

Reasons Why Few Patients With Acute Stroke Receive Tissue Plasminogen Activator

Kara Z. Bambauer, PhD; S. Claiborne Johnston, MD, PhD; Derek E. Bambauer, JD; Justin A. Zivin, MD, PhD

Despite the US Food and Drug Administration's approval in 1996, tissue plasminogen activator (tPA) therapy for acute ischemic stroke remains substantially underused. We reviewed 3 potential reasons for low rates of tPA use: poor patient education, physicians' perceived risk of legal liability from negative patient outcomes, and insufficient reimbursement. The recent addition of diagnosis-related grouping code 559 will provide higher payment for stroke patients treated with tPA, creating a natural experiment to examine our third reason.

Arch Neurol. 2006;63:661-664

Stroke is the third most common cause of death in the United States after heart disease and cancer.^{1,2} Tissue plasminogen activator (tPA) was proven useful for acute stroke therapy in 1995³ and was approved by the US Food and Drug Administration in 1996.⁴ It increases recovery from stroke symptoms by up to 50%³ with a low serious complication rate.⁵⁻⁹ However, only 3% to 8.5% of potentially eligible patients receive tPA.¹⁰ Ideally, more than 40% of all stroke patients should receive tPA. We propose 3 major obstacles preventing additional tPA use: poor public awareness of stroke symptoms, physician fear of legal liability, and insufficient funding for necessary facilities and personnel.

Surveys of the US population indicate that stroke is poorly understood.¹¹⁻¹³ People do not know stroke signs or symptoms and do not seek immediate care when they have one.¹⁴ Despite awareness campaigns, lack of public knowledge remains a problem.^{15,16} Compared with other diseases, stroke has received little publicity. Because few people know about stroke risk factors and symptoms, they do not

come into the emergency department quickly and are not offered tPA therapy. Better efforts are needed to educate the public, 911 responders, and emergency personnel about the signs and symptoms of stroke and the need to seek immediate attention at treatment centers that are able to handle acute stroke.

Another obstacle that limits tPA use is the fear of emergency department physicians and some neurologists that serious adverse effects are common.¹¹ While there is a 10-fold increase in intracerebral hemorrhage rate from administering intravenous tPA to patients with ischemic stroke, this is outweighed by the decreased rate of infarction. Tissue plasminogen activator has no net risk for acute stroke therapy. Nevertheless, tPA's hemorrhage potential has received disproportionate attention; for example, an American College of Emergency Physicians position article indicates that tPA is not yet standard care for acute stroke therapy.^{11,17}

Fear among emergency department doctors is problematic because most stroke patients are first treated by emergency medical staff. A survey of emergency department physicians found that 40% would not use tPA. Sixty percent cited risk of intracerebral hemorrhage as the reason for not using tPA, and one quarter of physicians cited the lack of (perceived) benefit,¹⁸ but when emergency medicine trainees were asked what they would prefer if

Author Affiliations: Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care, Boston, Mass (Dr K. Bambauer); Department of Neurology, University of California, San Francisco (Dr Johnston); Berkman Center for Internet & Society, Harvard Law School, Cambridge, Mass (Dr D. Bambauer); Department of Neurology, University of California San Diego, La Jolla (Dr Zivin).

they personally had a stroke, more than 88% said that they would want tPA treatment.¹⁹ While many emergency department physicians feel uncomfortable treating patients with acute stroke, increased hospital reimbursement may make new training programs possible, which will help these physicians feel as confident about treating patients with stroke as they are about treating patients with myocardial infarction.

To investigate whether physicians' fears of legal liability²⁰ are founded, we examined litigation involving stroke thrombolytic therapy. If an adverse response occurs after administering a drug, the patient may assume that the drug was responsible. However, failure to administer tPA may also generate litigation. Since few patients understand stroke symptoms and treatments (let alone risks from failure to treat), physicians may believe fewer lawsuits will follow negative results from failing to provide tPA than from tPA therapy itself.

