M1 Susceptibility Vessel Sign on T2* as a Strong Predictor for No Early Recanalization After IV-t-PA in Acute Ischemic Stroke

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Background and Purpose—In acute stroke patients treated with intravenous tissue plasminogen activator (t-PA), early recanalization of occluded arteries can improve the clinical outcome. The magnetic susceptibility effect of deoxygenated hemoglobin in red thrombi can present as hypointense signals on T2*-weighted gradient echo imaging. We investigated whether the gradient echo imaging M1 susceptibility vessel sign (M1 SVS) can predict no early recanalization after t-PA infusion.

Methods—Patients with internal carotid artery and M1 occlusion were prospectively studied. MRI studies, including DWI, T2*, and MRA, were performed before and within 30 minutes and 24 hours after t-PA infusion. The NIHSS score was obtained before and 7 days after t-PA administration. The relationship between the presence of the M1 SVS and no early recanalization and patient outcome was examined.

Results—A total of 48 patients (29 men; mean age, 74.6 ± 11.2 years) were enrolled. M1 SVS was present in 13 (27.1%) patients and absent in 35 (72.9%) patients. There were no significant differences in clinical characteristics between the 2 groups. Follow-up MRA within 30 minutes after t-PA infusion revealed that 20 (57.1%) of the 35 patients without the M1 SVS had early recanalization, but that none of the 13 patients with the M1 SVS had early recanalization (P = 0.0002). Seven days after t-PA infusion, dramatic improvement was more frequently observed in patients without the M1 SVS (51.4%) than in those with the M1 SVS (0%, P = 0.0007).

Conclusion—The M1 SVS on T2* appears to be a strong predictor for no early recanalization after t-PA therapy. (Stroke. 2009;40:3130-3132.)

Key Words: T2* recanalization • tissue plasminogen activator • outcome

Intravenous administration of tissue plasminogen activator (IV-t-PA) can improve clinical outcomes in patients with acute ischemic stroke.¹ Early arterial recanalization has been recognized as a marker of good outcome after t-PA infusion.²⁻⁴ However, about one-third of acute stroke patients treated with t-PA do not undergo recanalization.⁵

The magnetic susceptibility effect of deoxygenated hemoglobin in red thrombi may result in hypointense signals on T2*-weighted gradient echo imaging (GRE). Cho et al⁶ reported that red thrombi in occluded vessels were visualized as hypointense signals within vascular cisterns on T2*. They called such radiological findings the “GRE susceptibility vessel sign (GRE SVS).” The GRE SVS may reflect thrombus composition. Hemoglobin desaturation from oxyhemoglobin to deoxyhemoglobin occurs within a few hours. Thus, in hyperacute clot cases, the main component may still be oxyhemoglobin, and such emboli would not be identified as GRE SVS on T2*. In other words, the GRE SVS is present in older thrombi, which may be resistant to t-PA therapy.

We investigated whether acute stroke patients with the GRE SVS at the M1 portion of the middle cerebral artery (MCA), which we termed M1 SVS, had early recanalization after IV-t-PA, using serial magnetic resonance angiography (MRA) studies both before and immediately after t-PA administration. We also investigated the relationship between the M1 SVS and patient outcome.

Subjects and Methods

Consecutive patients with acute ischemic stroke treated with t-PA within 3 hours of stroke onset between October 2006 and October 2008 were studied prospectively. Of them, the patients with internal carotid artery (ICA) occlusion and proximal M1 occlusion on MRA before t-PA infusion were enrolled into the present study. Inclusion and exclusion criteria for intravenous t-PA were used in accordance with the Japan Alteplase Clinical Trial.⁷

Before t-PA infusion, all patients underwent MRI studies, including diffusion-weighted imaging (DWI), T2*, and MRA, to identify the occluded arteries. Next, follow-up MRA was performed within 30 minutes and 24 hours after the end of t-PA administration to identify the presence or absence of recanalization in the occluded...
arteries. The M1 SVS was defined as a hypointense signal of the horizontal of the MCA on T2* within a vascular cistern in corresponding symptomatic occlusive vessels. MRI was performed using a commercially available echo planar instrument operating on a 1.5-T unit (Signa EXCITE XL ver. 11.0; GE Healthcare).

Recanalization was graded as complete, partial, or no recanalization, as follows: (1) complete recanalization, reappearance of entire occluded artery and distal branch of vessels; (2) partial recanalization, restoration of part of the distal vessel supplied by an occluded artery; and (3) no recanalization, persistent occlusion. We used 3 measures of clinical recovery based on modifications of methods used in previous studies. “Dramatic improvement” was defined as a reduction of ≥10 in the total NIHSS score or complete recovery. “Good improvement” was defined as a reduction in the total NIHSS score of ≥4. “Worsening” was defined as an increase in the total NIHSS score of ≥4 or death.

Statistical analysis was performed using StatView version 5 statistical software to establish associations among no recanalization, clinical recovery, and clinical factors. Significance of intergroup differences was assessed using Fisher exact test for categorical variables and the Mann–Whitney U test and Kruskal–Wallis U test for continuous variables. Values of P<0.05 were considered statistically significant.

## Results

A total of 94 consecutive stroke patients were treated with t-PA. One patient was excluded because he had a pacemaker. Initial MRA demonstrated ICA occlusion in 22 patients and M1 occlusion in 26 patients. Thus, 48 patients (29 men, 19 women; mean age, 74.6±11.2 years) were enrolled into the present study.

The M1 SVS was present in 13 (27.1%) patients and absent in 35 (72.9%) patients. The Figure shows a patient with the M1 SVS. Table 1 shows the 2 groups’ clinical characteristics. There were no significant differences in the clinical characteristics between the 2 groups.

