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What imaging can disclose about suspected stroke and its Tx

Selecting useful modalities is key in early and later management of an acute ischemic event. This review—augmented by an at-a-glance table—can inform your care.

Stroke ranks second behind heart disease as the leading cause of mortality worldwide, accounting for 1 of every 19 deaths,[1] and remains a serious cause of morbidity. Best practices in stroke diagnosis and management can seem elusive to front-line clinicians, for 2 reasons: the rate of proliferation and nuance in stroke medicine and the fact that the typical scope of primary care practice exists apart from much of the diagnostic tools and management schema provided in stroke centers.[2] In this article, we describe and update the diagnosis of stroke and review imaging modalities, their nuances, and their application in practice.

Diagnosis of acute stroke

Acute stroke is diagnosed upon observation of new neurologic deficits and congruent neuroimaging. Some updated definitions favor a silent form of cerebral ischemia manifested by imaging pathology only; this form is not discussed in this article. Although there are several characteristically distinct stroke syndromes, there is no way to *clinically* distinguish ischemic pathology from hemorrhagic pathology.

Some common symptoms that should prompt evaluation for stroke are part of the American Stroke Association FAST mnemonic designed to promote public health awareness[3-5]:

- *F*ace drooping
- *A*rm weakness
- *S*peech difficulty
- *T*ime to call 911.

Other commonly reported stroke symptoms include unilateral weakness or numbness, confusion, word-finding difficulty, visual problems, difficulty ambulating, dizziness, loss of balance or coordination, and thunderclap headache. A stroke should also be considered in the presence of any new focal neurologic deficit.[3,4]

Stroke patients should be triaged by emergency medical services using a stroke screening scale, such as BE-FAST[5] (a modification of FAST that adds balance and eye assessments); the Los Angeles Prehospital Stroke Screen (LAPSS)[6,7]; the Rapid Arterial oCclusion Evaluation (RACE)[8]; and the Cincinnati Prehospital Stroke Severity Scale (CP-SSS)[9,10] (see "Stroke screening scales for early identification and triage" on page 444). Studies have not found that any single prehospital stroke scale is superior to the others for reliably predicting large-vessel occlusion; therefore, prehospital assessment is typically based on practice patterns in a given locale.[11] A patient (or family member or caregiver) who seeks your care for stroke symptoms should be told to call 911 and get emergency transport to a health care facility that can capably administer intravenous (IV) thrombolysis.[a]

First responders should elicit "last-known-normal" time; this critical information can aid in diagnosis and drive therapeutic options, especially if patients are unaccompanied at time of transport to a higher echelon of care. A point-of-care blood glucose test should be performed by emergency medical staff, with dextrose administered for a level < 45 mg/dL. Establishing IV access for fluids, medications, and contrast can be considered if it does not delay transport. A 12-lead electrocardiogram can also be considered, again, as long as it does not delay transport to a facility capable of providing definitive therapy. Notification by emergency services staff before arrival and transport of the patient to such a facility is the essential element of prehospital care, and should be prioritized above ancillary testing beyond the stroke assessment.[14]

Guidelines recommend use of the National Institutes of Health Stroke Scale (NIHSS; www.stroke.nih.gov/resources/scale.htm) for clinical evaluation upon arrival at the ED.[15] Although no scale has been identified that can reliably predict large-vessel occlusion amenable to endovascular therapy (EVT), no other score has been found to outperform the NIHSS in achieving meaningful patient outcomes.[16] Furthermore, NIHSS has been validated to track clinical changes in response to therapy, is widely utilized, and is free.

A criticism of the NIHSS is its bias toward left-hemispheric ischemic pathology.[17] NIHSS includes 11 questions on a scale of 0 to 42; typically, a score < 4 is associated with a higher chance of a positive clinical outcome.[18] There is no minimum or maximum NIHSS score that precludes treatment with thrombolysis or EVT.

Other commonly used scores in acute stroke include disability assessments. The modified Rankin scale, which is used most often, features a score of 0 (symptom-free) to 6 (death). A modified Rankin scale score of 0 or 1 is considered an indication of a favorable outcome after stroke.[19] Note that these functional scores are not *always* part of an acute assessment but can be done early in the clinical course to gauge the response to treatment, and are collected for stroke-center certification.