We hypothesized that physicians may not administer tPA because they fear being sued for medical malpractice if the patient has an adverse event after receiving the drug. To test this idea, we examined cases with claims against physicians over the role of tPA in treating patients with ischemic stroke. We queried the Lexis-Nexis Academic database that covers US state and federal case law. This database is comprehensive and commonly used by practicing attorneys. We searched the full text of each state's recorded cases for the terms *tissue plasminogen activator*, *t-PA*, and *tPA*. To ensure completeness, we repeated these searches for federal district courts, appellate courts, and the US Supreme Court. From these results, we excluded cases that did not involve a final decision, physicians, or use of tPA to treat stroke patients. These measures substantially reduced the number of cases in our analysis. For each case, we analyzed which party won and whether the case involved a claim based on administering tPA or failing to do so.

We identified 7 final decisions involving claims against physicians or other health care providers for stroke treatment involving tPA. All 7 involved claims for failing to administer tPA—the plaintiffs alleged harm from not receiving the drug. Defendants (medical personnel and providers) won 6 cases. One case was won by a plaintiff. All cases were recent, with the earliest being in 2002.

Final decisions by courts in medical malpractice cases are quite rare. From 1985 to 1999, 62.3% of medical malpractice claims ended in dismissal or withdrawal.²¹ Only 6.7% of cases resulted in a verdict, with defendants winning over 80% of these decisions.²¹ Thus, the vast majority of cases settle or terminate before the dispute is adjudicated and final decisions on the merits may not provide a representative sample of plaintiffs' initial claims. Data on settlements are not publicly available; many settlements have provisions mandating confidentiality. Nevertheless, our set (albeit small) of recorded final decisions suggests that physicians may be more likely to be sued for failing to treat a patient with stroke using tPA than for administering the drug inappropriately.

Although poor public awareness and physician fears are important, inadequate funding may be the most important obstacle to better stroke management. Tissue plasminogen activator therapy has both costs and benefits.

Costs include increased risk of intracranial hemorrhage³ and increased staff time and training. Benefits include decreased hospital stay,^{22,23} decreased rehabilitation costs,²² decreased nursing home costs,²² reduced dependency,²⁴ decreased stroke severity,²³ and higher likelihood of healthy survival during the first year after having a stroke.²⁵ Furthermore, tPA is not only a cost-effective therapy but a cost-saving one.²⁶

Tissue plasminogen activator savings accrue during the treated patient's lifetime. Many costs from improperly treated patients with stroke result from rehabilitative and nursing home care owing to stroke-related disability. As time since tPA treatment increases, benefits from rehabilitation services avoided also increase. Cost-saving treatments are relatively infrequent in commonly used health interventions,²⁷ which make tPA even more attractive.

To determine whether hospital expenditures for ischemic stroke vary with tPA use in actual practice, we compared hospital charges for patients treated with and without tPA using 2 large administrative databases. One cohort consisted of 13 078 patients with acute ischemic stroke seen in 1999 at 34 academic medical centers in the University Health Systems Consortium. Methods have been described in detail previously.²⁸ For this analysis, we used generalized estimating equations. Hospital charges reflect the total hospital bill, including charges for medications, nursing, imaging, other evaluation costs, and hotel costs, but not physician charges. Average hospital charges were \$36 188 for 284 patients receiving tPA and \$18 565 for patients who did not receive tPA ($P < .001$). After adjusting for age, race, sex, and payment source, the difference persisted (\$17 796 greater for those receiving tPA, $P < .001$).

Using identical methods, we analyzed discharge abstracts of all patients treated at nonfederal California acute care hospitals for ischemic stroke during 1998 to 2000 ($n = 113\,018$). Average charges were \$42 811 for those treated with tPA and \$25 195 for those who were not treated with tPA ($P < .001$). After adjusting for age, sex, race, and payment source with generalized estimating equations, the difference persisted (\$17 973 greater for those receiving tPA, $P < .001$). Thus, it costs substantially more to care for hospitalized patients with ischemic stroke who received tPA. Patients receiving tPA are typically more impaired neurologically partly because mild, rapidly improving deficits are an excluding factor for tPA and because patients with minor deficits often arrive at the hospital or emergency department later than patients with more severe illness.²⁹ Furthermore, patients who receive tPA may undergo more extensive evaluation.

