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Original Article

Prognostic prediction of thrombolytic therapy with rt-PA in acute ischemic stroke patients using an artificial intelligence model

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Abstract: Objective: Through the comparison of different prediction models, we hope to find a promising statistical method to evaluate the prognosis of patients with acute ischemic stroke (AIS) after thrombolytic therapy. Methods: Data of 518 patients who received thrombolytic therapy were retrospectively collected in this study. Among them, 362 patients met the eligibility criteria, so their data such as age, sex, smoking history, previous medical history, clinical and laboratory indicators were analyzed. According to the 3 month follow-up results, 266 patients were included in a good prognosis group (modified Rankin Scale (mRS) score ≤2) and 96 in a poor prognosis group (3≤mRS≤6). All variables with P<0.05 in univariant and multivariant analyses were assigned in logistic regression model and artificial neural network (ANN) model to predict neurological prognosis, and the performance of the two models were compared. Results: Age, NIHSS scores, the serum concentration of immediate glucose, APTT and MBP at admission were found to be the predictive factors through ANN and logistic regression analysis. The binary logistic regression model revealed that the percentage correction, the precision, recall and F1 score of the regression model were 79%, 69.23%, 37.50% and 48.65%, respectively. While those of ANN were 79.98%, 69.70%, 37.25%, and 49.66%, correspondingly. Conclusions: ANN model is as effective as a logistic regression model in predicting the prognosis of AIS after thrombolytic therapy with rt-PA. Moreover, ANN is slightly superior to logistic regression in accuracy, precision and F1 score.

Keywords: Acute ischemic stroke, prognosis, intra-venous thrombolytic therapy, artificial neural network, prediction model

Introduction

Stroke is a worldwide catastrophic disease with high morbidity, disability rate, and mortality. In 2013, the worldwide prevalence of stroke was 25.7 million, of which 10.3 million cases were new paroxysms and 6.5 million individuals died [1]. Among all reasons for death, stroke holds the second-leading cause behind ischemic cardiovascular disease with a mortality rate over 11.8% [2] and constitutes almost one-third of the death toll. Ischemic stroke comprises approximately 80% of all stroke cases [3]. In China, exceeding ischemic cardiovascular disease, stroke occupies the first-leading cause of death, as well as disability [4]. As a result, stroke places a heavy burden on the Chinese healthcare resources [5].

Up to now, intravenous recombinant tissue plasminogen activator (rt-PA) is the irreplaceable treatment for acute ischemic stroke (AIS) within 4.5 hours after onset according to the international guidelines [6]. However, the effect of thrombolytic therapy could be influenced by complications such as symptomatic intracranial hemorrhage (sICH), with an incidence differing from 4.87% to 7.3% in China [7]. Negative outcomes, including death, may still occur even with no sICH. Therefore, it is valuable for emer-

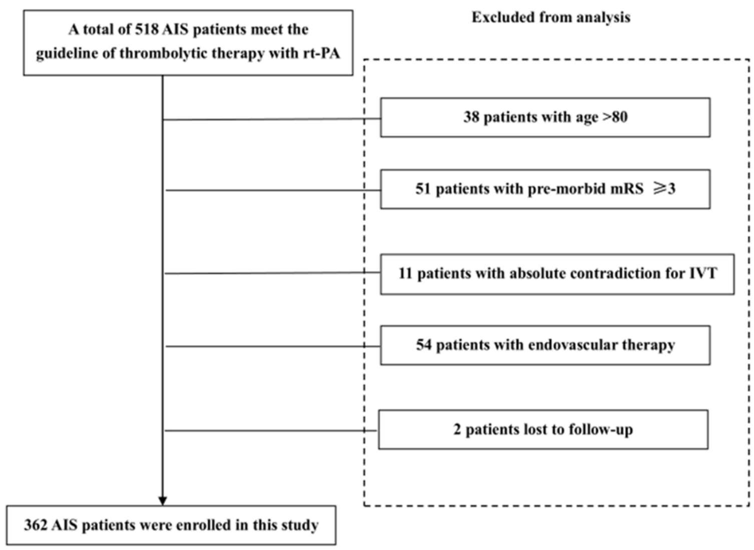

Figure 1. Enrollment of the study subjects. AIS: acute ischemic stroke; mRS: modified Rankin Scale; IVT: intravenous thrombolysis.

gency physicians to forecast the probable prognosis of patients before thrombolytic therapy, then formulate a beneficial individual treatment plan. Although a lot of research focuses on the risk factors for AIS patients with thrombolytic therapy, there are currently no definitive risk factors established. The main reason could be that the complicated risk factors are hard to calculate by popular statistics. The aim of this study was to find out a significant statistic model with superior accuracy and precision to predict the prognosis of Chinese patients with AIS treated with rt-PA, so as to provide reference for clinical decision-making.

