Development of an Ischemic Stroke Survival Score

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Background and Purpose—There has been substantial interest in identifying predictors of survival for stroke patients. Current instruments used for measuring stroke severity are confined to either neurological, functional, or disability measures. The purpose of this study was to develop a stroke survival score that combines instruments from different domains to better predict long-term survival.

Methods—We took advantage of a particularly broad array of clinical and physiological variables collected during the Stroke Treatment with Ancrod Trial. Four hundred fifty-three patients completed a battery of instruments at day 7 after stroke and were followed for 1 year.

Results—Of the 453 patients, 53% were male, 77% were aged 65 years or older, and 89% were white. One hundred nine patients (24%) died during the study period. Age was a highly significant predictor of mortality (P <0.001), but there were no statistically significant differences in 12-month survival with respect to sex, race, or educational level. The best model for predicting survival was the Ischemic Stroke Survival Score. This model included the Scandinavian Stroke Scale, Rapid Disability Rating Scale, age, and prior stroke. This model had substantially greater predictive power (R² = 0.30, c statistic = 0.86) than the Scandinavian Stroke Scale alone (R² = 0.20, c statistic = 0.78).

Conclusions—This study demonstrates that combining day 7 poststroke information from multiple domains substantially improves the ability to predict 12-month survival of ischemic stroke patients compared with data from a single domain. The high mortality rate emphasizes the importance of preventive measures for a disease that has identifiable and modifiable risk factors. (Stroke. 2000;31:2414-2420.)

Key Words: clinical trials  ■  outcome assessment  ■  prognosis  ■  stroke, acute  ■  survival

Stroke is the third leading cause of death in the United States, after heart disease and cancer.¹ There are at least 750,000 first-ever or recurrent strokes each year.²³ According to the Framingham Heart Study, approximately 29% of strokes result in death within 1 year, 31% of stroke patients need help caring for themselves, and 16% have to be institutionalized.⁴ Identifying stroke patients’ predictors of survival is becoming increasingly important for risk adjustment in the health policy arena.⁵ In addition, these predictors will enable clinicians to identify those stroke patients at a higher risk for early mortality and to provide patients and their caregivers with more accurate prognostic information.

How well can a neurological examination predict a stroke patient’s long-term survival? Most studies confirm the prognostic importance of level of consciousness and suggest that other elements of the neurological examination are also predictive of short-term survival.⁶⁻⁹ In addition, demographic variables have been identified as predictive of a stroke patient’s survival.¹ Previous studies of patients with other underlying disease conditions found that functional status and disability domains were also highly predictive of mortality.¹⁰⁻¹³

Three widely used instruments that address these domains are the Scandinavian Stroke Scale (SSS), Barthel Index (BI), and Rapid Disability Rating Scale (RDRS). The SSS¹⁴ has been used in many stroke studies as a measure of neurological functioning.¹⁵ This scale is reliable¹⁶ and has been validated in predicting short-term mortality and functional outcome,¹⁷ but its ability to predict long-term survival has not been examined. The BI¹⁸ has been extensively used in stroke for screening, monitoring, and rehabilitation.¹⁹ This instrument has been shown to be reliable and valid,²⁰ but it does not include items related to cognitive or perceptive function, which have been shown to have an influence on global outcome after stroke.²¹ The RDRS,²² which was developed as a measure of activities of daily living, is based on patient performance. This instrument is a reliable and valid measure of physical functioning applicable to the elderly,²³ but its ability to predict long-term survival has not yet been examined.

These current instruments for measuring severity of illness of persons with stroke are confined to either neurological, functional, or disability measures. Neither these nor other existing instruments incorporate measures from multiple

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domains. It is hypothesized that a system that combines domains will have greater predictive power of long-term survival. This in turn will allow clinicians to target appropriate services to their stroke patients and will allow researchers to adjust for prognosis in studies evaluating long-term outcome. To our knowledge, this was the first attempt to develop a 1-year ischemic stroke survival score from multiple varied domains. We are not aware of any other stroke survival systems that combine information from demographic, neurological, physiological, and functional status domains to predict long-term mortality for ischemic stroke patients.

