

AI-Based Precision Thrombolytic Therapy for Stroke: A Real-World Study Postprint

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Abstract

Background: Ischemic stroke (IS) has a sudden onset, narrow treatment time window, complex factors influencing treatment efficacy, and significant inter-patient variability. Therefore, treatment modality, drug type, dosage, and administration route all affect thrombolysis outcomes. Previous studies commonly used statistical methods to analyze factors influencing thrombolysis efficacy, while clinical applications of artificial intelligence algorithms remain rare in this domain.

Objective: Based on real-world data, to establish an artificial intelligence algorithm model for IS patients spanning from general patient characteristics and drug treatment modalities to recovery outcomes, enabling personalized precise thrombolytic therapy and providing data support for clinical medication decisions.

Methods: A retrospective study was conducted, extracting clinical information of IS patients (n=55,621) diagnosed at the Second Affiliated Hospital of Dalian Medical University from the Yidu Cloud research big data server system, covering January 1, 2001 to December 31, 2021. According to inclusion criteria, 1,855 IS patients with complete information were selected. Thrombolysis efficacy was evaluated based on the difference between admission and discharge National Institutes of Health Stroke Scale (NIHSS) scores, with patients divided into neurological function improvement group (difference ≥ 4 points, n=1,236) and control group (difference < 4 points, n=619). Following recommendations from three senior neurology experts through blinded review, combined with IS diagnosis and treatment guidelines and literature, potential factors influencing post-IS thrombolysis efficacy were compiled and categorized into five types: general patient characteristics, medication indicators, examination indicators, laboratory test indicators, and treatment modalities. First, univariate screening of influencing factors was performed, followed by dimensionality reduction using principal

component analysis. Logistic regression model, Support Vector Machine (SVM), C5.0 decision tree, Deep Neural Network (DNN), and Wide&Deep models were constructed for comparative evaluation to assess their prediction of thrombolysis efficacy in IS patients and determine the optimal model, then identify its optimal parameters. Clinical information of 1,855 patients was partitioned using random seeds 7 and 11 into training set (1,113 cases), validation set (371 cases), and test set (371 cases), where the training set was used to construct and train the model to discover patterns, the validation set to adjust model parameters, and the test set to evaluate the final model's generalization ability. Feature engineering was applied to construct a simplified model and evaluate its accuracy. Clinical information of IS patients was extracted from the Yidu Cloud research big data server system of Dalian Central Hospital (3,925 cases total) for external validation.

Results: A total of 26 patient features (i.e., influencing factors of thrombolysis efficacy) were included for model construction. After principal component analysis, they were reduced to 2 principal components with a cumulative variance contribution rate of 93.1%. Comparing the predictive value of Logistic regression model, SVM, C5.0 decision tree, DNN, and Wide&Deep models for thrombolysis efficacy, the Wide&Deep model demonstrated the best predictive performance with an accuracy of 81.5% and F-index of 87.1%. The area under the ROC curve was 0.753 for the training set and 0.793 for the test set. The optimal Wide&Deep model parameters were determined as: 7 hidden layers, 15 neurons per layer, with Sigmoid as the activation function. Feature engineering analysis of factors influencing neurological function improvement after thrombolysis treatment in IS patients showed that medication type, administration route, and dosage ranked among the top importance factors. The importance ranking from highest to lowest was: history of cerebrovascular disease, medication type, administration route, single dose, atherosclerosis, thrombolysis time window, use of anticoagulant drugs and blood-activating and stasis-resolving drugs, etc. After simplifying model variables, the Wide&Deep model achieved an accuracy of 0.819, and external validation after variable simplification achieved an accuracy of 0.801.

Conclusion: The Wide&Deep model exhibited excellent performance across all evaluation metrics. Factors influencing thrombolysis efficacy ranked from highest to lowest importance as: history of cerebrovascular disease, medication type, administration route, single dose, atherosclerosis, thrombolysis time window, use of anticoagulant drugs and blood-activating and stasis-resolving drugs, etc. Through artificial intelligence algorithms, this study can provide timely and effective personalized thrombolytic treatment plans for IS patients from the perspectives of influencing factors and individualized drug administration, holding positive significance for reducing the societal burden of the disease.

Full Text

Precise Thrombolytic Treatment for Stroke Using AI-based Algorithms: A Real-World Study

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Abstract

Background: Ischemic stroke (IS) is characterized by sudden onset, narrow therapeutic time window, complex factors influencing treatment efficacy, and diverse individual patient conditions. Treatment modality, drug type, dosage, and administration route all affect thrombolytic outcomes. While previous studies have primarily used statistical methods to analyze factors influencing thrombolytic efficacy, clinical applications of artificial intelligence (AI) algorithms in this domain remain rare.

