Elevations in Tissue Fluid-Attenuated Inversion Recovery Signal Are Related to Good Functional Outcome after Thrombolytic Treatment

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Background: Early elevations in the parenchymal signal intensity on T2-weighted images, including fluid-attenuated inversion recovery (FLAIR) sequences, within the ischemic territory are considered as a marker of successful recanalization following thrombolytic treatment. In this study, our aim was to assess whether quantitatively determined FLAIR hyperintensity increases could be predictive of improved functional outcome in patients with acute ischemic stroke. *Methods:* Patients receiving intravenous thrombolysis for proximal anterior circulation strokes were included in the study. FLAIR hyperintensity ratio was determined on magnetic resonance imaging obtained within 72 hours of symptom onset. Univariate and multivariate analyses were performed to determine predictors of good functional outcome at 90 days. *Results:* The study population was composed of 65 patients. The median (interquartile range) FLAIR hyperintensity ratio was significantly higher among patients with good functional outcome (modified Rankin Scale score ≤3 at day 90, 1.4 [1.2-1.7] versus 1.2 [1.1-1.4], $P = .005$). Patients with a FLAIR hyperintensity ratio of 1.3 or higher were 4.4 (95% confidence interval 1.6-12.7) times more likely to be independent functionally at the end of 3 months. Higher admission National Institutes of Health Stroke Scale score and age, together with lower FLAIR hyperintensity ratio ($P = .006$), were found to be significantly and independently related to unfavorable outcome at 90-day follow-up in multivariate analyses. *Conclusions:* Our findings suggest that a rise in FLAIR hyperintensity signal within the ischemic tissue is suggestive of favorable outcome in patients undergoing intravenous thrombolysis. This tissue marker of favorable outcome is irrespective of other parameters that are crucial in the prognosis of ischemic stroke, such as age and stroke severity. **Key Words:** Acute ischemic stroke—vasogenic edema—FLAIR ratio—thrombolysis.

Intravenous tissue plasminogen activator administered within 4.5 hours of symptom onset is accepted as a standard treatment in the setting of ischemic stroke. The positive influence of thrombolytic therapy on functional outcome is mediated through recanalization of occluded arteries.[1] One of the consequences of successful recanalization and accompanying microcirculatory reperfusion is the rapid shift of water from intravascular compartment to cerebral tissue via the dysfunctional blood–brain barrier, leading to development of early vasogenic edema.[2,3] While diffusion-weighted imaging (DWI), the hallmark of acute stroke imaging, is sensitive to cytotoxic edema, T2-weighted images, including

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fluid-attenuated inversion recovery (FLAIR) sequences, reflect the vasogenic process more accurately due to their sensitivity to water content in the tissue.[4] The amount of signal increase on FLAIR images can be quantified in a relative manner by comparison to the contralateral nonischemic hemisphere. An increase in this FLAIR hyperintensity ratio has been shown as a predictor of hemorrhagic conversion in patients with ischemic stroke.[4] In this regard, we sought to assess whether the degree of vasogenic edema, quantified as an increase in FLAIR hyperintensity ratio, could serve as a marker of thrombolytic treatment response and thereby predict improved functional outcome in patients with acute ischemic stroke.

Methods

The medical records and radiological studies of a consecutive series of acute ischemic stroke patients who were treated by intravenous thrombolysis in our medical center between 2006 and 2014 were retrospectively evaluated. The study was restricted to patients who had intracranial internal carotid artery or proximal middle cerebral artery (M1 and M2) occlusions demonstrated on admission computed tomography angiography studies and had undergone magnetic resonance imaging (MRI) within 72 hours of symptom onset. Patients receiving endovascular interventions or those with unreliable FLAIR ratio calculations (due to motion artifacts, severe leukoaraiosis, or parenchymal hematoma) were not included in the analyses. The present study was approved by the institutional review board.

