

Original Article

Early warning model for stroke recurrence in acute ischemic stroke patients based on traditional Chinese medicine syndrome theory

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Abstract: Objective: This study aimed to establish an early warning model for stroke recurrence in acute ischemic stroke patients based on Traditional Chinese Medicine (TCM) syndrome theory. Methods: This retrospective study collected the data of 1741 patients with ischemic stroke from 7 clinical centers between July 2016 and November 2019. Distance correlation coefficient, mutual information entropy, and statistical correlation test were used for univariate analysis. Cox proportional hazards regression model was applied to construct and validate the stroke recurrence warning model at different time. The area under the ROC curve (AUC) was used to evaluate the early warning ability of the model. Results: We successfully constructed the early warning model. The median follow-up time was 1.42 years (95% CI [1.37, 1.47]). Recurrence events occurred in 175 patients, with a cumulative recurrence rate of 10.05% (95% CI [8.64, 11.47]). The AUC of the model was 0.64±0.02 in the training set and 0.70±0.03 in the validation set. Conclusion: The TCM syndrome model can give an early warning for the recurrence of stroke and provide reference for the secondary prevention of ischemic stroke.

Keywords: Ischemic stroke, recurrence, early warning model, risk assessment tools, traditional Chinese medicine syndrome theory

Introduction

Stroke, with its high morbidity, mortality, and recurrence rates, presents a significant health-care challenge for middle-aged and elderly populations in China. It afflicts over two million individuals annually and is associated with an average fatality rate of 10-15%. Of those surviving the initial event, 50-70% experience sequelae. Recurrence rates are substantial, with 8.8% within 6 months, 15-30% within two years, and 20-47.7% within five years [1]. Therefore, secondary prevention of ischemic stroke is vital for reducing both recurrence and mortality [2]. Current predictive tools for risk assessment, however, are rare and have limited applicability. The foundational theory of “cure disease” in Traditional Chinese Medicine (TCM) is the theoretical basis of modern preventive medicine in TCM [3]. The theory of “treating disease with-

out disease” was first found in the concept that “The gentleman should think about the disease and prevent it” in Zhouyi, and its theory originated from the Huangdi Neijing [4]. As expressed in the text “Simple Questions, Four Qi Regulating Spirit”, the sage prioritizes prevention over treatment, embodying the TCM emphasis on health maintenance [5]. Contemporary interpretation of the “preventive treatment” theory aligns with modern medicine’s three-tier prevention strategy, encompassing pre-disease prevention, existing disease prevention, and post-disease recovery [6]. Consequently, developing an early warning system for ischemic stroke should emphasize both preventive strategies and rehabilitative care to mitigate recurrence risk.

Prevention of existing diseases in TCM centers on the principle of “change”, encompassing

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syndrome elements, micro-syndrome differentiation, and clinical presentation [6]. Initially, research on syndrome elements had identified hot syndrome (42%), phlegm syndrome (31%), blood stasis syndrome (31%), Yin deficiency syndrome (27%), qi deficiency syndrome (26%), and wind syndrome (9%) as prevalent within the at-risk stroke population [7]. Furthermore, modern TCM clinical research has integrated scientific technologies in material collection and syndrome differentiation, enhancing micro-level understanding of bodily structure, metabolism, and function. This approach synergizes with traditional macro-level diagnostic indicators and, through consistent clinical validation, progressively establishes a set of micro-indices for syndrome differentiation [8-10].

The relationship between syndromes, indicators, and symptoms is complex rather than linear. Therefore, monitoring micro indicators such as blood pressure, blood glucose, blood lipids, and imaging must converge with the four diagnostic pillars to inform syndrome differentiation and subsequent treatment. Clinical manifestations should concentrate on stroke precursor symptoms, including limb heaviness, dizziness, numbness, cephalgia, transient speech difficulties/aphasia, transient paralysis, muscle fibrillation, sensations of heat and cold, and constipation.