Objective: To establish AI algorithm models based on real-world data encompassing general patient characteristics, medication modalities, and recovery outcomes for IS patients, enabling individualized precise thrombolytic therapy and providing data support for clinical prescribing decisions.

Methods: A retrospective study design was employed. Clinical information of IS patients (n=55,621) diagnosed at the Second Affiliated Hospital of Dalian Medical University was extracted from the Yidu Cloud scientific research big data server system from January 1, 2001 to December 31, 2021. According to inclusion criteria, 1,855 IS patients with complete information were enrolled. Thrombolytic efficacy was evaluated based on the difference between admission and discharge National Institutes of Health Stroke Scale (NIHSS) scores, with patients divided into a neurological improvement group (score difference ≥ 4 points, n=1,236) and a control group (score difference < 4 points, n=619). Based on blinded recommendations from three senior neurologists and review of IS diagnosis/treatment guidelines and literature, potential factors associated with post-IS thrombolytic efficacy were compiled and categorized into five classes: general patient characteristics, medication indicators, examination indicators, laboratory test indicators, and treatment modalities. First, univariate screening of influencing factors was performed, followed by dimensionality reduction using principal component analysis. Logistic regression, support vector machine (SVM), C5.0 decision tree, deep neural network (DNN), and Wide&Deep models were constructed and compared to evaluate their performance in predicting thrombolytic efficacy, identify the optimal model, and determine its optimal parameters. Clinical information of 1,855 patients was split using random seeds 7 and 11 into a training set (1,113 cases), validation set (371 cases), and test set (371 cases). The training set was used to build and train models to discover patterns, the validation set to adjust model parameters, and the test set to evaluate the final model's generalization ability. Feature engineering was applied to construct a simplified model and assess its accuracy. External validation was

performed using clinical information of IS patients (n=3,925) extracted from the Yidu Cloud system of Dalian Central Hospital.

Results: Twenty-six patient characteristics (influencing factors of thrombolytic efficacy) were included for model construction. After dimensionality reduction by principal component analysis, two principal components were obtained with a cumulative variance contribution rate of 93.1%. Comparison of Logistic regression, SVM, C5.0 decision tree, DNN, and Wide&Deep models revealed that the Wide&Deep model achieved the best predictive performance with an accuracy of 81.5% and F-index of 87.1%. The area under the ROC curve was 0.753 for the training set and 0.793 for the test set. The optimal Wide&Deep model parameters were determined as: 7 hidden layers, 15 neurons per layer, and Sigmoid activation function. Feature engineering analysis of factors influencing neurological improvement after thrombolytic therapy showed that medication type, administration route, and dosage ranked among the most important factors, with importance ranking in descending order as: cerebrovascular disease history, medication type, administration route, single dose, atherosclerosis, thrombolytic time window, use of anticoagulant drugs and blood-activating stasis-removing drugs, etc. After simplifying model independent variables, the Wide&Deep model accuracy was 0.819, and external validation accuracy was 0.801.

Conclusion: The Wide&Deep model demonstrated excellent evaluation metrics. Factors influencing thrombolytic efficacy ranked in descending importance as: cerebrovascular disease history, medication type, administration route, single dose, atherosclerosis, thrombolytic time window, use of anticoagulant drugs and blood-activating stasis-removing drugs, etc. The AI algorithm can provide clinicians with timely and effective thrombolytic treatment plans for IS patients from the perspectives of influencing factors and individualized drug administration, which holds positive significance for reducing the social burden of the disease.

Keywords: Ischemic stroke; Thrombolytic drugs; Artificial intelligence algorithm; Wide&Deep model; Precision treatment

1. Methods

1.1 Study Subjects

A retrospective study design was employed. Clinical information of patients diagnosed with IS (n=55,621) at the Second Affiliated Hospital of Dalian Medical University was extracted from the Yidu Cloud scientific research big data server system, covering the period from January 1, 2001 to December 31, 2021. The inclusion criteria for IS patients were: (1) age >18 years, regardless of gender; (2) presence of responsible ischemic lesions confirmed by neuroimaging; (3) complete NIHSS scores at admission and discharge; and (4) indications

for thrombolysis. Exclusion criteria were: (1) critically missing key data such as medication dosage, treatment modality, or NIHSS scores that could not be retrieved; and (2) subjects designated as non-deidentified in ethical approval documents. Following application of inclusion criteria, a total of 1,855 IS patients were ultimately enrolled.

