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Medical Policy Manual

Topic: Computed Tomography (CT) Perfusion Imaging of the Brain

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Perfusion imaging using computed tomography (CT) is said to provide detailed study of cerebral blood flow which may assist in the identification of ischemic regions of the brain. It is being investigated for use in the evaluation of the following neurological conditions:

- Acute ischemic stroke: To identify the infarct core, and to identify at-risk brain regions (penumbra) that may be salvageable with successful intra-arterial thrombolysis beyond the standard 3-hour post-onset thrombolysis window. Additional potential uses of perfusion CT in acute stroke may include differential diagnosis (e.g., excluding stroke mimics such as transient ischemic attack and complex migraine), determination of stroke subtype, risk of early stroke following transient ischemic attack, and establishing prognosis.
- Subarachnoid hemorrhage (SAH) and cerebral vasospasm: As a potentially more accurate alternative to current diagnostic methods which include clinical examination, transcranial Doppler sonography, and digital subtraction angiography.
- Brain tumors: To assess tumor grade and prognosis, distinguish between recurrent tumor and radiation necrosis, and monitor tumor evolution and treatment response.
- Head trauma: To assess prognosis for functional outcome following traumatic brain injury.

Perfusion imaging using CT requires either a diffusible inert gas indicator such as xenon (Xe) or a non-diffusible indicator such as an iodinated contrast agent. The CT scanner is then used to capture images as the agent passes through the cerebral circulation and accumulates in the cerebral tissues.

Potential advantages of CT perfusion imaging are that it is less invasive than CT angiography and more widely available than MR imaging. Results from the CT perfusion studies allow calculation of regional cerebral blood volume, transit time, and regional cerebral blood flow.

Radiation Exposure

On November 9, 2010, the U.S. Food and Drug Administration (FDA) issued an update of their October 2008 Initial Communication about excess radiation during perfusion CT imaging. Together with state and local health authorities, the FDA has identified at least 385 patients who were exposed to excess radiation during CT perfusion scans. The has provided recommendations for facilities and practitioners and is continuing to work with manufacturers, professional organizations, and state and local public health authorities to investigate the scope and causes of these excess exposures and their potential public health impact. A November 9, 2010 update of this issue is available online at: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm185898.htm.

Regulatory Status

Several post-processing software packages have received 510(k) marketing clearance from the U.S. Food and Drug Administration (FDA) for use with a CT system to perform perfusion imaging.

MEDICAL POLICY CRITERIA

CT-based perfusion imaging of the brain is considered **investigational** for all indications, including but not limited to the diagnosis and management of the following:

1. Acute cerebral ischemia (stroke)
2. Brain tumors
3. Cerebral aneurysm
4. Cerebral vasospasm
5. Moyamoya disease
6. Subarachnoid hemorrhage
7. Traumatic brain injury

SCIENTIFIC EVIDENCE

Background

Validation of a diagnostic technology requires data regarding its technical performance, its diagnostic performance (i.e., sensitivity, specificity and positive and negative predictive value) compared to a gold

standard, and finally data regarding how the diagnostic information will be used in the management of the patient and whether beneficial health outcomes result.

Literature Appraisal

Acute Cerebral Ischemia (Stroke)

The current published literature on CT perfusion imaging focuses on technical capabilities and feasibility rather than clinical utility. A number of retrospective studies have indicated that blood flow values obtained using a diffusible gas indicator are accurate and also that the flow rates correlate with physiological changes such as the onset of neurological deficits.[1] The limited availability of medical-grade Xe gas is another issue with this approach to CT perfusion imaging. Because of more widespread availability, studies are also being done using non-diffusible tracers, i.e., contrast agents.[2,3] In 2008, studies reported on the use of CT perfusion imaging to identify infarcted tissue versus viable tissue (penumbra).[4-7] However, many studies evaluating use of thrombolytic therapy in acute stroke beyond 3 hours of symptom onset were based on magnetic resonance (MR) imaging with perfusion-diffusion mismatching.[8] As Lev commented in an editorial, although many investigators have advocated CT perfusion imaging as a reliable method for detecting both infarct core and penumbra, almost all the major clinical trials aimed at extending the time window for thrombolysis used advanced MR rather than CT imaging for triage.[9] The evidence is also not clear about how useful this technique is in differentiating reversible from irreversible ischemic cerebral tissue. In addition, the incremental impact of this technique on clinical decisions and clinical outcomes is not yet known. Prospective controlled studies have not been reported that demonstrate that use of perfusion CT imaging improves outcomes in patients with acute stroke.

