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ORIGINAL RESEARCH

Novel CT Image-Based Intracerebral Bleeding Risk Score for Patients With Acute Ischemic Stroke Undergoing Thrombolysis

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BACKGROUND: Symptomatic intracerebral hemorrhage (sICH) after intravenous recombinant tissue plasminogen activator in patients with acute ischemic stroke (AIS) remains a feared yet unpredictable complication. We aimed to develop and validate a new predictive model incorporating clinical variables and noncontrast head computed tomography imaging features to predict sICH in patients with AIS receiving intravenous recombinant tissue plasminogen activator.

METHODS AND RESULTS: The predictive model was derived from 808 patients with AIS in the derivation cohort in Southeast China, based on multivariable logistic regression analysis. External validation was conducted in a validation cohort from Central China. Discrimination, calibration, and clinical usefulness of the predictive model were assessed. We observed 32 sICH events among 808 patients with AIS in the derivation cohort, and 21 sICH events out of 612 participants in the validation cohort. The variables in the predictive model included cerebral small vessel disease burden and early infarct signs on head computed tomography scan, atrial fibrillation, age, systolic blood pressure, and initial National Institutes of Health Stroke Scale score. The fitted model showed promising discrimination (optimism-corrected C statistic of 0.80) and acceptable calibration (Hosmer and Lemeshow goodness of fit P=0.816) in the derivation cohort. External validation showed similar discrimination (C statistic 0.82 [95% CI, 0.72–0.91]) and calibration (Hosmer and Lemeshow goodness of fit P=0.866).

CONCLUSIONS: Our internally and externally validated prediction model for sICH in patients with AIS who received intravenous thrombolysis may facilitate individualized prediction for intracerebral bleeding risk after intravenous thrombolysis for acute ischemic stroke.

Key Words: acute ischemic stroke ■ intravenous thrombolysis ■ nomograph ■ predictive model ■ symptomatic intracranial hemorrhage

Symptomatic intracerebral hemorrhage (sICH) after intravenous thrombolysis using recombinant tissue plasminogen activator (r-tPA) in patients with acute ischemic stroke (AIS) remains a major feared complication.[1–3] Previous efforts have established several predictive models for sICH after intravenous thrombolysis, some of which only include clinical variables, such as the SPAN-100 (Stroke diagnosis using age and National Institutes of Health Stroke Scale [NIHSS]), and the Multicenter stroke survey score. The HAT (hemorrhage after thrombosis) score and some other scores incorporated both simple computed tomography (CT) image

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CLINICAL PERSPECTIVE

What Is New?

- The newly established CANES (CSVD [Cerebral small vessel disease], AF [Atrial fibrillation], initial National Institutes of Health Stroke Scale [NIHSS] score, Early infarct signs, Systolic blood pressure) model is the first to add computed tomography–visible cerebral small-vessel disease imaging markers in addition to early infarct signs to predict symptomatic intracranial hemorrhage after thrombolysis in patients with acute ischemic stroke.

What Are the Clinical Implications?

- The CANES score may provide indications for early identification of patients who are candidates for postprocedural intensive management to reduce the risk of symptomatic intracerebral hemorrhage.

Nonstandard Abbreviations and Acronyms

AIS	acute ischemic stroke
CSVD	cerebral small vessel disease
CT	computed tomography
HAT	hemorrhage after thrombosis
NIHSS	National Institutes of Health Stroke Scale
r-tPA	recombinant tissue plasminogen activator
SEDAN	sugar, early infarct sign, dense artery, age, and NIHSS
sICH	symptomatic intracerebral hemorrhage
SPAN-100	stroke diagnosis using age and NIHSS

features (ie, early infarct signs) and clinical variables.[4,5] However, the process of categorizing discrete/continuous variables into 2 or 3 risk groups, as used by the HAT and the SEDAN (sugar, early infarct sign, dense artery, age, and NIHSS) scores, is statistically inefficient and may decrease the predictive accuracy.[6]

