Glasgow Coma Scale Does Not Predict Outcome Post-Intra-Arterial Treatment for Basilar Artery Thrombosis

BACKGROUND AND PURPOSE: Evidence to guide patient selection for IA therapy in acute basilar artery thrombosis is lacking. The GCS is frequently used as a selection criterion, based on the view that higher GCS correlates with better neurologic outcome. This view has not been systematically studied. We hypothesize that low GCS does not correlate with poor outcome and that it should not preclude IA therapy.

MATERIALS AND METHODS: We included 40 consecutive patients with basilar artery thrombosis treated with IA therapy. Clinical characteristics, GCS, time to intervention, and postprocedural TIMI scores were collected. Recanalization was defined as TIMI grade 2 or 3; clinical outcome was measured by 90-day mRS.

RESULTS: Median patient age was 63.5 years. Most presented with gaze palsies (67.5%) or hemiparesis (45%). Median GCS was 9, the median time to intervention was 7.2 hours, and recanalization rate was 82.5%. Good neurologic outcome (mRS ≤ 1) occurred in 30%. There was no correlation between GCS and 90-day mRS (Spearman ρ = 0.174, P = .283). Equal numbers of patients with good neurologic outcome of mRS ≤ 1 (n = 12) had a GCS of ≤ 6 or > 6. In those with GCS ≤ 6 for > 3 hours, 33.3% had good neurologic outcome—a similar rate to that of the overall cohort. Statistical significance was demonstrated between time to IA therapy within 6 hours and mRS ≤ 2.

CONCLUSIONS: Low GCS score did not correlate with poor neurologic outcome in patients with acute basilar artery thrombosis managed with IA therapy. It is not appropriate to exclude patients from IA therapy on the basis of low GCS.

ABBREVIATIONS: ACT = activated clotting time; AICA = anterior inferior cerebellar artery; CI = confidence interval; GCS = Glasgow Coma Scale; IA = intra-arterial; IQR = interquartile range; mRS = modified Rankin Scale; SCA = superior cerebellar artery; TIMI = Thrombolysis In Myocardial Infarction; VA = vertebral artery

Acute basilar artery thrombosis is an infrequent but catastrophic subtype of posterior circulation ischemic stroke that carries a mortality rate of 80%–90% without treatment.1-4 Consequent thalamic, brain stem, and cerebellar infarction can result in herniation, hydrocephalus, and death. Achieving timely vascular recanalization is the aim of treatment5; however, evidence guiding appropriate patient selection for recanalization is lacking, in particular for IA recanalization.

The spontaneous recanalization rate is unclear but is likely poor,6 and Lindsberg and Mattle7 have suggested that death rates,6,7,10 and that recanalization is independently associated with reduced mortality and better functional outcome.5,9,11-14 Presenting clinical status, GCS score, age, and time to intervention influence the decision to proceed with IA therapy.5,15 There is little evidence to guide this decision because reported studies have had variable exclusion criteria (eg, tetraplegia for > 6 hours, bilateral mydriasis and extinct brain stem reflexes for > 1 hour, and extensive infarction on baseline imaging1); GCS score < 9 for > 6 hours;5 symptom onset of > 12 hours; and coma for > 4 hours).7

The GCS is frequently used as a selection criterion for IA treatment, with the view that high GCS is associated with better neurologic outcome.11,16,17 However, Tsao et al,18 who state that initial GCS predicts outcome following thrombolysis in posterior circulation stroke, had a total of 21 patients, of whom only 12 received IA therapy (9, urokinase; 3, IA tissue plasminogen activator). In addition, the patients of Tsao et al were treated without the use of mechanical thrombectomy, angioplasty, or stent insertion, so this small cohort may not be applicable to current patient cohorts with newer methods of revascularization. Ezaki et al16 used a GCS of 10 as an arbitrary
cutoff in assessing outcome, which does not acknowledge significant clinical differences from GCS 3–9.

We hypothesize that a low GCS of \( \leq 6 \) does not correlate with poorer neurologic outcome after IA treatment in acute basilar thrombosis and propose that low GCS should not preclude IA treatment.