Systematic Reviews

In 2009, the American Heart Association (AHA) Council on Cardiovascular Radiology and Intervention, Stroke Council, and the Interdisciplinary Council on Peripheral Vascular Disease published a scientific statement that included a review of the evidence on CT perfusion.[10] The scientific review determined that:

- Creation of accurate, quantitative CT perfusion has been validated in comparison with xenon-CT, positron emission tomography (PET), and MR perfusion. CT perfusion appears to have greater spatial resolution than MR perfusion, and MR perfusion may be more sensitive to contamination by large vascular structure, leading to the possibility that visual assessment of core/penumbra mismatch is more reliable with CT perfusion than with MR perfusion.
- Studies are evaluating various thresholds to predict the upper and lower limits of final infarct size, and outcome prediction studies suggest that CT perfusion has the potential to serve as a surrogate marker of stroke severity (final size of infarction), possibly exceeding current predictors of outcome such as the National Institutes of Health Stroke Score (NIHSS). Because of the superior quantitative capability compared to MR perfusion imaging, application of specific CT perfusion thresholds to predict tissue survival or infarction appears promising; however, it is essential that these thresholds be validated in larger patient cohorts for which reperfusion status is known.
- There is increasing but as yet indirect evidence that even relatively imprecise measures of core/penumbra mismatch may be used to select patients for treatment beyond a strict 3-hour time window for intravenous thrombolysis. Multimodal CT may also determine suitability for other therapies, such as mechanical clot retrieval and intra-arterial thrombolysis, and increase patient access to new treatments.

A systematic review from 2011 examined definitions and thresholds for MR and CT perfusion imaging.[11] Twenty papers on CT perfusion met the inclusion criteria for analysis of definitions, and 10 papers on CT perfusion (median sample size of 22) provided thresholds. The quality of the studies was generally poor. There were multiple definitions for tissue states. For example, there were 8 different definitions of at risk tissue, resulting in many-fold differences in the extent of tissue defined as tissue at risk. There was also considerable variability in quantitative thresholds. The review concluded that CT perfusion thresholds in stroke are derived from small numbers of patients, variable perfusion analysis methods and definitions of tissue states. As indicated in the 2009 AHA statement, thresholds should be validated in larger patient cohorts for which reperfusion status is known. Assessment of functional outcomes is also needed to evaluate if CT perfusion improves clinical outcomes.

Randomized Controlled Trials

No randomized controlled trials on CT perfusion imaging in the diagnosis and treatment of acute stroke were identified.

Nonrandomized Trials

Five relevant cohort studies have been identified that were published after the AHA review.

- In 2011, Bivard et al. reported a prospective clinical validation study of perfusion CT for acute (<6 hr) ischemic stroke in 314 consecutive patients.[12] This study attempted to define the technical CT parameters that best detect perfusion mismatches. If eligible, patients were treated with intravenous thrombolysis. All patients underwent baseline multimodal CT examination and follow-up MRI at 24 hours, with MRI used as the gold standard for tissue perfusion. The most accurate CT perfusion threshold at defining infarct core was determined to be cerebral blood flow less than 40% of contralateral with a relative delay time less than 2 sec (area under the curve [AUC] of 0.86). Using this threshold, the correlation between extent of CT perfusion mismatch tissue (the volume of "at-risk" tissue) salvaged from infarction and clinical improvement was R2=0.59 at 24 h (NIHSS) and R2=0.42 at 90 days (Rankin scale).
- Another 2011 report compared outcomes of 106 patients with acute stroke who were assessed with multimodal CT (CT/CT angiography [CTA]/CT perfusion) versus a cohort of 262 patients with acute stroke who were assisted without full multimodal brain imaging during a 5-year period.[13] Clinical and imaging data were collected prospectively, and all imaging studies were assessed by investigators blinded to prognostic data. The two groups were comparable at baseline with the exception of a greater percentage of patients with a time-to-treatment of greater than 3 hours (28% vs. 16%) and a greater percentage treated with endovascular therapy (26% vs. 11%, both respectively) in the multimodal CT group. Good outcome (modified Rankin scale score < 2) at 3 months was increased in the multimodal group compared with controls (adjusted odds ratio [OR] of 2.88) in models adjusted for age, gender, NIHSS, glucose, and treatment delay or modality. Fifty-six percent of patients assessed by multimodal CT had a Rankin score equal to or less than 2 in comparison with 41% of controls (p=0.008). In a sensitivity analysis, multimodal-assisted thrombolysis yielded superior benefits in those patients treated after 3 hours (adjusted OR, 4.48) than for patients treated within 3 hours (adjusted OR, 1.31). For patients treated after 3 hours, 63% of patients assessed by multimodal CT had a Rankin score equal to or less than 2 in comparison with 24% of controls. Mortality (14% and 15%) and symptomatic hemorrhage (5% and 7%m both respectively) were similar in the 2 groups. Randomized trials are needed to establish the value of multimodal CT to assist thrombolytic therapy in acute stroke.