Cerebral small vessel disease (CSVD) refers to a group of age-related pathological disorders that affect the brain microvasculature and cause most spontaneous intracerebral hemorrhage.[7] Previous studies showed that biomarkers of CSVD on magnetic resonance imaging were related to the risk of sICH after intravenous thrombolysis.[8,9] However, assessing imaging markers of CSVD with magnetic resonance imaging is not routinely accessible and increases time to treatment in emergency scenarios. A recent score to assess the total CSVD burden on noncontrast head CT scans based on the presence of 3 imaging markers (white matter lucencies, lacunes, and brain atrophy) showed good inter-rater agreement.[10] Moreover, the presence of CT-defined leukoaraiosis was associated with an increased risk of sICH after thrombolysis for AIS.[11] To our knowledge, the role of a more comprehensive assessment of CT-CSVD burden in sICH risk prediction has not been investigated. We aimed to develop and validate a novel bleeding nomogram incorporating imaging markers of CSVD and early infarct signs on noncontrast head CT scan, together with simple clinical variables, to predict sICH after intravenous thrombolysis for AIS.

METHODS

Data Sharing Statement

Persons interested in obtaining access to the data should contact the corresponding author.

Study Design, Setting, and Participants

A retrospective multicenter observational study was used to develop a prediction model for sICH after intravenous r-tPA in patients with AIS, using data from 3 teaching hospitals of Fujian Medical University in Southeast China between January 2016 and December 2022. The model was externally validated using a second retrospective observational data from 2 teaching hospitals in Central China. Patients were eligible if they received intravenous r-tPA within 4.5 hours after stroke onset. We excluded patients who underwent endovascular treatment following bridging intravenous thrombolysis because it was beyond the focus of the present study. We also excluded patients without imaging data of sufficient quality to assess initial baseline CT imaging features, including CSVD and early infarct signs. Both the derivation cohort and the validation cohort used the same eligibility criteria. This study protocol was reviewed and approved by Fujian Medical University Union Hospital Ethics Committee (NO. 2019KY076). Informed consent was waived due to the nature of our retrospective study with routine anonymous data.

Model Predictors

We selected 24 clinically relevant predictors of sICH through a systematic literature search using the search term ('ischemic stroke', 'cerebral infarct', 'hemorrhagic transformation', 'cerebral hemorrhage', 'intravenous thrombolysis', 'alteplase', and 'recombinant tissue plasminogen activator')[4–6,10] and expert clinical opinion, including demographics (age, sex, systolic and

diastolic blood pressure), clinical characteristics (smoking status, drinking, initial NIHSS, TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification, laboratory indicators (blood glucose before thrombolysis, platelet count, total cholesterol, low-density lipoprotein, triglycerides), CT-image features (CT-CSVD score, dense artery sign, early infarct signs, Alberta Stroke Program Early Ct Score [ASPECT] score), comorbidities (previous stroke, hypertension, diabetes, hyperlipidemia, atrial fibrillation, ischemic heart disease), and prescribed drugs (antithrombotics use before stroke).

CT-Image Assessment

All patients underwent a baseline head CT scan before intravenous thrombolysis, and a follow-up head CT scan was routinely performed at 24 hours or earlier if sICH after thrombolysis was suspected. Two trained neuro-radiologists blinded to clinical variables independently reviewed the noncontrast head CT images. The imaging markers of CSVD on noncontrast head CT were assessed as previously described. In brief, anterior and posterior white matter lucencies were graded using the van Swieten scale: absent (grade 0), restricted to the region adjoining the ventricles (grade 1), covering the entire region from the lateral ventricle to the cortex (grade 2).[12] Cortical and central atrophy were graded as none (grade 0), mild to moderate (grade 1), or severe (grade 2) against a standard template. A lacune was defined as a round or ovoid subcortical well-defined hypoattenuating lesion with a diameter of 3 to 15 mm in the territory of the perforating arteriole.[12] We calculated the total CT-CSVD score ranging from 0 to 3, which allocates 1 point for each of the following: severe white matter lucencies (grade 2), ≥2 lacunes, and severe central or cortical atrophy (grade 2).[12] Early infarct signs and dense artery sign (the appearance of a direct thrombus on nonenhanced CT) were reviewed as described.[13–16] Early infarct signs include visible hypodensities, insular ribbon sign, obscuration of the lentiform nucleus, superficial/absent lateral fissure, or cortical sulcus.[15] Dense artery sign refers to the appearance of direct thrombus imaging on a nonenhanced head CT.[16]