Material and methods

This retrospective study collected 518 AIS patients who were treated with rt-PA intravenously and hospitalized at Xinhua Hospital Affiliated to Shanghai Jiaotong University School of medicine from January 2010 to August 2017. After exclusion of ineligible patients, data of 362 patients were subjected to further analyses (**Figure 1**).

This study was conducted in accordance with the Helsinki Declaration. The study protocol was approved by the Ethics Committee of Xin Hua Hospital, Shanghai Jiao Tong University School of Medicine.

Inclusive criteria: patients were admitted into Xinhua Hospital after the onset, diagnosed with AIS according to the Diagnostic Criteria of National Cerebral Vascular Disease Conference in 1995, and met the guidelines modified by the American Heart Association/American Stroke Association for the early management of AIS regarding thrombolytic therapy [6]. Eligible patients with no absolute contraindications were treated with intravenous rt-PA at the discretion of the physician in charge [5, 6].

Exclusive criteria: (1) patients with missing data; (2) patients with infection or severe malnutrition at admission; (3) patients with severe liver and kidney dysfunction; (4) patients with malignant tumor or immune diseases; (5) patients with a history of ischemic stroke with a modified Rankin Scale (mRS) score of 3 to 6; (6) patients who received endovascular thrombectomy after thrombolysis.

Data collection

Baseline demographic data and cerebral vascular risk factors were collected, such as age, sex, time from onset to treatment (ONT), previous medical history of hypertension, diabetes, hyperlipidemia, atrial fibrillation, cardiovascular disease, and current smoking status. Clinical and laboratory data were collected after admission to the emergency room before thrombolytic therapy, such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), National Institute of Health Stroke Scale (NIHSS) score at admission, the immediate serum concentration of glucose, uric acid and lipid levels, as well as coagulation function, myocardial enzymes, electrolyte, and thyroid function indicators. At admission, all the patients underwent a head CT scan before thrombolysis and 24 hours after rt-PA treatment. Additionally, a CT scan was performed immediately after the neurological symptoms worsened after thrombolytic therapy if there was a worsening of neurological symptoms. All patients were treated with rt-PA (alteplase) intravenously with a standard dose of 0.9 mg/kg (maximum 90 mg). All patients were given 10% of the dose as a bolus within 1 min, and the remainder was infused over 60 minutes [7]. Neurologic impairment at admission was assessed by the NIHSS [8]. The prognosis of all patients was evaluated by modified Rankin Scale (mRS), which was measured by one or two physicians at 3-month follow-up visits after the onset of AIS [9]. A mRS score of 0-2 was considered as good prognosis, while a score of 3-6 indicated poor prognosis.

Statistical analysis

The statistical analysis was carried out with SPSS Statistics (version 24.0; SPSS, Chicago, IL) and SPSS Modeler (version 18.0). A chi-square test was used to compare classified variables, while an unpaired t-test was used to compare continuous variables. $P<0.05$ represented statistical significance in univariant analysis, which revealed the relationship with mRS. A multivariant analysis was applied to avoid confounding variables. Based on these positive factors, binary logistic regression model and artificial neural network (ANN) model were built. The odds ratios (ORs) of logistic regression model were reported with their 95% confidence intervals (CIs). Stepping forward was chosen as the way to process logistic regression. The ANN model evaluation was established to predict neurological prognosis. Because of the small amount of data, Twenty-fold Cross Validation was used to validate the ANN model to avoid data over-fitting and sampling errors as well as to gain more efficient information. Data were equally divided into twenty groups (Fold 1-20). Then, all positive variables selected from factor analysis were also enrolled in logistic regression model. The variables were regarded as the input of each ANN model with Multilayer Perception (MLP) Algorithm by SPSS Modeler. As for each model, SPSS Modeler automatically computed the number of units to build a network with one hidden layer so that the neural network could compute the "optimal" number of units in the hidden layer by itself. Each fold printed out a result of the model including the importance of variables, confusion matrix and receiver operating characteristic (ROC) curve. Then the models of folds were assembled to gain an average accuracy, which was a performance matric to evaluate the model. Besides, weighted sum was used to calculate the importance of predictive factors in each model. Among twenty ROC curves, an average ROC curve with its area under the curve (AUC) was calculated and printed out to compare with that of logistic regression.

