect on early or long-term dependency or long-term mortality [77].
- In a later 2014 meta-analysis of 16 trials (including ENOS) of antihypertensive medications that included over 19,000 patients with acute stroke, early blood pressure reduction had no effect on functional outcome (odds ratio 1.0, 95% CI 0.93-1.07) [76]. Similarly, a 2015 meta-analysis of 13 randomized trials (also including ENOS) and over 12,000 subjects found that blood pressure lowering started within three days of ischemic stroke onset did not alter the risk of death or dependency at three months or trial end point (relative risk, 1.04, 95% CI 0.96-1.13) [78].
- In two trials (COSSACS and ENOS) that evaluated over 2800 patients within 48 hours of stroke onset, continuing blood pressure treatment compared with stopping it temporarily had no effect on functional outcome (odds ratio 1.04, 95% CI 0.90-1.22) [76]. However, in the ENOS trial itself, the group assigned to continuing blood pressure treatment had an increased likelihood of hospital death or discharge to an institution, an increased risk of death or disability (Barthel index <60) at 90 days, and significantly lower cognition scores at 90 days compared with the group that stopped treatment, even though there was no difference in functional outcome between the two groups.

These results are not definitive for the reasons noted above.

Blood pressure goals ischemic stroke — Special considerations apply to blood pressure control in patients with acute ischemic stroke who are eligible for thrombolytic therapy. Before lytic therapy is started, treatment is recommended so that systolic blood pressure is ≤185 mmHg and diastolic blood pressure is ≤110 mmHg (table 6) [1]. The blood pressure should be stabilized and maintained at or

below 180/105 mmHg for at least 24 hours after thrombolytic treatment. This issue is discussed in detail separately. (See "Intravenous fibrinolytic (thrombolytic) therapy in acute ischemic stroke: Therapeutic use", section on 'Management of blood pressure'.)

For patients with ischemic stroke who are not treated with thrombolytic therapy, most consensus guidelines recommend that blood pressure **not** be treated acutely unless the hypertension is extreme (systolic blood pressure >220 mmHg or diastolic blood pressure >120 mmHg), or the patient has active ischemic coronary disease, heart failure, aortic dissection, hypertensive encephalopathy, acute renal failure, or pre-eclampsia/eclampsia [1,79]. When treatment is indicated, cautious lowering of blood pressure by approximately 15 percent during the first 24 hours after stroke onset is suggested [1].

Blood pressure management in acute ischemic stroke remains controversial. Current guidelines suggest that antihypertensive medications should be restarted at approximately 24 hours after stroke onset in patients with preexisting hypertension who are neurologically stable, unless a specific contraindication to restarting treatment is known [1]. However, patients with extracranial or intracranial large artery stenoses may require a slower reduction in blood pressure (eg, over 7 to 10 days after ischemic stroke), as some degree of blood pressure elevation may be necessary to maintain cerebral blood flow to ischemic brain regions.

If acute antihypertensive therapy is needed, intravenous agents are generally used. (See 'Choice of antihypertensive agent' below.)

Current guidelines note that vasopressors may be used to improve cerebral blood flow in rare cases when systemic hypotension is producing neurologic impairment, with close neurologic and cardiac monitoring [1]. At present, drug-induced hypertension is not recommended for the treatment of most patients with ischemic stroke outside the setting of a clinical trial [1].

Acute hemorrhagic stroke — In both intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH), the approach to blood pressure management must take into account the potential benefits (eg, reducing further bleeding) and risks (eg, reducing cerebral perfusion) of blood pressure lowering. Recommendations for blood pressure management in acute ICH and SAH are discussed in detail separately. (See "Spontaneous intracerebral hemorrhage: Treatment and prognosis", section on 'Blood pressure' and "Treatment of aneurysmal subarachnoid hemorrhage", section on 'Blood pressure control'.)

Choice of antihypertensive agent — In the acute phase of stroke, there is no clear evidence to support the use of any specific antihypertensive agent to achieve recommended blood pressure goals [1]. Nevertheless, reversible and titratable intravenous agents are best suited for precise blood pressure lowering. Consensus guidelines suggest intravenous labetalol and nicardipine as first-line antihypertensive agents if pharmacologic therapy is necessary in the acute phase, since they allow rapid and safe titration to the goal blood pressure (table 6) [1].

Intravenous nitroprusside should be considered second-line therapy since it carries added theoretical risks of increasing intracranial pressure or affecting platelet function, but in fact it is often needed. Medications likely to cause a prolonged or precipitous decline in blood pressure (eg, rapid-acting formulations of nifedipine) should be avoided. In addition, their use is associated with an increased risk of stroke, particularly in older adult patients [80].

ACUTE THERAPY — For eligible patients (table 2) with acute ischemic stroke, we recommend intravenous alteplase therapy, provided that treatment is initiated within three hours of clearly defined symptom onset. For patients who cannot be treated in less than 3 hours, we suggest intravenous alteplase therapy, provided that treatment is initiated within 3 to 4.5 hours of clearly defined symptom onset. The eligibility criteria and utility of thrombolytic therapy as well as the treatment of patients not eligible for thrombolysis are discussed separately. (See "Intravenous fibrinolytic (thrombolytic) therapy in acute ischemic stroke: Therapeutic use" and "Antithrombotic treatment of acute ischemic stroke and transient ischemic attack".)

Ischemic stroke management — In addition to intravenous thrombolysis with alteplase, a number of interventions for ischemic stroke are associated with either reduced disability, complications, or stroke recurrence, including:

- Antithrombotic therapy initiated within 48 hours of stroke onset (see "Antithrombotic treatment of acute ischemic stroke and transient ischemic attack", section on 'Aspirin')
- Prophylaxis for deep venous thrombosis and pulmonary embolism (see "Medical complications of stroke", section on 'VTE prophylaxis')
- Antithrombotic therapy at discharge (see "Antiplatelet therapy for secondary prevention of stroke" and "Atrial fibrillation: Anticoagulant therapy to prevent embolization")
- Lipid lowering therapy initiation [81] (see "Overview of secondary prevention of ischemic stroke" and 'Statin therapy' below)
- Blood pressure reduction, once the acute phase of ischemic stroke has passed (see "Antihypertensive therapy to prevent recurrent stroke or transient ischemic attack" and "Overview of secondary prevention of ischemic stroke")

  Management of blood pressure in the acute phase of ischemic stroke is discussed above (see 'Blood pressure management' above).
- Smoking cessation along with management of obesity, diabetes, and metabolic syndrome are unproven but generally recommended as well (see "Overview of secondary prevention of ischemic stroke" and "Overview of smoking cessation management in adults")

Appropriate and timely use of these therapies should be considered as soon as ischemic stroke is recognized. Utilization of these interventions may be improved by the use of standardized stroke care orders or critical pathways beginning with hospital admission through discharge [1,82].

