Patients with Low National Institutes of Health Stroke Scale Scores Have Longer Door-to-Needle Times: Analysis of a Telestroke Network

Archit Bhatt, MD, MPH, FAHA, Alexandra Lesko, BS, Lindsay Lucas, MS, Amit Kansara, MD, and Elizabeth Baraban, PhD

Background: The benefits of intravenous tissue-type plasminogen activator (IV-tPA) in acute ischemic stroke (AIS) are time dependent. Because emergency rooms quickly initiate a stroke alert with more severe symptoms, we hypothesized that patients with lower National Institutes of Health Stroke Scale (NIHSS) scores, indicating a less severe stroke, would have longer door-to-needle (DTN) times compared to patients with higher NIHSS scores. *Methods:* Data obtained from the 19-hospital Providence Stroke Registry were used to identify AIS patients who received IV-tPA within 4.5 hours of last-known-well. NIHSS scores were obtained prior to tPA administration at the time of emergency department presentation and categorized as low-NIHSS (score = 0-5) or high-NIHSS (score = 6-42) strokes. Median DTN times were collected for both groups as the primary outcome variable. Linear mixed-effects regression models were used to assess the effect of NIHSS scores on DTN and its 2 components: door-to-CT (DCT) and CT-to-needle (CTN) times. *Results:* We identified 692 AIS patients who received IV-tPA within 4.5 hours of last-known-well, with 198 patients presenting with low-NIHSS strokes and 494 patients with high-NIHSS strokes. In multivariable analysis, median DTN time was estimated to be 18% higher for low-NIHSS strokes than high-NIHSS strokes after adjusting for covariates ($P < .001$). Median DCT times were also higher for low-NIHSS (19 minutes) compared to high-NIHSS (11 minutes) strokes after adjusting for covariates ($P < .001$), whereas CTN times were unchanged ($P = .055$). *Conclusion:* In AIS patients receiving IV-tPA in a telestroke network, lower NIHSS scores were associated with longer DTN and DCT times. **Key Words:** Stroke—alteplase—NIHSS—thrombolysis.

Introduction

Intravenous tissue-type plasminogen activator (IV-tPA or IV-alteplase) is a highly effective treatment for acute ischemic stroke (AIS) patients if administered 4.5 hours from last-known-well, with outcomes strongly influenced by treatment time.[1-3] Although current guidelines for the treatment of AIS do not cite minor strokes as an independent exclusion criterion for IV-tPA,[2] minor stroke patients have historically experienced high rates of exclusion from IV-tPA treatment.[4,5] Fonarow et al found that 31% of minor stroke patients admitted within 2 hours of onset did not receive IV-tPA, solely because they were experiencing a mild or improving stroke.[6]

The consequences of exclusion for minor stroke patients are underscored by recent data. Approximately 20%-33% of patients with minor strokes (National Institutes of Health Stroke Scale; NIHSS ≤ 5) have unfavorable outcomes.[7-9] In addition, the International Stroke Trial

From the Providence Brain and Spine Institute, Portland, Oregon.
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Address correspondence to Archit Bhatt, MD, MPH, FAHA, 9427 SW Barnes Rd., Suite 595, Portland, OR 97225. E-mail: archit.bhatt@providence.org.
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(IST3) demonstrated that 20% of patients enrolled in the trial had NIHSS scores between 0 and 5,[10] compounding the need for better treatment options for minor stroke patients.

We hypothesize that the previously reported exclusion of treatment for minor stroke patients extends to a delay in treatment time for patients with lower NIHSS scores compared to higher NIHSS scores. The aim of this study was to assess differences in treatment times for patients with lower NIHSS scores (NIHSS ≤ 5) receiving IV-tPA compared to patients with higher NIHSS scores (NIHSS > 5) across a multistate telestroke network.

