PROVIDER LED ENTITY
Stroke and Related Conditions AUC
2024 Update

04/23/2024

Appropriateness of advanced imaging procedures* in patients with cerebrovascular disease 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
ACR	American College of Radiology
AHA	American Heart Association
AIS	Acute ischemic stroke
ASA	American Stroke Association
AUC	Appropriate Use Criteria
CAS	Carotid artery stenosis/stenting
CEA	Carotid endarterectomy
CT	Computed tomography
CTA	Computed tomographic angiography
CTP	CT perfusion
CTV	CT venography
CVA	Cerebrovascular accident
CVST	Cerebral venous sinus thrombosis
DWI	Diffusion weighted imaging
ECVD	Extracranial Carotid and Vertebral Artery Disease
ESVS	European Society for Vascular Surgery
ESO	European Stroke Organization
EVT	Endovascular thrombectomy
ICA	Internal carotid artery
ICH	Intracranial hemorrhage
LVO	Large vessel occlusion
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
MRP	MR perfusion
MRV	MR venography
NASCET	North American Symptomatic Carotid Endarterectomy Trial
NCCT	Noncontrast CT
NICE	National Institute for Health and Care Excellence
PLE	Provider Led Entity
SNIL	Silent new ischemic lesion
SVS	Society for Vascular Surgery
TIA	Transient ischemic attack
tPA	Tissue plasminogen activator
US	Ultrasound
USPSTF	U.S. Preventive Services Task Force

Appropriate Use Criteria: How to Use this Document

The RAYUS Radiology Quality Institute follows the recommendation framework defined by the Appraisal of Guidelines for Research & Evaluation (AGREE II), AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews) and a modified version of the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) to evaluate the strength of recommendations concerning advanced imaging. Considerations used to determine a recommendation are listed below.

Primary recommendation (green): A strong recommendation for imaging; there is confidence that the desirable effects of imaging outweigh its undesirable effects.

Alternative recommendation (yellow): A conditional recommendation for imaging; the desirable effects of imaging likely outweigh its undesirable effects, although some uncertainty may exist. The individual patient's circumstances, preferences, and values should be considered on a case-by-case basis. This may include: contraindication to the primary recommendation, specific clinical circumstances that require use of the alternative recommendation, or the primary recommendation has results that are inconclusive or incongruent with the patient's clinical diagnosis. Case-by-case indications to consider have been noted in brackets.

Recommendation against imaging (red): The undesirable effects of imaging outweigh any desirable effects. Additionally, the recommendation may be impractical or not feasible in the targeted population and/or practice setting(s).

PICO 1: Physical findings, radiographic signs, and/or risk factors suggestive of carotid artery stenosis in an otherwise asymptomatic patient:

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

Level of Evidence: CTA neck, MRA neck: low

Notes concerning applicability and/or patient preferences: None

Guideline and PLE expert panel consensus summary:

Screening

Routine screening for carotid artery stenosis is not recommended for:

- the general adult population (Krist [*USPSTF*] 2021, D recommendation; Naylor et al [ESVS] 2023: class III, level C recommendation; AbuRahma et al [SVS] 2022);
- asymptomatic patients who have no clinical manifestations of or risk factors for atherosclerosis (Brott et al [ACCF/AHA et al] 2011: Class III: No Benefit/Level of Evidence: C; AbuRahma et al [SVS] 2022: grade IB recommendation) or
- patients who have no risk factors for development of atherosclerotic carotid disease and no disease evidence on initial vascular testing (Brott et al [ACCF/AHA et al] 2011: Class III: No Benefit/Level of Evidence: C).

Screening for carotid stenosis has been found to reduce the risk of stroke when the prevalence of significant stenosis is ≥ 20% (AbuRahma et al [SVS] 2022). In selected asymptomatic patients who are at an increased risk of carotid stenosis, screening is suggested, especially if patients are willing to consider carotid intervention if significant stenosis is discovered. Such groups include patients:

- with two or more of the following traditional atherosclerotic 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 (Naylor et al [ESVS] 2023: class IIb, level B recommendation; AbuRahma et al [SVS] 2022: grade 2B recommendation; Brott et al [ACCF/AHA et al] 2011: Class IIb/Level of Evidence: C);

- with symptomatic peripheral artery disease, diabetes, atherosclerotic aortic aneurysm, or coronary artery disease/undergoing coronary artery bypass surgery (AbuRahma et al [SVS] 2022: grade 2B recommendation; Brott et al [ACCF/AHA et al] 2011: Class IIb/Level of Evidence: C);with a carotid bruit, which increases the likelihood of detecting significant stenosis (AbuRahma et al [SVS] 2022: grade 2B recommendation; Brott et al [ACCF/AHA et al] 2011: Class IIa/Level of Evidence: C);
- with silent brain infarction in the carotid territory [on advanced imaging] (AbuRahma et al [SVS] 2022: grade 2B recommendation; Smith et al [*AHA/ASA*] 2017); or
- with large (> 1.0 cm) silent intracranial hemorrhages on previous imaging (Smith et al [*AHA/ASA*] 2017).

In asymptomatic patients with suspected carotid stenosis, duplex ultrasonography (US), performed by a qualified technologist, is recommended as the initial diagnostic test to detect hemodynamically significant carotid stenosis (AbuRahma et al [SVS] 2022: grade 1B recommendation; Brott et al [ACCF/AHA et al] 2011: Class I/Level of Evidence: C). Carotid ultrasound is a very accurate and useful screening test, with 90% sensitivity and 94% specificity in the identification of clinically significant stenosis warranting surgical intervention (Pannell et al [ACR] 2023). It can, however, overestimate the degree of stenosis in those with contralateral or multivessel disease and can also underestimate the degree of stenosis in those with critical high-grade stenosis (Pennell et al [ACR] 2023).