Thrombolytic efficacy was evaluated based on the difference between admission and discharge NIHSS scores, with patients divided into a neurological improvement group (score difference ≥ 4 points, $n=1,236$) and a control group (score difference <4 points, $n=619$). This study was approved by the Ethics Committee of the Second Affiliated Hospital of Dalian Medical University (Approval No. [2020]043).

1.2 Research Indicators

Based on blinded recommendations from three senior neurologists and review of IS diagnosis/treatment guidelines and literature, potential factors associated with post-IS thrombolytic efficacy were compiled and categorized into five classes: general patient characteristics, medication indicators, examination indicators, laboratory test indicators, and treatment modalities, totaling 85 influencing factors. Patients with first-episode or recurrent IS and those with intracranial hemorrhage were included as confounding factors for control purposes.

1.3 Research Methods

1.3.1 Principal Component Analysis Principal component analysis is a dimensionality reduction technique that transforms multiple correlated variables into several principal components while preserving most of the original information. In this study, principal component analysis was employed for dimensionality reduction to improve model prediction efficiency.

1.3.2 Wide&Deep Model Construction and Evaluation The Wide&Deep model combines a wide component (a generalized linear model of the form $y=wTx+b$) with a deep component (a feedforward neural network), leveraging the advantages of both to achieve both memorization and generalization capabilities. The model architecture is illustrated in [Figure 1: see original paper]. Concurrently, SVM, Logistic regression, C5.0 decision tree, CART, and DNN models were constructed. Model performance was evaluated using metrics including accuracy (proportion of correctly classified samples), precision (proportion of true positive predictions among positive predictions), and sensitivity (proportion of true positives correctly identified), which is equivalent to recall and thus omitted in subsequent results. The dataset was randomly split using seeds 7 and 11 into training (1,113 cases), validation (371 cases), and test sets (371 cases). The training set was used for model construction and pattern discovery, the validation set for parameter tuning, and the test set for evaluating generalization performance. Patient neurological

improvement after thrombolysis served as the outcome variable (y), with 26 influencing factors including medication type (urokinase/alteplase/none), single dose, etiological classification, and thrombolytic time window as input variables. Model training was conducted for 100 epochs. Upon completion, model convergence performance was assessed by examining kernel and bias convergence, and data point distribution in three-dimensional coordinate systems to evaluate clustering characteristics. Comprehensive metrics including accuracy, recall, and F-score were calculated for thorough model evaluation.

1.3.3 Optimization of Wide&Deep Model Parameters GridSearchCV was employed to identify optimal model parameters. Fine-tuning was performed within the optimal parameter range, comparing activation functions (ReLU and Sigmoid), number of hidden layers (1, 3, 5, 7), and neurons per layer (10, 15, 30, 300). Model accuracy across training, validation, and test sets was compared under different conditions to determine the final network architecture parameters.

1.3.4 Model Variable Simplification via Feature Engineering Given the urgency of thrombolysis in IS patients, temporal complexity, treatment diversity, and numerous confounding factors, this study applied feature engineering to statistically significant factors from univariate screening. Key influencing factors were extracted and their importance compared based on weight magnitude to enhance model responsiveness and practicality. Factors were sorted by weight in descending order, and variables with cumulative percentage <90% were selected to construct a simplified model for accuracy evaluation.

1.3.5 External Validation of Wide&Deep Model After model development using data from the Second Affiliated Hospital of Dalian Medical University, external validation was performed using clinical information from 3,925 IS patients in the Yidu Cloud disease-specific database of Dalian Central Hospital. The predictive performance and generalization capability of the Wide&Deep model were evaluated based on accuracy metrics. The technical route of the study is illustrated in [Figure 2: see original paper].

1.4 Statistical Methods

SPSS 13.0 was used for data imputation and univariate screening. CART tree models were constructed to impute missing values for platelet count, low-density lipoprotein cholesterol (LDL-C), homocysteine, and other fields. Univariate screening of 85 influencing factors was performed. In addition to statistically significant indicators, variables recommended by senior neurologists were included in principal component analysis. Normally distributed continuous variables were expressed as $(\bar{x}\pm s)$ and compared between groups using independent samples t-test, including age, single dose, and white blood cell count (54 indicators). Categorical variables were expressed as relative frequencies and compared using

² test, including gender, hypertension, and antiplatelet drug use (31 indicators), with $P < 0.05$ considered statistically significant. Python 3.7 was used for principal component analysis and construction of DNN and Wide&Deep models using TensorFlow and Keras modules to identify optimal parameters and plot ROC curves. Concurrently, Logistic regression, SVM, and CART models were constructed, with accuracy, precision, and recall calculated for comprehensive evaluation.

