Initial Glasgow Coma Scale Score Predicts Outcome Following Thrombolysis for Posterior Circulation Stroke

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Background: Randomized trials of thrombolytic stroke treatment have either excluded patients with posterior circulation ischemia or used inclusion criteria making enrollment of these patients less likely. Consequently, there is less published information on thrombolytic therapy for posterior circulation stroke.

Objective: To determine effective thrombolytic treatment times for posterior circulation stroke and factors that might help predict clinical outcome.

Design: We describe our experience treating 21 consecutive patients with either intravenous or intra-arterial thrombolytic therapy for posterior circulation ischemic stroke between October 9, 1993, and February 19, 2001.

Main Outcome Measures: National Institutes of Health Stroke Scale, Glasgow Coma Scale, and modified Rankin Scale scores were evaluated at baseline, and the modified Rankin Scale was measured 3 months after stroke, with a good outcome being a modified Rankin Scale score of 2 or less.

Results: Nine patients received intravenous therapy; 12 patients received intra-arterial therapy. The median National Institutes of Health Stroke Scale score at onset was 20 (range, 2-39), and the median Glasgow Coma Scale score was 9 (range, 3-15). Twelve patients were treated within 8 hours of symptom onset (range, 1½ hours to 16 days). Nine patients (43%) had a modified Rankin Scale score of 2 or less at 3 months. The initial Glasgow Coma Scale score and treatment within 8 hours of symptom onset were each associated with good outcome, but the initial National Institutes of Health Stroke Scale score was not predictive.

Conclusions: Thrombolytic therapy for posterior circulation stroke may be beneficial even when initiated 8 hours after symptom onset. Level of consciousness, as measured by Glasgow Coma Scale score, seems to be a more important predictor of outcome than the initial National Institutes of Health Stroke Scale score.

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suggest that mortality rates are lower than previously assumed. Some patients have poor outcomes despite early and complete arterial recanalization while others have relatively good outcomes despite delays in treatment of up to 12 hours. This study was undertaken to further delineate acceptable times for treating posterior circulation thrombosis and to investigate factors that might be useful for predicting patient outcome.

Methods

Patient Selection

Retrospective medical record review was undertaken for 21 consecutive patients who received either IV or IA thrombolytic therapy for posterior circulation ischemic stroke at the University of California, San Francisco between October 9, 1993, and February 19, 2001. Stroke location was confirmed by a reviewing neurologist based on manifesting clinical signs and symptoms and radiological findings.

Main Outcome Measures

The National Institutes of Health Stroke Scale (NIHSS) score was calculated from the medical record at the time of hospital admission, at 1 day, at hospital discharge, and at the 3-month follow-up visit. Results were independently obtained by 2 of us (J.W.T. and D.C.B.). The Glasgow Coma Scale (GCS) score was determined from a description of the admission neurological examination findings and, again, the results were independently verified. Scoring bias owing to sedation or intubation was not found. The modified Rankin Scale (mRS) score was determined at the initial examination and at the 3-month follow-up visit from the patient interview or estimated from medical records. An mRS of 2 or less was considered a good outcome because this score signifies slight or no disability. There were no outcome differences for patients treated at the beginning of the study period vs those treated at the end of the study. Interrater reliability was highly correlated ($r = 0.97$, $r = 0.99$, respectively for NIHSS, GCS, and mRS, using Spearman rank correlation). Adjudication of differences in examiner scoring was made by consensus, and all analyses were performed using the consensus score. Blood flow through the occluded vessel, as seen by angiography, was scored using the Thrombolysis in Myocardial Infarction (TIMI) study criteria. Localization of the affected vascular territory was based on both clinical symptoms and radiological findings from computed tomography (CT) with magnetic resonance imaging (MRI), angiography, or both.

Statistical Analysis

Treatment outcomes were compared using the unpaired t test for continuous variables, the Wilcoxon rank sum test for ordinal variables (NIHSS, mRS, and GCS scores), and the Fisher exact test for unordered categorical and dichotomous variables. All statistical analyses were performed with Stata (version 7.0; Stata Corp, College Station, Tex) and Excel 98 (Microsoft, Seattle, Wash). Commonly measured clinical outcome variables were chosen for analysis to determine if any could predict patient outcomes. Time to thrombolysis was initially considered as an ordered, nonnormally distributed variable and was later dichotomized at 8 hours, as this appeared to be a reasonable clinical cutoff point based on the range of times to treatment. The GCS score was also initially considered as an ordered, nonnormally distributed variable and was later dichotomized at 8, as this is a clinical cutoff point often used to represent coma. Because these variables were not normally distributed, nonparametric univariate analyses were undertaken, but multivariable analyses were not performed.

Results

Twenty-one patients (14 males, 7 females) received thrombolytic therapy: 9 were given IV recombinant tissue plasminogen activator, 9 IA urokinase, and 3 IA recombinant tissue plasminogen activator. Their mean age was 61 ± 18 years (age range, 25-87 years). Twelve patients were treated within 8 hours of symptom onset (range, 1½ hours to 16 days). Seven patients were treated within 3 hours of symptom onset. Of the 5 patients treated between 3 and 8 hours of symptom onset, 2 were treated at 3 hours, 1 at 6 hours, and 2 at 8 hours. The median initial NIHSS score of all patients was 20 (range, 2-39), and the median GCS score was 9 (range, 3-15). One day after receiving thrombolytic therapy 17 patients (81%) showed improved NIHSS scores (12 patients improved ≥ 4 points on the NIHSS).

