Stroke



**BRIEF REPORT**

# Five-Year Outcome in Stroke Patients Submitted to Thrombolysis

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## Abstract

**Background and Purpose—**Little is known on long-term follow-up after thrombolysis in ischemic stroke patients because the majority of studies evaluated outcome at 3 to 12 months. We aimed to assess 5-year outcome after intravenous thrombolysis (IVT).

**Methods—**Cohort study based on the prospective registry of all consecutive ischemic stroke patients submitted to IVT in our Stroke Unit. Five-year outcome, including living settings, functional outcome, stroke recurrence, and mortality, was ascertained by telephonic interviews and additional review of clinical records. Multivariate analyses were performed to identify predictors of outcome and mortality. Excellent outcome was defined as modified Rankin scale 0 to 1.

**Results—**Five-year outcome was available for 155/164 patients submitted to IVT. At 5 years, 32.9% of patients had an excellent outcome (95% confidence interval (CI) =25.5–43.3) and mortality was 43.9% (95%CI=36.1–51.7). Increasing age (odds ratio =0.93, 95% CI =0.90–0.97) and increasing National Institute of Health Stroke Scale (NIHSS) 24 h after thrombolysis (odds ratio =0.81, 95% CI =0.74–0.90) were independently associated with a lower likelihood of an excellent 5-year outcome. Age (hazards ratio =1.07, 95% CI =1.03–1.11) and excellent functional outcome 3 months after thrombolysis (hazards ratio =0.28, 95%CI=0.12–0.66) were independently associated with mortality during follow-up.

**Conclusions—**One third of ischemic stroke patients have excellent 5-year outcome after IVT. Younger age, lower NIHSS 24 h after IVT, and excellent 3-month functional outcome are independent predictors of excellent 5-year outcome.

mortality stroke thrombolytic therapy treatment outcome

# Introduction

Thrombolytic therapy with intravenous alteplase (IVT) is an effective treatment in acute ischemic stroke when administered ≤4.5 h.[1] However, most studies addressing outcome have a relatively short follow-up period. Data on long-term outcome is scarce.[2–6] We aimed to assess 5-year outcome after IVT and to identify predictors of excellent outcome and long-term mortality.

# Methods

## Patients and Variables

Cohort study based on the prospective registry of consecutive ischemic stroke patients submitted to IVT in our hospital between February 2007 and February 2010. Clinical data were collected from the registry. Five-year outcome was ascertained by standardized telephone interviews to patients or carers when the patient was unable to provide information. Information on living settings, functional outcome (modified Rankin scale, mRS), stroke recurrence, and mortality was collected. Clinical records in our hospital and regional hospitals were reviewed to collect and confirm follow-up. Outcome was defined as excellent (mRS 0–1) or unfavorable (mRS 2–6). The study complies with the Helsinki Declaration and the local ethics committee requirements for clinical research.

## Statistical Methods

Groups of excellent and unfavorable outcome were compared using $\chi^2$, independent-samples *t*-student and Mann–Whitney U tests as appropriate. Binary logistic regression using 5-year outcome (dependent variable) and variables with $P<0.01$ in univariate analysis (covariates), and survival analysis with Cox proportional hazards regression model using out-of-hospital mortality as end-point were calculated. A sensitivity analysis using the multiple imputations method was performed to account for missing values. IBM SPSS Statistics (version 20) was used.

# Results

Five-year outcome was available for 155/164 patients (94.5%) consecutively submitted to IVT. Baseline characteristics are described in **Table 1**. Patients with excellent outcome had a lower median age ($P<0.001$), lower median admission National Institute of Health Stroke Scale (NIHSS; $P<0.001$), less frequently had Total Anterior Circulation Infarct syndrome ($P<0.001$), had lower NIHSS score 24 h after thrombolysis ($P<0.001$), and more frequently presented excellent outcome 3 months after thrombolysis ($P<0.001$). Mortality at 5 years was 43.9% (n=68), and survival curve is shown in **Figure**. In-hospital mortality during index stroke admission was 9.0% (n=14). Causes of out-of-hospital mortality were acute infectious disease (n=16), organ-specific terminal failure (n=7), stroke recurrence (n=6), neoplastic disease (n=6), sudden death (n=5), and unknown in 14 patients. At 3 months, 39.4% of patients had mRS 0 to 1, and mortality after 3 months was lower in this group ($P<0.001$; Figure I in the online-only Data Supplement). Seventy percent of the patients who were alive at 5 years had NIHSS 24 h after thrombolysis ≤10. Among the 87 patients alive at 5 years, 11 (12.6%) were living with relatives, 4 (4.6%)

were in a nursing home. Twelve of the 87 patients (13.8%) were professionally active at 5 years. Stroke recurred in 12 patients. Increasing age (odds ratio =0.93, 95% confidence interval =0.90–0.97) and increasing NIHSS 24 h after thrombolysis (odds ratio =0.81, 95% confidence interval =0.74–0.90) were independently associated with lower likelihood of excellent 5-year outcome (**Table 2**). Age (hazards ratio=1.07, 95% confidence interval =1.03–1.11) and excellent outcome at 3 months (hazards ratio =0.28, 95% confidence interval =0.12–0.66) were independently associated with mortality during follow-up (**Table 2**). Sensitivity analysis did not alter the results significantly (Table I in the online-only Data Supplement).

