Guidelines For Extending the Tissue Plasminogen Activator Treatment Window for Ischemic Stroke

To the Editor:

The anticipated recently published guidelines, regarding extending the tissue plasminogen activator (tPA) treatment window for ischemic stroke, are sure to garner much attention and discussion within the United States.1 Largely based on the European Cooperative Acute Stroke Study (ECASS) III trial results, the newly proposed 3- to 4.5-hour tPA treatment guidelines appropriately exclude patients >80 years, those with a baseline National Institutes of Health Stroke Scale score >25, and those with both a history of prior stroke and an established diagnosis of diabetes. What is unclear is why these guidelines fail to specify a blood glucose level >400 mg/dL as an exclusion criterion for tPA treatment, because these patients were excluded in the ECASS III trial and other randomized trials that provide the basis for the treatment of acute ischemic stroke with tPA.2–6

Similarly concerning, when the American Stroke Association updated their tPA treatment guidelines in 2003, a blood glucose level of <400 mg/dL was dropped from the list of “characteristics of patients with ischemic stroke who could be treated with tPA.”7 Because up to 60% of patients with acute stroke with hyperglycemia will not have a history of diabetes,8–10 excluding only patients with a history of diabetes, combined with a history of previous stroke, is insufficient and will miss a substantial number of hyperglycemic patients with stroke with stress hyperglycemia or undiagnosed diabetes. With compelling data demonstrating that an elevated serum glucose level is associated with an increased risk for intracranial hemorrhage after tPA treatment,11–13 and further data suggesting that hyperglycemia may counterbalance the beneficial effect of tPA-induced recanalization,14 the safety and efficacy of treating patients with a blood glucose level >400 mg/dL remains uncertain. Until data emerge that demonstrate an appropriate risk:benefit ratio in such patients, this exclusion criterion should be specified in the American Stroke Association’s expanded time window treatment recommendations. Additionally, given the currently available data, consideration should be given to reintroducing this exclusion criterion for patients with ischemic stroke evaluated for tPA treatment within the 3-hour window.

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Andrew W. Asimos, MD
Department of Emergency Medicine
Carolinas Medical Center
Charlotte, NC


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Andrew W. Asimos

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