Outcome

Our primary outcome was sICH per the ECASS-II (European Cooperative Acute Stroke Study-II) standard, defined as parenchymal hemorrhage on head CT with neurologic worsening (NIHSS ≥4 points) within 36 hours after thrombolytic treatment.[1]

Sample Size Calculation

We used the pmsampsize Package, R software (version 4.3.1) for sample size estimation. Our prespecified sample size calculation for model derivation assumed the prevalence of sICH is 0.06, an estimate of C statistic 0.8, and a maximum number of 24 predictor parameters in the model. Based on these inputs, a sample size of ≈2846 participants is required.[17] Our sample size is relatively low and therefore the predictive model will be at risk of overfitting. However, we have assessed the stability and generalization of the predictive model in the external validation.

Missing Data

Fully conditional specification[18] was used to multiply impute missing values in our derivation cohort using the MICE package (version 3.6.0) for R (version 4.3.1). The imputation models included all model covariates and binary event within each data set. We generated 10 imputed data sets based on the rule of thumb.[19] Missing data were assumed to be missing at random.[20] Predictor variables requiring imputation were baseline blood glucose (64 [7.9%]), blood platelet count (5 [0.6%]), serum lipid profile including total cholesterol, low-density lipoprotein, and triglycerides (20 [2.5%]), initial NIHSS (3 [0.4%]), TOAST classification (3 [0.4%]), and antiplatelet use before index stroke (14 [1.7%]). There were no missing data in the validation cohort.

Statistical Analysis

We compared the frequency of clinical characteristics and noncontrast head CT features between patients with and without sICH using the χ^2 test or Fisher's exact test for categorical variables and the Mann–Whitney *U* test for continuous variables.

Model Developed With the Imputation of Missing Data

For model development in the derivation cohort, predictors were selected by a least absolute shrinkage and selection operator algorithm in each of the 10 imputed data sets using the glmnet package (version 4.1-4). Variables for the predictive model were selected by majority vote (ie, if they were selected 5 or more times in the 10 imputed data sets).[21] The predictive model was constructed using multivariable logistic regression analysis and then re-estimated within each of the 10 imputed data sets, and the coefficients estimates were combined using Rubin's rule.[22] We established a nomogram to obtain the predictions for the risk of sICH.

Performance of the Predictive Models

Discrimination was assessed by calculating the C statistic, where a C statistic below 0.7 is considered poor, 0.7 to 0.8 is considered acceptable, and 0.8 or 0.9 or above is considered excellent or outstanding.[23,24] To check for significant differences between the observed and predicted risks of sICH, calibration of the predictive model was assessed using the Hosmer-Lemeshow

test and calibration plots. Calibration plots were generated separately in each imputed data set (1 illustrative example is shown for the predictive model).[25,26] Model performance measures were estimated in each imputed data set and combined using the Rubin's rules.[27]

Internal Validation

Bootstrap resampling for internal validation and estimation of the expected optimism were performed on the derivation cohort based on Harrell.[28–30] Briefly, internal validation was performed with 1000 bootstrapped samples based on each of imputed data sets separately.[29,30] The optimism-corrected C statistic of the internally validated within each imputed data set and averaged over the 10 imputed data sets were reported. As an important indicator of the validity of the established predictive model, the amount of optimism in the model gives an insight into how the model would perform when applied to new data sets.[31]

External Validation and Comparison With Other Models

We assessed the performance of the predicting score in the external validation cohort with discrimination and calibration. We additionally compared the discrimination of the novel predictive model to the conventional SPAN-100 score, the HAT score, and the SEDAN score in validation cohorts.[32]

Clinical Utility

The decision curve analysis was used to assess the clinical utility of the predictive model.[32] The decision curve analysis is a plot of net benefit against threshold probability.[33] We compared the clinical utility of the novel predictive model to the conventional SPAN-100 score, the HAT score, and the SEDAN score in validation cohorts.

Sensitivity and Subgroup Analyses

We performed a sensitivity analysis limited to patients with anterior circulation occlusion of 629 out 808 patients in the derivation cohort. We performed a separate analysis in the complete case data set of 711 patients who had available values for the 24 predictors in the derivation cohort. Subgroup analyses were performed to assess the performance of the model in patients identified stratified by sex.