**View inline** **View popup**

**Table 1.**

Characteristics of Patients According to Five-Year Outcome

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**Table 2.**

Binomial Logistic Regression and Multivariate Survival Analyses

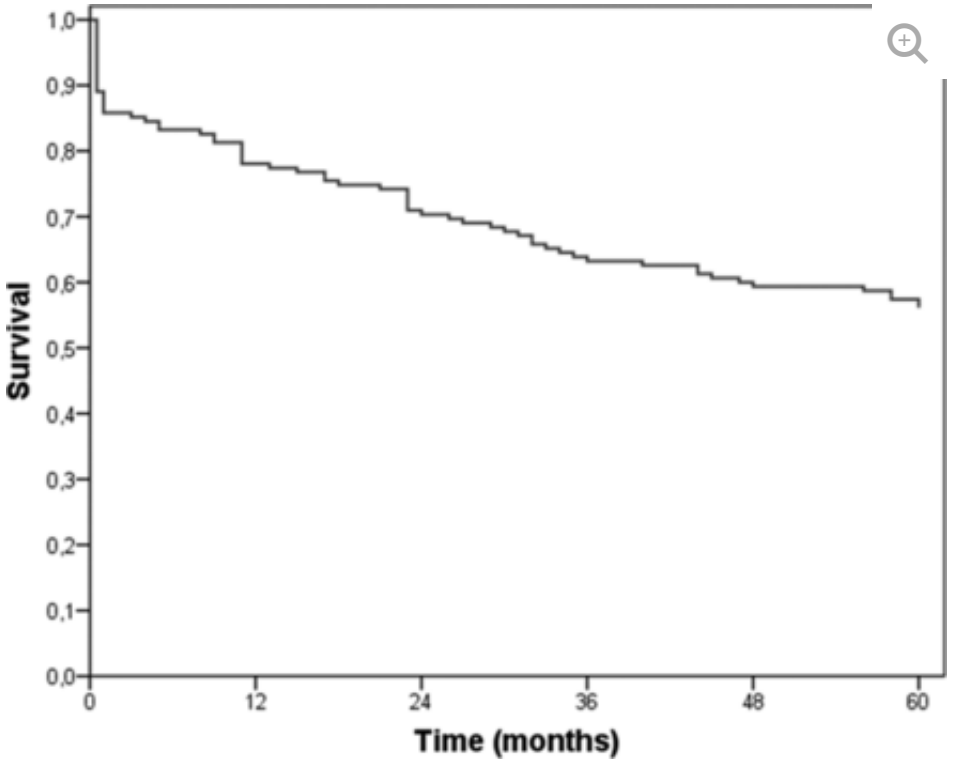


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**Figure.**

Survival curve.

## Discussion

Five years after IVT, 1/3 patients had excellent outcome (mRS 0–1) and almost 1/2 had died. Younger age and lower NIHSS 24 h after IVT were independent predictors of excellent 5-year outcome. Gensicke et al[4] found that higher admission stroke severity was a predictor of unfavorable outcome, but our analysis showed that when adjusted for NIHSS 24 h after IVT, admission stroke severity is no longer a predictor of long-term functional outcome. This suggests that neurological improvement after IVT is a robust predictor of an excellent 5-year outcome, irrespective of initial clinical severity. Studies with long-term follow-up (1–4 years) reported a cumulative mortality of 15% to 53% after IVT.[2–6] Only 3 studies[4–6] had follow-up >12 months, and ours is the first to include 5-year follow-up. Prethrombolytic era 5-year mortality in stroke patients admitted to Stroke Units ranged from 45 to 59.1%,[7,8] and despite lower 5-year mortality in our cohort, direct comparison has limited validity. Annual mortality rate was higher during the first year, decreasing gradually afterward. Age and 3-month outcome were the only independent predictors of 5-year mortality. Although clinical severity 24 h after thrombolysis did not have an impact on long-term mortality, this may be related to a floor effect of the NIHSS. However, excellent 3-month functional outcome was associated with 3.5-fold increase in the likelihood of being alive at 5 years. Our study is in line with observational community-based studies, which showed that ischemic stroke disability predicts 5-year and 7-year survival[9,10] and confirms that better short-term functional outcome after thrombolysis is associated with higher likelihood of being alive at 5 years.

## Conclusions

Approximately 1/3 patients had an excellent 5-year outcome after IVT. Clinical improvement 24 h after IVT is independently associated with excellent long-term outcome, and a better functional outcome at 3 months is associated with long-term survival.

## Acknowledgments

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## Disclosures

None.

## Footnotes

The online-only Data Supplement is available with this article at **http://stroke.ahajournals.org/lookup/suppl/doi:10.1161/STROKEAHA.115.009842/-/DC1**.

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