

Methods and Applications

Dynamic Prediction of 3-Month Recurrence After First-Ever Ischemic Stroke Using a Two-Stream Attention-LSTM Model — Henan Province, China, 2025

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ABSTRACT

Introduction: We aimed to develop a dynamic model for predicting 3-month recurrence after first-ever ischemic stroke using multimodal longitudinal data.

Methods: Patients with first-ever ischemic stroke admitted to a tertiary hospital in Zhengzhou, China between January 2023 and January 2025 were enrolled. Data on static baseline characteristics, discharge variables, and 1-month follow-up variables were collected. Imaging phenotypes were derived from diffusion-weighted imaging (DWI) and Fluid-Attenuated Inversion Recovery (FLAIR) using automated lesion segmentation and unsupervised clustering. The dataset was divided into training and validation sets (8:2) using a fixed random seed. Seven models were trained and evaluated: logistic regression, random forest (RF), support vector machine (SVM), XGBoost, multi-layer perceptron (MLP), standard Long Short-Term Memory (LSTM), and two-stream attention-LSTM. External validation was conducted at three independent hospitals. The predictive performance was assessed using the area under the curve (AUC), accuracy, sensitivity, specificity, and Brier score.

Results: Among 625 patients, recurrence occurred in 79 (12.64%) patients 3 months after discharge. In the validation set, the AUCs were ranked as follows: two-stream attention-LSTM (0.857); SVM (0.838); XGBoost (0.808); MLP (0.768); RF (0.761); standard LSTM (0.754); logistic regression with follow-up features (0.748); and discharge-only logistic regression (0.686). Two-stream attention LSTM identified key predictors, including dynamic changes in C-reactive protein, systolic blood pressure, and imaging phenotypes. External validation showed stable discrimination (pooled AUC=0.83) and good calibration.

Conclusion: Two-stream attention-LSTM

improved prediction of 3-month recurrence after first-ever ischemic stroke and may support early post-discharge risk stratification.

Recurrent ischemic stroke remains a major challenge for secondary prevention owing to associations with worse neurological outcomes, higher risks of disability/mortality, and a poorer long-term prognosis (1). Most prediction tools rely on static clinical information collected during hospitalization or at discharge and thus have a limited ability to capture dynamic changes during recovery (2). However, recurrence risk after first-ever ischemic stroke evolves over time under the combined influence of vascular burden, inflammatory activity, metabolic fluctuation, structural injury, and treatment adherence, particularly within the first 3 months post-discharge (3).

Machine/deep learning methods such as Support Vector Machine (SVM), Random Forest (RF), Multi-Layer Perceptron (MLP), and Long Short-Term Memory (LSTM) are well suited for modeling nonlinear relationships and temporal dependencies in clinical data (4). For recurrent stroke prediction, these approaches may provide additional value when multimodal/longitudinal information is available. However, many studies have used simple feature concatenation or single-stream models that may not adequately distinguish baseline susceptibility from short-term dynamic changes during recovery.

Herein, we analyzed a real-world longitudinal cohort of patients with first-ever ischemic stroke and developed multiple prediction models for recurrence within three months. The proposed two-stream attention-LSTM separately modeled static background factors and short-term follow-up features before integrating them for prediction, while the attention mechanism adaptively weighted the informative temporal signals. Model performance was

systematically compared to identify the optimal framework for early recurrence risk stratification after ischemic stroke.

METHODS

This study analyzed a real-world retrospective longitudinal cohort of patients with first-ever ischemic stroke comprising consecutive patients admitted to a tertiary hospital in Zhengzhou, China from January 2023–January 2025.

Acute ischemic stroke was diagnosed following the Chinese Guidelines for Endovascular Treatment of Acute Ischemic Stroke 2023, confirmed by neurologists and supported by brain MRI showing an acute ischemic lesion. Patients with complete baseline, imaging, and follow-up data were included, while those with non-ischemic/unclassifiable stroke, unavailable/inadequate MRI findings, severe systemic disease affecting prognosis/follow-up, or missing outcome data were excluded. Overall, 1,122 consecutive patients were screened. After excluding patients lacking brain MRI ($n=221$) or MRI-DWI/FLAIR sequences ($n=153$), those with substantial missing laboratory/biochemical data ($n=71$), and those lost to follow-up at one/three months ($n=52$), 625 patients were finally analyzed. The primary outcome was recurrent ischemic stroke within 3 months post-discharge, defined as a new focal neurological deficit distinguishable from the index event and supported by MRI-DWI evidence of a new acute ischemic lesion. Patients with symptom duration of <24 hours were considered recurrent cases if a new DWI lesion was present. Patients were assessed at discharge (T0), 1 month (T1), and 3 months (T2). Predictors from T0 to T1 were used to predict recurrence at T2.

