# A Case-Control Study of the Effectiveness of Tissue Plasminogen Activator on 6 Month Patients—Reported Outcomes and Health Care Utilization

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We examined the benefit of tissue plasminogen activator (tPA), delivered as part of usual stroke management, on patient-reported outcomes and health care utilization. Using a case control design, patients who received tPA as part of usual stroke management were compared with patients who would have received tPA had they arrived to the hospital within the therapeutic time window. Data were collected from surveys 6 months after stroke using standardized patient-reported outcome measures and questions about health care utilization. Demographic and medical data were acquired from hospital records. Patients were matched on stroke severity, age, race, and gender. Matching was done with 1:2 ratio of tPA to controls. Results were compared between groups with 1-tailed tests because of a directionally specific hypothesis in favor of the tPA group. The tPA (n = 78) and control (n = 156) groups were matched across variables, except for stroke severity, which was better in the control group; subsequent analyses controlled for this mismatch. The tPA group reported better physical function, communication, cognitive ability, depressive symptomatology, and quality of life/participation compared with the control group. Fewer people in the tPA group reported skilled nursing facility stays, emergency department visits, and rehospitalizations after their stroke compared with controls. Reports of other postacute services were not different between groups. Although it is known that tPA reduces disability, this is the first study to demonstrate the effectiveness of tPA in improving meaningful, patient-reported outcomes. Thus, use of tPA provides a large benefit to the daily lives of people with ischemic stroke. **Keywords:** Stroke—patient-reported outcomes—comparative effectiveness—health care utilization—tissue plasminogen activator—tPA—function.


## Introduction

The definitive National Institute of Neurological Disorders and Stroke (NINDS) rt-PA trial showed that persons who received tissue plasminogen activator (tPA) were 30% less likely to experience disabling symptoms at 90 days after stroke compared with those who had received a placebo.[1] Economic modeling from this same dataset indicated that the increased hospitalization costs associated with tPA are offset by savings from decreased postacute expenditures, including institutionalization.[2] Additional efforts since have refined our understanding of tPA delivery,[3-7] developed national guidelines for use

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of tPA,[8] and implemented national programs to increase and improve tPA use.[9-11]

Efficacy data have come primarily from clinical impairment scales, such as the National Institutes of Health Stroke Scale (NIHSS), and from brief disability scales, such as the modified Rankin scale, at 90 days after stroke. Although these scales are useful for large-scale clinical trials, they fail to capture many outcomes that are meaningful to stroke survivors.[12] Collection of outcome data at 90 days after stroke may be somewhat early because people have just completed postacute rehabilitation services and have yet to fully return to daily life.[12] Effectiveness data, indicating benefits of tPA as part of routine clinical care, have also been collected at 90 days after stroke and have used the same brief scales.[13-16] Thus, there are minimal data to confirm the effectiveness of routine use of tPA on patient-centered outcomes beyond 90 days after stroke. Given the resources invested at multiple levels across health care systems for implementing tPA protocols, it is necessary to understand its effectiveness with respect to the daily lives of stroke survivors.

The purpose of this study was to examine the real-world benefit of tPA, delivered as part of usual stroke management, on patient-reported outcomes and health care utilization. This was a pragmatic comparative effectiveness study conducted at a large, academic medical center. Given the abundance of efficacy data, we hypothesized that, at 6 months after stroke, persons who received tPA would report better function across multiple domains (physical function, cognition, communication), greater return to prestroke activities, and lower postacute health care utilization compared with people who did not receive tPA.

## Methods

This study was a retrospective case control analysis of prospectively collected data comparing outcomes in patients who received tPA as part of usual care with patients who would have received tPA had they arrived to the hospital within the therapeutic time window, that is, criteria other than time were met. At present, all persons with a diagnosis of stroke or transient ischemic attack from our hospital are contacted for a follow-up survey at 6 (±2 weeks) months after the event. People with stroke provided informed consent to have their data stored and used for research. Washington University Human Research Protection Office approved the database and studies using deidentified data. This sample includes people who received care at our hospital plus others who received tPA at a partner hospital and were transported to our facility for further care.

Data in this report were collected between February 2011 and October 2013. Follow-up surveys were completed via telephone (47% of sample), mail (33%), or e-mail (21%). Surveys could be completed by a patient or a caregiver. If a patient experienced another stroke within the 6-month follow-up period, the survey was completed 6 months from the new stroke. No survey data were collected from deceased individuals or their caregivers. Demographic and medical data regarding the stroke were acquired from hospital records, including NIHSS[17] at time of initial presentation to the emergency department, age, gender, race, marital status, education level, insurance coverage, date of stroke, side of stroke, and premorbid Barthel Index.[18,19]

Patient-reported outcomes were collected using valid, reliable, standardized questionnaires by trained personnel. Assessments administered were: the Stroke Impact Scale, a measure of self-perceived abilities in multiple domains affected by stroke[20-24]; the Patient Health Questionnaire 9-item version, a measure of depressive symptomatology[25,26]; the Reintegration to Normal Living Index, a measure of satisfaction with one's abilities to engage in daily life[27,28]; and the modified Rankin scale, a measure of global disability.[29-31] Modified Rankin scale scores were dichotomized to those with good outcome (scores of 0 or 1) and those with poor outcome (scores of 2 or higher). Additional items in the survey included questions about falls,[32-34] return to driving, and return to work.[35]

Health care utilization information was collected via self-report. This was chosen over extracting data from administrative records because the utilization records of our stroke population from a large geographic area are not contained in 1 or only a few databases, nor did we want to limit our sample to just people covered by Medicare. Procedures to minimize self-report bias (either over- or underreporting) were used as much as possible.[36] Patients reported if they had an inpatient rehabilitation facility stay, a skilled nursing facility stay, used home health services, used outpatient rehabilitation services, the number of physician office visits, visited an emergency department, and/or were readmitted to a hospital after discharge from the initial stroke-induced hospitalization.

tPA was administered according to hospital protocol, largely following the NINDS tPA trial and European Cooperative Acute Stroke Study III trial inclusion/exclusion criteria.[1,3,37] Patients who received tPA and the completed 6-month surveys were matched to patients with completed surveys who did not receive tPA. To be considered a match, the potential control had to satisfy the medical criteria[1,3,37] to receive tPA but arrive at the hospital outside of the therapeutic time window (beyond 4.5 hours). Patients receiving tPA and controls were matched on initial NIHSS score (±2 patients), age (±5 years), race, and gender. Matches were only searched for within ±12 months of date of stroke, in case any changes in hospital policies or programs had influenced care or outcomes. Matching was performed using a 1:2 ratio of tPA to controls. Personnel who collected survey data were separate and independent from personnel who assigned matches, and each was blinded to the activities and data of the others.