

Tenecteplase Averting Mechanical Thrombectomy in Emergent Large Vessel Occlusion

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Introduction: Tenecteplase has recently been studied as an alternative thrombolytic agent in acute stroke, with a possible superior effect in achieving reperfusion of large intracranial vessels.

Case Report: A 90-year-old female patient was admitted to our stroke unit because of acute onset of dysarthria, left-sided neglect, and hemiparesis. Brain computed tomography (CT) coupled with CT angiography and CT perfusion (postprocessed with the use of RAPID software) demonstrated right proximal middle cerebral artery occlusion with a large penumbra/small ischemic core pattern. The patient was subsequently treated with bolus tenecteplase infusion (0.25 mg/kg). Mechanical thrombectomy was abandoned because the patient has rapidly improved. The patient was discharged to her own home 4 days later with no neurological deficit and functionally independent (modified Rankin scale of 0).

Conclusion: This case exemplifies the potential of tenecteplase in achieving swift reperfusion in patients with large vessel occlusion associated with a substantial mismatch penumbral pattern.

Key Words: tenecteplase, reperfusion, acute stroke

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Intravenous thrombolysis with alteplase in acute ischemic stroke (AIS) patients eligible for mechanical thrombectomy remains the only systemic reperfusion therapy approved by the current international recommendations. However, its ability to achieve recanalization in patients with large vessel occlusion (LVO) is relatively low.¹ Tenecteplase is a genetically modified variant of alteplase, which presents some important pharmacological advantages:² greater fibrin specificity resulting in no fibrinogen depletion and lower incidence of systemic hemorrhage, increased resistance to plasminogen activator inhibitor-1, and longer serum half-life (up to 20 min) permitting bolus administration. It has been the standard of care for ST-segment elevation myocardial infarction since many years. In a recently published randomized trial (EXTEND-IA TNK),³

tenecteplase compared with alteplase (22% vs. 10%) exhibited superiority in achieving complete reperfusion in patients with acute LVO [especially those with middle cerebral artery (MCA) occlusion] scheduled to undergo mechanical thrombectomy. Moreover, the higher reperfusion rates with tenecteplase translated into better functional outcomes, quantified by modified Rankin Scale scores at 3 months.

CASE REPORT

A 90-year-old woman with a history of arterial hypertension was admitted to our emergency department because of acute onset of dysarthria, left-sided neglect, and hemiparesis (National Institutes of Health Stroke Scale score, 9). Brain computed tomography (CT) coupled with CT angiography and CT perfusion (postprocessed with the use of RAPID software) demonstrated right proximal MCA occlusion with a large penumbra of 76 mL, a small ischemic core of 5 mL, and a high mismatch ratio of 16.2 (Fig. 1A, B). Her blood pressure was initially 140/66 mm Hg, her blood glucose was 107 mg/dL, and the ECG revealed a previously unknown atrial fibrillation. The patient was subsequently treated with 11.75 mg bolus tenecteplase (dose, 0.25 mg/kg—off label administration after obtaining informed consent from the patient proxies). The time frame from the onset of symptoms to thrombolysis was 1 hour and 45 minutes. Twenty-five minutes after tenecteplase bolus infusion, the patient was transferred to the angi-suite. Before groin puncture, the patient was re-evaluated by a stroke neurologist that documented substantial clinical improvement (National Institutes of Health Stroke Scale score 2 points, because of persistent mild dysarthria and facial paresis). After discussion with the neuro-interventionalist, we decided not to proceed with the angiography. We also performed a transcranial Doppler evaluation that showed R-MCA recanalization consistent with the patient's significant clinical improvement. Repeat neuroimaging (Fig. 1C, D) with brain magnetic resonance imaging (MRI)/MR angiography and MR perfusion showed small but not quantifiable areas of increased hyperintensity (diffusion-weighted imaging sequences), no hypoperfusion areas, and complete MCA recanalization. There was also no evidence of hemorrhagic transformation on SWI sequences. After 4 days, the patient was discharged to her own home with no neurological deficit and functionally independent (modified Rankin scale of 0).