**Materials and Methods**

A retrospective single-center review was conducted of 40 consecutive patients with angiographically confirmed complete basilar artery thrombosis and immediate IA intervention between 1993 and 2009. Our comprehensive stroke referral service has 24-hour neurointerventional support, with treatment offered in the study population \( \leq 30 \) hours post–symptom onset. The only exclusion criterion was extensive infarction on preoperative CT with no limiting criteria for age or GCS.

Clinical parameters were identified through medical record review. “GCS” was defined at the lowest GCS score documented before IA therapy. “Time to IA intervention” was defined from the time of symptom onset, or from the time when the patient was last seen neurologically well, to the time of treatment onset. In the subgroup of patients with a variable clinical course followed by sudden onset of coma, time was defined from the sudden deterioration in clinical state.

Angiograms were reviewed by 2 neurointerventionists, with consensus opinion reached on clot location, collateral supply, and post-procedural TIMI score. Clot location was modeled on the methodology of Archer and Horenstein—proximal basilar (basilar origin to the origins of AICAs), midbasilar (origins of AICAs to origins of the SCA), and top of the basilar (origins of the SCAs to the basilar bifurcation). Involvement of the intra- or extradural VAs was also recorded; if either was involved bilaterally, this involvement was noted. Collateral supply from the posterior inferior cerebellar arteries via surface collaterals to the SCA territory and from the posterior communicating arteries to the basilar artery (when selective carotid angiography was performed) was also recorded.

TIMI was classified as grade 0, complete occlusion or no flow/perfusion of distal vasculature; grade 1, minimal flow/perfusion but with no opacification of distal vasculature; grade 2, partial obstruction leading to delayed opacification of distal vasculature; and grade 3, complete unimpeded perfusion of the distal vasculature regardless of whether residual stenosis was present. "Recanalization" was defined as TIMI grade 2 or 3.

After diagnostic angiography confirmed basilar artery thrombosis and intrathrombus placement of the microcatheter was achieved, an initial 200,000 U of urokinase with 5000 U of heparin was administered, followed by pulsed hand injections of further urokinase (maximum 1,000,000 U). Heparin bolus was administered according to weight with 70 U/kg to a maximum of 5000 U, followed by baseline and hourly ACT monitoring aiming at an ACT of 250. Total periods of thrombolysis were 1–2 hours, with repeat selective angiography every 15 minutes to assess recanalization. If flow disruption or occlusion persisted, angioplasty (percutaneous transarterial angioplasty) and/or stent placement was performed, particularly in athrombotic occlusions. If a full dose of intravenous thrombolysis had been administered, we proceeded to mechanical thrombectomy with the Merci retriever (Concentric Medical, Mountain View, California).

Postoperatively, heparin infusion was started at the end of the procedure when, in the opinion of the interventionist, rethrombosis or ongoing thromboembolism was a major risk, exceeding the estimated risk of hemorrhagic complication. This was monitored with an activated partial thromboplastin time of 60–65 as the target range, which was continued for 24 hours but was stopped if there was evidence of significant infarction or hemorrhage. If the underlying vessels were completely normal following lysis, confirming a diagnosis of embolus, heparin could be stopped at the end of the procedure.

Clinical outcome was assessed with 90-day mRS score obtained from the medical records. Primary analysis defined good neurologic outcome as mRS \( \leq 1 \), as stratified by Demchuk et al. A secondary analysis by using mRS \( \leq 2 \) as a good neurologic outcome was also performed for further comparison with the existing literature.

Statistical assessment was performed by the Clinical Epidemiology and Health Service Evaluation Unit (Royal Melbourne Hospital, Parkville, Australia). Data analysis was performed by using STATA10 (StataCorp, College Station, Texas) with a \( P \) value \( < .05 \) considered statistically significant. The Wilcoxon rank sum test was used to determine the differences between ordinal variables (eg, age), and the Spearman correlation was used to find the correlation between GCS and 90-day mRS scores. The Fisher exact test was used to determine the correlation between categoric variables. Stepwise logistic regression was used to find predictors of good neurologic outcome. Study approval was granted by the local research and ethics committee.