Statin therapy — Intensive lipid-lowering therapy with a statin is associated with a reduced risk of recurrent stroke and cardiovascular events, as discussed separately. (See "Overview of secondary prevention of ischemic stroke", section on 'Statin therapy'.)

A separate issue involves patients on statin therapy at the time of acute stroke. This issue was directly addressed in a single-center randomized controlled trial of 89 patients who were already treated with a statin and were assigned to continuation or cessation of statin therapy in the acute phase of ischemic stroke [83]. The rate of death or dependency at three months was significantly lower with continuation of statin treatment (39 versus 60 percent). The largest observational study, which evaluated over 12,000 subjects hospitalized with ischemic stroke, found that statin use before and during hospitalization was associated with improved outcome at hospital discharge and with improved survival at one year [84,85]. Furthermore, initiation of statin treatment early in hospitalization was associated with improved survival, while statin discontinuation early in hospitalization, even for a short period, was associated with decreased survival. Likewise, another uncontrolled study of 448 patients reported that new or continued statin treatment in the first 72 hours after acute ischemic stroke was associated with improved early and late (one-year) survival [86].

Based upon limited information, we suggest continuing statin treatment for patients receiving statin therapy prior to ischemic stroke onset. This suggestion is in accord with current guidelines [1].

An observational study of 2072 patients who received intravenous thrombolysis for acute ischemic stroke found that statin treatment started within 72 hours of thrombolysis was associated with a favorable functional outcome and a reduced risk of death at three months [87]. Of the 839 patients treated with statins, 65 percent were statin naïve. However, baseline differences in risk factors between the statin and no statin groups may have had a negative impact on the latter group. Therefore, data from

randomized controlled trials are needed to determine whether initiating statin therapy de novo in patients with acute ischemic stroke is beneficial.

SSRIs — There is some evidence from small randomized controlled trials suggesting that early initiation of selective serotonin-reuptake inhibitors (SSRIs) after ischemic stroke for patients with hemiparesis but without depression enhances motor recovery and reduces dependency [88-90]. However, it is unclear if this apparent benefit occurs through a reduction in poststroke depression or some other mechanism [91-93]. Larger trials are needed to determine the role of SSRIs for promoting recovery after ischemic stroke.

Intracranial hemorrhage management — The treatment of patients with intracerebral hemorrhage or subarachnoid hemorrhage is reviewed in detail elsewhere. (See "Spontaneous intracerebral hemorrhage: Treatment and prognosis" and "Treatment of aneurysmal subarachnoid hemorrhage".)

Neuroprotective treatment — Numerous neuroprotective agents have shown promising results in animal experiments. However, clinical trials have thus far failed to confirm consistent benefit [94-98]. This failure may be due, at least in part, to limitations of animal models of acute stroke and to shortcomings of clinical trials.

The search for effective neuroprotective treatment continues [96,99,100]. An updated list of all clinical trials for acute stroke, both in progress and completed, is available online at the Internet Stroke Center Trials Registry.

PREVENTION OF COMPLICATIONS — The prevention of medical complications of stroke is an important goal of stroke management, and this aspect of care begins with initial evaluation of the patient. Common acute and subacute medical problems associated with stroke include:

- Myocardial infarction
- Heart failure
- Dysphagia
- Aspiration pneumonia
- Urinary tract infection
- Deep vein thrombosis
- Pulmonary embolism
- Dehydration
- Malnutrition
- Pressure sores
- Orthopedic complications and contractures

The prevention, impact, and management of these complications are discussed separately. (See "Medical complications of stroke" and "Cardiac complications of stroke" and "Stroke-related pulmonary complications and abnormal respiratory patterns".)

Delirium, characterized by a disturbance of consciousness with decreased attention and disorganized thinking, is another potential complication of stroke [101]. In a meta-analysis of 10 prospective cohort studies, the incidence of post-stroke delirium ranged from 10 to 28 percent after the exclusion of one outlier study with a much higher rate [102]. Patients with delirium had longer hospital stays and higher inpatient and 12-month mortality rates. Risk factors for developing post-stroke delirium include preexisting cognitive decline, infection, and greater stroke severity [103]. (See "Diagnosis of delirium and confusional states" and "Delirium and acute confusional states: Prevention, treatment, and prognosis".)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have

about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient information: Stroke (The Basics)" and "Patient information: Hemorrhagic stroke (The Basics)")
- Beyond the Basics topics (see "Patient information: Stroke symptoms and diagnosis (Beyond the Basics)" and "Patient information: Ischemic stroke treatment (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- The main goals in the initial phase of acute stroke management are to ensure medical stability, to quickly reverse conditions that are contributing to the patient's problem, to determine if patients with acute ischemic stroke are candidates for thrombolytic therapy, and to begin to uncover the pathophysiologic basis of the neurologic symptoms. (See 'Initial assessment' above.)
- Important aspects of acute stroke evaluation and management include the following:
    - Assessing vital signs and ensuring stabilization of airway, breathing, and circulation (see 'Airway, breathing and circulation' above).
    - Obtaining a rapid but accurate history and examination to help distinguish between ischemic and hemorrhage stroke, and other disorders in the differential diagnosis (table 1) of acute stroke (see 'History and physical' above and 'Neurologic evaluation' above).
    - Obtaining urgent brain imaging (with CT or MRI) and other important laboratory studies, including cardiac monitoring during the first 24 hours after the onset of ischemic stroke (see 'Immediate laboratory studies' above and 'Neuroimaging' above and 'Cardiac studies' above).
    - Managing volume depletion and electrolyte disturbances (see 'Fluids' above).
    - Checking serum glucose. Low serum glucose (<60 mg/dL or 3.3 mmol/L) should be corrected rapidly. Normoglycemia is the desired goal while avoiding marked elevation of serum glucose. For patients who have elevated serum glucose concentrations >180 mg/dL (>10 mmol/L), we suggest treatment with insulin (**Grade 2C**).
    - Assessing swallowing and preventing aspiration (see 'Swallowing assessment' above and "Medical complications of stroke", section on 'Dysphagia and aspiration').
    - Optimizing head of bed position with respect to the risk of elevated intracranial pressure, aspiration, and the presence of comorbid cardiopulmonary disease; for patients in the acute phase of stroke who are at risk for elevated intracranial pressure, aspiration, cardiopulmonary decompensation, or oxygen desaturation, we recommend keeping the head in neutral alignment with the body and elevating the head of the bed to 30 degrees (**Grade 1C**); for patients in the acute phase of stroke who are not at risk for elevated intracranial pressure, aspiration, or worsening cardiopulmonary status, we suggest keeping the head of bed flat (0 to 15 degree head-of-bed position) (**Grade 2C**) (see 'Head and body position' above).
    - Evaluating and treating the source of fever; for patients with acute stroke, we suggest maintaining normothermia for at least the first several days after an acute stroke (**Grade 2C**) (see 'Fever' above).

