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

Jack W. Tsao, MD, DPhil; J. Claude Hemphill III, MD; S. Claiborne Johnston, MD, PhD; Wade S. Smith, MD, PhD; David C. Bonovich, MD

**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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**T**he first randomized study demonstrating the effectiveness of intravenous (IV) thrombolytic therapy in the treatment of acute stroke was published in 1995.1 Subsequently, the Prolyse in Acute Cerebral Thromboembolism II (PROACT II) trial demonstrated improved outcome in patients with angiography-documented middle cerebral artery occlusion treated with intra-arterial (IA) thrombolysis within 6 hours of symptom onset using prourokinase.2 However, patients who had posterior circulation strokes were less likely to be enrolled in the National Institute of Neurological Disorders and Stroke IV recombinant tissue plasminogen activator study (approximately 5% [J.W.T. review of primary data]). In PROACT II, patients who had posterior circulation strokes were specifically excluded. Other randomized studies have not found the same beneficial effect with thrombolytic therapy.3,8 In these studies, patients who had posterior circulation strokes were either excluded (Multicenter Acute Stroke Trial-Europe [MAST-E] and European Cooperative Acute Stroke Study [ECASS]) or inclusion criteria made enrollment of these patients less likely (the Multicenter Acute Stroke Trial-Italy [MAST-I], The Alteplase ThromboLysis for Acute Noninterventional Therapy in Ischemic Stroke [ATLANTIS], and Australian Streptokinase [ASK] trials did not publish the number of patients who had a posterior circulation stroke). Thus, the literature describing use of thrombolytic agents for posterior circulation thromboses is sparse.

Posterior circulation thrombosis, especially basilar artery occlusion, generally has been considered to have a poor prognosis, although more recent studies...
suggest that mortality rates are lower than previously as-
sumed. 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 circula-
tion thrombosis and to investigate factors that might be
useful for predicting patient outcome.

METHODS

PATIENT SELECTION

Retrospective medical record review was undertaken for 21 con-
secutive patients who received either IV or IA thrombolytic
therapy for posterior circulation ischemic stroke at the Uni-
versity of California, San Francisco between October 9, 1993,
and February 19, 2001. Stroke location was confirmed by a re-
viewing 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 neuro-
logical examination findings and, again, the results were inde-
pendently verified. Scoring bias owing to sedation or intuba-
tion 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 begin-
nning of the study period vs those treated at the end of the study.

STATISTICAL ANALYSIS

Treatment outcomes were compared using the unpaired t test
for continuous variables, the Wilcoxon rank sum test for or-
dinal variables (NIHSS, mRS, and GCS scores), and the Fisher
exact test for unordered categorical and dichotomous vari-
ables. All statistical analyses were performed with Stata (ver-
sion 7.0; Stata Corp, College Station, Tex) and Excel 98 (Mi-
crosoft, Seattle, Wash). Commonly measured clinical outcome
variables were chosen for analysis to determine if any could pre-
dict 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 di-
chotomized at 8, as this is a clinical cutoff point often used to
represent coma. Because these variables were not normally dis-
tributed, nonparametric univariate analyses were undertaken,
but multivariable analyses were not performed.

RESULTS

Twenty-one patients (14 males, 7 females) received throm-
bolytic therapy: 9 were given IV recombinant tissue plas-
minogen activator, 9 IA urokinase, and 3 IA recombi-
nant 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 be-
tween 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 grade 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).

