Intravenous Fibrinolysis Eligibility: A Survey of Stroke Clinicians' Practice Patterns and Review of the Literature

Felipe De Los Rios, MD,*¶ Dawn O. Kleindorfer, MD,* Amy Guzik, MD,† Santiago Ortega-Gutierrez, MD, MSc,|| Navdeep Sangha, MD,‡ Gyanendra Kumar, MD,§ James C. Grotta, MD,‡ Jin-Moo Lee, MD, PhD,§ Brett C. Meyer, MD,† Lee H. Schwamm, MD,# Pooja Khatri, MD,* and for the SPOTRIAS Investigators

Background: The indications and contraindications for intravenous (IV) recombinant tissue plasminogen activator (rtPA) use in ischemic stroke can be confusing to the practicing neurologist. Here we seek to describe practice patterns regarding decision-making among US stroke clinicians. *Methods:* Stroke clinicians (attending and fellow) from the 8 National Institutes of Health SPOTRIAS (Specialized Programs of Translational Research in Acute Stroke) centers were asked to complete a survey ahead of the 2012 SPOTRIAS Investigators' meeting. *Results:* A total of 51 surveys were collected (71% response rate). Most of the responders were attending physicians (68%). Only 18% of clinicians reported strictly adhering to current American Heart Association guidelines for treatment within 3 hours from symptom onset; this increased to 51% for the European Cooperative Acute Stroke Study (ECASS) III criteria in the 3 to 4.5 hours time frame. All clinicians treat eligible patients in the 3 to 4.5 hours time frame. The great majority will recommend rtPA in the following scenarios: (1) elderly individuals irrespective of age (97%); (2) severe stroke irrespective of National Institutes of Health Stroke Scale (NIHSS) (95%); or (3) suspected stroke with seizures at symptom onset (91%). None recommended rtPA in the setting of an international normalized ratio >1.7. Most clinicians defined mild strokes as an exclusion based on the perceived disability of the deficit (80%) rather than on a specific NIHSS threshold. *Conclusions:* Most surveyed stroke clinicians seem to find that the current IV rtPA eligibility criteria for the 3-hour time frame too restrictive. All would recommend rtPA to eligible patients in the 3 to 4.5 hours time frame despite the absence of an U.S. Food and Drug Administration (FDA)-approved indication. **Key Words:** Stroke—infarction—thrombolysis—stroke treatment—tissue plasminogen activator—rtPA.

From the *Department of Neurology and Rehabilitation Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio; †Department of Neuroscience, University of California San Diego, San Diego, California; ‡Department of Neurology, University of Texas, Houston, Texas; §Department of Neurology, Washington University, St. Louis, Missouri; ||Department of Neurology, Columbia University, New York, New York; ¶Department of Neurology, Sanna Healthcare Network, Lima, Peru; and #Department of Neurology, Harvard Medical School, Boston, Massachussets.

Received February 19, 2014; accepted March 29, 2014.

Supported by NIH, NINDS (R01 NS30678 and P50 NS044283-09).

The frontiers of intravenous fibrinolysis: a survey of stroke clinicians' practice patterns.

Address correspondence to Felipe De Los Rios, MD, Av. Aurelio Miro Quesada 1030, San Isidro, Lima, Lima 27, Peru. E-mail: delosrfe@ucmail.uc.edu.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2014.03.024

Fibrinolysis with recombinant tissue plasminogen activator (rtPA) is the pillar of current acute stroke therapy.[1-4] Despite its increased use in the United States, rtPA is still administered to only about 5% of patients with an acute ischemic stroke.[5] This is largely because of its strict inclusion and exclusion criteria.[6] These criteria are primarily taken from the pivotal National Institute of Neurological Disorders and Stroke (NINDS) study that led to FDA approval and expert opinion.[7] The NINDS study results have been replicated in real-life scenarios in multiple centers worldwide when these criteria are followed.[8,9]

Over the last decade, various publications have provided nonrandomized data on the outcome of patients treated with rtPA outside the established guidelines.[10-13] These reports, in addition to imaging advances and greater experience with intravenous (IV) rtPA, have led many to challenge the necessity of some of the current exclusion criteria.[7,14,15] However, there is also evidence that straying too far from established treatment protocols can lead to increased rates of complications.[16,17] Furthermore, the definitions of specific criteria have not been well delineated and discrepancies exist between the rtPA product label and current treatment guidelines (Table 1). In this context, we sought to describe practice patterns regarding IV rtPA decision-making among stroke clinicians from high-volume academic centers.

