A simple, valid, reliable, sensitive, and inexpensive tool to accurately measure patient outcome in stroke clinical trials would be highly valued.1 A surrogate measure that identifies early outcomes has been proposed.2–4 Early NIHSS score as a measure of stroke severity is highly predictive of 3-month outcome in acute ischemic stroke patients,2 and acute diffusion weighted imaging (DWI) data adds to the prediction.5 We hypothesized that the combination of day-5 NIHSS score and DWI volume in acute ischemic stroke (AIS) patients would be more predictive of 3-month clinical outcome than either alone.

**Background and Purpose**  
A simple, easily measured surrogate outcome measure for use in early treatment trials for acute ischemic stroke therapies would be highly valued. We hypothesized that day-5 NIH stroke scale score (NIHSS) and day-5 diffusion weighted imaging (DWI) volume would predict clinical outcome better than either alone and could be considered as a possible surrogate outcome in early phase acute stroke trials.

**Methods**  
The prospective Acute Stroke Accurate Prediction (ASAP) trial included a prespecified subgroup evaluated for early outcome. Logistic regression analysis was used to assess the prediction of modified Rankin (mRankin) of 0 or 1.

**Results**  
A total of 204 subjects completed the substudy, and 116 (57%) had excellent outcome at 3 months. The area under the ROC curve (AUC) for day-5 NIHSS predicting 3-month excellent outcome was 0.84; for DWI volume predicting outcome was 0.76, and for the multivariable model combining both was 0.84.

**Conclusions**  
The results of the early outcome substudy of the ASAP trial suggest that early stroke severity and infarct volume measures are predictive of 3-month excellent outcome. In our data set the DWI volume does not add clinically relevant information in predicting 3-month outcome. Validation of these results is required. (Stroke. 2009;40:1332-1333.)

**Key Words:** cerebral ischemia ■ prognosis ■ stroke outcome ■ models ■ statistical ■ surrogate

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Early clinical status is a strong predictor of 3-month outcome and may be useful in clinical and research settings. For proof of concept studies, use of a day-5 outcome may substantially reduce the time, cost, and frequency of subjects lost to follow-up while allowing an accurate determination of the appropriateness of proceeding to phase III trials. Additionally, this information may provide an imputation method for trials with early outcome information and a small number of patients missing final outcome data. The strong prediction supports a potential role for day-5 outcome. Once validated, our simple nomogram (supplemental Figure I) may be valuable in similar populations and may be useful in trials with adaptive designs and rapid accrual, as they may facilitate early adjustment of pretrial estimates of event rates. These potential benefits may, in some trials, outweigh the disadvantages of an imperfect but highly predictive estimate of 3-month outcome.

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**Disclosures**

None.

**References**


**Table. Patient Characteristics (n=204)**

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (IQ Range)</td>
<td>68 (56–78)</td>
</tr>
<tr>
<td>Median NIHSS score (IQ Range)</td>
<td>5.5 (3–11)</td>
</tr>
<tr>
<td>Median DWI volume, cc (IQ Range)</td>
<td>3.1 (0.3–19.7)</td>
</tr>
<tr>
<td>Female sex</td>
<td>96 (47%)</td>
</tr>
<tr>
<td>White race</td>
<td>175 (85.9%)</td>
</tr>
<tr>
<td>Lacune</td>
<td>62 (30%)</td>
</tr>
<tr>
<td>TPA treatment</td>
<td>31 (15%)</td>
</tr>
</tbody>
</table>

Day 5 status median (IQ range)

| NIHSS score | 4 (1–9) |
| DWI volume  | 5.64 (0.76–33.8) |

3-month outcome

| Death        | 15 (7.35%) |
| mRankin=0, 1 | 116 (57%)  |
| mRankin=5, 6*| 21 (10.29%)|

*mRankin of 5, 6 represents nursing home level disability (5) and death (6).
Clinical and Imaging Data at 5 Days as a Surrogate for 90-Day Outcome in Ischemic Stroke
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for the ASAP Investigators

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