Imaging modalities

Imaging is recommended within 20 minutes of arrival in the ED in a stroke patient who might be a candidate for thrombolysis or thrombectomy.[3] There, imaging modalities commonly performed are noncontrast-enhanced head computed tomography (NCHCT); computed tomography (CT) angiography, with or without perfusion; and diffusion-weighted magnetic resonance imaging (MRI).[20,21] In addition, more highly specialized imaging modalities are available for the evaluation of the stroke patient in specific, often limited, circumstances. All these modalities are described below and compared in the **TABLE**,[20,21] using the ACR Appropriateness Criteria (of the American College of Radiology),[21] which are guidelines for appropriate imaging of stroke, based on a clinical complaint. Separate recommendations and appraisals are offered by the most recent American Heart Association/American Stroke Association (AHA/ASA) guideline.[3]

NCHCT. This study should be performed within 20 minutes after arrival at the ED because it provides rapid assessment of intracerebral hemorrhage, can effectively corroborate the diagnosis of some stroke mimickers, and identifies some candidates for EVT or thrombolysis[3,21,22] (typically, the decision to proceed with EVT is based on adjunct imaging studies discussed in a bit). Evaluation for intracerebral hemorrhage is required prior to administering thrombolysis. Ischemic changes can be seen with variable specificity and sensitivity on NCHCT, depending on how much time has passed since the original insult. In all historical trials, CT was the only imaging modality used in the diagnosis of acute ischemic stroke (AIS) that suggested benefit from IV thrombolysis.[23-25]

Acute, subacute, and chronic changes can be seen on NCHCT, although the modality has limited sensitivity for identifying AIS (ie, approximately 75% within 6 hours after the original insult):

- *Acute* findings on NCHCT include intracellular edema, which causes loss of

There are several characteristically distinct stroke syndromes, but no way to differentiate ischemic and hemorrhagic pathologies clinically.

[a] Whether local emergency departments (EDs) should be bypassed in favor of a specialized stroke center is the subject of debate. The 2019 American Heart Association/American Stroke Association guidelines note the AHA's Mission: Lifeline Stroke EMS algorithm, which bypasses the nearest ED in feared cases of large-vessel occlusion if travel to a comprehensive stroke center can be accomplished within 30 minutes of arrival at the scene. This is based on expert consensus.[3,12,13]

the gray matter–white matter interface and effacement of the cortical sulci. This occurs as a result of increased cellular uptake of water in response to ischemia and cell death, resulting in a decreased density of tissue (hypoattenuation) in affected areas.
- *Subacute* changes appear in the 2- to 5-day window, including vasogenic edema with greater mass effect, hypoattenuation, and well-defined margins.[3,20,21]
- *Chronic* vascular findings on NCHCT include loss of brain tissue and hypoattenuation.

NCHCT is typically performed in advance of other adjunct imaging modalities.[3,20,21] Baseline NCHCT can be performed on patients with advanced kidney disease and those who have an indwelling metallic device.

CT angiography is performed with timed contrast, providing a 3-dimensional representation of the cerebral vasculature; the entire intracranial and extracranial vasculature, including the aortic arch, can be mapped in approximately 60 seconds. CT angiography is sensitive in identifying areas of stenosis > 50% and identifies clinically significant areas of stenosis up to approximately 90% of the time.[26] For this reason, it is particularly helpful in identifying candidates for an interventional strategy beyond pharmacotherapeutic thrombolysis. In addition, CT angiography can visualize aneurysmal dilation and dissection, and help with the planning of interventions—specifically, the confident administration of thrombolysis or more specific planning for target lesions and EVT.

It also can help identify a host of vascular phenomena, such as arteriovenous malformations, Moyamoya disease (progressive arterial blockage within the basal ganglia and compensatory microvascularization), and some vasculopathies.[20,27] In intracranial hemorrhage, CT with angiography can help evaluate for structural malformations and identify patients at risk of hematoma expansion.[22]

CT perfusion. Many stroke centers will perform a CT perfusion study,[28] which encompasses as many as 3 different CT sequences:
- NCHCT
- vertex-to-arch angiography with contrast bolus
- administration of contrast and capture of a dynamic sequence through 1 or 2 slabs of tissue, allowing for the generation of maps of cerebral blood flow (CBF), mean transit time (MTT), and cerebral blood volume (CBV) of the entire cerebral vasculature.

