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Perfusion Imaging in the 3 Hour Time Window Predicts a tPA-Associated Hemorrhage in Acute Ischemic Stroke

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Abstract

Perfusion imaging is being evaluated in acute ischemic stroke patients to identify those who may benefit from reperfusion therapies beyond standard thrombolytic time windows but limited data is available on its utility in patients presenting within standard thrombolytic time windows. We report a case of a patient presenting within the 3 hour time window where computerized tomographic perfusion imaging before intravenous thrombolysis identified a large volume of severely ischemic tissue and where intravenous tissue plasminogen activator (tPA) administration subsequently resulted in a fatal intracerebral hemorrhage. Whether perfusion imaging can predict an increased risk of tPA-associated symptomatic hemorrhage in patients presenting within standard thrombolytic time windows requires further study.

Introduction

Perfusion imaging is being evaluated as a tool to identify acute ischemic stroke patients who are most likely to benefit from reperfusion therapies beyond the standard time windows. It has also been hypothesized that patients with large volumes of severely ischemic tissue may be at greatest risk for reperfusion injury. A recent analysis of patients presenting within 3-6 hours from onset of symptoms found that magnetic resonance imaging (MR) perfusion weighted imaging ($T_{\max} > 8$ seconds) volume $> 85\text{cc}$ correlated with an increased hemorrhage risk after IV tPA.¹ Whether MR or computerized tomography (CT) perfusion can assist with selection of patients presenting within the standard time window for intravenous (IV) thrombolysis remains unclear.

Case report

A 72 year old woman was found by her grandson slumped over to the left on a bedside commode 19 minutes after her last seen normal time (LSNT). Her past history included

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diabetes, hypertension, congestive heart failure and atrial fibrillation. She had recently been discharged after a heart failure exacerbation and was not on anticoagulation.

She presented to our emergency room 73 minutes from her LSNT. Blood pressure was 129/66 mmHg and she was in atrial fibrillation with a rate of 114/min. Initial neurologic exam identified her to be somnolent but arousable to voice with right forced gaze deviation, left homonymous hemianopsia, left upper motor neuron facial weakness, moderate dysarthria, left hemiplegia, left hemianesthesia and neglect with National Institute of Health Score Scale (NIHSS) score of 21. CT head without contrast (Figures 1A, B) showed no intracerebral hemorrhage and Alberta Stroke Program Early CT Score (ASPECTS) of 8. While IV tPA was being mixed, patient underwent CT angiography (CTA) and CT perfusion (CTP) imaging (Figures 1D-F). CTA identified distal right M1 middle cerebral artery (MCA) occlusion (Figure 1C). CTP demonstrated prolonged mean transit time in the entire right MCA territory (Figure 1E) with decreased cerebral blood volume in the posterior division of the MCA but preserved cerebral blood volume in the anterior division of the MCA (Figure 1D) suggestive of penumbra. The stroke team re-confirmed the LSNT with the family. Within 30 minutes following tPA infusion, NIHSS score improved to 16 with improvement in level of consciousness and left arm and leg strength. Post-thrombolysis, blood pressure remained below 180/105 mmHg without anti-hypertensive therapy. While in the neuro-ICU, she was found to have a dilated and unreactive right pupil 6 hours after tPA administration. An emergent non-contrast head CT showed extensive hemorrhagic transformation in the right MCA distribution with midline shift and uncal herniation (Figure 1G). She was emergently intubated, transfused cryoprecipitate and initiated on hypertonic saline. Her examination rapidly declined to clinical brain death within 36 hours.

Discussion

Perfusion imaging provides information on key elements of ischemic pathophysiology including vessel occlusion, compensatory collateral flow, resultant hemodynamic changes and neurovascular injury in acute ischemic stroke.² Poor collateral circulation in our patient may have resulted in CTP evidence of a large volume of severely ischemic tissue even though our patient met eligibility criteria for IV thrombolysis within the 3 hour time window. While early ischemic changes in 3 areas on non-contrast head CT (ASPECT score 7) have been associated with an increased risk of tPA-associated hemorrhage,³ our patient's CT did not meet this criteria.

This case highlights the potential limitations of a time-based treatment approach to acute ischemic stroke. The American Heart Association/American Stroke Association has recommended that IV tPA should be administered to eligible patients up to 4.5 hours from LSNT, however 6.4% of patients treated within the 3 hour and 7.9% of patients treated within the 3 to 4.5 hour time windows were harmed as a result of symptomatic intracranial hemorrhage.⁴⁻⁶ While MRI mismatch [$PWI (T_{max} - 6 \text{ seconds}) \div DWI > 1.2$] identified large penumbra in a high percentage of patients presenting within 4.5 hours from stroke onset, 19% of patients within the 3 to 4.5 hour time window did not have mismatch in the EPITHET trial (personal communication, Stephen Davis, June 19, 2011). Whether perfusion imaging (CT or MR) can predict an increased risk of tPA-associated symptomatic

hemorrhage in patients presenting within the 4.5 hour time window requires further study. Any potential benefits from perfusion imaging in acute ischemic stroke treatment within the 4.5 hour time window can only be gained if its acquisition does not result in delays to IV tPA treatment.⁷

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Figure 1.

A & B: Non-contrast head CT showing minimal hypodensity and hyperdense M1 segment of the right MCA. C: CTA showing partial occlusion of the M1 segment of the right MCA. D: CT perfusion showing decreased cerebral blood volume (CBV) in the distribution of the posterior division of the right MCA but preserved CBV in the anterior division. E: Prolonged mean transit time in the entire right MCA distribution. F: Decreased cerebral blood flow in the distribution of the posterior division of the right MCA. G: Follow-up CT scan showing hemorrhagic transformation in the infarcted territory.