Protocol

Computed Tomography Perfusion Imaging of the Brain

(60149)

Medical Benefit		Effective Date: 01/01/16	Next Review Date: 03/19
Preauthorization	Yes	Review Dates: 11/14, 11/15, 11/16, 03/17, 03/18	

Preauthorization is required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With acute stroke who are being evaluated for thrombolysis	Interventions of interest are: • Computed tomography perfusion imaging	Comparators of interest are: • Standard workup without computed tomography perfusion imaging	Relevant outcomes include: • Overall survival • Test accuracy • Symptoms • Morbid events • Functional outcomes
Individuals: • With acute anterior large-vessel stroke who are being evaluated for mechanical embolectomy	Interventions of interest are: • Computed tomography perfusion imaging	Comparators of interest are: • Standard workup without computed tomography perfusion imaging	Relevant outcomes include: • Overall survival • Test accuracy • Symptoms • Morbid events • Functional outcomes
Individuals: • With acute stroke who are being evaluated for prognosis	Interventions of interest are: • Computed tomography perfusion imaging	Comparators of interest are: • Standard workup without computed tomography perfusion imaging	Relevant outcomes include: • Overall survival • Test accuracy • Symptoms • Morbid events • Functional outcomes
Individuals: • With subarachnoid hemorrhage and cerebral vasospasm	Interventions of interest are: • Computed tomography perfusion imaging	Comparators of interest are: • Clinical evaluation	Relevant outcomes include: • Overall survival • Test accuracy • Symptoms • Morbid events • Functional outcomes
Individuals: • With brain tumors	Interventions of interest are: • Computed tomography perfusion imaging	Comparators of interest are: • Magnetic resonance imaging	Relevant outcomes include: • Test accuracy • Symptoms • Morbid events • Functional outcomes

Description

Computed tomography perfusion (CTP) imaging provides an assessment of cerebral blood flow that may help identify ischemic regions of the brain. This technology is proposed to aid treatment decisions in patients being evaluated for acute ischemic stroke, subarachnoid hemorrhage, cerebral vasospasm, brain tumors, and head trauma.

Summary of Evidence

For individuals who have acute stroke who are being evaluated for thrombolysis who receive CTP imaging, the evidence includes nonrandomized comparative studies. Relevant outcomes are overall survival, test accuracy, symptoms, morbid events, and functional outcomes. One potential area of benefit is greater individualization of therapy for acute stroke by better defining at risk ischemic areas that may benefit from thrombolysis. Evidence from nonrandomized comparative studies has suggested that outcomes after thrombolysis are better in patients who have target mismatch on perfusion imaging than in patients without target mismatch and that patients with target mismatch treated after a three-hour time window have outcomes similar to patients treated within three hours. However, the therapeutic changes that would be associated with identifying specific target mismatch pattern on CTP are not well-defined. Therefore, randomized controlled trials are needed to determine with greater certainty whether a strategy employing CTP imaging improves health outcomes compared with traditional strategies for the treatment of acute stroke. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have acute anterior large-vessel stroke who are being evaluated for mechanical embolectomy who receive CTP imaging, the evidence includes a randomized controlled trial. Relevant outcomes are overall survival, test accuracy, symptoms, morbid events, and functional outcomes. CTP is one of the several approaches used in acute stroke to define viable ischemic tissue better and therefore may benefit from mechanical endovascular intervention. Alternative methods of patient selection for mechanical embolectomy have included time from stroke onset, multiphase computed tomography angiography, or Alberta Stroke Program Early CT score. One randomized controlled trial showed improved outcomes with mechanical embolectomy when patients were selected based on CTP results. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have acute stroke who are being evaluated for prognosis who receive CTP imaging, the evidence includes a retrospective analysis of data from large prospective randomized trials. Relevant outcomes are overall survival, test accuracy, symptoms, morbid events, and functional outcomes. Retrospective analysis of data from the MR CLEAN and DUST trials have found that the ischemic core detected on CTP imaging was predictive of functional outcomes. However, analysis of data from the DUST study found no improvement in a prediction model when CTP imaging was added to a basic model that used only patient characteristics and non-contrast computed tomography. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have suspected subarachnoid hemorrhage and cerebral vasospasm who receive CTP imaging, the evidence includes a prospective study. Relevant outcomes are overall survival, test accuracy, symptoms, morbid events, and functional outcomes. CTP imaging is being evaluated for the diagnosis of vasospasm and delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. One prospective study 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 determine whether CTP imaging in patients with aneurysmal subarachnoid hemorrhage leads to the early identification of patients at high risk for vasospasm or delayed cerebral ischemia, alters treatment decisions, and improves health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have brain tumors who receive CTP imaging, the evidence includes studies on diagnostic accuracy. Relevant outcomes are test accuracy, symptoms, morbid events, and functional outcomes. For indications such as brain tumors and head trauma, the data on CTP imaging are limited. One study assessed the diagnostic accuracy of CTP imaging to differentiate high-grade from low-grade gliomas. Prospective studies in an appropriate population of patients are needed to evaluate the sensitivity and specificity of CTP glioma grading, with histopathologic assessment of tumors as the independent reference standard. One prospective study performed receiver operating characteristic curve analysis to evaluate the diagnostic accuracy of volume perfusion computed tomography. This is the first report using volume perfusion computed tomography to differentiate gliomas; therefore, replication of these findings in an independent sample of patients is needed as well as clarification of the clinical utility of this information. Studies showing the consistency in the thresholds used are needed as are studies showing improvement in health outcomes with CTP imaging. No recent reports on the use of CTP imaging for the evaluation of brain tumors have been identified. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy

Computed tomography perfusion imaging may be considered **medically necessary** to select patients with anterior large-vessel stroke for mechanical embolectomy.

Computed tomography perfusion imaging of the brain is considered **investigational** for all other indications.

Policy Guidelines

Selection criteria for the EXTEND-IA trial included patients with an anterior large-vessel stroke who: were receiving tissue plasminogen activator (tPA); were able to receive endovascular therapy within six hours of stroke onset; were functionally independent prior to the stroke; and had evidence of salvageable brain tissue and an ischemic core with a volume of less than 70 mL on CT perfusion imaging.

Background

Acute Stroke

The goal of acute stroke thrombolytic treatment is to rescue the ischemic penumbra, an area of the brain that surrounds the infarct core and is hypoperfused but does not die quickly. Multimodal computed tomography (CT) and magnetic resonance imaging (MRI) can be used to assess the cerebral parenchyma, vasculature, and tissue viability in the acute ischemic stroke setting and are used to detect ischemic tissue and exclude hemorrhage and other conditions that mimic acute cerebral ischemia.

- Non-contrast CT is used to rule out intracranial hemorrhage, tumor, or infection. Diffusion-weighted MRI is used to identify acute infarction, and a gradient-recalled echo sequence is used to exclude intracerebral hemorrhage.
- CT angiography and magnetic resonance angiography are used to evaluate intra- and extracranial vasculature to detect the vascular occlusion and potentially guide therapy (e.g., intravenous thrombolysis or mechanical thrombectomy).

The approved therapy, use of an intravenous tissue plasminogen activator (tPA), requires only a non-contrast CT scan to exclude the presence of hemorrhage (a contraindication to use of the drug). Current guidelines are to administer tPA within the first three hours after an ischemic event, preceded by a CT scan. Many patients, however, do not present to the emergency department within the three-hour window, and thrombolysis carries a risk of intracranial hemorrhage. Thus, more sophisticated imaging may be needed to select the proper use of intra-arterial thrombolysis or mechanical thrombectomy in patients who present more than three hours after an ischemic stroke. Perfusion imaging is also being evaluated in the management of other neurologic conditions, such as subarachnoid hemorrhage and head trauma.