We conducted the analyses followed the framework for derivation and validation of prediction models discretely previously,[34] and the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) statement.[34] All analyses were conducted using the R version 4.3.1 software (http://www.R-project.org/). Two-tailed values of P <0.05 were considered statistically significant.

RESULTS

Study Population Characteristics

A total of 808 patients with AIS who received intravenous thrombolysis between January 2016 and December 2022 for outcomes and head CT scan features were available for the derivation cohort. Median age was 68 years (interquartile range 59–75), and men 533 (66.0%). A total of 32 participants experienced sICH, with a rate of 4.0% (95% CI, 2.8%–5.6%). In total, 612 patients were included in the validation cohort (median age 64 years [interquartile range 55–72], and men 413 [67.5%]), with 21 sICH (3.4% [95% CI, 2.2%–5.3%]) events observed. Baseline demographics, characteristics, and head CT scan features of the derivation and validation cohorts are shown in Table 1, compared by univariate analysis to patients without sICH.

Model Development

Table S1 summarizes the number of times each variable was retained across the imputed data sets. Four of the initial 24 potential predictors were selected in all 10 imputed data sets. We then constructed the multivariable logistic predictive models based on these 6 predictor variables (CSVD score, Atrial fibrillation, Age, initial NIHSS score, Early infarct signs, and Systolic blood pressure). A visualized nomogram predictive model (CANES; an acronym of the predictive factors) was then established (Figure 1). The CANES nomogram assigns a graphic preliminary score to each of the predictors with a point range from 0 to 100, which was then summed to generate the total score, finally converted into an individual probability of sICH ranging from 0 to 100%. The probability of sICH is obtained by drawing a vertical line between the total score line and the probability line. As shown in Figure 1, for a 75-year-old patient with AIS with atrial fibrillation, having an initial NIHSS score of 15, systolic blood pressure 180 mm Hg, early infarct signs, and a CSVD score of 2 on noncontrast head CT, the total CANES score was 188, indicating a probability of sICH of 39% after intravenous r-tPA. Table S2 shows the points of the CANES scale with their different values.

Discrimination, Calibration, and Internal Validation

The internal bootstrap validation of the predictive model showed promising discrimination (an optimism-corrected C statistic of 0.80 [95% CI, 0.79–0.80]; Table S3). The calibration plot revealed good predictive accuracy between the actual probability and predicted probability (Figure 2A). The Hosmer-Lemeshow test did not suggest lack of calibration (χ^2=4.436, P=0.816).

Table 1. Baseline Characteristics

Variables	Derivation (n=808)			Validation (n=612)		
	Non-sICH (n=776)	sICH (n=32)	*P* value	Non-sICH (n=591)	sICH (n=21)	*P* value
Age, y, median (IQR)	67 (59–75)	74.5 (68–80)	<0.001	64 (55–71)	74 (63–80)	0.001
Men, n (%)	513 (66.1)	20 (62.5)	0.817	401 (67.9)	12 (57.1)	0.428
Previous stroke, n (%)	117 (15.1)	7 (21.9)	0.314	139 (23.5)	2 (9.5)	0.187
Hypertension, n (%)	512 (66.0)	26 (81.3)	0.109	375 (63.5)	18 (85.7)	0.063
Diabetes, n (%)	160 (20.6)	11 (34.4)	0.100	100 (16.9)	3 (14.3)	0.984
Hyperlipidemia, n (%)	300 (38.7)	7 (21.9)	0.083	85 (14.4)	2 (9.5)	0.754
Atrial fibrillation, n (%)	198 (25.5)	20 (62.5)	<0.001	62 (10.5)	8 (38.1)	0.001
Initial NIHSS, median (IQR)	5 (3–10)	11 (6–16)	<0.001	4 (2–9)	14 (5–18)	<0.001
Systolic blood pressure, mm Hg, median (IQR)	150 (135–163)	155 (140–181)	0.041	150 (135–164)	172 (136–185)	0.007
Blood glucose before thrombolysis, mmol/L, median (IQR)	6.78 (5.94–8.31)	8.13 (6.55–10.92)	0.002	6.7 (5.81–8.35)	7.31 (6.82–9.56)	0.081
CT-CSVD score, n (%)			<0.001			0.605
0	556 (71.6)	14 (43.8)		264 (44.7)	9 (42.9)	
1	154 (19.8)	11 (6.7)		192 (32.5)	8 (38.1)	
2	61 (7.9)	5 (15.6)		121 (20.5)	3 (14.3)	
3	5 (0.6)	2 (6.3)		14 (2.4)	1 (4.8)	
Dense artery sign, n (%)	168 (21.7)	13 (40.6)	0.021	54 (9.1)	6 (28.6)	0.012
Visible hypodensities, n (%)			<0.001			0.018
NA	484 (62.2)	7 (21.9)		436 (73.8)	11 (52.4)	
<1/3 MCA	223 (28.7)	10 (31.3)		126 (21.3)	6 (28.6)	
≥1/3 MCA	69 (8.9)	15 (46.9)		29 (4.9)	4 (19.1)	
Insular ribbon sign, n (%)	193 (24.9)	21 (65.6)	<0.001	70 (11.8)	6 (28.6)	0.035
Obscuration of the lentiform nucleus, n (%)	154 (19.9)	15 (46.9)	<0.001	63 (10.7)	6 (28.6)	0.023
Superficial/absent lateral fissure or cortical sulcus, n (%)	90 (11.6)	17 (53.1)	<0.001	63 (10.7)	8 (38.1)	0.001
Early infarct signs, n (%)	408 (52.6)	28 (87.5)	<0.001	164 (27.8)	11 (52.4)	0.027