Conversely, in the domain of disease prevention and recovery, the emphasis is placed on predisposing factors, including susceptibility constitution, risk factors, and triggers [11, 12]. Initially, the constitution types considered high-risk for cerebral infarction, namely phlegm-dampness, blood stasis, qi deficiency, and Yin deficiency, should be monitored during the primary prevention phase of stroke. Furthermore, susceptibility factors encompass characteristics such as personality, habits, and lifestyle choices that are associated with the onset of ischemic stroke. These factors include age, dietary patterns, smoking and alcohol use, impatience, obesity, and medical history. Drawing from Chen Wuzhe's Theory of Three Causes and One Disease Syndrome Prescription from the Song Dynasty, disease etiologies are categorized by external, internal, and neither strictly internal nor external causes. External factors include climatic changes and circadian rhythms; emotions and overexertion are con-

sidered internal causes; while postural strain, dietary irregularities, and constipation are classified as not strictly internal or external causes [13, 14]. Research has indicated that prevalent triggers for stroke include sudden changes in weather, emotional disturbances, and specific eating patterns. Notably, cold conditions, anger, and morning fatigue after fasting have been identified as principal factors in the onset of ischemic stroke.

Within the concept of "prevention before illness", modern medicine's incorporation of TCM principles in constructing an early warning system for ischemic stroke recurrence risk is significant. This system utilizes the symptomatic expressions of TCM syndrome elements in existing ischemic stroke indices to establish a preliminary framework. The framework is refined through a consensus among experts, questionnaire surveys, the application of data mining, and artificial intelligence technologies. It encompasses a comprehensive set of risk assessment and early warning indicators, including TCM syndromes, constitutional analysis, psychological factors, risk elements, and biological samples. There are few reports on the early warning signs for ischemic stroke recurrence within TCM that use recurrence and other outcome events as evaluation indicators. Consequently, conducting novel systematic research to develop a new risk assessment and early warning model for ischemic stroke, grounded in TCM's multidimensional and integrative data, holds substantial clinical value.

Materials and methods

Participants and data extraction

In this retrospective analysis, clinical data from patients who experienced ischemic stroke were collected from eight clinical centers (Beijing University of Chinese Medicine, Dongzhimen Hospital Affiliated to the Capital University of Medical Sciences, Beijing Tiantan Hospital, Hospital of Guangdong Province, Changchun University of Chinese Medicine Affiliated Hospital, Henan University First Affiliated Hospital of Traditional Chinese Medicine, Beijing University of Chinese Medicine Hospital, Taiyuan East Hospital of Traditional Chinese Medicine). Over the course of three years and four months, data from 1,741 ischemic stroke patients were

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collected, from July 2016 to November 2019. Comprehensive details regarding the study's content and associated risks were recorded for each case, following the acquisition of informed consent from the patients or their legal representatives. The research protocol received ethical approval from the Ethics Committee of Bao'an Central Hospital of Shenzhen, ensuring adherence to stringent ethical standards.

Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosis of cerebral infarction consistent with TOAST classification as either large-artery atherosclerosis or small-artery occlusion, as confirmed by CT or MRI examination [15]; (2) assessment with Carotid Artery Color Doppler Ultrasound; (3) age between 35 and 80 years inclusive; (4) diagnosis of cerebral infarction established within the previous year.

Exclusion criteria: (1) cases of transient ischemic attack, hemorrhagic stroke, or mixed stroke; (2) cerebral infarction as per TOAST classification attributable to cardioembolic sources, other defined etiologies, or classified as cryptogenic; (3) individuals younger than 35 years or older than 80 years; (4) patients unable to participate in clinical data collection due to poor compliance.

Definition of ischemic stroke recurrence

Recurrence of ischemic stroke was determined in accordance with the diagnostic criteria set forth in the Chinese guidelines for stroke [16]. A recurrence was confirmed when a patient met three or more of the following criteria: First, acute cerebral or retinal ischemic episodes with focal neurological symptoms or signs persisting for over 24 hours. Second, acute cerebral or retinal ischemic events with focal symptoms or signs lasting less than 24 hours, yet corroborated by neuroimaging evidence of a new infarct. Third, worsening of an initial vascular ischemic stroke, evidenced by an increase in the NIHSS score from the primary ischemic event (excluding the effects of post-infarct hemorrhagic transformation or symptomatic intracranial hemorrhage), which persisted for more than 24 hours and was accompanied by novel ischemic alterations on head MRI or CT scan.

Follow-up

Follow-up data were systematically collected by trained coordinators who employed a standardized script during telephone interviews at each participating hospital. These interviews were conducted at 3, 6, and 12 months following the onset of symptoms of the index event. Data on recurrent strokes were gathered and examined during hospitalization and at each follow-up interval post-index event. The primary focus of this analysis was on the incidence of recurrent strokes within the 12-month period after the initial symptom onset.