**Results**

Of the 40 patients, 62.5% were men. Median age was 63.5 years with an IQR of 47–77 years. The clinical presentation included gaze palsy (68%), hemiparesis (45%), quadriaparesis (10%), and locked-in syndrome (5%). Sex and cardiovascular risk factors (type 2 diabetes mellitus, hypercholesterolemia, and hypertension) or previous stroke or ischemic heart disease was not significantly associated with functional outcome.

The median GCS was 9 (IQR, 5–14). In 1 patient, the angiogram was not available for review; information on clot location, treatment, and recanalization was available from the procedural report, but TIMI and collaterals could not be assessed.

Clot location in the basilar artery (proximal, \( n = 12 \); mid, \( n = 18 \); or top-of-the-basilar, \( n = 5 \)) and presence of collaterals did not demonstrate any significant correlation with good neurologic outcome by Spearman analysis. Five patients had thrombus extending from the intradural VAs, of which 3 were bilateral. Nine had involvement of the extradural VAs, of which 2 were bilateral. In both the primary and secondary analyses, if thrombus extended from the VAs, 83% had a poor neurologic outcome. This is compared with 64% without VA involvement in patients with mRS > 1 and 57% in patients with mRS > 2.

Tables 1 and 2 reveal key clinical and angiographic data in those with 90-day mRS of \( \leq 1 \) and >1 and mRS of \( \leq 2 \) and >2, respectively.

Median time to IA intervention was 7.2 hours (IQR, 5–12.5 hours). IA therapy included IA urokinase (95%), mechanical thrombectomy with the Merci device (7.5%), angioplasty (35%), and stent insertion (17.5%). Mean urokinase dose was 769,000 U. Mean procedural time to recanalization was 101 \( \pm 36.8 \) minutes. There was no correlation between mean procedural time and good neurologic outcome by the Student \( t \) test. Recanalization occurred in 82.5% (\( n = 33 \)). TIMI 3 was achieved in 26 patients; TIMI 2 in 7; TIMI 1 in 4; and TIMI 0 in 2 patients. There were 3 intraoperative complications—2 vesi-
sel perforations and 1 dissection. Five patients (12.5%) had complicating intracranial hemorrhages; 4 of these patients died within 90 days. Overall, the 90-day mortality rate was 32.5% (n/H1100513). Causes included intracranial hemorrhage (n/H110054), extensive infarction or acute hydrocephalus (n/H110053), failure to make neurologic recovery (n/H110053), respiratory failure (n/H110052), and retroperitoneal hematoma (n/H110051).

Most outcome assessments were available at 3 months. Two mRS scores were taken at 2 months; 2 mRS scores, at 1 month; and 1 mRS score, at 12 months. Figures 1 and 2 illustrate the distribution of mRS scores for patients with presenting GCS scores of ≤6 and >6, respectively. Good neurologic outcome (mRS ≤ 2) occurred in 30% (95% CI, 16.6–46.5); Secondary analysis demonstrated good neurologic outcome (mRS ≤ 2) in 33% of cases. Stepwise logistic regression assessing GCS, age, recanalization, and time to IA intervention demonstrated that only time to IA intervention was a significant predictor of good neurologic outcome (with mRS ≤ 2). Those treated beyond 6 hours from symptom onset had less chance of good neurologic outcome (mRS ≤ 2) (odds ratio 0.106; 95% CI, 0.023–0.488).

