Evaluating outcomes of extended thrombolytic therapy for ischemic stroke

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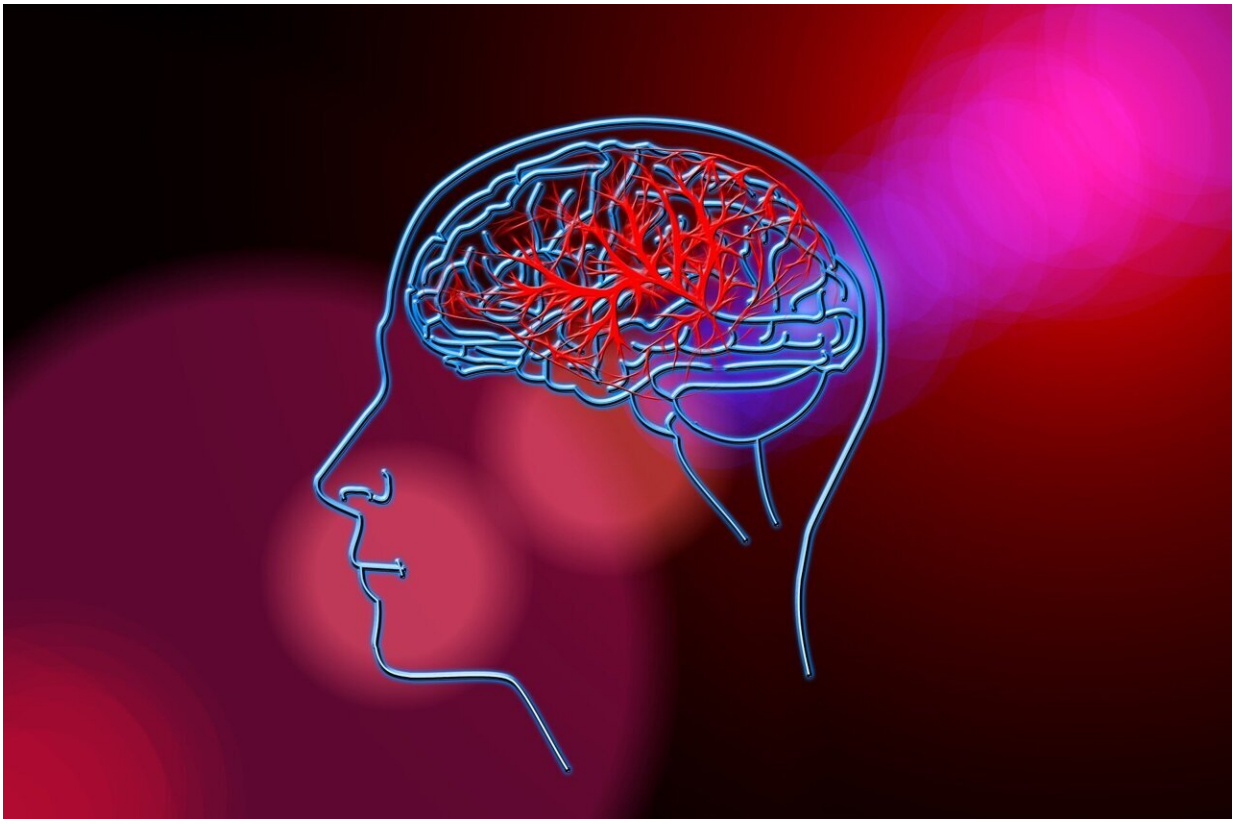

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Thrombolytic therapy administered longer after the onset of ischemic stroke than current recommendations did not demonstrate improved clinical outcomes as compared to placebo, according to a recent trial

published in the *New England Journal of Medicine*.

Minjee Kim, MD, associate professor in the Ken and Ruth Davee Department of Neurology's Division of Neurocritical Care, was a co-author of the study.

Ischemic stroke occurs when a blood vessel supplying blood to the brain is blocked or reduced, and accounts for nearly 90% of all strokes, according to statistics from the American Stroke Association.

Thrombolytic therapy is generally considered the standard of care for eligible patients within 4.5 hours after the onset of acute ischemic stroke . Thrombolytic agents, such as alteplase and tenecteplase, break down blood clots and restore blood flow to the brain. However, efforts to extend this treatment time frame have remained limited due to patients having an increased risk of bleeding in the brain or intracranial hemorrhage.

In the current clinical trial, investigators aimed to test whether intravenous tenecteplase administered in a longer time frame, 4.5 to 24 hours after stroke onset, may benefit patients who had a large-vessel occlusion of the internal carotid artery or middle cerebral artery and who had evidence of salvageable brain tissue as determined by perfusion imaging.

A total of 458 patients were enrolled across 112 medical institutions in the U.S. and Canada, including Northwestern Memorial Hospital. Of the patients, 228 were randomized to receive tenecteplase and 230 to receive placebo. Additionally, more than 75% of the patients underwent mechanical thrombectomy, the current standard of care, after receiving either tenecteplase or placebo.

The primary outcome was neurological disability at day 90, measured by

the modified Rankin Scale (mRS). Safety outcomes included death and symptomatic intracranial hemorrhage.

Overall, the investigators did not observe a significant difference in the distribution of neurological disability at 90 days between the two patient groups. The rate of intracranial hemorrhage was similar in the two groups—3.2% in the tenecteplase group versus 2.3% in the placebo group—as well as 90-day mortality—19.7% versus 18.2%, respectively.

"Overall, the null finding of the study was somewhat disappointing," Kim said. "A possible contribution to this result may be that most patients received the study drug after they were transferred to a comprehensive stroke center, not at the hospital where they initially presented with stroke symptoms. Although we do not know what would have happened if they received the study drug earlier, this speaks to the challenges of emulating real-life scenarios in clinical trials."

On the other hand, Kim said the trial results did demonstrate that tenecteplase given during an extended (4.5 to 24 hours) time window appeared safe without increased mortality or severe bleeding in the brain and that mechanical thrombectomy, the current standard of care, is effective for patients.

"Overall, this clinical trial was executed well, with substantial contributions to the field. I want to thank everyone on the Northwestern team, including clinicians, staff, and research personnel working together across disciplines of Vascular Neurology, Emergency Medicine, Interventional Neuroradiology, Neurosurgery, and Neurocritical Care. We successfully randomized 29 patients at Northwestern, which placed Northwestern as one of the top five highest-enrolling sites out of 112 centers," Kim said.

More information: Gregory W. Albers et al, Tenecteplase for Stroke

at 4.5 to 24 Hours with Perfusion-Imaging Selection, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2310392