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CDI Quality Institute PLE Stroke AUC

2020 Update

Appropriateness of advanced imaging procedures* in patients with stroke/cerebrovascular accident (CVA) and the following clinical presentations or diagnoses:

*Including MRI, MR angiography, MR venography, MR perfusion, CT, CT angiography, CT venography, CT perfusion, nuclear medicine, SPECT, PET, PET/CT

Abbreviation list:

ACEP	American College of Emergency Physicians	GCS	Glasgow Coma Scale
		ICA	Internal carotid artery
ACR	American College of Radiology	ICH	Intracranial hemorrhage
AHA	American Heart Association	LVO	Large vessel occlusion
AIS	Acute ischemic stroke	MCA	Middle cerebral artery
ASA	American Stroke Association	MRA	Magnetic resonance angiography
AUC	Appropriate Use Criteria	MRI	Magnetic resonance imaging
CAS	Carotid artery stenosis/stenting	MRP	MR perfusion
CEA	Carotid endarterectomy	MRV	MR venography
CT	Computed tomography	NASCET	North American Symptomatic Carotid Endarterectomy Trial
CTA	Computed tomographic angiography	NCCT	Noncontrast CT
CTP	CT perfusion	NICE	National Institute for Health and Care Excellence
CTV	CT venography		
CVA	Cerebrovascular accident	PET	Positron emission tomography
CVST	Cerebral venous sinus thrombosis	PLE	Provider Led Entity
DWI	Diffusion weighted imaging	SIGN	Scottish Intercollegiate Guidelines Network
ECST	European Carotid Surgery Trial		
ECVD	Extracranial Carotid and Vertebral Artery Disease	SNIL	Silent new ischemic lesion
		TIA	Transient ischemic attack
ESVS	European Society for Vascular Surgery	tPA	Tissue plasminogen activator
		US	Ultrasound
ESO	European Stroke Organization	USPSTF	U.S. Preventive Services Task Force

Physical findings, radiographic signs, and/or risk factors suggestive of carotid artery stenosis in an otherwise asymptomatic patient†:

- Green – *
- Yellow – MRA neck (for any of the following):
    - to further characterize hemodynamically significant carotid artery stenosis detected or suspected on duplex carotid ultrasound,
    - in patients with an indeterminate or nondiagnostic duplex carotid ultrasound, or
    - when ultrasound is not available
- Yellow – CTA neck (for any of the following):
    - to further characterize hemodynamically significant carotid artery stenosis detected or suspected on duplex carotid ultrasound,
    - in patients with an indeterminate or nondiagnostic duplex carotid ultrasound, or
    - when ultrasound is not available
- Yellow – MRA head in patients with established carotid artery stenosis **and** who are being evaluated for carotid stenting
- Yellow – CTA head in patients with established carotid artery stenosis **and** who are being evaluated for carotid stenting
- Red – CT head; MRI brain; CT perfusion; MR perfusion; CT venography; MR venography

†Screening for asymptomatic carotid artery disease is not recommended in the general adult population without signs, symptoms or risk factors.

*Duplex carotid ultrasound is indicated for the initial evaluation of asymptomatic patients at high risk for, with signs of, or with radiographic evidence of carotid artery stenosis.

<u>Level of Evidence:</u> CTA neck, MRA neck: n/a

<u>Notes concerning applicability and/or patient preferences:</u> none

<u>Guideline and PLE expert panel consensus summary:</u>
Routine screening for carotid artery stenosis (CAS) is not recommended for:

- the general adult population (LeFevre [*USPSTF*] 2014, D recommendation);
- asymptomatic patients who have no clinical manifestations of or risk factors for atherosclerosis (Brott et al. 2011, Class III: No Benefit/Level of Evidence: C; Naylor et al. [*ESVS*] 2018, Class III/Level of Evidence: B); or
- patients who have no risk factors for development of atherosclerotic carotid disease and no disease evidence on initial vascular testing (Brott et al. 2011, Class III: No Benefit/Level of Evidence: C).

Screening for carotid artery stenosis (CAS) might be considered in asymptomatic patients with:

- two or more of the following risk factors: hypertension, hyperlipidemia, tobacco smoking, a family history in a first-degree relative of atherosclerosis manifested < age 60 years, or a family history of ischemic stroke (Brott et al. 2011, Class IIb/Level of Evidence: C);

- symptomatic [peripheral arterial disease] PAD, coronary artery disease (CAD), or atherosclerotic aortic aneurysm;(Brott et al. 2011, Class IIb/Level of Evidence: C).
- a carotid bruit (Brott et al. 2011, Class IIa/Level of Evidence: C);
- silent brain infarction in the carotid territory [on advanced imaging] (Smith et al. [*AHA/ASA*] 2017); or
- large (> 1.0cm) silent [intracranial] hemorrhages [on advanced imaging] (Smith et al. [*AHA/ASA*] 2017).

In asymptomatic patients with … suspected carotid stenosis, duplex ultrasonography, performed by a qualified technologist in a certified laboratory, is recommended as the initial diagnostic test to detect hemodynamically significant carotid stenosis (Brott et al. 2011, Class I/Level of Evidence: C).

Duplex carotid ultrasound is indicated for the initial evaluation of asymptomatic patients at high risk for, with signs of, or with radiographic evidence of carotid artery stenosis (Expert panel consensus opinion; Naylor et al. [*ESVS*] 2018, Class I/Level of Evidence: A).

It is reasonable to repeat duplex ultrasonography annually by a qualified technologist to assess the progression or regression of disease and response to therapeutic interventions in patients with atherosclerosis who have had stenosis > 50% detected previously. Once stability has been established over an extended period or the patient's candidacy for further intervention has changed, longer intervals or termination of surveillance may be appropriate (Brott et al. 2011).

Duplex US surveillance enables monitoring of disease progression in the contralateral ICA, which is more common than ipsilateral restenosis, with progression being dependent on disease severity at the time of CEA. The data are, however, conflicting as to its benefit (Naylor et al. [*ESVS*] 2018).

Computed tomographic angiography and/or magnetic resonance angiography are recommended for evaluating the extent and severity of extracranial carotid stenosis (Naylor et al. [*ESVS*] 2018, Class I/Level of Evidence: A).

When carotid endarterectomy is being considered, it is recommended that duplex ultrasound stenosis estimation be corroborated by computed tomographic angiography or magnetic resonance angiography, or by a repeat duplex ultrasound performed by a second operator (Naylor et al. [*ESVS*] 2018, Class I/Level of Evidence: A).

When carotid stenting is being considered, it is recommended that any duplex ultrasound study be followed by computed tomographic angiography or magnetic resonance angiography which will provide additional information on the aortic arch, as well as the extra- and intracranial circulation (Naylor et al. [*ESVS*] 2018, Class I/Level of Evidence: A).

If duplex US or MRA neck without IV contrast are positive, consider follow-up with CTA or contrast-enhanced MRA. CE-MRA is superior to noncontrast TOF-MRA because it is less affected by slow and turbulent flow, particularly at the carotid bifurcation (Salmela et al. [ACR] 2017).

In *asymptomatic patients with structural lesion on physical examination (cervical bruit) and/or risk factors*, the *American College of Radiology* recommends US duplex Doppler carotid (8), MRA neck without IV contrast (8), MRA neck without and with IV contrast (8), CTA neck with IV contrast (8), CT head perfusion with IV contrast (5), MRI head perfusion with IV contrast (5), MRI head without IV contrast (5), MRI head without and with IV contrast (5), and CT head without IV contrast (5) (Salmela et al. [ACR] 2017).

Clinical notes:

- Carotid artery disease is responsible for 10%-20% of strokes (Salmela et al. [ACR] 2017; Brott et al. 2011).
- The major risk factors for carotid artery stenosis include older age, male sex, hypertension, smoking, hypercholesterolemia, diabetes mellitus, and heart disease (LeFevre [*USPSTF*] 2014).

Imaging notes:

- Duplex US is operator dependent and can have difficulty with artifact due to calcified plaque and is limited in the evaluation of near occlusion, tandem lesions, and lesions at the distal carotid and carotid origin (Salmela et al. [ACR] 2017).
- Although MRA has slightly higher sensitivity and specificity than US to determine carotid stenosis and occlusion, the usefulness of either procedure may be determined by other factors, such as availability. Computed tomography angiography (CTA) has a sensitivity and specificity similar to MRA for carotid occlusion and similar to US for the detection of severe stenosis (Irimia et al. 2010).
- The advantage of computed tomographic angiography (CTA) and MR angiography (MRA) is the ability to simultaneously image the aortic arch, supra-aortic trunks, carotid bifurcation, distal ICA, and the intracranial circulation, which is mandatory in patients being considered for carotid artery stenting (CAS) (Naylor et al. [*ESVS*] 2018).
- Ensure that carotid imaging reports clearly state which criteria (ECST or NASCET) were used when measuring the extent of carotid stenosis (*NICE* 2019).

Evidence update (2016-present): There was no new low, moderate or high quality evidence significantly affecting the evidence and recommendations included in the guidelines cited above.

