# IV tPA for acute ischemic stroke

## Times are changing

Larry B. Goldstein, MD

Correspondence to
Dr. Goldstein:
larry.goldstein@uky.edu

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Based on evidence that the administration of IV tissue plasminogen activator (tPA) improved the outcomes of selected patients with acute ischemic stroke, the US Food and Drug Administration (FDA) approved its use for this purpose in 1996, leading to a revolution in stroke care.[1] Following its introduction into routine clinical practice, stroke began to be viewed as a medical emergency, similar to myocardial infarction, with effective treatment dependent or early symptom recognition and patient transport to facilities capable of conducting rapid evaluations and IV tPA administration. There were, however, considerable barriers that slowed adoption; even 8 years after FDA approval, IV tPA was being given to only about 1%–2% of stroke patients.[2]

What was anticipated to be a revolutionary change became evolutionary. Transformation of the structure and organization of stroke care delivery were needed, and in part led to recommendations for the development of primary stroke centers and stroke care systems, each having benefits beyond the administration of IV tPA.[3,4] For example, patients with intracerebral or subarachnoid hemorrhage cared for at primary stroke center–certified hospitals had lower risk-adjusted mortality rates compared to those at treated noncertified hospitals.[5] Additional innovations include the use of telemedicine to support management decisions at hospitals without stroke care expertise and the advent of mobile stroke units to speed treatment. Although there was no difference in the rate of use of IV tPA in the United States between 2001 and 2004, the rate doubled from 2005 to 2009, with a conservative estimate indicating that 3.4%–5.2% of patients with ischemic stroke were treated at the end of the decade.[6]

In the current issue of *Neurology*®, Domino et al.[7] specifically address changes in the rate of use of IV tPA for acute ischemic stroke in a biethnic community (Mexican Americans and non-Hispanic whites) without an academic medical center. Using active and passive surveillance, they found that similar to the nation as a whole, IV tPA use remained at 2% from 2000 to 2006, but then increased to 11% by 2012. Limitations in the data preclude analysis of the specific reasons for the improvement, but it was noted that 2 of the 7 participating hospitals were certified by the Joint Commission as Primary Stroke Centers during this period—one in 2009 and the second in 2010. Although thought to contribute to the increase in treatment rates, hospital-specific data were not analyzed. In addition, the certifications followed the beginning of the improvement in IV tPA treatment rates in 2006 by 3–4/year (i.e., the increase in rates preceded certification by several years). Another study found that early primary stroke center–certified hospitals had better outcomes than noncertified hospitals even before the program began.[8] Whether the overall improvement in treatment rates in this community was directly related to changes in the 2 primary stroke center hospitals or other factors is not known. Given the characteristics of the community in which the study was conducted, including the race/ethnic composition of the population, generalization to other areas of the country might be limited. The overall improvement in treatment rates, however, is encouraging and indicates that there can be considerable gains in stroke-related care even in the absence of a locally available academic medical center.

In the Brain Attack Surveillance in Corpus Christi (BASIC) population, the likelihood of receiving IV tPA decreased with increasing age (relative rate 0.77, 95% confidence interval [CI] 0.69 to 0.85 per 10 years).[7] This may have reflected the view that the benefits and risks of thrombolytic treatment are inversely proportional to age. Although older patients have relatively poorer outcomes and higher rates of intracerebral hemorrhage than younger patients, treatment with IV tPA still improves their likelihoods of being independent at 3 months, and is now equally recommended for those over and under age 80 years.[9] The improvement in treatment rates was also less in those with less severe compared to more severe deficits as reflected in baseline NIH Stroke Scale (NIHSS) scores: treatment rates for those at the 25th percentile of NIHSS scores increased from 0.74% in 2000 (95% CI 0.28%–1.98%) to 1.47% in 2012 (95% CI 0.50%–4.26%), compared to 1.88% in 2000 (95% CI 0.85%–4.18%) to 5.92% in 2012 (95% CI 3.25%–10.79%) for those at the 75th percentile.[7] This was likely based on the perception that patients with minor stroke symptoms would not have a meaningful treatment-related functional improvement. It is now

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From the Department of Neurology, Kentucky Neuroscience Institute, University of Kentucky, Lexington.

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recognized, however, that some minor stroke symptoms can be disabling, and that these patients also benefit from thrombolytic treatment. Although data were not available to determine the reasons patients were or were not treated with IV tPA in the BASIC project, treatment rates may further increase as these disparities are addressed.

A second revolution in acute stroke treatment based on clinical trials showing that endovascular clot retrieval improves outcomes of selected patients with large vessel occlusions is upon us.[10] The infrastructure and expertise required to safely and effectively provide this therapy is not trivial. Community hospitals located in regions similar to those involved in the BASIC project will need to develop protocols for the triage, immediate management, and prompt referral of suitable patients to endovascular-capable centers while considering that the chances of benefit decline rapidly with the lag between symptom onset and recanalization. Although the rates of treatment with IV tPA are improving, changing times and new therapeutic options are also adding additional complexity to the organization of stroke care systems.


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## DISCLOSURE

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## REFERENCES


1. Furlan AJ. Thrombolysis for acute ischemic stroke: update on the beginning of a revolution. Cleve Clin J Med 1998; 65:185–190.
2. Marler JR, Goldstein LB. Stroke: tPA and the clinic. Science 2003;301:1677.
3. Schwamm LH, Pancioli A, Acker JE III, et al. Recommendations for the establishment of stroke systems of care: recommendations from the American Stroke Association's Task Force on the Development of Stroke Systems. Circulation 2005;111:1078–1091.
4. Alberts MJ, Hademenos G, Latchaw RE, et al. Recommendations for the establishment of primary stroke centers. JAMA 2000;283:3102–3109.
5. Lichtman JH, Jones SB, Leifheit-Limson EC, Wang Y, Goldstein LB. 30-day mortality and readmission after hemorrhagic stroke among Medicare beneficiaries in Joint Commission Primary Stroke Center-certified and noncertified hospitals. Stroke 2011;42:3387–3391.
6. Adeoye O, Hornung R, Khatri P, Kleindorfer D. Recombinant tissue-type plasminogen activator use for ischemic stroke in the United States: a doubling of treatment rates over the course of 5 years. Stroke 2011;42: 1952–1955.
7. Domino JS, Baek J, Meurer WJ, et al. Emerging temporal trends in tissue plasminogen activator use: results from the BASIC project. Neurology 2016;87:2184–2191.
8. Lichtman JH, Allen NB, Wang Y, Watanabe E, Jones SB, Goldstein LB. Stroke patient outcomes in US hospitals before the start of the Joint Commission Primary Stroke Center certification program. Stroke 2009;40: 3574–3579.
9. Demaerschalk BM, Kleindorfer DO, Adeoye OM, et al. Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2016;47:581–641.
10. The Lancet. The stroke care revolution. Lancet Neurol 2015;14:341.