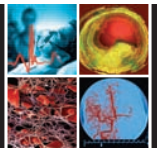
DIAGNOSIS OF TIA AND STROKE IN THE ED: HOW CAN THIS BE MADE MORE CONSISTENT?



Brian A. Stettler, MD
Assistant Professor and Residency Director, Department of Emergency Medicine,
University of Cincinnati College of Medicine,
Member, Greater Cincinnati/Northern Kentucky Stroke Team, Cincinnati, OH

OBJECTIVES:

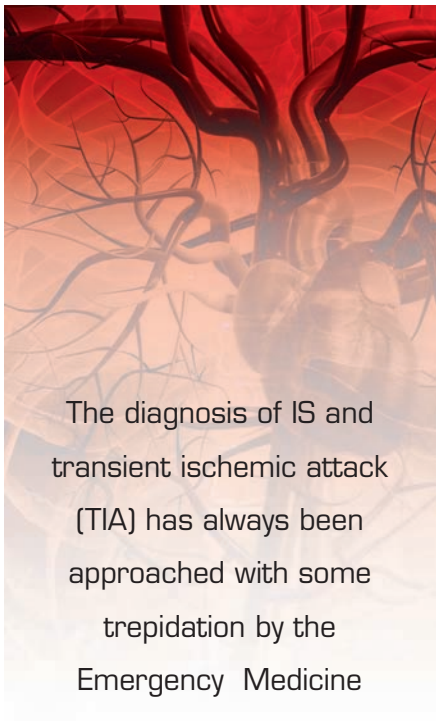
1. Delineate the useful historical points in establishing a diagnosis of TIA.
2. Describe the use of imaging in the diagnosis of TIA.
3. Describe the use of imaging in the diagnosis of acute stroke.

INTRODUCTION

Ischemic Stroke (IS) is a disease process that kills and disables millions of individuals world-wide every year. While there are treatments available both for prevention as well as to minimize the effects of the stroke in the first few hours, the first step in treatment of the disease is the formulation of an accurate diagnosis.[1] The diagnosis of IS and transient ischemic attack (TIA) has always been approached with some trepidation by the Emergency Medicine community, partly due to the potential complexity of the presentation and disease process, and partly due to a lack of training in neurologic emergencies among emergency physicians.[2] Using the history, physical examination, and technological tools available in the emergency department (ED), the diagnosis of TIA and IS can be made reliably to improve patient care and outcomes.

Central to making an accurate diagnosis of TIA is understanding the definition. Previously, TIA was defined as a sudden, focal neurologic deficit lasting less than 24 hours, presumed to be of vascular origin, and confined to an area of the brain or eye perfused by a specific artery. This definition was originally established in the 1970's and was based on the assumption of complete resolution of the ischemia if the patient's symptoms resolved. Newer imaging techniques have shown in many cases, that while the symptoms of the TIA resolve, small cerebral infarcts remain.

New definitions of TIA have been proposed which emphasize most TIAs resolve within one hour. TIAs lasting longer than this frequently demonstrate an area of persistent ischemia within the affected vascular territory on MRI and are therefore an infarct, not a TIA. One proposed definition of TIA is "…a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms lasting less than one hour, and without evidence of acute infarction." The authors of this definition compare TIA to unstable angina. This is done to emphasize both the usually short course of the symptoms and also the danger of progression to a much more severe disease process.[3] The reliability of a diagnosis of TIA



The diagnosis of IS and transient ischemic attack (TIA) has always been approached with some trepidation by the Emergency Medicine community, partly due to the potential complexity of the presentation and disease process, and partly due to a lack of training in neurologic emergencies among emergency physicians.

varies widely depending on what is used as the gold standard, but significant variability is seen even among neurologists when presented with the same history, physical examination, and diagnostic studies.