2. Results

2.1 Modeling Dataset and Univariate Screening

The inclusion process for 1,855 IS patients is shown in [Figure 3: see original paper]. A total of 85 influencing factors were initially considered. Based on clinical expert opinion, 26 factors were selected for model construction: age, diabetes, atrial fibrillation, atherosclerosis, hemorrhagic disease history, cerebrovascular disease history, hypertension, single thrombolytic dose, medication type, administration route, thrombolytic time window, antiplatelet drug use, anticoagulant drug use, other blood-activating stasis-removing drugs, thrombectomy, bridging therapy, admission NIHSS score, platelet count, LDL-C, cystatin C, homocysteine, degree of responsible vessel stenosis, focal neurological deficit, infarct location, infarct size, and etiological classification. Vessel stenosis was defined as mild (<50%), moderate (50-69%), or severe (70-99%). Focal neurological deficit referred to symptoms of weakness, numbness, or language impairment in IS patients.

Significant differences between control and neurological improvement groups were observed for age, diabetes, atrial fibrillation, atherosclerosis, hemorrhagic disease history, cerebrovascular disease history, hypertension, single dose, medication type, administration route, thrombolytic time window, antiplatelet drug use, anticoagulant drug use, other blood-activating drugs, thrombectomy, admission NIHSS score, platelet count, degree of responsible vessel stenosis, focal neurological deficit, and infarct location ($P < 0.05$). No significant differences were found for bridging therapy, LDL-C, cystatin C, homocysteine, infarct size, or etiological classification ($P > 0.05$), as shown in .

2.2 Principal Component Analysis Results

The 26 influencing factors were reduced to two principal components with variance contribution rates of 65.6% and 27.5%, respectively, and a cumulative variance contribution rate of 93.1%, as presented in .

2.3 Comparison of Data Mining Models

Logistic regression, C5.0 decision tree, CART, SVM, DNN, and Wide&Deep models were evaluated for their ability to predict neurological improvement after

thrombolysis. The Wide&Deep model achieved the highest accuracy, precision, specificity, and F-index, demonstrating superior performance, as shown in .

2.4 Wide&Deep Model Parameters and Accuracy

Using ReLU and Sigmoid activation functions, the optimal number of hidden layers was explored (1, 3, 5, 7 layers) with neurons per layer varied (10, 15, 30, 300). The final optimal parameters were determined as: Sigmoid activation function, 7 hidden layers, and 15 neurons per layer, as illustrated in [Figure 4: see original paper]. The Wide&Deep model achieved training set accuracy of 0.816, validation set accuracy of 0.828, and test set accuracy of 0.844, demonstrating high predictive performance. The accuracy curve is shown in [Figure 5: see original paper]. The ROC curve analysis revealed an AUC of 0.753 for the training set and 0.793 for the test set, indicating good predictive performance and generalization capability without overfitting, as shown in [Figure 6: see original paper].

2.5 Feature Engineering and External Validation

Feature engineering analysis of factors influencing neurological improvement after thrombolysis revealed that medication type, administration route, and dosage ranked among the most important factors. The importance ranking in descending order was: cerebrovascular disease history, medication type, administration route, single dose, atherosclerosis, thrombolytic time window, use of anticoagulant drugs and blood-activating stasis-removing drugs, etc., as presented in . To enhance model applicability, variable simplification was performed, yielding a Wide&Deep model accuracy of 0.819. External validation using data from Dalian Central Hospital demonstrated an accuracy of 0.800, confirming good generalization and predictive performance.

3. Discussion

3.1 Application of AI Algorithms in Drug Selection

This study demonstrates that the Wide&Deep model effectively predicts neurological improvement in IS patients from thrombolytic influencing factors, achieving a test set accuracy of 0.844. The influencing factors include medication type, single dose, and administration route. By combining individual patient characteristics with medication regimen indicators, the model can recommend different thrombolytic treatment outcomes to clinicians for decision support, benefiting more patients. Six models were constructed and comprehensively evaluated, with the Wide&Deep neural network selected as the optimal algorithm. The Wide&Deep approach, which integrates the generalization capability of deep neural networks with the memorization performance of linear models, has been rarely reported in previous studies and substantially enhances predictive performance.