Results

Baseline characteristics

Of the 362 patients enrolled in this study, 266 patients were included in a good prognosis group (mRS≤2) and 96 in a poor prognosis group (3≤mRS≤6) according to the 3 months follow-up results. The baseline characteristics were analyzed by univariant analysis (**Table 1**). The median age of patients in the good prognosis group was significantly younger than that in the poor prognosis group (64 vs. 69; $P<0.01$). In the 362 patients, the ratio of good prognosis to poor prognosis in males was 178:49, with a good prognosis rate of 78.41%, while those in females were 88:47 and 65.19%, respectively. It seemed that male patients tended to achieve better prognosis than females. In addition, the patients with a previous medical history of atrial fibrillation and diabetes mellitus did not achieve the same good prognosis as those without (53 vs. 31 and 49 vs. 27, respectively; both $P<0.05$). Patients with lower SBP and MBP tended to recover better than those with higher SBP and MBP (146 vs. 153 and 101 vs. 104, respectively; both $P<0.05$), while DBP was unconcerned. Patients in the good prognosis group had lower NIHSS score compared with the poor prognosis group (5 vs. 12; $P<0.01$). Laboratory variables serum concentration of immediate blood glucose, APTT and fibrinogen were found to be statistically related to the prognosis of AIS patients (7.4 vs. 9.8; $P<0.01$, 31.4 vs. 29.9; $P<0.05$, 3.1 vs. 3.3; $P<0.05$, respectively). To mitigate the impact of confounding factors, a multivariant analysis was conducted. The results of interaction among variables that were significant in univariant analysis did not yield any significant difference, which meant that enrolling these ten single factors into the regression model was the only possible option.

Predictive factors in different statistic methods

Through ANN and logistic regression models, five variables, age, NIHSS at admission, immediate blood glucose, APTT and MBP, were found

Table 1. Baseline characteristics

	Good prognosis group (n=266)	Poor prognosis group (n=96)	P
Age (Years)	64.05±9.83	69.16±9.54	<0.001
Sex			0.006
Male	178	49	
Female	88	47	
Smoking history	93	24	0.070
Previous medical history			
Hypertension	178	64	0.960
Coronary heart disease	41	15	0.960
Atrial fibrillation	53	31	0.014
Diabetes	49	27	0.045
Clinical indicators before thrombolytic therapy			
SBP (mmHg)	146.2±20.9	153.2±22.9	0.006
DBP (mmHg)	77.9±13.1	80.0±13.6	0.167
MBP (mmHg)	100.6±13.2	104.4±14.2	0.019
NIHSS score	5.0 (2.0-8.0)	12.0 (8.0-24.0)	<0.001
ONT (min)	173.9±64.4	183.3±70.8	0.232
Laboratory indicators			
Glucose	7.4±6.4	9.8±5.0	<0.001
PLT	197.0±56.0	206.7±77.8	0.267
TT	14.8±6.0	14.4±2.5	0.458
APTT	31.4±6.6	29.9±4.0	0.037
D-Dimer	1.4±10.4	1.6±10.1	0.910
Fibrin degradation products	4.1±14.5	7.5±22.9	0.178
INR	1.4±6.0	1.0±0.2	0.542
PT	11.6±6.4	11.4±1.8	0.757
Fibrinogen	3.1±0.8	3.3±0.8	0.023
Antithrombin activity	95.7±16.5	94.4±16.7	0.504

Note: ONT: Onset-to-needle-time; SBP: Systolic Blood Pressure; DBP: diastolic blood pressure; MBP: Mean Blood Pressure; NIHSS: National Institute of Health stroke scale; PLT: blood platelet; TT: thrombin time; APTT: activated partial thromboplastin time; INR: International Normalized Ratio; PT: prothrombin time.

to have predictive value for the prognosis of AIS after thrombolytic therapy. The predicted values of all variables after ANN are shown in **Table 2**, and those of the logistic regression are shown in **Table 3**.