The risk of stroke after TIA is around ten percent in the first 90 days in most population-based studies, although the estimates vary from 4-20% depending on the population selected.[4-8] Importantly, studies agree that half of these strokes will occur within the first 48 hours after the initial TIA, highlighting the need for an expeditious evaluation and urgent treatment to avoid permanent neurologic deficit. The most recent update to the guidelines for the management of TIA published by the American Heart Association (AHA) Council on Stroke state that "A TIA should be promptly evaluated because delaying diagnosis risks preventable stroke." They further state that "Hospitalization is often justified to expedite evaluation and lessen the possibility of stroke."[9,10]

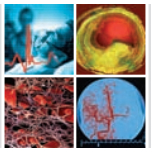
The History and Physical Examination in TIA and Stroke Diagnosis

The greatest difficulty associated with the diagnosis of TIA in the ED is that most patients are asymptomatic at the time of presentation. The diagnosis must be constructed from the historical information provided by patients and family, which is often incomplete or unreliable. It is imperative to acquire details of what actually occurred, what part of the body seemed not to work correctly, and how long each aspect or event lasted. Specific questions related to cranial nerves, such as clarity of speech, coughing or gagging when attempting to swallow, double vision, and associated vertigo are all relevant to the diagnosis and will not necessarily be brought to light without direct questioning of the patient and family. The duration of the symptoms is critical, as an event that lasted only a second or two is less worrisome than an event that lasted minutes to hours. Evaluate for positive symptoms as well as negative symptoms. Positive symptoms, or those that are present during the event which were not there previously, such as flashing lights in the visual field or tingling on the body, are less indicative of focal ischemia than negative symptoms. Negative symptoms indicate loss of function which previously existed, such as loss of speech, strength or loss of sensation. In general, negative symptoms are suggestive of acute ischemia. The ischemic brain tends to halt function rather than discharging inappropriately, such as the flashing lights sometimes described in an acute migrainous attack.

History is key in all aspects of the diagnosis of TIA. One of the main historical points which confounds the diagnosis of TIA and stroke is the presence or description of a period of generalized confusion. While confusion which resolves may be indicative of a brief period of aphasia or language difficulty, it more commonly represents global cerebral dysfunction, such as is found in a hypotensive episode or non-convulsive seizure. In the case of an episode of confusion, it is important to try to obtain history from family or friends regarding the patient's actions during this period, as well as trying to have the patient more completely explain what is meant by confusion. Often the aphasic patient whose symptoms have resolved will describe knowing what he or she wanted to say, but being unable to say it or being unable to appropriately complete the action attempted.

While not specifically designed as adjuncts to diagnosis, several aids exist to attempt to risk-stratify TIA regarding which patients may progress to stroke.[4] Among his patients diagnosed with TIA, five factors were found to be independently associated with risk of stroke. These five factors included diabetes, age greater than 60 years, symptom duration longer than 10 minutes, weakness, and speech impairment.

Similarly, Rothwell and colleagues found age greater than 60 years, speech disturbance, unilateral weakness, symptom duration longer than 10 minutes, and hypertension (blood pressure greater than 140/90) also correlated with risk of stroke in a population diagnosed with TIA.[11] This study was not designed to evaluate the accuracy of the diagnosis of TIA, but does point to the presence of these five factors being associated with a more likely diagnosis of TIA as opposed to another, non-ischemic pathology. It is important in trying to establish the diagnosis of TIA from the patient's history to also evaluate their past medical history. Patients with



vascular disease or risk factors for vascular disease such as diabetes and hypertension are more likely to have cerebral ischemia as the cause of their presentation than those without vascular disease. Also a history of smoking, or family history of early vascular disease should be elicited in the history as these entities increase a patient's risk for TIA.