DISCUSSION

Tenecteplase has recently been studied as an alternative thrombolytic agent for AIS. Five randomized controlled studies and 5 observational studies have been conducted since 2005.⁴ They used various different tenecteplase doses as well as various approaches to imaging selection criteria and reported different results. Pooled individual patient data meta-analysis of the 2 studies which used multimodal neuroimaging during the acute phase,^{5,6} showed improved recanalization and better clinical outcomes in patients with LVO,⁷ and target mismatch on CT perfusion⁸ who were treated with tenecteplase at a dose of 0.25 mg/kg as opposed to alteplase standard treatment. Furthermore, a recently published network

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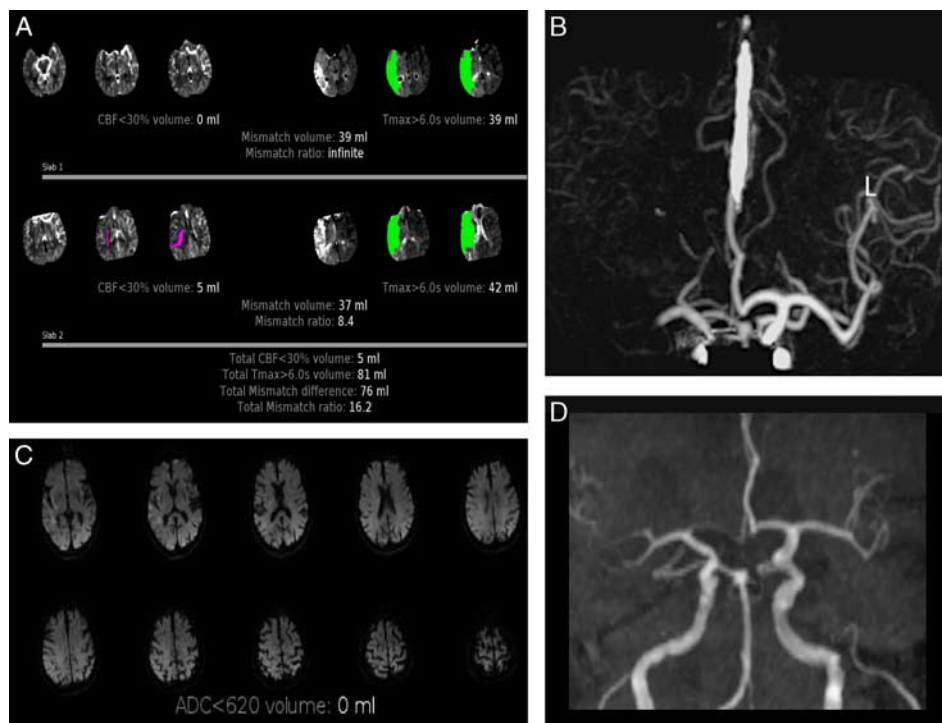


FIGURE 1. Baseline and follow-up neuroimaging. CT perfusion mismatch map (A) with RAPID software demonstrating a small region (5 mL) of severe cerebral blood flow reduction (infarct core is shown in pink) and a substantial penumbra region of 81 mL (shown in green) resulting in a 76 mL mismatch difference (mismatch ratio, 16.2). CT angiography (B) documenting right proximal MCA occlusion. Repeat neuroimaging following tenecteplase bolus: brain MRI (axial diffusion-weighted imaging sequences) demonstrating small areas of increased signal in the posterior MCA territory (C). MR perfusion with RAPID software was unable to identify any area of restricted diffusion (infarct core, 0 mL) using the $620 \times 10^6 \text{ mm}^2/\text{s}$ threshold. Time-of-flight angiography (D) showing complete right MCA recanalization. ADC indicates apparent diffusion coefficient; CBF, cerebral blood flow; CT, computed tomography; MCA, middle cerebral artery; MRI, magnetic resonance imaging.

meta-analysis of 5 randomized controlled trials demonstrated a potentially superior effect of tenecteplase compared with alteplase in achieving both recanalization and early neurological improvement without significant differences regarding safety profiles.⁹ Ongoing trials will further address the questions of optimal tenecteplase dose (0.25 vs. 0.4 mg/kg) and the subgroup of patients with AIS (LVOs) that may potentially benefit additionally from tenecteplase reperfusion therapy compared with the current standard of care (alteplase). Interestingly, the recently published guidelines of the European Stroke Organisation (ESO)/European Society for Minimally Invasive Neurological Therapy (ESMINT) on mechanical thrombectomy in AIS suggested the use of tenecteplase in patients with confirmed LVO (on the basis of expert opinion).¹⁰ Following the publication of EXTEND-IA TNK trial, we have revised our institutional protocol regarding systemic thrombolytic treatment in patients with AIS presenting with a LVO in the time frame of 4.5 hours. On the basis of EXTEND-IA TNK results, we now prefer treating the patients with 0.25 mg/kg tenecteplase (instead of 0.9 mg/kg alteplase) before proceeding to the angi suite for mechanical thrombectomy.

The present case adds to the existing literature¹¹ by exemplifying the potential of tenecteplase in achieving swift reperfusion and averting mechanical thrombectomy in patients with LVO associated with a substantial mismatch penumbral pattern. Even in the era of endovascular therapies, a more potent systemic thrombolytic therapy may offer earlier

recanalization, prevent from potential interventional complications (especially in older patients), and even facilitate mechanical thrombectomy by reducing the number of passes required to achieve reperfusion.

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