In 1995,1 a 2-part randomized trial showed the efficacy of intravenous tissue plasminogen activator (tPA) when given within 3 hours of onset of symptoms of acute ischemic stroke. Postmarketing studies have demonstrated that intravenous recombinant tPA can be administered appropriately in a wide variety of hospitals setting. If treatment guidelines2 are carefully followed, intravenous tPA for acute ischemic stroke is feasible and shows safety and efficacy comparable to the results from the study by the National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group.3–6 However, although the persuasive results of that study have launched some enthusiasm, safety and efficacy concerns about the use of thrombolysis for ischemic stroke prevail among many neurologists because of the risk of hemorrhage and the small proportion of suitable patients. Further concerns are nourished by a report from “the real world” in which the translation of study results into daily clinical practice seemed to be less easy and more harmful than expected.6,7

In European countries, there is little information about early outcomes after intravenous application of tPA for stroke patients treated in community-based settings. In this issue of Stroke, Heuschmann et al report the largest experience from the German Stroke Registers Study Group (Arbeitsgemeinschaft Deutscher Schlaganfall Register [ADSR]). ADSR is a network of regional stroke registers that combines data from 104 academic and community hospitals throughout Germany and represents ≈5% of all acute stroke hospitals in Germany. Therefore, the description reflects the special situation of the German healthcare system. The main result of this study is that the experience level of an individual hospital in tPA treatment influences stroke mortality. The experience of an individual hospital in administration of tPA was based on the study of Katzan and colleagues.7 Patients receiving tPA in hospitals that administered ≤5 thrombolytic therapies in 2000 had an increased risk of in-hospital mortality (odds ratio, 3.3; 95% confidence interval, 1.1 to 9.9). The next step within the ADSR network should be the audit of causes for early in-hospitals deaths and detailed evaluation of potential protocol violations.

Thrombolytic therapy for acute stroke will not have a major impact on death and dependency unless it is accessible to more patients. Concerns exist regarding the impact of implementing a treatment that only a limited number of stroke patients might be eligible for and that has an associated excess risk of intracerebral hemorrhage.5 Thrombolysis for acute ischemic stroke, for instance, may have a substantial effect on stroke outcome but has no more overall effect in the population than a much less potent treatment such as aspirin unless it can be given safely to more than a small minority of patients.9 About 3% of all ischemic strokes and 10.4% of patients admitted within 3 hours of stroke onset were treated with tPA in the hospitals of the ADSR network. These proportions were comparable to previous multicenter studies reporting on rates of tPA use outside clinical trials from 1.6%10 to 6.3%.11

Increasing the proportion of patients with acute ischemic stroke who are treated with tPA is an important challenge facing contemporary physicians. In the ADSR network, thrombolytic therapy was administered more often in neurological departments, in hospitals providing stroke unit services, and in centers treating >100 ischemic stroke patients per year. Accordingly, the prehospital and hospital infrastructure needs to be streamlined to handle ischemic stroke with high priority.12 Further widespread and repetitive public education is needed to increase awareness of warning signs, stroke risk factors, and availability of treatment. The last factor should not be underestimated because stroke has been widely thought to be untreatable.

The generalized efficacy and safety of tPA depend on a network involving an efficient connection between emergency physicians and stroke neurologists. In this setting, tPA can be safely given to acute ischemic stroke patients in rural and community hospitals with or without on-site neurology. In addition, regardless of hospital size, a system for expedited stroke workups can be set up and successfully implemented by a stroke team. In such facilities, it is very likely that these patients will be under the direct care of emergency and/or primary care physicians. To assist physicians in these cases, community hospitals and their physicians must have access to 24-hour neuroscience support. Such neuroscience backup will come only from larger regional medical centers. These regional centers should also assist with or provide community hospitals with physician education and address their concerns regarding tPA therapy. Ultimately, such programs will provide the opportunity for patients to receive stroke therapies that previously were unavailable and may contribute to the decrease in tPA-related morbidity observed in hospitals less trained in acute stroke management.11

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References


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