In the April issue of *Stroke*, we have yet another study on the safety of tissue-type plasminogen activator (tPA) for patients with stroke mimics (SM). Zinkstok et al. conducted a multicenter retrospective analysis of patients with SM treated with tPA at primary and community hospitals. With 100 patients reported in the largest series to date, the authors found, like all the previous cohort studies, a low rate of symptomatic intracerebral hemorrhage and death.2,3 There were no instances of orolingual edema or fatal intracerebral hemorrhages.

The incidence of SM in their cohort among all tPA-treated patients was on the lower end of other reports: 2% to 31%.2,6-6 This rate is also much lower than the 7% misdiagnosis rate reported for emergency departments in which tPA was administered without a stroke team evaluation.7 In fact, some community centers report as high as 25% to 29% of patients with SM.8,9 The variability in incidence from one report to another is likely because of a lack of a standardized definition of SM.4 In this study, the authors used the Hand criteria to define SM as patients in whom clinical details did not suggest a vascular pathogenesis but who had an alternate final diagnosis convincingly explain their symptoms. SM also were diagnosed in cases in which additional diagnostic tests did not assist in determining an alternate diagnosis and the physician was convinced on clinical grounds that the symptoms were not caused by cerebral ischemia.

MRI with diffusion-weighted sequences was not part of their SM definition, which likely explains, in part, the low incidence of SM in this cohort. Neuroimaging before and after treatment in the absence of an alternative diagnosis other than acute cerebral ischemia also could have allowed the authors to distinguish an averted stroke from SM.5 However, as the authors point out, primary and community hospitals often do not have MRI. Therefore, this study does add novel information on the safety of tPA in SM at community hospitals where advanced imaging may not be available to distinguish stroke from other causes of acute neurological deficits. Although brain imaging can help guide the diagnosis of stroke, we agree with the authors that bedside clinical assessment is still essential to help differentiate SM from true stroke. Unfortunately, in this study, it is not clear which clinical assessments the clinicians used to differentiate SM from true stroke.

However, to add to the validity of their findings, SM were more likely to be younger and women than patients with acute ischemic stroke, similar to previous studies.2,3 In addition, the authors also found, as previously reported, that global aphasia with minimal or no paresis was associated with SM. In the report by Scott and Silbergleit,2 global aphasia without hemiparesis was 10-times more frequent in the SM group than in the acute ischemic stroke group. Yet, this clinical feature seems not distinctive enough to assign individual patients to one or the other group.

Overall, this article supports the concept that we proposed in our study5 that even in acute emergency cases in which the diagnosis of stroke is not completely certain, the benefit of rapid treatment with tPA likely outweighs the minimal risk of complications associated with tPA in SM.

At this point, we would encourage an end to reporting further retrospective studies on the safety of tPA for SM. Let us now focus on trying to differentiate with more certainty SM from acute ischemic strokes and tackle the question articulated by Saver and Barsan10 in their editorial—in cases of uncertainty, how can we remain swift in administering tPA but become more sure that we are treating an acute ischemic stroke? Prospective studies are needed to identify and to validate a panel of variables, including clinical features, imaging, and perhaps biomarkers that can confidently and rapidly separate SM from AIS.

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**Disclosures**

None.

**References**


**Key Words:** ischemic stroke ■ mimics ■ rtPA
Tissue-Type Plasminogen Activator for Stroke Mimics: Continuing to Be Swift Rather Than Delaying Treatment to Be Sure
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