Thrombolysis in Large Diffusion-Weighted Imaging Lesions: Lower Chance but Still a Chance

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Background: We sought to investigate whether early thrombolytic treatment can result in favorable functional outcome even in patients with large diffusion-weighted imaging (DWI) lesions. *Materials and Methods:* We analyzed 566 patients who received intravenous alteplase within 4.5 hours from onset, initially underwent DWI and magnetic resonance angiography, and had acute infarction confined to anterior circulation. DWI lesion volumes were measured semiautomatically. The association between DWI lesion volume and 3-month outcome in patients who achieved early recanalization was assessed. The DWI lesion volume cutoff, which predicts unfavorable outcome despite recanalization, was determined. In patients with large DWI lesions, the distributions of modified Rankin Scale (mRS) score were compared according to the recanalization status. *Results:* Four hundred thirty-six patients achieved early recanalization. Among these patients, 283 (65%) patients had a favorable functional outcome (mRS score 0-2). DWI lesion volume (odds ratio [OR], 1.38 per 10 mL; 95% confidence interval [CI], 1.22-1.56) was an independent variable associated with poor outcome, along with hypertension (OR, 1.87; 95% CI, 1.12-3.10), National Institutes of Health Stroke Scale (NIHSS) score (OR, 1.13; 95% CI, 1.08-1.19), and onset-to-needle time (OR, 1.08 per 10 minutes; 95% CI, 1.03-1.13). The DWI lesion of 60 mL or higher highly predicted an unfavorable outcome with a positive predictive value of 95.3%. In patients with a DWI lesion of 60 mL or higher, recanalization had no benefit for an mRS score of 0-2 but was significantly associated with an mRS score of 0-3 (OR, 4.64; 95% CI, 1.08-19.97). *Conclusions:* Despite early recanalization, the probability of favorable outcome is low in patients with a DWI lesion of 60 mL or higher. Nevertheless, the benefit of recanalization still persists in large DWI lesions. **Key Words:** Thrombolysis—diffusion-weighted imaging—MRI—outcome.

Introduction

The thrombolytic treatment within the time window is of proven benefit in patients with acute ischemic stroke.[1,2] However, we occasionally encounter patients with large diffusion-weighted imaging (DWI) lesions within the time window. In thrombolysis studies, a large lesion volume on pretreatment DWI has been known to be associated with unfavorable outcome.[3,4] However, these data have been derived from studies where patients were treated beyond 3 hours. An early thrombolysis study showed that the initial DWI lesion volume was not an independent predictor of outcome.[5]

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As for the endovascular treatment, a previous study showed that none of the 6 patients with a DWI lesion higher than 70 mL benefited from recanalization.[6] Accordingly, most endovascular treatment trials excluded patients with a large infarct core and the current guidelines address the uncertainty of treatment benefit in patients with a large infarct core.[7-11] The Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands trial was the only endovascular treatment trial that did not exclude patients with a large infarct core and subsequently needed a much larger sample size to show the benefit of reperfusion treatment.[12,13] In contrast, a recent registry data showed that favorable outcome was achieved in one third of patients with DWI lesions higher than 70 mL after successful endovascular recanalization.[14]

Whether to exclude patients with large DWI lesions for thrombolysis may be dependent on whether early DWI lesion can benefit from reperfusion or not. Generally, the DWI lesion is considered as an ischemic core that is not reversible with reperfusion.[15] Moreover, reperfusion in large DWI lesions may increase the risk of symptomatic intracerebral hemorrhage (ICH).[16] On the contrary, there are studies about the possibility of diffusion lesion reversal in the early time window.[17,18]

Therefore, whether to withhold thrombolytic treatment in patients with large DWI lesion is unsettled. We sought to investigate if thrombolytic treatment in early time window can result in favorable functional outcome even in patients with large DWI lesions.

Materials and Methods

Subjects

We retrospectively reviewed data from the prospectively collected stroke registry of our stroke center. Consecutive patients with acute ischemic stroke who were admitted between January 2009 and December 2016 were considered if they received intravenous alteplase within 4.5 hours from onset, initially underwent DWI and magnetic resonance angiography (MRA), and had acute infarction confined to the anterior circulation. We excluded patients who received alteplase from other hospitals, had a prestroke modified Rankin Scale (mRS) score of 2 or higher, and had no data about the recanalization status of large vessels after thrombolysis. In our stroke registry, demographic features and risk factors were recorded, including hypertension, diabetes mellitus, dyslipidemia, current cigarette smoking, previous stroke, atrial fibrillation, and history of coronary heart disease. The National Institutes of Health Stroke Scale (NIHSS) score was measured at the time of admission. As for the time variables, stroke onset time, hospital arrival time, alteplase treatment time, and magnetic resonance imaging (MRI) scan time were recorded. The mRS score was assessed 3 months after stroke through a telephone interview.

Imaging Protocol

According to our institutional policy, candidates for thrombolytic treatment had undergone immediate MRI scan, including DWI, fluid-attenuated inversion recovery, gradient echo, and MRA. In most cases, the alteplase was started when the patient was undergoing an MRI scan. If the MRI was not available immediately, we performed a computed tomography (CT) scan and started the alteplase afterward. Even in such cases, MRI was usually performed within 50 minutes from the hospital arrival. After the alteplase treatment, patients with proximal large-vessel occlusion proceeded to additional endovascular treatment according to the decision of the vascular neurologists. All patients were admitted to the stroke unit for neurological monitoring. On hospital day 2, a follow-up CT scan was performed to check for any intracerebral bleeding. For those who had large-vessel occlusion on the initial MRI, CT angiography was performed to assess the recanalization status.

Imaging Variables

The DWI lesion volume was measured in a semiautomatic manner. Using the picture archiving and communicating system, all areas of abnormal hyperintense signal on each section were calculated by drawing the border of the lesion manually in each slice of the DWI. Then, the volume was calculated as the sum of the hyperintense area in each slice multiplied by the slice thickness and interslice gap. Large-vessel occlusion was defined by the presence of occlusion in the internal carotid artery, in M1, in M2, and in the anterior cerebral artery. Recanalization of the large vessel was assessed in 2 ways. For those who underwent endovascular treatment, achievement of modified treatment in cerebral infarction grade 2b–3 recanalization was defined as recanalization. For patients in whom endovascular treatment was not performed, the recanalization was defined as the recanalization of the primary arterial occlusive lesion score of II or III on the follow-up CT angiography performed on hospital day 2.[19] Symptomatic ICH was defined according to the National Institute of Neurological Disorders and Stroke definition.[1]

The Impact of Early DWI Lesion Volume on Stroke Outcome

To investigate the impact of early DWI lesion volume on stroke outcome, we excluded the recanalization failure cases and evaluated the association between the DWI lesion volume and the 3-month mRS score in patients who achieved early recanalization, that is, patients who achieved recanalization or who did not have large-vessel occlusion on initial MRA. Participants were assigned to the 2 groups according to the dichotomized 3-month functional outcome (mRS score 0-2 as favorable outcome and mRS