The Stroke-Thrombolytic Predictive Instrument Provides Valid Quantitative Estimates of Outcome Probabilities and Aids Clinical Decision-Making

Bart M. Demaerschalk, MD, MSc, FRCP(C)

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Computerized clinical decision support systems are increasingly popular in health sciences and have been demonstrated to improve practitioner performance. For an emergency closely related to ischemic stroke, acute myocardial infarction, a thrombolytic predictive instrument was developed for real-time use in emergency medical-service settings to identify patients likely to benefit from thrombolysis and to facilitate the earliest possible use of this therapy. A similar instrument, designed for ischemic stroke, could also prove to be useful. Thrombolysis for ischemic stroke remains underused even under ideal circumstances. Approximately 40% of emergency physicians in a national survey report that they would not use recombinant tissue plasminogen activator (rt-PA) for stroke, citing the risk of symptomatic intracranial hemorrhage and relative lack of benefit. Similar results were reported by Bobrow et al in a survey of the Arizona chapter of the American College of Emergency Physicians. Only 52% of the emergency physicians who responded to the survey indicated that they would endorse rt-PA use for stroke under ideal conditions. Physicians’ perceptions of risks and benefits of rt-PA for stroke are not uniformly accurate. Merino et al reported that only 11% (95% CI, 0 to 22) of surveyed emergency medicine physicians and neurologists could correctly convey the expected magnitude of beneficial effect of rt-PA, and that only 39% (95% CI, 21 to 57) could accurately report the expected rate of symptomatic and fatal intracranial hemorrhage of rt-PA. This misperception may interfere with their willingness to endorse this treatment. It would be helpful to draw a distinction between true and perceived efficacy and between true and perceived harm associated with rt-PA for stroke.

In this issue of Stroke, Kent et al developed a Stroke-Thrombolytic Predictive Instrument (TPI) to aid physicians considering thrombolysis for a patient with acute ischemic stroke. The authors used data from 5 major randomized clinical trials testing rt-PA in acute ischemic stroke. They developed logistic regression equations using clinical variables as potential predictors of a good outcome (defined as modified Rankin Scale score = 5) with and without use of rt-PA. To predict good outcome, the rt-PA treatment, age, diabetes, stroke severity, gender, prior stroke, systolic blood pressure, and time from symptom onset significantly affected prognosis. To predict catastrophic outcome, only age, stroke severity, and serum glucose significantly affected prognosis; rt-PA did not. The Stroke-TPI that was created is capable of predicting good and bad functional outcomes for acute ischemic stroke patients with and without thrombolysis.

Consider the following 2 acute ischemic stroke scenarios: In the first scenario, a 77-year-old woman with a history of diabetes mellitus presented to the emergency department relatively late in the course of her stroke symptoms. Her systolic blood pressure was 140 mm Hg, her serum glucose was 15.2 mmol/L, and her National Institute of Health Stroke Scale (NIHSS) score was low, only 5. By the time she had her intravenous lines placed, blood tests drawn and processed, and computed tomography of brain conducted and interpreted, the 3-hour window was nearly closed, at 179 minutes. The treating physician, patient, and accompanying family members had a critical decision to make and essentially no time in which to make it. The physician drew on traditionally available resources and clinical experience. In the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study, on average, an acute ischemic stroke patient treated with rt-PA might expect an absolute risk reduction ranging from 11% to 15%, depending on the functional outcome scale. The physician attempted to balance that estimated treatment effect with the potential risk of harm from a symptomatic intracranial hemorrhage, quoted as 6.4%. The physician acknowledged that the later the treatment is administered, the lower the likelihood of a favorable outcome. A summary of postmarketing reports of rt-PA use in ischemic stroke has demonstrated that failure to adhere to indications and contraindications outlined in the guidelines, including time window, is associated with an increased risk of hemorrhagic complications. Finally, the treating physician’s common experience has been that there is invariably a good spontaneous recovery associated with a mild stroke, NIHSS score of 5, regardless of treatment. Ultimately, a decision was made to withhold rt-PA as the perceived risk outweighed the perceived benefit.