CT indicates computed tomography; CSVD, cerebral small vessel disease; IQR, interquartile range; MCA, middle cerebral artery; NA, not applicable; NIHSS, National Institutes of Health Stroke Scale; and sICH, symptomatic intracerebral hemorrhage.

External Validation and Comparison With Conventional Prediction Models

Upon external validation, the CANES prediction model showed similar discrimination (C statistic: 0.82 [95% CI, 0.72–0.91]; Figure 3). The calibration plot indicated good predictive accuracy (Figure 2B). The Hosmer-Lemeshow test did not suggest a lack of calibration (χ^2=3.899, *P*=0.866). In addition, we compared the 4 predictive models (the SPAN-100 score, the HAT score, the SEDAN score, and the CANES model) in the validation cohort and found that the CANES model had the highest discrimination (Figure 3).

Clinical Utility Analysis

Decision curve analysis was used to facilitate the comparison among 4 different prediction models (the CANES, the SPAN-100, the HAT, and the SEDAN scores) in the validation cohort, based on the assumptions that no one is at risk for sICH (all negative) or the assumption that all are at risk for sICH (all positive). The net benefits of the CANES, the SPAN-100, the HAT, and the SEDAN scores for identifying sICH conditional on different decision thresholds are shown in Table 2. Figure 4 shows that the CANES model had a greater net benefit than the SPAN-100 score, the HAT score, and SEDAN score. For example, using the CANES model at a cut-off of 4% risk of sICH resulted in a predicted net benefit of 15 for every 1000 participants, which was significantly higher than the SEDAN score (6 per 1000), the SPAN-100 (4 per 1000), and the HAT score (8 per 1000).

Sensitivity and Subgroup Analysis

Sensitivity analysis limited to patients with anterior circulation occlusion confirmed the predictive performance of the CANES model (an optimism-corrected C statistic of 0.78 [95% CI, 0.77–0.79]; Table S4). Complete case data set analysis yielded consistent findings with the primary analysis (an optimism-corrected C statistic of 0.81 [95% CI, 0.75–0.88]; Table S4). The C statistics