Methods

We invited all stroke attendings and fellows (stroke clinicians) from SPOTRIAS (Specialized Programs of Translational Research in Acute Stroke) centers to participate in a survey regarding their acute stroke practice patterns. SPOTRIAS is a national network of 8 specialized stroke treatment and research centers funded by the NINDS of the National Institutes of Health with a goal of reducing disability and mortality through collaborative laboratory and clinical investigation (www.spotrias.org). At the time of the survey, there were 8 SPOTRIAS sites: University of California Los Angeles, University of California San Diego, University of Texas Houston, Washington University in St. Louis, Columbia University, Partners (Massachusetts General Hospital and Brigham and Women's Hospital), NINDS Intramural Program, and the University of Cincinnati.

Stroke clinicians who had made the decision to prescribe or recommend fibrinolytic therapy to at least 1 patient with a diagnosis of acute ischemic stroke within the previous 12 months were asked to complete the survey; residents were excluded. The survey consisted of questions about their treatment of patients with acute ischemic stroke (Appendix e-1).

A pilot survey modeled on the 2007 American Heart Association (AHA) guidelines,[18] 2009 AHA science advisory on the expansion of treatment time windows,[19] and the rtPA product label was administered to stroke clinicians at the University of Cincinnati on March 26, 2012. Feedback from this pilot survey was used to modify and expand the questions, creating the study survey (Appendix e-1). The study survey was then distributed to the principal investigators of each SPOTRIAS center to share among their faculty and fellows by email and an additional opportunity was given at the 2012 SPOTRIAS investigators' meeting. Data collection took place during the months of April and May 2012. The surveys were designed, stored, and analyzed online using SurveyMonkey software (www.surveymonkey.com). All questions required a single answer unless stated otherwise. Because of wording differences between the pilot and final surveys, data from the pilot survey were not included for this analysis. To include data from the University of Cincinnati, a second survey including questions present only in the final survey but not in the pilot survey was distributed. The replies from this second survey are also included in this analysis and were used to calculate our response rate. In addition, questions 5 and 6 (Appendix e-1) were excluded from this article because of concerns by those interviewed regarding the ambiguity of the wording and difficulty in interpretation of results.

All data collection was finalized on May 17, 2012. We report only the data regarding IV fibrinolysis. This study was given exempt status by the University of Cincinnati Institutional Review Board.

Results

We estimated that our survey population of interest consisted of 70 stroke clinicians (attending physician members of each institution's stroke team and vascular neurology fellows) within the SPOTRIAS network. We collected 51 surveys (71% response rate), including 4 physicians who did not treat an acute stroke patient in the previous 12 months and whose responses were excluded. A total of 47 responses remained available for analysis.

Most (2/3) of the responders were attending physicians at academic institutions (66%, n = 31). Approximately 1/3 of respondents were stroke fellows (32%, n = 15). The remaining physicians worked primarily in the community (2%).

Specific survey results are described as follows:

(A) Question: *"Which potential rtPA exclusion criteria do you "bend" for patients with a perceived disabling stroke? Multiple answers allowed."*

Only 18% (n = 7) of responders would adhere strictly to AHA guidelines and insert criteria. The most frequently waived criterion (49%, n = 18) was having a previously secured intracranial aneurysm. Responses for each individual criterion are presented in Figure 1.

(B) Question: *"What additional ECASS III rtPA contraindication criteria do you "bend" for patients with a*