In the second scenario, a young woman age 51 presented to the emergency department with a severe ischemic stroke, NIHSS score of 29. Her systolic blood pressure was 165 mm Hg, serum glucose was 13.1 mmol/L, and after all her examinations, diagnostic tests, and brain imaging were performed, 2 hours had already elapsed since symptom onset. Once again, a critical treatment decision had to be made. The prevailing thought that ran through the mind of the treating physician was that the woman’s prognosis was invariably extremely
poor, based on the clinical stroke severity at presentation.\textsuperscript{10,11} Additionally, the physician was reminded that a very high NIHSS score was at least a relative contraindication to administration of rt-PA. The physician recalled that the stroke severity was an independent predictor of symptomatic intracranial hemorrhage. Most patients with a symptomatic intracranial hemorrhage experienced a severe stroke (NIHSS score $>20$). The physician estimated the risk of such a hemorrhage in this woman to exceed 17%.\textsuperscript{12} After presenting the pros and cons to the family, the collective decision was that rt-PA was probably futile and even potentially harmful. The family grieved but felt that they understood the logic behind withholding rt-PA therapy.

In these fictional examples, the evidence-based and experience-based clinical decision-making is vulnerable to potential errors in judgment. Only some of the available evidence was used by the decision-making parties. Most of the physicians’ predictive estimates of prognosis were nonquantitative, imprecise, and even vague. Even the quoted quantitative estimates of various potential outcomes of effect and harm with or without rt-PA were hard to interpret for patients, family members, and clinicians.

Now imagine the same 2 clinical scenarios with the Stroke-TPI available for use by the treating physician. In the first case, the following patient characteristics were entered into the Stroke-TPI on a handheld computer system: age 77 years, female gender, diabetes, no prior stroke, $140$ mm Hg systolic blood pressure, glucose of $15.2$ mmol/L, NIHSS score of 5, and a symptom onset to treatment time of 179 minutes. The patient-specific predictions of outcome probabilities were instantly calculated and presented. As the physician had suspected, the probability of a normal or near-normal outcome without rt-PA was already quite good, at 48%, and the probability of having a catastrophic outcome was truly low, at only 13%. What was incredibly valuable was the estimate of a normal or near-normal outcome after administration of rt-PA in this woman, 72%. This quantity could easily be compared with the 48% chance of a good outcome without treatment, yielding an impressive 24% absolute risk difference. It is this risk difference that was formerly falsely perceived, by the decision-making parties, to be low or even negligible. Given this valuable, tailored, applicable, quantitative information, a different conclusion might have been reached—to treat—despite the mild stroke and late symptom onset to treatment time.

In the second case, these patient characteristics were entered: age 51 years, female gender, no diabetes or prior stroke, $165$ mm Hg systolic blood pressure, serum glucose of $13.1$ mmol/L, NIHSS score of 29, and 122 minutes from symptom onset to treatment time. The patient-specific predictions of outcome probabilities were calculated and presented. It was confirmed that the probability of a catastrophic outcome was very high, 51%, whether rt-PA was used or not. It was also confirmed that the probability of a good outcome, without rt-PA, was extremely low, 4%. What was better presented using the Stroke-TPI tool was the 9% probability of a good outcome with administration of rt-PA. If the husband of this woman was presented quantitative estimates of various outcomes, in this fashion, the ultimate treatment decision may have been a different one. Although he already appreciated that there was a fifty-fifty chance of catastrophic outcome regardless of treatment choice, he could now see that his wife had a 1 in 11 (9%) chance of making a good recovery with rt-PA versus a 1 in 25 (4%) chance without rt-PA. Armed with this quantitative information, a treatment attempt with rt-PA might not seem quite so futile. These case examples illustrate how this predictive instrument could potentially support point-of-care physician decision-making and counseling of patients and families.

A few limitations exist. The authors point out that the predictive equations are based on outcomes achieved in major randomized clinical trials. Thus, the outcome predictions may not be reliable for patients who are not well represented in the database (eg, the very elderly and those with pre-existing disability) and for instances when there is less than strict adherence to treatment protocols. The Stroke-TPI appears to be a well-conceived, valid, and potentially useful predictive instrument. The next natural step would be to study the effect it has on physician clinical decision-making and on patient outcomes.

Disclosures

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References


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