Suspected transient ischemic attack(s) (TIA):

Brain imaging:

- **Green** – MRI brain‡
- **Green** – CT head
- **Yellow** – CT perfusion in patients unable to undergo MRI

Carotid imaging:

- **Green** – MRA neck*
- **Yellow** – CTA neck in patients unable to undergo MRI*†

Intracranial vascular imaging:

- **Yellow** – MRA head (for either of the following):
  - when an extracranial source of ischemia is not identified, or
  - when intervention for significant carotid stenosis detected by carotid duplex ultrasonography is planned
- **Yellow** – CTA head† in patients unable to undergo MRI (for either of the following):
  - when an extracranial source of ischemia is not identified, or
  - when intervention for significant carotid stenosis detected by carotid duplex ultrasonography is planned
- **Red** – CT venography; MR venography; MR perfusion

‡ MRI of the brain should include diffusion-weighted imaging and gradient recalled imaging or susceptibility-weighted imaging (see imaging notes below).

*Duplex carotid ultrasound is also accurate for evaluation of the carotid arteries and can be used to evaluate patients with TIA.

†MRA is the preferred imaging modality as CTA requires the use of IV iodinated contrast and exposes the patient to ionizing radiation (Salmela et al. [ACR] 2017)

Level of Evidence: CT head without contrast, MRA neck without contrast: high; MRI brain without contrast: high for diagnostic accuracy/low for management change; CTA neck with contrast, MRA neck without and with contrast: high for carotid imaging/low for any one modality; MRA head without contrast: low; CT perfusion, MR perfusion: very low

Notes concerning applicability and/or patient preferences: Consulting and reporting requirements are not required for orders for applicable imaging services made by ordering professionals under the following circumstances (*42 C.F.R. § 414.94. 2015*):

- Emergency services when provided to individuals with emergency medical conditions.
- For an inpatient and for which payment is made under Medicare Part A.

Guideline and PLE expert panel consensus summary:
Patients presenting with suspected acute or recent TIA…should undergo an initial assessment that includes brain imaging, non-invasive vascular imaging, 12-lead ECG, echocardiography if indicated, and laboratory investigations (Boulanger et al 2018).

In patients with *carotid territory or vertebrobasilar TIA, initial screening study*, the *American College of Radiology* recommends MRI head without and with IV contrast (9), MRI head without IV contrast (8), MRA head and neck without IV contrast (8), MRA head and neck without and with IV contrast (8), CT head without IV contrast (8), CTA head and neck with IV contrast (8), US duplex Doppler carotid (5), CT head perfusion with IV contrast (5), and MRI head perfusion with IV contrast (5) (Salmela et al. [ACR] 2017).

Brain imaging –
After specialist assessment in the TIA clinic, consider MRI (including diffusion-weighted and blood-sensitive sequences) to determine the territory of ischemia, or to detect hemorrhage or alternative pathologies. (*NICE* 2019).

When feasible, physicians should obtain MRI with diffusion-weighted imaging to identify patients at high short-term risk for stroke (Lo et al. [*ACEP*] 2016, Level C recommendation).

If noncontrast brain MRI is not readily available, it is reasonable for physicians to obtain a noncontrast head CT as part of the initial TIA workup to identify TIA mimics [or intracranial hemorrhage]. However, noncontrast head CT should not be used to identify patients at high short-term risk for stroke (Lo et al. [*ACEP*] 2016, Level C recommendation).

Do not offer CT brain scanning to people with a suspected TIA unless there is clinical suspicion of an alternative diagnosis that CT could detect (*NICE* 2019). *The expert panel noted that CT is often obtained in patients presenting with TIA to exclude intracranial hemorrhage* (PLE expert panel consensus opinion).

CTP may play a role to evaluate for ischemia when MRI is contraindicated or cannot be performed. (Salmela et al. [ACR] 2017

Carotid imaging –
The initial evaluation of patients with transient retinal or hemispheric neurological symptoms of possible ischemic origin should include noninvasive imaging for the detection of ECVD (Brott et al. 2011, Class I/Level of Evidence: C). When feasible, physicians should obtain cervical vascular imaging (e.g., carotid ultrasonography, CTA, or MRA) to identify patients at high short-term risk for stroke (Lo et al. [ACEP] 2016, Level C recommendation).

Duplex ultrasonography is recommended to detect carotid stenosis in patients:

- who develop focal neurological symptoms corresponding to the territory supplied by the left or right internal carotid artery ECVD (Brott et al. 2011, Class I/Level of Evidence: C); and with nonspecific neurological symptoms when cerebral ischemia is a plausible cause (Brott et al. 2011, Class IIb/Level of Evidence: C).

In patients with acute, focal ischemic neurological symptoms corresponding to the territory supplied by the left or right internal carotid artery, magnetic resonance angiography (MRA) or computed tomography angiography (CTA) is indicated to detect carotid stenosis when sonography either cannot be obtained or yields equivocal or otherwise nondiagnostic results (Brott et al. 2011, Class I/Level of Evidence: C).

In patients whose symptoms suggest posterior cerebral or cerebellar ischemia, MRA or CTA is recommended rather than ultrasound imaging for evaluation of the vertebral artery (Brott et al. 2011, Class I/Level of Evidence: C).

MRA without contrast is reasonable to assess the extent of disease in patients with symptomatic carotid atherosclerosis and renal insufficiency or extensive vascular calcification (Brott et al. 2011, Class IIa/Level of Evidence: C).

It is reasonable to use MRI systems capable of consistently generating high-quality images while avoiding low-field systems that do not yield diagnostically accurate results (Brott et al. 2011, Class IIa/Level of Evidence: C).

CTA is reasonable for evaluation of patients with clinically suspected significant carotid atherosclerosis who are not suitable candidates for MRA because of claustrophobia, implanted pacemakers, or other incompatible devices (Brott et al. 2011, Class IIa/Level of Evidence: C).

Intracranial vascular imaging –
When an extracranial source of ischemia is not identified in patients with transient retinal or hemispheric neurological symptoms of suspected ischemic origin, CTA, MRA, or selective cerebral angiography can be useful to search for intracranial vascular disease (Brott et al. 2011, Class IIa/Level of Evidence: C).

When intervention for significant carotid stenosis detected by carotid duplex ultrasonography is planned, MRA, CTA, or catheter-based contrast angiography can be useful to evaluate the severity of stenosis and to identify intrathoracic or intracranial vascular lesions that are not adequately assessed by duplex ultrasonography (Brott et al. 2011, Class IIa/Level of Evidence: C).

When noninvasive imaging is inconclusive or not feasible because of technical limitations or contraindications in patients with transient retinal or hemispheric neurological symptoms of suspected ischemic origin, or when noninvasive imaging studies yield discordant results, it is reasonable to perform catheter-based contrast angiography to detect and characterize extracranial and/or intracranial cerebrovascular disease (Brott et al. 2011, Class IIa/Level of Evidence: C).

Clinical notes:

- TIA is conventionally defined as a syndrome of acute neurological dysfunction referable to the distribution of a single brain artery and characterized by symptoms that last < 24 hours (Brott et al. 2011; Salmela et al. [ACR] 2017).
- Patients with carotid territory symptoms include those with (i) hemi-sensory impairment (numbness, paresthesia of face/arm/leg); (ii) hemimotor deficits (weakness of face/arm/leg, or limb clumsiness), and (iii) higher cortical dysfunction (dysphasia/aphasia, visuospatial problems) (Naylor et al. [*ESVS*] 2018).
- TIA may present as amaurosis fugax which is defined as transient impairment or loss of vision in one eye (Naylor et al. [*ESVS*] 2018).
- Frequent causes of transient neurological symptoms that can mimic TIA include migraine aura, seizures, syncope, peripheral vestibular disturbance and functional/anxiety disorder (Nadarajan et al. 2014).
- Neurologic studies have shown that approximately one-third of all TIAs have evidence of infarction at presentation (Lo et al. [*ACEP*] 2016).

- The risk of acute ischemic stroke after TIA ranges from 3.5-10% at 2 days, 5-10% at 7 days, and 9.2-17% at 90 days (Lo et al. [*ACEP*] 2016). The 10-year risk for suffering a stroke, myocardial infarction, or death in a TIA patient is as high as 43% (e.g., Clark et al. 2003; van Wijk et al. 2005).
- Evidence showed that risk prediction scores (ABCD2 and ABCD3) used in isolation are poor at discriminating low and high risk of stroke after TIA (NICE 2019).
- The *NICE* 2019 committee agreed, based on their clinical experience and the limited predictive performance of risk scores, that all cases of suspected TIA should be considered as potentially high risk for stroke. Also, because there is no reliable [risk stratification tools] for TIA, it is important to urgently confirm or refute the diagnosis of a suspected TIA with specialist opinion. This is particularly so because in practice, a significant proportion of suspected TIA (30% to 50%) will have an alternative diagnosis (that is, TIA-mimic). Therefore, it was agreed that everyone who has had a suspected TIA should have specialist assessment and investigation within 24 hours of the onset of symptoms (NICE 2019).

<u>Imaging notes:</u>

- The primary goal of imaging is to identify serious TIA mimics and to identify patients at high short-term risk for stroke, commonly defined as occurring within 2-7 days after the initial TIA event (Lo et al. [*ACEP*] 2016).
- MRI is superior to CT scan in terms of diagnostic sensitivity for small strokes and may provide additional information that could guide diagnosis, prognosis, and management decision-making. Decisions regarding MRI scanning should be based on MRI access, availability, and timing of appointments (Boulanger et al. 2018).
- Both DWI and cervical vascular imaging predict short-term risk for stroke in patients presenting with suspected TIA (Lo et al. [*ACEP*] 2016).
- An example of a stroke-protocol for an MRI brain includes DWI, ADC, T1, T2, FLAIR, and T2 GRE or SWI sequences. This combination of sequences allows for identification of other causes for the patient's symptoms, for the detection of ischemia, and for estimation of the age of the infarct (PLE expert panel consensus statement).
- If there is concern for carotid artery dissection, axial fat-suppressed T1-weighted images through the neck should be obtained (Salmela et al. [ACR] 2017).
- The NICE [2019] committee discussed the possible risks of not offering CT brain imaging to everyone with a suspected TIA. They agreed that, in the absence of clinical 'red flag' indicators (for example, headache, anticoagulation, head injury, repetitive stereotyped events), it is rare for a CT scan to reveal an alternative diagnosis needing a different referral pathway.
- Vascular imaging is recommended to identify significant symptomatic extracranial carotid artery stenosis for which patients should be referred for possible carotid revascularization (*NICE* 2019).
- Carotid ultrasonography may be used to exclude severe carotid stenosis because it has accuracy similar to that of MRA or CTA (Lo et al. 2016 [*ACEP*], Level C Recommendation).
- Ensure that carotid imaging reports clearly state which criteria (ECST or NASCET) were used when measuring the extent of carotid stenosis (*NICE* 2019).

