Thrombolysis in Stroke of an Undetermined Onset Time
Is Plain and Simple Good Enough?
Magdy H. Selim, MD, PhD; Carlos A. Molina, MD, PhD

Thrombolytic therapy remains the most effective treatment strategy for acute ischemic stroke to date. The vast majority of patients who present with stroke-like symptoms, in whom onset time is suspected to be ≥3 to 4.5 hours and cannot be established reliably, are not considered for thrombolytic therapy according to standard practice guidelines. This is largely attributed to concerns over the potential for limited effectiveness of therapy at a delayed time window and fear of hemorrhagic complications. However, the time of stroke onset is unknown in a significant proportion of patients—up to one-quarter of acute ischemic stroke patients either wake up with stroke symptoms or the time they were last seen well cannot be ascertained on presentation. For some, this uncertainty about the time of stroke symptoms onset may be the only reason why they are deemed ineligible for thrombolytic therapy. The clinical and radiological features in a substantial number of these patients are similar to those of patients with a known time of stroke onset. Hence, the question: Why should these patients be deprived of a proven effective therapy?

As Drs Adams and Alexandrov point out, the decision making requires careful balance of the potential benefit versus harm. Let us examine the risk of thrombolysis-related hemorrhage in our patient. Although her National Institutes of Health Stroke Scale score seems high, she is relatively young and her head computed tomography scan shows no signs of large infarctions or hypodensity. Assuming that she is not affected with diabetes mellitus and that her serum glucose and blood pressure levels are not exceedingly high, her risk of symptomatic or fatal hemorrhage after thrombolysis should not be dissimilar from her counterparts with an established stroke-onset time. We agree that the effectiveness of thrombolysis diminishes as time goes by, but our patient is severely disabled and is more likely than not to remain with significant residual disability with supportive medical care alone. So, yes! We would consider thrombolysis. The question then becomes whether or not other tests are needed first. Not necessarily, although vascular imaging, such as computed tomography angiography showing vascular occlusion, would strongly reinforce our decision to treat this patient with thrombolytic therapy. The pros and cons of thrombolysis in this peculiar situation should be thoroughly discussed with the patient and her family before contemplating thrombolytic therapy.

There are several ongoing efforts to use advanced imaging strategies, such as diffusion-weighted imaging/fluid attenuated inversion recovery mismatch, or serum biomarkers as surrogate measures to estimate the timing since stroke onset; or perfusion imaging to determine the extent of salvageable brain tissue to aid with the decision making of whether or not to use thrombolysis in a patient with stroke with an undetermined time of symptom onset. We welcome these studies, anxiously await their results, and would encourage enrolling our patient in one of these studies if feasible. It is important to point out, however, that these advanced imaging strategies will result in further delays in initiating thrombolysis and may only be available at academic institutions and advanced stroke centers.

Accumulating data suggest that the Alberta Stroke Program Early Computed Tomography score (ASPECTS) provides a surrogate estimate of the infarct extent as seen on diffusion-weighted imaging; and that after thrombolysis the functional outcomes of patients with an unknown time of stroke onset, who otherwise meet all other eligibility criteria for thrombolysis and their plain computed tomography scan shows an ASPECTS ≥7, are similar to those who are treated within 3 to 4.5 hours of stroke onset. However, most of these data are retrospective and are limited by selection bias. Prospective randomized trials of thrombolytic therapy based on plain computed tomography scan findings and perhaps additional vascular imaging in patients like ours are certainly needed.

Disclosures
None.

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1496
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A correction is needed in the article, “Individual patient data subgroup meta-analysis of surgery for spontaneous supratentorial intracerebral hemorrhage” (Stroke 43:1496–1504).

In the Abstract, the first section of the Results section omitted the words, “…randomization was.” That passage has been updated to read, “Meta-analysis indicated that there was improved outcome with surgery if randomization was undertaken within 8 hours of ictus.”

In the Conclusions the first sentence omitted the words, “if the decision is made” and that passage has been updated to read, “Our data suggest that improved outcomes can be achieved with early surgery if the decision is made within 8 hours of ictus.”

The online version of the article has been updated with these corrections.