Demographic characteristics, lifestyle factors, comorbidities, medication use, laboratory indicators, and imaging data were collected from the electronic medical record system, stroke registry database, and follow-up platform. At T1, the following 17 post-discharge dynamic variables were collected through scheduled follow-up assessment: use of antihypertensive, antidiabetic, lipid-lowering, anticoagulant, and antiplatelet drugs; body mass index (BMI); systolic blood pressure; Low-Density Lipoprotein Cholesterol (LDL-C); High-Density Lipoprotein Cholesterol (HDL-C); Triglyceride (TG); Total Cholesterol (TC); fasting blood glucose; Glycated Hemoglobin (HbA1c); C-reactive protein; homocysteine; albumin; and uric acid. Medication

variables were coded as binary indicators, while clinical/laboratory variables were analyzed as continuous measures using the same definitions and units as those used at discharge (T0). Static background factors, including demographic characteristics, baseline comorbidities, and imaging phenotypes, were modeled separately from the T1 dynamic follow-up features. For non-sequential models, delta features (T1–T0) were constructed for continuous follow-up variables to capture short-term changes; for sequential models, T0 and T1 values were retained as ordered temporal inputs.

Imaging data were primarily derived from DWI and FLAIR sequences. After standardized preprocessing and multimodal registration, lesion regions were segmented using a pretrained nnU-Net model, and imaging heterogeneity scores were calculated to generate structured imaging phenotypes through unsupervised clustering (Supplementary Figure S1, available at <https://weekly.chinacdc.cn/>). For non-sequential models, delta features (T1–T0) were constructed to represent short-term changes. For sequential modeling, predictors were reformatted into temporal tensors with static background factors and dynamic follow-up features represented in separate streams.

The dataset was divided into training and validation sets (8:2) using a fixed random seed after feature engineering processing (Supplementary Figure S2, available at <https://weekly.chinacdc.cn/>). Seven models (LR, RF, SVM, XGBoost, MLP, long short-term memory (LSTM), and two-stream attention-LSTM) were developed. In the proposed two-stream attention-LSTM, static background factors and short-term follow-up features were modeled through separate branches and integrated for risk prediction, while an attention mechanism adaptively weighted informative temporal signals during recovery. External validation was conducted in three tertiary Grade A hospitals affiliated with Zhengzhou University, and included 340 patients (92, 138, and 110 from centers A, B, and C, respectively). All external samples were subjected to the same preprocessing pipeline, and the final optimized model was directly applied without retraining/parameter updating. Model performance was evaluated using ROC curve analysis, AUC, accuracy, sensitivity, specificity, F1-score, and Brier score. DeLong tests, calibration curves, and decision curve analyses were applied to assess discrimination, calibration, and clinical net benefits. A two-tailed test was applied, with statistical significance set at $\alpha=0.05$.

All preprocessing, model development, and evaluation were conducted in Python 3.10 with Anaconda environment management. Deep learning models were implemented in TensorFlow 2.20/Keras on PyCharm 2025.2.4, whereas conventional machine learning models were implemented using Scikit-learn (version 1.6.1; Scikit-learn developers/Inria, Paris, France) and XGBoost (version 2.1.4; Distributed Machine Learning Community, Seattle, WA, USA). Reproducibility was ensured by fixing random seeds for NumPy and TensorFlow.

RESULTS

Baseline Characteristics of Patients with First-ever Ischemic Stroke

Among 625 patients with first-ever ischemic stroke, 40 (6.4%) and 79 (12.64%) experienced recurrence at 1 and 3 months post-discharge, respectively, indicating a cumulative increase in recurrence risk during early recovery. Patients with recurrence had a higher burden of vascular risk factors and adverse imaging findings. In particular, diabetes, coronary heart disease, and high-heterogeneity imaging phenotypes were more common in the recurrent group. In the overall cohort, the baseline prevalence of hypertension, dyslipidemia, and diabetes were 65.12%, 43.52%, and 25.92%, respectively. Baseline characteristics according to recurrence outcomes among participants followed up within 3 months are shown in Table 1 and

Supplementary Table S1 (available at <https://weekly.chinacdc.cn/>).

Performance of the Two-stream Attention-LSTM Model

The two-stream attention-LSTM model comprised a 24-unit static branch, a 16-unit bidirectional LSTM dynamic branch, and a 16-unit classification head. The model demonstrated a strong and stable discriminative performance, with an AUC of 0.895 in the training set and 0.857 in the validation set (Figure 1A), indicating good generalization with only limited performance attenuation from training to validation. At the cohort level, the model assigned nearly equal average attention weights to T0 and T1, both close to 0.50 (Figure 1B), indicating that baseline status and short-term follow-up information jointly contributed to recurrence prediction. However, at the individual level, temporal attention weights showed substantial heterogeneity (Figure 1C), indicating that the model adaptively shifted its temporal focus according to patient-specific clinical trajectories. Permutation importance analysis further demonstrated clear hierarchical differences in feature contributions at a baseline AUC of 0.857 (Figure 1D).

Performance Comparison of Multiple Models

As in Figure 2, the two-stream attention-LSTM consistently demonstrated the best overall performance

TABLE 1. Continuous T0 characteristics of participants with T2 follow-up.