Predictive model of different statistic methods

Through the result of logistic regression analysis, we can model the prediction as follows.

$$P = \frac{e^{(5.819+(-0.045 * Age)+(-0.154 * \text{NIHSS at admission})+(-0.102 * \text{glucose})+(0.102 * \text{APTT})+(-0.026 * \text{MBP}))}}{1 + e^{(5.819+(-0.045 * Age)+(-0.154 * \text{NIHSS at admission})+(-0.102 * \text{glucose})+(0.102 * \text{APTT})+(-0.026 * \text{MBP}))}}$$

ANN can fit any nonlinear function through reasonable network structure configuration, so it can also be used to deal with nonlinear systems or black box models with relatively complex internal expression [10]. Different from logistic regression model, we adjusted the training model by setting numbers of hidden layer neurons. The training process was conducted using a similar approach as that of an ANN model.

Predictive ability of different statistic methods

By univariant analysis, we successfully identified several predictive variables associated with the response variable, mRS. Ten positive variables such as age, NIHSS score, and Glucose, whose *p* value were below 0.05 in **Table 1**, were regarded as the predictive variables in the following two models.

Table 2. Predictive factors in ANN model

	Predictive importance
Age (Years)	0.161
NIHSS at admission	0.119
Glucose	0.198
APTT	0.124
MBP	0.103

Note: ANN: artificial neural network; NIHSS: National Institute of Health stroke scale; APTT: activated partial thromboplastin time; MBP: Mean Blood Pressure.

Table 3. Predictive factors in binary logistic regression model

	Good prognosis group (n=266)	Poor prognosis group (n=96)
Age (Years)	0.45	0.002
NIHSS on admission	0.154	<0.001
Glucose	0.101	<0.001
APTT	-0.102	<0.001
MBP	0.026	0.009

Note: ANN: artificial neural network; NIHSS: National Institute of Health stroke scale; APTT: activated partial thromboplastin time; MBP: Mean Blood Pressure. B = regression coefficient β.

The binary logistic regression model built with these ten variables revealed that the percentage correction of the regression model was 79%. According to the confusion matrix, the precision was 69.23%, and recall was 37.50%. After computing, the F1 score of logistic regression model was found to be 48.65%. The results of variables in the equation are shown in **Table 3**. Age, NIHSS score at admission, MBP, serum concentration of glucose and APTT were found to be associated with prognosis independently. The ROC curve of logistic regression equation is displayed in **Figure 2**. The AUC of logistic regression model was 0.77.

Then, ANN model also used positive variables in **Table 1** as inputs. In order to reduce the variance and avoid overfitting, twenty-fold cross-validation was used. The results of the model in each fold are displayed in **Table 4** with AUCs, and the average ROC curve is displayed in **Figure 2**. According to the weighted sum of importance, blood glucose was found to be the most important predictive factor for prognosis. Besides, age, APTT, NIHSS on admission and MBP appeared to be important factors in pre-

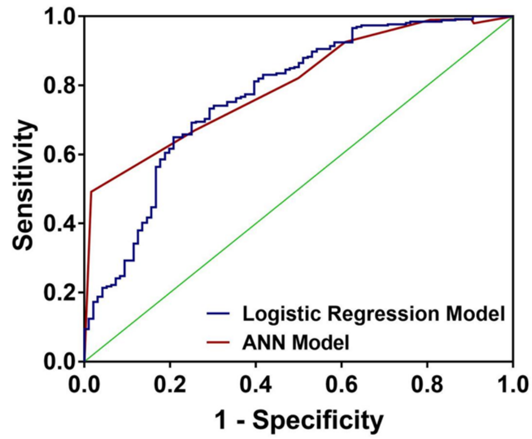

Figure 2. ROC curve of ANN and logistic regression. ROC: receiver operating characteristic; ANN: artificial neural network.

diction. To summarize the results, average of accuracy, precision, recall and F1 score were calculated as the final result of ANN, which were 79.98%, 69.70%, 37.25%, and 49.66%, respectively. The comparison of the two models is shown in **Table 5**.