It can be difficult to be certain of a diagnosis of TIA or stroke in the setting of symptoms referable to the posterior circulation. There is little published population-based data on posterior circulation ischemia. Caplan and colleagues describe their experience with the New England Medical Center Posterior Circulation Registry and the findings of this patient population.[12] They found less than one percent of their patients presented with only one symptom, including dizziness or vertigo. While dizziness and vertigo were present in 54% of their population with basilar artery disease, it was commonly associated with other findings, most often speech and swallowing difficulty found in 74% of patients. In their population with proven posterior circulation ischemia, 41% presented with headache as a primary symptom, which is unusual for anterior circulation ischemia. These findings reinforce that while TIA involving the posterior circulation can be more challenging to diagnose, a complete history, specifically asking about symptoms such as diplopia, speech slurring, difficulty swallowing, and difficulty reaching for objects or coordinating movements should aid in establishing the diagnosis. In a patient with complaints of dizziness plus another symptom, such as one of those described above, the diagnosis of TIA must be considered as more likely in the differential diagnosis, and must be convincingly replaced by an alternative diagnosis if a patient is to be dispositioned to home.

The history in evaluating a patient with persistent symptoms suspicious for acute ischemic stroke is similar to TIA, but also focuses on determining when the patient was last known to be neurologically normal, or at their neurologic baseline, if the patient has a previous deficit. The potential for treatment of the stroke exists if the patient is less than three hours from the time in which they were last known to be normal. The emergency physician (EP) is tasked with determining this time as closely as possible, even if required to contact outside sources, such as calling the nursing home or relatives that live with the patient. It is important if the patient is transported by EMS, to query the medics on when the patient was last normal and make certain the time quoted is not the time in which the patient was found abnormal, but when the patient was at his or her baseline. This inquiry should be performed during the initial physical examination to save minutes which may prove valuable in facilitating treatment.

While TIA patients typically have a normal physical examination by the time of arrival to the ED, stroke patients continue to have suggestive findings on physical examination. The most important aspect of the physical examination is to ensure it is complete and does not leave untested areas of the brain which could lead to the correct diagnosis. In order to make the diagnosis of stroke more consistent, approach the physical examination consistently with every patient. Most of what is needed regarding mental status, orientation, fluency, and quality of speech will be learned while taking the history. Little more will have to be added, unless performing a formal National Institute of Health Stroke Scale (NIHSS). While speaking with the patient regarding the history which brought them to the ED, specifically note the rate of speech and words chosen, whether an unusual amount of time is taken to formulate a sentence, or any inappropriate words are used in trying to relate the events of the day. If the patient seems to be mildly dysarthric, ask a family member or friend accompanying the patient if the speech sounds normal to them.

When proceeding to the examination, make certain to test visual fields in every patient. While patients with a visual field cut may sometimes complain of this, frequently they do not and may have significant infarcts in the occipital area which would otherwise go unnoticed. Take a few seconds to look at the extraocular movements of each patient. Posterior circulation infarcts which begin as mild but can progress may be unmasked by elucidating the diplopia and dysconjugate gaze of a patient with a cranial nerve deficit. In addition to strength testing, make certain to have every patient walk. Impending

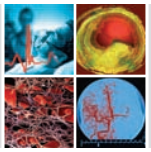
disaster from completion of a posterior circulation infarct can sometimes be identified by uncovering a patient's ataxia on gait analysis which otherwise may have gone unnoticed. A complete physical examination, including cranial nerves, visual fields, strength, and gait analysis will only require a few minutes. Only when this is normal can one truly exclude a diagnosis of stroke in the setting of worrisome complaints, although the history may still suggest TIA. If the patient presents with an abnormal physical examination and the stroke is less than three hours since the time the patient was last witnessed as being normal, consider performing a quick NIHSS to gather a more formal assessment of the patient's physical disability. Do not let this delay placement of a call to the Neurology or the stroke team regarding treatment if the patient meets inclusion criteria for t-PA therapy. Overall, EPs are excellent at making an accurate diagnosis of ischemic stroke. Scott and colleagues demonstrated in a consecutive sample of 151 patients treated for stroke in the ED, based on history and physical as well as a non-contrasted head CT and without a stroke team, the ED diagnosis was accurate 96% of the time in comparison to the hospital discharge diagnosis.[13]