- The management of blood pressure in acute stroke depends on the type of stroke. (See 'Blood pressure management' above.)
    - For patients with acute ischemic stroke who will receive thrombolytic therapy, antihypertensive treatment is recommended so that systolic blood pressure is ≤185 mmHg and diastolic blood pressure is ≤110 mmHg (table 6). This issue is discussed in detail separately. (See "Intravenous fibrinolytic (thrombolytic) therapy in acute ischemic stroke: Therapeutic use", section on 'Management of blood pressure'.)
    - For patients with acute ischemic stroke who are **not** treated with thrombolytic therapy, we suggest treating high blood pressure only if the hypertension is extreme (systolic blood pressure >220 mmHg or diastolic blood pressure >120 mmHg), or if the patient has another clear indication (active ischemic coronary disease, heart failure, aortic dissection, hypertensive encephalopathy, acute renal failure, or pre-eclampsia/eclampsia) (**Grade 2C**). When treatment is indicated, we suggest cautious lowering of blood pressure by approximately 15 percent during the first 24 hours after stroke onset (**Grade 2C**). (See 'Blood pressure goals ischemic stroke' above.)
    - In both intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH), the approach to blood pressure lowering must account for the potential benefits (eg, reducing further bleeding) and risks (eg, reducing cerebral perfusion). Recommendations for blood pressure management in acute ICH and SAH are discussed in detail separately (See 'Acute hemorrhagic stroke' above and "Spontaneous intracerebral hemorrhage: Treatment and prognosis", section on 'Blood pressure' and "Treatment of aneurysmal subarachnoid hemorrhage", section on 'Intracranial pressure'.)
- For eligible patients (table 2) with acute ischemic stroke, we recommend intravenous alteplase therapy, provided that treatment is initiated within three hours of clearly defined symptom onset. For patients who cannot be treated in less than 3 hours, we suggest intravenous alteplase therapy, provided that treatment is initiated within 3 to 4.5 hours of clearly defined symptom onset. The eligibility criteria and utility of thrombolytic therapy as well as the treatment of patients not eligible for thrombolysis are discussed separately. (See "Intravenous fibrinolytic (thrombolytic) therapy in acute ischemic stroke: Therapeutic use" and "Reperfusion therapy for acute ischemic stroke" and "Antithrombotic treatment of acute ischemic stroke and transient ischemic attack".)
- In addition to intravenous alteplase treatment, a number of interventions for ischemic stroke are associated with either reduced disability, complications, or stroke recurrence, including (see 'Acute therapy' above):
    - Antithrombotic therapy initiated within 48 hours of stroke onset. (See "Antithrombotic treatment of acute ischemic stroke and transient ischemic attack", section on 'Aspirin'.)
    - Prophylaxis for deep venous thrombosis and pulmonary embolism. (See "Medical complications of stroke", section on 'VTE prophylaxis'.)
    - For patients receiving statin therapy prior to stroke onset, we suggest continuing statin treatment (**Grade 2C**). (See 'Statin therapy' above.)

ACKNOWLEDGMENT — The editorial staff at UpToDate would like to acknowledge Walter J Koroshetz, MD, who contributed to an earlier version of this topic review.

REFERENCES

1. Jauch EC, Saver JL, Adams HP Jr, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013; 44:870.
2. Hemphill JC 3rd, Greenberg SM, Anderson CS, et al. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2015; 46:2032.
3. Connolly ES Jr, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/american Stroke Association. Stroke 2012; 43:1711.
4. Goldstein LB, Samsa GP. Reliability of the National Institutes of Health Stroke Scale. Extension to non-neurologists in the context of a clinical trial. Stroke 1997; 28:307.
5. Kothari R, Hall K, Brott T, Broderick J. Early stroke recognition: developing an out-of-hospital NIH Stroke Scale. Acad Emerg Med 1997; 4:986.
6. Goldstein LB, Simel DL. Is this patient having a stroke? JAMA 2005; 293:2391.
7. Generalized efficacy of t-PA for acute stroke. Subgroup analysis of the NINDS t-PA Stroke Trial. Stroke 1997; 28:2119.
8. Adams HP Jr, Davis PH, Leira EC, et al. Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). Neurology 1999; 53:126.
9. Adams HP Jr, del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Stroke 2007; 38:1655.
10. Michaels AD, Spinler SA, Leeper B, et al. Medication errors in acute cardiovascular and stroke patients: a scientific statement from the American Heart Association. Circulation 2010; 121:1664.
11. Rodriguez GJ, Cordina SM, Vazquez G, et al. The hydration influence on the risk of stroke (THIRST) study. Neurocrit Care 2009; 10:187.
12. Burns JD, Green DM, Metivier K, DeFusco C. Intensive care management of acute ischemic stroke. Emerg Med Clin North Am 2012; 30:713.
13. Weir CJ, Murray GD, Dyker AG, Lees KR. Is hyperglycaemia an independent predictor of poor outcome after acute stroke? Results of a long-term follow up study. BMJ 1997; 314:1303.
14. Bruno A, Biller J, Adams HP Jr, et al. Acute blood glucose level and outcome from ischemic stroke. Trial of ORG 10172 in Acute Stroke Treatment (TOAST) Investigators. Neurology 1999; 52:280.
15. Capes SE, Hunt D, Malmberg K, et al. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. Stroke 2001; 32:2426.
16. Dave JA, Engel ME, Freercks R, et al. Abnormal glucose metabolism in non-diabetic patients presenting with an acute stroke: prospective study and systematic review. QJM 2010; 103:495.
17. Béjot Y, Aboa-Eboulé C, Hervieu M, et al. The deleterious effect of admission hyperglycemia on survival and functional outcome in patients with intracerebral hemorrhage. Stroke 2012; 43:243.
18. Allport L, Baird T, Butcher K, et al. Frequency and temporal profile of poststroke hyperglycemia using continuous glucose monitoring. Diabetes Care 2006; 29:1839.
19. Lindsberg PJ, Roine RO. Hyperglycemia in acute stroke. Stroke 2004; 35:363.
20. Parsons MW, Barber PA, Desmond PM, et al. Acute hyperglycemia adversely affects stroke outcome: a magnetic resonance imaging and spectroscopy study. Ann Neurol 2002; 52:20.
21. Bruno A, Levine SR, Frankel MR, et al. Admission glucose level and clinical outcomes in the NINDS rt-PA Stroke Trial. Neurology 2002; 59:669.
22. European Stroke Initiative Executive Committee, EUSI Writing Committee, Olsen TS, et al. European Stroke Initiative Recommendations for Stroke Management-update 2003. Cerebrovasc Dis 2003; 16:311.

