Research Article

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# Demographic characteristics of patients who recovered or worsened after intravenous thrombolysis within 24 hours of acute ischemic stroke

Yusuf İnanç[1], Zülfikar Arlıer[2], Semih Giray[1], Yılmaz İnanç[3]

[1]Department of Neurology, Gaziantep University School of Medicine, Gaziantep, Turkey
[2]Department of Neurology, Başkent University Adana Application Hospital, Adana, Turkey
[3]Department of Neurology Kahraman Maraş Sütçüimam University School of Medicine, Kahramanmaraş, Turkey

**Abstract**

**Objective:** The aim of this study was to evaluate the demographics of patients who experienced recovery or worsening after receiving intravenous thrombolytic treatment within 24 hours of the onset of acute ischemic stroke (AIS).

**Methods:** This retrospective study included patients with AIS who were admitted to emergency units within 4.5 hours of AIS between January 2012 and December 2015. Recovery was defined as a decrease of ≥4 points in the National Institutes of Health Stroke Scale (NIHSS) score within 24 hours (group I), and worsening was defined as an increase of ≥4 points in NIHSS score within 24 hours compared with admission (group II).

**Results:** The study included a total of 86 patients comprising 55.8% males, with a mean (±SD) age of 61.1 (±13.1) years. The mean patient age was similar in both sexes. Of the total 86 patients, 80.2% experienced recovery within 24 hours (group I) and symptoms worsened in 19.8% (group II). No significant sex or age difference was determined in terms of recovery. Patients receiving thrombolysis within 1-3 hours had a higher recovery ratio compared with patients who received treatment within 3-4.5 hours. Patients without diabetes mellitus had a better recovery ratio compared with those with diabetes mellitus.

**Conclusion:** A relatively high recovery rate was determined at 24 hours after thrombolysis in patients with AIS. Demographic characteristics were not determined to be contributing factors to this outcome, but the time to thrombolytic treatment and having diabetes mellitus were observed to be more significant predictors of patient recovery.

**Keywords:** Acute ischemic stroke, recover, worsening

## INTRODUCTION

Acute ischemic stroke (AIS) is defined as a sudden loss of blood flow to a certain location of the brain, resulting in a loss of neurologic function. Stroke may lead to major disabilities and is also one of the leading causes of death worldwide. In the United States of America (USA), stroke is reported as the third leading cause of death. It is estimated that approximately 795,000 people per year experience a stroke as either a first or recurrent attack. Of all strokes, 87% are ischemic and 10% are intracerebral hemorrhage strokes (1).

Intravenous recombinant tissue plasminogen activator treatment within 4.5 hours of the onset of ischemic stroke is beneficial and significantly improves the clinical outcome (2).

In AIS, dramatic recovery (DR) is an early and stable favorable clinical outcome and also a good predictor of prognosis (3). Various studies have reported that DR occurs in 20-40% of patients with middle cerebral artery stroke after receiving thrombolytic treatment (4-6). Different time points have been considered for the evaluation of DR in different studies and these time windows vary from 1 hour (4) to 24 hours (5) and may even go up to 7 days (5) after the initiation of thrombolytic treatment. In general, the magnitude of clinical improvement is measured by the National Institutes of Health Stroke Scale (NIHSS) score at 24 hours after treatment.

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**Corresponding Author:** Yusuf İnanç **E-mail:** yusufinanc77@hotmail.com **Submitted:** 24 November 2017 **Accepted:** 5 December 2017

In contrast to DR in AIS, neurologic worsening is another common outcome with significant morbidity and mortality. The prevalence of neurologic worsening has been reported as 13-38% and worsening is usually defined using an increase in NIHSS scores (7).

The aim of this study was to evaluate the demographic characteristics of patients who experienced recovery or worsening after receiving intravenous thrombolytic treatment within 24 hours of the onset of AIS.

## METHODS

This study was a multicenter, retrospective, observational, cross-sectional study of patients with AIS who were treated in the Emergency Departments of Başkent University Adana Training and Research Hospital, and medical faculty hospitals of Gaziantep University and Kahraman Maraş Sütçüimam University. Ethics committee approval was received for this study from the ethics committee of Gaziantep University (date: 16-5-2016, approval number: 2016-156). The study included the data of patients who were admitted to the study centers within 4.5 hours of the onset of an AIS and received intravenous thrombolytic treatment between January 2012 and December 2015.

The patients were categorized into 2 groups: group I (patients who recovered) and group II (patients who worsened). Recovery was defined as a decrease of ≥4 points in the NIHSS score within 24 hours, and worsening was defined as an increase of ≥4 points in the NIHSS score within 24 hours compared with admission. Clinical outcome was measured using the Modified Rankin Scale (mRS) in 2 categories as 1) very good outcome (mRS score 0-1) and 2) good outcome (mRS score 0-2).