Outcome measures

Predictors of stroke recurrence encompass a broad array of factors including demographic characteristics such as gender, age, education level, and body mass index; clinical assessments including blood pressure, evaluations of neurological deficit, neural functional recovery, and onset of dysphagia; medical history details of hypertension, previous cerebral infarction, coronary heart disease, diabetes, dyslipidemia, and intracranial hemorrhage; family history of stroke, hypertension, coronary heart disease, and diabetes; personal behaviors such as smoking and alcohol use, sleep quality, and exercise; medication regimens including TCM, western medicine, and specific stroke treatments; TCM syndrome characteristics and physical features; psychological factors evaluations including anxiety and depression; laboratory examination indexes such as blood lipid levels, coagulation profiles, and homocysteine; and imaging examinations that account for the number and area of infarcts observed on head MRI/CT scans, intracranial vascular stenosis, and occlusion seen in MRA/CTA, and the nature of carotid artery plaques determined by neck vascular Doppler ultrasound. These factors collectively served as multidimensional indices for observing and analyzing the risk of stroke recurrence.

Constructing an early warning model

The study divided the included cases into five geographical regions, with 60% of the cases randomly selected from each region's datasets to form the training set for model construction, while the remaining 40% constituted the test

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dataset for model validation. This sampling procedure was iteratively conducted 100 times, generating 100 distinct pairs of training (S1-S100) and test sets (S1-S100). To evaluate the predictive performance, four analytical models - logistic regression, random forest, support vector machine, and Cox proportional hazard regression - were applied across these 100 randomized training and test data sets. The models' efficacy was assessed using recall and Area Under the Curve (AUC) values as predictive metrics. Given its predictive accuracy, data characteristic suitability, and interpretability within the context of this study, the Cox proportional hazards regression model was ultimately selected for modeling the recurrence of ischemic stroke.

Statistical analysis

Descriptive statistics encompassed frequency counts, means, standard deviations, medians, and quartile measures. For measured data, values were expressed as mean \pm standard deviation for normally distributed data and as median with interquartile range for non-normally distributed data. Counted data were presented as frequency and percentage. The t-test, Chi-square test, and covariance analyses in R software were utilized to assess the statistical correlations of independent variables, with the t-test applied to continuous variables and the Chi-square test for categorical variables. Distance correlation coefficients were calculated using the DCOR function from R's energy toolkit, while information entropy was determined with the Multi-information function of the InfoTheo package. Longitudinal data analysis employed GLMM and GEE approaches, with the GLMM model constructed using the LME4 package and GEE model through the Geepack package in R software. The Cox proportional hazards regression model for cross-sectional data analysis and predictions was facilitated using the survival package's correlation functions, with competitive hazard models executed by the CMPSK package. Model performance was evaluated using discrimination, negative predictive value, specificity, recall rate, and F score as metrics. The AUC values for all models were computed with the pROC package in R, which also generated the corresponding ROC curves. For competing risks models, the CUMINC function from the CMPSK package calculated cumulative rates of stroke recur-

rence and pre-recurrence mortality, considering competing events. Kaplan-Meier estimates for cumulative recurrence rates, excluding competing times, were derived using the Survfit function from the Survival package. *P*-values were determined using a two-tailed probability approach, with a median value <0.15 for variable screening and <0.05 for model coefficient estimation considered significant. Descriptive statistics analyses were conducted with the SPSS V.22.0, while the remaining statistical modeling and graphical representations were performed using R version 3.6.1.

Results

Patient characteristics

There were significant differences between the two groups in terms of age, history of hypertension, history of diabetes mellitus, history of angina pectoris, cerebral hemorrhage, and smoking ($P < 0.05$) (**Table 1**).

TCM syndrome characteristics

As shown in **Table 2**, there was a statistically significant difference between two groups in term of qi deficiency syndrome ($P < 0.05$).

Univariate analysis

The results of univariate analysis showed that age, cerebral hemorrhage, coronary heart disease myocardial infarction, angina pectoris, history of coronary heart disease, history of diabetes, smoking history, and qi deficiency constitution were associated with ischemic stroke recurrence ($P < 0.05$) (**Table 3**).