The potential utility of perfusion imaging for acute stroke is as follows:

- identification of brain regions with extremely low cerebral blood flow, which represent the core
- identification of patients with at risk brain regions (acutely ischemic but viable penumbra) that may be salvageable with successful intra-arterial thrombolysis beyond the standard three-hour window
- triage of patients with at risk brain regions to other available therapies, such as induced hypertension or mechanical clot retrieval
- decisions regarding intensive monitoring of patients with large, abnormally perfused brain regions
- biologically based management of patients who awaken with a stroke for which the precise time of onset is unknown.

Additional potential uses of CTP in acute stroke may include the following:

- detection and differential diagnosis (e.g., excluding stroke mimics such as transient ischemic attack, complex migraine, seizure, conversion disorders, hypoglycemia, brain tumors)
- determination of stroke subtype
- determination of stroke extent, including additional vascular territories at risk
- identification of patients at high early risk of stroke following transient ischemic attack
- determining the need for blood pressure management
- establishing prognosis.

Similar information can be provided by CT and MRI regarding infarct core and penumbra. However, multimodal CT has a short protocol time (five to six minutes) and, because it can be performed with any modern CT equipment, is more widely available in the emergency department setting. CTP is performed by capturing images as an iodinated contrast agent bolus passes through the cerebral circulation and accumulates in the cerebral tissues. (Older perfusion methodologies such as single-photon emission CT and xenon-enhanced CT scanning use a diffusible tracer.) The quantitative perfusion parameters are calculated from density changes for each pixel over time with the commercially available deconvolution-based software, in which cerebral blood flow is equal to regional cerebral blood volume divided by mean transit time. CT angiography and CTP imaging require ionizing radiation and iodinated contrast. It is estimated that typical CTP imaging deposits a slightly greater radiation dose than a routine unenhanced head CT (≈ 3.3 mSv).

Subarachnoid Hemorrhage and Cerebral Vasospasm

Cerebral vasospasm is a major cause of morbidity and mortality following aneurysmal subarachnoid hemorrhage in patients who survive the initial hemorrhage and can be seen in about two-thirds of patients with aneurysmal subarachnoid hemorrhage. The typical onset of cerebral vasospasm occurs three to five days after hemorrhage, with maximal narrowing on digital subtraction angiography at five to 14 days. Currently, the diagnosis of vasospasm and the management decisions rely on clinical examination, transcranial Doppler sonography, and digital subtraction angiography. Although symptomatic vasospasm affects 20% to 30% of patients with aneurysmal subarachnoid hemorrhage, not all patients with angiographic vasospasm manifest clinical symptoms, and the symptoms can be nonspecific. Also, patients do not always have both clinical and imaging findings of vasospasm.

Due to these limitations, more accurate and reliable methods to detect cerebral vasospasm are being investigated.

Brain Tumors

The current standard for tumor grading is a histopathologic assessment of tissue. Limitations of histologic assessment include sampling error due to regional heterogeneity and interobserver variation. These limitations can result in inaccurate classification and grading of gliomas. Because malignant brain tumors are characterized by neovascularity and increased angiogenic activity, perfusion imaging has been proposed as a method to assess tumor grade and prognosis. Also, perfusion imaging can be repeated and may help to assess the evolution of tumors and the treatment response. Traditionally, perfusion imaging of brain tumors has been performed with MRI, which can estimate tumor blood volume, blood flow, and permeability. More recently, CTP imaging has been investigated for glioma grading. Potential advantages, compared with magnetic resonance perfusion, include the wider availability, faster scanning times, and lower cost. CTP imaging may also be used to distinguish recurrent tumor from radiation necrosis.

Regulatory Status

Several postprocessing software packages (e.g., Siemens' syngo® Perfusion-CT, GE Healthcare's CT Perfusion 4, Philips Medical System's Brain Perfusion Option) have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for use with a CT system to perform perfusion imaging. The software is being distributed with new CT scanners. FDA product code: JAK.

Related Protocol

Endovascular Procedures for Intracranial Arterial Disease (Atherosclerosis and Aneurysms)

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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