<u>Evidence update (2016-present):</u>

Coutts et al. (2019) conducted a multicenter cohort study to establish frequency of acute infarction defined by diffusion restriction detected on MRI scans among 1,028 patients (mean age 63) with mild focal neurologic, but low-risk, symptoms. All patients had minor focal neurologic event(s) of any duration or motor/speech symptoms of short duration ($\leq$ 5 min), with no previous stroke, and were referred to neurology within 8 days of symptom onset, where they underwent detailed neurologic assessment prior to brain MRI. A total of 139 patients (13.5%) had an acute stroke as defined by MRI scan (DWI positive) and final diagnosis was revised in 308 patients (30.0%) after undergoing brain MRI. There were 7 (0.7%) recurrent strokes at 1 year, and DWI-positive brain MRI scan was associated with increased risk of recurrent stroke (RR, 6.4; 95% CI, 2.4 - 16.8) at 1 year. Absence of a DWI-positive lesion on brain MRI scan had a 99.8% NPV for recurrent stroke. Factors associated with MRI evidence of stroke in multivariable modeling were older age (odds ratio [OR], 1.02; 95% CI, 1.00 - 1.04), male sex (OR, 2.03; 95% CI, 1.39 - 2.96), motor/speech symptoms (OR, 2.12; 95% CI, 1.37 - 3.29), ongoing symptoms at assessment (OR, 1.97; 95% CI, 1.29-3.02), no prior identical symptomatic event (OR, 1.87; 95% CI, 1.12 - 3.11), and abnormal results of initial neurologic examination (OR, 1.71; 95% CI, 1.11 - 2.65). The authors conclude that patients with TIA and symptoms traditionally considered low risk carry a substantive risk of acute stroke as defined by diffusion restriction (DWI positive) on brain MRI scan. Early MRI is required to make a definitive diagnosis (moderate level of evidence).

Ottaviani et al. (2016) conducted a prospective study on the prognostic value of ABCD2 score with or without imaging tests (urgent carotid ultrasound (CUS) or unenhanced head CT (UHCT)) in 186 patients presenting with TIA within 24h of symptoms onset. In patients with TIA, 12 ischemic strokes (6.5%) occurred: four (7.1%) in patients with ABCD2 score < 4 and 8 (6.2%) in those with score ≥ 4. Internal carotid stenosis of ≥ 50% was found in 15 patients (8.1%) and associated with high risk for stroke (odds ratio 4.5, 95% confidence interval 1.1–18.8). An acute ischemic lesion consistent with the neurological deficit was revealed by UHCT in 15 patients (8.1%), and associated with a trend of increasing stroke risk (odds ratio 2.5, 95% confidence interval 0.5–12.5). Patients without, with at least one, or with both positive imaging tests showed incremental stroke risk at both 7 days (2.5, 12.5, and 33%) and 30 days (5, 12.5, and 33%) (P<0.05 for both). The authors conclude that simple imaging tests showed added prognostic value to ABCD2 score in TIA patients. Urgent CUS together with UHCT should be performed in all TIA patients regardless of ABCD2 score (high level of evidence).

Amarenco et al. (2016) conducted a multicenter prospective registry on the contemporary profile, etiologic factors, and outcomes in patients (mean age 66.1) with a TIA or minor ischemic stroke within the previous 7 days who receive care in health systems that offer urgent evaluation by stroke specialists. Kaplan–Meier estimate of 1-year event rate of composite cardiovascular outcome was 6.2% (95% CI: 5.5-7.0), and estimates of stroke rate at days 2, 7, 30, 90, and 365 were 1.5%, 2.1%, 2.8%, 3.7%, and 5.1%, respectively. Multiple infarctions on brain imaging, large-artery atherosclerosis, and an ABCD score of 6 or 7 were each associated with more than a doubling of stroke risk. The authors observed a lower rate of cardiovascular events after TIA or minor stroke than that in historical cohorts. This may reflect a contemporary risk of recurrent cardiovascular events among patients with a TIA or minor stroke who are admitted to TIA clinics and who receive risk-factor control and antithrombotic treatment as recommended by current guidelines. Findings suggest that limiting urgent assessment to patients with an ABCD score of ≥ 4 would miss approximately 20% of those with early recurrent strokes. Multiple infarctions on neuroimaging and large-artery atherosclerotic disease were also strong independent predictors of recurrent vascular events (low level of evidence).

Suspected acute stroke within the treatment window for thrombolytic or endovascular therapy:

Brain imaging:

- **Green** – CT head without contrast or CT without and with contrast
- **Green** – MRI brain‡
- **Green** – MR cerebral perfusion
- **Green** – CT cerebral perfusion
- **Yellow** – CT head with contrast in patients with findings of intracranial hemorrhage on noncontrast CT

Vascular imaging:

- **Yellow** – MRA head and/or neck without contrast in patients who are candidates for endovascular therapy
- **Yellow** – CTA head and/or neck in patients who are candidates for endovascular therapy
- **Red** – CT venography, MR venography

‡MRI of the brain should include diffusion weighted imaging and gradient recalled images (GRE) or susceptibility-weighted imaging (SWI) (see technical notes below).

Level of Evidence: CT head without contrast, MRI brain without contrast, CTA head without and with contrast, CTA neck with contrast, MRA neck without and with contrast MRA head without contrast, MRA neck without contrast, CT perfusion, MR perfusion: high

Notes concerning applicability and/or patient preferences: Consulting and reporting requirements are not required for orders for applicable imaging services made by ordering professionals under the following circumstances (*42 C.F.R. § 414.94. 2015*):

- Emergency services when provided to individuals with emergency medical conditions.
- For an inpatient and for which payment is made under Medicare Part A.

MRI scanning can be challenging to obtain urgently in an ED setting. This must be considered in decision-making and not delay decisions regarding EVT eligibility (Boulanger et al. 2018; Powers et al. [*AHA /ASA*] 2019, Class I (strong) Recommendation / Level of Evidence A).

Guideline and PLE expert panel consensus summary

Brain Imaging -

All patients with suspected acute stroke should undergo emergent or immediate brain imaging with NCCT or MRI (Boulanger et al. 2018: Evidence Level A; *NICE* 2019; Irimia et al. 2010, Class I/Level A).

Rapid neuroimaging with CT or MRI is recommended to distinguish ischemic stroke from intracerebral hemorrhage (ICH) (Hemphill et al. [*AHA/ASA*] 2015, Class I/Level of Evidence: A; Irimia et al. 2010, Class I/Level A).

Noncontrast head CT is often obtained first to assess for hemorrhage or large infarct (Salmela et al. [ACR] 2017).

Perform brain imaging immediately with a non-enhanced CT for people with suspected acute stroke if any of the following apply (*NICE* 2019):

- Indications for thrombolysis or thrombectomy
- On anticoagulant treatment
- A known bleeding tendency
- A depressed level of consciousness (Glasgow Coma Score < 13)
- Unexplained progressive or fluctuating symptoms
- Papilledema, neck stiffness or fever
- Severe headache at onset of stroke symptoms.

MRI has a higher sensitivity than conventional CT for the documentation of infarction within the first hours of stroke onset, lesions in the posterior fossa, identification of small lesions, and documentation of vessel occlusion and brain edema (Irimia et al. 2010, Class I/Level A).

CTP may play a role to evaluate for ischemia when MRI is contraindicated or cannot be performed. (Salmela et al. [ACR] 2017).

MRI with diffusion weighted and gradient echo sequences is recommended for the diagnosis of acute stroke syndromes in patients who are not severely ill, especially where neurological deficit is mild and the clinical likelihood is that the lesion is small or lies in the posterior fossa (*SIGN* 2008, B recommendation).

In conjunction with MRI and magnetic resonance angiography (MRA), perfusion and diffusion MR are very helpful for the evaluation of patients with acute ischemic stroke (Irimia et al. 2010, Class I/Level A).

Imaging patients for possible intravenous thrombolysis -
All patients with suspected acute ischemic stroke who arrive within 4.5 h and are potentially eligible for intravenous thrombolysis should undergo immediate brain imaging with non-contrast CT (NCCT) without delay to determine eligibility for thrombolysis (Boulanger et al. 2018: Evidence Level A).

Noncontrast CT (NCCT) is effective to exclude ICH before IV alteplase administration (Powers et al. [*AHA/ASA*] 2019, Class I (strong) Recommendation / Level of Evidence: A).

Magnetic resonance imaging (MRI) is effective to exclude ICH before IV alteplase administration (Powers et al. [*AHA/ASA*] 2019, Class I (strong) Recommendation / Level of Evidence: B-NR).