Information related to demographics, stroke risk factors, time from stroke onset to thrombolysis, time from stroke onset to imaging, and 90-day functional outcome was abstracted in all patients from a prospectively collected departmental stroke database. MRI was performed using 1.5-T scanners (MAGNETOM Tim, Siemens, Erlangen, Germany; and Intera/Achieva, Philips, Best, The Netherlands). FLAIR images were obtained with the following acquisition parameters: repetition time 8000-9000 milliseconds, echo time 90-100 milliseconds, inversion time 2000-2100 milliseconds, matrix 224×256, slice thickness 5 mm with 10% interslice distance, and field of view 220-240 mm. The FLAIR hyperintensity ratio was determined by a previously described and validated method, in which signal intensities were measured in regions of interests (ROIs) within the ischemic and nonischemic hemispheres (2 consecutive slices, 1 cortical and 1 subcortical measurement performed in each slice from the ipsilateral and contralateral hemisphere); each measurement from the ischemic hemisphere was then divided to its corresponding pair from the normal hemisphere and the resulting 4 sets of ratios from each patient were averaged to calculate the FLAIR hyperintensity ratio of the patient (Fig 1).[4] DWI was used to verify placement of ROIs within the ischemic tissue; the mirror locations were then selected to place the corresponding ROIs within the contralateral hemisphere. Care was taken not to place ROIs on regions with evidence of hemorrhagic conversion.

Categorical variables were expressed as N (%) and continuous variables as median (interquartile range [IQR]). The primary outcome measure in our cohort of patients with proximal anterior circulation strokes was the proportion of patients achieving a modified Rankin Scale score of 3 or lower at the end of 90 days. Groupwise comparisons among categorical variables were performed by using the chi-square test and among continuous variables by using the Mann–Whitney *U*-test. The Spearman test was used to assess correlation among continuous variables. A logistic regression model with 90-day modified Rankin Scale score as the dependent variable was developed to determine independent factors associated with

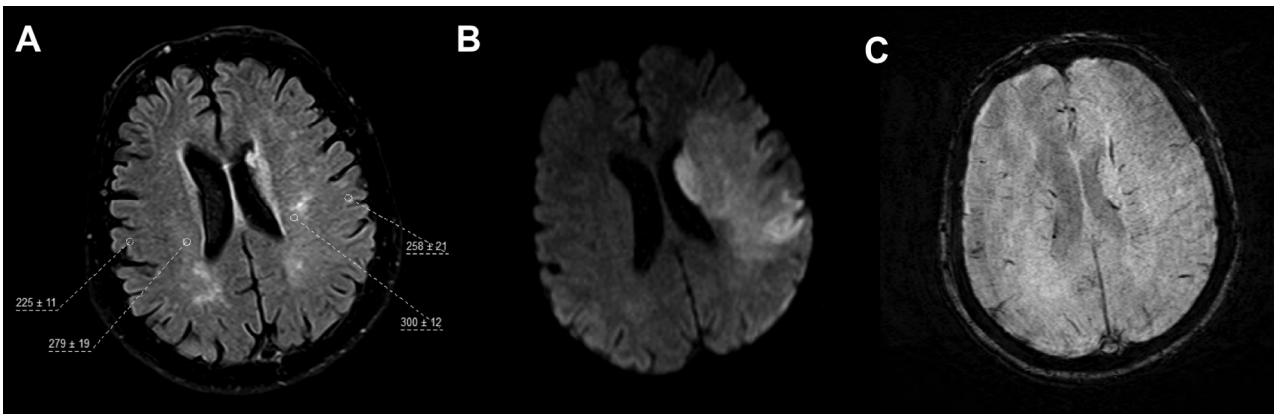

Figure 1. *Two consecutive FLAIR slices are used for determination of FLAIR hyperintensity ratio. On each FLAIR slice, 1 ROI is placed on a cortical area and another on a subcortical area (A) within the corresponding DWI bright region (B). Care is taken not to place ROIs on top of white matter hyperintensities or regions with evidence of hemorrhagic conversion per susceptibility-weighted images (C). The FLAIR intensity level within each ROI is divided by the intensity level of the mirror area in the contralateral nonischemic hemisphere (258/225 = 1.15 and 300/279 = 1.08 in the current example). A total of 4 sets of ratios originating from 2 slices are then averaged to calculate the FLAIR hyperintensity ratio of the patient. Abbreviations: DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; ROI, region of interest.*