23. Stroke Hyperglycemia Insulin Network Effort (SHINE) Trial. http://clinicaltrials.gov/ct2/show/NCT01369069 (Accessed on March 21, 2013).
24. Bruno A, Durkalski VL, Hall CE, et al. The Stroke Hyperglycemia Insulin Network Effort (SHINE) trial protocol: a randomized, blinded, efficacy trial of standard vs. intensive hyperglycemia management in acute stroke. Int J Stroke 2014; 9:246.
25. Bellolio MF, Gilmore RM, Ganti L. Insulin for glycaemic control in acute ischaemic stroke. Cochrane Database Syst Rev 2014; 1:CD005346.
26. Schwarz S, Georgiadis D, Aschoff A, Schwab S. Effects of body position on intracranial pressure and cerebral perfusion in patients with large hemispheric stroke. Stroke 2002; 33:497.
27. Wojner-Alexander AW, Garami Z, Chernyshev OY, Alexandrov AV. Heads down: flat positioning improves blood flow velocity in acute ischemic stroke. Neurology 2005; 64:1354.
28. Toole JF. Effects of change of head, limb and body position on cephalic circulation. N Engl J Med 1968; 279:307.
29. Caplan LR, Sergay S. Positional cerebral ischaemia. J Neurol Neurosurg Psychiatry 1976; 39:385.
30. Silver FL, Norris JW, Lewis AJ, Hachinski VC. Early mortality following stroke: a prospective review. Stroke 1984; 15:492.
31. Frank JI. Large hemispheric infarction, deterioration, and intracranial pressure. Neurology 1995; 45:1286.
32. Hacke W, Schwab S, Horn M, et al. 'Malignant' middle cerebral artery territory infarction: clinical course and prognostic signs. Arch Neurol 1996; 53:309.
33. Poca MA, Benejam B, Sahuquillo J, et al. Monitoring intracranial pressure in patients with malignant middle cerebral artery infarction: is it useful? J Neurosurg 2010; 112:648.
34. Wijdicks EF, Sheth KN, Carter BS, et al. Recommendations for the management of cerebral and cerebellar infarction with swelling: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2014; 45:1222.
35. Rowat AM, Wardlaw JM, Dennis MS, Warlow CP. Patient positioning influences oxygen saturation in the acute phase of stroke. Cerebrovasc Dis 2001; 12:66.
36. Tyson SF, Nightingale P. The effects of position on oxygen saturation in acute stroke: a systematic review. Clin Rehabil 2004; 18:863.
37. Summers D, Leonard A, Wentworth D, et al. Comprehensive overview of nursing and interdisciplinary care of the acute ischemic stroke patient: a scientific statement from the American Heart Association. Stroke 2009; 40:2911.
38. Fernández-Crehuet R, Díaz-Molina C, de Irala J, et al. Nosocomial infection in an intensive-care unit: identification of risk factors. Infect Control Hosp Epidemiol 1997; 18:825.
39. AVERT Trial Collaboration group, Bernhardt J, Langhorne P, et al. Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised controlled trial. Lancet 2015; 386:46.
40. Ginsberg MD, Busto R. Combating hyperthermia in acute stroke: a significant clinical concern. Stroke 1998; 29:529.
41. Greer DM, Funk SE, Reaven NL, et al. Impact of fever on outcome in patients with stroke and neurologic injury: a comprehensive meta-analysis. Stroke 2008; 39:3029.
42. Saini M, Saqqur M, Kamruzzaman A, et al. Effect of hyperthermia on prognosis after acute ischemic stroke. Stroke 2009; 40:3051.
43. Phipps MS, Desai RA, Wira C, Bravata DM. Epidemiology and outcomes of fever burden among patients with acute ischemic stroke. Stroke 2011; 42:3357.
44. Prasad K, Krishnan PR. Fever is associated with doubling of odds of short-term mortality in ischemic stroke: an updated meta-analysis. Acta Neurol Scand 2010; 122:404.
45. den Hertog HM, van der Worp HB, van Gemert HM, et al. The Paracetamol (Acetaminophen) In Stroke (PAIS) trial: a multicentre, randomised, placebo-controlled, phase III trial. Lancet Neurol 2009; 8:434.
46. Den Hertog HM, van der Worp HB, Tseng MC, Dippel DW. Cooling therapy for acute stroke. Cochrane Database Syst Rev 2009; :CD001247.