Diagnosis and Imaging in TIA

Conventional imaging, particularly non-contrasted head computed tomography (CT), is rarely useful in making a consistent diagnosis of TIA, as the images are typically normal. The utility of noncontrasted head CT in the setting of suspected TIA largely exists to establish alternate pathology and does little to "rule in" the diagnosis. Most estimates place the findings of a non-vascular lesion accounting for neurologic symptoms in suspected TIA at approximately one percent of all scans performed. Douglas performed a retrospective analysis of patients seen in the ED for TIA who underwent a head CT, and had a new infarct seen, despite complete resolution of symptoms. Patients were then followed for 90 days and the odds ratio for clinical stroke within 90 days was determined. Of patients with a new infarct on CT, the odds ratio for a stroke at 90 days was 4 (95% CI 1.16 – 14.4) after adjustment for confounding variables.[14] While the number of patients in the study with a new infarct was small, the study supports the utility of this imaging modality in the setting of suspected TIA. Some patients will be seen to have cerebral ischemia even in the absence of symptoms, and this can firmly establish the diagnosis of TIA/IS.

There has been significant effort recently focusing on the evaluation of TIA using diffusion-weighted imaging (DWI) of MRI. This imaging modality is attractive for several reasons. The first is a positive lesion on DWI confirms the diagnosis of TIA in a patient not currently symptomatic, and eliminates many of the TIA mimics, similar to positive biomarkers in acute coronary syndrome. This possibility of confirmation of diagnosis does not exist with CT, as CT is much less sensitive for acute ischemia than DWI. In multiple series of patients evaluated for TIA, around forty percent of patients show DWI-positivity, with a range from 21 – 68%.[15-20] Kidwell et al. studied 42 patients with DWI who presented with symptoms of TIA. Twenty of the 48 patients (42%) demonstrated a DWI hyperintense lesion; despite this finding only two of the 20 DWI-positive patients remained symptomatic.[16] Diffusion-weighted imaging becomes positive early in an ischemic insult. Positive DWI tends to occur much more often in TIAs which last greater than one hour, with some studies demonstrating a correlation with duration of TIA and likelihood of positive DWI. DWI-positivity has been shown in TIAs lasting only ten minutes, however, and may still have a place in the diagnosis of patients with short duration of symptoms. It is very unlikely, however, DWI will be positive in a patient with only seconds to a few minutes of symptomatology.

The utility of DWI in the evaluation of TIA is still being defined. The patient with positive DWI most likely has a higher risk of subsequent stroke. In addition, the lack of a lesion on DWI does not refute the diagnosis of TIA, and these patients still have significant risk of future ischemia. Presently, DWI should most likely be regarded as a specific but insensitive test for transient focal cerebral ischemia, serving to confirm the diagnosis in some cases. In the setting of a compelling history, the diagnosis of TIA should remain likely and the evaluations continue, regardless of cerebral imaging results.



Diagnosis and Imaging in Acute Stroke

The non-contrasted CT of the brain has become the standard approach to imaging of the patient who presents with an acute neurologic deficit. It is the most readily available imaging modality in most EDs. The ability of CT to establish a consistent diagnosis of IS, however, depends on time from symptom onset and the area of the brain involved. Non-contrasted CT is the gold standard for detection of acute hemorrhage and can provide a good method of screening for mass lesions which may mimic acute stroke. Non-contrasted CT does lack sensitivity for ischemic changes in hyperacute stroke, but CT interpretation can be improved through the use of standardized measures and experience.

While the sensitivity of non-contrasted head CT for ischemic changes in the hyperacute period is variable and ranges from 31-75%, there are certain hallmarks of ischemic injury that can be found.[21,22] Loss of differentiation between the gray matter and white matter, especially in the basal ganglia, loss of the "insular ribbon," effacement of the sulci, mass effect from edema, and areas of hypodensity are all early changes indicative of ischemia. Even experienced radiologists and stroke physicians, however, have difficulty in accurately and reproducibly identifying the presence of early ischemic change on non-contrasted CT.