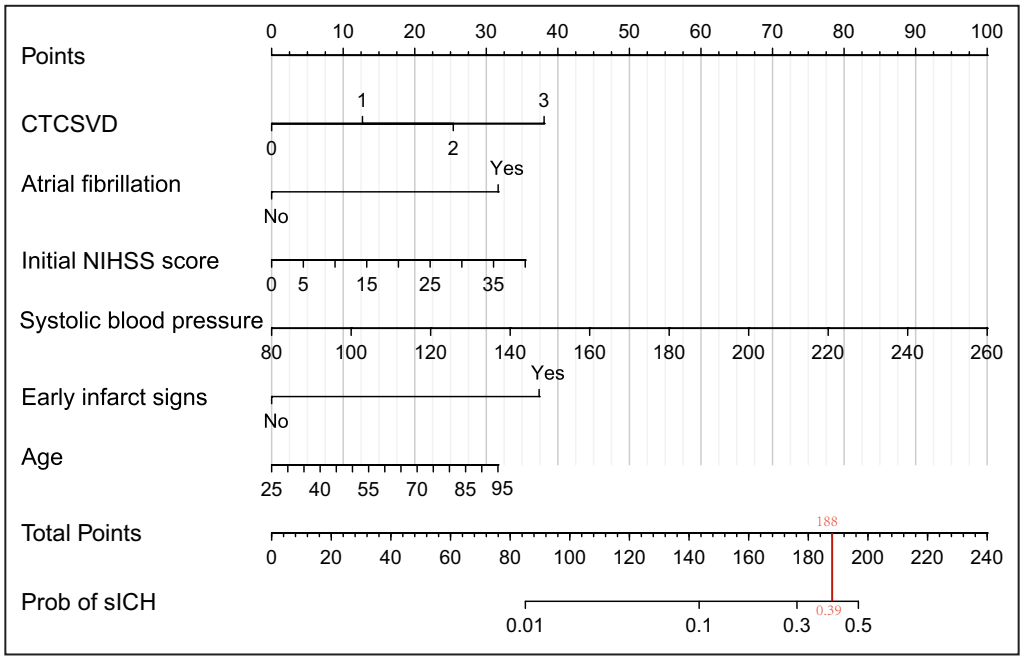

Figure 1. Prediction nomogram for sICH.
CANES indicates CSVD (Cerebral small vessel disease), AF (Atrial fibrillation), initial NIHSS [National Institutes of Health Stroke Scale] score, Early infarct sign, Systolic blood pressure; and sICH, symptomatic intracerebral hemorrhage.

of the CANES model were similar across subgroups of patients identified according to different sex (Table S5).

DISCUSSION

We developed and validated a novel noncontrast CT image–based predictive model for sICH after intravenous r-tPA in patients with AIS. The newly established CANES model incorporates 6 readily accessible variables at bedside, yielding better discriminative ability than the SPAN-100, the HAT, and the SEDAN scores, and may have good clinical usefulness throughout the range of sICH risk. Moreover, the CANES score was visualized using a nomogram for ease of practical use to provide an individualized probability estimation of the event based on the individual's disease characteristics without averaging or combining within a category.[35]

To be clinically practical and easily applied at bedside, a risk-predicting tool using information easily obtained before the administration of intravenous thrombolysis to balance the risk of sICH is favored. Some prediction models are now available to estimate an individual's probability of sICH after intravenous r-tPA.[36–38] The simplest model, the SPAN-100 index, which incorporates only age and NIHSS, failed to predict sICH satisfactorily in our derivation and validation cohorts as well as in several previous studies.[37,39,40] The HAT score incorporates early infarct signs on noncontrast head CT scan in addition to clinical parameters.[36] However, data concerning the predictive power of the HAT score for sICH are inconsistent.[41–43] Our data showed that compared with the SPAN-100, the HAT, and the SEDAN scores, the new established CANES score had the highest discriminative performance. Variables in the CANES model can be easily obtained using clinical examination and simple, routinely acquired nonenhanced CT brain imaging. Thus, identification of individuals at higher risk of sICH with the CANES score may be feasible and may facilitate postthrombolysis management. For instance, for patients who are at a high risk of sICH, postthrombolysis imaging control and more intensive blood pressure monitoring should be anticipated. The ENCHANTED (Enhanced Control of Hypertension and Thrombolysis) stroke study showed that compared with the guideline blood pressure management group, the frequency of sICH was lower but not significantly different in the intensive blood pressure group.[44]

In line with some previous studies,[45] our data showed the predictive value of early infarct signs for sICH after intravenous thrombolysis. The new established CANES model is the first to add CT-visible CSVD imaging markers in addition to early infarct signs. The severity of these biomarkers may reflect the frailty of the small vessels within the brain, which could influence susceptibility to intracerebral hemorrhage. Moreover, these biomarkers are familiar in stroke clinical practice and readily achievable with adequate education in centers delivering intravenous thrombolysis. Although magnetic resonance imaging–visible

imaging markers of CSVD (ie, microbleeds) might have prognostic value for predicting sICH after intravenous thrombolysis,[46] these variables are neither readily assessable nor available within the narrow time window of intravenous thrombolysis. The established CANES model might offer an advantage over the use of magnetic resonance imaging, providing an ease-of-use tool in the clinical setting.