In patients with AIS who awake with stroke symptoms or have unclear time of onset > 4.5 hours from last known well or at baseline state, MRI to identify diffusion-positive FLAIR-negative lesions can be useful for selecting those who can benefit from IV alteplase administration within 4.5 hours of stroke symptom recognition (Powers et al. [*AHA/ASA*] 2019, Class IIa (moderate) Recommendation / Level of Evidence: B-R).

Imaging patients for possible endovascular thrombectomy (less than 6 h) -
All patients with suspected acute ischemic stroke who arrive within 6 h and are potentially eligible for EVT should undergo immediate brain imaging non-contrast CT and CT angiography (CTA) without delay, from arch-to-vertex including the extra- and intra-cranial circulation, to identify large vessel occlusions eligible for endovascular thrombectomy (Boulanger et al. 2018: Evidence Level A; *NICE* 2019; Powers et

al. [*AHA/ASA*] 2019, Class I (strong) Recommendation / Level of Evidence: A; Wahlgren et al. [*ESO*] 2016; Grade A/Level 1a).

In patients who are potential candidates for mechanical thrombectomy, imaging of the extracranial carotid and vertebral arteries, in addition to the intracranial circulation, may be reasonable to provide useful information on patient eligibility and endovascular procedural planning (Powers et al. [*AHA/ASA*] 2019, Class IIb (moderate) Recommendation /Level of Evidence: C-EO).

MRA or CTA may be used to define the vascular anatomy for treatment planning in the acute setting, however should not delay treatment with thrombolytic or endovascular therapy (PLE expert panel consensus opinion).

Advanced CT imaging such as CT perfusion (CTP) or multiphase or dynamic CTA (to assess pial collateral vessels) can be considered as part of initial imaging to aid patient selection [Boulanger et al. 2018: Evidence Level B]. However, this must not substantially delay decision and treatment with intravenous thrombolysis with alteplase or EVT treatment. If there are signs of hemorrhage on initial CT images, there is no need to proceed to CTP imaging as part of initial imaging and CTA should be completed based on the clinical judgment of the treating physician.

When evaluating patients with AIS within 6 hours of last known normal with LVO and an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of $\geq$ 6, selection for mechanical thrombectomy based on CT and CTA or MRI and MRA is recommended in preference to performance of additional imaging such as perfusion studies (Powers et al. [*AHA/ASA*] 2019, Class I (strong) Recommendation / Level of Evidence: B-NR).

In patients with *new focal neurologic defect, fixed or worsening, less than 6 hours, suspected stroke,* the *American College of Radiology* recommends CT head without IV contrast (9), MRI head without IV contrast (8), MRI head without and with IV contrast (8), MRA head and neck without IV contrast (8), MRA head and neck without and with IV contrast (8), CTA head and neck with IV contrast (8), CT head perfusion with IV contrast (6), MRI head perfusion with IV contrast (5), and arteriography cervicocerebral (5) (Salmela et al. [ACR] 2017).

Imaging patients for possible endovascular thrombectomy (extended window 6-24 h) -
All patients with suspected ischemic stroke who arrive at 6–24 h after stroke onset (late presentation and stroke on awakening with unknown onset time) and are potentially eligible for late window EVT treatment should undergo immediate brain imaging with NCCT with CTA and CTP, or MRI with MRA and MRP [Boulanger et al. 2018: Evidence Level B].

CTP has shown some promise in identifying patients who may benefit from therapy outside the accepted treatment window (Salmela et al. [ACR] 2017). Add CT perfusion imaging (or MR equivalent) if thrombectomy might be indicated beyond 6 hours of symptom onset (*NICE* 2019).

When selecting patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation, obtaining CTP or DW-MRI, with or without MRI perfusion, is recommended to aid in patient selection for mechanical thrombectomy, but only when patients meet other eligibility criteria from one of the RCTs that showed benefit from mechanical thrombectomy in this extended time window (Powers et al. [*AHA/ASA*] 2019, Class I (strong) Recommendation / Level of Evidence: A).

Duplex carotid ultrasound:
For patients with suspected LVO who have not had noninvasive vessel imaging as part of their initial imaging assessment for stroke, noninvasive vessel imaging should then be obtained as quickly as possible (e.g., during alteplase infusion if feasible) (Powers et al. [*AHA/ASA*] 2019).

Duplex carotid ultrasound is not typically performed prior to thrombolytic or endovascular treatment for acute stroke. Evaluation of the extracranial carotid arteries is typically performed in the context of risk assessment and secondary prevention after treatment for the acute stroke (PLE expert panel consensus opinion; Brott et al. 2011).

Patients with intracranial hemorrhage –
[In patients with ICH] CTA and contrast-enhanced CT may be considered to help identify patients at risk for hematoma expansion (Class IIb; Level of Evidence: B), and CTA, CT venography, contrast-enhanced CT, contrast-enhanced MRI, magnetic resonance angiography and magnetic resonance venography, and catheter angiography can be useful to evaluate for underlying structural lesions including vascular malformations and tumors when there is clinical or radiological suspicion (Hemphill et al. [*AHA/ASA*] 2015, Class IIa/Level of Evidence: B).

In patients with *clinically suspected parenchymal hemorrhage (hematoma), not yet confirmed)* recommends CT head without IV contrast (9), MRI head without IV contrast (8), MRI head without and with IV contrast (7), and CT head without and with IV contrast (5) (Salmela et al. [ACR] 2017).

Clinical notes:

- Ischemic stroke is responsible for 87% of all strokes (Salmela et al. [ACR] 2017).
- In many patients, the diagnosis of ischemic stroke can be made accurately on the basis of the clinical presentation and either a negative NCCT or one showing early ischemic changes, which can be detected in the majority of patients with careful attention (Powers et al. [*AHA*/*ASA*] 2019).
- In patients eligible for IV alteplase, because benefit of therapy is time dependent, treatment should be initiated as quickly as possible and not delayed for additional multimodal neuroimaging, such as CT and MRI perfusion imaging (Powers et al. [*AHA*/*ASA*] 2019).

Imaging notes:

- Timely access to CT or MR perfusion [or MRI with DWI] scanning can be used to demonstrate a perfusion mismatch and to determine the extent of the ischemic core, especially in patients beyond 6h from last known well, including patients with stroke on awakening (Boulanger et al. 2018; PLE expert panel consensus opinion).
- Imaging techniques for determining infarct and penumbra sizes can be used for patient selection and correlate with functional outcome after mechanical thrombectomy (Wahlgren et al. [*ESO*] 2016, Grade B, Level 1b/KSU Grade B).
- It may be reasonable to incorporate collateral flow status into clinical decision making in some candidates to determine eligibility for mechanical thrombectomy (Powers et al. [*AHA/ASA*] 2019).
- In patients with suspected intracranial LVO and no history of renal impairment, who otherwise meet criteria for mechanical thrombectomy, it is reasonable to proceed with CTA if indicated in patients before obtaining a serum creatinine concentration (Powers et al. [*AHA/ASA*] 2019).
- Patients with radiological signs of large infarcts may be unsuitable for thrombectomy (Wahlgren

et al. [*ESO*] 2016; Grade B/Level 2a).

- An example of a stroke-protocol MRI includes DWI, ADC, T1, T2, FLAIR, and T2 GRE or SWI sequences. This combination of sequences allows for identification of other causes for the patient's symptoms and allows the estimation of the age of the infarct (PLE expert panel consensus statement).
- It is reasonable to use MRI systems capable of consistently generating high-quality images while avoiding low-field systems that do not yield diagnostically accurate results (Brott et al. 2011).

<u>Evidence update (2017-present):</u>
Ryu et al. (2017) conducted a systematic review and meta-analysis of 13 studies regarding the utility of perfusion imaging in determining treatment eligibility in patients with acute stroke (994 treated with aid of perfusion imaging [multimodal CT scan and MRI performed as a part of stroke assessment] and 1819 treated with standard care) and in predicting clinical outcome. Of patients treated with aid of perfusion imaging, 51.1% experienced a favorable clinical outcome at 3-mo follow-up compared with 45.6% of those treated with standard care (p=0.06). Random effects modeling suggested a trend towards favoring perfusion imaging-based treatment (OR 1.29, 95% CI 0.99 to 1.69; p=0.06). Studies using multimodal therapy showed largest effect size favoring perfusion imaging (OR 1.89, 95% CI 1.44 to 2.51; p<0.01). The authors concluded that perfusion imaging may represent a complementary tool to standard radiographic assessment in enhancing patient selection for reperfusion therapy (moderate level of evidence).

Thomalla et al. (2019) conducted a multicenter randomized trial to determine whether patients with stroke with unknown time of onset and features suggesting recent cerebral infarction on MRI would benefit from thrombolysis with the use of IV alteplase. Included patients (n = 503) had an ischemic lesion visible on MRI diffusion-weighted imaging but no parenchymal hyperintensity on fluid-attenuated inversion recovery (FLAIR), which indicated that stroke had occurred approximately < 4.5 hours prior. Patients for whom thrombectomy was planned were excluded. Of the enrolled patients, 254 were randomly assigned to receive alteplase and 249 to receive placebo. A favorable outcome at 90 days was reported in 131 of 246 patients (53.3%) in the alteplase group and in 102 of 244 patients (41.8%) in the placebo group (adjusted OR, 1.61; 95% CI, 1.09 - 2.36; P = 0.02). There were 10 deaths (4.1%) in the alteplase group and 3 (1.2%) in the placebo group (OR, 3.38; 95% CI, 0.92 - 12.52; P = 0.07). The rate of symptomatic intracranial hemorrhage was 2.0% in the alteplase group and 0.4% in the placebo group (OR, 4.95; 95% CI, 0.57 - 42.87; P = 0.15).The authors conclude that, in patients with acute stroke with an unknown time of onset, IV alteplase guided by a mismatch between diffusion-weighted imaging and FLAIR in the region of ischemia resulted in a significantly better functional outcome than placebo at 90 days (high level of evidence).

