Validating the Stroke-Thrombolytic Predictive Instrument in a Population in the United Kingdom

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Background and Purpose—This study aimed to test the explanatory qualities of the Stroke-Thrombolytic Predictive Instrument (S-TPI) when applied to patients treated in routine practice.

Methods—S-TPI predictions were compared with observed outcomes in terms of normal/near-normal (modified Rankin Scale score, ≤1) and catastrophic outcome (modified Rankin Scale score, ≥5) at 3 months. Logistic regression was used to calibrate and expand the S-TPI.

Results—The S-TPI overestimated probability of catastrophic outcomes and overestimated the probability of a normal/near normal outcome above 0.4 and underestimated those below. Calibrating the S-TPI minimized discrepancies between predicted and observed outcomes, in the case of normal/near-normal outcomes, where including additional predictors (serum glucose and signs of current infarction on pretreatment brain scan) further reduced discrepancies between predicted and observed outcomes.

Conclusions—The explanatory power of the S-TPI in thrombolytic-treated patients can be improved to reflect outcomes seen in routine practice. (Stroke. 2012;43:3378-3381.)

Key Words: acute stroke ■ clinical decision support ■ predictive models ■ thrombolysis

Predictive equations are useful to support clinical decision-making about thrombolysis with recombinant tissue plasminogen activator in acute stroke and to communicate risk/benefit information to patients and families.1 The Stroke-Thrombolytic Predictive Instrument2 (S-TPI) provides patient-specific predictions at 3 months for the likelihood of a normal/near-normal outcome (modified Rankin scale score, ≤1: no symptoms or slight disability), referred to as a normal outcome hereafter, and of catastrophic outcome (modified Rankin Scale score ≥5: severe disability/death).

A single-center cohort study (N=301) reported the S-TPI had reasonable external validity when applied to patients treated in routine practice but overestimated and underestimated probabilities for normal and catastrophic outcomes, respectively.3 We aimed to identify sources of prediction discrepancies between the S-TPI and outcomes in a larger population of patients treated in routine practice and to identify extensions that enhance the explanatory properties of the S-TPI.

Materials and Methods

Calibration curves were used to establish how predictions from the S-TPI corresponded with outcomes in the Safe Implementation of Treatments in Stroke United Kingdom (SITS-UK)4 population treated with recombinant tissue plasminogen activator between December 2002 and February 2010 in United Kingdom centers (N=4022).

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Original S-TPI Predictions of Outcomes in SITS-UK Data
Calibration curves for predicted probability of the S-TPI of normal and catastrophic outcomes in the SITS-UK population are shown in Figure A and B. The S-TPI underpredicts the probability of catastrophic outcomes in the SITS-UK population; for example, a predicted \( P = 0.60 \) equates to an actual observed \( P = 0.50 \) (Figure A). The S-TPI overpredicts the probability of normal outcomes in the SITS-UK population (Figure B). At low probabilities of normal outcome, the overprediction is reversed and the S-TPI underpredicts.

Calibration for Normal Outcomes
The parameter estimates for the calibrated S-TPI are shown in Table 2. The S-TPI prediction is retained \( (1.3770; P = 0.0117) \). No prediction discrepancy is associated with diabetes, previous stroke, and systolic blood pressure. Prediction discrepancy is associated with male gender, age, and National Institutes of Stroke Scale score. Of the additional predictors, infarction on pretreatment brain scan and serum glucose are also found to be associated with a normal outcome. Figure C shows the improved areas under the curve (0.754–0.766) for the calibrated S-TPI models for all cases, including those who did not survive to 3 months, reflecting the S-TPI finding of an absence of association between treatment with recombinant tissue plasminogen activator and death.

Calibration for Catastrophic Outcomes
The SITS-UK population risk of catastrophic outcome was greater than predicted by the S-TPI (Table 2). No receiver-operating curve is shown for catastrophic outcome because the parsimonious recalibrating does not affect the ranking of case, but the area under the curve is 0.784.

Discussion
Consistent with previous research, we found evidence that the S-TPI overestimates the probability of a normal outcome and underestimates the probability of a catastrophic outcome in treated patients. The strength of the calibrated S-TPI model is its applicability to current practice because the predictions are adjusted using data about patients routinely treated up to year 2010, and it includes additional patient characteristics.

In terms of weaknesses, there may have been bias in the routine practice data. For example, I possible reason for the overprediction of normal outcomes is that United Kingdom clinicians (compared with European/North America clinicians) may assign lower modified Rankin Scale scores to patients with similar levels of disability. Studies assessing inter-rater reliability of modified Rankin Scale scores show only modest agreement, with a kappa of \(<0.5\). Prediction discrepancies associated with men and additional predictors mean that untreated outcomes cannot be estimated using the calibrated model. Like the S-TPI, our model predicts no overall harm from treatment; its use as a guide for clinical decision-making is only warranted when thrombolytic treatment is considered to have no association with increased mortality (an assumption more valid at a population level than an individual level) or used with separate predictors of harmful outcomes.
Conclusion
Notwithstanding the assumption about the association between treatment and death, our findings suggest that recalibrated S-TPI is a good basis for predicting outcomes at 3 months in treated patients and its explanatory power can be improved to reflect outcomes seen in routine practice.

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References
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