- Sztriha et al. evaluated whether CT perfusion imaging mismatch could help to select ischemic stroke patients for thrombolysis between 3 and 6 hours.[14] A cohort of 254 thrombolysed patients were studied; 174 (69%) were thrombolysed at 0-3 hours using non-contrast CT, and 80 (31%) were thrombolysed at 3-6 hours by using CT perfusion mismatch criteria, defined as a cerebral blood volume ASPECTS [Alberta Stroke Program Early CT Score] of at least 7 and an ASPECTS mismatch of at least 2. Baseline characteristics were comparable in the 2 groups. Efficacy endpoints included disability at 3 months, as assessed by the Rankin score. Safety endpoints included overall mortality, any intracerebral hemorrhage, and symptomatic intracerebral hemorrhage. At 3 months, there were no differences between patients thrombolysed at 0-3 hours or at 3-6 hours in symptomatic intracerebral hemorrhage (3% vs. 4%), or in any intracerebral hemorrhage (7% vs. 9%). There were also no differences at 3 months in mortality (16% vs. 9%) or the modified Rankin scale score 0-2 (55% vs. 54%, respectively for all). The NIHSS score was the only independent determinant of a favorable functional outcome at 3 months (Rankin score of 0-2; odds ratio [OR]: of 0.89) in patients treated using CT perfusion mismatch criteria beyond 3 hours. This study is limited by the lack of a control group of patients without CT perfusion. The authors also noted that results of this study cannot be generalized to patients with symptoms in the posterior circulation, an area where CT perfusion is known to underperform.
- Rai et al. evaluated rates of recanalization and functional outcomes in a cohort of 99 patients selected by CT perfusion for treatment with endovascular stroke therapy and compared results with historical controls from the MERCI [Mechanical Embolus Removal in Cerebral Ischemia], Multi-MERCI, and Penumbra device trials that treated all comers.[15] Patients were included if they had anterior circulation symptoms at presentation with a baseline NIHSS score of 8 or greater and intracerebral vascular occlusion on admission CT angiography correlating with the neurologic deficit. There was no cut-off time for treatment. The type of endovascular therapy involved intra-arterial thrombolytics in 33.3% of patients, mechanical device in 24.2%, and both thrombolytics and mechanical thrombectomy in 42.4%. Successful recanalization was achieved in 55.6%, with a good outcome in 41.4% of patients. The recanalization rate in this study was not significantly different from the 46% for MERCI and 68% for Multi-MERCI but was significantly lower than the 82% recanalization rate in the Penumbra trial. In patients who were successfully recanalized, good outcomes were obtained in 67% of patients in this study in comparison with 46% in MERCI, 49% in Multi-MERCI, and 29% in Penumbra. The rate of futile recanalization (defined as a poor outcome despite successful recanalization) was 33% compared with 54% in MERCI, 51% in Multi-MERCI, and 71% for Penumbra. A small cerebral blood volume abnormality and large mean transit time-cerebral blood volume mismatch were strong predictors of a good outcome. This study is limited by the comparison of a retrospective cohort with results from prospective device trials and by the reliance on recanalization rates as the primary outcome rather than clinical measures.
- In 2013, Sheth et al. reported a retrospective study of the effect of multi-modal CT on outcomes from endovascular therapy in 556 patients from 10 stroke centers. [16] Patients were included if they presented within 8 hours of symptom onset and were then divided into groups based on the imaging modality employed prior to treatment. Non-contrast CT was used in 51% of patients, CT perfusion in 34%, and MRI in 14% of patients. Patients were selected for endovascular therapy based on specific imaging criteria. Non-contrast CT patients had significantly lower median times to groin puncture (61 min.) compared with CT perfusion (114 min.) or MRI (124 min.). There were no differences in clinical outcomes, hemorrhage rates, or final infarct volumes among the groups. This study is limited by the retrospective analysis and differences between groups at baseline. Patients selected for endovascular treatment by non-contrast CT alone had a higher baseline NIHSS score and were more likely to have been transferred from an outside facility. In addition, there was limited information regarding the patients who did not proceed to endovascular therapy.