MRA has slightly higher sensitivity and specificity than US to determine carotid stenosis and occlusion, however is not indicated in initial screening for carotid artery disease (AbuRahma et al [SVS] 2022; Irimia et al 2010) unless ultrasound is non diagnostic or not available (PLE expert panel consensus opinion). Magnetic resonance angiography (MRA) can provide three-dimensional images and has advantages over CTA which include absence of radiation and avoidance of iodinated-based contrast materials (AbuRahma et al [SVS] 2022).

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). CTA is also able to evaluate the extent of vessel calcification, can evaluate for associated aortic arch disease, and is less likely to overestimate the severity of carotid stenosis compared with MRA (AbuRahma et al [SVS] 2022). However, CTA is generally not appropriate for screening purposes, and the requirement for radiation and the use of contrast are significant limitations (AbuRahma et al [SVS] 2022).

Neither MRI or CT of the head is indicated in the initial workup of the asymptomatic patient with a carotid bruit (Pannell et al [ACR] 2023). There is also no literature to support the use of perfusion imaging or venography for the initial detection of hemodynamically significant carotid disease in asymptomatic patients (Pannell et al [ACR] 2023).

Further Characterization of Stenosis

For patients undergoing evaluation of the extent and severity of extracranial carotid stenoses, duplex ultrasound, CTA, and/or MRA are recommended (Naylor et al [ESVS] 2023: class I, level B recommendation). MRA or CTA of the neck can be useful for further workup of the asymptomatic patient with a carotid bruit, particularly when multivessel cerebrovascular disease or very severe stenosis is present (Pannell et al [ACR] 2023). However, either modality can underestimate or overestimate the degree of stenosis in certain scenarios (Pannell et al [ACR] 2023). CTA head or MRA head may also be useful for treatment planning for those with an established diagnosis of asymptomatic carotid stenosis (Pannell et al [ACR] 2023).

Surveillance
In patients with a 50-60% asymptomatic carotid stenosis who would consider a future carotid endarterectomy or carotid artery stenting (if indicated), it is reasonable to offer annual duplex ultrasound surveillance performed by a qualified technologist to assess progression or regression of disease and response to therapeutic interventions (Brott et al 2011; Naylor et al [ESVS] 2023). Once stability has been established over an extended period, longer intervals or termination of surveillance may be appropriate (Brott et al 2011). If a patient would not consent to any future carotid intervention, surveillance is typically not indicated (Naylor et al [ESVS] 2023). Neither MRI or CT of the head is indicated in the routine surveillance imaging of asymptomatic carotid disease (Pannell et al [ACR] 2023).

Evaluation for Treatment
When intervention for significant carotid stenosis is planned, MRA or CTA 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 C evidence). For patients where carotid endarterectomy is being considered, it is recommended that the duplex ultrasound stenosis estimate be corroborated by CTA or MRA, or by a repeat duplex ultrasound performed by a second operator (Naylor et al [ESVS] 2023: class I, level B recommendation). Similarly, for a patient where carotid artery stenting is being considered, it is recommended that any duplex ultrasound study be followed by CTA or MRA, which will provide additional information on the aortic arch, as well as the extra- and intracranial circulation (Naylor et al [ESVS] 2023: class I, level B recommendation).

<u>Clinical and imaging notes:</u>

- Asymptomatic carotid artery stenosis refers to stenosis in persons without a history of ischemic stroke, transient ischemic attack, or other neurologic symptoms referable to the carotid arteries (Krist et al [USPSTF] 2021).
- Although carotid artery stenosis is a risk factor for stroke, it causes a relatively small proportion (10-20%) of strokes (Krist et al [USPSTF] 2021; Brott et al 2011).
- The presence of asymptomatic carotid artery stenosis is low in the general population but increases with age (Krist et al [USPSTF] 2021).
- Carotid stenosis is divided into three categories based on the degree of stenosis including mild (< 50%), moderate (50-69%), and severe (> 70%) stenosis, with moderate and severe having a higher probability of hemodynamic significance (Pannell et al [ACR] 2023).
- Cervical carotid bruit is an important diagnostic sign of potential underlying carotid stenosis, as these patients are > 50% more likely to harbor hemodynamically significant internal carotid stenosis (Pannell et al [ACR] 2023).
- In units which base management decisions in patients with atherosclerotic carotid disease on duplex ultrasound measurement, it is recommended that reports should state which measurement method is used (e.g., ECST, NASCET) (NICE 2019; Naylor et al [ESVS] 2023).

<u>Evidence update (2016-present):</u>
High Level of Evidence
Cassola et al (2022) in a *Cochrane Library* systematic review, estimated the accuracy of duplex ultrasound (DUS) in individuals with symptomatic carotid stenosis verified by either digital subtraction angiography (DSA), CTA, or MRA. NASCET criteria for carotid stenosis measures were used, and studies were excluded if they included < 70% of symptomatic patients. In total, 22 studies were included (n = 4,957 carotid arteries). Risk of bias varied considerably across studies, and individual studies were

generally of moderate to low quality. For DUS versus DSA, for < 50% carotid artery stenosis, summary sensitivity was 0.63 (95% CI: 0.48 to 0.76) and summary specificity was 0.99 (95% CI: 0.96 to 0.99); for the 50% to 99% range, summary sensitivity was 0.97 (95% CI: 0.95 to 0.98) and summary specificity was 0.70 (95% CI: 0.67 to 0.73); for the 70% to 99% range, summary sensitivity was 0.85 (95% CI: 0.77 to 0.91) and summary specificity was 0.98 (95% CI: 0.74 to 0.90); for occlusion, summary sensitivity was 0.91 (95% CI: 0.81 to 0.97) and summary specificity was 0.95 (95% CI: 0.76 to 0.99). There was little evidence that compared DUS with CTA or MRA. The authors conclude that this review provides evidence that the diagnostic accuracy of DUS is high, especially in discriminating between the presence or absence of significant carotid artery stenosis (< 50% or 50%-99%). This evidence, plus its less invasive nature, supports the early use of DUS for the detection of carotid artery stenosis.

