Original Article

The PLAN score can predict poor outcomes of intracerebral hemorrhage

Wanliang Du[1], Xingquan Zhao[1,2], Yilong Wang[1,3], Guitao Zhang[4], Jiming Fang[5], Yuesong Pan[4], Liping Liu[1], Kehui Dong[1], Gaifen Liu[1,4], Yongjun Wang[1,2,3,4,6]; on behalf of the China National Stroke Registry (CNSR) Investigators

[1]Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing 100070, China; [2]Beijing Key Laboratory of Translational Medicine for Cerebrovascular Disease, Beijing 100070, China; [3]Center of Stroke, Beijing Institute for Brain Disorders, Beijing 100070, China; [4]China National Clinical Research Center for Neurological Diseases, Beijing 100070, China; [5]Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada; [6]Advanced Innovation Center for Human Brain Protection, Capital Medical University, Beijing 100070, China

Contributions: (I) Conception and design: Y Wang, G Liu, W Du; (II) Administrative support: X Zhao, Y Wang, L Liu, C Wang, K Dong; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: G Liu, Y Pan; (V) Data analysis and interpretation: G Liu, J Fang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Yongjun Wang; Gaifen Liu. Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing 100070, China. Email: yongjunwang@ncrcnd.org.cn; liugaifen1997@163.com.

Background: For patients hospitalized after acute ischemic stroke (AIS), the preadmission comorbidities, level of consciousness (LOC), age and neurologic deficit (PLAN) score can help to identify those who may have a poor outcome. Implementing the PLAN score in other types of stroke may also have predictive value. Our study aimed to evaluate the PLAN score's prognostic accuracy in predicting 1-year mortality and severe disability after intracerebral hemorrhage (ICH).

Methods: We analyzed data found in the China National Stroke Registry (CNSR) of 2,453 hospitalized patients in 132 urban Chinese hospitals, diagnosed with ICH from September 2007 to August 2008. The outcomes analysis included 30-day mortality, modified Rankin Scale score (mRS) of 5–6 at discharge, and 1-year mortality. Univariate and multivariate analysis was performed, and we calculated consistency statistics (C statistic). We evaluated the PLAN score performance using area under the curve (AUC) calculations.

Results: We found that the 30-day mortality was 12.6%, the frequency of a mRS 5–6 at discharge was 20.6%, and 1-year mortality was 21.9%. The PLAN score had good predictive value in 30-day mortality (C statistic, 0.82), death or severe dependence at discharge (0.84), and 1-year mortality (0.82).

Conclusions: In patients hospitalized for ICH, the 30-day mortality, death or severe dependence at discharge and 1-year mortality can be predicted by the PLAN score. Similarly to patients hospitalized after AIS, the PLAN score can help to identify patients likely to have poor outcomes following hospitalization for ICH.

Keywords: Intracerebral hemorrhage (ICH); acute ischemic stroke (AIS); outcomes; PLAN score

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Introduction

Spontaneous intracerebral hemorrhage (ICH) is a sudden and life-threatening event that accounts for 10–15% of all stroke cases (1,2). Mortality rates for ICH patients are as high as 46–48% and with only 32.8–42.4% of patients being able to function independently by 1 year post-ICH hospitalization (3,4).

At the time of admission, it is important to evaluate the possibility of death and severe disability to make rational treatment decisions for ICH patients. Making these decisions quickly is also important to help determine if patients are eligible for clinical trials, which will help assess

the use of novel therapies in ICH. These considerations necessitate the development of a model that will help clinicians efficiently stratify patients for accurate assessment of therapeutic efficacy using varying treatment modalities and help predict the prognosis of ICH.