Variable	No recurrence (mean±SD)	Recurrence (mean±SD)	<i>t</i>	<i>P</i>
Age (years)	65.34±12.02	67.68±11.59	-1.630	0.104
BMI	25.90±4.13	25.83±4.59	0.142	0.887
Systolic blood pressure (mmHg)	141.47±16.61	147.29±19.31	-2.852	0.004
LDL-C (mmol/L)	2.84±0.80	2.76±0.80	0.780	0.436
HDL-C (mmol/L)	1.21±0.28	1.22±0.30	-0.116	0.908
TG (mmol/L)	1.65±0.77	1.57±0.77	0.863	0.389
TC (mmol/L)	4.75±0.88	4.67±1.03	0.716	0.474
FBG (mmol/L)	6.57±1.91	6.91±2.05	-1.446	0.149
HbA1c (%)	6.79±1.14	6.96±1.25	-1.244	0.214
CRP (mg/L)	4.14±3.96	5.51±5.20	-2.753	0.006
HCY (μmol/L)	14.00±4.42	14.65±4.67	-1.220	0.223
Albumin (g/L)	40.24±3.60	40.00±3.31	0.567	0.571
Uric acid (μmol/L)	362.58±86.10	374.82±92.80	-1.170	0.242

Abbreviation: SD=standard deviation; BMI=body mass index; LDL-C=low-density lipoprotein cholesterol; HDL-C=high-density lipoprotein cholesterol; TG=triglyceride; TC=total cholesterol; FBG=fasting blood glucose; HbA1c=glycated hemoglobin A1c; CRP=C-reactive protein; HCY=homocysteine.