Low Level of Evidence

Poorthuis et al (2021) used a large contemporary screened population to develop a new risk score for predicting asymptomatic carotid stenosis (ACS) and to identify those at moderate (≥ 50%) and severe (≥ 70%) risk. Individual participant data from volunteers who attended commercial vascular disease screening clinics in the USA and UK were used. A total of 596, 469 participants were included in the data (mean age 62, 36% male, 41% current or former smoker). Carotid duplex assessment was conducted by trained staff using dedicated vascular ultrasound instruments. Participants underwent bilateral examination of the carotid arteries with measurement of the highest peak systolic velocity (PSV) and end diastolic velocities of each common carotid and internal carotid artery. Results found that predictors of ≥ 50% and ≥ 70% ACS were age, sex, current smoking, diabetes mellitus, prior stroke/TIA, coronary artery disease, peripheral arterial disease, blood pressure, and blood lipids. Targeted screening among the highest decile of predicted risk identified around 40% of all cases with ≥ 50% ACS.

PICO 2: Suspected transient ischemic attack(s) (TIA):

Carotid (extracranial) imaging:

- Green – **Duplex carotid ultrasound**
- Green – **MRA neck**
- Yellow – **CTA neck**
    - patient unable to undergo MRI

Brain (intracranial) imaging:

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

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

*Venography imaging is appropriate for patients with suspected CVT, which is addressed in PICO 6 below.

Level of Evidence: CT head without contrast, MRA neck without contrast: high; MRI head 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: None

Guideline and PLE expert panel consensus summary:
Transient ischemic attacks are self-limited focal neurologic deficits resulting from a temporary interruption in blood supply to the brain, with no permanent clinical deficit or demonstrated infarct on subsequent imaging (Pannell et al [ACR] 2023). Although symptoms may resolve within a short period of time, typically < 1 hour, the risk for subsequent stroke is high. Therefore, expeditious initial imaging is important, requiring rapid vascular imaging of the cervical carotid arteries in addition to brain parenchymal imaging (Pannell et al [ACR] 2023). 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).

Carotid (extracranial) 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 extracranial carotid and vertebral artery disease (ECVD) (Brott et al [ACCF/AHA et al] 2011: Class I/Level of Evidence: C). When

feasible, physicians should obtain cervical vascular imaging (e.g., carotid ultrasonography, CTA, or MRA) In patients with symptomatic TIA who are candidates for revascularization, noninvasive cervical carotid imaging with carotid ultrasonography, CTA, or MRA is recommended to screen for stenosis (Kleindorfer et al [AHA/ASA] 2021: class 1, level B-NR recommendation) and to identify patients at high short-term risk for stroke (Lo et al [ACEP] 2016, Level C recommendation).

Ultrasound

Duplex carotid ultrasound is a useful test in the initial evaluation of the extracranial vasculature in the workup of TIA, as it is noninvasive and has similar accuracy to MRA or CTA for evaluating the degree of carotid stenosis (Pannell et al [ACR] 2023; Lo et al [ACEP] 2016: level C recommendation). Duplex ultrasonography can 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 [ACCF/AHA et al] 2011: class I, level C evidence) and with nonspecific neurological symptoms when cerebral ischemia is a plausible cause (Brott et al [ACCF/AHA et al] 2011: class IIb, level C evidence).

MRA or CTA

In patients with acute, focal ischemic neurological symptoms corresponding to the territory supplied by the left or right internal carotid artery, MRA (or 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 C evidence). MRA of the neck can be useful for screening extracranial vascular disease in the initial workup and triage of patients presenting with TIA (Heran et al 2024: strong recommendation, moderate quality of evidence; Pannell et al [ACR] 2023). Noncontrast MRA may overestimate the degree of carotid stenosis when compared with contrast-enhanced MRA, particularly in cases of high-grade stenosis (Pannell et al [ACR] 2023). CTA of the neck can rapidly evaluate the extracranial vasculature and is useful in the initial workup and triage of patients presenting with carotid territory TIA, particularly those who are not suitable candidates for MRA because of claustrophobia or implanted pacemakers (Brott et al [ACCF/AHA et al] 2011: Class IIa, level C evidence; Pannell et al [ACR] 2024). However, heavy calcification or calcified plaque on both sides of the lumen can lead to overestimation of the stenosis on CTA (Pannell et al [ACR] 2023), however newer CT technologies such as photon counting CT will limit this deficiency (expert committee consensus opinion).

Brain (intracranial) imaging

MRI

Brain imaging (MRI or CT) should be completed as soon as possible following TIA to confirm the diagnosis (Heran et al 2024: strong recommendation, moderate quality of evidence; Kleindorfer et al [AHA/ASA] 2021: class 1, level B-NR recommendation). MRI is the most sensitive test for acute infarct, and a noncontrast MRI of the head (including diffusion-weighted and blood-sensitive sequences) is typically sufficient for the routine assessment of uncomplicated TIA to determine the territory of ischemia, to evaluate for silent infarcts or to detect hemorrhage or alternative pathologies (Pannell et al [ACR] 2023; NICE 2019; Lo et al [ACE] 2016, level C recommendation). MRI brain scanning is superior to head CT in terms of diagnostic sensitivity for identifying small ischemic lesions in patients presenting clinically with a TIA or minor stroke and can provide additional information to guide decisions about diagnosis, prognosis, and treatment (Heran et al 2024). It is also particularly useful in lower-risk patients with transient symptoms where the presence of ischemia would change their management (Heran et al 2024). If the initial head imaging (CT or MRI) does not demonstrate a symptomatic cerebral infarct, follow-up MRI is reasonable to predict risk of early stroke and to support the diagnosis (Kleindorfer et al [AHA/ASA] 2021: class 2a, level B-NR recommendation). MRI without and with IV contrast may be useful in the secondary workup of patients who present with transient focal neurological symptoms (Pannell et

al [ACR] 2023).

CT
CT head without IV contrast is useful for the initial evaluation of TIA to exclude alternative etiologies (intracranial hemorrhage, infection, intracranial mass) and evaluate for early ischemic changes (Pannell et al [ACR] 2023; NICE 2019). 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; NICE 2019).