47. The Intravascular Cooling in the Treatment of Stroke 2/3 Trial (ICTuS2/3). http://clinicaltrials.gov/ct2/show/NCT01123161 (Accessed on June 15, 2011).
48. Candelise L, Gattinoni M, Bersano A, et al. Stroke-unit care for acute stroke patients: an observational follow-up study. Lancet 2007; 369:299.
49. Meretoja A, Roine RO, Kaste M, et al. Effectiveness of primary and comprehensive stroke centers: PERFECT stroke: a nationwide observational study from Finland. Stroke 2010; 41:1102.
50. Di Carlo A, Lamassa M, Wellwood I, et al. Stroke unit care in clinical practice: an observational study in the Florence center of the European Registers of Stroke (EROS) Project. Eur J Neurol 2011; 18:686.
51. Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke. Cochrane Database Syst Rev 2013; 9:CD000197.
52. Alberts MJ, Latchaw RE, Jagoda A, et al. Revised and updated recommendations for the establishment of primary stroke centers: a summary statement from the brain attack coalition. Stroke 2011; 42:2651.
53. Alberts MJ, Latchaw RE, Selman WR, et al. Recommendations for comprehensive stroke centers: a consensus statement from the Brain Attack Coalition. Stroke 2005; 36:1597.
54. Alberts MJ. Stroke centers: proof of concept and the concept of proof. Stroke 2010; 41:1100.
55. Middleton S, McElduff P, Ward J, et al. Implementation of evidence-based treatment protocols to manage fever, hyperglycaemia, and swallowing dysfunction in acute stroke (QASC): a cluster randomised controlled trial. Lancet 2011; 378:1699.
56. European Stroke Organisation (ESO) Executive Committee, ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovasc Dis 2008; 25:457.
57. Qureshi AI. Acute hypertensive response in patients with stroke: pathophysiology and management. Circulation 2008; 118:176.
58. Aiyagari V, Gorelick PB. Management of blood pressure for acute and recurrent stroke. Stroke 2009; 40:2251.
59. Wallace JD, Levy LL. Blood pressure after stroke. JAMA 1981; 246:2177.
60. Leonardi-Bee J, Bath PM, Phillips SJ, et al. Blood pressure and clinical outcomes in the International Stroke Trial. Stroke 2002; 33:1315.
61. Okumura K, Ohya Y, Maehara A, et al. Effects of blood pressure levels on case fatality after acute stroke. J Hypertens 2005; 23:1217.
62. Bath PM. How to manage blood pressure in acute stroke. J Hypertens 2005; 23:1135.
63. Berge E. Should high blood pressure be lowered in the acute stroke? J Hypertens 2011; 29:1478.
64. Oliveira-Filho J, Silva SC, Trabuco CC, et al. Detrimental effect of blood pressure reduction in the first 24 hours of acute stroke onset. Neurology 2003; 61:1047.
65. Vlcek M, Schillinger M, Lang W, et al. Association between course of blood pressure within the first 24 hours and functional recovery after acute ischemic stroke. Ann Emerg Med 2003; 42:619.
66. Castillo J, Leira R, García MM, et al. Blood pressure decrease during the acute phase of ischemic stroke is associated with brain injury and poor stroke outcome. Stroke 2004; 35:520.
67. Mistri AK, Robinson TG, Potter JF. Pressor therapy in acute ischemic stroke: systematic review. Stroke 2006; 37:1565.
68. Rordorf G, Cramer SC, Efird JT, et al. Pharmacological elevation of blood pressure in acute stroke. Clinical effects and safety. Stroke 1997; 28:2133.
69. Rordorf G, Koroshetz WJ, Ezzeddine MA, et al. A pilot study of drug-induced hypertension for treatment of acute stroke. Neurology 2001; 56:1210.
70. Hillis AE, Barker PB, Beauchamp NJ, et al. Restoring blood pressure reperfused Wernicke's area and improved language. Neurology 2001; 56:670.
71. Marzan AS, Hungerbühler HJ, Studer A, et al. Feasibility and safety of norepinephrine-induced arterial hypertension in acute ischemic stroke. Neurology 2004; 62:1193.
72. Saver JL. Time is brain--quantified. Stroke 2006; 37:263.

73. He J, Zhang Y, Xu T, et al. Effects of immediate blood pressure reduction on death and major disability in patients with acute ischemic stroke: the CATIS randomized clinical trial. JAMA 2014; 311:479.
74. Sandset EC, Bath PM, Boysen G, et al. The angiotensin-receptor blocker candesartan for treatment of acute stroke (SCAST): a randomised, placebo-controlled, double-blind trial. Lancet 2011; 377:741.
75. Robinson TG, Potter JF, Ford GA, et al. Effects of antihypertensive treatment after acute stroke in the Continue or Stop Post-Stroke Antihypertensives Collaborative Study (COSSACS): a prospective, randomised, open, blinded-endpoint trial. Lancet Neurol 2010; 9:767.
76. ENOS Trial Investigators, Bath PM, Woodhouse L, et al. Efficacy of nitric oxide, with or without continuing antihypertensive treatment, for management of high blood pressure in acute stroke (ENOS): a partial-factorial randomised controlled trial. Lancet 2015; 385:617.
77. Wang H, Tang Y, Rong X, et al. Effects of early blood pressure lowering on early and long-term outcomes after acute stroke: an updated meta-analysis. PLoS One 2014; 9:e97917.
78. Lee M, Ovbiagele B, Hong KS, et al. Effect of Blood Pressure Lowering in Early Ischemic Stroke: Meta-Analysis. Stroke 2015; 46:1883.
79. National Institute for Health and Clinical Excellence. Stroke: The diagnosis and acute management of stroke and transient ischaemic attacks. Royal College of Physicians, London 2008. http://www.nice.org.uk/CG068 (Accessed on February 01, 2011).
80. Jung SY, Choi NK, Kim JY, et al. Short-acting nifedipine and risk of stroke in elderly hypertensive patients. Neurology 2011; 77:1229.
81. Yeh PS, Lin HJ, Bai CH, et al. Effect of in-hospital initiation of lipid-lowering therapy on six-month outcomes in patients with acute ischemic stroke or transient ischemic attack. Am J Cardiol 2010; 105:1490.
82. California Acute Stroke Pilot Registry Investigators. The impact of standardized stroke orders on adherence to best practices. Neurology 2005; 65:360.
83. Blanco M, Nombela F, Castellanos M, et al. Statin treatment withdrawal in ischemic stroke: a controlled randomized study. Neurology 2007; 69:904.
84. Flint AC, Kamel H, Navi BB, et al. Statin use during ischemic stroke hospitalization is strongly associated with improved poststroke survival. Stroke 2012; 43:147.
85. Flint AC, Kamel H, Navi BB, et al. Inpatient statin use predicts improved ischemic stroke discharge disposition. Neurology 2012; 78:1678.
86. Ní Chróinín D, Callaly EL, Duggan J, et al. Association between acute statin therapy, survival, and improved functional outcome after ischemic stroke: the North Dublin Population Stroke Study. Stroke 2011; 42:1021.
87. Cappellari M, Bovi P, Moretto G, et al. The THRombolysis and STatins (THRaST) study. Neurology 2013; 80:655.
88. Mead GE, Hsieh CF, Lee R, et al. Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery. Cochrane Database Syst Rev 2012; 11:CD009286.
89. Chollet F, Tardy J, Albucher JF, et al. Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial. Lancet Neurol 2011; 10:123.
90. Mead GE, Hsieh CF, Hackett M. Selective serotonin reuptake inhibitors for stroke recovery. JAMA 2013; 310:1066.
91. Chollet F. Selective serotonin reuptake inhibitors may be helpful in most patients with stroke. Stroke 2012; 43:3150.
92. Marshall RS. Should every patient with stroke be on selective serotonin reuptake inhibitors? No. Stroke 2012; 43:3152.
93. Selim MH, Molina CA. Poststroke treatment with selective serotonin reuptake inhibitors: a journey from sadness to motor recovery. Stroke 2012; 43:3154.
94. Dávalos A, Alvarez-Sabín J, Castillo J, et al. Citicoline in the treatment of acute ischaemic stroke: an international, randomised, multicentre, placebo-controlled study (ICTUS trial). Lancet 2012; 380:349.
95. Reza Noorian A, Nogueira R, Gupta R. Neuroprotection in acute ischemic stroke. J Neurosurg Sci 2011; 55:127.