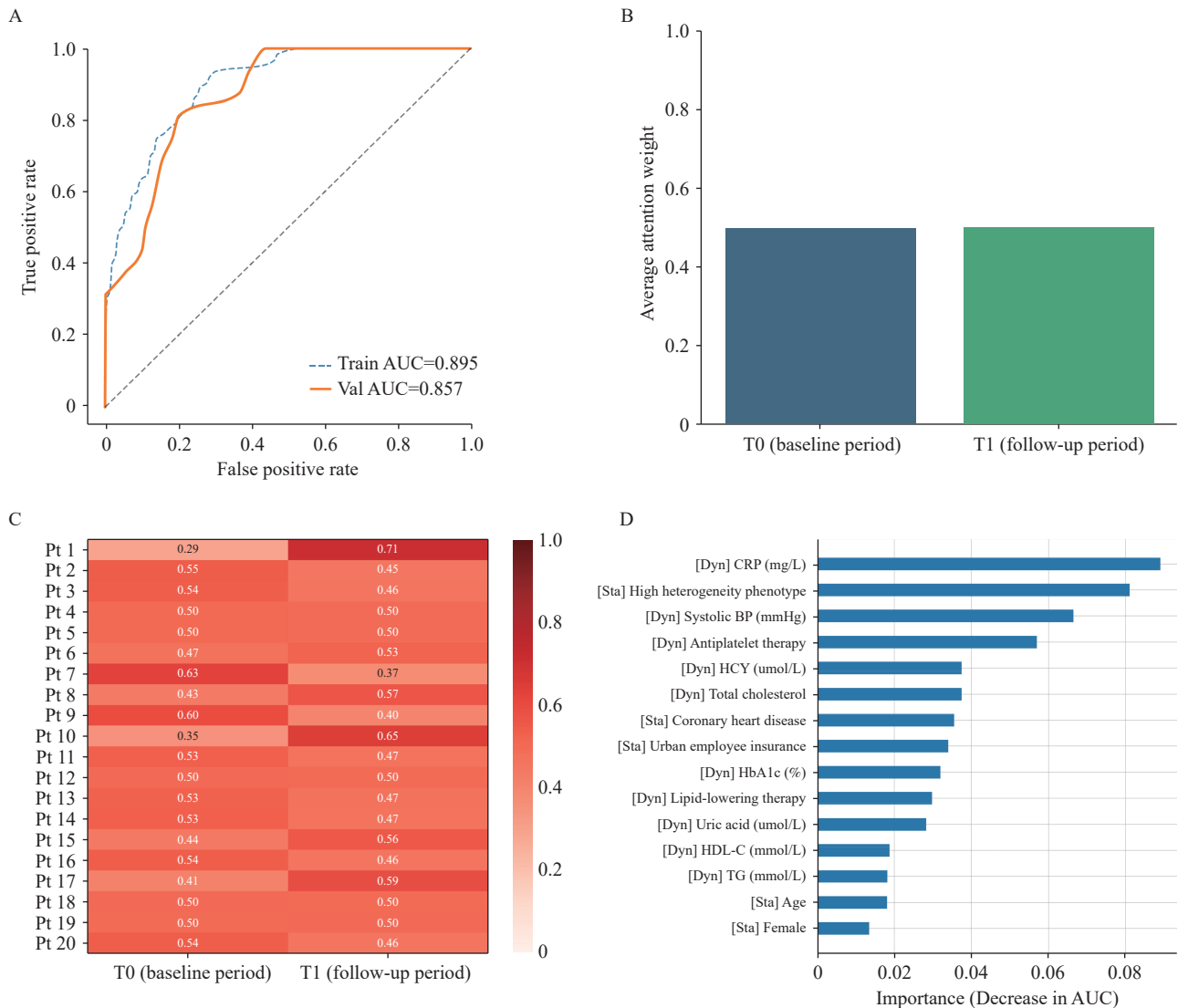


FIGURE 1. Prediction result graph based on two-stream attention-LSTM. (A) ROC curve of the training and validation sets of the two-stream attention-LSTM model; (B) Global time attention weight distribution of the two-stream attention-LSTM model; (C) Heatmap of time attention distribution for the first 20 patients at T0/T1; (D) Importance ranking chart of feature substitution in the two-stream attention-LSTM mode.

Abbreviation: LSTM=long short-term memory; ROC=receiver operating characteristic; AUC=area under the curve; Pt=patient.

among all models. In the validation set, its ROC curve was the outermost and closest to the upper-left corner (Figure 2A and Table 2), with the highest AUC of 0.857, outperforming logistic regression based on T0 only (AUC=0.686) or with T1 features (AUC=0.748), random forest (AUC=0.761), XGBoost (AUC=0.808), MLP (AUC=0.768), standard LSTM (AUC=0.754), and SVM (AUC=0.838). Pairwise DeLong tests further confirmed that the superior discrimination of the two-stream attention-LSTM was statistically significant when compared with most competing models, including the SVM, random forest, XGBoost,

MLP, and standard LSTM (Figure 2B), indicating that its performance advantage was not attributable to random variation. In addition, calibration analysis showed that the prediction probabilities of the two-stream attention-LSTM were in better agreement with the observed recurrence frequencies than those of other models (Figure 2C), suggesting a more reliable risk estimation. Decision curve analysis also demonstrated that the two-stream attention-LSTM provided the broadest range of positive net benefits across clinically relevant threshold probabilities (Figure 2D), supporting its superior clinical utility for recurrence