The interplay of these 3 sequences drives characterization of lesions (ie, CBF = CBV/MTT). An infarct is characterized by low CBF, low CBV, and elevated MTT. In penumbral tissue, MTT is elevated but CBF is slightly decreased and CBV is normal or increased. Using CT perfusion, areas throughout the ischemic penumbra can be surveyed for favorable interventional characteristics.[20,29]

A CT perfusion study adds at least 60 seconds to NCHCT. This modality can be useful in planning interventions and for stratifying appropriateness of reperfusion strategies in strokes of unknown duration.[3,30] CT perfusion can be performed on any multidetector CT scan but (1) requires specialized software and expertise to interpret and (2) subjects the patient to a significant radiation dose, which, if incorrectly administered, can be considerably higher than intended.[20,26,27]

Diffusion-weighted MRI. This is the most sensitive study for demonstrating early ischemic changes; however, limitations include lack of availability, contraindication in patients with metallic indwelling implants, and duration of the study—although, at some stroke centers, diffusion-weighted MRI can be performed in ≤ 10 minutes.

MRI and NCHCT have comparable sensitivity in detecting intracranial hemorrhage. MRI is likely more sensitive in identifying areas of microhemorrhage: In diffusion-weighted MRI, the sensitivity of stroke detection increases to > 95%.[31] The modality relies on the comparable movement of water through damaged vs normal neuronal tissue. Diffusion-weighted MRI does not require administration of concomitant contrast, which can be a benefit in patients who are allergic

> **Commonly used scoring systems in acute stroke include disability assessments—not always part of the acute assessment but undertaken early in the clinical course to gauge response to treatment.**

TABLE

Imaging modalities in acute stroke care: Pros, cons, and when to consider[20,21]

Modality	Pros	Cons	When should it be performed?	ACR Appropriateness Criteria[a]	
				New focal neurologic defect (fixed or worsening); < 6 h; suspected stroke	> 6 h; suspected stroke
NCHCT	Rapid Widely available	Radiation burden Limited sensitivity for ischemia	Whenever acute stroke is considered in association with NIHSS	**9**	**8**
CT angiography (head and neck)	More sensitive than NCHCT Helps with anatomic determination of stenosis Also useful for evaluating for aneurysm Can be performed concomitantly with CT perfusion	Larger radiation burden Requires contrast load Neck must also be assessed	When at a facility where endovascular therapy is available	**8**	**8**
CT perfusion	More sensitive than NCHCT Can help determine candidacy for intervention In combination with CT angiography	Larger radiation burden Not widely available Mistakes in calibration can result in very large radiation burden	When at a facility where mechanical thrombectomy is available and there is potential uncertainty about onset of symptoms	**6**	**5**
Diffusion-weighted MRI	Heightened sensitivity in detecting ischemia	Not readily available A significantly longer study (about 15 min) Patients with an indwelling metallic device are not candidates	When the patient does not have a contraindication to MRI	**8**	**8**
MRI with perfusion	With addition of perfusion to diffusion, areas of reversible ischemia can be isolated Highly specific and sensitive	Depending on which MRI and software packages are implemented, small intracranial hemorrhages might not be demonstrated Can take longer to perform Patients with an indwelling metallic device are not a candidate	—	**8**	**8**

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TABLE

Imaging modalities in acute stroke care: Pros, cons, and when to consider[20,21] (*cont'd*)

Modality	Pros	Cons	When should it be performed?	ACR Appropriateness Criteria[a]	
				New focal neurologic defect (fixed or worsening); < 6 h; suspected stroke	> 6 h; suspected stroke
MR angiography	Highly specific and sensitive visualization of intracranial and extracranial vasculature	Results in contrast burden Can be performed near the time of onset of symptoms, but is a slow study to obtain A patient with a contraindication to MRI is not a candidate Neck also must be assessed	When readily available OR When there is: • concern of aneurysm • desire to obtain intracranial and extracranial assessment of stenosis in a single study	**8**	**8**
Transcranial Doppler imaging	No radiation Accurate when performed by an expert sonographer	Highly technician-dependent Not widely available Difficult to obtain in a timely manner	Usually, at an academic center: • in unstable patients • in patients who cannot receive contrast OR • as an adjunct to other imaging modalities	No ACR Appropriateness Criteria	
Carotid duplex ultrasonography	Noninvasive Useful in evaluating the course of embolic cardiovascular accident Screening test of choice for examining extracranial vasculature	Gives reliable information only about extracranial vasculature Technician-dependent Should not be used as the sole modality for diagnosis	Extracranial vasculature should always be assessed during initial admission of a patient with expected stroke	**2**	**2**
Angiography	Gold standard Diagnostic Especially helpful in intracranial hemorrhage when no pathology has been identified noninvasively If the patient is a candidate for intervention, could be undertaken concomitantly	Invasive Results in contrast burden Not an ideal study in hemorrhage Carries risk of stroke	Before intervention, when large-vessel disease is highly suspected and intervention is planned	**5**	**6**