96. Sahota P, Savitz SI. Investigational therapies for ischemic stroke: neuroprotection and neurorecovery. Neurotherapeutics 2011; 8:434.
97. Tymianski M. Can molecular and cellular neuroprotection be translated into therapies for patients?: yes, but not the way we tried it before. Stroke 2010; 41:S87.
98. Ginsberg MD, Palesch YY, Hill MD, et al. High-dose albumin treatment for acute ischaemic stroke (ALIAS) Part 2: a randomised, double-blind, phase 3, placebo-controlled trial. Lancet Neurol 2013; 12:1049.
99. Hill MD, Martin RH, Mikulis D, et al. Safety and efficacy of NA-1 in patients with iatrogenic stroke after endovascular aneurysm repair (ENACT): a phase 2, randomised, double-blind, placebo-controlled trial. Lancet Neurol 2012; 11:942.
100. Wu TC, Grotta JC. Hypothermia for acute ischaemic stroke. Lancet Neurol 2013; 12:275.
101. Balami JS, Chen RL, Grunwald IQ, Buchan AM. Neurological complications of acute ischaemic stroke. Lancet Neurol 2011; 10:357.
102. Shi Q, Presutti R, Selchen D, Saposnik G. Delirium in acute stroke: a systematic review and meta-analysis. Stroke 2012; 43:645.
103. Oldenbeuving AW, de Kort PL, Jansen BP, et al. Delirium in the acute phase after stroke: incidence, risk factors, and outcome. Neurology 2011; 76:993.

Topic 1126 Version 41.0

GRAPHICS

Acute stroke differential diagnosis

Migraine aura
Seizure with postictal paresis (Todd paralysis), aphasia, or neglect
Central nervous system tumor or abscess
Functional deficit (conversion reaction)
Hypertensive encephalopathy
Head trauma
Mitochondrial disorder (eg, mitochondrial encephalopathy with lactic acidosis and stroke-like episodes or MELAS)
Multiple sclerosis
Posterior reversible encephalopathy syndrome (PRES)
Spinal cord disorder (eg, compressive myelopathy, spinal dural arteriovenous fistula)
Subdural hematoma
Syncope
Systemic infection
Toxic-metabolic disturbance (eg, hypoglycemia, exogenous drug intoxication)
Transient global amnesia
Viral encephalitis (eg, herpes simplex encephalitis)
Wernicke encephalopathy

Graphic 69869 Version 6.0

Eligibility criteria for the treatment of acute ischemic stroke with recombinant tissue plasminogen activator (alteplase)

Inclusion criteria
Clinical diagnosis of ischemic stroke causing measurable neurologic deficit
Onset of symptoms <4.5 hours before beginning treatment; if the exact time of stroke onset is not known, it is defined as the last time the patient was known to be normal
Age ≥18 years
Exclusion criteria
Historical
Significant stroke or head trauma in the previous three months
Previous intracranial hemorrhage
Intracranial neoplasm, arteriovenous malformation, or aneurysm
Recent intracranial or intraspinal surgery
Arterial puncture at a noncompressible site in the previous seven days
Clinical
Symptoms suggestive of subarachnoid hemorrhage
Persistent blood pressure elevation (systolic ≥185 mmHg or diastolic ≥110 mmHg)
Serum glucose <50 mg/dL (<2.8 mmol/L)
Active internal bleeding
Acute bleeding diathesis, including but not limited to conditions defined in 'Hematologic'
Hematologic
Platelet count <100,000/mm^3*
Current anticoagulant use with an INR >1.7 or PT >15 seconds*
Heparin use within 48 hours and an abnormally elevated aPTT*
Current use of a direct thrombin inhibitor or direct factor Xa inhibitor with evidence of anticoagulant effect by laboratory tests such as aPTT, INR, ECT, TT, or appropriate factor Xa activity assays
Head CT scan
Evidence of hemorrhage
Evidence of a multilobar infarction with hypodensity involving >33 percent of the cerebral hemisphere
Relative exclusion criteria¶
Only minor and isolated neurologic signs
Rapidly improving stroke symptoms
Major surgery or serious trauma in the previous 14 days
Gastrointestinal or urinary tract bleeding in the previous 21 days
Myocardial infarction in the previous three months

Seizure at the onset of stroke with postictal neurologic impairments
Pregnancy
Additional relative exclusion criteria for treatment from 3 to 4.5 hours from symptom onset
Age >80 years
Oral anticoagulant use regardless of INR
Severe stroke (NIHSS score >25)
Combination of both previous ischemic stroke and diabetes mellitus

aPTT: activated partial thromboplastin time; ECT: ecarin clotting time; INR: international normalized ratio; PT: prothrombin time; NIHSS: National Institutes of Health Stroke Scale; TT: thrombin time.

* Although it is desirable to know the results of these tests, thrombolytic therapy should not be delayed while results are pending unless (1) there is clinical suspicion of a bleeding abnormality or thrombocytopenia, (2) the patient is currently on or has recently received anticoagulants (eg, heparin, warfarin, a direct thrombin inhibitor, or a direct factor Xa inhibitor), (3) use of anticoagulants is not known. For patients without recent use of oral anticoagulants or heparin, treatment with intravenous tPA can be started before availability of coagulation test results but should be discontinued if the INR, PT, or aPTT exceed the limits stated in the table.