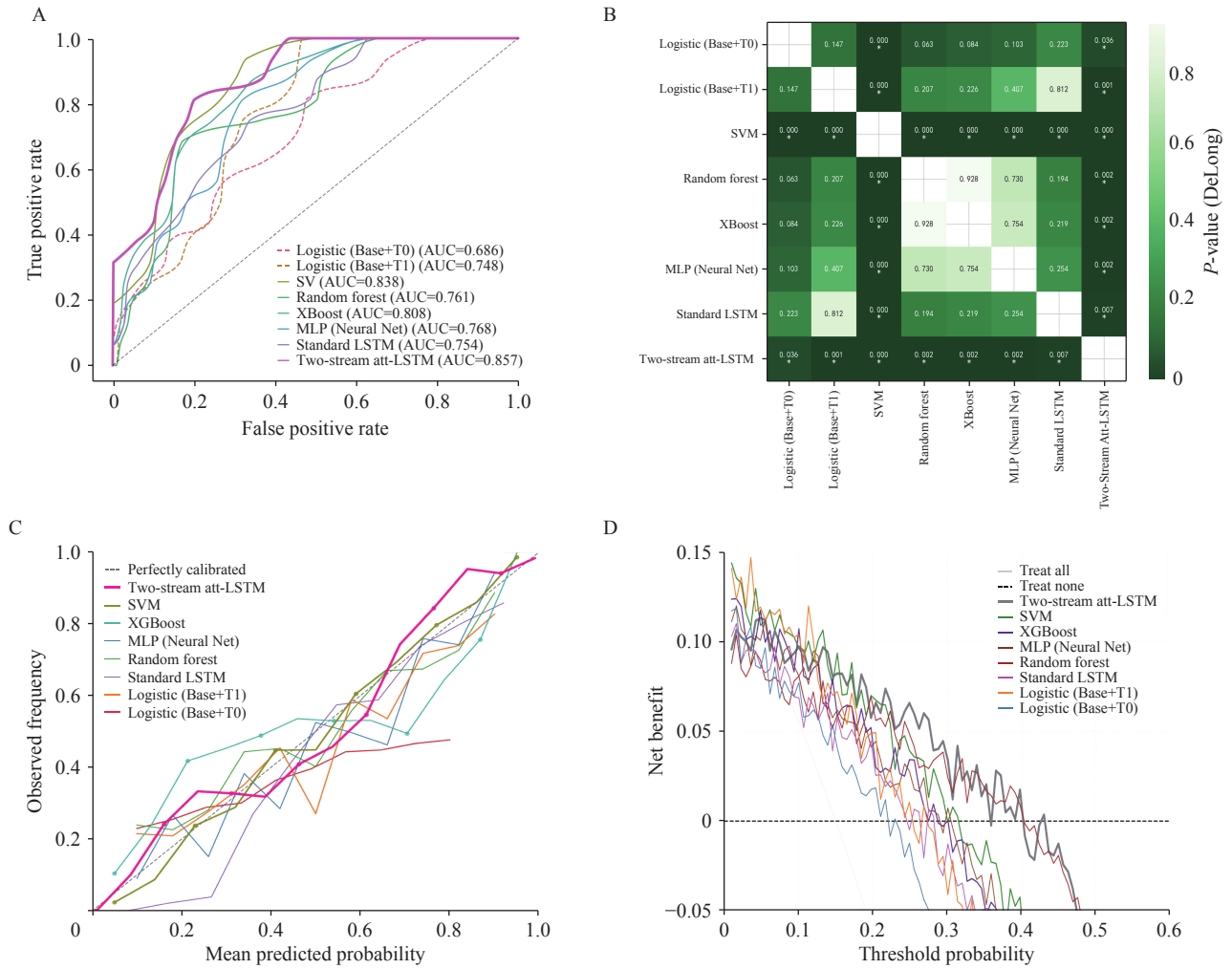


FIGURE 2. Performance comparison diagram of each model. (A) ROC curves of the validation sets for each prediction model; (B) Heatmap for pairwise comparison of DeLong test; (C) Calibration curve of validation set; (D) Analysis of decision curve.

Abbreviation: ROC=receiver operating characteristic; AUC=area under the curve.

TABLE 2. Performance summary of each of the prediction models in the internal validation set.

Model	AUC (95% CI)	Threshold	Accuracy	F1 Score	Sensitivity	Specificity	Kappa	Brier score
Two-Stream Att-LSTM	0.857 (0.738, 0.976)	0.477	0.792	0.480	0.750	0.798	0.370	0.219
SVM	0.838 (0.713, 0.963)	0.125	0.696	0.424	0.875	0.670	0.286	0.092
XGBoost	0.808 (0.675, 0.941)	0.492	0.672	0.388	0.813	0.651	0.240	0.238
MLP	0.768 (0.627, 0.909)	0.508	0.688	0.381	0.750	0.679	0.235	0.214
Random Forest	0.761 (0.619, 0.903)	0.525	0.800	0.444	0.625	0.826	0.335	0.200
Standard LSTM	0.754 (0.611, 0.897)	0.503	0.664	0.344	0.688	0.661	0.188	0.231
Logistic (Base+T1)	0.748 (0.604, 0.892)	0.255	0.584	0.366	0.938	0.532	0.201	0.190
Logistic (Base+T0)	0.686 (0.534, 0.838)	0.326	0.552	0.300	0.750	0.523	0.120	0.201

Abbreviation: CI=confidence interval; AUC=area under the curve; SVM=support vector machine; MLP=multi-layer perceptron.

risk stratification after ischemic stroke. External validation was performed in three independent hospitals to assess model generalizability. The external validation cohort included 340 patients, with 92, 138,

and 110 from centers A, B, and C, respectively. In external validation, the final Two-Stream Attention-LSTM model showed stable discrimination across centers, with AUCs of 0.84 (0.76, 0.92), 0.81 (0.74,

0.88), and 0.83 (0.76, 0.90), respectively, and a pooled AUC of 0.83 (0.79, 0.87), together with overall good calibration.

DISCUSSION

Compared with conventional statistical methods, machine/deep learning algorithms are better suited for modeling nonlinear relationships, high-dimensional data, and temporal dependencies (5). Herein, two-stream attention-LSTM showed the best overall performance, suggesting that short-term recurrence after a first-ever ischemic stroke may be better characterized when baseline vulnerability and recovery-phase evolution are modeled simultaneously (6). This superiority could be explained by two methodological strengths: First, the two-stream framework separately modeled static background factors and short-term dynamic follow-up features before integrating them for prediction, enabling distinguishing of stable baseline susceptibility from evolving post-discharge risk signals. Second, the attention mechanism adaptively weighted informative temporal signals, enabling the focus on clinically relevant changes during early recovery (7). This design is well-suited for recurrent stroke prediction as recurrence risk evolves under the combined influence of vascular burden, inflammatory activity, hemodynamic fluctuation, structural injury, and treatment response (8).

Another important implication is that short-term follow-up information provides prognostic value beyond the discharge status alone. The identified predictors support this interpretation, indicating that persistent inflammatory activity (9), insufficient blood pressure control, and adverse imaging-defined structural characteristics (10) may play central roles. The observed protective associations for continued antihypertensive and lipid-lowering therapies are also clinically plausible, possibly reflecting better adherence to secondary prevention and more effective control of modifiable vascular risk factors. The association between the payment method and recurrence further indicates that socioeconomic factors and healthcare accessibility may influence post-stroke outcomes. However, payment method should be interpreted as a proxy marker, rather than a direct causal factor. Clinically, these findings support the combined use of multimodal baseline features and short-term dynamic follow-up information to predict recurrence. In settings with limited follow-up resources, simpler models, such as logistic regression, may still be useful,

while more advanced deep-learning approaches may add value when richer longitudinal information is available.

