

Door-to-needle times in acute ischemic stroke

How low can we go?

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IV human recombinant tissue plasminogen activator (rt-PA) is the best proven and most effective treatment for acute ischemic stroke. The benefits of rt-PA are highly dependent on the time elapsed since stroke symptoms.¹ Accordingly, the Brain Attack Coalition recommends that the time from emergency room arrival to initiation of rt-PA (that is, the “door-to-needle” time) should be 60 minutes or less.²

Are patients actually receiving rt-PA within 60 minutes in clinical practice? Unfortunately, recent studies clarify that they are not. Data from the large American Heart Association/American Stroke Association Get With The Guidelines–Stroke program and the multinational Safe Implementation of Treatment in Stroke–International Stroke Thrombolysis Register registry showed that median door-to-needle times were 75 minutes and 65 minutes, respectively.^{3,4} Among 641 US hospitals reporting ≥ 10 rt-PA–treated patients, only 6.7% treated more than half of their patients within 60 minutes.³

Clearly, neither US nor European hospitals are meeting the proposed 60-minute door-to-needle benchmark. Either the Brain Attack Coalition’s benchmark is unrealistic and unfeasible—except possibly in very experienced stroke centers or in the context of prospective clinical trials—or a large number of hospitals are missing out on processes of care that could reduce door-to-needle times. So, which is it?

This issue of *Neurology*® provides a convincing answer by Meretoja et al.⁵ In this single center retrospective cohort study from Helsinki University Central Hospital, a succession of improvements to their rt-PA protocols resulted in a substantial reduction in median door-to-needle times over a 10-year period. A strikingly low median door-to-needle time of 20 minutes was achieved, with 94% of patients treated within 60 minutes. Innovative strategies to reduce door-to-needle time included obtaining history and provisional consent for rt-PA by telephone in the field, and bypassing the emergency department to

take patients directly from emergency medical transport to the CT scanner.

This remarkable improvement in door-to-needle time contributed to a 45-minute shortening of the time from stroke onset to treatment between 1999 and 2011. According to the pooled rt-PA trial data, reducing onset-to-treatment time by 45 minutes should result in an approximate 0.16 absolute increase in the odds ratio for good recovery for rt-PA compared to placebo.¹ For a hypothetical “average” patient in the 1995 National Institute of Neurological Disorders and Stroke trial with a 26% chance of good outcome on placebo but a 1.70-fold increase in the odds of good outcome with rt-PA, increasing that odds ratio from 1.70 to 1.86 would increase the probability of a good outcome with tPA treatment from 37% to 40%. This is a modest shift in an individual’s expected outcome, but similar improvements averaged over the tens of thousands of patients treated annually with rt-PA⁶ could save hundreds of patients per year from a lifetime of disability.

Meretoja et al. have demonstrated that door-to-needle times of 60 minutes—indeed, much less than 60 minutes—can be consistently achieved. Given this, it is an ethical imperative for us to work toward similar results in our own hospitals. However, changing practices may not be easy. For many hospitals, emulating the protocols used by Helsinki University Central Hospital will require substantial changes to systems of care involving not only neurologists, but also others involved in emergency medical services and in emergency medicine and radiology departments. Additionally, it is important that enough time be reserved for accurate clinical evaluation, including identification of contraindications to rt-PA. Patient safety must not be sacrificed for the sake of speed.

Fortunately, there is some help for hospitals seeking advice on how to reduce their door-to-needle times. In 2010 the American Heart Association/American Stroke Association launched the Target: Stroke Initiative—accessible at www.targetstroke.org.

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org—designed to help hospitals enact strategies to reduce door-to-needle times with the ultimate goal of treating more than half of their patients in 60 minutes or less. Registered hospitals can access information on strategies and care pathways for acute stroke, and share examples of best practices.⁷

By showing us how rapidly rt-PA can be given, Meretoja et al. also show us the limits of what rt-PA can achieve. Despite a remarkable reduction in treatment times, 60% or more of their patients still had poor outcomes throughout the years of their study. Unfortunately, rt-PA usually fails to recanalize occluded arteries⁸ and fails to help patients whose arteries have spontaneously recanalized, with the consequent risk of hemorrhage. Clearly, rt-PA is not a panacea. Better ways are needed to quickly identify patients with an occluded artery but who still have viable brain, and better drugs or devices are needed to recanalize the occluded artery.⁹ Randomized controlled trials to test new approaches must remain a priority.

Are the door-to-needle times achieved by Meretoja et al. the limit, or can we reduce times further? It is hard to imagine a system better optimized for timely administration of rt-PA. Nonetheless, one should not discount the possibility of further innovations to reduce door-to-needle times. Ruling out hemorrhage in the field during transport, for example, by as-yet undiscovered biomarkers, might be one way to further shorten times. Additionally, a renewed emphasis on prehospital care is warranted, including public education to activate emergency response systems immediately when stroke symptoms occur, coupled with triage and rapid transport to the nearest stroke center by emergency medical services. Improvements in the speed of prehospital care will further shorten the time from stroke onset to rt-PA administration, even after hospital door-to-needle times are minimized.

For current and future treatments, door-to-needle times less than 60 minutes should be the rule, not the exception—now it is up to us to make it so.

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