Acute Stroke Patients With Mild-to-Moderate Pre-existing Disability Should Be Considered for Thrombolysis Treatment

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Background: Thrombolytic therapy in patients with pre-existing disability presenting with acute ischemic stroke (AIS) is controversial because of concerns regarding poor outcomes and futility of treatment. We hypothesized that a similar proportion of patients with and without pre-existing disability would return to their premorbid functional status following thrombolysis. *Methods:* This was a retrospective study at a single high-volume academic primary stroke center. All patients with AIS treated with intravenous alteplase between January 2005 and July 2016 were included. Premorbid functional status was assessed using modified Rankin scale (mRS) and dichotomized as independent premorbid (mRS 0-1) or disabled premorbid (mRS 2-4) groups for comparison. Functional outcome was assessed by mRS at 90 days and compared between groups. *Results:* Six hundred eighty patients independent premorbid (mean age 71.8 ± 13.1 years, 57.9% male) and 140 disabled premorbid (mean age 82.1 ± 8.7 years, 40.7% male) were included. Patients with pre-existing disability were older and had more vascular risk factors and more severe stroke on presentation ($P < 0.05$). A greater proportion of patients in the disabled premorbid group were dead at 90 days (35.7% versus 12.8%, $P < 0.05$). At 90 days, among patients with premorbid mRS 0, 1, 2, 3, and 4: 25%, 38%, 32%, 30%, and 25% of them returned to their respective premorbid mRS status. *Conclusions:* Irrespective of premorbid functional level, approximately one fourth to one third of thrombolyzed patients had returned to their premorbid functional levels at 90 days. Thrombolytic treatment should be considered in patients with mild-to-moderate pre-existing disability, taking into account the value placed on the chance of a return to premorbid functional status.

Key Words: Acute ischemic stroke—thrombolysis—pre-existing disability—modified Rankin scale

Introduction

Thrombolysis with intravenous alteplase is the standard treatment for patients with acute ischemic stroke (AIS); however, treatment of patients with pre-existing disability remains controversial. These patients are often excluded in acute stroke thrombolysis studies due to the conventional dichotomous analysis of outcome assessments. In practice, patients with pre-existing disability may be excluded from thrombolytic treatment because of concerns about poor outcomes and the potential futility of treatment. However, patients and caregivers may place a high value on the possibility of a return to premorbid functioning even if treatment is associated with the possibility of death.

Published data on the outcomes of thrombolysis for patients with premorbid disability is limited. Pre-existing disability (modified Rankin scale [mRS] >1) is reported in up to 12.5% of treated cases in registry studies,[1-3] with a greater proportion (24.8%) among patients more than 80 years old.[4] In a subgroup analysis of a large Eastern

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European cohort, more than one third of thrombolyzed patients with premorbid mRS greater than or equal to 3 returned to their premorbid functional status post-thrombolytic treatment.[3]

We hypothesized that a similar proportion of patients with and without pre-existing disability would return to their premorbid functional status following intravenous thrombolysis.

Methods

This was a retrospective study at a single, high-volume academic primary stroke center. The departmental stroke database was interrogated for all patients treated with intravenous alteplase between January 2005 and July 2016. All treated patients underwent 24-hour post-treatment brain computed tomography. Age, gender, vascular risk factors, premorbid mRS, initial National Institutes of Health Stroke Scale (NIHSS) score, onset and door-to-needle time, length of stay, symptomatic intracranial haemorrhage (sICH) and asymptomatic ICH (aICH), discharge destinations, mortality, and 3-month mRS were evaluated and compared between groups.

Included patients were categorized as independent premorbid (mRS 0-1) or disabled premorbid (mRS 2-4). The sICH was defined by the presence of parenchymatous hemorrhage type 2 on the 24-hour post-thrombolysis scan combined with neurological deterioration with greater than or equal to 4 points increase from baseline NIHSS score.[1] The study was approved as a quality assurance study by our institutional Human Research and Ethics Committee, with no written informed consent required.

Statistical Analysis

The frequency distributions of categorized variables were compared by using Fisher's exact test and Student's t test as appropriate. The significance level was set at $P < 0.05$. Multivariable regression analysis was used to explore variables associated with mortality and poor functional outcome at 90 days. The analysis was performed using Stata 14 (StataCorp LP, College Station, TX).

Results

Patient Characteristics

Two thousand six hundred and ninety-three patients were admitted to our center with AIS within the thrombolysis window (3 hours from symptoms onset for the years 2005-2008, 4.5 hours from the year 2009 to 2016). Eight hundred twenty patients (30.4%) were treated with intravenous alteplase and included in the analysis. Mean age was 73.5 years (±13.0) and 54.8% were male. There were 680 and 140 patients without and with pre-existing disability, respectively. No patients with premorbid mRS 5 were treated with thrombolysis. Among the 262 patients with mRS 3 and 159 patients with premorbid mRS 4, 162 (60.3%) and 119 (74.8%), respectively, were excluded from alteplase treatment. Most commonly the exclusion reason was documented due to their poor premorbid function. Other exclusion reasons included history of ICH, terminal illness, NIHSS more than 22, and current anticoagulant use.

Patients with pre-existing disability were significantly older, more likely to be female and to have vascular risk factors, and had more severe stroke (baseline NIHSS 12.3 versus 10.4, $P < 0.05$) on presentation (Table 1). These

Table 1. *Patient characteristics*

Groups (premorbid status)	Independent group (mRS 0-1)	Disabled group (mRS 2-4)
Number	680	140
Age (mean + SD, years)*	71.8 ± 13.1	82.1 ± 8.7
Male (%)*	57.9	40.7
Comorbidities (%)		
Atrial fibrillation*	35.4	48.6
Hypertension*	63.2	77.1
Hypercholesterolemia	39.3	35.0
Diabetes*	14.4	27.1
Previous history of Stroke*	15.2	27.1
IHD/CCF*	18.1	35.0
Smoker*	13.7	4.3
Ex-smoker	12.8	12.9
Baseline NIHSS (median)*	9.0	12.0
Onset-to-needle time (minutes, median)*	148.5	160.0
Door-to-needle time (minutes, median)	68.0	73.0
Length of stay (days, median)	6.0	8.0

Abbreviations: CCF, congestive cardiac failure; IHD, ischaemic heart disease; NIHSS, the National Institutes of Health Stroke Scale; SD, standard deviation.

*$P < 0.05$.