

Neurology residency program as factor associated with thrombolysis utilization in acute stroke

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Despite strong evidence on the safety and efficacy of IV alteplase up to 4.5 hours after ischemic stroke (IS) symptom onset¹ and increased use of thrombolysis over recent decades, this treatment remains underused and accessible to only a fraction of patients. The rate of thrombolysis in the United States is 3.4%–5.2% of all stroke cases.² Several studies have identified barriers to thrombolysis delivery,³ but other as yet unmeasured factors may also underlie these barriers, thereby influencing rates of thrombolysis utilization and access.

In this issue of *Neurology*®, Moradiya et al.⁴ investigate the role that hospital academic status may have on thrombolysis use for acute IS. They present a retrospective serial cross-sectional cohort study comparing rates of thrombolysis utilization in hospitals with neurology residencies (NR) and in other teaching (OT) and nonteaching (NT) hospitals. They extracted data for 2000 to 2010 from the Nationwide Inpatient Sample (NIS), a publicly available national database of an approximate 20% sample of all admissions in nonfederal US hospitals containing anonymized basic patient information and hospital characteristic data. Patients with a primary or secondary diagnosis of IS and, among them, those who received thrombolysis, identified by using *ICD-9-CM* codes, were included in the analysis. Thrombolysis rates for NR, OT, and NT were calculated, stratified, and controlled by data available in NIS. All 3 hospital types showed increasing thrombolysis utilization (NR more than OT/NT), but NR had a higher thrombolysis rate (3.74% ± 0.24% [standard error]) compared to OT (2.28% ± 0.11, $p < 0.001$) and NT (1.44% ± 0.06%, $p < 0.001$). Interestingly, discrepancies were greatest in elderly patients. In multivariable analysis, NR was an independent predictor of higher thrombolysis utilization (odds ratio [OR] 1.51, 95% confidence interval [CI] 1.44–1.59 [NR vs OT], and OR 1.82, 95% CI 1.73–1.91 [NR vs NT]) regardless of other independent predictors: younger age, male sex, Caucasian ethnicity, private insurance, lower modified Charlson comorbidity index, urban location, higher hospital stroke case volume, more recent calendar

year, and Joint Commission–Primary Stroke Center certification.

These results have implications for clinical and organizational operations, not only for the US but also for other countries' health care systems. Other data suggest that academic status and residency programs may improve the efficiency of general stroke management.^{5,6} The independent association between the presence of a neurology residency program and higher rates of thrombolysis use in this study could represent both direct and indirect influences on stroke treatment in the acute setting. Direct effects may include a higher number of dedicated in-training personnel that, with the back-up of senior attending neurologists, is more prone to follow acute stroke treatment guidelines; 24/7 in-hospital availability that could make thrombolytic therapy possible at any moment of the day and week; and more comfort with potential treatment-related adverse events. Indirect effects may include a review of local procedures with the development/implementation of specific evidence-based in-hospital treatment protocols, a better infrastructural organization in terms of logistics, in-hospital delay reduction, neuroimaging appropriateness and interpretation, stroke mimic differential diagnosis, and better resource allocation.

Most study limitations are related to data extraction from national administrative databases like NIS: inaccuracies in *ICD-9* coding for thrombolysis utilization that may have caused thrombolysis rate underestimation (although study results did not change when only hospitals coding at least one thrombolytic infusion in a given year were considered); or potential inclusion of patients electively admitted for secondary stroke prevention–related vascular procedures (e.g., endarterectomy, carotid stenting). Moreover, a lack of information in NIS may have affected results. NIS does not include differences in prehospital stroke management; stroke onset time that could allow calculation of thrombolysis rates among eligible cases; thrombolysis modalities, as intra-arterial thrombolysis requires technical expertise and logistic/economic resources that NR hospitals are more likely to have; duration of hospital use of IV

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thrombolysis (more likely longer for NR), as this could influence the learning curve and number of treatments; and number of hospitals involved in telestroke networks.

Despite these weaknesses, the study by Moradiya et al. provides a new point of view for further evaluation of barriers to thrombolysis delivery in IS patients that should be confirmed in prospective studies including assessments of other unexplored factors potentially explaining the higher rate of thrombolysis in NR. The implementation of neurology/neurovascular/stroke medicine training programs can be neither the only nor the immediate solution to the thrombolysis underuse issue. In the meantime, in order to increase the number of eligible persons who could benefit from this treatment, regardless of age and socioeconomic factors, it is crucial to continue promoting multimodal interventions: public educational campaigns to improve the awareness of stroke symptoms and stroke as an emergency whose successful treatment is extremely time-dependent; continuing educational programs for hospital personnel; improvement of physicians' awareness of and confidence in treatment safety, even when patients are treated despite the presence of relative contraindications, like advancing age⁷; coordinated actions, supported by legislation, targeting creation of regional systems of care and preferential pathways (including direct transportation to referral specialized centers) for stroke cases and reduction of onset-to-door/in-hospital delays; implementation of current guidelines; and revision of some relative exclusion criteria. Equally important are cost-effective strategies, also involving NT hospitals, aimed at making stroke care more standardized and at improving outcome by encouraging adherence to guidelines.⁸ Performance measurement and recognition awards, like those adopted by the American Heart Association's Get With The Guidelines–Stroke program, will aid this process.⁸ Administratively, better definition of recommendations and requirements/criteria for stroke center certification^{9,10} and postcertification monitoring of the delivered quality of care will be necessary, as will creation of infrastructures dedicated to stroke centers with multidisciplinary team and neuroimaging capabilities, including implementation of telestroke networks, improved coding methods, and physician reimbursement incentives for thrombolytic

utilization. Finally, it is fundamental to promote basic and translational research and randomized controlled clinical trials aimed at extending therapeutic time windows and evaluating novel thrombolytic/neuroprotective drugs or diagnostic neuroimaging methods.

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