Strengths and Limitations

Our study has several strengths. First, predictors were selected by the least absolute shrinkage and selection operator algorithm, which combines shrinkage and variable selection and is promising when prediction and parsimony are goals of predictive modeling.[29] Moreover, our derivation and validation of the CANES model in a diverse cohort of patients from China suggests acceptable applicability and consistent performance. Our findings should be interpreted within the context of its limitations. First, this study includes all the drawbacks of retrospective observational design; further prospective validation of the CANES score is needed. Although the size of the development sample is relatively small, the external validation means that the small sample size is less of a negative. Second, our

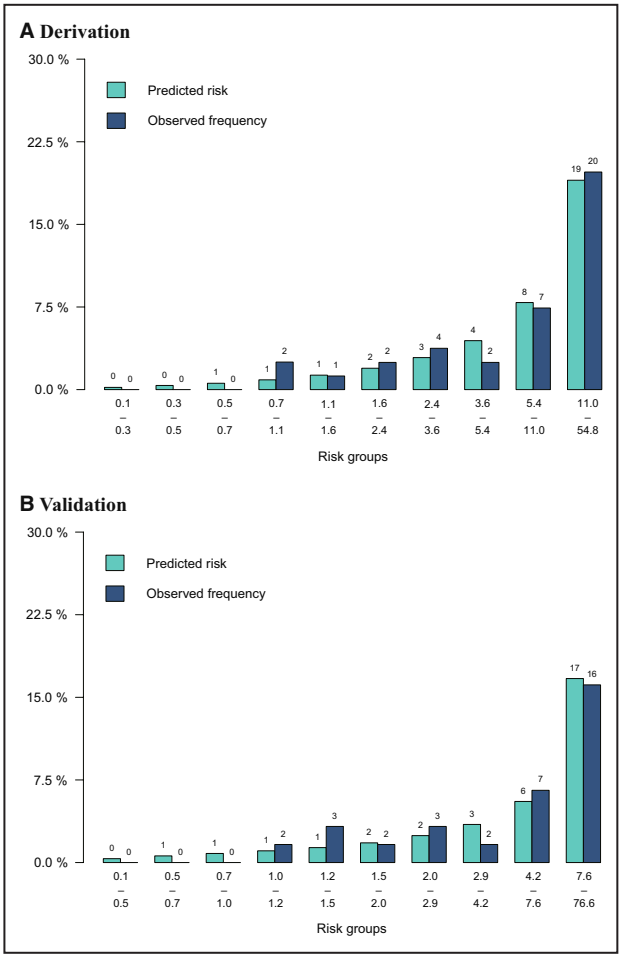

Figure 2. Calibration plot for CANES.
A, Derivation, (**B**) Validation. These plots show the proportion of patients with sICH as both predicted by the model and as observed in the derivation cohort (**A**) and validation cohort (**B**). CANES indicates CSVD (Cerebral small vessel disease), AF (Atrial fibrillation), initial NIHSS [National Institutes of Health Stroke Scale] score, Early infarct signs, Systolic blood pressure; and sICH, symptomatic intracerebral hemorrhage.