Follow-up MRA within 30 minutes after t-PA infusion revealed recanalization in 20 patients (complete in 14 patients, partial in 6) and no recanalization in 28. Interestingly, all 13 patients with the M1 SVS had no recanalization (Table 2). However, 20 (57.1%) of the 35 patients without the M1 SVS had recanalization (P=0.0002). One patient with the M1 SVS did not have follow-up MRA 24 hours after t-PA infusion because of severe stroke. Of the remaining 12 patients with the M1 SVS, complete recanalization 24 hours after t-PA infusion was not observed in any patient, but partial recanalization was seen in 7 patients (58.3%). Of the 35 patients without the M1 SVS, 26 (72.9%) had recanalization (partial in 12 patients and complete in 14 patients; P=0.4653).

Table 2 shows the neurological recovery of patients with and without the M1 SVS on T2*. At 24 hours after t-PA infusion, dramatic improvement was more frequently observed in patients without the M1 SVS (34.2%) than in patients with the M1 SVS (0%; P=0.021). At 7 days after t-PA infusion, dramatic improvement was more frequently observed in patients without the M1 SVS (51.4%) than in patients with the M1 SVS (0%; P=0.0007). However, worsening was more frequently observed in patients with the M1 SVS (46.2%) than in patients without the M1 SVS (14.3%; P=0.0475).

## Discussion

The present study demonstrated that no patient with the M1 SVS had early recanalization after t-PA therapy, and that such patients had poor outcomes. Thus, the M1 SVS on T2* appears to be a strong predictor for no early recanalization after t-PA therapy.
Table 2. Neurological Recovery of Patients With and Without M1 SVS on T2*

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<tr>
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<th>M1 SVS on T2*</th>
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<tr>
<td></td>
<td>With n=13</td>
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<td></td>
<td>P</td>
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<tr>
<td>Recanalization after t-PA infusion</td>
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<tr>
<td>Within 1 hour</td>
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<td>Partial</td>
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<td>Complete</td>
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<td>24 hours</td>
<td>7/12 (58.3%)</td>
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<tr>
<td>Partial</td>
<td>7/12</td>
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<tr>
<td>Complete</td>
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<td>24 hours after t-PA infusion</td>
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<tr>
<td>Dramatic recovery</td>
<td>0</td>
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<td>Good improvement</td>
<td>2 (15.4%)</td>
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<tr>
<td>Worsening</td>
<td>2 (15.4%)</td>
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<tr>
<td>7 days after t-PA infusion</td>
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<tr>
<td>Dramatic recovery</td>
<td>0</td>
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<tr>
<td>Good improvement</td>
<td>3 (23.1%)</td>
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<tr>
<td>Worsening</td>
<td>6 (46.2%)</td>
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Clot dissolution depends on clot size, the site of occlusion, clot composition, surface area of the clot exposed to blood flow, and penetration of t-PA into the clot structure.\(^8\) Old and large thrombi may be more resistant to thrombolysis than fresh and small thrombi. Blood goes though sequential stages of degradation from oxyhemoglobin to deoxyhemoglobin, methemoglobin, and then hemosiderin. Deoxyhemoglobin, methemoglobin, and hemosiderin can be detected as signal loss on T2*.\(^9\) If the main component of hyperacute clots is oxyhemoglobin, T2* cannot demonstrate them as hypointense (the M1 SVS) on T2*. Patients without the M1 SVS had more fresh clots than those with the M1 SVS. Furthermore, the M1 SVS may be a sign of a more extensive thrombus. In fact, 8 of 13 patients with the M1 SVS had ICA occlusion. Therefore, t-PA therapy may be effective in patients without the M1 SVS compared with those with the M1 SVS.

Cho et al\(^{10}\) reported that the GRE SVS might predict cardioembolic stroke. In the present study, 11 of 13 patients with the GRE SVS had cardioembolic stroke, which was compatible with Cho’s results. Schellinger et al\(^{10}\) reported that the GRE SVS did not predict the therapeutic effect of IV-t-PA therapy. They studied ICA (n=9), M1 (n=13), P1 (n=5), A1 (n=1), and branch (n=16) occlusion. However, we assessed the presence of the M1 SVS at the proximal M1 and ICA occlusion and excluded P1, A1, and branch occlusion from our study. They did not assess the recanalization rate in patients with the SVS of each artery, and the early recanalization rate in patients with the SVS of M1 and ICA occlusion was not mentioned. We believe that some of their patients with the SVS of P1, A1, and branch occlusion had early recanalization because the embolus size in such patients was small compared with ICA and M1 occlusion. This may have resulted in the apparent discrepancy between Schellinger’s and our results.

The present study had several limitations. Our MRI parameters for DWI and T2* were a slice thickness of 5 mm and an interslice gap of 2 mm. An MRI protocol with a gap of 2 mm might be not the ideal protocol for the detection of vessel signs if the vessel was 2 to 3 mm thick. Secondly, the use of MRA is somewhat inaccurate for detecting vessel occlusion or stenosis.\(^{11}\) Third, MRI cannot be performed in patients in whom metallic materials, such as pacemakers and metal clips, have been implanted. One such patient was excluded from our study. Finally, the rates of recanalization may have been lower because the dose of t-PA (0.6 mg/kg)\(^7\) is lower in Japan than the internationally approved dosage of 0.9 mg/kg.

In conclusion, M1 SVS on T2* appears to be a strong predictor for no early recanalization after t-PA therapy.

Disclosures

None.

References

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