Nine patients (43%) had a good outcome (mRS score of ≤ 2) at 3 months. Three of these patients received IA therapy, 1 each with initial TIMI flow grades of 0, 2, and 3. In the 9 patients who received IA therapy and had poor outcomes, 5 had an initial flow grade of 0, 1 had a flow grade of 1, and 3 had a flow grade of 2. Two patients with fluctuating symptoms were treated with delayed IA therapy (at 7 and 16 days), and 1 had a good outcome (basilar artery occlusion and a TIMI flow grade of 2). The Table summarizes the association of various other characteristics with outcome. The only characteristics predictive of good outcome were time to thrombolysis and GCS score at stroke presentation. Specifically, disability at stroke onset, as measured by the NIHSS (including analysis of the subset of NIHSS questions assessing consciousness), was not statistically associated with outcome. When time to thrombolysis was dichotomized at 8 hours after stroke onset, a significant treatment effect on 3-month outcome was seen. The median mRS score of the group of patients treated within 8 hours was 1.5 compared with 4 for the group treated at times greater than 8 hours ($P = .04$, Wilcoxon rank sum test). At presentation the median mRS score in the 2 groups was not significantly different—4.5 vs 4.0, respectively. Two of the 5 patients treated between 3 and 8 hours had a good outcome (1 was treated at 5 hours and 1 at 8 hours). Dichotomizing initial GCS score also demonstrated that patients with an initial GCS score greater than 8 were more likely to have a good outcome, with a median 3-month mRS score of 2, compared with 5.5 for those patients with an initial GCS score of 8 or less ($P = .008$, Wilcoxon rank sum test). Sensitivity analysis done after excluding the 2 patients with fluctuating symptoms (treated at 7 and 16 days) did not change the study results. In fact, in this slightly smaller cohort, treatment time and GCS cutoff points were even more strongly predictive of outcome ($P = .01$ and $P = .003$, respectively), and no good outcomes were observed in patients treated after 8 hours. Overall, 1 intracranial hemorrhage was observed within...
Posterior circulation stroke is often associated with poor patient outcomes. Several studies, however, have demonstrated that good outcomes, even in comatose patients, can be achieved with arterial recanalization much later than the accepted 3-hour window for IV thrombolysis. This study was undertaken to investigate factors that might help to predict patient outcomes in posterior circulation stroke, as well as to further examine effective thrombolytic treatment times.

The NIHSS score is frequently used to quantitate the severity of stroke symptoms, with a score of 20 or more predictive of poor outcomes in one study. The NIHSS score may be less useful for predicting outcomes in posterior circulation stroke, however, because patients may have a high NIHSS score (≥20) with preserved consciousness. In addition, the scale appears weighted toward anterior circulation stroke symptoms. The NIHSS scores of our patients did not predict outcomes. Thus, we sought to determine whether other scales for evaluating initial clinical presentation might be more useful for predicting treatment efficacy.

Our data revealed that a high presenting GCS score (≥9) was predictive of good patient outcome. There are only 3 articles that directly examined the relationship between the initial GCS score and the clinical outcome in patients with posterior circulation stroke. In the 45 patients described by Schwarz et al, those who had lower presenting GCS scores had worse clinical outcomes. In the study by Cross et al, 24 total patients with basilar artery thromboses were described, with 12 patients (50%) having an initial GCS score of 8 or less. At the 90-day follow-up visit, only 3 of these 12 patients were alive and only 1 had an mRS score of 2 or less. One possible confounding factor was that 75% of patients were treated at times greater than 8 hours. Other reports also identify tetraparesis and coma as independent predictors of poor clinical outcome. Only 4 of 10 patients (treated at 6, 8, 26, and 26 hours after symptom onset) had a good outcome in the study by Mitchell et al, while Grond et al reported 3 of 5 patients had a good outcome when treated within 3 hours of symptom onset. Thus, we believe that formal assessment of the presenting GCS score may be useful in guiding treatment decisions and assessing prognosis in patients with posterior circulation stroke.

The currently accepted times for initiating thrombolytic therapy in anterior circulation stroke are 3 hours for IV therapy and 6 hours for IA therapy. However, treatment windows have not been well delineated for posterior circulation thrombolysis, with some studies suggesting windows as long as 8 to 12 hours may still be clinically beneficial. In our study, 12 (57%) of 21 patients were treated within 8 hours of symptom onset with good outcomes in 8 (75%) of the 12, including 2 (40%) of 5 patients treated between 3 and 8 hours. Moreover, the risk for hemorrhage was low even in those patients treated after 8 hours. Comparison of these data suggests IA therapy may have been detrimental to patients (Table, P=.09). However, this could be explained by a small sample size resulting in a large type II error or may be a result of the data, which indicate that patients with a 90-day mRS score greater than 2 were also treated at significantly later times (and, thus, were ineligible for IV therapy) and were sicker at presentation (significantly worse presenting GCS scores).

In this study, the patients receiving the greatest benefit not only were treated within 8 hours of symptom onset but also had a GCS score greater than 8. Further studies with a larger cohort are needed to confirm both our findings—that late thrombolysis can still be beneficial and that initial GCS score can help predict patient outcome. Such studies are also necessary to better define acceptable times for initiating thrombolytic therapy for posterior circulation stroke.
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REFERENCES