Provost et al. (2019) compared workflow and functional outcome in acute ischemic stroke patients screened by MRI or CT before treatment in the randomized THRACE trial (tPA and thrombectomy or tPA alone). A total of 401 patients from 25 centers were included: 299 patients underwent MRI and 102 had CT before treatment. Median baseline NIHSS score was 18 in both groups. MRI scan duration (median [interquartile range]) was longer than CT (MRI: 13 minutes [10–16]; CT: 9 minutes [7–12]; P < 0.001). Stroke-onset-to-imaging time (MRI: median 114 minutes [89–138]; CT: 107 minutes [88–139]; P=0.19), onset-to-IV tPA time (MRI: 150 minutes [124–179]; CT: 150 minutes [123–180]; P=0.38) and onset-to-angiography suite time (MRI: 200 minutes [170–250]; CT: 213 minutes [180–246]; P=0.57) did not differ between groups. Imaging modality was not significantly associated with functional outcome in the multivariable analysis. The authors conclude that, although MRI scan duration is a few minutes longer than CT, workflow demonstrates that real world application of MRI for acute stroke evaluation before treatment can be accomplished as rapidly as CT-based selection paradigms (low level of evidence).

Albers et al. (2018) conducted a multicenter randomized open-label trial on therapeutic efficacy of endovascular therapy (thrombectomy) plus standard medical therapy (endovascular-therapy group; n = 92) compared to standard medical therapy alone (medical-therapy group; n = 90) in patients with stroke onset 6-16 hours prior to thrombectomy. Patients had occlusion of the cervical or intracranial internal carotid artery or the proximal middle cerebral artery on CTA or MRA and initial infarct volume (ischemic core) of < 70 ml, a ratio of volume of ischemic tissue to initial infarct volume of ≥ 1.8, and an absolute volume of potentially reversible ischemia (penumbra) of ≥ 15 ml on CT or MR perfusion. Median growth volume of the infarct region between baseline and 24 hours was 23 ml in the endovascular-therapy group and 33 ml in the medical-therapy group (p=0.08). Reperfusion > 90% of the initial perfusion lesion at 24 hours was more common in the endovascular-therapy group than medical-therapy group (79% vs. 18%, p<0.001). The percentage of patients with complete recanalization of the primary arterial occlusive lesion at 24 hours on CTA or MRA was higher for endovascular-therapy group than medical therapy group (78% vs. 18%, p<0.001). Mortality at 90 days was 14% for endovascular therapy group and 26% for medical-therapy group (p=0.05). The rate of symptomatic intracranial hemorrhage did not differ significantly between groups (7% vs. 4%; p=0.75). The authors conclude that among patients with acute ischemic stroke due to large-vessel occlusion who had favorable findings on perfusion imaging, endovascular therapy 6-16 hours after stroke onset plus standard medical therapy resulted in less disability and higher rates of functional independence at 3 mo than standard medical therapy alone (high level of evidence).

Nogueira et al. (2018) conducted a multicenter prospective randomized open-label trial on therapeutic efficacy of thrombectomy plus standard care (thrombectomy group; n = 107; mean age 69.4) compared to standard care alone (control group; n = 99; mean age 70.7) in patients with occlusion of the intracranial internal carotid artery or proximal middle cerebral artery who had last been known to be well 6-24 hours earlier, and who had a mismatch between severity of clinical deficit and the infarct volume. Mismatch criteria was defined according to age with NIHSS > 10, MRS < 2. Mean score on the utility-weighted modified Rankin scale at 90 days was 5.5 in the thrombectomy group as compared with 3.4 in the control group (adjusted difference [Bayesian analysis], 2.0 points; 95% credible interval, 1.1 to 3.0; posterior probability of superiority, >0.999), and rate of functional independence at 90-d was 49% in the thrombectomy group vs. 13% in the control group (adjusted difference, 33 percentage points; 95% credible interval, 24 to 44; posterior probability of superiority, >0.999). Rate of symptomatic intracranial hemorrhage did not differ significantly between the two groups (6% in thrombectomy group and 3% in control group, P=0.50), nor did 90-d mortality (19% and 18%, respectively; P=1.00). The authors conclude that outcomes for disability were better with thrombectomy plus standard medical care than with standard medical care alone among patients with acute stroke who received treatment 6-24 hours after they had last been known to be well and who had a mismatch between severity of the clinical deficit and the infarct volume, which was assessed with the use of diffusion-weighted MRI or perfusion CT and measured with the use of automated software (high level of evidence).

Mokin et al. (2017) analyzed the accuracy of various relative cerebral blood volume (rCBV) and relative cerebral blood flow (rCBF) thresholds for predicting 27-h infarct volume. Patients from the SWIFT PRIME study who achieved complete reperfusion based on time until the residue function reached its peak > 6 s perfusion maps obtained at 27-h were included. Final infarct volume was determined on MRI (fluid-attenuated inversion recovery images) or CT scans obtained 27-h after symptom onset. Among the 47 subjects, the following baseline CT perfusion thresholds most accurately predicted the actual 27-h infarct volume: rCBV=0.32, median absolute error (MAE) = 9 mL; rCBV=0.34, MAE=9 mL; rCBF=0.30, MAE=8.8 mL; rCBF=0.32, MAE=7 mL; and rCBF=0.34, MAE=7.3. The authors conclude that brain regions with rCBF 0.30-0.34 or rCBV 0.32-0.34 thresholds provided the most accurate prediction of infarct volume in patients who achieved complete reperfusion with MAEs of $\leq$ 9 (low level of evidence).

Yoo et al. (2016) examined the effect of the baseline Alberta Stroke Program Early CT Score (ASPECTS) on the safety and efficacy of intraarterial treatment in a subgroup analysis of the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN). Imaging criteria for inclusion were a CT or MRI scan ruling out hemorrhage, and CT, magnetic (MR), or digital subtraction angiography showing occlusion of the intracranial internal carotid artery, middle cerebral artery (M1 or M2 segments), or anterior cerebral artery (A1 or A2 segments). A total of 496 patients, 232 (47%) in the intraarterial treatment and usual care group and 264 (53%) in the usual care alone group, were included in the subgroup analysis. The authors graded ASPECTS on baseline non-contrast CT images. The authors estimated intraarterial treatment effect by using multivariable ordinal logistic regression analysis to calculate the adjusted common odds ratio [for a shift towards a better functional outcome according to the modified Rankin Scale (mRS) score for intraarterial treatment and usual care than for usual care alone]. An interaction term was used to test for interaction with prespecified ASPECTS subgroups: 0–4 (large infarct) versus 5–7 (moderate infarct) versus 8–10 (small infarct). The authors found that, contrary to findings from previous studies suggesting that only patients with non-contrast CT ASPECTS of > 7 benefit from intraarterial treatment, data from this study suggest that patients with ASPECTS 5-7 should be treated (low level of evidence).

Suspected stroke in patients who are not candidates for thrombolytic or endovascular therapy or confirmed stroke in patients after thrombolytic or endovascular therapy for risk stratification/secondary prevention:

- **Green** – CT head without contrast
- **Green** – MRI brain‡
- **Yellow** – CT head with contrast, CTA head, and/or CT venography to evaluate for an underlying vascular lesion in patients with intracranial hemorrhage
- **Yellow** – MRA head and/or MR venography to evaluate for an underlying vascular lesion in patients with intracranial hemorrhage

Carotid imaging:

- **Green** – MRA or CTA neck with contrast*
- **Red** – CT perfusion; MR perfusion

‡MRI of the brain should include diffusion weighted imaging and gradient recalled imaging (GRE) or susceptibility-weighted imaging (SWI) (see technical notes below).

*Duplex carotid ultrasound is also accurate for evaluation of the carotid arteries and can be used to evaluate patients for carotid artery stenosis following stroke.

Level of Evidence: CT head without contrast, MRI brain without contrast: moderate; CTA head without and with contrast: moderate for intracranial vascular imaging/very low for modality; CTA neck with contrast, MRA head without contrast; MRA neck without and with contrast, MRA neck without contrast: low

Notes concerning applicability and/or patient preferences: Consulting and reporting requirements are not required for orders for applicable imaging services made by ordering professionals under the following circumstances (*42 C.F.R. § 414.94. 2015*):

- Emergency services when provided to individuals with emergency medical conditions.
- For an inpatient and for which payment is made under Medicare Part A.

Guideline and PLE expert panel consensus summary:
All patients admitted to hospital with suspected acute stroke should receive brain imaging evaluation on arrival. In most cases, noncontrast CT (NCCT) will provide the necessary information to make decisions about acute management (Powers et al. [*AHA/ASA*] 2018, Class I (strong) Recommendation: /Level of Evidence: B-NR).

Rapid neuroimaging with CT or MRI is recommended to distinguish ischemic stroke from intracerebral hemorrhage (ICH) (Hemphill et al. [*AHA/ASA*] 2015, Class I/Level of Evidence: A).