The purpose of this study was 2-fold: (1) to determine which demographic, neurological functioning, and disability measures are independent predictors of survival; and (2) to develop an ischemic stroke survival score that is more predictive of 12-month mortality than data from a single domain. Our analysis took advantage of a particularly broad array of clinical and physiological variables collected during the Stroke Treatment with Ancrod Trial (STAT).24

Subjects and Methods

Patients

These data were collected as part of STAT, a phase III multicenter, randomized, placebo-controlled, double-blind, parallel-group trial designed to assess the safety and efficacy of ancrod for the treatment of acute ischemic stroke.24 Study entry criteria are listed in Table 1. Patient demographics were collected at baseline, and a battery of instruments was used at day 7 after stroke. All neurological evaluations and stroke scale assessments performed in STAT were conducted in a consistent manner by trained evaluators. The only outcome collected at 1 year after stroke was the patient’s survival status. This was determined by physician telephone contact or by contact with other sources responsible for the care of the patient.

Scandinavian Stroke Scale

The SSS14 has been used in many stroke studies as a measure of neurological functioning.13 The SSS assessment involves evaluations of level of consciousness, motor function, disorders of cranial nerves, cutaneous sensitivity, gait, and speech. These parameters reflect the severity of the patient’s neurological deficit. The maximum attainable total score in this study was 46 points. This score represented normal function but excluded gait. Gait assessment was contraindicated since bed rest was encouraged during the first week of the trial. Therefore, a patient with no impairment received a score of 46, whereas maximum impairment produced a score of 0.

For the purpose of STAT, patients with mild strokes were excluded, since it was assumed that patients with mild strokes would not benefit significantly from ancrod. Therefore, only patients with a cumulative SSS score <40 immediately before entry were admitted in STAT. There was no lower limit, ie, patients with a score of 0 were eligible. Each patient’s neurological function was evaluated daily during the first week, but only the day 7 poststroke assessment was used in this study to be consistent with the other instruments.

In 1995, Edwards et al17 examined the validity of the SSS for 84 consecutive stroke patients admitted to a neurology/neurosurgery intensive care unit. They used structural equation modeling, a technique that merges the analytic procedures of factor analysis and multiple regression to examine its reliability and construct validity. They also analyzed the predictive validity, sensitivity, and specificity of the scale in predicting short-term mortality and concluded that the SSS was reliable and valid for use in stroke patients.

The interrater reliability of the SSS is very good, with κ scores up to 0.912 being reported.16 However, completion of this scale should only be performed by a clinician. It is more time consuming than the BI, but it still rarely takes >10 minutes to complete.
may even be administered over the telephone.27 The BI is so widely used that the score is likely to be understood by other professionals, thus making the measure more valuable in multidisciplinary care.

**Rapid Disability Rating Scale**

The RDRS22 was originally developed in 1967 and then revised in 1982.21 Linn and Linn23 reported the findings of 2 nurses who independently rated the same 100 disabled patients. Intraclass correlations ranged from \( r = 0.62 \) to a high of \( r = 0.98 \); all items were statistically significant. Reliability was also demonstrated by testing a subset of the same 50 patients twice within a 3-day period. Test-retest values ranged from \( r = 0.58 \) to \( r = 0.96 \) between the first and second ratings by Pearson product moment correlations. Linn and Linn23 also examined the validity of the RDRS. Measurements were made on 845 men at the time of transfer from a general medical hospital to community nursing homes. Thirty percent of the patients died within 6 months after nursing home placement. The items on the scale were used to predict mortality by discriminant function analysis. For accuracy of classification, the scale correctly identified patients who would die 72% of the time.23

The RDRS is based on the patient’s performance; it measures disability and also includes levels of mobility. There are 17 questions covering the following: eating, bathing, dressing, toileting, grooming, walking, mobility, adaptive tasks, communication, hearing, sight, diet, incontinence, medication, mental confusion, uncooperativeness, and depression. The individual items are scored in increments of 1 point, with 3 points representing no impairment and 0 points extreme impairment. Therefore, a score of 51 represents no disability, and 0 represents complete disability.