Discussion

This study found that the ANN model, similar to logistic regression, could be used to predict the prognosis of AIS after thrombolytic therapy with rt-PA. Moreover, it is slightly superior to logistic regression in accuracy, precision and F1 score.

Thrombolytic therapy plays an inimitable role in treatments of AIS, but unfortunately, not every patient can benefit from this therapy. Therefore, it is of great significance for doctors, patients and their families to predict a general outcome for individual patients before thrombolytic therapy. Despite continuous studies, there are currently no alternative biomarkers. Up to now, research on the prognosis of AIS has focused on the relativity between certain biomarkers and prognosis. Several risk factors were identified to be associated with the prognosis, including NIHSS score at admission, the serum concentration of glucose [7], ONT [11], age, hypertension, smoking [12], the mean platelet volume [13], previous medical history of diabetes mellitus, cardiovascular disease, ischemic stroke [14], et al. But no definitive biomarkers have been confirmed to be associated with the prognosis after thrombolysis. We believe that the biomarkers associated with the prognosis

Table 4. Predicted strength of ANN model with twenty-folds

	Accuracy	Precision	Recall	F score	AUC	Hidden Layer Neurons
Fold 1	0.7222	0.75	0.4285	0.5454	0.558	4
Fold 2	0.7778	0.5	0.25	0.3333	0.821	4
Fold 3	0.8333	1	0.5714	0.7272	0.831	5
Fold 4	0.7778	0.75	0.5	0.6000	0.833	5
Fold 5	0.8333	0	0	\	0.938	6
Fold 6	0.7778	1	0.25	0.4000	0.846	5
Fold 7	0.8889	0.5	0.5	0.5000	0.812	3
Fold 8	0.7778	1	0.25	0.4000	0.846	3
Fold 9	0.7778	1	0.5	0.6667	0.653	5
Fold 10	0.7778	0.67	0.4	0.5009	0.908	3
Fold 11	0.8333	1	0.25	0.4000	0.482	5
Fold 12	0.7778	0.6	0.6	0.6000	0.738	6
Fold 13	0.8333	1	0.4	0.5714	0.785	5
Fold 14	0.8889	0.17	0.75	0.2772	0.964	6
Fold 15	0.7778	0.67	0.4	0.5009	0.769	5
Fold 16	0.7778	0	0	\	0.875	2
Fold 17	0.8889	1	0.5	0.6667	0.786	4
Fold 18	0.6842	0.33	0.2	0.2491	0.507	5
Fold 19	0.7895	1	0.5	0.6667	0.705	3
Fold 20	0.8	1	0.2	0.3333	0.693	5
Average	0.7998	0.6970	0.3725	0.4966	0.77	

Note: ANN: artificial neural network; AUC: area under the curve. Since the sum of data was not large enough, we randomly divided them into twenty sets (Fold 1-20). Each Fold above recorded the results of each set we used to training.

Table 5. Predictive strength in different models

	Logistic Regression Model	ANN Model
Accuracy	79.00%	79.98%
Precision	69.23%	69.70%
Recall	37.50%	37.25%
F1 Score	48.65%	49.66%
AUC	0.77	0.77
Predictive Factors	Age, NIHSS on admission, Blood Glucose, APTT, MBP	Blood Glucose, Age, APTT, NIHSS on admission, MBP

Note: ANN: artificial neural network; AUC: area under the curve; MBP: Mean Blood Pressure; NIHSS: National Institute of Health stroke scale; APTT: activated partial thromboplastin time.

of thrombolytic therapy in AIS patients are not a single entity but a combination of multiple factors. Therefore, this study attempted to find the risk factors and establish a prognostic model for emergency physicians before making thrombolytic decisions in AIS patients.