This study had several limitations. This was primarily a retrospective study, and residual selection/information biases cannot be excluded. As inclusion depended on imaging availability, data completeness, and follow-up accessibility, bias may compromise model performance estimate accuracy and model generalizability. Despite external validation, the development cohort was derived from a single center, meaning broader validation in more diverse populations is needed. Further, only two major observation points were used for temporal modeling, which may not fully capture the long-term recurrence trajectories.

Overall, the proposed framework provides a promising approach for dynamic recurrence prediction, warranting further validation in larger multicenter studies.

Conflicts of interest: No conflicts of interest.

Ethical statements:: Approved by the Ethics Committee of Zhengzhou University (No. 2025-96).

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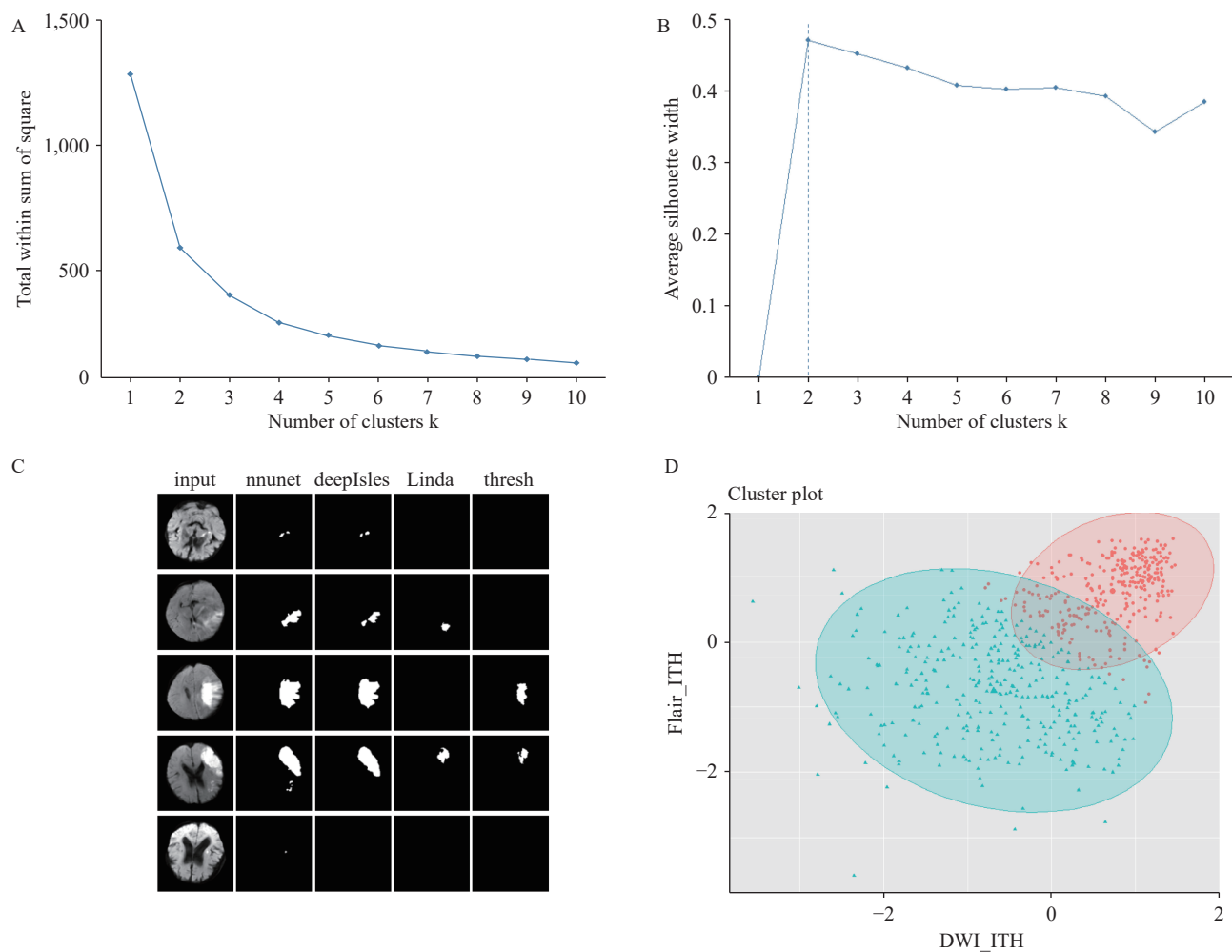
SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Categorical T0 characteristics of participants with T2 follow-up.