The RDRS is a reliable and valid measure of physical functioning applicable to the elderly.23 It can serve as an indicator of an elderly person’s response to treatment, or it can be used in other areas when assessment of the need for care or level of disability is required. It has not been as widely used and validated as the BI; it is also more time consuming and evaluates some of the same functions as the BI. However, the RDRS may be more precise in differentiating between different possible responses since it has 4 categories per item, while the BI has only 3. This may make the RDRS a better predictor of long-term mortality.

**Demographic Data**

The following demographic variables were collected at baseline: sex, age, race, education, and handedness. These were included in the analysis since they are often predictive of a stroke patient’s long-term survival.1

**Data Analysis**

The statistical analysis was performed in 4 steps. First, the full data set was randomly divided in half, creating “training” and “validation” data sets, and a crude analysis of 12-month mortality by different patient demographics and characteristics was performed on the training data set. Next, logistic regression techniques were used to develop and compare multivariate regression models predicting probability of death at 12 months from the training data set. In step 3, the “best” model identified in step 2 was tested on the validation data set. The predictive value approach suggested by Harrel et al29 was used, and values of the c statistic were computed. The c statistic equals the area under a receiver operating characteristic curve when the response is binary.30 This measures how well models discriminate between patients who lived and those who died. A c statistic of 0.5 indicates no ability to discriminate, while a value of 1.0 indicates perfect discrimination.31 Finally, the best model coefficients were reestimated with the full data set. These coefficients were then used to calculate survival scores for each patient, and we examined 12-month survival by quartile of patients.

**Results**

Of the 500 patients enrolled in STAT, 453 had a day 7 poststroke assessment. The major reason for the reduction in study size was the high short-term mortality (ie, 46 of 500 patients [9.2%] died within 7 days after stroke, and 1 patient was not assessed at day 7 after stroke). Of the 453 patients, 53% of the patients were male, 77% were aged 65 years or older, 89% were white, and 75% had <12 years of education. Both ancrord and placebo patients were included in the analysis since there was no difference in 1-year mortality by treatment (32.7% versus 32.5%).

All 453 patients completed the SSS assessment, but 44 patients did not complete the BI and 45 patients had missing RDRS data. The SSS data were complete because greater emphasis was placed on this instrument at day 7. Fortunately, 44 of the missing patients did not complete both the BI and RDRS, and an additional patient had missing RDRS data. Therefore, complete day 7 data were available for 408 patients.

In January 1999, 12-month survival data collection was completed for all 453 patients with day 7 poststroke information. Of these, 109 (24%) died during the study period. Age was a highly significant predictor \((P<0.001)\) of 12-month survival, but there were no statistically significant differences in mortality with respect to sex, educational level, smoking status, or handedness in the full or training data set (Table 2). In the full data set there was a difference in mortality by race (25% versus 14%; \(P=0.067\)), but white patients were on average 2 years older than nonwhite patients, and there were 8% fewer white patients younger than 65 years than nonwhite patients (22% versus 30%). Since age is a very strong predictor of mortality, it appeared that the difference in age distribution between whites and nonwhites caused the...
The difference in mortality and not the race. This was confirmed by finding no significant difference in mortality by race when controlling for age ($P = 0.266$).

The day 7 poststroke SSS assessment performed well in the training data set. Twelve-month mortality rates were 64.7% for individuals with SSS of 0 to 20, 30.4% for SSS 21 to 30, and 10.8% for SSS 31 to 46 ($P = 0.001$). In addition, the RDRS performed well: 12-month mortality rates were 63.9% for individuals with RDRS 0 to 20, 25.0% for RDRS 21 to 40, and 1.6% for RDRS 41 to 51 ($P = 0.001$). BI and history of prior stroke were also highly predictive of long-term mortality (Table 3).