Despite the substantial expense of administering tPA and caring for hospitalized stroke patients, tPA reimbursement rates have not reflected the time and complexity involved. The American Academy of Neurology recommends that physicians bill using Current Procedural Terminology (CPT) evaluation and management codes (99221-99223 for initial hospital care, 99291-99292 for critical care, and 99356-99357 for prolonged inpatient service).³⁰ Others recommend 99251 to 99255 for initial inpatient consultation.¹¹ Codes for tPA admin-

istration (37195), physician standby services (99360), and phone consultations (99371-99373) are not covered by Medicare and many private insurance companies.¹¹ Two attempts to combine these CPT codes in 2002 to bill for tPA administration calculated reimbursement rates between \$445 and \$460.^{11,20} Similar reimbursement rates exist for reading 4 electroencephalograms, injecting Botox into 1 extremity, and spending 1 hour with a critically ill stroke patient.¹¹

There are several problems with these coding procedures and reimbursement rates. First, multiple providers cannot bill for the same procedures for the same patient on the same day. Therefore, there is no incentive for integrated care teams if multiple providers cannot be reimbursed for administering tPA.²⁰ Second, some carriers will not cover critical care codes on the same day as inpatient evaluation and management codes and will not cover prolonged service codes, which leads to insufficient reimbursement for individual providers.³⁰ Third, the lack of reimbursement for such codes means that there is little incentive for busy neurologists to interrupt other work or personal time to help emergency department physicians administer tPA.²⁰ Inpatient billing demonstrates a similar problem. Diagnosis-related grouping (DRG) codes are required to bill for inpatient services, yet DRG codes have not reflected modern advances in stroke therapy, such as tPA, that are more costly than traditional stroke care. Diagnosis-related grouping code 014, the previous code for stroke care (with or without tPA), is reimbursed at less than \$6000.³¹

In August 2005, the Centers for Medicare and Medicaid Services created DRG code 559 to increase reimbursement for stroke patients treated with tPA. In 2006, the base payment for DRG code 014 (intracranial hemorrhage or cerebral infarction) will be \$6417. For DRG code 559, the base payment is currently \$11 578. Implementing this higher rate of reimbursement for Medicare patients is an important first step in recognizing the additional complexity and expense of administering tPA. We hypothesize that the new DRG's higher reimbursement will increase tPA use for stroke patients. Furthermore, improved reimbursement for treating stroke patients with tPA will create incentives for potentially reluctant neurologists to develop expertise and devote time to treating patients for ischemic stroke with thrombolysis. With higher tPA reimbursement rates under DRG code 559, improved treatment facilities, better-trained neurologists, and broader organizational structures will be possible (though not always achieved).

The 2002 National Institute of Neurological Disorders and Stroke report outlining "Incentives for Enhancing Stroke Care"²⁰ recommends ways to improve financial incentives for using tPA to treat stroke patients. These include (1) allowing simultaneous reimbursement for multiple providers from multiple specialties who contribute on the same day to a patient's stroke treatment; (2) providing Medicare reimbursement for all CPT codes listed above; (3) encouraging private insurance reimbursement of these CPT codes; (4) creating new CPT codes for acute resuscitative and chronic stroke care; and (5) modifying DRG code 014 reimbursement rates to reflect costs of modern stroke treatment. The Centers for

Medicare and Medicaid Services responded to the fifth recommendation by creating DRG code 559 but the increase will not cover the therapy's real costs.

We recommend that reimbursement rates of the CPT code for tPA administration (37195) be increased to incorporate provider (both physician and staff) time and intensity of service for tPA administration. Adjusting stroke-related CPT codes will make tPA treatment more feasible for providers, especially because not all stroke patients are eligible for Medicare, and thus are not affected by changes in DRG payments.