Multivariate analysis

Multivariate analysis showed that age ($P = 0.013$), smoking history ($P = 0.03$), cerebral hemorrhage ($P = 0.02$), history of coronary heart disease ($P = 0.021$), and qi deficiency constitution ($P = 0.021$) were independent risk factors for the recurrence of ischemic stroke (**Table 4**).

Construction of early warning model for ischemic stroke recurrence

With recurrence as the outcome event, the influencing factors for recurrence were as follows: $X_1 =$ age, $X_2 =$ past history - cerebral

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Table 1. Comparison of demographic data and clinical characteristics between the two groups

| Indicator | Recurrent group (n = 175) | Non-recurrent group (n = 1566) | χ^2/t | P |
|-----------------------|---------------------------|--------------------------------|------------|-------|
| Age (years) | 62.51±9.34 | 52.98±11.61 | -0.221 | 0.021 |
| Sex | | | 0.642 | 0.382 |
| Male | 109 | 997 | | |
| Female | 66 | 569 | | |
| Hypertension | 121 | 1005 | 11.713 | 0.002 |
| Diabetes Mellitus | 87 | 400 | 6.654 | 0.022 |
| Angina pectoris | 66 | 50 | 12.323 | 0.003 |
| Myocardial infarction | 17 | 18 | 2.213 | 0.342 |
| Cerebral hemorrhage | 20 | 1 | 12.872 | 0.003 |
| Smoking | 157 | 946 | 8.292 | 0.041 |
| Onset solar term | | | 3.561 | 0.242 |
| Beginning of spring | 20 | 100 | | |
| Sting | 27 | 117 | | |
| Qingming Festival | 25 | 226 | | |
| Guyu | 22 | 243 | | |
| Beginning of summer | 23 | 289 | | |
| Autumn wind | 26 | 298 | | |
| Beginning of Winter | 52 | 293 | | |

Table 2. Comparison of TCM syndrome characteristics between the two groups

| | Recurrent group (n = 175) | Non-recurrent group (n = 1566) | χ^2 | P |
|--------------------------|---------------------------|--------------------------------|----------|-------|
| Internal wind syndrome | 64 | 500 | 3.286 | 0.062 |
| Internal fire syndrome | 100 | 177 | 2.587 | 0.089 |
| Phlegm dampness syndrome | 164 | 700 | 1.301 | 0.871 |
| Blood stasis syndrome | 185 | 701 | 2.505 | 0.051 |
| Qi deficiency syndrome | 170 | 501 | 7.505 | 0.011 |
| Yin deficiency syndrome | 21 | 16 | 1.028 | 0.320 |

Note: TCM: Traditional Chinese Medicine.

Table 3. Univariate analysis

| Predictive factor | P | Distance correlation coefficient | Mutual information entropy value |
|--|-------|----------------------------------|----------------------------------|
| Age | 0.103 | 0.054 | 0.003 |
| Cerebral hemorrhage | 0.012 | 0.058 | 0.012 |
| Coronary heart disease myocardial infarction | 0.232 | 0.043 | 0.001 |
| Angina pectoris | 0.062 | 0.034 | 0.002 |
| History of coronary heart disease | 0.031 | 0.072 | 0.002 |
| History of diabetes | 0.124 | 0.024 | 0.003 |
| Smoking history | 0.123 | 0.038 | 0.003 |
| Qi deficiency constitution | 0.001 | 0.067 | 0.005 |

hemorrhage, X3 = family history - coronary heart disease, X4 = continuous smoking history, X5 = Qi deficiency syndrome score. The risk early warning model is: $H(t|X) = H_0(t) \exp(0.027 * X_1 + 1.241 * X_2 + 0.459 * X_3 + 0.027 * X_4 + 0.573 * X_5)$.

Fitting results of Cox proportional hazards regression model

The average AUC of the Cox proportional hazards model on 100 training sets (S1-S100) was 0.64 ± 0.02 (**Figure 1**).