To construct our ischemic stroke survival score, we used the training data set and began with the SSS. We developed a baseline logistic model to predict 12-month mortality using the SSS and then added the BI and RDRS. Each significant bivariate analysis variable was individually input into the baseline model. Variables were also dropped from the model if they no longer made a significant contribution to the $R^2$ value. Table 4 reports the proportionate increase (or decrease) in odds of mortality from the least severe category for each variable. From the analysis of the training data set, the most parsimonious model with the best $R^2$ value included the SSS, RDRS, prior history of stroke, and age. We call this model the Ischemic Stroke Survival Score (ISSS). In Table 5, the $R^2$ for the SSS alone was 0.20. It improved to 0.22 when age was added; however, the $R^2$ for the ISSS was 0.30 ($P<0.001$). The ISSS was also highly correlated with time to death ($r = -0.43$, $P<0.001$).

The ISSS was validated by applying the best model, and its coefficients were estimated from the training data set to the validation data set. Table 5 reports the c statistics, which improved from 0.78 with the SSS alone to 0.86 for the ISSS system. Next, we reran the best model and reestimated the coefficients, standard errors, odds ratios, and their 95% CIs for the full data set (Table 6). The odds ratio for each component of the ISSS was in the same direction and similar in magnitude to those observed in the training set data set (Table 4). This suggests that the coefficients were relatively stable.
Finally, to provide clinicians with an estimate of the relationship between a patient’s ISSS and 12-month survival, we examined survival by quartile of patients. In this analysis, we estimated each patient’s survival score by using coefficients obtained from the full data set. This was done to maximize the stability of the coefficients. Patients in the lowest quartile (survival scores of 0.0 to 1.80) had a 12-month mortality rate of 1.7%. Similarly, patients in quartiles 2, 3, and 4 had ranges of 1.81 to 3.34, 3.35 to 4.89, and 4.90 to 6.90, with mortality rates of 8.8%, 22.9%, and 63.7%, respectively (P<0.001).

**Discussion**

This study demonstrates the strength of combining day 7 poststroke information from multiple domains in improving the ability to predict 12-month survival of patients who have had an ischemic stroke compared with data from a single domain. The addition of measures on age, history of prior stroke, and activities of daily living increases the ability to predict 12-month survival of patients who have had a stroke, and activities of daily living increases the ability to predict 12-month survival of patients who have had a stroke.

The inclusion of these measures improves the ability of the SSS to predict 12-month survival from 78% to 86% with the use of the c statistic. Therefore, by combining information from multiple domains and creating a new stroke survival score, the clinician’s ability to assess the prognosis of stroke patients has been substantially improved.

It is to be expected that the combination of information on clinical and physiological measures along with functional status will produce a more accurate prediction of survival than data from a single domain. In the logistic analysis of the training data set, each measure was statistically significant after controlling for the other measures (Table 4). There are obvious trade-offs in choosing outcome measures that are more accurate predictors of survival but require increased resources in data collection. The ISSS requires information on age, neurological functioning, history of prior stroke, and activities of daily living. This involves both chart review and patient report. This information is relatively easy to obtain, but it can be time consuming. Therefore, a real trade-off may exist between the cost of data and the validity and accuracy of the stroke survival measure.

There was a degree of overlap between the SSS and the RDRS, illustrated by a high Pearson correlation (r=0.80, P<0.001). However, there is considerable variability between these 2 instruments. They do not ask the same questions, and they explore different domains. There was significant overlap in questions between the RDRS and the BI, and therefore they were very highly correlated (r=0.87, P<0.001). When we examined the ISSS model using the BI instead of the RDRS, the model still performed well (R²=0.26, c=0.82), but not as well as the model using the RDRS (R²=0.30, c=0.86). We believe that the ISSS model was superior since the BI measures only the physical aspects of stroke disability, whereas the RDRS also covers cognitive functioning and mental health, including questions about communication, uncooperativeness, mental confusion, and depression.