Despite its efficacy and cost-effectiveness, tPA treatment for stroke patients remains underused. Patients' lack of information about the drug's benefits, physicians' fears of legal liability for administering tPA, and insufficient reimbursement are 3 potential reasons for its underuse. We suggest 3 steps to reduce these barriers. First, public education efforts should be increased. Second, physicians should be informed that legal risk may be greater for failing to administer tPA than for using it. Finally, reimbursement mechanisms such as stroke-related CPT and DRG codes should be altered to make providing tPA less financially burdensome for providers. Future research can examine whether increased reimbursement rates under DRG code 559 will improve tPA access for eligible stroke patients.

Accepted for Publication: October 6, 2005.

Correspondence: Justin A. Zivin, MD, PhD, Department of Neurosciences, University of California San Diego, 9500 Gilman Dr, La Jolla, CA 92093 (jzivin@ucsd.edu).

Author Contributions: *Study concept and design:* K. Bambauer, Johnston, D. Bambauer, and Zivin. *Acquisition of data:* Johnston and D. Bambauer. *Analysis and interpretation of data:* K. Bambauer, Johnston, and D. Bambauer. *Drafting of the manuscript:* K. Bambauer, Johnston, D. Bambauer, and Zivin. *Critical revision of the manuscript for important intellectual content:* K. Bambauer, Johnston, D. Bambauer, and Zivin. *Statistical analysis:* Johnston. *Administrative, technical, and material support:* K. Bambauer and D. Bambauer. *Study supervision:* K. Bambauer, Johnston, D. Bambauer, and Zivin.

Funding/Support: Dr Bambauer has support from a pharmaceutical policy fellowship and the Thomas O. Pyle Fellowship through Harvard Pilgrim Health Care Foundation.

REFERENCES

1. American Stroke Association. What is stroke? Available at: <http://www.strokeassociation.org/presenter.jhtml?identifier=3030066>. Accessed March 13, 2006.
2. World Health Organization. Death from stroke. Available at: http://www.who.int/cardiovascular_diseases/en/cvd_atlas_16_death_from_stroke.pdf. Accessed December 8, 2004.
3. Tissue plasminogen activator for acute ischemic stroke: the National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. *N Engl J Med*. 1995; 333:1581-1587.
4. A systems approach to immediate evaluation and management of hyperacute stroke: experience at eight centers and implications for community practice and patient care. The National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study Group. *Stroke*. 1997;28:1530-1540.
5. Schmulling S, Grond M, Rudolf J, Heiss WD. One-year follow-up in acute stroke patients treated with rtPA in clinical routine. *Stroke*. 2000;31:1552-1554.
6. Tanne D, Bates VE, Verro P, et al. Initial clinical experience with IV tissue plas-