A large number of case series have been published that have retrospectively assessed how CT perfusion at admission might facilitate clinical decision making and predict outcomes in patients with suspected acute ischemic stroke. Prospective trials are needed to evaluate the impact of this technology on health outcomes.

Conclusion

Four recent cohort studies described how CT perfusion can be used in clinical care to select patients for endovascular therapy. However, these trials lack concurrent control groups and, therefore do not provide relevant evidence on the comparative efficacy of this approach compared to alternative strategies. A fifth stratified cohort study found shorter time to treatment and no difference in clinical outcomes in patients who underwent CT perfusion compared with non-contrast CT or MRI. Randomized trials are needed to establish with greater certainty the value of CT perfusion to assist decision making for thrombolytic or mechanical therapy in acute stroke.

Subarachnoid Hemorrhage and Cerebral Vasospasm

Systematic Reviews and Meta-Analyses

A 2010 meta-analysis on the diagnostic accuracy of CTA and CT perfusion for cerebral vasospasm found three studies with a total of 64 patients that met the inclusion criteria and contained the appropriate data for statistical analysis.[17] In these studies, "vasospasm" was defined on CT perfusion as a perfusion deficit demonstrating prolonged mean transit time and decreased cerebral blood flow. However, there were no standardized thresholds of mean transit time and cerebral blood flow to determine vasospasm, contributing to the heterogeneity among these studies. For this meta-analysis, "angiographic vasospasm" was defined as evidence of arterial narrowing compared with the parent vessel or with a baseline examination, with both symptomatic and asymptomatic patients included. In comparison with digital subtraction angiography, CT perfusion pooled estimates had 74% sensitivity and 93% specificity. Given the small sample size and the heterogeneity in the CT perfusion data, these results are considered preliminary.

Randomized Controlled Trials

No randomized controlled trials on CT perfusion imaging in the diagnosis and treatment of subarachnoid hemorrhage or cerebral vasospasm were identified.

Nonrandomized Trials

- In 2011, Sanelli et al. reported a prospective study with 97 patients that evaluated the accuracy of CT perfusion to diagnose delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage.[18] CT perfusion was performed between days 6 and 8 in asymptomatic patients and on the day of clinical deterioration in symptomatic patients. Perfusion maps were qualitatively evaluated by 2 neuroradiologists who were blinded to clinical and imaging data and compared to the reference standard. Based on a multistage hierarchical reference standard that incorporated both imaging and clinical criteria, 40 patients (41%) were diagnosed with delayed cerebral ischemia. Overall diagnostic accuracy for CT perfusion, determined from receiver operating characteristic (ROC) curves, was 93% for cerebral blood flow, 88% for mean transit time, and 72% for cerebral blood volume. The study also sought to determine a quantitative threshold for delayed cerebral ischemia with CT perfusion, although it was noted that absolute thresholds may not be generalizable due to

differences in scanner equipment and post-processing methods. Clinical outcomes of the delayed cerebral ischemia group included 19 patients (48%) with no permanent neurologic deficit, 16 (40%) with permanent neurologic deficit, and 5 (13%) who died during hospitalization.