Perfusion imaging
While CT head perfusion is not typically used for the initial assessment of TIA, it has been found to identify abnormalities in the setting of TIA in up to one-third of cases (Pannell et al [ACR] 2023).

Venography
There is no relevant literature to support the use of MR venography or CT venography for evaluation of TIA in the absence of suspicion for cerebral venous thrombosis (CVT) (Pannell et al [ACR] 2023).

CTA or MRA
When an extracranial source of ischemia is not identified in patients with transient retinal or hemispheric neurological symptoms of suspected ischemic origin, CTA head or MRA head can be useful to search for intracranial vascular disease (Brott et al 2011: class IIa, level C evidence). MRA or CTA is also recommended over ultrasound imaging for evaluation of the vertebral artery in those whose symptoms suggest posterior cerebral or cerebellar ischemia (Brott et al [ACCF/AHA et al] 2011: class I, level C evidence). In patients with TIA, imaging of the intracranial large arteries and the extracranial vertebrobasilar arterial system with MRA or CTA can be effective to identify atherosclerotic disease, dissection, moyamoya, or other etiologically relevant vasculopathies (Kleindorfer et al [AHA/ASA] 2021: class 2a, level C-LD recommendation). CTA of the head can rapidly evaluate the intracranial vasculature for underlying intracranial atherosclerosis and other intracranial steno-occlusive diseases, which may be useful in the secondary workup and triage of patients presenting with TIA (Pannell et al [ACR] 2023). MRA of the head is an alternative modality to evaluate intracranial steno-occlusive disease and may be useful in the initial workup and triage of patients presenting with TIA. Without the need for IV contrast, MRA may be preferable to CTA in patients with renal impairment, contrast allergy, or repeat presentations (Pannell et al [ACR] 2023).

<u>Clinical notes:</u>

- 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).
- Approximately one-third of all TIAs have evidence of infarction at presentation (Lo et al [*ACEP*] 2016).
- In patients with TIA or minor stroke, evidence of acute ischemia with chronic ischemia or microangiopathy significantly increases the risk of subsequent stroke within 90 days of index visit. The combination of all three findings results in the greatest early risk (Ferguson et al 2023).
- 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 (i.e., a 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).

- Transient neurological symptoms that can mimic TIA include migraine aura, seizures, syncope, peripheral vestibular disturbance, and functional/anxiety disorder (Nadarajan et al 2014).

Imaging notes:

- 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).
- 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.
- Carotid imaging reports should clearly state which criteria (e.g., ECST, NASCET) were used when measuring the extent of carotid stenosis (*NICE* 2019).
- Typically, noncontrast time-of-flight (TOF) MRA technique is sufficiently sensitive to screen for culprit intracranial lesions in the setting of suspected TIA (Pannell et al [ACR] 2023).

Evidence update (2016-present):

High 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 $\geq$ 4. Internal carotid stenosis of $\geq$ 50% was found in 15 patients (8.1%) and associated with high risk for stroke (OR = 4.5, 95% CI: 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 (OR = 2.5, 95% CI: 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.

Moderate Level of Evidence

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 (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.

Low Level of Evidence

Bala et al (2022), in a post hoc analysis of a large, prospective multicenter cohort study, examined the prevalence and risk factors associated with intracranial atherosclerotic disease in patients with low-risk transient or persistent neurologic events (defined as nonmotor or nonspeech symptoms of any duration, or motor or speech symptoms of $\leq$ 5 minutes duration). A total of 661 patients with mean age of 62 years were included and all underwent MR brain imaging. Intracranial atherosclerotic disease was found in 81 (12.3%) patients, with the majority (n = 65) being asymptomatic. The most frequent location was in the posterior cerebral artery (29%). Age was the only factor associated with intracranial atherosclerotic disease (adjusted OR = 1.9; 95% CI: 1.6-2.5). The authors conclude that evaluation of the intracranial arteries could be valuable in establishing the etiology of such low-risk events.

PICO 3: Suspected acute stroke within the treatment window for thrombolytic or endovascular therapy:

- **Green – CT head**
- **Green – MRI head**[‡]
- **Green – CTA head and/or neck**
- **Yellow – MRA head and/or neck**
- **Yellow – CT perfusion head**
- **Yellow – MR perfusion head**
- **Yellow – Duplex carotid ultrasound**
- **Red – CT venography*, MR venography***

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

*Venography imaging is appropriate for patients with suspected CVT, which is addressed in PICO 6 below.

Level of Evidence: CT head without contrast, MRI head 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:
MRI scanning can be challenging to obtain urgently, and this must be considered in decision-making and not delay decisions regarding eligibility for therapy (Powers et al [*AHA/ASA*] 2019: class I (strong) recommendation, level A evidence; Pannell et al [ACR] 2023).

Guideline and PLE expert panel consensus summary
Imaging for suspected intracranial hemorrhage (ICH)
It is essential to exclude ICH before administration of IV thrombolytic therapy or before the initiation of EVT (Pannell et al [ACR] 2023). Either a noncontrast CT (strong recommendation, level A evidence) or MRI (strong recommendation, level B-NR evidence) is effective to exclude ICH before IV alteplase administration (Powers et al [*AHA/ASA*] 2019). No existing clinical decision scale can differentiate intracerebral hemorrhage from other diseases with high sensitivity or specificity in the absence of neuroimaging (Greenberg et al [AHA/ASA] 2022).

Brain imaging is essential to distinguish ICH from ischemic stroke and determine ICH volume (Greenberg et al [AHA/ASA] 2022). In patients presenting with stroke-like symptoms, rapid neuroimaging with CT or MRI is recommended to confirm the diagnosis of spontaneous ICH (Greenberg et al [AHA/ASA] 2022: class 1, level B-NR recommendation). CT is the most widely used imaging modality to confirm (or rule out) the presence of ICH because of its widespread availability, rapidity, high diagnostic accuracy, and ease (Greenberg et al [AHA/ASA] 2022; Heran et al 2024: strong recommendation, moderate quality of evidence). However, MRI with echo-planar gradient echo or susceptibility-weighted sequences also can detect hyperacute ICH with high accuracy (Greenberg et al [AHA/ASA] 2022).