Several prognostic tools have been developed for ICH, including the ICH score (5), intracerebral hemorrhage grading scale (ICH-GS) (6), Essen-ICH score (7), max-ICH score (8), the simplified ICH score (sICH score) (9), ICH functional outcome score (ICH-FOS) (10), modified ICH (MICH) score (11), ICH outcomes project (ICHOP) score (12), and the functional outcome (FUNC) score (13). Even more of these prognostic tools have been developed for acute ischemic stroke (AIS), including the acute stroke registry and analysis of Lausanne (ASTRAL) score (14), preadmission comorbidities, level of consciousness (LOC), age and neurologic deficit (PLAN) score (15), ischemic stroke predictive risk score (IScore) (16), the Bologna outcome algorithm for stroke (BOAS) (17), Get with the Guidelines Stroke (GWTG-Stroke) risk model (18), totaled health risks in vascular events (THRIVE) score (19), subtype, Oxfordshire Community Project classification, age and prestroke modified Rankin (SOAR) score (20), and thrombolytic predictive instrument (TPI) score (21). In these prediction models, during the acute phase of a stroke, the most important predictors of outcome are patient age and stroke severity (22). Other important predictors of outcome are related to the presence of comorbid medical conditions and functional status prior to stroke onset (23). Predictive assessment of poor outcomes in AIS may share similarities with predicting poor outcomes in ICH. Of the models mentioned, the PLAN score is desirable because of its simplicity and integration multiple factors including preadmission comorbidities, LOC, age, and neurologic focal deficit (15). The ease of use in calculating PLAN scores may be valuable in the time-sensitive setting of ICH hospitalization. We used PLAN scoring in an analysis of ICH patients in the China National Stroke Registry (CNSR) to determine if it can help predict poor outcomes following ICH hospitalization.

Methods

Study design

We conducted this study using the CNSR, the largest stroke registry in China. The CNSR is sponsored by the Chinese Ministry of Health and is a national, multicenter, and prospective registry. The CNSR recruited patients from September 2007 to August 2008 who suffered from acute cerebrovascular disease. These patients were from 132 participating centers in 27 provinces and 4 municipalities spanning the entirety of China, including Hong Kong SAR (24). To minimize the variations among different areas due to factors such as infrastructure, hospital size, population composition, as well as maximize the geographic and demographic representativeness, participating centers were strategically chosen from the west, east, and central areas of China. The total number of patients in the CNSR is 22,216 consecutive eligible patients. Signed, written informed consent was obtained from every enrolled patient or their legal guardian.

Eligibility criteria

The cohort used in this study included CNSR patients who were ≥18 years of age with a primary diagnosis of ICH. We excluded patients diagnosed with transient ischemic attack, ischemic stroke, or subarachnoid hemorrhage. ICH diagnoses were based on the World Health Organization criteria combined with brain computerized tomography (CT) imaging. ICH patients in this study also must have presented to hospital no more than 14 days after symptom onset and be >18 years old. Exclusion criterion included tumor-induced ICH, unavailable data of ICH hematoma volume, primary intraventricular hemorrhage (IVH), >2 pre-stroke modified Rankin Scale score (mRS), patients who did not agree take part in the study, and those who were lost during follow-up. The central institutional review board at Beijing Tiantan Hospital and ethical committees at each participating center of the CNSR approved the scientific use of the registered data for this study.

Data collection

Patient demographics (e.g., age, gender) were recorded upon admission. Baseline vascular risk factors included stroke history (confirmed from a medical chart), hypertension (history of hypertension or use of antihypertensive medicine), diabetes mellitus (history of diabetes mellitus or use of hypoglycemic drug), dyslipidemia (history of dyslipidemia or use of lipid-lowering medicine), atrial fibrillation (history of atrial fibrillation based on the confirmation of at least one electrocardiogram, or onset of arrhythmia during hospitalization), cardiovascular disease, active smoking, moderate or heavy alcohol consumption