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Table 4. Multivariate analysis

| Factor | Cox coefficient | Cox risk ratio | Standard deviation | Test statistic | P | 95% lower confidence limit | 95% confidence upper limit |
|--|-----------------|----------------|--------------------|----------------|-------|----------------------------|----------------------------|
| Age | 0.020 | 1.203 | 0.007 | 2.450 | 0.013 | 1.003 | 1.048 |
| Smoking history | 0.383 | 1.473 | 0.176 | 2.402 | 0.030 | 1.048 | 2.204 |
| History - cerebral hemorrhage | 1.056 | 2.843 | 0.348 | 2.643 | 0.020 | 1.056 | 2.012 |
| History - Coronary Heart Disease and Angina Pectoris | 0.498 | 1.673 | 0.234 | 1.974 | 0.062 | 0.978 | 2.802 |
| History - Coronary Heart Disease and Myocardial Infarction | 0.421 | 1.542 | 0.431 | 0.976 | 0.421 | 0.987 | 2.743 |
| History - coronary heart disease | 0.802 | 2.234 | 0.342 | 2.291 | 0.021 | 1.092 | 4.621 |
| History - diabetes history | 0.436 | 1.642 | 0.302 | 1.531 | 0.234 | 0.873 | 2.761 |
| Qi deficiency constitution | 0.343 | 1.465 | 0.156 | 2.345 | 0.021 | 1.056 | 1.976 |

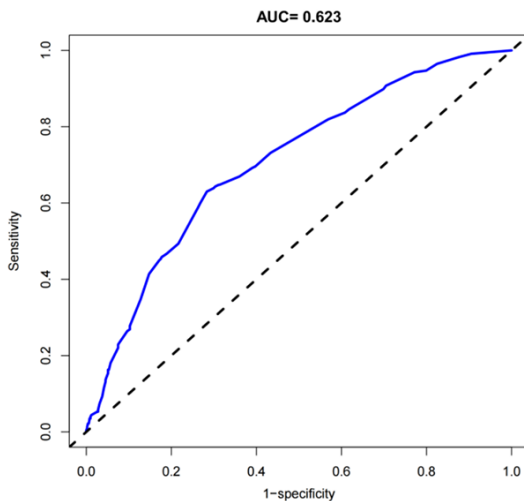


Figure 1. ROC curve of training set of TCM syndrome model (S = 91). Note: TCM: Traditional Chinese Medicine.

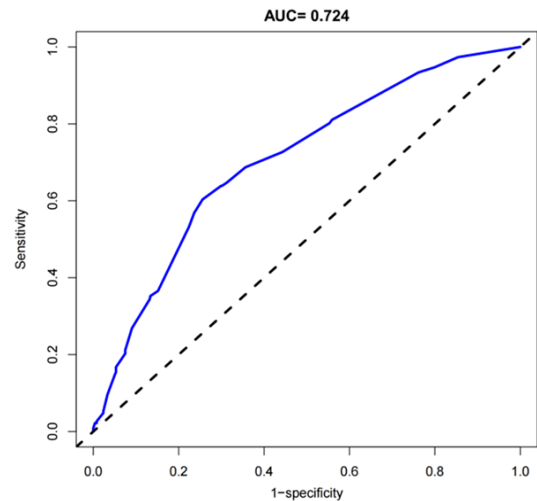


Figure 2. ROC curve of TCM syndrome model test set (S = 91). Note: TCM: Traditional Chinese Medicine.

Model verification

The average AUC of the Cox proportional hazards regression model on 100 test sets (S1-S100) was 0.70 ± 0.03 (Figure 2).

Construction of risk score

This study constructed a risk assessment tool for ischemic stroke recurrence based on the Cox proportional hazards regression model. That is, based on the recurrence risk assessment Tools in syndrome of Traditional Chinese Medicine (TCM-RRATS), according to the corresponding table of risk probability at various time periods, the ROC curve was used to classify high, medium, and low risk groups. The predicted total score of -13-3 was associated with low risk, score of 4-19 (90 d)/14 (180/360 d)/17 (720/900 d) with medium risk, and score of 20 (900 d)/15 (180/360 d)/18 (720/900 d)-46 with high risk.

Predictive effect

TCM-RRATS risk score (Supplementary Table 1) was used to predict the risk of stroke recurrence in 1741 patients with ischemic stroke. The high, medium, and low risk of stroke recurrence were divided into different time periods. The recurrence rate in each time period is shown in Figure 3. The study found that the TCM syndrome model could predict 95.42% of recurrences.