If there are signs of hemorrhage on initial CT images, CTA should be completed based on clinical judgment (Heran et al 2024). In patients with spontaneous ICH, CTA within the first few hours of ICH onset may be reasonable to identify patients at risk of subsequent hematoma expansion (HE)

(Greenberg et al [AHA/ASA] 2022: class 2b, level B-NR recommendation).

If there are signs of hemorrhage on initial CT images, there is no need to proceed with CT perfusion as part of initial imaging (Heran et al 2024).

Imaging for consideration of thrombolytic therapy:
Brain imaging (CT or MRI) should be completed as soon as possible following suspected stroke to confirm the diagnosis (Heran et al 2024: strong recommendation, moderate quality of evidence; Kleindorfer et al [AHA/ASA] 2021: class 1, level B-NR recommendation; *NICE* 2019; Irimia et al 2010, Class I/Level A).

CT
Noncontrast CT of the head is essential in the initial evaluation of stroke to exclude other potential etiologies for the patient's symptoms and to evaluate for early ischemic changes (Pannell et al [ACR] 2023). Additionally, areas of early ischemic change can be used to estimate the extent of irreversible tissue damage (Pannell et al [ACR] 2023). In many patients, the diagnosis of ischemic stroke can be made accurately based on the clinical presentation and either a negative NCCT or one showing early ischemic changes, which can be detected in many patients with careful attention (Powers et al [*AHA*/*ASA*] 2019).

MRI
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 recommendation, level A evidence). In patients who awake with stroke symptoms or have unclear time of onset, MRI to identify diffusion-positive FLAIR-negative lesions can also 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 B-R evidence). For some wake-up strokes or anterior circulation strokes with large infarcts, SWI-MRI and FLAIR sequences are necessary to determine eligibility for thrombolytics (Pannell et al [ACR] 2023).

CTA or MRA
CTA or MRA may be used to define the vascular anatomy for treatment planning in the acute setting, however, should not delay treatment with thrombolytic therapy (PLE expert panel consensus opinion). With this in mind, patients with suspected ischemic stroke due to large vessel occlusion who are potentially eligible for intravenous thrombolysis can undergo immediate non-contrast CT combined with CTA of the head and neck when performed and interpreted without delay (Heran et al 2024: strong recommendation, high quality of evidence). CTA is the first-line vascular imaging test for stroke patients and the most rapid means of assessing extracranial vasculature in the setting of stroke (Heran et al 2024: conditional recommendation, low quality of evidence; Pannell et al [ACR] 2023). CTA of the head and neck from aortic arch to vertex, performed at the time of initial brain CT, is ideal for assessing both extracranial and intracranial circulation (Heran et al 2024: strong recommendation, moderate quality of evidence). Stroke due to large vessel occlusion (LVO) is a true medical emergency in which the rapidity of diagnosis afforded by CTA is a strongly relevant clinical consideration (Pannell et al [ACR] 2023). If CTA is not possible, MRA for extracranial vascular imaging is a reasonable alternative for assessment of the carotid vessels, and selection should be based on availability, patient characteristics, and time (Heran et al 2024: conditional recommendation, low quality of evidence; PLE expert panel consensus opinion).

Perfusion imaging
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 perfusion imaging (Powers et al [*AHA/ASA*] 2019). Therefore, in some situations, CT perfusion of the head may not always be necessary (Pannell et al [ACR] 2023). When indicated in this scenario, the rapidity of diagnosis afforded by CT perfusion (as opposed to MR perfusion) is a relevant clinical consideration in most settings (Pannell et al [ACR] 2023).

Ultrasound
Although sensitive and specific in the detection of extracranial vascular disease, duplex carotid Doppler does not provide the information necessary to determine eligibility for thrombolytics or thrombolysis (Pannell et al [ACR] 2023). 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).

Venography
There is no relevant literature to support the use of CT venography or MR venography in the evaluation of suspected ischemic stroke in the absence of suspicion for CVT (Pannell et al [ACR] 2023).

Imaging for consideration of endovascular therapy (EVT):
Diagnosing an acute stroke patient with an LVO who may be a candidate for EVT requires advanced imaging, which has been associated with better EVT outcomes (Lo et al [ACEP] 2023). 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 C-EO evidence).

EVT is indicated in patients with suspected ischemic stroke due to LVO based on imaging selection, and most often performed with immediate head and neck imaging, including extracranial and intracranial arteries (Heran et al 2024: strong recommendation, high quality of evidence). MRA or CTA can be used to aid patient selection, define the vascular anatomy for treatment planning in the acute setting, and identify atherosclerotic disease, dissection, moyamoya, or other relevant vasculopathies; however, it should not delay treatment with endovascular therapy (Heran et al 2024: strong recommendation, moderate quality of evidence; Kleindorfer et al [AHA/ASA] 2021; PLE expert panel consensus opinion). Combination head and neck imaging can be rapidly acquired together to further elucidate the etiology of stroke and may be useful for endovascular surgical planning for EVT in LVO (Pannell et al [ACR] 2023). Specifically, it is recommended that all patients with suspected acute ischemic stroke who arrive within six hours and are potentially eligible for EVT undergo immediate non-contrast CT and CTA without delay, from arch-to-vertex including the extra- and intra-cranial circulation, to identify large vessel occlusions eligible for endovascular thrombectomy (*NICE* 2019; Powers et al [*AHA/ASA*] 2019: class I (strong) recommendation, level A evidence; Wahlgren et al [*ESO*] 2016: grade A recommendation, level 1a evidence). Although sensitive and specific in the detection of the extent of irreversible ischemia, LVO, and extracranial vascular disease, MRI head and TOF MRA of the head and/or MRA of the neck may delay EVT in the setting of stroke, which possibly detracts from the usefulness of this procedure due to the potential harm of delayed treatment (Pannell et al [ACR] 2023).