- Sanelli et al. also reported a retrospective study of the development of vasospasm in 75 patients with aneurysmal subarachnoid hemorrhage who had an earlier CT perfusion assessment (likely overlap in subjects with the study described above).[19] Based on a multistage reference standard, 28 patients (37%) were classified as vasospasm. CT perfusion values (cerebral blood flow and mean transit time) on days 0-3 were found to be significantly lower in the vasospasm group. Optimal thresholds were then determined for cerebral blood flow (50% sensitivity and 91% specificity), mean transit time (61% sensitivity and 70% specificity) and cerebral blood volume (36% sensitivity and 89% specificity). Clinical outcomes of the vasospasm group included 15 patients (54%) with no permanent neurologic deficit, 11 (39%) with permanent neurologic deficit, and 2 (7%) who died during hospitalization.

Conclusion

CT perfusion is being evaluated for the diagnosis of vasospasm and delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. A prospective trial showed a qualitative measure of cerebral blood flow to have 93% accuracy for the detection of delayed cerebral ischemia with lower accuracy for cerebral blood volume. Prospective trials are needed to evaluate whether CT perfusion in patients with aneurysmal subarachnoid hemorrhage leads to the early identification of patients at high risk for vasospasm/delayed cerebral ischemia, alters treatment decisions, and improves health outcomes.

Brain Tumors

Systematic Reviews

A 2011 review by Jain indicated that most of the literature on the utility of perfusion imaging for glioma grading is based on various MR perfusion techniques.[20] One study compared CT perfusion with conventional MRI in 19 patients.[21] With a cutoff point of greater than 1.92 normalized cerebral blood volume (nCBV), there was sensitivity of 85.7% and specificity of 100% to differentiate high-grade gliomas. There were no significant differences in nCBV between grade III or IV tumors. A subsequent study by Jain and colleagues correlated CT perfusion findings with histopathologic grade in 32 patients with astroglial tumors.[22] Eight additional patients with oligodendrogliomas were excluded from analysis because of the known higher blood volume compared with astroglial tumors. Of the 32 patients included in the study, 8 had low-grade gliomas and 24 had high-grade gliomas. In this selected set of patients, CT perfusion showed significant differences in the grade III and grade IV tumors. Prospective studies in an appropriate population of patients are needed to evaluate the sensitivity and specificity of CT perfusion glioma grading, with histopathologic assessment of tumors as the independent reference standard.

Randomized Controlled Trials

No randomized controlled trials on CT perfusion imaging in the diagnosis and treatment of brain tumors were identified.

Nonrandomized Trials

In 2011, Xyda et al. reported a prospective study of the feasibility and efficacy of volume perfusion CT (VPCT) for the preoperative assessment of cerebral gliomas in 46 consecutive patients with suspected cerebral gliomas.[23] (Whereas typical perfusion CT covers a relatively narrow range of brain tissue, the VPCT system with multispiral acquisition covers the entire tumor.) Two blinded readers independently evaluated VPCT by drawing volumes of interest (VOIs) around the tumor according to maximum intensity projection volumes. The VOIs were mapped onto the cerebral blood volume, flow, and permeability perfusion datasets, which correspond to histopathologic microvascular density. VPCT was followed by stereotactic biopsy or surgery to evaluate the histopathology of the tumor and classified into low-grade (I and II) and high-grade (III and IV). The diagnostic power of the perfusion parameters were analyzed by receiver operating characteristic (ROC) curve analysis. Permeability demonstrated the highest diagnostic accuracy (97% sensitivity, 100% specificity), positive predictive value (100%), and negative predictive value (94%) to identify or exclude high-grade tumors. Potential uses of VPCT are to guide biopsy and to monitor low-grade gliomas. This is the first report using VPCT to differentiate gliomas; therefore, replication of these findings in an independent sample of patients is needed.

Conclusion

The evidence on CT perfusion imaging for the diagnosis and management of brain tumors is limited to a small feasibility study for preoperative assessment of cerebral gliomas. Large prospective trials are needed to verify the diagnostic accuracy of CT perfusion imaging in differentiating low- and high-grade tumors, and to determine whether the information provided by this imaging adds significant value compared with conventional imaging in this patient population.

