Protocol Deviations before and after Treatment with Intravenous Tissue Plasminogen Activator in Community Hospitals

Eric E. Adelman, MD,* Phillip A. Scott, MD,† Lesli E. Skolarus, MD,* Allison K. Fox, MS,† Shirley M. Frederiksen, MS,† and William J. Meurer, MD†

Background: Protocol deviations before and after tissue plasminogen activator (tPA) treatment for ischemic stroke are common. It is unclear if patient or hospital factors predict protocol deviations. We examined predictors of protocol deviations and the effects of protocol violations on symptomatic intracerebral hemorrhage (sICH). *Methods:* We used data from the Increasing Stroke Treatment through Interventional Behavior Change Tactics trial, a cluster-randomized, controlled trial evaluating the efficacy of a barrier assessment and educational intervention to increase appropriate tPA use in 24 Michigan community hospitals, to review tPA treatments between 2007 and 2010. Protocol violations were defined as deviations from the standard tPA protocol, both before and after treatment. Multilevel logistic regression models were fitted to determine if patient and hospital variables were associated with pretreatment or post-treatment protocol deviations. *Results:* During the study, 557 patients (mean age 70, 52% male, median National Institutes of Health Stroke Scale score 12) were treated with tPA. Protocol deviations occurred in 233 (42%) patients: 16% had pretreatment deviations, 35% had post-treatment deviations, and 9% had both. The most common protocol deviations included elevated post-treatment blood pressure, antithrombotic agent use within 24 hours of treatment, and elevated pretreatment blood pressure. Protocol deviations were not associated with sICH, stroke severity, or hospital factors. Older age was associated with pretreatment protocol deviations (adjusted odds ratio [OR], .52; 95% confidence interval [CI], .30-.92). Pretreatment deviations were associated with post-treatment deviations (adjusted OR, 3.20; 95% CI, 1.91-5.35). *Conclusions:* Protocol deviations were not associated with sICH. Aside from age, patient and hospital factors were not associated with protocol deviations. **Key Words:** Stroke—thrombolysis—emergency department—tPA.

From the *Stroke Program, Department of Neurology, University of Michigan Medical School, Ann Arbor, Michigan; and †Department of Emergency Medicine, University of Michigan Medical School, Ann Arbor, Michigan.

Received June 6, 2015; revision received July 24, 2015; accepted August 23, 2015.

Ms. Fox is current affiliated with the Oakland University William Beaumont School of Medicine, Rochester, Michigan.

This study was funded by National Institute of Neurological Disorders and Stroke: R01 NS050372.

Address correspondence to Eric E. Adelman, MD, Stroke Program, University of Michigan Medical School, 1500 East Medical Center Drive, 1914 Taubman Center, SPC 5316, Ann Arbor, MI 48109-5316. E-mail: eriadelm@med.umich.edu.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2015.08.036

Introduction

Protocols for the administration of intravenous (IV) tissue plasminogen activator (tPA) for acute ischemic stroke have been adapted from the National Institute of Neurological Disorders and Stroke (NINDS) tPA trial[1] and are recommended by guidelines.[2] Previous studies have shown that protocol deviations before and immediately after tPA are common[3-16]; however, the clinical implications of these deviations are uncertain. Some studies have found that protocol deviations are associated with symptomatic intracerebral hemorrhage (sICH) and poor outcome,[3,9-13] whereas other reports have not found this association.[4-8,15-19] Because poor outcomes have been associated with protocol deviations, identifying predictors of these deviations may be useful to improve the quality of acute stroke care. Predictors of protocol deviations are not well understood. Most prior studies examining protocol deviations evaluated small numbers of patients, were retrospective reviews of a single center's experience, or both. Using prospectively collected data from the Increasing Stroke Treatment through Interventional Behavior Change Tactics (INSTINCT) trial,[20] we aimed (1) to determine if patient or hospital factors were associated with protocol deviations and (2) to examine the effects of protocol deviations before or immediately after tPA on sICH.

Methods

The INSTINCT Trial was a multicenter, cluster-randomized, controlled trial evaluating the efficacy of a barrier assessment and educational intervention to increase appropriate tPA use in emergency departments (EDs) in Michigan community hospitals. The methods and results of the INSTINCT Trial have been described previously.[20] Briefly, community hospitals in Michigan's Lower Peninsula were randomly selected and matched with a geographically separated partner hospital with ±20% of the index hospital's annual stroke admissions. This process was repeated for a total of 12 hospital dyads. One hospital in each pair received INSTINCT intervention and the other hospital served as a control. Complete data on the physician cohort staffing the INSTINCT EDs have previously been reported.[21] In brief, 80% of the physician cohort completed emergency medicine residencies and 85% were board certified in emergency medicine. No significant interhospital differences in staff were identified. INSTINCT had complete capture of tPA use for ischemic stroke between 2007 and 2010.

This study was a post hoc secondary analysis of the final INSTINCT dataset. All clinical information from the chart was abstracted using a previously described instrument with a high inter-rater reliability (kappa = .74).[14] The chart abstracters were not aware of this analysis at the time the data were collected.

Protocol deviations were defined as deviations from the recommendations outlined in the American Heart Association guidelines at the time the trial was conducted.[22] All hospitals used guideline concordant protocols to treat patients with tPA. As the European Cooperative Acute Stroke Study III (ECASS III)[23] was published during the INSTINCT Trial, protocol deviations for time to treatment were defined as treatment with IV tPA at more than 4.5 hours for patients who met ECASS III criteria, and treatment at more than 3 hours for others. Current guidelines support the expanded treatment window.[2] Pretreatment blood pressure deviations were defined as treating a patient with IV tPA despite a blood pressure of greater than 185/110 (defined as the last documented pretreatment blood pressure before tPA administration). Post-tPA hypertension was defined as 2 consecutive blood pressure readings, at least 30 minutes apart, greater than 180 mmHg systolic or 105 mmHg diastolic within the first 24 hours of tPA treatment. The patients were classified as having pretreatment deviations, post-treatment deviations, or both. In contrast to the primary INSTINCT analysis,[20] we used nursing reviewer assessment of protocol deviations rather than physician ascertainment. This allowed for an evaluation of an extended set of variables that were not assessed by physician reviewers.

Study Covariates

Covariates were chosen based on a priori beliefs regarding which clinical and hospital factors would be associated with protocol deviations. Medical comorbidities, antiplatelet use, and neurological consultation were obtained from the medical record. Hypertension, diabetes, hyperlipidemia, and antiplatelet use were defined as a history of these conditions documented in the medical record or if the patient was taking medications to treat these conditions. Symptomatic intracerebral hemorrhage (sICH) was defined as radiographic ICH with associated clinical worsening based on a retrospective review of the hospital chart (NINDS tPA trial definition[1]). Inpatient mortality and modified Rankin Scale score at discharge were abstracted based on previously described methods.[14] Hospital size and Joint Commission Primary Stroke Center (JC PSC) certification were self-reported by the participating hospitals. Five hospitals were JC PSC certified before the INSTINCT Trial and 3 hospitals obtained JC PSC certification during the trial. None of the hospitals had other forms of stroke certification. The University of Michigan and local institutional review boards approved the INSTINCT Trial.

Statistical Analysis

Descriptive statistics were computed for demographic and clinical characteristics. Patient and hospital characteristics and the presence of protocol deviations were compared using chi-squared tests for categorical