Perfusion imaging
Perfusion imaging can be used as part of initial imaging to aid patient selection for EVT; however,

advanced imaging must not substantially delay decision-making and treatment (Heran et al 2024: strong recommendation, moderate quality of evidence; Lo et al [ACEP] 2023). When evaluating patients within 6 hours of last known normal with LVO, 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 B-NR evidence).

All patients with suspected ischemic stroke due to LVO arriving 6 to 24 hours after stroke symptom onset (including stroke on awakening or with unknown onset time) and who may potentially benefit from this late window EVT should undergo immediate brain imaging with NCCT, CTA and CT perfusion; or MRI with MRA and MR perfusion (Heran et al 2024: strong recommendation, moderate quality of evidence; Lo et al [ACEP] 2023; Pannell et al [ACR] 2023; Powers et al [*AHA/ASA*] 2019: class I (strong) recommendation, level A evidence; Irimia et al 2010, class I recommendation, level A evidence). The CT approach may be more practical and more readily available than the MR approach, and choice of imaging modality should be based on most immediate availability, local resources, and time considerations (Heran et al 2024; Pannell et al [ACR] 2023; NICE 2019; PLE expert panel consensus opinion). MRI perfusion is sensitive and specific in the detection of reversible ischemia, so long as it does not delay EVT in the setting of stroke due to LVO (Pannell et al [ACR] 2023).

Ultrasound
Although sensitive and specific in the detection of extracranial vascular disease, duplex carotid Doppler does not provide the information necessary to determine eligibility for EVT (Pannell et al [ACR] 2023). However, it is noninvasive and is accurate in evaluating the degree of carotid stenosis, making it a useful test for the evaluation of the extracranial vasculature to determine eligibility for CEA or stenting if this information has not already been obtained from other vascular imaging (Pannell et al [ACR] 2023).

Venography
There is no relevant literature to support the use of CT venography or MR venography in the evaluation of suspected ischemic stroke in the absence of suspicion for CVT (Pannell et al [ACR] 2023).

Clinical notes:

- Approximately 10% of strokes per year are intracerebral hemorrhages, defined by brain injury attributable to acute blood extravasation into the brain parenchyma from a ruptured cerebral blood vessel (Greenberg et al [AHA/ASA] 2022).
- Ischemic stroke is responsible for 87% of all strokes (Kleindorfer et al [AHA/ASA] 2021).
- The standard window for intravenous thrombolysis is 4.5 hours and the standard time window for EVT is 6 hours. However, patients may be considered eligible beyond these windows based on clinical factors and neuroimaging findings (Heran et al 2024).
- Rarely, brain tumors or other conditions can mimic ischemic stroke, and MRI without and with IV contrast may be helpful in the secondary workup of patients presenting with stroke-like symptoms (Pannell et al [ACR] 2023).

Imaging notes:

- For patients with ICH, identification of a spot sign on CTA or contrast-enhanced CT or certain imaging features on NCCT such as heterogenous densities within the hematoma or irregularities at its margins may help to identify patients at risk for hematoma expansion (Greenberg et al [AHA/ASA] 2022).

- 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 6 hours from last known well, including patients with stroke on awakening (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).
- 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).
- For some wake-up strokes and some anterior circulation strokes with large infarcts, SWI-MRI and FLAIR sequences are necessary to determine eligibility for EVT, respectively (Pannell et al [ACR] 2023). 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).

Evidence update (2017-present):

High 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 (DWI) 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 DWI and FLAIR in the region of ischemia resulted in a significantly better functional outcome than placebo at 90 days.

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 $\geq$ 1.8, and an absolute volume of potentially reversible ischemia (penumbra) of $\geq$ 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.

Moderate Level of Evidence

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 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: 0.99-1.69; p=0.06). Studies using multimodal therapy showed largest effect size favoring perfusion imaging (OR= 1.89, 95% CI: 1.44-2.51; 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.

Low Level of Evidence

Jadhav et al (2022) performed a subanalysis of pooled data from randomized controlled trials comparing EVT with usual care for acute ischemic stroke due to anterior circulation LVO and within 6 hours from last known well. Good functional outcome (Rankin Scale score 0-2) was compared between randomized patients with and without CT perfusion baseline imaging. A total of 1,348 patients were analyzed, of which 610 (45.3%) underwent CT perfusion prerandomization. Results found that CT perfusion baseline imaging compared to baseline noncontrast CT with CTA yielded similar rates of good outcome (OR = 1.05 [95% CI: 0.82–1.33], adjusted OR = 1.04, [95% CI: 0.80–1.35]). The authors conclude that EVT treatment effect in the 0- to 6-hour time window was similar in patients with and without baseline CT perfusion imaging.

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 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 significantly 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.

PICO 4: 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:

Brain imaging:

- **Green – CT head**
- **Green – MRI head**[‡]
- **Yellow – CTA head**
- **Yellow – CT venography***
- **Yellow – MRA head**
- **Yellow – MR venography***
- **Red – CT perfusion; MR perfusion**

Carotid imaging:

- **Green – CTA neck**
- **Green – MRA neck**
- **Green – Duplex carotid ultrasound**

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

*Venography imaging is appropriate for patients with suspected CVT, which is addressed in PICO 6 below.

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: None

Guideline and PLE expert panel consensus summary:

Brain Imaging

All patients with suspected acute stroke should receive brain imaging with NCCT or MRI. 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). In patients with delayed presentation of strokes, noncontrast CT of the head is essential to evaluate for complications such as hemorrhagic conversion, mass effect, and herniation (Pannell et al [ACR] 2023). 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 patients suspected of having ischemic stroke, if initial head imaging (CT or MRI) does not demonstrate a cerebral infarct, follow-up MRI is also reasonable to predict risk of early stroke and to support the diagnosis (Kleindorfer et al [AHA/ASA] 2021).