Two imaging modalities which can help firmly establish a diagnosis of acute stroke, if uncertainty remains after a complete history and physical examination include computed tomographic angiography (CTA) and cerebral perfusion CT (CTP). CTA takes advantage of the widespread availability of CT scanners in EDs to allow a non-invasive look at the cerebral vasculature to assess for stenosis or occlusion. The axial cuts, or source images, are reformatted into a three-dimensional projection which allows visualization of the circle of Willis as well as proximal portions of the MCA, anterior cerebral artery (ACA) and vertebrobasilar system. The advantages of CTA include its speed and availability as compared to magnetic resonance angiography (MRA) as well as its ability to demonstrate occlusion of the cerebral vessels, thus firmly establishing a diagnosis of ischemia if uncertainty remains. For example, in a patient with right arm weakness suspected to be cerebral ischemia but with a history of seizure adding Todd's paralysis into the differential diagnosis, absence of the left middle cerebral artery (MCA) on CTA would be considered diagnostic of a left MCA stroke instead of seizure.

Lev et al. used CTA in 44 consecutive patients who presented within six hours of onset of symptoms to assess for occlusion of a cerebral vessel prior to angiographic correlation with conventional angiography.[23] Of 224 vessels studied with diagnostic angiography after CTA, the sensitivity of CTA for large-vessel occlusion was 98.4% with a specificity of 98.1% and overall accuracy of 98.2%. The CTA added an average of only 11.7 ± 4.2 minutes to the study time, with an estimated 3 minutes required for reconstruction and review. They concluded CTA was highly accurate in the detection of large vessel occlusion and may be valuable for the diagnosis of stroke and potential triage of patients to intra-arterial fibrinolysis. Even in the absence of documented occlusion on CTA, lacunar infarct can still produce the symptoms seen on clinical examination stroke cannot be excluded based on normal CTA, but merely "ruled in" by an abnormal study.

In some situations, CTP can be used as an adjunct to CTA and can demonstrate tissue with decreased perfusion, thus aiding in establishing the diagnosis of acute stroke. This technology suffers from similar insensitivity in the posterior cranial fossa as other CT imaging. Schramm et al. compared perfusion CT with perfusion-weighted MRI (PWI) and DWI to determine correlation between the two studies.[24] In this study, 22 patients underwent both CT and MRI within six hours of onset of acute neurologic deficit. This study found no significant difference between perfusion CT lesion volume and PWI on MRI. Further, PCT evidence of infarction correlated well with DWI. This suggests good reproducibility between CTP and MRI for evaluation of ischemic stroke. The perfusion CT averages approximately 10 minutes to complete and can be performed on most spiral CT scanners with the addition of imaging software, making it more accessible to EDs in real-time.

The standard method for evaluation of ischemic stroke is investigation by MRI. Diffusion-weighted imaging demonstrates a hyperintense signal in the setting of acute ischemia and is thought to be positive in most patients after only minutes of ongoing symptoms. While there are case reports of delayed DWI-positivity, most patients with acute ischemia will have a positive study in real-time. Studies involving MRI in the hyperacute time period are small but encouraging. Röther et al., in a non-randomized study, used MRI to evaluate 139 patients for open-label use of rt-PA within six hours of onset of presumed ischemic injury.[25] Patients with DWI-positivity treated with rt-PA did significantly better (OR 0.20, 95%CI 0.05-0.83). Typical MRI protocols in the hyperacute time period add only 20 minutes to overall treatment time. DWI benefits from being one of the few imaging modalities which can, in most cases, rule out the diagnosis of ischemia in the setting of normal imaging and symptom duration of at least an hour.

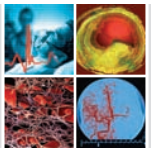
Magnetic resonance angiography (MRA) is the final piece in the puzzle of hyperacute MRI for ischemic stroke. MRA performed of the Circle of Willis can document occlusion or stenosis in the proximal vessels with three-dimensional imaging. It is non-invasive, requires no contrast, and further adds information about the possible risks and benefits of fibrinolysis. The downside to the use of MRI in the acute evaluation of ischemic stroke is the lack of availability of the hardware and technologists. However, as CT improves its ability to provide imaging of perfusion defects and angiography, need for MRI in the acute phase may decrease.