Among all kinds of machine learning models, ANNs have gained popularity in artificial intelligence research. Medical scientists have shown increased interest in utilizing ANN models for prognostic research in cancer and the prediction of image construction in radiology. Some argued that ANNs hold promise as a new avenue for clinical research on predicting prognosis [15]. Still, no related articles on stroke have been published [16]. Prediction models were only found in vascular occlusion on radiology research and differentiating cerebral ischemia from stroke mimics [17, 18]. Univariant and multivariant analyses are commonly used for prognosis prediction. Univariant analysis exhibited the relationship among variables and the prognosis, leaving the interrelationship and relative strength out of account. However, it neglected the synthetic action. To be more specific, it could not evaluate the value of the analysis when other factors were taken into consideration. Multivariant analysis can reveal the independent relationship between single variables and prognosis, with consideration of relative strength. Since medical data are linear inseparable, linear regression with a simple line to divide data may greatly influence medical diagnosis in reality, and logistic regression has to recognize a specific relationship among factors [19]. Many clinical models are based on logistic regression, which could estimate the odds ratio or approximate relative risk of a factor at different levels and explain each risk factor [20]. However, for some nonlinear influencing factors, logistic regression may get suboptimal results [21].

From this perspective, ANNs not only consider relationship and relative strength, but mimic the workings of the brain due to its self-study function, which is a unique working method in ANNs [18]. Thus, ANNs tend to be nearly perfect for self-improvement of accuracy and specificity on projects with the increasing sample size. Besides, ANNs are able to recognize the relationship between input and output as well as possible implicit interactions in inputs by itself [22]. Therefore, ANNs were deemed to be a new avenue for predicting the prognosis of diseases. But there has been no evidence shown that ANNs could obtain the same scientific and accurate predictive value as the conventional statistic methods did on predicting prognosis of AIS patients after thrombolytic therapy.

In light of this research background, our study focused on the comparison between ANN and logistic regression models, trying to illustrate that ANN is a viable model for clinical prediction, with AIS patients after thrombolytic therapy as the study population. We used the same variables, which came from the result of factor analysis, as the input into the two models. After training and testing models, we got same predictive factors from the two models. For the ANN model (**Table 2**), we got all variables with their importance in each fold and calculated the weighted sum with threshold of 0.1. These 5 predictive variables reflected the relative importance of each predictor in the ANN model. **Table 3** displays final variables and their parameters filtered into the binary logistic regression model. Although the importance of variables of the logistic regression model was not presented, it was clear that both models selected same significant prediction variables in building models. As shown in **Table 5**, the main important predictors in ANN were as same as those in logistic regression.

NIHSS, age, serum concentration of glucose, APTT and MBP was identified as prognostic factors for prognosis in AIS patients after thrombolytic therapy. Although NIHSS score does not fully reflect the severity of certain types of strokes (such as posterior circulation stroke), it has been regarded as a convenient tool on the cut-off point for thrombolytic therapy [23, 24]. The relationship between age and prognosis of AIS seemed suspended. According to the guidelines, patients aged 80 and older have a narrower window of only 3 hours after onset for receiving intravenous thrombolytic therapy [25]. Age of 80 and older is considered to be a major predictor of sICH-related death, independent from characteristics related to sICH severity [26, 27]. It was reported that serum concentration of glucose was associated with the vascular recanalization rate and the mortality [28, 29]. In this study, it was paradoxical that the serum concentration of immediate glucose was associated with the prognosis while the previous medical history of diabetes mellitus was irrelevant. It was widely believed that serum concentration of immediate glucose reflected the physical stress state, which could be stimulated by severe diseases, such as stroke. Glucose control in the early stage of thrombolytic therapy with rt-PA could shrink the volume of cerebral infarction focus, reduce brain edema and decrease the morbidity of sICH [30]. In AIS, the formation of thrombi plays a central role. As the thrombus formation progresses, the coagulation and anti-coagulation functions are mobilized accordingly. In this study, we identified the relationship between APTT and prognosis, while other coagulation parameters such as PT, and D-dimer, were irrelevant. Blood pressure is an important determinant of functional outcomes in AIS patients treated with intravenous rt-PA [31]. Intensive blood pressure reduction was recommended in the study of ENCHANTED [32]. In this study, MBP was independently related to prognosis, while SBP and DBP were not. In the following discussion, we would evaluate the two models through evaluation metrics.