ACR, American College of Radiology; CT, computed tomography; MRI, magnetic resonance imaging; NCHCT, noncontrast-enhanced head computed tomography; NIHSS, National Institutes of Health Stroke Scale.

[a] ACR Appropriateness Criteria relate to American College of Radiology recommendations on imaging,[21] based on a clinical complaint. Rating scale:

- 1-3 Imaging usually is not appropriate.
- 4-6 Imaging may be appropriate.
- 7-9 Imaging usually is appropriate.

to gadolinium-based contrast agents or have advanced kidney disease that precludes the use of contrast. It typically does not result in adequate characterization of extracranial vasculature.

Other MRI modalities. These MRI extensions include magnetic resonance (MR) perfusion and MR angiography. Whereas diffusion-weighted MRI (discussed above) offers the most rapid and sensitive evaluation for ischemia, fluid-attenuated inversion recovery (FLAIR) imaging has been utilized as a comparator to isolated diffusion-weighted MRI to help determine stroke duration. FLAIR signal positivity typically occurs 6 to 24 hours after the initial insult but is negative in stroke that occurred < 3 hours earlier.[32]

MRI is limited, in terms of availability and increased study duration, especially when it comes to timely administration of thrombolysis. A benefit of this modality is less radiation and, as noted, superior sensitivity for ischemia. Diffusion-weighted MRI combined with MR perfusion analysis can help isolate areas of the ischemic penumbra. MR perfusion is performed for a similar reason as CT perfusion, although logistical execution across those modalities is significantly different. Considerations for choosing MR perfusion or CT perfusion should be made on an individual basis and based on available local resources and accepted local practice patterns.[26]

In the subacute setting, MR perfusion and MR angiography of the head and the neck are often performed to identify stenosis, dissection, and more subtle mimickers of cerebrovascular accident not ascertained on initial CT evaluation. These studies are typically performed well outside the window for thrombolysis or intervention.[26] No guidelines specifically direct or recommend this practice pattern. The superior sensitivity and cerebral blood flow mapping of MR perfusion and MR angiography might be useful for validating a suspected diagnosis of ischemic stroke and providing phenotypic information about AIS events.

Transcranial Doppler imaging relies on bony windows to assess intracranial vascular flow, velocity, direction, and reactivity. This information can be utilized to diagnose stenosis or occlusion. This modality is principally used to evaluate for stenosis in the anterior circulation (sensitivity, 70%-90%; specificity, 90%-95%).[20] Evaluation of the basilar, vertebral, and internal carotid arteries is less accurate (sensitivity, 55%-80%).[20] Transcranial Doppler imaging is also used to assess for cerebral vasospasm after subarachnoid hemorrhage, monitor sickle cell disease patients' overall risk for ischemic stroke, and augment thrombolysis. It is limited by the availability of an expert technician, and therefore is typically reserved for unstable patients or those who cannot receive contrast.[20]

Carotid duplex ultrasonography. A dynamic study such as duplex ultrasonography can be strongly considered for flow imaging of the extracranial carotids to evaluate for stenosis. Indications for carotid stenting or endarterectomy include 50% to 79% occlusion of the carotid artery on the same side as a recent transient ischemic attack or AIS. Carotid stenosis > 80% warrants consideration for intervention independent of a recent cerebrovascular accident. Interventions are typically performed 2 to 14 days after stroke.[33] Although this study is of limited utility in the hyperacute setting, it is recommended within 24 hours after nondisabling stroke in the carotid territory, when (1) the patient is otherwise a candidate for a surgical or procedural intervention to address the stenosis and (2) none of the aforementioned studies that focus on neck vasculature have been performed.