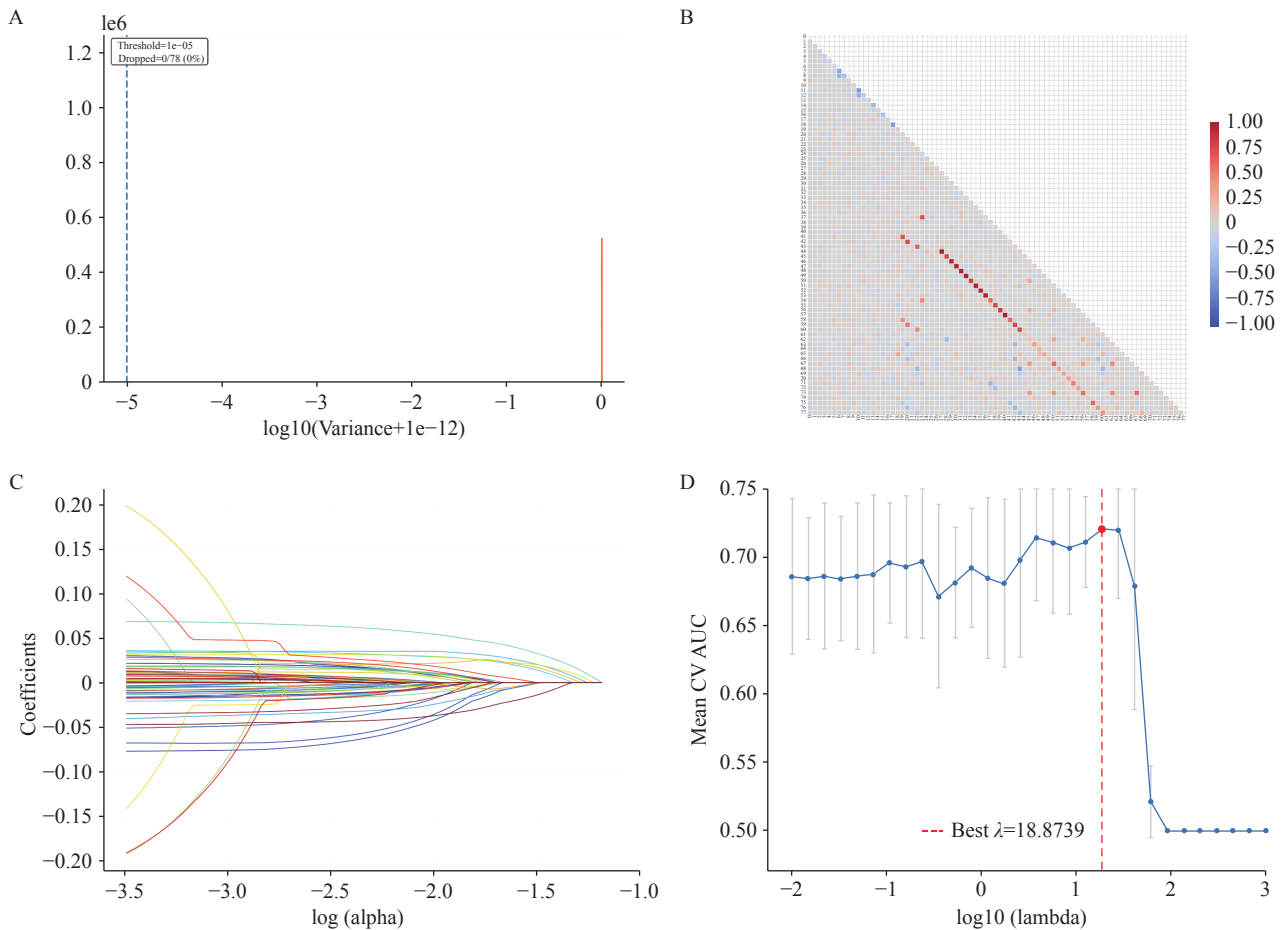
Variable	Total <i>n</i> (%)	No recurrence <i>n</i> (%)	Recurrence <i>n</i> (%)	χ^2	<i>P</i>
Sex					
Male	347 (55.52)	306 (56.04)	41 (51.90)	0.480	0.488
Female	278 (44.48)	240 (43.96)	38 (48.10)		
Ethnicity					
Han	575 (92.00)	502 (91.94)	73 (92.41)	0.020	0.887
Others	50 (8.00)	44 (8.06)	6 (7.59)		
Marital status					
Married	428 (68.48)	373 (68.32)	55 (69.62)	0.108	0.991
Unmarried	105 (16.80)	92 (16.85)	13 (16.46)		
Divorced	53 (8.48)	47 (8.61)	6 (7.59)		
Widowed	39 (6.24)	34 (6.23)	5 (6.33)		
Education level					
Primary school or below	110 (17.60)	98 (17.95)	12 (15.19)	0.917	0.821
Junior high school	223 (35.68)	196 (35.90)	27 (34.18)		
High school or technical secondary school	172 (27.52)	147 (26.92)	25 (31.65)		
College or above	120 (19.20)	105 (19.23)	15 (18.99)		
Family history of stroke					
No	496 (79.36)	438 (80.22)	58 (73.42)	1.949	0.163
Yes	129 (20.64)	108 (19.78)	21 (26.58)		
Payment method					
Self-pay	93 (14.88)	69 (12.64)	24 (30.38)	17.473	0.001
Urban employee insurance	358 (57.28)	323 (59.16)	35 (44.30)		
Urban-rural resident insurance	106 (16.96)	94 (17.22)	12 (15.19)		
Commercial insurance	68 (10.88)	60 (10.99)	8 (10.13)		
Smoking status					
Never smoked	310 (49.60)	272 (49.82)	38 (48.10)	0.465	0.793
Former smoker	160 (25.60)	141 (25.82)	19 (24.05)		
Current smoker	155 (24.80)	133 (24.36)	22 (27.85)		
Alcohol drinking status					
Never drank	335 (53.60)	293 (53.66)	42 (53.16)	0.643	0.725
Former drinker	220 (35.20)	190 (34.80)	30 (37.97)		
Current drinker	70 (11.20)	63 (11.54)	7 (8.86)		
Exercise					
Never	182 (29.12)	158 (28.94)	24 (30.38)	0.070	0.965
Occasionally	257 (41.12)	225 (41.21)	32 (40.51)		
Regularly	186 (29.76)	163 (29.85)	23 (29.11)		
Hypertension					
No	218 (34.88)	180 (32.97)	38 (48.10)	6.959	0.008
Yes	407 (65.12)	366 (67.03)	41 (51.90)		