Statistical analysis was performed using SPSS 22.0 (IBM Corp.; Armonk, NY, USA). The Shapiro-Wilk test was used to test univariate normality and variance homogeneity was evaluated using Levene's test. When comparing two independent groups in terms of quantitative data, the independent samples t-test was used with bootstrapping as a parametric test. Categorical variables were evaluated using Pearson's Chi-square test with the Monte Carlo Simulation technique and exact results of the Fisher exact test. When a significant difference was detected, odds ratio (OR) was used to determine the most significant risk factor and the results are presented with confidence intervals (CIs). Quantitative variables are presented as mean ±standard deviation [SD] and range (minimum-maximum), and categorical variables as number (n) and percentage (%). All variables were analyzed at 95% confidence intervals and a p value of <0.05 was accepted as statistically significant.

Written informed consent was obtained from the parents of the patients who participated in this study.

## RESULTS

The study included a total of 86 patients with AIS, comprising 55.8% males with a mean age of 61.1±13.1 years (range, 24-79 years). The mean patient age was similar in both sexes (males: 64.1 years, females 58.7 years; p>0.05). Of the total 86 patients, 69 (80.2%) experienced recovery within 24 hours of AIS (group I) and symptoms worsened in 17 patients (19.8%; group II). Patients who recovered were younger than those who worsened (mean age 59.8 vs. 66.3 years) although the difference was not statistically significant (p=0.068). No significant sex difference was determined in terms of recovery (Table 1).

The mean NIHSS scores on admission were similar in group I (14.4) and in group II (14.1). At 24 hours after admission, the mean NIHSS score decreased to 4.1 (±3.8) in group I and increased to 16.9 (±4.3) in group II, resulting in a significant difference between the groups (p=0.001) (Table 1).

The time to tissue plasminogen activator treatment had a positive impact on recovery. Patients receiving thrombolysis within 1-3 hours had a higher recovery ratio compared with

**Table 1. Demographic characteristics and NIHSS scores at admission and 24 hours after admission**

| | Worsening (n=17) | | Recovery (n=69) | | Total (n=86) | | |
|---|---|---|---|---|---|---|---|
| | Mean ±STD. | Max.-Min. | Mean ±STD. | Max.-Min. | Mean ±STD. | Max.-Min. | p |
| **Age (years)** | | | | | | | |
| Admission | 66.29±12.08 | 78-34 | 59.80±13.14 | 79-24 | 61.08±13.13 | 79-24 | 0.068 |
| **NIHSS Score** | | | | | | | |
| Admission | 14.06±4.39 | 20-6 | 14.38±5.66 | 25-4 | 14.31±5.42 | 25-4 | 0.789 |
| 24 hours | 16.88±4.34 | 24-9 | 4.07±3.84 | 16-0 | 6.60±6.46 | 24-0 | 0.001 |
| | N | % | N | % | N | % | |
| **Gender** | | | | | | | |
| Female | 7 | 41.2% | 31 | 44.9% | 38 | 44.2% | >0.99 |
| Male | 10 | 58.8% | 38 | 55.1% | 48 | 55.8% | |

NIHSS: National Institutes of Health Stroke Scale; STD: standard deviation; max: maximum; min: minimum

**Table 2. Clinical characteristics of the patients**

| | Worsening (n=17) | | Recovery (n=69) | | Total (n=86) | | |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | p |
| **Time to TPA treatment** | | | | | | | |
| 1-2 hours | 1 | 5.9% | 9 | 13.0% | 10 | 11.6% | 0.045 |
| 2-3 hours | 3 | 17.6% | 30 | 43.5% | 33 | 38.4% | |
| 3-4.5 hours | 13 | 76.5% | 30 | 43.5% | 43 | 50.0% | |
| **Symptomatic hemorrhage within 36 hours - NIHSS≥4)** | | | | | | | |
| No | 11 | 64.7% | 69 | 100.0% | 80 | 93.0% | <0.001 |
| Yes | 6 | 35.3% | 0 | 0.0% | 6 | 7.0% | |
| **Very good outcome (mRS 0-1)** | | | | | | | |
| No | 17 | 100.0% | 30 | 43.5% | 47 | 54.7% | <0.001 |
| Yes | 0 | 0.0% | 39 | 56.5% | 39 | 45.3% | |
| **Good outcome (mRS 0-2)** | | | | | | | |
| No | 16 | 94.1% | 18 | 26.1% | 34 | 39.5% | <0.001 |
| Yes | 1 | 5.9% | 51 | 73.9% | 52 | 60.5% | |
| **Mortality** | | | | | | | |
| No | 6 | 35.3% | 66 | 95.7% | 72 | 83.7% | <0.001 |
| Yes | 11 | 64.7% | 3 | 4.3% | 14 | 16.3% | 40 (8.7-200)* |
| **Diabetes** | | | | | | | |
| No | 7 | 41.2% | 49 | 71.0% | 56 | 65.1% | 0.026 |
| Yes | 10 | 58.8% | 20 | 29.0% | 30 | 34.9% | 3.5 (1.2-10.5)* |
| **Cardiac failure** | | | | | | | |
| No | 12 | 70.6% | 63 | 91.3% | 75 | 87.2% | 0.037 |
| Yes | 5 | 29.4% | 6 | 8.7% | 11 | 12.8% | 4.4 (1.2-16.7)* |

NIHSS: National Institutes of Health Stroke Scale; mRS: modified rankin scale; TPA: tissue plasminogen activator; STD: standard deviation; max: maximum; min: minimum
*Odds Ratio (95% Confidence interval)

those who received treatment within 3-4.5 hours (p=0.045) (Table 2).