MRA head and CTA head are indicated in this clinical scenario to evaluate for an underlying vascular lesion in patients with intracranial hemorrhage, or when their use changes patient management (PLE

expert panel consensus opinion). CTA of the head is a rapid and highly sensitive means of evaluating the intracranial vasculature for underlying intracranial atherosclerosis, LVO, and other intracranial steno-occlusive diseases, which may be useful in the management of late presenting strokes (Pannell et al [ACR] 2023). MRA of the head can also be useful for workup of late presenting stroke when there is no indication for urgent EVT (Pannell et al [ACR] 2023).

CT venography or MR venography of the head may be useful to exclude CVT as a potential etiology in the setting of typical hypertensive hemorrhage (Pannell et al [ACR] 2023). MR venography may be particularly useful if suggested by features of hemorrhage on initial CT imaging or the diagnosis is in doubt based on contrast-enhanced MRI (Pannell et al [ACR] 2023).

While head perfusion imaging may detect an underlying lesion not identified by other imaging modalities in some cases of late presenting stroke, it is not generally used as a first-line test (Pannell et al [ACR] 2023).

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). Current guidelines recommend noninvasive imaging of the cervical carotid arteries for patients with minor stroke who are candidates for CEA or stenting, within 24 hours of hospitalization or 48 hours of onset due to the high early risk of recurrent stroke in patients with symptomatic carotid stenosis (Pannell et al [ACR] 2023).

CTA of the neck is a rapid and highly sensitive means of evaluating the extracranial vasculature underlying carotid stenosis and other steno-occlusive disease of the cervical vasculature (Pannell et al [ACR] 2023). MRA of the neck can obtain similar information when there is no need for rapid triage and vascular diagnosis, but may tend to overestimate the degree of carotid stenosis in the absence of contrast administration (Pannell et al [ACR] 2023). 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 [ACCF/AHA 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 [ACCF/AHA 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 [ACCF/AHA et al] 2011: Class iIa/Level of Evidence: C).

US duplex carotid Doppler is useful for assessing the degree of carotid stenosis in anterior circulation infarcts due to the noninvasive nature of this examination, the high degree of accuracy, and the absence of time pressure of EVT candidacy associated with delayed presenting strokes (Pannell et al [ACR] 2023). 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 [ACCF/AHA et al] 2011: Class I/Level of Evidence: C); and
- with nonspecific neurological symptoms when cerebral ischemia is a plausible cause (Brott et al [ACCF/AHA et al] 2011: Class iIb/Level of Evidence: C).

<u>Clinical and imaging notes:</u>

- Survivors of stroke face risk of recurrent stroke as high as 4%-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 based on clinical presentation and either a negative NCCT or one showing early ischemic changes, which can be detected in most patients with careful attention (Powers et al [*AHA*/*ASA*] 2019).
- Rarely, brain tumors or other conditions can mimic ischemic stroke, and MRI without and with IV contrast can be helpful in the secondary workup of patients presenting with stroke-like symptoms (Pannell et al [ACR] 2023).
- 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).
- 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):

High 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 patients) 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).

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.

Moderate Level of Evidence

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.

Low 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.

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.

PICO 5: Follow-up of extracranial carotid artery disease treated with carotid endarterectomy or stenting:

- Green – **Duplex carotid ultrasound**
- Yellow – **MRA neck** (either of the following)
    - ultrasound is not available
    - nondiagnostic or inconclusive ultrasound
- Yellow – **CTA neck** (either of the following)
    - ultrasound is not available, or
    - nondiagnostic or inconclusive ultrasound
- Red – **CT perfusion; MR perfusion; CTA head; CT head; CT neck; MRA head; MRI head; CT venography; MR venography**

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:
For patients who have undergone an open or endovascular vertebral artery intervention, serial non-invasive imaging surveillance may be considered (Naylor et al [ESVS] 2023: class IIb, level C recommendation). Noninvasive imaging of the extracranial carotid arteries is reasonable 1 month, 6 months, and annually after carotid endarterectomy or revascularization to assess patency and exclude the development of new or contralateral lesions (Brott et al [ACCF/AHA et al] 2011: Class iIa/Level of Evidence: C). Once stability has been established over an extended period, surveillance at longer intervals may be appropriate (Brott et al [ACCF/AHA et al] 2011: Class iIa/Level of Evidence: C). Termination of surveillance is reasonable when the patient is no longer a candidate for intervention (Brott et al [ACCF/AHA et al] 2011: Class iIa/Level of Evidence: C).

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

Clinical and imaging notes:

- After carotid endarterectomy or carotid artery stenting, about 5-10% will develop an asymptomatic recurrent narrowing within the treated artery called re-stenosis. However, this very rarely causes patients to experience another TIA or stroke (Naylor et al [ESVS] 2023).

PICO 6: Suspected cerebral venous thrombosis (CVT):

- Green – **MRI head**
- Green – **MR venography head**
- Yellow – **CT head** (either of the following)
    - patient unable to undergo MRI
    - MRI or MR venography is not available
- Yellow – **CT venography head** (either of the following)
    - patient unable to undergo MRI
    - MRI is not available
- Yellow – **Duplex carotid ultrasound**
- Red – **CTA head; CTA neck; MRA head; MRA neck; CT perfusion; MR perfusion; CT neck**

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

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus summary:
Conventional CT or MRI is often the first test obtained in patients with nonspecific acute presentations and may show signs that increase suspicion for CVT (Saposnik et al [AHA] 2024). MRI of the head is a useful initial examination in the workup of CVT; contrast is not always required for structural brain imaging but adds to the overall MRI evaluation and is commonly administered when MRI is performed together with MRV (Pannell et al [ACR] 2023). Noncontrast CT of the head can evaluate for hemorrhagic complication and alternative etiologies (Pannell et al [ACR] 2023).