Discussion

In this study, we analyzed the implications and potential impacts of our findings on stroke management strategies. The integration of TCM syndrome differentiation theory into models for predicting stroke recurrence notably enhances the precision of risk assessment and the customization of treatment plans for patients. This approach allows for a more holis-

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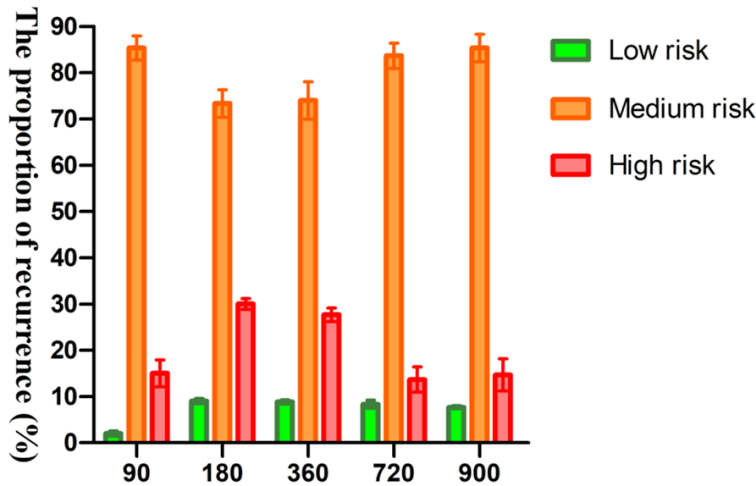


Figure 3. Risk division of TCM syndrome model. Note: TCM: Traditional Chinese Medicine.

tic evaluation by incorporating both traditional risk factors and the unique patterns of imbalance within an individual's body, thus providing a more accurate prediction of stroke recurrence risk. Moreover, our analysis identified age, smoking history, previous instances of cerebral hemorrhage, a history of coronary heart disease, and a qi deficiency constitution as independent risk factors for the recurrence of ischemic stroke, further underscoring the value of personalized preventive strategies.

Our analysis identified age as an independent risk factor for recurrent ischemic stroke ($P = 0.013$), highlighting the increased susceptibility to stroke as individuals age. This vulnerability is attributed to the progressive narrowing and reduced flexibility of blood vessels over time, elevating the risk of clots [17, 18]. Furthermore, advanced age is often accompanied by additional stroke risk factors, including hypertension, diabetes, and cardiovascular diseases [19, 20]. In managing recurrent ischemic stroke among older patients, healthcare professionals must consider age and overall health. This may necessitate more intensive treatment approaches, such as elevated medication dosages or enhanced monitoring, to avert further strokes. Lifestyle adjustments, including dietary changes and physical activity, are also advised to mitigate the risk of recurrence in the elderly.

Smoking history emerged as another independent risk factor for recurrent ischemic stroke ($P = 0.03$). Studies have established that indi-

viduals with a smoking history face a significantly increased risk of a second ischemic stroke when compared to non-smokers [21, 22]. The detrimental effects of smoking on the cardiovascular system, such as vascular damage, heightened blood pressure, and the promotion of blood clot formation, are well-documented contributors to stroke incidence [23-25]. Effective reduction of recurrent ischemic stroke risk among former smokers necessitates the implementation of smoking cessation programs. These programs might encom-

pass counseling, nicotine replacement therapy, and additional support measures. Moreover, for individuals with a smoking history, healthcare providers are advised to vigilantly monitor and manage coexisting stroke risk factors, including hypertension, elevated cholesterol levels, and diabetes, to prevent further ischemic events.

Cerebral hemorrhage has been identified as an independent risk factor for the recurrence of ischemic stroke ($P = 0.02$). The occurrence of cerebral hemorrhage elevates the likelihood of subsequent strokes, including ischemic types, due to the disruption of normal blood flow, inflammation, and damage to the brain tissue surrounding the hemorrhage [26-28]. To mitigate the risk of recurrence in individuals with a history of cerebral hemorrhage, it is crucial to employ precise diagnostic measures and therapeutic approaches. Strategies should encompass rigorous monitoring of blood pressure and cholesterol, alongside other cardiovascular risk indicators. Lifestyle interventions, including adherence to a nutritious diet, engaging in regular physical activity, and promoting smoking cessation, are recommended. Moreover, the prescription of medications to address coexisting conditions such as hypertension, diabetes, and atrial fibrillation, which heighten stroke risk, may be necessary. In certain scenarios, surgical or minimally invasive procedures may be needed to manage specific risk elements or complications arising from cerebral hemorrhage.