Conventional (digital subtraction) angiography is the gold standard for mapping cerebrovascular disease because it is dynamic and highly accurate. It is, however, typically limited by the number of required personnel, its invasive nature, and the requirement for IV contrast. This study is performed during intra-arterial intervention techniques, including stent retrieval and intra-arterial thrombolysis.[26]

Impact of imaging on treatment

Imaging helps determine the cause and some characteristics of stroke, both of which

> Knowledge of historic details of the event, the patient (eg, known atrial fibrillation), and findings on imaging can facilitate communication between the primary care physician and inpatient teams.

Stroke screening scales for early identification and triage

National Institutes of Health Stroke Scale
www.stroke.nih.gov/resources/scale.htm

FAST
www.stroke.org/en/help-and-support/resource-library/fast-materials

BE-FAST
www.ahajournals.org/doi/10.1161/STROKEAHA.116.015169

Los Angeles Prehospital Stroke Screen (LAPSS)
http://stroke.ucla.edu/workfiles/prehospital-screen.pdf

Rapid Artery Occlusion Evaluation (RACE)
www.mdcalc.com/rapid-arterial-occlusion-evaluation-race-scale-stroke

Cincinnati Prehospital Stroke Severity Scale (CP-SSS)
https://www.mdcalc.com/cincinnati-prehospital-stroke-severity-scale-cp-sss

can help determine therapy. Strokes can be broadly subcategorized as hemorrhagic or ischemic; recent studies suggest that 87% are ischemic.[34] Knowledge of the historic details of the event, the patient (eg, known atrial fibrillation, anticoagulant use, history of falls), and findings on imaging can contribute to determine the cause of AIS, and can facilitate communication and consultation between the primary care physician and inpatient teams.[35]

Best practices for stroke treatment are based on the cause of the event.[3] To identify the likely cause, the aforementioned characteristics are incorporated into one of the scoring systems, which seek to clarify either the cause or the phenotypic appearance of the AIS, which helps direct further testing and treatment. (The ASCOD[36] and TOAST[37] classification schemes are commonly used phenotypic and causative classifications, respectively.) Several (not all) of the broad phenotypic imaging patterns, with myriad clinical manifestations, are reviewed below. They include:

- *Embolic stroke*, which, classically, involves end circulation and therefore has cortical involvement. Typically, these originate from the heart or large extracranial arteries, and higher rates of atrial fibrillation and hypercoagulable states are implicated.
- *Thrombotic stroke*, which, typically, is from large vessels or small vessels, and occurs as a result of atherosclerosis. These strokes are more common at the origins or bifurcations of vessels. Symptoms of thrombotic stroke classically wax and wane slightly more frequently. Lacunar strokes are typically from thrombotic causes, although there are rare episodes of an embolic source contributing to a lacunar stroke syndrome.[38]

There is evidence for using MRI discrepancies between diffusion-weighted and FLAIR imaging to time AIS findings in so-called wake-up strokes.[39] The rationale is that strokes < 4.5 hours old can be identified because they would have abnormal diffusion imaging components but normal findings with FLAIR. When these criteria were utilized in considering whether to treat with thrombolysis, there was a statistically significant improvement in 90-day modified Rankin scale (odds ratio = 1.61; 95% confidence interval, 1.09-2.36), but also an increased probability of death and intracerebral hemorrhage.[39]

A recent multicenter, randomized, open-label trial, with blinded outcomes assessment, showcased the efficacy of thrombectomy as an adjunct when ischemic brain territory was identified without frank infarction, as ascertained by CT perfusion within the anterior circulation. This trial showed that thrombectomy could be performed as long as 16 hours after the patient was last well-appearing and still result in an improved outcome with favorable imaging characteristics (on the modified Rankin scale, an ordinal score of 4 with medical therapy and an ordinal score of 3 with EVT [odds ratio = 2.77; 95% confidence interval, 1.63-4.70]).[29] A 2018 multicenter, prospective, randomized trial with blinded assessment of endpoints extended this idea, demonstrating that, when there was mismatch of the clinical deficit (ie, high NIHSS score) and infarct volume (measured on diffusion-weighted MRI or CT perfusion), thrombectomy as late as 24 hours after the patient was last known to be well was beneficial for lesions in the anterior circulation—specifically, the intracranial internal carotid artery or the proximal middle cerebral artery.[40] JFP

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This trial showed that thrombectomy could be performed as long as 16 hours after the patient was last well-appearing and still result in an improved outcome.

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