While building the ANN model with MLP, we set one hidden layer with automatic number of neurons to get more precise results in each fold. The MLP algorithm can change connection weights and learn itself after comparing the number of errors in the output and the expected result in every processed piece of data through back propagation. Specific numbers of neurons in the model of each fold are recorded in **Table 4**, as well as accuracy, precision, recall and F1 score. After computing the average of these evaluation metrics, we got an accuracy of 79.98%, a precision of 69.70%, a recall of 37.25% and an F1 score of 49.66%. Then, we found that ANN had the similar evaluation metric results as logistic regression did. As shown in **Table 5**, logistic regression model got an accuracy of 79.00%, a precision of 69.23%, a recall of 37.50% and an F1 score of 48.65%. Specifically, the accuracy, precision and F1 score of ANN model were slightly better than those of logistic regression model. Recall represented the ability of a classification model to identify all relevant instances, which presented the ability of a classification model to return only relevant instances. From the results of two models, we found the logistic regression model might have an advantage in identification, and ANN model might be more efficient in returning positive prognosis. Since higher recall would result in lower precision, we then focused on F1 score. The F1 score of ANN model was 1.01%, higher than that of logistic regression model. The basic model equation and network of the two models were different. Logistic regression focused on the independent relationship between variables and prognosis, while ANN showed comprehensive influences among variables and prognosis with different relative weight coefficient [32, 33]. The interrelationship among variables might change the patients' fundamental vascular condition, degree of nerve damage, and establishment of collateral circulation, which might be the exact determinants to the prognosis. In fact, logistic regression model is sensitive to the multi-co linearity of independent variables [34]. To illustrate, when two highly correlated independent variables, such as NIHSS in the analysis, are included in the model simultaneously, it can result in a weaker regression coefficient for one of the variables, which may not meet the expected outcome. Moreover, clinical data are complex, multidimensional and nonlinear in nature. In this situation, logistic regression may not be adept at modeling complex interactions among nonlinear factors. However, ANN is flexible and requires less domain knowledge for development, which is ideally suitable for complex clinical data. This advantage of ANN model could be the reason why it performed better than logistic regression model in some evaluation metrics.

AUC was used to reflect the performance of classifiers. In general, AUC above 0.7 indicates a strong performance of the prediction model [35]. In this study, it was evident that both models were reliable on prediction, with an AUC of both 0.77, showing high diagnostic value. According to the diagram, the average ROC of the ANN model was nearly coincident with the ROC of the logistic regression model while the False Positive Rate was increasing. It should be noted that logistic regression needs to converse the nonlinear features before dealing with them. Thus, logistic regression is limited in some situations. On the contrary, ANN models do not need to consider whether the independent variables meet a normality. Besides, ANN can identify complex nonlinear relationships between variables. It can integrate and analyze the existing massive data with limited data samples. Generally, it should be considered from the aspects of the number of layers of the network, the number of neurons in each layer, and the choice of transfer function. Based on its structure, ANN with MLP can potentially perform better on larger training dataset [36], so it could be one of the further research directions in the future.

Currently, logistic regression and ANN are popular models in clinical medicine. ANN with its nonlinear systems could be better suited than the logistic regression model in clinical prognosis prediction, which has been proven in this study. Thus, with enlarging databases in the future, the ANN model could be a better predictive method for prognosis of AIS patients after thrombolytic therapy.

The limitation of this study is its non-randomized single-center retrospective study design, but this pilot study indicated the potential application of ANN in predicating the prognosis of patients with AIS after thrombolytic therapy. Given the differences in demographics at baseline, there is possible physician preference, which tends to prioritize patients perceived with more severe stroke and with greater potential for rehabilitation. Therefore, selection bias cannot be excluded. Because of the small sample size, we cannot exclude the possibility that the conclusion may be influenced by residual confounding factors. Further studies are warranted to verify the ANN model until it is stable enough on the risk prediction.

Technically, the ANN model has advantages over conventional statistical methods and risk prediction models. It could account for relationships among independent variables, reflecting complex relationships between continuous and categorical independent variables and the outcome, and quantifying the weights of independent variables regarding their impact upon the outcome. This pilot study indicated that the ANN model could be similar to logistic regression in predicting the prognosis of AIS patients after thrombolytic therapy with rt-PA. Moreover, ANN is slightly superior to logistic regression in accuracy, precision and F1 score.

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Disclosure of conflict of interest

None.

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