

Safety of Intravenous Tissue Plasminogen Activator Administration with Computed Tomography Evidence of Prior Infarction

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Background: Prior stroke within 3 months excludes patients from thrombolysis; however, patients may have computed tomography (CT) evidence of prior infarct, often of unknown time of origin. We aimed to determine if the presence of a previous infarct on pretreatment CT is a predictor of hemorrhagic complications and functional outcomes after the administration of intravenous (IV) tissue plasminogen activator (tPA). *Methods:* We retrospectively analyzed consecutive patients treated with IV tPA at our institution from 2009-2011. Pretreatment CTs were reviewed for evidence of any prior infarct. Further review determined if any hemorrhagic transformation (HT) or symptomatic intracerebral hemorrhage (sICH) were present on repeat CT or magnetic resonance imaging. Outcomes included sICH, any HT, poor functional outcome (modified Rankin Scale score of 4-6), and discharge disposition. *Results:* Of 212 IV tPA-treated patients, 84 (40%) had evidence of prior infarct on pretreatment CT. Patients with prior infarcts on CT were older (median age, 72 versus 65 years; $P = .001$) and had higher pretreatment National Institutes of Health Stroke Scale scores (median, 10 versus 7; $P = .023$). Patients with prior infarcts on CT did not experience more sICH (4% versus 2%; $P = .221$) or any HT (18% versus 14%; $P = .471$). These patients did have a higher frequency of poor functional outcome at discharge (82% versus 50%; $P < .001$) and were less often discharged to home or inpatient rehabilitation center (61% versus 73%; $P = .065$). *Conclusions:* Visualization of prior infarcts on pretreatment CT did not predict an increased risk of sICH in our study and should not be viewed as a reason to withhold systemic tPA treatment after clinically evident strokes within 3 months were excluded. **Key Words:** Acute ischemic stroke—thrombolysis—safety—symptomatic intracerebral hemorrhage—computerized tomography.
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Introduction

Systemic thrombolytic therapy has been shown to improve clinical outcomes in patients with acute ischemic stroke.¹ The most feared adverse effect of intravenous (IV) tissue plasminogen activator (tPA) is symptomatic intracerebral hemorrhage (sICH) because of the high associated morbidity and mortality.² Generally, tPA protocols derived from the original National Institute of Neurological Disorders and Stroke tPA trial¹ aim to exclude patients who are considered to be at high risk for sICH. One of these exclusions is a history of stroke within the preceding 3 months. Unfortunately, patients may not be able to report this history and physicians may have to use their best judgment when the pretreatment CT scan reveals evidence of prior infarction.

Pretreatment magnetic resonance imaging (MRI) studies have shown that absolute volume on diffusion weighted imaging^{3,4} and fluid attenuated inversion recovery hyperintensities within the area of diffusion restriction are associated with increased risk of hemorrhagic transformation (HT) after IV thrombolysis.⁵ However, given the current lack of adequate MRI availability and the extended study duration compared with CT, the application of these findings is of limited value in clinical practice. Several indicators on the pretreatment CT scan have been identified as risk factors for sICH, including early ischemic changes and a hyperdense middle cerebral artery sign.^{6,7} Unfortunately, changes associated with previous infarcts have not been well studied to determine their risk of sICH. The purpose of this study was to determine if there is a relationship between evidence of prior infarction on pretreatment CT, either lacunar or cortical, and subsequent sICH in patients receiving IV tPA.

Methods

Study Population and Variable Definition

We retrospectively identified all consecutive IV tPA-treated patients who presented to our tertiary care center from 2008-2011 using our prospectively collected stroke registry. Patients were excluded if they were transferred from another institution. Patient demographic, clinical, and imaging data were extracted from the medical record. Stroke severity was measured using the National Institutes of Health Stroke Scale (NIHSS) score. Pretreatment CTs were reviewed for evidence of any prior infarct by neurologists blinded to follow-up imaging. The definition of a prior infarct was at the clinical discretion of the neurologist and confirmed by an independent review by a neuroradiologist. We did not distinguish these prior infarctions as symptomatic or asymptomatic. Patients with evidence of prior infarct were subdivided into prior lacunar or prior cortical infarcts. These groups were not

mutually exclusive as patients could have evidence of both prior lacunar and cortical infarcts. After all pretreatment head CTs were reviewed, repeat CT or MRI was evaluated to determine if hemorrhage was present.

Outcomes of interest included any HT on follow-up CT or MRI, sICH (defined as a type 2 parenchymal hemorrhage with deterioration in the NIHSS score of ≥ 4 points or death⁸), poor functional outcome (defined as a modified Rankin Scale score of 3-6), and favorable discharge disposition (being discharged to home or an inpatient rehabilitation center). We compared admission, clinical, and discharge information between patients who had evidence of prior infarct compared with those who did not have prior evidence of infarct.

Statistics

Demographic and clinical data were recorded throughout admission and compared between groups using chi-square and *t* tests with nonparametric equivalents when appropriate. Crude and adjusted logistic regression analyses were conducted to assess the relationship between evidence of prior infarct and outcomes of interest. Adjustment variables for the multivariable logistic regression models were chosen based on baseline differences between the 2 groups and clinical significance. As this was an exploratory analysis, no adjustments were made for multiple comparisons.⁹ An alpha of .05 was set as the level of significance.

Results

Baseline Demographic Information

Of 212 IV tPA-treated patients, 84 (40%) had evidence of prior infarct on pretreatment CT. Lacunes were seen in 55 patients (26%), whereas 47 patients (22%) had evidence of prior cortical strokes. Both lacunar and cortical infarcts were found in 17 patients (8%). Patients with prior infarcts on CT were older (mean age, 72 versus 65 years; $P = .001$), were more likely to have a history of hypertension (85% versus 71%; $P = .024$) or congestive heart failure (19% versus 9%; $P = .026$), were more often on antiplatelet agents before admission (49% versus 31%; $P = .007$), and had higher pretreatment NIHSS scores (median, 10 versus 7; $P = .023$). Demographic variables are fully listed in [Table 1](#) for the dichotomized groups.

Stroke Outcomes

As shown in [Table 2](#), patients with prior infarcts on CT did not experience significantly more sICH (4% versus 2%; $P = .221$) or HT of any type (18% versus 14%; $P = .471$). Patients with evidence of prior stroke on pretreatment CT were discharged to home or inpatient rehabilitation center less often, albeit not statistically significantly (61% versus 73%; $P = .065$), and had higher frequencies of poor functional outcome at discharge (82% versus 50%; $P < .001$).

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