Modest Association between the Discharge Modified Rankin Scale Score and Symptomatic Intracerebral Hemorrhage after Intravenous Thrombolysis

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Background: Thirty- and 90-day modified Rankin Scale (mRS) scores are used to monitor adverse outcome or symptomatic intracerebral hemorrhage (sICH) in ischemic stroke patients after intravenous (IV) thrombolytic therapy. Discharge mRS scores are more readily available and could serve as a proxy for 30- or 90-day mRS data. Our goal was to evaluate agreement between the discharge mRS score and sICH. Additionally, we tested for correlations between the discharge mRS score and 8 clinical scores developed to predict sICH or adverse outcomes based on 90-day mRS data. *Methods:* Clinical data were analyzed from 210 patients receiving IV thrombolysis from January 2009 till December 2013 at the Yale New Haven Hospital. Agreement between sICH and the discharge mRS score was assessed using linear kappa. Eight clinical scores were calculated for each patient and compared with the discharge mRS score by univariate logistic regression. Goodness of fit was tested by receiver operating characteristic (ROC) analysis and by Hosmer–Lemeshow statistics. *Results:* We found only modest agreement between sICH and unfavorable discharge mRS scores (mRS ≥5), with kappa .22, $P = .0001$. All 8 clinical scores tested showed good agreement with discharge mRS score of 5 or more (ROC area >.7). *Conclusions:* The discharge mRS score shows only modest agreement with sICH and therefore cannot be recommended as a proxy for 30- or 90-day mRS data. However, the discharge mRS score correlates strongly with clinical scores predicting long-term adverse outcome; therefore, assessment of discharge mRS scores may be of some clinical benefit. **Key Words:** Ischemic stroke—hemorrhagic transformation—IV thrombolysis—alteplase—modified Rankin scale—symptomatic intracerebral hemorrhage.
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The Rankin Scale was modified by the United Kingdom Transient Ischaemic Attack study group to measure overall independence after a stroke.[1] This modified Rankin Scale (mRS) gives a better indication of the patient's ability to look after themselves in daily life and shows moderate-to-good interobserver agreement.[2] Thirty- or 90-day mRS scores are routinely used to measure long-term functional deficits after ischemic stroke. They are particularly useful for monitoring adverse outcomes associated with symptomatic intracerebral hemorrhage (sICH) in ischemic stroke patients treated with intravenous (IV) thrombolysis (rt-PA), because standard dose

rt-PA administration carries a significant risk of subsequent sICH—up to 6%-30% depending on the sICH definition in use.[3-5] Long-term mRS scores are not readily available at many stroke centers because they require structured interviews performed by trained and certified raters.[6] Discharge mRS scores on the other hand are routinely assessed at most stroke centers and are strong independent predictors of disability at 90 days, although they showed only modest agreement with 90-day mRS scores in 1 study.[7] Discharge mRS scores are an attractive alternative to long-term mRS scores for assessing functional outcome in ischemic stroke patients after rt-PA therapy.

A number of other clinical scores have been developed to predict sICH or adverse outcome in patients undergoing IV thrombolytic therapy, including the Stroke-Thrombolytic Predictive Instrument (Stroke-TPI),[8] iSCORE,[9] DRAGON ([hyper]Dense cerebral artery sign/early infarct signs on admission CT scan, prestroke modified Rankin Scale (mRS) score, Age, Glucose level at baseline, Onset-to-treatment time, and baseline National Institutes of Health Stroke Scale),[10] Stroke Prognostication using Age and NIH Stroke Scale-100 (SPAN-100),[11] Acute Stroke Registry and Analysis of Lausanne (ASTRAL),[12] Post-thrombolysis Risk Score (PRS),[13] Hemorrhage After Thrombolysis,[14] SEDAN (Sugar, Early infarct signs and [hyper]Dense cerebral artery sign on admission computed tomography scan, Age, and NIH Stroke Scale on admission),[15] and Safe Implementation of Treatments in Stroke Symptomatic Intracerebral Hemorrhage (SITS-ICH) scores.[16] Several of these scores were developed to predict patient outcomes based on 90-day mRS scores; however, their correlation with discharge mRS scores have not been previously tested. In this study, we investigated agreement between discharge mRS scores and the presence of sICH. Additionally, we tested for correlations between discharge mRS scores and 8 clinical scores for predicting sICH or long-term adverse outcome after rt-PA administration.

Methods

Patient Data

Demographic and clinical data were retrospectively analyzed from all consecutive patients (n = 210) who had a principal or secondary discharge diagnosis of ischemic stroke and received IV rt-PA therapy from January 2009 until July 2013 at Yale New Haven Hospital.[17] Patients transferred from an outside institution after IV rt-PA administration were excluded, as were patients who subsequently underwent intra-arterial rt-PA or neurointerventional procedures with mechanical clot retrieval devices. One patient was excluded because of incomplete data. Eligibility criteria for IV rt-PA treatment were applied following the American Heart Association guidelines.[18] This study was approved by the Yale Human Investigation Committee and the Yale Human Research Protection Program.

Imaging Data

Computed tomography (CT) or magnetic resonance imaging scans were performed on each patient before IV rt-PA treatment, at 24 hours after treatment, and subsequent to any observed clinical deterioration. Neuroradiologic assessment of hypodense CT lesions, hyperdense vessels, and intracerebral hemorrhage was performed on each patient by a trained neurologist (H.A.). Stroke severity was assessed by National Institute of Health Stroke Scale (NIHSS) score at baseline.

Clinical Scores and Outcome Data

The discharge mRS score was calculated for each patient as a continuous variable and discharge mRS scores of 5 or more and 4 or more as binary variables. Eight clinical scores were also calculated for each patient: Stroke-TPI, DRAGON, SPAN-100, ASTRAL, PRS, Hemorrhage After Thrombolysis, SEDAN, and SITS-ICH. Detailed derivations of each score have been published elsewhere[8,9,11-15] and are summarized in Table 1. The iSCORE was excluded because, similar to other authors' concerns,[19] it required detailed patient records including history of renal dialysis and congestive heart failure, which are not readily available in the hyperacute stroke setting. For the Stroke-TPI score, parameter estimates for predicting mRS scores of 5 or more without ASPECTS scores were used.[8] Rather than deriving probabilities from the inverse logit function, parameter estimates were calculated directly for each patient and summed to generate a raw score, which allowed more meaningful comparison with the other scores. All other clinical scores were calculated as previously published.

Statistical Analysis

Agreement between sICH and discharge mRS score of 5 or more or mRS scores of 4 or more was assessed using linear weighted kappa, which measures agreement between 2 raters or metrics after excluding the effect of chance.[20] Univariate logistic regression was performed using each clinical score as an independent variable and discharge mRS, discharge mRS scores of 5 or more, or discharge mRS scores of 4 or more as the dependent variable. Goodness of fit was tested using Hosmer–Lemeshow statistics and areas under the receiver operating characteristic (ROC) curve using the DeLong method.[21] P values less than .05 (2-tailed) were considered statistically significant. All analyses were performed using STATA 13 software package (StataCorp LP, College Station, TX).