Either non-contrast computed tomography (CT) or magnetic resonance imaging (MRI) should be used for the definition of stroke type and treatment of stroke. MRI has a higher sensitivity than conventional CT for the documentation of infarction within the first hours of stroke onset, lesions in the posterior fossa, identification of small lesions, and documentation of vessel occlusion and brain edema (Irimia et al. 2010, Class I/Level A).

MRI with diffusion weighted and gradient echo sequences is recommended for the diagnosis of acute stroke syndromes in patients who are not severely ill, especially where neurological deficit is mild and the clinical likelihood is that the lesion is small or lies in the posterior fossa; or in patients who present late (after one week) (*SIGN* 2008, B recommendation).

In patients with ICH, CTA and contrast-enhanced CT may be considered to help identify patients at risk for hematoma expansion (Class IIb; Level of Evidence B), and CTA, CT venography, contrast-enhanced CT, contrast-enhanced MRI, magnetic resonance angiography and magnetic resonance venography, and catheter angiography can be useful to evaluate for underlying structural lesions including vascular malformations and tumors when there is clinical or radiological suspicion (Hemphill et al. [*AHA/ASA*] 2015, Class IIa/Level of Evidence: B).

MRA head and CTA head are not indicated in this clinical scenario unless it is used to evaluate for an underlying vascular lesion in patients with intracranial hemorrhage, or unless it changes patient management (PLE expert panel consensus opinion).

Carotid imaging –
Evaluation of the extracranial carotid arteries is typically performed in the context of risk assessment and secondary prevention after treatment for the acute stroke (PLE expert panel consensus opinion; Brott et al. 2011).

Duplex ultrasonography is recommended to detect carotid stenosis in patients:

- who develop focal neurological symptoms corresponding to the territory supplied by the left or right internal carotid artery ECVD (Brott et al. 2011, Class I/Level of Evidence: C); and
- with nonspecific neurological symptoms when cerebral ischemia is a plausible cause (Brott et al. 2011, Class IIb/Level of Evidence: C).

Duplex ultrasound (as first-line), computed tomographic angiography and/or magnetic resonance angiography are recommended for evaluating the extent and severity of extracranial carotid stenosis (Naylor et al. [*ESVS*] 2017, Class I/Level of Evidence: A).

In patients with acute, focal ischemic neurological symptoms corresponding to the territory supplied by the left or right carotid artery, magnetic resonance angiography (MRA) or computed tomography angiography (CTA) is indicated to detect carotid stenosis when sonography either cannot be obtained or yields equivocal or otherwise nondiagnostic results (Brott et al. 2011, Class I/Level of Evidence: C).

In patients whose symptoms suggest posterior cerebral or cerebellar ischemia, MRA or CTA is recommended rather than ultrasound imaging for evaluation of the vertebral artery (Brott et al. 2011, Class I/Level of Evidence: C).

MRA without contrast is reasonable to assess the extent of disease in patients with symptomatic carotid atherosclerosis and renal insufficiency or extensive vascular calcification (Brott et al. 2011, Class IIa/Level of Evidence: C).

CTA is reasonable for evaluation of patients with clinically suspected significant carotid atherosclerosis who are not suitable candidates for MRA (Brott et al. 2011, Class IIa/Level of Evidence: C).

Clinical notes:

- Survivors [of stroke] face risks of recurrent stroke as high as 4% to 15% within a year after incident stroke, and 25% by 5 years (Brott et al. 2011).
- In many patients, the diagnosis of ischemic stroke can be made accurately on the basis of the clinical presentation and either a negative NCCT or one showing early ischemic changes, which can be detected in the majority of patients with careful attention (Powers et al. [*AHA*/*ASA*] 2019).
- Once the diagnosis of acute stroke has been made, the patient has been stabilized, thrombolytic and endovascular therapy has been administered if appropriate, evaluation is directed to establishing the vascular territory involved, the cause and the pathophysiology of the event. Treatment is then directed at risk stratification and secondary prevention (Brott et al. 2011; PLE expert panel consensus opinion).

Imaging notes:

- Ensure that carotid imaging reports clearly state which criteria (ECST or NASCET) were used when measuring the extent of carotid stenosis (*NICE* 2019). An example of a stroke-protocol MRI includes DWI, ADC, T1, T2, FLAIR, and T2 GRE or SWI sequences. This combination of sequences allows for identification of other causes for the patient's symptoms and allows the estimation of the age of the infarct (PLE expert panel consensus opinion).
- It is reasonable to use MRI systems capable of consistently generating high-quality images while avoiding low-field systems that do not yield diagnostically accurate results (Brott et al. 2011).
- If there is concern for carotid artery dissection, axial fat-suppressed T1-weighted images through the neck should be obtained (Salmela et al. [ACR] 2017).

Evidence update (2016-present):
Georgakis et al. (2019) conducted a systematic review and meta-analysis to explore the long-term prognostic significance of white matter hyperintensities (WMH) in patients with ischemic stroke. A total of 104 studies (n = 71,298 patients with ischemic stroke and examining the association of WMH at baseline with the outcomes of interest over a follow-up period of ≥ 3 months) were included. Moderate/severe WMH at baseline were associated with increased risk of dementia (RR 2.17, 95% CI 1.72–2.73), cognitive impairment (RR 2.29, 95% CI 1.48–3.54), functional impairment (RR 2.21, 95% CI 1.83–2.67), any recurrent stroke (RR 1.65, 95% CI 1.36–2.01), recurrent ischemic stroke (RR 1.90, 95% CI 1.26–2.88), all-cause mortality (RR 1.72, 95% CI 1.47–2.01), and cardiovascular mortality (RR 2.02, 95% CI 1.44–2.83). The associations followed dose-response patterns for WMH severity and were consistent for both MRI- and CT-defined WMH. The results remained stable in sensitivity analyses adjusting for age, stroke severity, and cardiovascular risk factors, in analyses of studies scoring high in quality, and in analyses adjusted for publication bias. The authors conclude that, in patients with ischemic stroke, both the presence and extent of WMH are associated with substantially increased risk of multiple long-term outcomes (moderate level of evidence).

Kauw et al. (2018) conducted a systematic review and meta-analysis to identify both clinical and imaging predictors of recurrent ischemic stroke. A total of 10 articles (n = 212,864 patient with ischemic stroke) were included. Results of the analysis found that: past history of stroke or TIA was a predictor of recurrent ischemic stroke (pooled RR 2.5, 95% CI 2.1–3.1); small vessel strokes were associated with a lower risk of recurrence than large vessel strokes (pooled RR 0.3, 95% CI 0.1–0.7); patients with stroke of an undetermined cause had a lower risk of recurrence than patients with large artery atherosclerosis

(pooled RR 0.5, 95% CI 0.2–1.1). The authors found no studies using CT or ultrasound for the prediction of recurrent ischemic stroke. The following MRI findings were predictors of recurrent ischemic stroke: multiple lesions (pooled RR 1.7, 95% CI 1.5–2.0), multiple stage lesions (pooled RR 4.1, 95% CI 3.1–5.5), multiple territory lesions (pooled RR 2.9, 95% CI 2.0–4.2), chronic infarcts (pooled RR 1.5, 95% CI 1.2–1.9), and isolated cortical lesions (pooled RR 2.2, 95% CI 1.5–3.2) (moderate level of evidence).
Kang et al. (2016) conducted a prospective study on the reliability of silent new ischemic lesions (SNIL) at 5 days (5D) or 30 days (30D) after acute ischemic stroke to predict recurrent ischemic stroke (IS) in 270 patients (mean age 62.81) with acute IS confirmed by initial DWI performed within 24-h of symptom onset. In patients with acute IS, 5D- and 30D-SNIL independently predicted recurrent IS (hazard ratio [95% confidence interval] 2.9 [1.3–6.4] and 9.6 [4.1–22.1], respectively). In patients with acute IS, 5D- and 30D-SNIL independently predicted composite vascular events of recurrent IS, TIA, ACS, and vascular death (HR = 2.4 [1.3–4.5] and 6.1 [3.1–12.4], respectively). The authors conclude that patients with a SNIL within the first few weeks after index stroke have increased risk of recurrent IS or vascular events (high level of evidence).

Streifler et al. (2016) evaluated the impact of prior cerebral infarction in patients previously enrolled in the Asymptomatic Carotid Surgery Trial: a large study (n = 3,120) with 10-y follow-up in which participants whose carotid stenosis had not caused symptoms for at least 6 mo were randomly allocated to either immediate or deferred carotid endarterectomy. Of these, 2333 patients with baseline brain imaging (CT or MRI) were identified and divided into two groups irrespective of treatment assignment, 1331 with evidence of previous cerebral infarction, (history of ischemic stroke or TIA > 6 months prior to randomization or radiological evidence of an asymptomatic infarct: group 1) and 1,002 with normal imaging and no prior stroke or TIA (group 2). At 10-y follow-up, stroke was more common among patients with cerebral infarction before randomization (absolute risk increase 5.8% (1.8–9.8), p=0.004), and risk of stroke and vascular death were also higher in this group (absolute risk increase 6.9% (1.9–12.0), p=0.007). The authors conclude that asymptomatic carotid stenosis patients with prior cerebral infarction have higher stroke risk at long-term follow-up than those without prior infarction. Evidence of prior ischemic events might help identify patients in whom carotid intervention is particularly beneficial (low level of evidence).