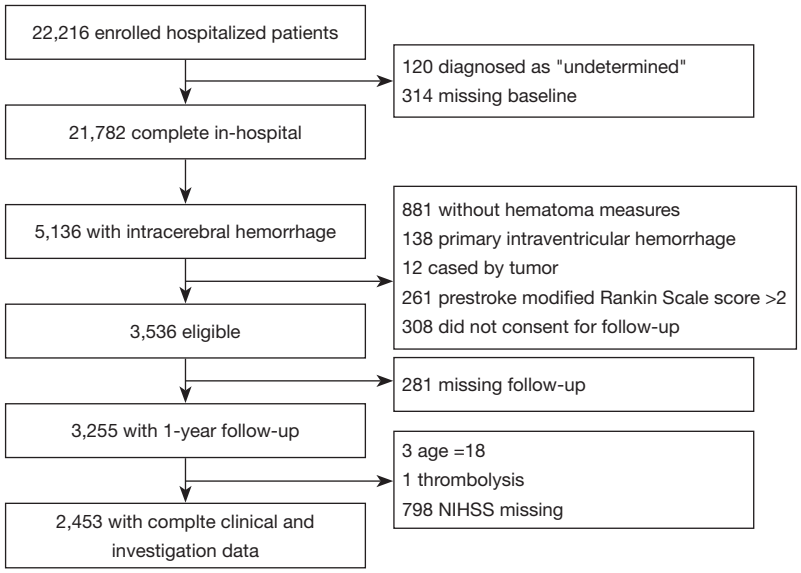

Figure 1 Selection method for defining intracerebral hemorrhage patient eligibility.

(≥2 standard alcoholic beverages a day), body mass index (BMI, weight in kilograms divided by the square of height in meters), and medication history including antihypertensive, antiplatelet, anticoagulant, lipid-lowering, and hypoglycemic agents. Other risk factors such as cancer (prior or concurrent, active or metastatic) and lung disease were also noted. We used mRS to evaluate pre-stroke functional status and the National Institute of Health Stroke Scale (NIHSS) and Glasgow Coma Scale (GCS) to assess the severity of neurological impairment within 24 hours of admission. Routine laboratory tests data were recorded. To acquire information on mRS, death, and the corresponding dates of outcomes, all patients' functional outcomes were evaluated via telephone follow-up at 3, 6, and 12 months post-ICH hospitalization. Telephone follow-up was uniform for all study subjects using a shared, standardized interview protocol administered by trained interviewers.

Statistical analyses

The calculation of patients' PLAN score was performed as described in the original article (15). For descriptive analysis, we used percentages for categorical variable and mean with standard deviation (SD) for continuous variables. To compare categorical variables, we used a χ^2 test and for the continuous variables, we used the *t*-test or Wilcoxon rank sum test for continuous variables. PLAN score was used to divide the CNSR cohort into six risk categories. A logistic regression model was applied for evaluation of PLAN score's poor outcome predictive value using 30-day mortality, mRS 5–6 at discharge, and 1-year mortality. Area under the curve (AUC) from the C statistic was used to establish prediction score performance. A C statistic of 1.0 indicates a perfect prediction, whereas a C statistic of 0.5 indicates that the prediction does not differ from a random prediction. All tests were 2-tailed. $P<0.05$ was deemed statistically significant. SAS version 9.4 statistical software (SAS Institute Inc., Cary, North Carolina, USA) was used for all analyses.

Results

Five thousand one hundred and thirty-six of the 22,216 CNSR patients were diagnosed with ICH and screened for eligibility for this study. Using the previously described exclusion criteria, we excluded 881 patients who had no hematoma measurement data, 138 with primary IVH, 12 with ICH secondary to an intracranial tumor, 261 with a pre-stroke mRS >2,308 who did not consent for follow-up, 281 lost to follow-up, three 18-year-old patients, one patient with ICH secondary to thrombolysis, and 798 patients without NIHSS. The remaining 2,453 patients were analyzed in *Figure 1*.

The mean age of these ICH patients was 62.17± 12.95 years and 946 (38.6%) were female. Patient demographics and clinical characteristics at baseline are summarized in *Table 1*.