Continued

Variable	Total <i>n</i> (%)	No recurrence <i>n</i> (%)	Recurrence <i>n</i> (%)	χ^2	<i>P</i>
Diabetes mellitus					
No	463 (74.08)	420 (76.92)	43 (54.43)	18.184	<0.001
Yes	162 (25.92)	126 (23.08)	36 (45.57)		
Coronary heart disease					
No	499 (79.84)	446 (81.68)	53 (67.09)	9.135	0.003
Yes	126 (20.16)	100 (18.32)	26 (32.91)		
Dyslipidemia					
No	353 (56.48)	312 (57.14)	41 (51.90)	0.772	0.38
Yes	272 (43.52)	234 (42.86)	38 (48.10)		
Atrial fibrillation					
No	558 (89.28)	486 (89.01)	72 (91.14)	0.327	0.568
Yes	67 (10.72)	60 (10.99)	7 (8.86)		
Peripheral vascular disease					
No	557 (89.12)	484 (88.64)	73 (92.41)	1.006	0.316
Yes	68 (10.88)	62 (11.36)	6 (7.59)		
Carotid plaque					
No	381 (60.96)	335 (61.36)	46 (58.23)	0.284	0.594
Yes	244 (39.04)	211 (38.64)	33 (41.77)		
Antihypertensive drugs					
No	124 (19.84)	108 (19.78)	16 (20.25)	0.010	0.922
Yes	501 (80.16)	438 (80.22)	63 (79.75)		
Antidiabetic drugs					
No	380 (60.80)	344 (63.00)	36 (45.57)	8.801	0.003
Yes	245 (39.20)	202 (37.00)	43 (54.43)		
Lipid-lowering drugs					
No	228 (36.48)	204 (37.36)	24 (30.38)	1.452	0.228
Yes	397 (63.52)	342 (62.64)	55 (69.62)		
Anticoagulants					
No	509 (81.44)	443 (81.14)	66 (83.54)	0.265	0.607
Yes	116 (18.56)	103 (18.86)	13 (16.46)		
Antiplatelet drugs					
No	201 (32.16)	180 (32.97)	21 (26.58)	1.290	0.256
Yes	424 (67.84)	366 (67.03)	58 (73.42)		



SUPPLEMENTARY FIGURE S1. Feature engineering results. (A) Within-cluster sum of squares; (B) Average silhouette coefficient; (C) Clustering results of different models; (D) Clustering performance with the optimal number of clusters ($k=2$). Abbreviation: nnU-Net=no-new-Net; Deep ISLES=Deep Ischemic Stroke Lesion Segmentation; LINDA=Lesion Identification with Neighborhood Data Analysis; threshold=threshold-based method; FLAIR ITH=FLAIR-based intralesion heterogeneity; DWI ITH=DWI-based intralesion heterogeneity.



SUPPLEMENTARY FIGURE S2. Radiomics and unsupervised clustering results. (A) Feature variance distribution; (B) Collinearity assessment heatmap; (C) LASSO regression coefficient paths; (D) Cross-validation tuning curve for L1-regularized logistic regression based on mean AUC.

Note: In panel A, near-zero variance filtering of candidate predictors. The distribution of variable variance was evaluated using $\log_{10}(\text{variance} + 10^{-12})$. The blue dashed line indicates the predefined variance threshold of 1×10^{-5} . No variables were removed during this step. In panel C, LASSO coefficient path plot. Each colored line represents one candidate predictor. The regression coefficients changed with the regularization parameter alpha, and predictors with coefficients shrunk to zero were excluded during feature selection.

Abbreviation: Mean CV AUC=mean area under the receiver operating characteristic curve across cross-validation folds.