Venography is the optimal test to confirm a diagnosis of CVT (Saposnik et al [AHA] 2024). The combination of MRV of the head along with MRI is an essential component of the workup of CVT in most cases, as it can confirm the presence of thrombus (Pannell et al [ACR] 2023; Irimia et al 2011: class II recommendation, level B evidence). CT venography allows clear depiction of the superficial and deep cerebral venous system, however, has a lower sensitivity compared to MRI (Saposnik et al [AHA] 2024). CTV of the head useful for rapid evaluation, when MRI is contraindicated or when MRI artifacts are suspected that could obscure the diagnosis (Pannell et al [ACR] 2023). If findings are unclear on noncontrast MRV, further imaging with contrast-enhanced CTV or MRV should be considered (Pannell et al [ACR] 2023). Contrast-enhanced MRV has a sensitivity and specificity comparable to that of CTV but allows better characterization between the low-flow state and hypoplastic sinus (Saposnik et al [AHA] 2024).

In the absence of concern for an alternative diagnosis, there is no relevant literature to support the use of CTA or MRA in the initial evaluation of CVT (Pannell et al [ACR] 2023).

While some studies demonstrate a potential role for its use in prognostic evaluation of the ischemic penumbra in the setting of CVT, perfusion imaging is typically a follow-up imaging study after the diagnosis of CVT (Pannell et al [ACR] 2023).

There is no relevant literature to support the use of carotid Doppler in the setting of CVT, however ultrasound assessment of the adjacent venous structures could yield information about the extent of

the thrombus if extending into the neck (Pannell et al [ACR] 2023).

Clinical and imaging notes:

- CVT is an uncommon cause for stroke, accounting for only 0.5-3% of all strokes, and may present with headache (up to 90% of cases), seizure (20-40%), or decreased level of consciousness due to venous ischemic or hemorrhagic complications (Pannell et al [ACR] 2023; Saposnik et al [AHA] 2024).
- Imaging features suggesting venous infarction with hemorrhage may include atypical distributions not matching arterial vascular territories, infarcts with cortical sparing, typical parasagittal or temporoparietal location, or dural venous/cortical venous hyperdensity on noncontrast CT suggestive of thrombus (Pannell et al [ACR] 2023).
- CVT on CT or MRI may be suspected by 1) direct visualization of the thrombus, 2) the absence of venous filling, and 3) imaging of the consequences of venous obstruction at the tissue level and at the vascular level (Saposnik et al [AHA] 2024).
- Volumetric MRI sequences are essential for contrast-enhanced MRV, and delayed postcontrast imaging can further increase the sensitivity for detection of T1 isointense thrombus (Pannell et al [ACR] 2023).
- MRV can be performed without contrast, with time-of-flight (TOF) or phase-contrast techniques, or with a contrast-enhanced technique (Saposnik et al [AHA] 2024).
- 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 2011).

Evidence update (2015-present):

Low Level of Evidence

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.

PICO 7: Suspected central nervous system (CNS) vasculitis presenting with stroke:

Head imaging:

- Green – **MRI head**[‡]
- Green – **CT head**
- Green – **MRA head**
- Green – **CTA head**

Neck imaging:

- Yellow – **MRA neck**
- Yellow – **CTA neck**
- Red – **CT neck; CT perfusion; MR perfusion; CT venography; MR venography**

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

Level of Evidence: CT head, MRI head 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: None.

Guideline and PLE expert panel consensus summary:
All patients with suspected acute stroke should undergo emergent or immediate brain imaging with NCCT or MRI (*NICE* 2019; Irimia et al 2010, Class I/Level A). When there is strong clinical suspicion of CNS vasculitis, brain imaging is important for supporting the diagnostic process and directing biopsy (Ledbetter et al [ACR] 2021).

MRI head is useful for evaluation of CNS vasculitis given its superior soft-tissue characteristics of the brain parenchyma and vessel walls; although parenchymal abnormalities on MRI have considerable overlap with other CNS diseases (Ledbetter et al [ACR] 2021). 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).

CTA head or MRA head can both be useful for imaging CNS vasculitis. However, specificity of vascular luminal imaging is limited by considerable overlap with other cerebrovascular disease, such as atherosclerosis, and sensitivity is limited to resolution as vasculitis can involve small distal arteries. (Ledbetter et al [ACR] 2021). MRA offers the advantage of being radiation free (Ledbetter et al [ACR] 2021). While there is no specific literature to support the use of MRA of the neck in the diagnosis of large vessel vasculitis, MRA can be used to assess vascular damage, such as aneurysm, stenosis, or occlusion (Aghayev et al [ACR] 2021).

Clinical and imaging notes:

- CNS vasculitis refers to inflammation and destruction of the blood vessels of the brain, spinal cord, or meninges (Ledbetter et al [ACR] 2021).

- Primary CNS vasculitis is a rare cause of stroke, affects predominantly younger populations (mean age at presentation of 45 years), and is slightly more prevalent in men (Kleindorfer et al [AHA/ASA] 2021). Referral to a healthcare professional with stroke expertise should be considered for patients with a suspected uncommon cause of stroke, including suspected cerebral vasculitis (Heran et al 2024).
- The diagnosis of primary CNS vasculitis is challenging because of its nonspecific and varied symptoms (Ledbetter et al [ACR] 2021).
- Imaging exams with CNS vasculitis demonstrate numerous nonspecific findings, such as infarcts, white matter injury, mass lesions, meningeal enhancement, or hemorrhage. Characteristic vessel imaging findings may include multifocal stenosis and dilatation of the intracranial vasculature as well as characteristic pattern of vessel wall inflammation (Ledbetter et al [ACR] 2021).
- 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):

Low Level of Evidence

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.

Guideline exclusions:

- Cardiac imaging
- Detection or follow-up of isolated intracranial aneurysm
- Detection or follow-up of cerebrovascular malformation(s)
- Suspected or known subarachnoid hemorrhage
- MR arterial spin labelling
- Transcranial Doppler (TCD) ultrasonography
- Pediatric patients,
- Pregnant patients, and
- Post processing or AI applications.

AUC Revision History:

Revision Date:	New AUC Clinical Scenario(s):	Approved By:
04/07/2020	n/a	CDI Quality Institute's Multidisciplinary Committee
04/23/2024	n/a	RAYUS Radiology 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.rayusradiology.com/ple**

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Appropriateness of Advanced Imaging in Patients with Stroke and Related Conditions: Bibliography

04/23/2024

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