ASTRAL Score Predicts 5-Year Dependence and Mortality in Acute Ischemic Stroke

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Background and Purpose—The ASTRAL score was externally validated showing remarkable consistency on 3-month outcome prognosis in patients with acute ischemic stroke. The present study aimed to evaluate ASTRAL score’s prognostic accuracy to predict 5-year outcome.

Methods—All consecutive patients with acute ischemic stroke registered in the Athens Stroke Registry between January 1, 1998, and December 31, 2010, were included. Patients were excluded if admitted >24 hours after symptom onset or if any ASTRAL score component was missing. End points were 5-year unfavorable functional outcome, defined as modified Rankin Scale 3 to 6, and 5-year mortality. For each outcome, the area under the receiver operating characteristics curve was calculated; also, a multivariate Cox proportional hazards analysis was performed to investigate whether the ASTRAL score was an independent predictor of outcome. The Kaplan–Meier product limit method was used to estimate the probability of 5-year survival for each ASTRAL score quartile.

Results—The area under the receiver operating characteristics curve of the score to predict 5-year unfavorable functional outcome was 0.89, 95% confidence interval 0.88 to 0.91. In multivariate Cox proportional hazards analysis, the ASTRAL score was independently associated with 5-year unfavorable functional outcome (hazard ratio, 1.09; 95% confidence interval, 1.08–1.10). The area under the receiver operating characteristics curve for the ASTRAL score’s discriminatory power to predict 5-year mortality was 0.81 (95% confidence interval, 0.78–0.83). In multivariate analysis, the ASTRAL score was independently associated with 5-year mortality (hazard ratio, 1.09, 95% confidence interval, 1.08–1.10). During the 5-year follow-up, the probability of survival was significantly lower with increasing ASTRAL score quartiles (log-rank test <0.001).

Conclusions—The ASTRAL score reliably predicts 5-year functional outcome and mortality in patients with acute ischemic stroke. (Stroke. 2013;44:00-00.)

Key Words: ASTRAL score ■ functional outcome ■ modified Rankin Scale ■ mortality ■ stroke prognosis

Prognostication of outcome in cerebrovascular diseases has been a rapidly developing field. Physicians need to estimate the patient’s prognosis, families need to design long-term supportive care and rehabilitation, and researchers need to compare baseline status or interpret study results to compare a strong driving force for the development of prognostic scores in cerebrovascular medicine. However, currently validated stroke prognostic models do not expand the predictive horizon >12 months and the applicability for longer time periods remains, therefore, questionable.

The recently developed ASTRAL score is based on 6 items readily available on arrival of the stroke patient in the emergency department. It has been externally validated in 2 independent cohorts showing remarkable consistency on predicting 3-month functional outcome. The aim of this study was to evaluate ASTRAL score’s prognostic accuracy to predict 5-year outcome in patients with acute ischemic stroke.

Patients and Methods

Data Selection
All consecutive, first-ever acute ischemic stroke patients admitted in Alexandra University Hospital in Athens, Greece, between January 1, 1998, and December 31, 2010, were included in the study. They were investigated on the basis of a standard diagnostic protocol and all data were prospectively entered into the Athens Stroke Registry, a computerized stroke databank as previously described. Patients were
excluded from the analysis if any of the ASTRAL score components were not available or if admitted later than 24 hours after symptom onset (or last proof of good health in case of unknown onset stroke).

All patients were examined at admission by a stroke physician. Stroke severity was assessed with the National Health Institute Stroke Scale Score (NIHSS). All patients were treated according to current guidelines. Stroke pathogenesis was classified according to the Trial of Org 10172 in Acute Stroke Treatment criteria. Cerebrovascular risk factors and previous evidence of cardiovascular disease were recorded using previously described definitions.

ASTRAL score was calculated on the basis of age (1 point for every 5 years), severity (1 point for every admission NIHSS point), time delay between symptom onset or last proof of good health (in case of unknown onset stroke) and admission (2 points if >3 hours), presence of any new visual field defect (2 points), glucose at admission (1 point if >7.3 or <3.7 mmol/L), and level of consciousness (3 points if impaired).

The estimation of the presence of visual field defect was based on the third item of the NIHSS, whereas level of consciousness was judged from item 1a on the NIHSS.

All patients or one of their relatives provided written informed consent for inclusion in this registry. The Institutional Ethics Committee approved the scientific use of the data contained in the database.

**Follow-up and Outcome Assessment**

Patients were followed up prospectively at 1, 3, 6, and 12 months after discharge and yearly thereafter. Follow-up was routinely performed in the outpatient clinic by physicians. In case of patients with severe handicap who were not able to attend the outpatient clinic, follow-up was assessed by a telephone interview or at the patient’s residence. Patient records, information from general practitioners, family physician’s records, and death certificates were used to register death and define its cause. The end points of the study were unfavorable functional outcome—defined as modified Rankin Scale (mRS) >2—and overall mortality at 5 years.

**Statistical Analysis**

To investigate the prognostic value of the ASTRAL score to predict 5-year functional outcome and overall mortality, we assessed the discriminatory power of the score (ie, the degree to which the prognostic score enables the discrimination between patients with favorable and unfavorable outcome by calculating the area under the receiver operating characteristics curve [AUC]).

To further assess whether the ASTRAL score is an independent predictor of 5-year functional outcome and mortality, univariate Cox proportional hazard analyses were performed. ASTRAL score (as a continuous covariate), sex, arterial hypertension, diabetes mellitus, smoking, coronary artery disease, atrial fibrillation, dyslipidemia, heart failure, peripheral artery disease, valvular heart disease, systolic and diastolic blood pressure at admission (as a continuous covariate), and Trial of Org 10172 in Acute Stroke Treatment category were included in the analysis. For each outcome, a second analysis was performed analyzing ASTRAL score as a categorical covariate stratified into quartiles. Thrombolysis was not included as a covariate because of the small number of thrombolysed patients in the cohort. Those covariates which were found to be associated with outcome in the univariate analysis at a P=0.1 level (to minimize the risk of type II errors) were included in the multivariate Cox proportional hazard analyses. Associations are presented as hazard ratios (HRs) with 95% confidence intervals (CIs). In the multivariate analyses, the level of statistical significance was set at 95% (P=0.05).

In order to further investigate the association between the ASTRAL score and survival, the Kaplan–Meier product limit method was used to estimate the probability of 5-year survival for each ASTRAL quartile; the log-rank test was used to compare the probability of survival between the quartiles. For patients lost during follow-up, survival data were censored at the last date they were known to be alive.

For continuous variables, data are summarized as medians and interquartile range. Categorical data are presented as absolute numbers and percentages. The χ² test was used to compare dichotomous or categorical variables; continuous variables were compared with the ANOVA test.

All statistical analyses were performed with the Statistical Package for Social Science version 15.0 for Windows (SPSS Inc, Chicago, IL).

**Results**

From the entire cohort of 1701 patients with first-ever ischemic stroke, 42 (2.5%) were excluded because ≥1 of the 6 covariates of the ASTRAL score were unavailable. Among these 42 patients, age, NIHSS on admission, and level of consciousness were recorded in all patients. Four patients had missing glucose values, 7 had missing visual field evaluation data, 5 had missing onset to admission time, and in 26 patients >1 component of the ASTRAL score were missing. Also, 139 patients (8.1%) were excluded because of admission delay of >24 hours after the onset of symptoms or last proof of good health. Finally, 1520 patients (median age, 72 years; interquartile range, 63–78; 955 men [62.8%]) were included in the analysis. The baseline characteristics of the patients are summarized in Table 1.

The AUC for ASTRAL score’s discriminatory power to predict 5-year unfavorable functional outcome was 0.89 (95% CI, 0.88–0.91; Figure I in online-only Data Supplement). In multivariate Cox analysis, the ASTRAL score (analyzed as a continuous covariate) was independently associated with 5-year unfavorable functional outcome (HR, 1.09 [95% CI, 1.08–1.10]; Table 2). Increasing values of the ASTRAL score were associated with an escalating worsening of functional outcome (HR, 2.34 [95% CI, 1.44–3.79] for quartile 2; HR, 5.45 [95% CI, 3.46–8.56] for quartile 3; and HR, 12.35 [95% CI, 7.87–19.35] for quartile 4 with quartile 1 used as a reference).

The AUC for the ASTRAL score’s discriminatory power to predict 5-year mortality was 0.81 (95% CI, 0.78–0.83; Figure II in online-only Data Supplement). In multivariate Cox analysis, the ASTRAL score (analyzed as a continuous covariate) was independently associated with 5-year mortality (HR, 1.09 [95% CI, 1.08–1.10]; Table 2). The ASTRAL score remained an independent predictor of 5-year mortality when analyzed in quartiles (HR, 2.01 [95% CI, 1.19–3.41]; HR, 3.80 [95% CI, 2.31–6.27]; and HR, 10.81 [95% CI, 6.62–17.65], respectively, for quartiles 2, 3, and 4 compared with quartile 1).

During the 5-year follow-up period, the probability of survival was significantly lower with increasing ASTRAL score quartiles (log-rank test <0.001; Figure). Mean survival was 57.4 (95% CI, 56.2–58.5), 53.0 (95% CI, 51.2–54.8), 46.0 (95% CI, 43.4–48.5), and 27.3 (95% CI, 24.3–30.2) months in the first, second, third, and fourth ASTRAL score quartile, respectively.
Discussion

The ASTRAL score was originally developed and externally validated to predict 3-month functional outcome after acute ischemic stroke. The present study aimed to investigate whether the ASTRAL score can predict reliably disability and a hard end point (ie, mortality) in the long term (ie, 5 years). The results showed that the score can be used reliably to predict 5-year functional outcome and mortality, thus extending its applicability. To our knowledge, no prognostic model has been previously validated for the prediction of stroke outcome in such a long-run. The ASTRAL score is the first prognostic score validated to predict stroke outcome >12 months. The combination of speed (rapid calculation within minutes after emergency department arrival), simplicity and reliability in long-term prediction of a frequently used clinical end point (independence using the mRS), and mortality highlight the role the ASTRAL score as a valuable clinical and research tool.

Several prognostic scores have been introduced to predict stroke outcome, such as the score by Weimar et al, the score by Counsell et al (the Six Simple Variable score), the Bologna Outcome Algorithm for Stroke scale, the iScore, the PLAN score, and the Get With the Guidelines risk model. Among them, the only scores that were validated to predict stroke mortality in the long term are the PLAN score, the iScore, and the Six Simple Variable score; however, in all 3 cases, this was limited to 12-month follow-up. The PLAN score incorporates 9 clinical variables (ie, preadmission dependence, cancer, congestive heart failure, atrial fibrillation, level of consciousness, age, significant/total weakness of the leg, weakness of the arm, and aphasia/neglect) and was shown to predict 12-month

Table 1. Demographics, Clinical Characteristics on Admission, Cerebrovascular Risk Factors, History of Cardiovascular Disease, Thrombolysis, and Hospitalization Time Data of the 1520 Study Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients</th>
<th>Quartile 1 n=404 (5–18)</th>
<th>Quartile 2 n=380 (19–23)</th>
<th>Quartile 3 n=367 (24–34)</th>
<th>Quartile 4 n=369 (35–59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
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</tr>
<tr>
<td>Age, y 72 (63–78)</td>
<td></td>
<td>62 (54–69)</td>
<td>73 (66–78)</td>
<td>75 (68–80)</td>
<td>76 (70–83)</td>
</tr>
<tr>
<td>Sex, men* 955 (62.8%)</td>
<td></td>
<td>299 (74.0%)</td>
<td>253 (66.6%)</td>
<td>22 (60.2%)</td>
<td>182 (49.3%)</td>
</tr>
<tr>
<td>Admission data</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Systolic blood pressure, mmHg 150 (140–170)</td>
<td></td>
<td>150 (130–170)</td>
<td>150 (140–170)</td>
<td>160 (140–180)</td>
<td>150 (139–170)</td>
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<tr>
<td>Diastolic blood pressure, mmHg 85 (80–90)</td>
<td></td>
<td>85 (80–90)</td>
<td>85 (80–90)</td>
<td>90 (80–93)</td>
<td>80 (80–90)</td>
</tr>
<tr>
<td>NIHSS at admission* 6 (2–16)</td>
<td></td>
<td>2 (1–3)</td>
<td>4 (2–6)</td>
<td>11 (8–14)</td>
<td>22 (19–25)</td>
</tr>
<tr>
<td>Glucose on admission, mmol/L* 5.78 (5.06–6.94)</td>
<td></td>
<td>5.78 (5.06–6.94)</td>
<td>6.28 (5.28–6.94)</td>
<td>6.28 (5.28–5.85)</td>
<td>6.50 (5.33–8.50)</td>
</tr>
<tr>
<td>Time from symptom onset to admission, min* 130 (65–250)</td>
<td></td>
<td>120 (60–200)</td>
<td>157.5 (90–373)</td>
<td>135 (65–245)</td>
<td>125 (60–233)</td>
</tr>
<tr>
<td>Impaired level of consciousness* 320 (21.1%)</td>
<td></td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>21 (5.7%)</td>
<td>299 (81.0%)</td>
</tr>
<tr>
<td>Visual field defect* 662 (43.6%)</td>
<td></td>
<td>60 (14.9%)</td>
<td>119 (31.3%)</td>
<td>181 (49.3%)</td>
<td>302 (81.8%)</td>
</tr>
<tr>
<td>History of cardiovascular disease or risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hypertension* 1070 (70.4%)</td>
<td></td>
<td>250 (61.9%)</td>
<td>269 (70.8%)</td>
<td>292 (73.6%)</td>
<td>259 (70.2%)</td>
</tr>
<tr>
<td>Diabetes mellitus 414 (27.2%)</td>
<td></td>
<td>83 (20.5%)</td>
<td>123 (32.4%)</td>
<td>98 (26.7%)</td>
<td>110 (29.8%)</td>
</tr>
<tr>
<td>Smoking* 476 (31.3%)</td>
<td></td>
<td>190 (47.0%)</td>
<td>107 (28.2%)</td>
<td>93 (25.3%)</td>
<td>86 (23.3%)</td>
</tr>
<tr>
<td>Dyslipidemia* 544 (35.8%)</td>
<td></td>
<td>185 (45.8%)</td>
<td>141 (37.1%)</td>
<td>125 (34.1%)</td>
<td>93 (25.2%)</td>
</tr>
<tr>
<td>Coronary artery disease† 294 (19.3%)</td>
<td></td>
<td>57 (14.1%)</td>
<td>74 (19.5%)</td>
<td>77 (21.0%)</td>
<td>86 (23.3%)</td>
</tr>
<tr>
<td>Atrial fibrillation* 515 (33.9%)</td>
<td></td>
<td>54 (13.4%)</td>
<td>109 (28.7%)</td>
<td>150 (40.9%)</td>
<td>202 (54.7%)</td>
</tr>
<tr>
<td>Heart failure* 105 (6.9%)</td>
<td></td>
<td>11 (2.7%)</td>
<td>18 (4.7%)</td>
<td>35 (9.6%)</td>
<td>41 (11.1%)</td>
</tr>
<tr>
<td>Valvular heart disease† 89 (7.1%)</td>
<td></td>
<td>18 (5.3%)</td>
<td>18 (5.8%)</td>
<td>35 (1.7%)</td>
<td>18 (6.0%)</td>
</tr>
<tr>
<td>In-hospital data</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Thrombolysis* 51 (3.4%)</td>
<td></td>
<td>0 (0.0%)</td>
<td>5 (1.3%)</td>
<td>22 (6.0%)</td>
<td>24 (6.5%)</td>
</tr>
<tr>
<td>Hospitalization time, d* 9 (6–15)</td>
<td></td>
<td>7 (5–9)</td>
<td>8 (5–11)</td>
<td>11 (8–15)</td>
<td>16 (11–23)</td>
</tr>
</tbody>
</table>

Data are presented as medians (interquartile range) and absolute numbers (percentages) for continuous and categorical variables, respectively. Percentages refer to a total of recorded values. P values are for comparison between quartile groups. NIHSS indicates National Health Institute Stroke Scale Score; and TOAST, Trial of Org 10172 in Acute Stroke Treatment.

*P≤0.001; †P≤0.01.
stroke mortality reliably (AUC 0.84). However, it has only been validated internally and not externally. The iScore was initially introduced for the prediction of 12-month stroke mortality and was later validated to predict also disability (mRS=3–5) or institutionalization at discharge, and clinical response and risk of hemorrhagic complications after stroke thrombolysis. Compared with the iScore’s discriminatory power of 12-month mortality in the Ontario Stroke Audit (AUC 0.78), the ASTRAL score performed at least similarly to predict 5-year mortality (AUC 0.81). A caveat for the iScore is the need for recalibration/validation in other specific populations. The Six Simple Variable score includes 6 simple variables (age, living alone before stroke, prestroke mRS≤2, normal verbal component of the Glasgow Coma Scale, ability to lift both arms, and ability to walk without help) and at 12 performed, as well as or better than other simple predictive systems for the prediction of 12-month outcome.

The strengths of our study are the large size of the validation cohort, the hard end points, the long follow-up, and the confirmation of the results using several analytic methodologies. On the contrary, the study is limited by the fact that it is a single-center study and that only patients with first-ever stroke were included. Also, for a proportion of patients, mRS was assessed during a telephone interview and not in person; however, it was previously shown that telephone assessment of mRS is reliable and can be used in clinical studies. Finally, it is surprising that both atrial fibrillation and cardioembolic stroke remain in the multivariate model as independent predictors of unfavorable outcome. Given the borderline significance of the atrial fibrillation (95% CI, 1.03–2.63), it could be possible that this represents a type I statistical error (false-positive result).

In conclusion, the ASTRAL is a simple score available immediately after emergency department arrival that reliably predicts 5-year functional outcome and mortality in patients with first-ever stroke. Further validation of the ASTRAL score in other cohorts would be welcome.

Disclosures

None.

References


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Figure e1: ROC curve of ASTRAL score’s predictive power of unfavorable functional outcome.

AUC: 0.89 (95% CI: 0.88-0.91)  
\( p < 0.001 \)

Diagonal segments are produced by ties.
Figure e2: ROC curve of ASTRAL score’s predictive power of mortality.

AUC: 0.81 (95% CI 0.78-0.83)
p = 0.001

Diagonal segments are produced by ties.