Clinical Practice Statement

tPA and Ischemic Stroke: Focused Update of 2010 Clinical Practice Advisory from the American Academy of Emergency Medicine

Chair: Steve Rosenbaum, MD FAAEM

Authors:	William J. Meurer, MD FAAEM	MS University of Michigan
	Bradley Barth, MD FAAEM	University of Kansas Medical Center
	Michael Abraham, MD FAAEM	University of Maryland
	Jerome R. Hoffman, MA MD FAAEM	University of California, Los Angeles

The authors disclosed no commercial relationships or conflicts of interest.

Reviewers: Wan-Tsu W. Chang, MD FAAEM
David Farcy, MD FAAEM
Gary Gaddis, MD FAAEM
Robert Sherwin, MD FAAEM

Reviewed and approved by the AAEM Board of Directors (3/17/2017)

Executive Summary:

No new studies published between 2010 and 2016 meaningfully reduced uncertainty regarding our understanding of the benefits and harms of tPA for acute ischemic stroke. Discussions regarding benefit and harm should occur for patients and risk prediction scores may facilitate or expedite the conversation.

Background and Purpose:

In 2010, AAEM issued a clinical practice advisory reviewing the available evidence for tissue plasminogen activator (tPA) in acute ischemic stroke. The objective of this focused review is to assess the impact of new evidence regarding tPA in acute ischemic stroke that has emerged since 2010. The previous specific recommendations, which remain controversial today, were:

1. tPA is an effective treatment for stroke when given in academic medical centers and prepared stroke centers.
2. Emergency physicians should have necessary resources (i.e. stroke team) to optimally care for suspected stroke patients.
3. Hospitals should formulate a plan for timely care of patient with suspected acute stroke.

This current update, neither endorses nor rejects the 2010 statement but instead, addresses two primary questions for the clinician: 1) is there any applicable, new, high quality evidence that the benefits of tPA are

justified in light of the harms associated with it, and 2) if so, does the evidence clarify which patients, if any, are most likely to benefit from the treatment.

Methods:

We used the AAEM methodology for an expedited literature review. We searched for published papers between January 1, 2010 and October 1, 2016. We classified and synthesized the available, additional, high quality evidence.

Results and Conclusions:

Between 2010 and 2016 little or no additional high-quality prospective data emerged on the utilization of tPA in acute ischemic stroke (AIS). Therefore, uncertainty remains over whether benefits gained from the use of tPA in AIS do or do not exceed potential harms. This places the emergency physician in a difficult situation that is both subject to time constraints and clinical equipoise. The benefits of the use of tPA in AIS has been neither proven nor disproven for all nominally eligible patients, leading to challenges in the clinical arena. Since the last AAEM CPC statement, one large randomized trial was reported, but it had major methodological issues regarding blinding and selection bias. A number of incremental meta-analyses were also published. The grading tables are located at the end of the document.

Based on the available data, the major conclusions that can be made since our 2010 statement are:

1. No new studies meaningfully reduced uncertainty regarding the benefits and harms of tPA for acute ischemic stroke. tPA is possibly an effective treatment for stroke when given under the right circumstances, however more than half those patients treated with tPA have no change in long-term outcome when compared to their initial prognosis. Currently, there are insufficient data to definitively demonstrate a robust benefit from using tPA in AIS.
    a. Emergency physicians should understand the shortcomings of the existing data and have a discussion with patients about the potential benefits and harms associated with tPA. The decision aids described in the 2010 paper are no longer active web links. Currently, the iScore seems to provide most helpful prognostic information (http://www.sorcan.ca/iscore/).
2. Based on published literature, the symptomatic intracranial hemorrhage rate is approximately 6%. This is subject to the inherent effects of reporting bias, where higher or lower rates may not be published.
3. Evidence on mild/improving stroke is inadequate to make a clear recommendation. A focus on the likelihood a patient will be incrementally disabled by their current stroke symptoms may be more helpful for decision making with patients and families.
4. Patients treated earlier have a greater chance of a good outcome despite generally having more severe presentations. This time association is likely confounded by early spontaneous improvement. Early tPA treatment and spontaneous improvement likely contribute to observed better outcomes in earlier treated patients. The relative contributions of each remain uncertain.

5. Older patients and those with severe strokes have a lower likelihood of a good outcome, but uncertainty about the magnitudes of the benefits and harms in these groups remains substantial.
6. Dedicated stroke units appear to reduce death and dependency. This effect appears larger in magnitude than the impact of tPA and is potentially available to a much greater proportion of stroke patients.