The Future of Diagnosis in TIA and Stroke

While evaluation in the ED using an accurate and complete history and physical examination, coupled with advanced imaging, is an excellent standard upon which to base diagnosis, several tools are in the process of development which may aid EPs in the diagnosis and treatment of acute cerebral ischemia. One such tool is telemedicine. Internet-based systems are now being used to allow stroke team evaluation of patients who present to hospitals without 24-hour neurologic expertise. If a patient is identified as likely having an acute stroke, a telemedicine system is activated which allows a stroke team member to interact with the physician and patient at the remote hospital and view radiologic images. The stroke team member can then provide input into the decision to treat with fibrinolytics, transfer, or offer expertise on other acute diagnostic and management issues. One example of such a system was described by Schwamm and colleagues, who treated 75% of patients with acute stroke at the remote hospital who were eligible for t-PA.[26] Every EP involved in the study felt the telemedicine conferencing improved patient care.

Another tool undergoing experimental evaluation for the future diagnosis of stroke and TIA is biomarkers in the setting of cerebral ischemia. Many pre-clinical and clinical trials have been performed on serum samples of proteins in patients with confirmed diagnosis of cerebral ischemia. The ultimate goal is to find a protein, much like troponin in cardiac ischemia, which would rapidly diagnose cerebral ischemia with high sensitivity and specificity. While a single marker which performs this task rigorously has not yet been identified, recent work has focused on a panel of biomarkers used in concert to increase specificity. Lynch and colleagues described a panel of four markers which achieved 90% sensitivity and specificity for the diagnosis of stroke.[27] While encouraging, this area still has significant questions to be answered, including the timing in which the markers become positive after symptom onset and the continued need for near 100% sensitivity without sacrificing specificity.

The presentation of acute cerebral ischemia can be variable, but the consequences of missing the diagnosis are grave. In addition, over diagnosis of processes such as TIA can consume valuable resources and result in unnecessary hospitalizations. Future tools may help streamline the diagnosis and management of cerebral ischemia in the ED. Currently, however, the cornerstone of diagnosis of TIA and stroke remains an accurate, complete, history and physical examination. When coupled with thoughtful use of cerebral imaging and an overall cautious approach, the diagnosis will rarely be missed.