Traumatic Brain Injury (TBI)

Evidence for CT perfusion imaging in TBI is limited to case series evaluating whether admission perfusion CT is prognostic for functional outcomes. Metting et al studied admission CT perfusion in 67 patients with mild brain injury and normal admission noncontrast CT.[24] Extended Glascow Coma Outcome Scale and return to work were evaluated at six months after the injury. The authors reported a correlation between decreased admission cerebral blood flow and volume, and decreased functional level scores. CT perfusion did not predict return to work. Similarly, Wintermark et al studied Glascow Outcome Scale three months after injury in patients with severe head trauma and reported perfusion CT to be an independent prognostic factor.[25] The same investigators also studied the feasibility of using CT perfusion to characterize cerebral vascular autoregulation in 42 patients with severe head trauma and cerebral edema.[26] The authors reported that this technique was able to provide direct and quantitative assessment of cerebral vascular autoregulation and may have the potential in the future to guide brain edema therapy and monitor treatment response. No studies were found for the use of CT perfusion in patient management.

Conclusion

The available case series on the use of CT perfusion imaging in patients with TBI do not permit conclusions on the value of CT perfusion imaging in determining prognosis or to guide treatment decisions. Larger prospective trials are needed to determine whether this imaging can be used to improve functional outcomes following TBI.

Clinical Practice Guidelines and Position Statements

Acute Ischemic Stroke

- The 2012 American Heart Association (AHA) and American Stroke Association (ASA) guidelines for management of aneurysmal subarachnoid hemorrhage recommended that perfusion imaging with CT or MR can be useful to identify regions of potential brain ischemia (Class IIa; Level of Evidence B).[27] The guidelines stated that there are emerging data that perfusion imaging demonstrating regions of hypoperfusion may be more accurate for identification of delayed cerebral ischemia than anatomic imaging of arterial narrowing or changes in blood flow velocity by transcranial Doppler. The guidelines concluded that CT perfusion is a promising technology, although repeat measurements are limited by the risks of dye load and radiation exposure.

- The 2013 AHA and ASA guidelines for the early management of adults with acute ischemic stroke recommended that multimodal CT and magnetic resonance imaging (MRI) may provide additional information that will improve diagnosis of ischemic stroke (Class I, Level of Evidence A).[28] The recommendations related to CT perfusion and MRI perfusion and diffusion imaging changed since the last update of this guideline. The current recommendation is that these imaging techniques, including measures of infarct core and penumbra, be considered for patient selection for acute reperfusion therapy beyond the time windows for fibrinolysis. "These techniques provide additional information that may improve diagnosis, mechanism, and severity of ischemic stroke and allow more informed clinical decision making. The recommendation was rated as class IIb, level of evidence B, defined as usefulness/efficacy less well established by evidence or opinion based on data from a single RCT or nonrandomized studies.

- In a 2013 joint statement on imaging for acute stroke and transient ischemic attack patients, the American Society of Neuroradiology (ASNR), American College of Radiology (ACR), and the Society of NeuroInterventional Surgery made the following recommendations:[29]

  Imaging for Detection of Viable Tissue
  "Although perfusion imaging has been incorporated into acute stroke imaging algorithms at some institutions, its clinical utility has not been proved... there is no clear consensus on the optimal perfusion parameter that is most predictive of tissue viability and outcome."

  Imaging of Collateral Vessels
  "Perfusion imaging may be considered to assess the target tissue "at risk" for reperfusion therapy. However, the accuracy and usefulness of perfusion imaging to identify and differentiate viable tissue have not been well-established."

  Stroke with Unknown Time of Onset
  "If acute reperfusion therapy is considered, multimodal MR imaging or CT with perfusion imaging is recommended to evaluate viable tissue, as the time clock is not applicable. However, there is no firm evidence supporting imaging selection for treatment in this patient population."

- In 2009, the American Heart Association (AHA) issued a scientific statement on imaging of acute ischemic stroke.[10] The statement included the following recommendations regarding perfusion imaging:

  Perfusion-Derived Values
  Quantitative thresholds of tissue that is dead or destined to die versus tissue that is still living and may be salvageable are the goal of all perfusion techniques. Although the performance of such studies may be considered to identify and differentiate the ischemic penumbra and infarct core, their accuracy and usefulness have not been well established (Class IIb, Level of Evidence B).

Clinical Role of Perfusion Imaging

- The admission volumes of infarct core and ischemic penumbra may be significant predictors of clinical outcome, possibly exceeding the prognostic value of admission NIHSS score [National Institutes of Health Stroke Score] (Class IIb, Level of Evidence B).

