Predictors of Long-term Outcome after Intravenous or Intra-arterial Recombinant Tissue Plasminogen Activator Treatment in the Eastern Hungarian Thrombolysis Database

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Background: This prospective single-center study aimed to identify features determining long-term outcome after thrombolysis in a Central European stroke population. *Methods:* Between 1 January, 2004, and 31 December, 2010, 415 patients were treated with recombinant tissue plasminogen activator at the Department of Neurology, University of Debrecen. Stroke severity by the National Institute of Health Stroke Scale score (NIHSSS) and imaging findings by the Alberta Stroke Programme Early Computed Tomography score (ASPECTS) were evaluated on admission and 1 day later. The modified Rankin Scale (mRS) at 3 months and case fatality at 1 year were evaluated. Independent predictors of outcome were identified by multivariate testing. *Results:* Data of 369 patients were analyzed. Median NIHSSS was 12 (interquartile range [IQR], 8-17) on admission and 10 (IQR, 5-16) at 24 hours. Arterial occlusion was found in 55%. Symptomatic intracerebral hemorrhage (SICH) was detected in 3.8%. Outcome was significantly worse, and SICH was more frequent in intra-arterially treated patients. At 3 months, one third of the patients were independent (mRS ≤2), and 23% were dead. At 1 year 2 of 3 patients were alive. Significant independent predictors of disability at 3 months were 24-hour NIHSSS, admission ASPECTS, admission glucose level, and treatment modality. Only the 24-hour NIHSSS was a significant predictor of case fatality at 1 year. *Conclusions:* Although short-term outcome was similar, the 3-month and 1-year outcomes were worse than data from previous reports. A more efficient health care program should be implemented after stroke to maintain the favorable effect of thrombolysis in the long term. **Key Words:** Ischemic stroke—thrombolysis—predictors—outcome.

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Introduction

The National Institute of Neurological Disorders and Stroke (NINDS) study proved the efficacy of thrombolysis with recombinant tissue plasminogen activator (rtPA) within 3 hours of stroke onset.[1] The European Cooperative Acute Stroke Study (ECASS) III trial established the benefits of intravenous (IV) rtPA in the time window of 3-4.5 hours,[2] also confirmed by real-life data from the Safe Implementation of Treatment in Stroke (SITS) International Stroke Thrombolysis Register.[3] There are only few data on predictors of long-term outcome after rtPA treatment in stroke. Favorable outcome at 1 year after rtPA administration within 3 hours was reported by Kwiatowski et al.[4] A recent meta-analysis of data of 7012 patients indicates that IV rtPA increases the proportion of patients with favorable outcome.[5] In the Virtual International Stroke Trials Archive, considerable geographic differences were seen in stroke outcome of patients participating in clinical trials.[6] For this reason we assume that long-term outcome after rtPA treatment in stroke may also differ regionally and set forth to present patient characteristics and to identify factors with impact on long-term outcomes of rtPA-treated stroke patients in Hungary.

Methods

Subjects

Between 1 January, 2004, and 31 December, 2010, 415 patients were treated with rtPA at the Department of Neurology, University of Debrecen, with a catchment area of 600,000 inhabitants and 600-700 acute stroke hospitalizations per year. For IV treatment, the time window from symptom onset was 3 hours until October 2008, and 4.5 hours afterward. Intra-arterial (IA) use of rtPA was approved by the Local Research Ethics Committee of the University of Debrecen with a 6-hour time window. Cases where treatment indication did not follow the guidelines[7,8] were excluded, and 369 patients' data were analyzed. Four patients were lost to long-term follow-up (Fig 1).

Database

A database was created recording age, gender, time of stroke onset, time of arrival to the hospital, time of the computed tomography (CT) scan result, time of administration of rtPA, previous medical history (hypertension, diabetes mellitus, atrial fibrillation, heart failure, self reported smoking, and alcohol consumption habits), on-admission stroke severity (including the National Institute of Health Stroke Scale score [NIHSSS]),[9] pre-stroke modified Rankin Scale (mRS) score,[10,11] systolic and diastolic blood pressure before the initiation of rtPA administration, serum glucose, international normalized ratio, activated partial thromboplastin time, cholesterol, triglyceride, on-admission CT/computed tomography angiography (CTA) scan, digital subtraction angiography if performed, and a follow-up (24 hours ± 2 hours) CT scan. We registered the NIHSSS at 24 hours, medications for secondary prevention, mRS at 3 months, and survival status at 1 year.

Imaging

A non-contrast CT was performed on admission. Arterial occlusion (trunk or at least 1 branch of any large artery) was identified by CTA. CT was repeated 1 day after treatment and in case of clinical deterioration. The Alberta Stroke Programme Early Computed Tomography score (ASPECTS) was determined unblinded to patient characteristics and was stratified to 7 and less (group I-severe) and above 7 (group II-mild).[12,13] Hemorrhagic infarction or parenchymal hematoma was defined according to the ECASS.[14,15] We used 3 definitions for symptomatic intracerebral hemorrhage (SICH): the SITS, the ECASS, and the NINDS criteria.[1,14,16]

Treatment

IV treatment was administered according to guidelines.[7,8] Of these 202 cases with CTA-proven vessel occlusion, IA thrombolysis was performed in 46 patients, and in 12 cases, treatment started IV and was followed by IA administration ("bridging" therapy). For IA intervention, repeated doses of 5 mg rtPA was given, until opening of the artery or the maximum IV dose was reached. It was individually decided which treatment modality was used by the treating physician who consulted with the neuroradiologist.

Outcomes

The NIHSSS and case fatality were evaluated the day after admission. The mRS was used to assess outcome at 3 months and dichotomized to favorable (mRS 0-2) and unfavorable (mRS >2).[17] Survival status was evaluated at 1 year.

Statistical Analysis

Statistical analysis was carried out using the SPSS for Windows 19.0 (SPSS Inc, Chicago, IL). Categorical variables were assessed with the Pearson χ^2 test. Binary logistic regression analysis was used to assess outcome at 3 months and at 1 year. Logistic regression models were used to identify the independent predictors of 3-month disability and 1-year case fatality. The analysis was preformed with the multivariate general linear model. In the models, disability at 3 months (mRS >2), and case fatality at 1 year were the dependent variables, and those factors that were found to be associated with outcome by univariate analyses were entered as confounding