Table 1 Characteristics of intracerebral hemorrhage cohorts in CNSR

Characteristic	N (%)
Age	62.17±12.95
Female gender	946 (38.6)
Preadmission dependence	1,977/2,430 (81.4)*
Cancer	36 (1.5)
Stroke or TIA	650 (26.5)
Dementia	34 (1.4)
Hypertension	1,685 (68.7)
Hyperlipidemia	190 (7.7)
Atrial fibrillation	35 (1.4)
Diabetes mellitus	217 (8.8)
Congestive heart failure	14 (0.6)
Myocardial infarction	37 (1.5)
Reduced LOC	895 (36.5)
Facial weakness	1,661 (67.7)
Arm weakness	1,481 (60.4)
Leg weakness	1,488 (60.7)
Neglect	343 (14.0)
Aphasia	1,163 (47.4)
Dysphagia	179 (7.3)
Visual field defect	438 (17.9)
30-day mortality	310 (12.6)
mRS 5–6 at discharge	505 (20.6)
1-year mortality	537 (21.9)

*, denominator maybe different due to missing data. LOC, level of consciousness; mRS, modified Rankin Scale score; TIA, transient ischemic attack.

Univariate analysis showed age, preadmission dependence, reduced LOC, arm weakness, leg weakness, aphasia and/or neglect were significantly associated with 30-day mortality, mRS 5–6 at discharge, and 1-year mortality (P<0.001). Atrial fibrillation was only significantly associated with mRS 5–6 at discharge. However, cancer and congestive heart failure were not associated with mortality (*Table 2*).

Multivariable analysis showed age, reduced LOC, aphasia and/or neglect were significantly predictive of 30-day mortality, mRS 5–6 at discharge, and 1-year mortality (Ps<0.001). Arm weakness was only significantly associated with mRS 5–6 at discharge. Pre-admission dependence, cancer, atrial fibrillation, congestive heart failure, and leg weakness were not significantly associated with mortality (*Table 3*).

Figure 2 shows that 30-day mortality, mRS 5–6 at discharge, and 1-year mortality after ICH onset increased gradually as PLAN score increased.

AUC values were used to estimate the accuracy of the PLAN score in predicting poor outcome. The PLAN score showed good discriminatory power with AUC values of 0.82, 0.84 and 0.82 at 30-day discharge and 1-year follow-ups, respectively (*Figure 3*). This was consistent even after grouping by age and gender, as the PLAN score still showed good discriminatory power as all the AUC values were still ≥0.80 (*Table 4*).

Discussion

The CNSR is a large-scale stroke registry well-suited for the evaluation of PLAN score predictive value in ICH patients. Using this database, we found that the PLAN score reliably predicted poor outcomes following ICH hospitalization. Our study represents the first assessment of the predictive ability of the PLAN score in ICH using a nationwide cohort.

It is well-established that stroke risk prognostic scores can improve clinician accuracy in predicting clinical outcomes (25). The PLAN score was developed in Canada (15) and validated in several AIS populations with varying ethnicities (26,27), and a Scottish mixed stroke patient cohort (88% AIS, 12% ICH) (25). In our study, we found that the PLAN score had performed well in predicting the 30-day mortality (C statistics: 0.82; 95% CI, 0.70–0.84), mRS 5–6 at discharge (C statistics: 0.84; 95% CI, 0.83–0.86) and 1-year mortality (C statistics: 0.82; 95% CI, 0.80–0.84), which is similar to the predictive ability in AIS patients (15,25-27).

In the past two decades, several prognostic tools have been developed for ICH. Hemphill *et al.* introduced the ICH score (5) in 2001, which were followed by a number of modified and pragmatic ICH scoring methods (6-12). The original ICH score was used to predict 30-day mortality (C statistics: 0.825; 95% CI, 0.811–0.838) and 1-year mortality (C statistics: 0.798; 95% CI, 0.783–0.811) (5). The ICH-GS score assessed 30-day mortality (C statistics: 0.830; 95% CI, 0.817–0.843) and 1-year mortality (C statistics: 0.814; 95% CI, 0.800–0.827) (6) along with the ICH-FOS score, which also predicted 30-day mortality (C statistics: 0.836;

Table 2 Univariate analysis on the association between selected variables and outcomes