REFERENCES

1. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue Plasminogen Activator for Acute Ischemic Stroke. N Engl J Med 1995;333(24):1581-8.
2. Stettler BA, Jauch EC, Kissela B, Lindsell CJ. Neurologic Education in Emergency Medicine Training Programs. Acad Emerg Med 2005;12(9):909-11.
3. Albers GW, Caplan LR, Easton JD, et al. Transient Ischemic Attack -- Proposal for a new definition. N Engl J Med 2002;347(21):1713-6.
4. Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after Emergency Department diagnosis of TIA. JAMA 2000;284(22):2901-6.
5. Coull AJ, Lovett JK, Rothwell PM. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. BMJ 2004;328(7435):326-.
6. Hill MD, Yiannakoulias N, Jeerakathil T, Tu JV, Svenson LW, Schopflocher DP. The high risk of stroke immediately after transient ischemic attack: A population-based study. Neurology 2004;62(11):2015-20.
7. Eliasziw M, Kennedy J, Hill MD, Buchan AM, Barnett HJM. Early risk of stroke after a transient ischemic attack in patients with internal carotid artery disease. CMAJ 2004;170(7):1105-9.
8. Lisabeth LD, Ireland JK, Risser JMH, et al. Stroke risk after transient ischemic attack in a population-based setting. Stroke 2004;35(8):1842-6.
9. Feinberg W, Albers G, Barnett H, et al. Guidelines for the management of transient ischemic attacks. From the Ad Hoc Committee on Guidelines for the Management of Transient Ischemic Attacks of the Stroke Council of the American Heart Association. Circulation 1994;89(6):2950-65.
10. Albers GW, Hart RG, Lutsep HL, Newell DW, Sacco RL. Supplement to the Guidelines for the Management of Transient Ischemic Attacks A Statement From the Ad Hoc Committee on Guidelines for the Management of Transient Ischemic Attacks, Stroke Council, American Heart Association. Stroke 1999;30(11):2502-11.
11. Rothwell P, Giles M, Flossmann E, et al. A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack. Lancet 2005;366(9479):29-36.
12. Voetsch B, DeWitt LD, Pessin MS, Caplan LR. Basilar artery occlusive disease in the New England Medical Center Posterior Circulation Registry. Arch Neurol 2004;61(4):496-504.
13. Scott P, Silbergleit R. Misdiagnosis of stroke in tissue plasminogen activator-treated patients: Characteristics and outcomes. Ann Emerg Med 2003;42(5):611-8.
14. Douglas VC, Johnston CM, Elkins J, Sidney S, Gress DR, Johnston SC. Head computed tomography findings predict short-term stroke risk after transient ischemic attack. Stroke 2003;34(12):2894-8.
15. Rovira A, Rovira-Gols A, Pedraza S, Grive E, Molina C, Alvarez-Sabin J. Diffusion-weighted MR imaging in the acute phase of transient ischemic attacks. AJNR Am J Neuroradiol 2002;23(1):77-83.
16. Kidwell CS, Alger JR, Di Salle F, et al. Diffusion MRI in patients with transient ischemic attacks. Stroke 1999;30(6):1174-80.
17. Winbeck K, Bruckmaier K, Etgen T, von Einsiedel HG, Rottinger M, Sander D. Transient ischemic attack and stroke can be differentiated by analyzing early diffusion-weighted imaging signal intensity changes. Stroke 2004;35(5):1095-9.
18. Purroy F, Montaner J, Rovira A, Delgado P, Quintana M, Alvarez-Sabin J. Higher risk of further vascular events among transient ischemic attack patients with diffusion-weighted imaging acute ischemic lesions. Stroke 2004;35(10):2313-9.
19. Restrepo L, Jacobs MA, Barker PB, Wityk RJ. Assessment of transient ischemic attack with diffusion- and perfusion-weighted imaging. AJNR Am J Neuroradiol 2004;25(10):1645-52.
20. Crisostomo RA, Garcia MM, Tong DC. Detection of diffusion-weighted MRI abnormalities in patients with transient ischemic attack: correlation with clinical characteristics. Stroke 2003;34(4):932-7.
21. Patel SC, Levine SR, Tilley BC, et al. Lack of clinical significance of early ischemic changes on computed tomography in acute stroke. JAMA 2001;286(22):2830-8.
22. Barber PA DA, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. Lancet 2000;355(9216):1670-4.
23. Lev MH, Farkas J, Rodriguez VR, et al. CT angiography in the rapid triage of patients with hyperacute stroke to intraarterial thrombolysis: accuracy in the detection of large vessel thrombus. J Comput Assist Tomogr 2001;25(4):520-8.
24. Schramm P, Schellinger PD, Klotz E, et al. Comparison of perfusion computed tomography and computed tomography angiography source images with perfusion-weighted imaging and diffusion-weighted imaging in patients with acute stroke of less than 6 hours duration. Stroke 2004;35(7):1652-8.
25. Rother J, Schellinger PD, Gass A, et al. Effect of intravenous thrombolysis on MRI parameters and functional outcome in acute stroke <6 hours. Stroke 2002;33(10):2438-45.
26. Schwamm LH, Rosenthal ES, Hirshberg A, et al. Virtual TeleStroke support for the Emergency Department evaluation of acute stroke. Acad Emerg Med 2004;11(11):1193-7.
27. Lynch JR, Blessing R, White WD, Grocott HP, Newman MF, Laskowitz DT. Novel diagnostic test for acute stroke. Stroke 2004;35(1):57-63.