Andersen et al. (2016) conducted an observational cohort study on the association of silent lacunes and risk of ischemic stroke recurrence, death, and cardiovascular events in a cohort of 786 patients (mean age 59.5 years) with incident ischemic stroke and no atrial fibrillation (AF). Number of silent lacunes were assessed on brain MRI as none, single, or multiple. In 168 (21.5%) patients, at least one silent lacune was present, and in 87 (11.1%) patients, multiple silent lacunes were found. Patients with at least one silent lacune were older (mean age 66.1 vs. 57.7, p < 0.001). During a median follow-up time of 2.9 years, 53 recurrent ischemic strokes, 76 deaths, and 96 cardiovascular events were observed. Incidence rates per 100 person-years of ischemic stroke recurrence were 1.6, 2.5, and 5.0 for none, single, and multiple silent lacunes, respectively. The authors conclude that an increasing number of silent lacunes was associated with increasing incidence rates of ischemic stroke recurrence. Risk of death or cardiovascular events was not significantly influenced by presence of silent lacunes (low level of evidence).

Amarenco et al. (2016) conducted a multicenter prospective registry on the contemporary profile, etiologic factors, and outcomes in patients (mean age 66.1) with a TIA or minor ischemic stroke within the previous 7 days who receive care in health systems that offer urgent evaluation by stroke specialists. Kaplan–Meier estimate of 1-year event rate of composite cardiovascular outcome was 6.2% (95% CI: 5.5-7.0), and estimates of stroke rate at days 2, 7, 30, 90, and 365 were 1.5%, 2.1%, 2.8%, 3.7%, and

5.1%, respectively. Multiple infarctions on brain imaging, large-artery atherosclerosis, and an ABCD score of 6 or 7 were each associated with more than a doubling of stroke risk. The authors observed a lower rate of cardiovascular events after TIA or minor stroke than that in historical cohorts. This may reflect a contemporary risk of recurrent cardiovascular events among patients with a TIA or minor stroke who are admitted to TIA clinics and who receive risk-factor control and antithrombotic treatment as recommended by current guidelines. Findings suggest that limiting urgent assessment to patients with an ABCD score of $\geq$ 4 would miss approximately 20% of those with early recurrent strokes. Multiple infarctions on neuroimaging and large-artery atherosclerotic disease were also strong independent predictors of recurrent vascular events (low level of evidence).

Follow-up of extracranial carotid artery disease treated with carotid endarterectomy or stenting:

- **Green** – *
- **Yellow** – MRA neck (for either of the following):
  - in patients for whom ultrasound is not available, or
  - for patients who have had a nondiagnostic or inconclusive ultrasound
- **Yellow** – CTA neck (for either of the following):
  - in patients for whom ultrasound is not available, or
  - for patients who have had a nondiagnostic or inconclusive ultrasound
- **Red** – CT perfusion; MR perfusion; CTA head; CT head; CT neck; MRA head; MRI brain; CT venography; MR venography

*Duplex carotid ultrasound can be used to follow lesions in the extracranial carotid arteries and can be used to follow progression of disease in the contralateral artery after medical or invasive therapy.

Level of Evidence: CT head without contrast, MRI brain without contrast: moderate; CT perfusion, MR perfusion, CTA head without and with contrast, CTA neck with contrast, MRA head without contrast, MRA neck without and with contrast, MRA neck without contrast, CT head with contrast, CT head without and with contrast, MRA head with contrast, MRA head without and with contrast, CTA head without and with contrast: very low (none)

Notes concerning applicability and/or patient preferences: none

Guideline and PLE expert panel consensus summary:
Noninvasive imaging of the extracranial carotid arteries is reasonable 1 month, 6 months, and annually after CEA or revascularization to assess patency and exclude the development of new or contralateral lesions. Once stability has been established over an extended period, surveillance at longer intervals may be appropriate. Termination of surveillance is reasonable when the patient is no longer a candidate for intervention (Brott et al. 2011, Class IIa/Level of Evidence: C).

Serial follow-up assessment most commonly involves duplex ultrasound imaging. Imaging by CTA or MRA may also be helpful for surveillance after carotid angioplasty and stenting (CAS), particularly when Doppler interrogation is difficult because of a superior anatomic location of the region of interest (Brott et al. 2011).

Serial non-invasive imaging of the extracranial vertebral arteries may be considered in patients who have undergone open or endovascular interventions (Naylor et al. [*ESVS*] 2018, Class IIb/Level of Evidence: C).

Clinical/Technical notes: none

Evidence update (no date limit):
There was no new low, moderate or high quality evidence significantly affecting the evidence and recommendations included in the guidelines cited above.

Suspected cerebral venous thrombosis (CVT):

- **Green** – MRI brain
- **Green** – MR venography
- **Yellow** – CT head* when the patient is unable to undergo MRI or when MRI is not available
- **Yellow** – CT venography* when the patient is unable to undergo MRI or when MRI is not available
- **Red** – CTA head; CTA neck; MRA head; MRA neck; CT perfusion; MR perfusion; CT neck

*CT utilizes ionizing radiation and iodinated contrast, however is often more available in the acute or urgent setting.

Level of Evidence: CT head, MRI brain without contrast, CTA head without and with contrast, MRA head without and with contrast: low

Notes concerning applicability and/or patient preferences: Consulting and reporting requirements are not required for orders for applicable imaging services made by ordering professionals under the following circumstances (*42 C.F.R. § 414.94. 2015*):

- Emergency services when provided to individuals with emergency medical conditions.
- For an inpatient and for which payment is made under Medicare Part A.

Guideline and PLE expert panel consensus summary:
Although a plain CT or MRI is useful in the initial evaluation of patients with suspected cerebral venous thrombosis (CVT), a negative plain CT or MRI does not rule out CVT. A venographic study (either CTV or MRV) should be performed in suspected CVT if the plain CT or MRI is negative or to define the extent of CVT if the plain CT or MRI suggests CVT (Saposnik et al. [*AHA/ASA*] 2011, Class I/Level of Evidence: C).

An MRV or CTV should be performed if hemorrhage location, relative edema volume, or abnormal signal in the cerebral sinuses on routine neuroimaging suggests cerebral vein thrombosis (Hemphill et al. [*AHA/ASA*] 2015).

MRI with [MRV] is recommended for the diagnosis and follow-up of cerebral venous thrombosis (Class II, Level B). Alternatively, CT venography is accurate and can be used for the same purpose (Irimia et al. 2010, Class III/Level C).

In patients with previous CVT who present with recurrent symptoms suggestive of CVT, repeat CTV or MRV is recommended (Saposnik et al. [*AHA/ASA*] 2011, Class I/Level of Evidence: C).

An early follow-up CTV or MRV is recommended in CVT patients with persistent or evolving symptoms despite medical treatment or with symptoms suggestive of propagation of thrombus (Saposnik et al. [*AHA/ASA*] 2011, Class I/Level of Evidence: C).

A follow-up CTV or MRV at 3 to 6 months after diagnosis is reasonable to assess for recanalization of the occluded cortical vein/sinuses in stable patients (Saposnik et al. [*AHA/ASA*] 2011, Class IIa/Level of Evidence: C).

Intra-arterial four-vessel angiography has long been the gold standard for establishing the diagnosis of CVST but today magnetic resonance imaging (MRI) and magnetic resonance [venography (MRV)] are regarded the best tools both for the diagnosis and follow-up of CVST. Cranial computed tomography (CCT) alone is not sufficient but diagnosis can be established in combination with CT angiography although the use of iodinated contrast fluid and ionizing radiation remains a disadvantage which makes it inappropriate for follow-up examinations (Einhaupl et al. [*EFNS*] 2010*).

In patients with *suspected dural venous sinus thrombosis,* the *American College of Radiology* recommends MR venography head without and with IV contrast (9), MR venography head without IV contrast (8), CT venography head with IV contrast (8), MR venography head and neck without and with IV contrast (8), CT head without and with IV contrast (7), CT head without IV contrast (7), MRI head without and with IV contrast (7), MRI head without IV contrast (7), CT venography head and neck with IV contrast (7), CT head with IV contrast (6), MR venography head and neck without IV contrast (6), and catheter venography cervicocerebral (5) (Salmela et al. [ACR] 2017).

* This guideline did not pass the AGREE II total score or rigor of development scaled domain score cutoff. It was included, however, because of its direct relevance to this clinical scenario.

<u>Clinical notes:</u>

- CVT is an uncommon cause for stroke, affecting 0.5%-2% of stroke patients (Salmela et al. [ACR] 2017; Saposnik et al. [*AHA/ASA*) 2011).
- Patients can present with headaches, seizures, or decreased level of consciousness (Saposnik et al. [*AHA/ASA*] 2011).
- In patients with headache associated with atypical features, imaging of the cerebral venous system is reasonable to exclude CVT (Class IIa/Level of Evidence C). For patients with isolated headache, the proper strategy for identification of CVT is much less clear (Saposnik et al. [AHA/ASA] 2011). The vast majority of patients with isolated headache will not have CVT (PLE expert panel consensus opinion; Saposnik et al. [*AHA/ASA*] 2011).
- Factors that may suggest the diagnosis [of CVT] and thus prompt imaging evaluation include a new atypical headache; headache that progresses steadily over days to weeks despite conservative treatment; and thunderclap headache (Saposnik et al. [*AHA/ASA*] 2011).
- Predisposing conditions for CVT and principles in favor of a cause-and-effect relationship include prothrombotic conditions, pregnancy, puerperium, oral contraceptives, parameningeal infections, or cancer (Saposnik et al. [*AHA/ASA*] 2011).
- In patients with lobar ICH of otherwise unclear origin or with cerebral infarction that crosses typical arterial boundaries, imaging of the cerebral venous system should be performed (Saposnik et al. [*AHA/ASA*], Class I/Level of Evidence).
- In patients with the clinical features of idiopathic intracranial hypertension, imaging of the cerebral venous system is recommended to exclude CVT (Saposnik et al. [*AHA/ASA*], Class I/ Level of Evidence C).
- In patients with a history of CVT who complain of new, persisting, or severe headache, evaluation for CVT recurrence and intracranial hypertension should be considered (Saposnik et al. [*AHA/ASA*] 2011, Class I/Level of Evidence C).