Methods

Data Source

Diagnostic and outcome patient data were manually abstracted from each hospital's medical record and entered into the American Stroke Association's Get with the Guidelines Stroke Patient Management Tool (GWTG). The data were combined into a single stroke registry.

Study Population

The Providence Telestroke Network based in Oregon and southern Washington consists of 17 partner site facilities and 2 hub facilities: a Comprehensive Stroke Center and a Primary Stroke Center. Eligible subjects were IV-tPA-treated patients presenting with signs and symptoms of ischemic stroke over the age of 18, who arrived at the emergency room within 4.5 hours from "last-known-well," between January 2009 and September 2015. Subjects were excluded for the following reasons: experienced an in-hospital stroke; comfort care measures were initiated on day 1; last-known-well to door times greater than 4.5 hours; had missing or unknown arrival times, admit NIHSS scores, or arrival mode; or had a zero or negative door-to-needle (DTN) time, door-to-CT (DCT) time, or CT-to-needle (CTN) time. Each stroke was considered an independent event, regardless of whether it was first admittance or readmittance.

Statistical Analysis

The primary outcome variable was DTN time, defined as the time in minutes from hospital arrival to IV-tPA delivery. The primary independent variable was stroke severity: patients who presented with an admit NIHSS score of 5 or less were considered "low-NIHSS strokes" and those with an admit NIHSS score of 6 or more were considered "high-NIHSS strokes." Patient characteristics for the 2 groups were summarized as percentages, means (standard deviation), or medians (interquartile range; IQR), as appropriate. A linear mixed-effects regression model was used to measure the difference in DTN between low-NIHSS and high-NIHSS stroke patients after adjusting for patient characteristics and treatment-related factors (further defined below). A hospital-specific random intercept (random effect) was included in the model to account for patient clustering within the hospital. DTN followed a normal distribution only after performing logarithmic transformation. Therefore, the natural log of DTN was used for all parametric analyses, and all results are reported as median DTN.

In Model 1, the following patient characteristics and treatment-related factors were added to the model as covariates based on literature review: age, gender, weekend or evening admission compared to daytime admission, telestroke usage (defined as remote evaluation by a neurologist using video technology), arrival time, and mode of arrival (private car or ambulance).[3,11-16] Two additional covariates, the year that the patient was discharged and a composite variable indicating the presence of one or more of the following stroke risk factors: dyslipidemia, diabetes, atrial fibrillation, or hypertension, were also added to Model 1. Because of low sample sizes of nonwhite patients, race was excluded as a covariate from the analysis. Daytime admission occurred between 8:00 a.m. and 4:00 p.m., Monday to Friday, with all other hours or major holidays considered weekend or evening admission. Telestroke was defined as stroke consult facilitated by the use of remote audiovisual technology at our hub facilities with 1 of our 17 partner sites. Arrival time was defined as the time from last-known-well to hospital arrival. Backward elimination (with a threshold of $P \leq .05$) was used to find significant covariates of DTN from the above covariates. In Model 2, the predictor of interest, stroke severity indicator variable, was then included with all significant covariates. This inferential model examined whether stroke severity constituted an important explanatory factor after all other significant factors were accounted for. Interactions between stroke severity and all significant main effects were tested one at a time in the final model. To verify the appropriateness of the models, histograms and scatterplots of residuals and predicted values were examined. All tests were two tailed with alpha equal to .05; P values < .05 were considered statistically significant. R and SPSS v22.0 software (SPSS Inc., Chicago, IL) were used for all statistical analyses and graphics.[17-19]

Secondary analyses were performed to examine the 2 components of DTN time: (1) DCT time, the time in minutes from hospital arrival to a computerized tomography (CT) scan; and (2) CTN time, the time in minutes from a CT scan to IV-tPA delivery. The same model-building process used to estimate DTN as a function of stroke severity was also used to estimate DCT and CTN as a function of stroke severity.

This study was approved by the Institutional Review Board of Providence Health and Services with waiver of informed consent (IRB #14-108).