Patients without diabetes mellitus had a better recovery ratio compared than those with diabetes mellitus (p=0.026, OR: 3.5, 95% CI:[1.2-10.5]) and lower mean serum glucose levels were detected in patients who recovered compared with patients who worsened (120 vs. 174 mg/dL, p<0.001). Symptomatic hemorrhage was detected in 6 patients within 36 hours of the onset of stroke and no hemorrhage was observed in patients who recovered (p<0.001) (Table 2).

Of the total patients, 54.7% did not have a good outcome. In group I, a very good outcome was determined in 56.5% of patients, as expected (p<0.001). On the basis of the mRS, 60.5% of patients had a good outcome (p<0.001; Table 2).

A cerebrovascular event leading to death was observed in 16.3% of patients and mortality was not observed in the majority (95.7%) of the patients in group I (p=0.037, OR: 40, 95% CI:[8.7-200]) (Table 2).

No cardiac failure was detected in 87.2% of the total patient group. No cardiac failure developed in 91.3% of group I (p=0.037, OR: 4.4, 95% CI:[1.2-16.7]) (Table 2).

An evaluation was made of other factors including the hemispheric side of the stroke (right, left or both), location of circulation (anterior or posterior), Trial of ORG 10172 in Acute Stroke Treatment (TOAST) Classification (atherosclerotic, cardioembolic, small-vessel occlusion, other, or cryptogenic), presence of hemorrhagic transformation, hypertension, chronic kidney disease, hyperlipidemia, history of smoking, antiplatelet treatment, atrial fibrillation, and previous stroke. No significant difference was determined between group I and group II in terms of these factors.

## DISCUSSION

In the current study, an examination was made of the clinical outcomes of patients with AIS who received intravenous thromboembolic treatment within 4.5 hours of stroke onset and the demographic characteristics were compared in patients who recovered or worsened.

At 24 hours after the intravenous thrombolytic treatment, a very high rate of recovery (80.2%) was determined in the current study population. In a recent study, Gill et al. examined 435 patients with AIS who underwent thrombolysis and reported a NIHSS score reduction of 5 points at 24 hours after the thrombolysis (8). The results of the current study revealed a higher reduction of 10 points in the recovery group (group I). The time to thrombolytic treatment was compared in both studies and was not found to be a reason for this difference.

Stroke can occur at any age, although it occurs in older people more frequently. In the USA, three-quarters of all strokes occur in people aged over 65 years, and the risk of stroke more than doubles after the age of 55 years. However, the predictive value of age on stroke outcome is still controversial. According to the current study results, patient age was similar in patients with good or poor outcomes, suggesting that age is not a predictor of clinical outcome. Numerous reports are available mentioning the association between age and poor outcome. Some of these studies examined the Functional Independence Measure (FIM) as a measure of outcome and compared the results at discharge to baseline. Bagg et al. reported that age was not a significant predictor of outcome in terms of FIM change (9). Similarly, Luk et al. mentioned in their report that age was not an independent predictor for good outcome, and therefore recommended that older patients should receive the same intensive rehabilitation as younger stroke patients (10). The current study results are in line with these two reports and also seem to indicate that age is not a predictor of clinical outcome.

Sex difference in stroke has been studied in many local and multinational studies and has been found, in general, to be more common in females. Compared with males, females are reported to have a higher risk of stroke and are more likely to experience recurrent stroke. More severe strokes are observed in females than males (1). A poorer recovery after ischemic stroke has been reported for female patients compared with males in many studies (11-13). In the current study, no sex difference was determined in terms of stroke outcome at 24 hours after initiation of thromboembolic treatment.

The importance of time to initiation of intravenous tissue-plasminogen activator has been mentioned in many studies and reviews (2, 14). The current study results are in line with published literature suggesting that early treatment initiation is associated with a better recovery in AIS.

In general, patients with AIS with diabetes mellitus have poorer outcomes and this is not linked with intracerebral hemorrhage (15, 16). The results of the current study demonstrated a better rate of recovery of patients without diabetes, which is similar to findings in the published literature. Although no symptomatic hemorrhage was detected in the patients who recovered, no further investigation was undertaken in the current study to reveal the relationship between hemorrhage and diabetes.

In patients with AIS, a relatively high recovery rate was determined at 24 hours after intravenous thrombolytic treatment compared with findings in the published literature. However, demographic characteristics such as age and sex are not contributory factors in this outcome. The time to thrombolytic treatment and having diabetes mellitus were more significant predictors for patient recovery.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Gaziantep University School of Medicine (2016-156).

**Informed Consent:** Written informed consent was obtained from the parents of the patients who participated in this study.

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