Characteristic	30-day mortality		mRS 5–6 at discharge		1-year mortality	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age	1.26 (1.14–1.38)	<0.001	1.31 (1.21–1.42)	<0.001	1.47 (1.35–1.59)	<0.001
Preadmission dependence	1.66 (1.26–2.20)	<0.001	1.94 (1.54–2.44)	<0.001	2.53 (2.03–3.16)	<0.001
Cancer, %	1.39 (0.57–3.37)	0.465	1.72 (0.84–3.51)	0.140	2.04 (1.03–4.06)	0.042
Stroke or TIA, %	1.40 (1.09–1.81)	0.010	1.63 (1.32–2.01)	<0.001	1.83 (1.49–2.25)	<0.001
Dementia, %	2.53 (1.17–5.48)	0.018	3.51 (1.78–6.93)	<0.001	4.12 (2.09–8.13)	<0.001
Atrial fibrillation, %	3.25 (1.58–6.70)	0.001	3.32 (1.70–6.51)	0.001	2.14 (1.07–4.27)	0.032
Diabetes mellitus, %	1.37 (0.94–2.01)	0.106	0.89 (0.62–1.27)	0.519	1.48 (1.09–2.03)	0.013
Congestive heart failure, %	3.89 (1.29–11.68)	0.016	2.92 (1.01–8.44)	0.049	2.70 (0.93–7.81)	0.067
Myocardial infarction, %	1.63 (0.71–3.74)	0.251	1.24 (0.58–2.65)	0.572	1.33 (0.64–2.76)	0.448
Reduced LOC	8.85 (6.62–11.83)	<0.001	9.56 (7.59–12.04)	<0.001	6.58 (5.33–8.14)	<0.001
Arm weakness	6.79 (4.66–9.88)	<0.001	9.28 (6.75–12.77)	<0.001	4.51 (3.52–5.78)	<0.001
Leg weakness	6.24 (4.32–8.99)	<0.001	8.26 (6.07–11.24)	<0.001	4.67 (3.63–6.00)	<0.001
Neglect	8.02 (6.14–10.46)	<0.001	8.68 (6.78–11.12)	<0.001	7.13 (5.59–9.10)	<0.001
Aphasia	7.33 (5.34–10.06)	<0.001	7.28 (5.70–9.30)	<0.001	4.47 (3.60–5.54)	<0.001
Aphasia and/or neglect	7.31 (5.31–10.06)	<0.001	6.84 (5.36–8.71)	<0.001	4.37 (3.53–5.43)	<0.001
Dysphagia	2.22 (1.53–3.21)	<0.001	2.44 (1.77–3.37)	<0.001	2.12 (1.54–2.92)	<0.001
Visual field defect	5.84 (4.52–7.53)	<0.001	5.89 (4.70–7.37)	<0.001	4.40 (3.53–5.50)	<0.001

LOC, level of consciousness; mRS, modified Rankin Scale score; OR, odds ratio; TIA, transient ischemic attack.

Table 3 Multivariate analyses

Characteristic	30-day mortality		mRS 5–6 at discharge		1-year mortality	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age	1.22 (1.10–1.35)	<0.001	1.33 (1.21–1.46)	<0.001	1.48 (1.35–1.62)	<0.001
Preadmission dependence	1.23 (0.90–1.69)	0.188	1.53 (1.16–2.03)	0.003	2.10 (1.62–2.72)	<0.001
Cancer, %	1.58 (0.57–4.33)	0.378	2.20 (0.91–5.35)	0.081	1.91 (0.84–4.36)	0.124
Atrial fibrillation, %	3.16 (1.31–7.63)	0.010	3.87 (1.65–9.08)	0.002	1.60 (0.71–3.64)	0.258
Congestive heart failure, %	3.15 (0.85–11.64)	0.086	2.09 (0.56–7.76)	0.272	1.67 (0.47–5.92)	0.431
Reduced LOC	4.57 (3.30–6.32)	<0.001	4.87 (3.75–6.33)	<0.001	4.19 (3.26–5.37)	<0.001
Arm weakness	2.20 (1.12–4.35)	0.023	3.11 (1.77–5.44)	<0.001	1.56 (0.97–2.52)	0.070
Leg weakness	1.22 (0.63–2.38)	0.557	1.42 (0.82–2.46)	0.206	1.56 (0.97–2.53)	0.068
Aphasia and/or neglect	3.04 (2.13–4.34)	<0.001	2.66 (2.01–3.51)	<0.001	1.91 (1.48–2.47)	<0.001
C statistic	0.82 (0.80–0.85)	0.760*	0.85 (0.83–0.87)	0.063*	0.81 (0.79–0.83)	0.336*

*, HL-test P value for C statistics. LOC, level of consciousness; mRS, modified Rankin Scale score; OR, odds ratio.