¶ The available data suggest that under some circumstances – with careful consideration and weighting of risk-to-benefit – patients may receive fibrinolytic therapy despite one or more relative contraindications. In particular, there is now consensus that patients who have a persistent neurologic deficit that is potentially disabling, despite improvement of any degree, should be treated with tPA in the absence of other contraindications. Any of the following should be considered disabling deficits:

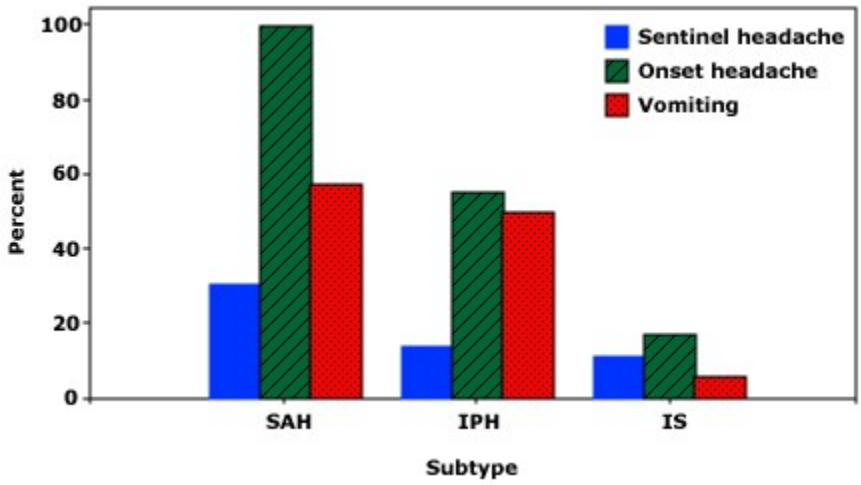
- Complete hemianopsia: ≥2 on NIHSS question 3, or
- Severe aphasia: ≥2 on NIHSS question 9, or
- Visual or sensory extinction: ≥1 on NIHSS question 11, or
- Any weakness limiting sustained effort against gravity: ≥2 on NIHSS question 5 or 6, or
- Any deficits that lead to a total NIHSS >5, or
- Any remaining deficit considered potentially disabling in the view of the patient and the treating practitioner using clinical judgement.

Adapted from:

1. *Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 2008; 359:1317.*
2. *Del Zoppo GJ, Saver JL, Jauch EC, et al. Expansion of the time window for treatment of acute ischemic stroke with intravenous tissue plasminogen activator. A science advisory from the American Heart Association/American Stroke Association. Stroke 2009; 40:2945.*
3. *Jauch EC, Saver JL, Adams HP Jr, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013; 44:870.*
4. *Re-examining Acute Eligibility for Thrombolysis (TREAT) Task Force:, Levine SR, Khatri P, et al. Review, historical context, and clarifications of the NINDS rt-PA stroke trials exclusion criteria: Part 1: rapidly improving stroke symptoms. Stroke 2013; 44:2500.*

Graphic 71462 Version 13.0

Headache and vomiting in stroke subtypes



The frequency of sentinel headache, onset headache, and vomiting in three subtypes of stroke: subarachnoid hemorrhage (SAH), intraparenchymal (intracerebral) hemorrhage (IPH), and ischemic stroke (IS). Onset headache was present in virtually all patients with SAH and about one-half of those with IPH; all of these symptoms were infrequent in patients with IS.

Data from: Gorelick PB, Hier DB, Caplan LR, et al, Neurology 1986; 36:1445.

Graphic 60831 Version 3.0

Acute stroke syndromes according to vascular territory and mechanism

Artery involved	Syndrome	Pathophysiology
Anterior cerebral artery	Motor and/or sensory deficit (leg >> face, arm) Grasp, sucking reflexes Abulia, paratonic rigidity, gait apraxia	Embolic > atherothrombotic
Middle cerebral artery	Dominant hemisphere: aphasia, motor and sensory deficit (face, arm > leg > foot), may be complete hemiplegia if internal capsule involved, homonymous hemianopia Non-dominant hemisphere: neglect, anosognosia, motor and sensory deficit (face, arm > leg > foot), homonymous hemianopia	Embolic > atherothrombotic
Posterior cerebral artery	Homonymous hemianopia; alexia without agraphia (dominant hemisphere); visual hallucinations, visual perseverations (calcarine cortex); sensory loss, choreoathetosis, spontaneous pain (thalamus); III nerve palsy, paresis of vertical eye movement, motor deficit (cerebral peduncle, midbrain)	Embolic > atherothrombotic
Penetrating vessels	Pure motor hemiparesis (classic lacunar syndromes) Pure sensory deficit Pure sensory-motor deficit Hemiparesis, homolateral ataxia Dysarthria/clumsy hand	Small artery (lacunar) infarct
Vertebrobasilar	Cranial nerve palsies Crossed sensory deficits Diplopia, dizziness, nausea, vomiting, dysarthria, dysphagia, hiccup Limb and gait ataxia Motory deficit Coma Bilateral signs suggest basilar artery disease	Embolic = atherothrombotic
Internal carotid artery	Progressive or stuttering onset of MCA syndrome, occasionally ACA syndrome as well if insufficient collateral flow	Atherothrombotic > embolic

Graphic 75487 Version 4.0

National Institutes of Health Stroke Scale (NIHSS)

Administer stroke scale items in the order listed. Record performance in each category after each subscale exam. Do not go back and change scores. Follow directions provided for each exam technique. Scores should reflect what the patient does, not what the clinician thinks the patient can do. The clinician should record answers while administering the exam and work quickly. Except where indicated, the patient should not be coached (ie, repeated requests to patient to make a special effort).

Instructions	Scale definition	Score
1a. Level of consciousness: The investigator must choose a response if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.	0 = **Alert;** keenly responsive. 1 = **Not alert;** but arousable by minor stimulation to obey, answer, or respond. 2 = **Not alert;** requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped). 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and areflexic.	_____
1b. LOC questions: The patient is asked the month and his/her age. The answer must be correct - there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues.	0 = **Answers** both questions correctly. 1 = **Answers** one question correctly. 2 = **Answers** neither question correctly.	_____
1c. LOC commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him or her (pantomime), and the result scored (ie, follows none, one or two commands). Patients with trauma, amputation, or other physical	0 = **Performs** both tasks correctly. 1 = **Performs** one task correctly. 2 = **Performs** neither task correctly.	_____

impediments should be given suitable one-step commands. Only the first attempt is scored.		
2. Best gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored, but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI), score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements, and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.	0 = **Normal.** 1 = **Partial gaze palsy;** gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present. 2 = **Forced deviation,** or total gaze paresis not overcome by the oculocephalic maneuver.	_____
3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat, as appropriate. Patients may be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia, is found. If patient is blind from any cause, score 3. Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a 1, and the results are used to respond to item 11.	0 = **No visual loss.** 1 = **Partial hemianopia.** 2 = **Complete hemianopia.** 3 = **Bilateral hemianopia** (blind including cortical blindness).	_____
4. Facial palsy: Ask - or use pantomime to encourage - the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barriers obscure	0 = **Normal** symmetrical movements. 1 = **Minor paralysis** (flattened nasolabial fold, asymmetry on smiling). 2 = **Partial paralysis** (total or near-total paralysis of lower face). 3 = **Complete paralysis** of one or both sides (absence of facial movement in the upper and lower face).	_____