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A history of coronary heart disease has been recognized as an additional independent risk factor for recurrent ischemic stroke ($P = 0.021$). Coronary heart disease contributes to the development of atherosclerosis, a condition that heightens the likelihood of blood clot formation and subsequent obstruction of cerebral blood flow, leading to stroke [29, 30]. To mitigate the risk of recurring ischemic stroke in individuals with a history of coronary heart disease, prioritizing lifestyle changes is crucial. These changes include adopting a balanced diet, engaging in consistent physical activity, and quitting smoking. The prescription of medications such as antiplatelet agents, statins, and antihypertensive drugs is also central to stroke risk reduction strategies. Furthermore, diligent monitoring of blood pressure, cholesterol, and glucose levels - is essential for managing the risk of a subsequent stroke. In select cases, surgical interventions like coronary artery bypass grafting or angioplasty may be needed to enhance cardiac blood flow and diminish stroke risk.

Qi deficiency constitution has also been identified as another independent risk factor for recurrent ischemic stroke ($P = 0.021$). This association is attributed to the diminished state of Qi, which may result in compromised circulation and inadequate nourishment to the brain, thereby elevating the risk of stroke recurrence [31]. Treatment approaches aimed at mitigating this risk should focus on fortifying Qi. This can be achieved through a combination of acupuncture, herbal medicine, dietary adjustments, and lifestyle changes. By enhancing the Qi and fostering overall health and well-being, it's possible to decrease the likelihood of experiencing another ischemic stroke in individuals with a Qi deficiency constitution.

In contrast to existing research, this study introduces an innovative early warning model for stroke recurrence in patients with acute ischemic stroke, leveraging the principles of TCM syndrome theory. This theory offers a distinct perspective on the mechanisms underlying stroke recurrence, thereby complementing the prevailing western medical methodologies [32]. The incorporation of TCM concepts into the early warning model expands opportunity for personalized and comprehensive stroke management. Additionally, the fusion of TCM syn-

drome theory within this model potentially increases the precision and efficacy of recurrence predictions among acute ischemic stroke patients. By accounting for individual symptom patterns of and the specific disharmonies within the body as interpreted by TCM, the model is poised to suggest more customized and focused preventive measures against subsequent strokes. This integrative and person-centered approach to stroke prevention is in line with the emerging preference for personalized medicine and integrative healthcare solutions.

Our study, while pioneering in its approach, acknowledges several limitations and areas for improvement. Firstly, the acceptance of TCM syndrome theory is not widespread in western medical practice, which narrows the receptive audience. Additionally, the inherently subjective nature of diagnosing TCM syndromes could lead to variability and bias in outcome. Secondly, the relatively small sample size of our study might compromise the statistical significance and the reliability of our results. Expanding the sample size would bolster the credibility of the early warning model's effectiveness. Lastly, our study may have overlooked various confounding factors that influence stroke recurrence, including lifestyle habits, existing health conditions, and adherence to prescribed medication regimens. Neglecting these elements may result in imprecise risk evaluations. Despite the innovative potential of the early warning model grounded in TCM syndrome theory for predicting stroke recurrence, further investigation with more extensive sample sizes, longer monitoring periods, and more accounting for confounding variables is essential to affirm its efficacy.

Overall, the study contributes to the expanding body of research on stroke recurrence prediction by introducing a TCM-based early warning model. Future studies should validate and refine this model, as well as explore synergies between TCM and western medicine in stroke management.

Disclosure of conflict of interest

None.

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Supplementary Table 1. Brief table of TCM-RRATS risk score

| Predicted risk factor | Score |
|---|-------|
| Age | |
| >30~40 | 0 |
| >40~50 | 2 |
| >50~60 | 4 |
| >60~70 | 6 |
| >70~80 | 8 |
| >80~90 | 10 |
| Past history - Cerebral hemorrhage | 9 |
| Family history - Coronary heart disease | 3 |
| NIHSS>4 points | 2 |
| Continuous smoking history | 4 |
| Exercise | -3 |
| Antiplatelet aggregation drug | -4 |
| Traditional Chinese medicine intervention | 5 |
| Number of infarct lesions ≥ 3 (including large infarcts) | 2 |
| Severe or more severe intracranial artery stenosis | -3 |
| Severe or more severe cervical artery stenosis | 4 |
| Mixed plaques | 4 |
| Endogenous wind syndrome | 1 |
| The fire certificate | -1 |
| Phlegm dampness syndromes | -2 |
| Qi deficiency syndrome | 2 |

Note: NIHSS: National Institutes of Health Stroke Scale.