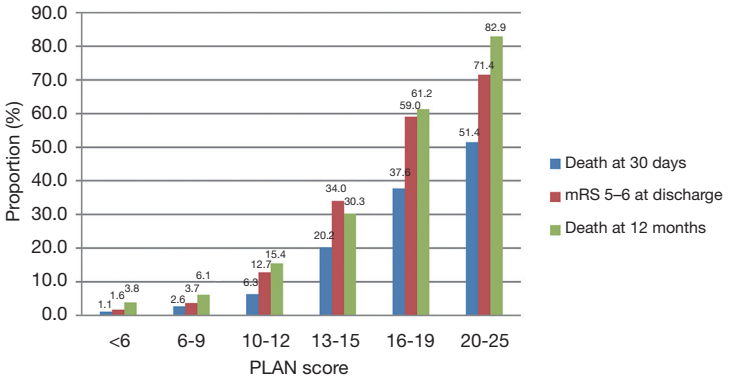

Figure 2 Trends of poor outcome as the PLAN score increasing.

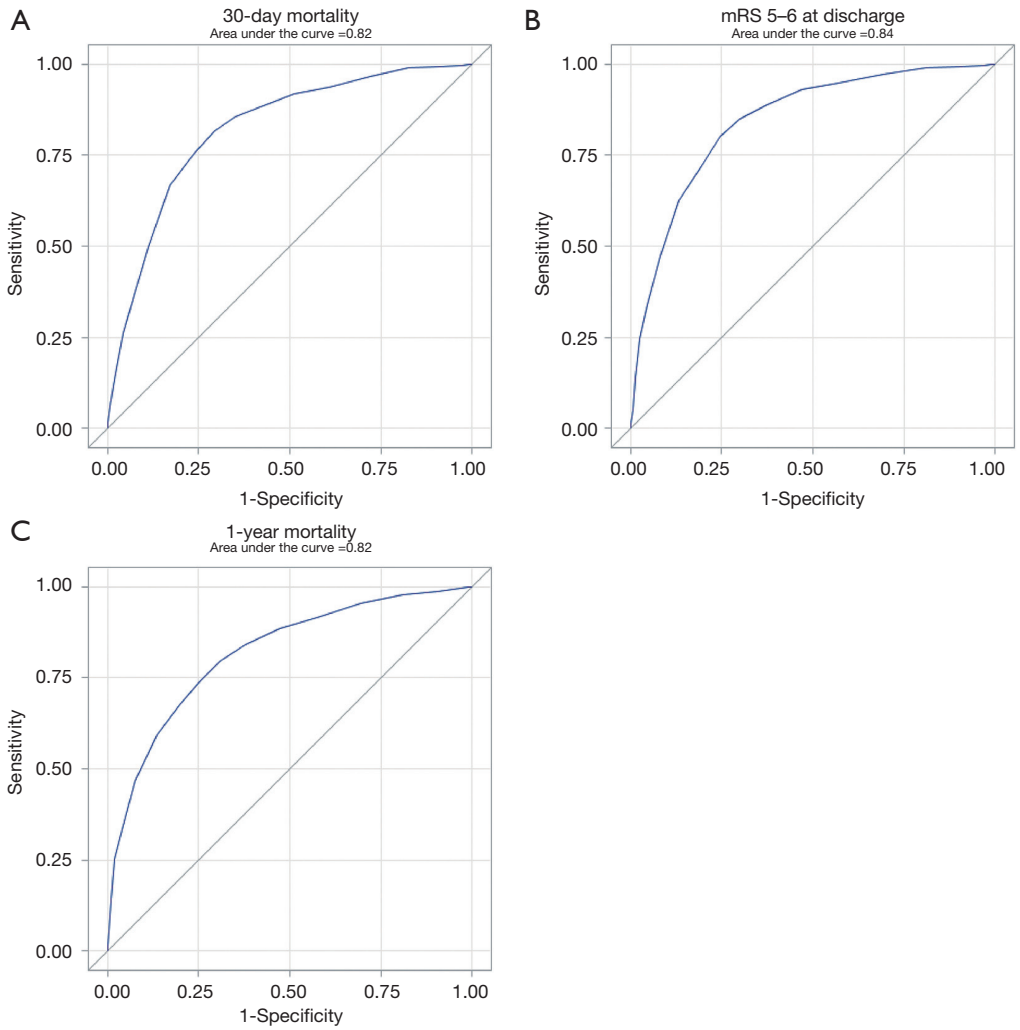

Figure 3 Receiver-operating characteristic curves of the PLAN score for prediction of 30-day mortality (A), mRS 5–6 at discharge (B), and 1-year mortality (C).

Table 4 C statistics of the PLAN score in the ICH cohort and subgroup analysis

PLAN score	30-day mortality	mRS 5–6 at discharge	1-year mortality
All	0.82 (0.70–0.84)	0.84 (0.83–0.86)	0.82 (0.80–0.84)
Age, years			
<70	0.81 (0.78–0.85)	0.84 (0.81–0.86)	0.80 (0.77–0.83)
≥70	0.82 (0.78–0.85)	0.84 (0.81–0.87)	0.82 (0.78–0.85)
Sex			
Men	0.82 (0.79–0.85)	0.85 (0.82–0.87)	0.82 (0.80–0.85)
Women	0.82 (0.78–0.86)	0.84 (0.81–0.87)	0.81 (0.77–0.84)

95% CI, 0.822–0.848) and 1-year mortality (C statistics: 0.836; 95% CI, 0.822–0.848) (10). Those prognostic models use similar variables, such as age, GCS score, ICH volume, ICH location, NIHSS score, and serum glucose, along with a few variables that required a significant waiting period such as CT and detailed lab exams. Clinical grading scales must be reliable, accurate, and practical and to-date none of these prognostic tools have been universally accepted in routine clinical practice. The PLAN score, which was developed as a bedside prediction rule for death and severe disability following AIS, addresses issues of practicality and efficiency by only requiring basic information such as preadmission comorbidities, LOC, age, and neurologic focal deficit, which are all established risk factors that can be evaluated by non-specialist clinicians. The simplicity and high predictive value of the PLAN score may allow it to have widely accepted use for prediction of poor outcomes in post-hospitalization ICH patients.