Table 1: Summary of key angiographic and clinical data with 90-day mRS

<table>
<thead>
<tr>
<th></th>
<th>mRS ≤ 1 (n = 12)</th>
<th>mRS &gt; 1 (n = 28)</th>
<th>P Value</th>
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<tr>
<td>GCS</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤6</td>
<td>6</td>
<td>10</td>
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<tr>
<td>&gt;6</td>
<td>6</td>
<td>18</td>
<td></td>
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<tr>
<td>Time to IA intervention</td>
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<td></td>
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<tr>
<td>≤6 Hours</td>
<td>7</td>
<td>7</td>
<td>0.07</td>
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<tr>
<td>&gt;6 Hours</td>
<td>5</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Recanalization</td>
<td>11</td>
<td>22</td>
<td>0.65</td>
</tr>
<tr>
<td>Procedure time (mean)</td>
<td>95.9 ± 13.0</td>
<td>103.5 ± 7.2</td>
<td>0.59</td>
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<td>TIMI score</td>
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<td>1</td>
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<td>6</td>
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<tr>
<td>3</td>
<td>10</td>
<td>16</td>
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Table 2: Summary of key angiographic and clinical data with 90-day mRS

<table>
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<tr>
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<th>mRS &gt; 2 (n = 26)</th>
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<tr>
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<tr>
<td>&gt;6</td>
<td>8</td>
<td>16</td>
<td></td>
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<tr>
<td>Time to IA intervention</td>
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<td></td>
<td>.01</td>
</tr>
<tr>
<td>≤6 Hours</td>
<td>9</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>&gt;6 Hours</td>
<td>5</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Recanalization</td>
<td>13</td>
<td>20</td>
<td>.39</td>
</tr>
<tr>
<td>Procedure time (mean)</td>
<td>94.7 ± 11.3</td>
<td>104.7 ± 7.5</td>
<td>.47</td>
</tr>
<tr>
<td>TIMI score</td>
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<td>2</td>
<td>2</td>
<td>5</td>
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<tr>
<td>3</td>
<td>11</td>
<td>15</td>
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Fig 1. Distribution of mRS for GCS ≤ 6.

Fig 2. Distribution of mRS for GCS > 6.
come. This improved to 54% if time to IA intervention was ≤6 hours (P = .07). In the secondary analysis, if recanalization occurred, 39% had a good neurologic outcome (mRS ≤ 2), compared with 17% if recanalization did not occur (P = .391).

Of those who were recanalized, if time to IA intervention was >6 hours, 20% had a good neurologic outcome (mRS ≤ 2). This improved to 69% if time to IA intervention was ≤6 hours (P = .01).

**Discussion**

Early diagnosis and treatment are paramount in acute basilar artery thrombosis. While an acute onset of quadriplegia or locked-in state may be perceived as a common presentation, basilar artery thrombosis presents in a heterogeneous manner, and there should be a low threshold for investigation in the appropriate clinical setting. Ferbert et al. studied 85 patients and there should be a low threshold for investigation in the basilar artery thrombosis presents in a heterogeneous manner, locked-in state may be perceived as a common presentation, early diagnosis and treatment are paramount in acute basilar artery thrombosis.

The spontaneous recanalization rate in acute basilar artery occlusion, in whom sudden neurologic decline, including quadriplegia or locked-in state, occurred in only 20. Admission symptoms and signs were variable and included vertigo, headache, hemihyperesthesia, and oculomotor disturbance. Eleven percent were locked-in, and 18% were quadriplegic compared with 5% locked-in and 5% quadriplegic in our study.

The natural history of acute basilar artery thrombosis managed with antiplatelets and/or anticoagulants is poor. Hacke et al. reported 19 of 22 deaths (86%) in a cohort of patients who received antiplatelet or anticoagulant therapy, while Schoneville et al. described dependency rates (mRS 4–5) of ≤65% and mortality rates of 40% in a similar subgroup of patients. The spontaneous recanalization rate in acute basilar artery thrombosis is unknown but is suggested to be no higher than 20% within 12–24 hours. This compares with IA thrombolysis that can achieve recanalization rates as high as 92%. The recanalization rate in our study population was comparable at 82.5%.