<u>Imaging notes:</u>

- Direct signs [of CVT] on unenhanced CT are the cord sign, corresponding to thrombosed cortical veins, and the dense triangle sign, corresponding to a thrombus in the superior sagittal sinus, and, on enhanced CT of the sagittal sinus, the delta sign (Irimia et al. 2010, Saposnik et al. [*AHA/ASA*] 2011).

- Indirect signs such as local hypodensities caused by edema or infarction, hyperdensities secondary to hemorrhagic infarction, or brain swelling and small ventricles suggest the diagnosis of CVT (Irimia et al. 2010).
- Contrast-enhanced CT may show enhancement of the dural lining of the sinus with a filling defect in the vein or sinus (Saposnik et al. [*AHA/ASA*] 2011).
- Gradient echo T2 susceptibility-weighted images combined with magnetic resonance can be useful to improve the accuracy of CVT diagnosis (Saposnik et al. [*AHA/ASA*] 2011, Class IIa/Level of Evidence B).
- If there is suspicion for CVT after the initial NCCT is performed in the acute setting, CTV can be quickly performed while the patient is still on the CT scan table. In a less acute setting or an acute setting where MRI is readily available without contraindications, contrast-enhanced brain MRI and MRV are often performed for optimal evaluation (Salmela et al. [ACR] 2017).
- Catheter cerebral angiography can be useful in patients with inconclusive CTV or MRV in whom a clinical suspicion for CVT remains high (Saposnik et al. [*AHA/ASA*] 2011, Class IIa/Level of Evidence C).

Evidence update (2015-present):
Xu et al. (2018) conducted a meta-analysis to assess the accuracy of CT and MRI in the differential diagnosis of cerebral venous thrombosis (CVT) and cerebral venous sinus thrombosis (CVST). A total of 24 articles (n = 4,595 cases) were included. The pooled sensitivity for CT–CVT/CT–CVST groups was 0.79 (95% CI: 0.76, 0.82)/0.81(95% CI: 0.78, 0.84), and pooled specificity was 0.90 (95% CI: 0.89, 0.91)/0.89 (0.88, 0.91), with an area under the curve (AUC) for the summary receiver operating characteristic (SROC) of 0.9314/0.9161, respectively. No significant heterogeneity or publication bias was observed. For MRI–CVT/MRI–CVST, the pooled sensitivity was 0.82 (95% CI: 0.78, 0.85)/0.80 (95% CI: 0.76, 0.83), and pooled specificity was 0.92 (95% CI: 0.91, 0.94)/0.91(0.89, 0.92), with an AUC for the SROC of 0.9221/0.9273, respectively. The authors conclude that both CT and MRI have a high level of diagnostic accuracy in the differential diagnosis of CVT and CVST. Either could be chosen as an alternative sub-optimal gold standard (vs. MRV or CTV), especially in emergency (low level of evidence).

Alons et al. (2015) conducted a meta-analysis of 8 studies on the diagnostic accuracy and diagnostic yield of the D-dimer test in 636 patients with isolated headache and suspected CVT. A total of 45 (7.5%) CVT patients had a negative D-dimer. Sensitivity of D-dimer for diagnosing CVT was 97.8 % (95 % CI: 88.2–99.6 %), specificity was 84.9 % (95 % CI: 81.8–87.7 %), PPV was 33.1 % (95 % CI: 25.2–41.7 %), and NPV was 99.8 % (95 % CI: 98.9–100 %). The authors conclude that D-dimers have a high negative predictive value in patients with isolated headache for excluding CVT (moderate level of evidence).

Suspected central nervous system (CNS) vasculitis presenting with stroke:

- **Green** – CT head without contrast
- **Green** – MRI brain‡
- **Green** – MRA head
- **Green** – CTA head
- **Yellow** – CT head with contrast in patients who are unable to undergo MRI

Neck imaging:

- **Yellow** – MRA neck if systemic large vessel vasculitis is suspected
- **Yellow** – CTA neck if systemic large vessel vasculitis is suspected
- **Red** – CT neck; CT perfusion; MR perfusion; CT venography; MR venography

‡ MRI of the brain should include diffusion-weighted imaging and gradient recalled imaging or susceptibility-weighted imaging (see technical notes below).

Level of Evidence: CT head, MRI brain without contrast, CTA head without and with contrast, CTA neck with contrast, MRA head without and with contrast: low

Notes concerning applicability and/or patient preferences: Consulting and reporting requirements are not required for orders for applicable imaging services made by ordering professionals under the following circumstances (*42 C.F.R. § 414.94. 2015*):

- Emergency services when provided to individuals with emergency medical conditions.
- For an inpatient and for which payment is made under Medicare Part A.

Guideline and PLE expert panel consensus summary:
All patients with suspected acute stroke should undergo emergent or immediate brain imaging with NCCT or MRI (Boulanger et al. 2018: Evidence Level A; *NICE* 2019; Irimia et al. 2010, Class I/Level A).

Noncontrast head CT is often obtained first to assess for hemorrhage or large infarct (Salmela et al. [ACR] 2017).

MRI has a higher sensitivity than conventional CT for the documentation of infarction within the first hours of stroke onset, lesions in the posterior fossa, identification of small lesions, and documentation of vessel occlusion and brain edema (Irimia et al. 2010, Class I/Level A).

In the evaluation of CNS vasculitis, CE-MRI and MRA of the head and neck are the initial imaging studies of choice to evaluate for vessel narrowing/dilation/occlusion of large- and medium-vessels, scattered white matter T2 hyperintensities, and scattered infarcts in different vascular territories (Salmela et al. [ACR] 2017).

In patients with *central nervous system vasculitis,* the *American College of Radiology* (Salmela et al. [ACR] 2017) recommends MRI head without and with IV contrast (8), MRA head without and with IV contrast (8), MRA head without IV contrast (8), arteriography cervicocerebral (8), CTA head with IV contrast (8), MRA head and neck without and with IV contrast (7), MRA head and neck without IV contrast (7), CTA head and neck with IV contrast (7), MRI head without IV contrast (7), and CT head without IV contrast (5).

Clinical notes:

- The clinical presentation [of CNS vasculitis] is highly variable and includes ischemic stroke, hemorrhagic stroke, seizure, migraine, psychiatric disease, and cognitive decline (Salmela et al. [ACR] 2017).
- US can be used in the evaluation for extracranial vasculitis, including fibromuscular dysplasia and giant cell arteritis decline (Salmela et al. [ACR] 2017).
- Conventional angiography remains the gold standard imaging study for evaluation of large- and medium-vessel narrowing, dilation, or occlusion in CNS vasculitis (Salmela et al. [ACR] 2017).
- If MRA is negative and vasculitis is still suspected, conventional angiography should then be performed (Salmela et al. [ACR] 2017).

Imaging notes:

- Direct imaging findings of CNS vasculitis include vessel wall enhancement and thickening, and indirect imaging findings include vessel narrowing, dilation, occlusion, and a beaded appearance as well as scattered nonspecific white-matter T2 hyperintensities on MRI, scattered infarcts in different vascular territories, perfusion defects, and hemorrhage (Salmela et al. [ACR] 2017).
- High-resolution contrast-enhanced MRI at 3T can be used to evaluate for direct signs of vasculitis, including wall thickening and enhancement in large- and medium-sized vessels (Salmela et al. [ACR] 2017).
- An example of a stroke-protocol for an MRI brain includes DWI, ADC, T1, T2, FLAIR, and T2 GRE or SWI sequences. This combination of sequences allows for identification of other causes for the patient’s symptoms, for the detection of ischemia, and for estimation of the age of the infarct (PLE expert panel consensus statement).

Evidence update (no date limit):

Boulouis et al. (2017) conducted a case series of 60 patients (mean age 45) with primary angiitis of the central nervous system (PACNS). Acute ischemic lesions were observed in 75% of patients at time of diagnosis. The most common MRI finding observed in 42% of patients was multiterritorial, bilateral, distal acute stroke lesions after small to medium artery distribution, with a predominant carotid circulation distribution. Seventy-seven percent of MRA studies were abnormal, revealing proximal/distal stenoses in 57% and 61% of patients, respectively. The authors conclude that PACNS diagnosis with neuroimaging remains difficult given the wide variety of imaging characteristics and the poor specificity of each finding taken separately (low level of evidence).

Guideline exclusions:

- Cases meeting the definition of a suspected or confirmed emergency medical condition
- Cardiac imaging
- Blunt or penetrating trauma
- Detection or follow-up of isolated intracranial aneurysm
- Detection or follow-up of cerebrovascular malformation(s)
- Suspected or known subarachnoid hemorrhage (thunderclap headache)
- MR arterial spin labelling
- Transcranial Doppler (TCD) ultrasonography
- Pediatric patients and
- Pregnant patients.

AUC Revision History:

Revision Date:	New AUC Clinical Scenario(s):	Posting Date:	Approved By:
04/07/2020	n/a	04/13/2020	CDI Quality Institute's Multidisciplinary Committee

Information on our evidence development process, including our conflicts of interest policy is available on our website at **https://www.mycdi.com/ple**