Table summarizes the association of various other character-
istics with outcome. The only characteristics predic-
tive 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 con-
sciousness), was not statistically associated with out-
come. 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 pre-
sentation 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). Di-
chotomizing initial GCS score also demonstrated that pa-
tients 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 out-
comes were observed in patients treated after 8 hours.
Overall, 1 intracranial hemorrhage was observed within


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Table. Patient Characteristics by Outcome After Posterior Circulation Thrombolysis*  

<table>
<thead>
<tr>
<th>Variable</th>
<th>mRS Score = 2 (n = 9)</th>
<th>mRS Score &gt; 2 (n = 12)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>63 ± 13</td>
<td>60 ± 22</td>
<td>.66</td>
</tr>
<tr>
<td>Male</td>
<td>7 (78)</td>
<td>7 (58)</td>
<td>.64</td>
</tr>
<tr>
<td>Hours to thrombolysis, median (range)</td>
<td>3 (1.5-384)</td>
<td>16.5 (2.8-168)</td>
<td>.02</td>
</tr>
<tr>
<td>Agent</td>
<td></td>
<td></td>
<td>.18</td>
</tr>
<tr>
<td>rtPA</td>
<td>7 (78)</td>
<td>5 (42)</td>
<td></td>
</tr>
<tr>
<td>Urokinase</td>
<td>2 (22)</td>
<td>7 (58)</td>
<td>.09</td>
</tr>
<tr>
<td>Route</td>
<td></td>
<td></td>
<td>.99</td>
</tr>
<tr>
<td>Intra-arterial</td>
<td>3 (33)</td>
<td>9 (75)</td>
<td></td>
</tr>
<tr>
<td>Intravenous</td>
<td>6 (66)</td>
<td>3 (25)</td>
<td></td>
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<tr>
<td>Race</td>
<td></td>
<td></td>
<td>.99</td>
</tr>
<tr>
<td>White (including Hispanic)</td>
<td>6 (67)</td>
<td>8 (67)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>3 (33)</td>
<td>3 (25)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>0 (0)</td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>Premorbid conditions</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Coronary artery disease</td>
<td>4 (44)</td>
<td>3 (25)</td>
<td>.32</td>
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<tr>
<td>Atrial fibrillation</td>
<td>2 (22)</td>
<td>3 (25)</td>
<td>.99</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6 (67)</td>
<td>6 (50)</td>
<td>.66</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2 (22)</td>
<td>3 (25)</td>
<td>.99</td>
</tr>
<tr>
<td>NIHSS score at presentation, median (range)</td>
<td>13 (4-59)</td>
<td>28 (2-37)</td>
<td>.20</td>
</tr>
<tr>
<td>GCS score at presentation, median (range)</td>
<td>14 (5-15)</td>
<td>6 (3-15)</td>
<td>.02</td>
</tr>
<tr>
<td>Rankin Scale score at presentation, median (range)</td>
<td>4 (3-5)</td>
<td>5 (1-5)</td>
<td>.13</td>
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<tr>
<td>Vascular localization</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Basilar artery</td>
<td>5 (55)</td>
<td>18 (83)</td>
<td>.18</td>
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<tr>
<td>Vertebral artery</td>
<td>2 (22)</td>
<td>2 (17)</td>
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<tr>
<td>Posterior cerebral artery</td>
<td>2 (22)</td>
<td>0 (0)</td>
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</tr>
</tbody>
</table>

Abbreviations: GCS, Glasgow Coma Scale; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; rtPA, recombinant tissue plasminogen activator.

*Data are given as the number (percentage) unless otherwise indicated. †P values calculated using the unpaired t test for continuous variables, the Fisher exact test for dichotomous and categorical variables, and the Wilcoxon rank sum test for ordinal variables.

36 hours. The patient, whose clinical outcome was unaffected, received IA recombinant tissue plasminogen activator therapy at 8 hours with bleeding, localized to the cerebellum, occurring in the setting of hypertension and heparin anticoagulation therapy. Six patients died between days 2 to 14 of medical complications (3 of stroke, 1 of myocardial infarction); 5 (83.3%) had an initial GCS score of 8 or less.

COMMENT

Posterior circulation stroke is often associated with poor patient outcomes.9,17 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.1-5,16-19 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.20 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.21 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.13,14,24 In the 45 patients described by Schwarz et al,24 those who had lower presenting GCS scores had worse clinical outcomes. In the study by Cross et al,13,14 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.12,17,18 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,17 while Grond et al19 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.1,2 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.13,14,16-19 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.
REFERENCES


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