Recanalization is associated with a significant survival benefit, particularly when data from multiple studies are included. Seventy-three percent (95% CI, 54.5%–86.8%) of those who were recanalized survived at 90 days, compared with 33% (95% CI, 4.3%–77.7%) of those who were not recanalized (P = .15). A larger sample size may have resulted in a significant survival benefit, but in the examination of 83 patients by in Eckert et al., mortality reduction from 72% to 54% with recanalization was not significant. Ten of the 14 recanalized patients examined by Hacke et al. had a favorable neurologic outcome (defined as no, minimal, or moderate neurologic deficit). In our study population, 33% of those recanalized had a good neurologic outcome of mRS ≤ 1, compared with 16% if recanalization did not occur. Our definition is stricter, with mRS ≤ 1 (ie, no symptoms at all, no significant disability despite symptoms, and able to carry out all usual duties and activities). This is not dissimilar to the study of Eckert et al, in which 30% of those who were recanalized had a 3-month Barthel index of >90, compared with 10% of those who were not recanalized. Of our 6 patients who were unable to be recanalized (TIMI, 0 or 1) and were managed medically, 4 died and 1 had severe disability (mRS 5).

Of those who were recanalized, there was a trend toward more frequent good neurologic outcome (mRS ≤ 1) with earlier treatment (20% if treated >6 hours compared with 54% if treated ≤6 hours, P = .07). In the secondary analysis (mRS ≤ 2 as a good neurologic outcome), statistical significance was demonstrated between time to IA intervention and good outcome, increasing from 20% if it was >6 hours to 69% if, within 6 hours (P = .01). These findings add strength to the study of Eckert et al., in which, with just over double the sample size, a significant improvement in favorable neurologic outcome was reported (Barthel index, >90) from 7% to 36% if treatment could be performed within 6 hours. Eckert et al. subsequently concluded that endovascular treatment is not reasonable if patients present with a persistent severe neurologic deficit like tetraplegia and coma for >6 hours.

There was no correlation with GCS and 90-day mRS. Of the 12 patients with a mRS ≤ 1, six had GCS ≤ 6, the same number as those with GCS > 6.

Although time to IA intervention may be a confounding factor in this assessment, of the 15 patients with GCS ≤ 6 for >3 hours, a third had good neurologic outcome (mRS ≤ 1) at 90 days. This is a rate to similar that of the overall cohort of 40, with 30% good neurologic outcome overall. There were 10 patients with GCS of ≤6 and >6 hours to IA intervention. Three had an mRS score of 5, and 4 were dead at 90 days. However, notable cases include a 79-year-old patient with GCS 6 treated at 6 hours with a 90-day mRS of 1. An 82-year-old patient with a GCS of 6 who was treated at 12 hours made a full neurologic recovery with an mRS 0 at 3-month review. A 63-year-old patient with a GCS score of 3 for >3 hours was treated at 5 hours, with a 90-day mRS of 1 after IA lysis.

There are weaknesses in our study; it was a retrospective case review with a small sample size. Similar to treatment in other stroke referral centers, preoperative anticoagulation was variable, particularly when referred from external institutions. Clinical follow-up was not fully standardized, with 4 of 40 patients (12%) with mRS 4 died and 1 had severe disability (mRS 1, coma for >6 hours).

Failure of Recanalization | Recanalization | P Value
--- | --- | ---
90-Day mortality (n = 6) | 4 (67%) | 9 (27%) | .15
90-Day mRS | .85
≤1 | 1 (17%) | 11 (33%) | .391
>1 | 5 (83%) | 22 (67%) | .391
90-Day mRS | .391
≤2 | 1 (17%) | 13 (39%) | .90
>2 | 5 (83%) | 20 (61%) | .90

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**Table 3: Recanalization compared with 90-day mortality and mRS**

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**Table 3: Recanalization compared with 90-day mortality and mRS**
wires, and new mechanical thrombectomy devices. Nonetheless, it represents 16 years of consecutive angiographically proved basilar thromboses in routine clinical comprehensive stroke care settings.

**Conclusions**

GCS is frequently used as a selection criterion for IA therapy in acute basilar artery thrombosis based on the view that higher GCS correlates with better neurologic outcome. However, when systematically studied, there was no correlation between GCS and neurologic outcome at 90 days. Thus, we propose that it is not appropriate to exclude patients from IA therapy on the basis of low GCS scores. Continuing data collection by our neurointerventional group will provide further data to confirm our current findings on a larger sample population.

**Acknowledgments**

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**References**