- There is increasing but as yet indirect evidence that even relatively imprecise measures of core/penumbra mismatch may be used to select patients for treatment beyond a strict 3-hour time window for intravenous thrombolysis. Together with vascular imaging, these approaches may determine suitability for other therapies such as mechanical clot retrieval and intra-arterial thrombolysis, as well as provide a surrogate marker for treatment efficacy (Class IIb, Level of Evidence B).

- The 2011 American College of Radiology (ACR) Appropriateness Criteria® noted that CT stroke protocols combining a brain non-contrast CT, CT angiography, and CT perfusion may produce a relative radiation level of 1-10 mSv, and repeated use of this protocol in an individual patient may result in high radiation exposure to the scalp and eyes. The ACR provided the following ratings for CT head perfusion with contrast:[30]

  - Rating of 2 (usually not appropriate) for asymptomatic individuals with structural lesion on physical examination (cervical bruit) and/or risk factors
  - Rating of 6 (may be appropriate) if directly employed in decision making and planning treatment for carotid territory or vertebrobasilar transient ischemic attack; initial screening survey
  - Rating of 6 (may be appropriate) for a new focal neurologic defect, fixed or worsening; less than 3 hours, if CT is used for planning treatment such as thrombectomy
  - Rating of 6 (may be appropriate) for a new focal neurologic defect, fixed or worsening; 3 to 24 hours, if CT is used for planning treatment such as thrombectomy within 8 hours of symptom onset
  - Rating of 5 (may be appropriate) for a new focal neurologic defect, fixed or worsening; longer than 24 hours, if used for decision making or planning treatment such as angioplasty and stenting

Other Indications

- The 2013 ACR, American Society of Neuroradiology (ASNR), and Society for Pediatric Radiology (SPR) guideline for the performance of CT perfusion listed indications including but not limited to the following:[31]
  - For adults:
    1. Brain
       - Primary indications:
         - Acute neurological change suspicious for stroke
         - Suspected vasospasm following subarachnoid hemorrhage
         - Cerebral hemorrhage with secondary local ischemia
       - Secondary indications:
         - Follow-up of acute cerebral ischemia or infarction in the subacute or chronic phase of recovery

- To assist in planning, and evaluating the effectiveness of therapy for cervical or intracranial arterial occlusive disease (as an isolated test or in combination with a cerebrovascular reserve challenge)
- In patients with contraindication to magnetic resonance imaging (MRI) or with devices or material in or close to the field of view that would result in nondiagnostic MRI scans
- CT perfusion scanning may also be helpful in the setting of acute traumatic brain injury
- Intracranial tumors

2. Head and Neck
   - Primary indications:
     - Evaluation of the vascular status of solid tumors where MRI is degraded due to susceptibility artifact from air-containing spaces or from surgical clips or dental work
   - Secondary indications:
     - Follow-up of tumor response to therapy

- For children
  - At the time of this guideline revision there are no data to support a role of CT brain perfusion imaging in pediatric stroke.
  - It may be reasonable to use CT brain perfusion imaging in individual patients under 18 years of age for the same indications listed for adults, but the increased risk to the pediatric patient associated with radiation exposure obligates the practitioner to apply a higher threshold to any decision to use this technique and to strongly consider MRI as an alternative.

Summary

While computed tomography (CT) perfusion imaging of the brain may hold promise for improving care of patients with various neurological conditions, including the potential individualization of thrombolytic therapy in acute stroke, current evidence remains insufficient to determine whether patient health outcomes are improved with use of this technique. Randomized clinical trials are needed in which a strategy employing CT perfusion imaging in the treatment of acute stroke is compared with traditional strategies. Because the impact of CT perfusion imaging of the brain on clinical outcomes is not known, this technique is considered investigational for all indications, including but not limited to acute stroke.

For indications other than acute stroke such as subarachnoid hemorrhage and cerebral vasospasm, traumatic brain injury, and brain tumors, the data on CT perfusion imaging of the brain are limited. Because the impact of CT perfusion imaging on clinical outcomes is not known, this technique is considered investigational for all indications.

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CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	0042T	Cerebral perfusion analysis using computed tomography with contrast administration, including post-processing of parametric maps with determination of cerebral blood flow, cerebral blood volume, and mean transit

CODES	NUMBER	DESCRIPTION
		time
HCPCS	None	