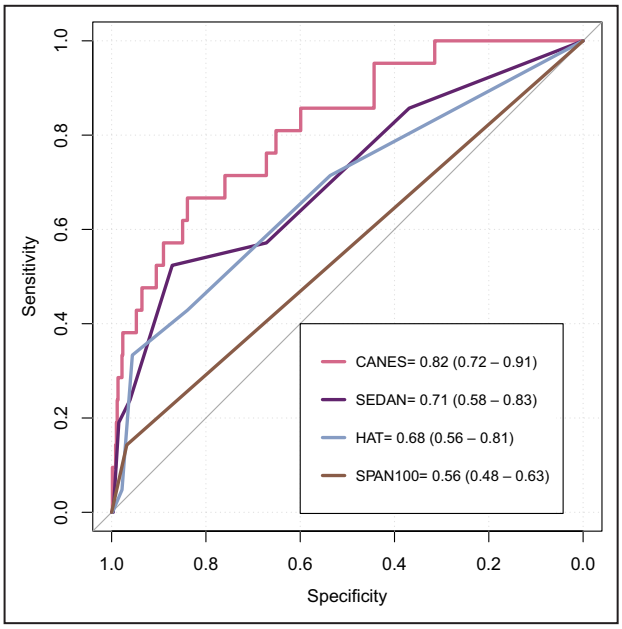

Figure 3. Discrimination of the prediction models.
CANES indicates CSVD (Cerebral small vessel disease), AF (Atrial fibrillation), initial NIHSS [National Institutes of Health Stroke Scale] score, Early infarct signs, Systolic blood pressure; HAT, hemorrhage after thrombolysis; SEDAN, Sugar, early infarct signs, dense artery, age, and NIHSS; and SPAN-100, Stroke prognostication using age and NIHSS.

Table 2. Net Benefit

Risk threshold	ALL	CANES	SEDAN	HAT	SPAN-100
0.00	0.034	0.034	0.034	0.034	0.034
0.01	0.025	0.026	0.025	0.025	0.025
0.02	0.015	0.020	0.017	0.015	0.015
0.03	0.004	0.016	0.010	0.011	0.004
0.04	−0.006	0.015	0.006	0.008	0.004
0.05	−0.017	0.012	0.011	0.007	0.003
0.06	−0.027	0.013	0.010	0.005	0.003
0.07	−0.038	0.011	0.009	0.008	0.003
0.08	−0.050	0.010	0.005	0.008	0.002
0.09	−0.061	0.010	0.004	0.007	0.002
0.10	−0.073	0.009	0.004	0.007	0.001

CANES indicates CSVD (Cerebral small vessel disease), AF (Atrial fibrillation), initial NIHSS score, Early infarct signs, Systolic blood pressure; SPAN-100, Stroke prognostication using age and NIHSS; HAT, Hemorrhage after thrombolysis; and SEDAN, Sugar, early infarct signs, dense artery, age, and NIHSS.

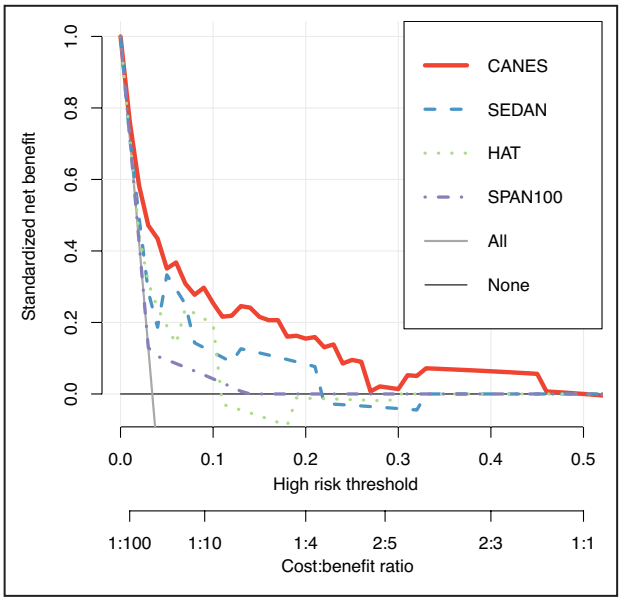

Figure 4. Clinical usefulness assessed using the DCA. DCA indicates decision curve analysis; CANES, CSVD (Cerebral small vessel disease), AF (Atrial fibrillation), initial NIHSS [National Institutes of Health Stroke Scale] score, Early infarct signs, Systolic blood pressure; HAT, hemorrhage after thrombolysis; SEDAN, Sugar, early infarct signs, dense artery, age, and NIHSS; and SPAN-100, Stroke prognostication using age and NIHSS.

primary outcome was only based on the ECASS II definition. However, previous studies have shown that the ECASS II definition had the highest inter-rater agreement and the largest contribution to the worst outcomes.[47,48] Third, unmeasured confounding variables, including CT perfusion parameters, are not available to assess their possible association with sICH. Finally, our established CANES model was developed and validated in Chinese patients with stroke; whether our findings may be generalizable to other ethnic populations needs to be validated.

CONCLUSIONS

The present study showed good performance of the established CANES model for sICH after intravenous r-tPA. The CANES score may provide indications for early identification of patients who are candidates for postprocedural intensive management to reduce the risk of sICH.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S5

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