Despite the proposed benefits of using PLAN in ICH patients, we acknowledge a few limitations of this study. First, only hospitalized patients were included, while those who died in the emergency department or sought treatment in the outpatient setting were not considered in our study. Second, misjudgment of patients' functional outcome evaluation may be present because interviewees might not be able to give accurate answers during the follow-up phone interview. Although prior studies have shown that assessment of the mRS through structured telephone is reliable and comparable with face-to-face interviews (28). Third, the predictions performed at first assessment were mostly within 24 hours after ICH onset, yet predictions performed >24 hours from onset are more accurate and over the first 24 hours, the association between stroke severity and 90-day mRS strengthens (29). Despite these limitations, a reliable method of early prediction should be used to inform vital early clinical decision-making and discussions regarding prognosis with patients and relatives. Further validation of the PLAN score is needed in non-Asian ICH populations. Future work must also examine whether the PLAN score can improve prediction of ICH patient outcomes when compared to the assessment of experienced stroke-specialized clinicians.

Conclusions

The PLAN score can predict 30-day mortality, death or severe dependence at discharge, and 1-year death after ICH hospitalization. This score was developed originally for use in AIS, but it may also help identify ICH patients who could develop poor outcomes following hospitalization. Further studies are needed to validate the PLAN score for use in ICH patients from different ethnic backgrounds.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The central institutional review board at Beijing Tiantan Hospital and ethical committees at each participating center of the CNSR approved the scientific use of the registered data for this study. Written informed consent was obtained from every enrolled patient or their legal guardian.

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