- minogen activator for acute ischemic stroke: a multicenter survey. The t-PA Stroke Survey Group. *Neurology*. 1999;53:424-427.
7. Buchan AM, Barber PA, Newcommon N, et al. Effectiveness of t-PA in acute ischemic stroke: outcome relates to appropriateness. *Neurology*. 2000;54:679-684.
 8. Albers GW, Bates VE, Clark WM, Bell R, Verro P, Hamilton SA. Intravenous tissue-type plasminogen activator for treatment of acute stroke: the Standard Treatment with Alteplase to Reverse Stroke (STARS) Study. *JAMA*. 2000;283:1145-1150.
 9. Wang DZ, Rose JA, Honings DS, Garwacki DJ, Milbrandt JC. Treating acute stroke patients with intravenous tPA: the OSF stroke network experience. *Stroke*. 2000;31:77-81.
 10. Arora S, Broderick JP, Frankel M, et al. Acute stroke care in the US: results from 4 pilot prototypes of the Paul Coverdell National Acute Stroke Registry. *Stroke*. 2005;36:1232-1240.
 11. Kleindorfer D, Kissela B, Schneider A, et al. Eligibility for recombinant tissue plasminogen activator in acute ischemic stroke: a population-based study. *Stroke*. 2004;35:e27-e29.
 12. Fontanarosa PB, Winker MA. Timely and appropriate treatment of acute stroke: what's missing from this picture? *JAMA*. 1998;279:1307-1309.
 13. Kothari R, Sauerbeck L, Jauch E, et al. Patients' awareness of stroke signs, symptoms, and risk factors. *Stroke*. 1997;28:1871-1875.
 14. Williams LS, Bruno A, Rouch D, Marriott DJ. Stroke patients' knowledge of stroke: influence on time to presentation. *Stroke*. 1997;28:912-915.
 15. Schneider AT, Pancioli AM, Khoury JC, et al. Trends in community knowledge of the warning signs and risk factors for stroke. *JAMA*. 2003;289:343-346.
 16. Johnston SC, Fayad PB, Gorelick PB, et al. Prevalence and knowledge of transient ischemic attack among US adults. *Neurology*. 2003;60:1429-1434.
 17. American College of Emergency Physicians. Use of intravenous tPA for the management of acute stroke in the emergency department. Available at: <http://www.acep.org/webportal/PracticeResources/issues/clin/UseIntravenousTPAManagementAcuteStrokeED.htm>. Accessed March 13, 2006.
 18. Brown DL, Barsan WG, Lisabeth LD, Gallery ME, Morgenstern LB. Survey of emergency physicians about recombinant tissue plasminogen activator for acute ischemic stroke. *Ann Emerg Med*. 2005;46:56-60.
 19. Kunnel B, Heller M. Thrombolytics and stroke: what do emergency medicine residents perceive? *Acad Emerg Med*. 1999;6:1174-1176.
 20. Schneider SM, Goldstein LB, Adams JG, et al. Incentives for enhancing stroke care. National Institute of Neurological Disorders and Stroke, National Institutes of Health Web site. Available at: http://www.ninds.nih.gov/news_and_events/proceedings/stroke_2002/acute_stroke_incentives.htm. Accessed December 12-13, 2002.
 21. Nathanson MJ. It's the economy (and combined ratio), stupid: examining the medical malpractice litigation crisis myth and the factors critical to reform. *Pennsylvania State Law Review*. 2004;108:1077-1122.
 22. Fagan SC, Morgenstern LB, Petitta A, et al. Cost-effectiveness of tissue plasminogen activator for acute ischemic stroke: NINDS rt-PA Stroke Study Group. *Neurology*. 1998;50:883-890.
 23. Jorgensen HS, Nakayama H, Raaschou HO, Olsen TS. Acute stroke: prognosis and a prediction of the effect of medical treatment on outcome and health care utilization. The Copenhagen Stroke Study. *Neurology*. 1997;49:1335-1342.
 24. Wardlaw JM, del Zoppo G, Yamaguchi T. Thrombolysis for acute ischaemic stroke. *Cochrane Database Syst Rev*. 2000;2:CD000213.
 25. Sandercock P, Berge E, Dennis M, et al. Cost-effectiveness of thrombolysis with recombinant tissue plasminogen activator for acute ischemic stroke assessed by a model based on UK NHS costs. *Stroke*. 2004;35:1490-1497.
 26. Chambers MG, Koch P, Hutton J. Development of a decision-analytic model of stroke care in the United States and Europe. *Value Health*. 2002;5:82-97.
 27. Stone PW, Teutsch S, Chapman RH, Bell C, Goldie SJ, Neumann PJ. Cost-utility analyses of clinical preventive services: published ratios, 1976-1997. *Am J Prev Med*. 2000;19:15-23.
 28. Johnston SC, Fung LH, Gillum LA, et al. Utilization of intravenous tissue-type plasminogen activator for ischemic stroke at academic medical centers: the influence of ethnicity. *Stroke*. 2001;32:1061-1068.
 29. Barber PA, Zhang J, Demchuk AM, Hill MD, Buchan AM. Why are stroke patients excluded from TPA therapy? an analysis of patient eligibility. *Neurology*. 2001;56:1015-1020.
 30. American Academy of Neurology. Coding for t-PA infusion-related physician work. Available at: http://www.aan.com/professionals/coding/archives/0602_cod_tpa.cfm. Accessed November 21, 2004.
 31. Kleindorfer D, Hill MD, Woo D, et al. A description of Canadian and United States physician reimbursement for thrombolytic therapy administration in acute ischemic stroke. *Stroke*. 2005;36:682-687.