The BI has long been considered the gold standard in assessing functional status and outcome in both stroke trials and observational studies. However, in this analysis the BI was not a statistically significant independent predictor of 12-month mortality after controlling for SSS, RDRS, age, and prior history of stroke. Researchers have recently discussed the inadequacy of using measures such as the BI to capture the full impact of stroke-related disability. They recommend that other measures be used in addition to the BI, which has a ceiling effect and captures only physical function. This ceiling effect relates to the lack of sensitivity of the BI in differentiating stroke patients with milder impairments. However, this ceiling effect was not observed in our study since we examined only moderate to severe strokes, and the only outcome analyzed was 12-month survival.

Stroke affects not only physical functioning but also emotion, memory and thinking, communication, and role function. Focus group interviews with patients and caregivers have demonstrated that these factors should be assessed as sequelae of stroke. Furthermore, the results of the recent study of Duncan et al demonstrated that in addition to the physical aspects of disability, emotion and participation also predict a patient’s future stroke recovery. Therefore, the part of the RDRS related to cognitive functioning and mental health is expected to be particularly important for stroke.

**TABLE 5. Comparison of R² and c Statistics for Age, SSS, RDRS, Prior Stroke, and ISSS: Training (n=226) and Validation (n=227) Data Sets**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Training Set</th>
<th>Validation Set</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.10</td>
<td>0.66</td>
</tr>
<tr>
<td>RDRS</td>
<td>0.25</td>
<td>0.81</td>
</tr>
<tr>
<td>SSS</td>
<td>0.20</td>
<td>0.78</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>0.08</td>
<td>0.59</td>
</tr>
<tr>
<td>ISSS (multivariate analysis)</td>
<td>0.30</td>
<td>0.86</td>
</tr>
</tbody>
</table>

*The c statistic equals the area under a receiver operating characteristic curve.

**TABLE 6. Results for ISSS Model: Full Data Set (n=453)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>SE</th>
<th>Odds Ratio*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>1.810</td>
<td>0.525</td>
<td>6.10</td>
<td>2.18, 17.10</td>
</tr>
<tr>
<td>65–79</td>
<td>2.325</td>
<td>0.535</td>
<td>10.23</td>
<td>3.58, 29.20</td>
</tr>
<tr>
<td>≥80</td>
<td>1.556</td>
<td>0.420</td>
<td>4.74</td>
<td>2.08, 10.80</td>
</tr>
<tr>
<td>SSS</td>
<td>0.948</td>
<td>0.368</td>
<td>2.58</td>
<td>1.25, 5.31</td>
</tr>
<tr>
<td>21–30</td>
<td>0.232</td>
<td>0.497</td>
<td>10.20</td>
<td>3.85, 27.05</td>
</tr>
<tr>
<td>RDRS</td>
<td>1.537</td>
<td>0.454</td>
<td>4.65</td>
<td>1.91, 11.31</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>0.682</td>
<td>0.322</td>
<td>1.98</td>
<td>1.05, 3.72</td>
</tr>
</tbody>
</table>

*Proportionate increase (or decrease) in odds of mortality in comparison with 1.0, with all other variables held constant.
patients and may help to explain why the RDRS was better at predicting long-term survival than the BI.

The SSS and RDRS are both ordinal scales, whereas the ISSS is a continuous variable that gives each patient a survival score ranging from 0.0 to 6.9. Clinicians have the ability to calculate scores for their individual patients to assess their prognosis. This can be achieved by using the coefficients estimated from the full data set, displayed in Table 4. For example, a 70-year-old patient (1.810), with SSS between 0 and 20 (1.556), RDRS between 21 and 40 (1.537), and prior history of stroke (0.682) would have a survival score of 5.585. In our population, such individuals would fall into the most severe quartile of patients, with an expected 12-month mortality of 63.7%, assuming that they survived to day 7 after stroke. Alternatively, a 60-year-old patient with SSS between 21 and 30 (0.948), RDRS between 21 and 40 (1.537), and no history of prior stroke would have a score of 2.485. This individual would fall into our second least severe quartile, with an expected 12-month mortality of 8.8%. In addition, researchers could use the raw survival scores directly as covariates to adjust for baseline imbalances in their statistical analyses.

The model was validated by applying coefficients obtained from the training data set (Table 4) to the validation data set. We also compared the training data set coefficients with the coefficients obtained from the full data set (Table 6). Although these values are similar, the coefficients based on the full data set are more stable. Therefore, we recommend that clinicians use the coefficients based on the full data set when assessing the severity of their patient’s illness. In addition to this internal validation, external validation is also an important next step for further study.

A number of studies have identified factors that predict functional outcome after stroke34–36 and stroke mortality.37–39 In addition, several studies have predicted stroke mortality by combining multiple factors.5,8 For example, Fullerton et al8 examined the ability of 21 factors to predict 6-month mortality for 206 consecutively admitted acute stroke patients. Iezzoni et al8 compared the ability of 5 severity measures to predict in-hospital death for stroke patients. The 5 severity-adjusted predictions were generated from clinical data and discharge abstracts. Our study varies in several ways. First, we used 12-month mortality instead of 6-month or inpatient mortality. Second, the previous studies used all strokes, whereas we examined a more homogeneous group of moderate to severe ischemic strokes. Finally, we used data collected during a clinical trial instead of data from a convenience sample or large administrative database. Therefore, this study is, to our knowledge, the first to evaluate the accuracy of combining prognostic measures from different domains in predicting 12-month ischemic stroke mortality.

In our univariate analysis, factors such as age, neurological functioning, history of prior stroke, disability, and activities of daily living were important predictors of survival. Previous work among patients with other underlying conditions (eg, AIDS, rheumatoid arthritis) have demonstrated that measures of health status and functional status are highly predictive of mortality.10–13 Our finding that activities of daily living were associated with 12-month survival after controlling for age, prior stroke, and neurological functioning is an important contribution to earlier studies of stroke survival.

This study has a number of limitations. First, the study cohort included 453 moderate to severe ischemic stroke patients from a North American multicenter clinical trial. Therefore, the study findings are probably not generalizable to all stroke patients, since patients with intracerebral and subarachnoid hemorrhages have a much poorer prognosis. It is expected, however, that these results are generalizable to the population of ischemic stroke patients who represent approximately 85% of all strokes.3 Obviously, the vast majority of mild ischemic strokes would probably fall into the least severe quartile of the ISSS.

Second, the 3 physiological instruments were administered 7 days after stroke, within a time window of 1 day. Therefore, the study findings may not hold true for ischemic stroke patients who are measured within a few days of stroke onset, but we expect the findings to hold true if the instruments are administered between 5 and 9 days after stroke. Still, we recommend that clinicians using this tool administer the instruments as close to day 7 as possible.

Third, while we observed univariate associations between survival and several other variables, these measures were not independent predictors after controlling for SSS and RDRS. The relatively small study size did not allow us to include a large number of predictors with potentially modest effects in our model. We doubt that the ISSS would be improved substantially by incorporating any of these measures. The relationships between some of these variables are likely to be very complex; therefore, further study with a larger cohort seems warranted.

Fourth, this study assessed only survival at 1 year after stroke. Logistic regression techniques and not Cox proportional hazard models were used because <50% of the patients had died at the conclusion of the trial. Therefore, the study had limited scope since it only examined 1 outcome at 1 time point. Further examination of the performance of the ISSS in predicting other important outcomes would have been of interest. In particular, cause of death, physical functioning, and health-related quality of life at various time points after stroke would provide further insight into stroke prognosis. Future studies could examine the prognostic importance of data on other risk factors, such as smoking, diabetes, hypertension, hyperlipidemia, and obesity, and disease states, such as coronary heart disease, peripheral vascular disease, and renal failure.

In summary, our results suggest that age, disability, neurological functioning, and history of prior stroke are all important independent predictors of 12-month mortality. The ISSS combines all of these measures into a continuous survival score, which better predicts 12-month survival than data from a single domain. Mortality prediction can be refined with more data and external validation. The ISSS should therefore be considered a “work in progress,” with further investigation needed. Providing accurate prognostic tools is particularly important both for researchers in the health policy arena and for clinicians to help care for their patients. Our study suggests that the relationship between stroke patient characteristics and long-term survival is ex-
tremely complex and may be best assessed by a combination of measures from different domains.

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References


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