3.2 Analysis of Factors Influencing IS Thrombolytic Treatment Outcomes

Current research primarily focuses on clinical observation of thrombolytic drugs, analysis of drug efficacy and safety, and exploration of influencing factors, typically with sample sizes ranging from dozens to hundreds. Prospective studies often compare basic treatment groups with thrombolytic drug-added groups, concluding with statistical comparisons of efficacy outcomes. However, discussion of thrombolytic treatment selection, including dosage and administration methods, remains limited. For factor exploration, multivariate Logistic regression is commonly employed after univariate screening, but studies based on big data algorithms and real-world comprehensive data are scarce. This study's predictive model can input patient-related factors, including exhaustive thrombolytic treatment options (medication type, single dose, administration route), to identify optimal treatment combinations through algorithmic computation, providing theoretical references for clinical decision-making and enhancing IS treatment outcomes.

Feature engineering variable simplification identified key factors influencing post-treatment thrombolytic efficacy: medication type, administration route, single dose, and cerebrovascular disease history. Cerebrovascular disease history ranked first with a weight of 988.87, as patients with cardiovascular and cerebrovascular disease history are more prone to IS onset due to conditions such as hemorrhagic cerebrovascular disease, ischemic cerebrovascular disease, cerebral insufficiency, hypertensive encephalopathy, and arteriosclerosis or stenosis that cause cerebrovascular hemodynamic changes. Univariate screening revealed significant differences in medication type, administration route, and single dose between neurological improvement and control groups ($P < 0.001$), confirming the substantial impact of medication factors on treatment efficacy. Medication type ranked second with a weight of 670.44 (22.68% contribution). This study focused on alteplase and urokinase as primary thrombolytic agents. For IS onset within 4.5 hours, patients should be strictly screened according to indications and contraindications and administered recombinant tissue-type plasminogen activator (rt-PA). For onset within 6 hours, urokinase is relatively safe and effective, though its indications and contraindications require updating. The AI model can provide individualized recommendations for medication type, dosage, and administration route based on patient-specific characteristics, thrombolytic time window, and NIHSS scores.

Administration route ranked third with a weight of 510.73 (17.28% contribution). During intravenous thrombolysis, administration occurs via either bolus injection or pump infusion, with pump infusion requiring 10% of the drug as a bolus followed by the remainder infused over 1 hour. Administration route is therefore a crucial factor in optimizing thrombolytic efficacy. Single dose ranked fourth with a weight of 142.85 (4.83% contribution). Guidelines recommend rt-PA at 0.9 mg/kg or low-dose rt-PA at 0.6 mg/kg, with lower bleeding risk but no reduced disability rate, requiring individualized decisions based on disease

severity and bleeding risk. For urokinase, the recommended dose is 100-150 U. The AI model can recommend optimal thrombolytic drug dosages for new patients, combining individual characteristics to provide treatment options for medication type (alteplase or urokinase), single dose, and administration route (pump infusion or intravenous drip) to assist clinical decision-making.

3.3 AI and Future Medicine

With the continuous advancement of big data and AI industries, AI technology is increasingly permeating daily life. In healthcare, AI is expanding its development space and application prospects, demonstrating growing value in pathology diagnosis, assisted diagnosis and treatment, medical imaging recognition, and drug development. AI will further integrate with healthcare, becoming an important support for clinical decision-making.

3.4 Urgency of IS Treatment and Social Burden

Stroke imposes enormous global economic impact. According to the “Heart Disease and Stroke Statistics-2020 Update,” direct and indirect economic losses from stroke reached \$45.5 million, with estimated direct medical costs of \$28 million. In China, stroke is the second leading cause of death after cancer. This study provides references for selecting thrombolytic regimens based on different patient characteristics, deeply explores factors influencing thrombolysis, and offers data support for health economic decision-making in IS, optimizing clinical decisions to achieve higher treatment benefits at lower costs.

This study has limitations. With 1,855 IS patients, the Wide&Deep model achieved 81.5% accuracy, demonstrating good predictive performance. Model accuracy could be further improved with larger datasets. Future work will incorporate multi-center data for external validation to continuously assess and refine model performance.

In summary, AI algorithm results indicate that factors influencing thrombolytic efficacy rank in descending importance as: cerebrovascular disease history, medication type, administration route, single dose, atherosclerosis, thrombolytic time window, and use of anticoagulant and blood-activating stasis-removing drugs. This provides clinical decision-making references and enables individualized precise treatment for IS patients, holding positive significance for reducing disease-related social burden.

Author Contributions: SHEN Huiwen contributed to data collection, statistical analysis, and manuscript drafting. LIN Yongzhong proposed the primary research indicators. CHEN Shuliang developed inclusion/exclusion criteria. ZHANG Lihong was responsible for subject selection. MA Chunye contributed to manuscript revision. MA Deyuan participated in data collection and organization. ZHANG Ce was responsible for quality control, manuscript review, and overall study supervision. All authors approved the final manuscript.

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Note: Figure translations are in progress. See original paper for figures.

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