the face, these should be removed to the extent possible.		
5. Motor arm: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine). Drift is scored if the arm falls before 10 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** limb holds 90 (or 45) degrees for full 10 seconds. 1 = **Drift;** limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 = **Some effort against gravity;** limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = **No effort against gravity;** limb falls. 4 = **No movement.** UN = **Amputation** or joint fusion, explain:_____ **5a. Left arm** **5b. Right arm**	_____
6. Motor leg: The limb is placed in the appropriate position: hold the leg at 30 degrees (always tested supine). Drift is scored if the leg falls before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic leg. Only in the case of amputation or joint fusion at the hip, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** leg holds 30-degree position for full 5 seconds. 1 = **Drift;** leg falls by the end of the 5-second period but does not hit bed. 2 = **Some effort against gravity;** leg falls to bed by 5 seconds, but has some effort against gravity. 3 = **No effort against gravity;** leg falls to bed immediately. 4 = **No movement.** UN = **Amputation** or joint fusion, explain:_____ **6a. Left leg** **6b. Right leg**	_____
7. Limb ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion, the examiner should record the score as untestable (UN), and clearly write	0 = **Absent.** 1 = **Present in one limb.** 2 = **Present in two limbs.** UN = **Amputation** or joint fusion, explain:_____	_____

the explanation for this choice. In case of blindness, test by having the patient touch nose from extended arm position.		
8. Sensory: Sensation or grimace to pinprick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for hemisensory loss. A score of 2, "severe or total sensory loss," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will, therefore, probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (item 1a=3) are automatically given a 2 on this item.	0 = **Normal;** no sensory loss. 1 = **Mild-to-moderate sensory loss;** patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched. 2 = **Severe to total sensory loss;** patient is not aware of being touched in the face, arm, and leg.	_____
9. Best language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For this scale item, the patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet and to read from the attached list of sentences. Comprehension is judged from responses here, as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in a coma (item 1a=3) will automatically score 3 on this item. The examiner must choose a score for the patient with stupor or limited cooperation, but a score of 3 should be used only if the patient is mute and follows no one-step commands.	0 = **No aphasia;** normal. 1 = **Mild-to-moderate aphasia;** some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response. 2 = **Severe aphasia;** all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = **Mute, global aphasia;** no usable speech or auditory comprehension.	_____
	0 = **Normal.**	_____

10. Dysarthria: If patient is thought to be normal, an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barriers to producing speech, the examiner should record the score as untestable (UN), and clearly write an explanation for this choice. Do not tell the patient why he or she is being tested.	1 = **Mild-to-moderate dysarthria;** patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = **Severe dysarthria;** patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. UN = **Intubated** or other physical barrier, explain:_____	
11. Extinction and inattention (formerly neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosognosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.	0 = **No abnormality.** 1 = **Visual, tactile, auditory, spatial, or personal inattention** or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = **Profound hemi-inattention or extinction to more than one modality;** does not recognize own hand or orients to only one side of space.	_____
		_____

Adapted from: Goldstein LB, Samsa GP, Stroke 1997; 28:307.

Graphic 61698 Version 4.0

Stroke outcome at three months in the placebo group of the NINDS trial

Baseline NIHSS score	Percent with favorable outcome (three-month NIHSS score = 0 or 1)
Age <60 y	
0-9	42
10-14	18
15-20	27
>20	12
Age 61-68 y	
0-9	37
10-14	25
15-20	25
>20	0
Age 69-75 y	
0-9	54
10-14	27
15-20	0
>20	0
Age >75 y	
0-9	36
10-14	15
15-20	6
>20	0

NIHSS: National Institutes of Health Stroke Scale.

Adapted from: NINDS t-PA Stroke Study Group, Stroke 1997; 28:2119.

Graphic 81859 Version 4.0

Potential approaches to arterial hypertension in patients with acute ischemic stroke who are candidates for acute reperfusion therapy

Patient otherwise eligible for acute reperfusion therapy except that blood pressure is >185/110 mmHg
Labetalol 10 to 20 mg intravenously over 1 to 2 minutes, may repeat one time; **or**
Nicardipine 5 mg/hour intravenously, titrate up by 2.5 mg/hour every 5 to 15 minutes, maximum 15 mg/hour; when desired blood pressure reached, adjust to maintain proper blood pressure limits; **or**
Other agents (hydralazine, enalaprilat, etc) may be considered when appropriate
If blood pressure is not maintained at or below 185/110 mmHg, do **not** administer rtPA
Management to maintain blood pressure at or below 180/105 mmHg during and after acute reperfusion therapy
Monitor blood pressure every 15 minutes for 2 hours from the start of rtPA therapy, then every 30 minutes for 6 hours, and then every hour for 16 hours
If systolic blood pressure is >180 to 230 mmHg or diastolic is >105 to 120 mmHg:
Labetalol 10 mg intravenously followed by continuous infusion 2 to 8 mg/min; **or**
Nicardipine 5 mg/hour intravenously, titrate up to desired effect by 2.5 mg/hour every 5 to 15 minutes, maximum 15 mg/hour
If blood pressure is not controlled or diastolic blood pressure >140 mmHg, consider intravenous sodium nitroprusside

rtPA: recombinant tissue-type plasminogen activator.

Graphic 50725 Version 13.0

Disclosures

Disclosures: **Jamary Oliveira Filho, MD, MS, PhD** Nothing to disclose. **Scott E Kasner, MD** Grant/Research/Clinical Trial Support: WL Gore and Associates [PFO, stroke (HELEX, GSO devices)]; AstraZeneca [Stroke (Ticagrelor)]. Consultant/Advisory Boards: Medtronic [Stroke, atrial fibrillation (CoreValve, REVEAL)]; Merck [Stroke]; Pfizer [Stroke]; Novartis [Stroke]; GSK [Stroke]; AbbVie [Stroke]; Daiichi Sankyo [Stroke]; Boehringer Ingelheim [Stroke]. **John F Dashe, MD, PhD** Nothing to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy