External Validation of the ASTRAL Score to Predict 3- and 12-Month Functional Outcome in the China National Stroke Registry

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Background and Purpose—The ASTRAL score was recently introduced as a prognostic tool for acute ischemic stroke. It predicts 3-month outcome reliably in both the derivation and the validation European cohorts. We aimed to validate the ASTRAL score in a Chinese stroke population and moreover to explore its prognostic value to predict 12-month outcome.

Methods—We applied the ASTRAL score to acute ischemic stroke patients admitted to 132 study sites of the China National Stroke Registry. Unfavorable outcome was assessed as a modified Rankin Scale score ≥2 at 3 and 12 months. Areas under the curve were calculated to quantify the prognostic value. Calibration was assessed by comparing predicted and observed probability of unfavorable outcome using Pearson correlation coefficient.

Results—Among 3755 patients, 1473 (39.7%) had 3-month unfavorable outcome. Areas under the curve for 3 and 12 months were 0.82 and 0.81, respectively. There was high correlation between observed and expected probability of unfavorable 3- and 12-month outcome (Pearson correlation coefficient: 0.964 and 0.963, respectively).

Conclusions—ASTRAL score is a reliable tool to predict unfavorable outcome at 3 and 12 months after acute ischemic stroke in the Chinese population. It is a useful tool that can be readily applied in clinical practice to risk-stratify acute stroke patients. (Stroke. 2013;44:00-00.)

Key Words: ASTRAL score ■ China National Stroke Registry

Recently, the ASTRAL score was developed from the Acute Stroke Registry and Analysis of Lausanne (ASTRAL) registry for the prediction of 3-month functional outcome in patients with acute ischemic stroke and performed well in a double external validation in 2 European stroke registries: It is a useful tool for clinical practice and stroke research. Up to date, it has not been validated in non-European populations.

The purpose of our study was to validate the ASTRAL score in the China National Stroke Registry (CNSR), a nationwide prospective stroke registry, and moreover to explore its prognostic value to predict 12-month outcome.

Methods
The data set was derived from the CNSR. Full details of the rationale, design, and baseline information of the CNSR were published previously. Patients’ follow-up was assessed during a central telephone structured interview at 3-, 6-, and 12-months by blinded trained interviewers (graduate medical students). The study was approved by the central Ethics Committee at Beijing Tiantan Hospital, Capital Medical University. Written informed consent was obtained from all patients or from their legal representatives.

Unfavorable outcome was defined as modified Rankin Scale ≥2. Patients with a prestroke modified Rankin Scale >2, admitted >24 hours after symptom onset, or without follow-up assessment were excluded from the analysis. ASTRAL score was calculated in a manner identical to that reported in the original article. It assigns points to 6 categories: age (1 point for every 5 years), admission glucose level (1 point for glucose ≥3.7 mmol/L based on previous observations), impaired level of consciousness (3 points for any level of unconsciousness). Patients were excluded if any of the components of the ASTRAL score were not available.

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Statistical Analysis

Patient characteristics were summarized as mean values and SD for continuous parameters, or absolute count and percentage for categorical parameters. \( \chi^2 \) test was used to compare categorical parameters; Student \( t \) test for continuous. The discriminatory power of the score (c-statistic) was assessed by the area under the receiver-operator curves and 95% confidence intervals. Calibration was assessed by comparing predicted and observed probability of unfavorable outcome using Pearson correlation coefficient. Level of significance was set at 5% (2-sided test). All analyses were performed with SAS software version 9.2 (SAS Institute Inc, Cary, NC).

Results

Data set included 3522 patients who were registered in the CNSR from September 2007 to August 2008, met the inclusion criteria of the original publication, and had complete follow-up information (Figure I in the online-only Data Supplement). Baseline characteristics of the patients in the CNSR and the ASTRAL cohort are summarized in the Table. Figure II in the online-only Data Supplement presents the frequency of events for any given value of the ASTRAL score.

In the CNSR cohort, an ASTRAL score of 26 indicates a 50% likelihood of unfavorable outcome at 3 and 12 months. Figure 1 presents the calibration plot of the ASTRAL score in the CNSR cohort. On receiver-operator curves analysis, the ASTRAL score displayed good discriminatory power; the c-statistic for the discrimination between patients with favorable and unfavorable 3-month outcome was 0.82 (95% confidence interval, 0.81–0.83), which was similar to the c-statistic for the 12-month outcome 0.82 (95% confidence interval, 0.80–0.83; Figure 2). There was a high correlation between observed and expected probability of unfavorable 3- and 12-month outcome (Pearson correlation coefficient, 0.964 and 0.963, respectively).

Discussion

The present analysis validated externally the ASTRAL score in a large population of consecutive Chinese stroke patients. Also, it extended for the first time the prognostic role of the ASTRAL score to predict functional outcome at 12 months after ischemic stroke.

The ASTRAL score was recently introduced as a simple and accurate tool to predict 3-month functional outcome in stroke patients admitted within 24 hours after stroke onset. The accurate discriminatory power of the score, which was also confirmed in the present study, emphasizes the potential of the ASTRAL score as a useful risk stratification tool that can be applied in routine clinical practice and stroke research. The present report represents the first external validation of the ASTRAL score in an Asian population. A good performance of the score was seen despite significant baseline differences between the original and the validation cohorts.

We found a significantly higher unadjusted risk of unfavorable stroke outcome at 3 months in the CNSR (39.7%) compared with the ASTRAL registry (34%), despite a lower age

![Figure 1](https://example.com/figure1.png)

*Figure 1.* Calibration plot of the ASTRAL score in the China National Stroke Registry cohort. Dots represent the actual rates of unfavorable outcome, and the vertical lines represent the 95% confidence intervals. The continuous line represents the predicted probability of unfavorable outcome. mRS indicates modified Rankin Scale.
Although methodological heterogeneity may account for some of the differences, it is possible that the gap between clinical practice and the guidelines contributes to the higher proportion of unfavorable stroke outcome in CNSR. Evidence-based therapeutic and preventive measures are available for ischemic stroke but remain underused in China.5

Strengths of this study include the large sample size of consecutive stroke patients and the prospective and multicenter design of the CNSR. In addition, we explored the discrimination and calibration power of ASTRAL score to predict unfavorable outcome at 12 months, thus extending its prognostic role over a longer time window.

Our study also has potential limitations. There could be a selection bias; our study sites may represent the institutes with more resources and expertise than those in rural areas. Therefore, we might have underestimated the risk of unfavorable stroke outcome in the Chinese population. However, this enrollment bias should not affect the accuracy of the ASTRAL score as an integral predictive tool. Second, the follow-up assessment was performed by telephone interviews rather than clinical examination in person, which may have biased the modified Rankin Scale results. However, the telephone assessment of the modified Rankin Scale with a structured interview was shown recently to have a good agreement with face-to-face assessment.6 Finally, <50% of the overall CNSR cohort was included in the present analysis (mean age, 64.9 years; SD, 12.3 years; 37.8% women, median National Institutes of Health Stroke Scale, 4 [interquartile range, 2–8] in the excluded patients), which may have introduced selection bias to the analysis.

In conclusion, the ASTRAL score is a reliable tool to predict unfavorable outcome at 3 and 12 months after acute ischemic stroke in the Chinese population.

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Disclosures
None.

References
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Figure 1: Flow diagram of patients included in the analysis.
*: ≥1 of the following: age, NIHSS, onset-to-admission delay, range of visual field defect, glucose, level of consciousness.
Figure 2: Frequency of events at any given value of the ASTRAL score. The red sigmoid curve represents the association between the ASTRAL score and predicted probability of 3-months unfavorable outcome in the CNSR (Red line).