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# Analysis of clinical characteristics and diagnostic prediction of Qi deficiency and blood stasis syndrome in acute ischemic stroke

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ABSTRACT

**Objective** To explore the clinical characteristics and methods for syndrome differentiation prediction, as well as to construct a predictive model for Qi deficiency and blood stasis syndrome in patients with acute ischemic stroke (AIS).

**Methods** This study employed a retrospective case-control design to analyze patients with AIS who received inpatient treatment at the Neurology Department of The First Hospital of Hunan University of Chinese Medicine from January 1, 2013 to December 31, 2022. AIS patients meeting the diagnostic criteria for Qi deficiency and blood stasis syndrome were stratified into case group, while those without Qi deficiency and blood stasis syndrome were stratified into control group. The demographic characteristics (age and gender), clinical parameters [time from onset to admission, National Institutes of Health Stroke Scale (NIHSS) score, and blood pressure], past medical history, traditional Chinese medicine (TCM) diagnostic characteristics (tongue and pulse), neurological symptoms and signs, imaging findings [magnetic resonance imaging-diffusion weighted imaging (MRI-DWI)], and biochemical indicators of the two groups were collected and compared. The indicators with statistical difference ($P < 0.05$) in univariate analysis were included in multivariate logistic regression analysis to evaluate their predictive value for the diagnosis of Qi deficiency and blood stasis syndrome, and the predictive model was constructed by receiver operating characteristic (ROC) curve analysis.

**Results** The study included 1 035 AIS patients, with 404 cases in case group and 631 cases in control group. Compared with control group, patients in case group were significantly older, had extended onset-to-admission time, lower diastolic blood pressure, and lower NIHSS scores ($P < 0.05$). Case group showed lower incidence of hypertension history ($P < 0.05$). Regarding tongue and pulse characteristics, pale and dark tongue colors, white tongue coating, fine pulse, astringent pulse, and sinking pulse were more common in case group. Imaging examinations demonstrated higher proportions of centrum semiovale infarction, cerebral atrophy, and vertebral artery stenosis in case group ($P < 0.05$). Among biochemical indicators, case group showed higher proportions of elevated fasting blood glucose and glycated hemoglobin (HbA1c), while lower proportions of elevated white blood cell count, reduced hemoglobin, and reduced high-density lipoprotein cholesterol (HDL-C) ($P < 0.05$). Multivariate logistic regression analysis identified significant predictors for Qi deficiency and blood stasis syndrome including: fine pulse [odds ratio (OR) = 4.38], astringent pulse (OR = 3.67), superficial sensory abnormalities (OR = 1.86), centrum semiovale infarction (OR = 1.57),

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cerebral atrophy (OR = 1.55), vertebral artery stenosis (OR = 1.62), and elevated HbA1c (OR = 3.52). The ROC curve analysis of the comprehensive prediction model yielded an area under the curve (AUC) of 0.878 [95% confidence interval (CI) = 0.855 – 0.900].

**Conclusion** This study finds out that Qi deficiency and blood stasis syndrome represents one of the primary types of AIS. Fine pulse, astringent pulse, superficial sensory abnormalities, centrum semiovale infarction, cerebral atrophy, vertebral artery stenosis, elevated blood glucose, elevated HbA1c, pale and dark tongue colors, and white tongue coating are key objective diagnostic indicators for the syndrome differentiation of AIS with Qi deficiency and blood stasis syndrome. Based on these indicators, a syndrome differentiation prediction model has been developed, offering a more objective basis for clinical diagnosis, and help to rapidly identify this syndrome in clinical practice and reduce misdiagnosis and missed diagnosis.

## 1 Introduction

Acute ischemic stroke (AIS) is a significant medical condition that poses a serious threat to human health, accounting for more than 70% of all stroke cases [1]. Stroke was the second leading cause of death globally, accounting for 11.6% of total deaths, following ischemic heart disease. Approximately 12.2 million new cases of stroke occurred worldwide in 2019 [2]. AIS not only inflicts significant health damage to patients but also places a substantial economic burden on families and society due to the extended rehabilitation period, which necessitates prolonged rehabilitation treatment and care. It is characterized by a high incidence rate, mortality rate, and disability rate. In recent years, although various treatments such as intravenous thrombolysis and mechanical thrombectomy have achieved significant therapeutic effects in restoring cerebral blood flow and improving prognosis, their application is limited by the narrow therapeutic time window for intravenous thrombolysis, the stringent conditions required for mechanical thrombectomy, and numerous contraindications. As a result, only a minority of patients can benefit from thrombolysis and thrombectomy [3, 4]. The vast majority of patients continue to depend on internal medicine treatment. Traditional Chinese medicine (TCM) has shown definite therapeutic effects in treating AIS, and the integration of TCM with western medicine in the internal treatment of stroke is of significant therapeutic importance for improving patient prognosis and reducing disability [5, 6].

AIS falls within the scope of “Stroke” in TCM and is categorized as “Zhong Zangfu (stroke affecting meridians and collaterals, 中脏腑)” or “Zhong Jingluo (stroke affecting Zangfu organs, 中经络)” depending on the presence of unconsciousness. The earliest understanding of stroke etiology in TCM is documented in the *Huangdi Neijing* (《黄帝内经》, *Inner Cannon of Huangdi*), which identifies Qi deficiency as the fundamental cause of stroke. Qingren WANG, a physician from the Qing Dynasty, elaborated on the relationship between “Qi deficiency” and “blood stasis”, establishing Qi deficiency with blood stasis syndrome as the pathological foundation of stroke. Current clinical studies have confirmed that “Qi deficiency” and “blood stasis” constitute the pathological basis of AIS, with Qi deficiency and blood stasis syndrome being its fundamental diagnostic pattern. However, due to its relatively mild symptoms, the syndrome is often overlooked by both medical professionals and patients, resulting in misdiagnosis, missed diagnoses, and delayed treatment. This can lead to severe conditions and adverse outcomes, such as recurrent cerebral infarction [7].

Syndrome differentiation and treatment are fundamental components of TCM in disease management. However, the diagnosis of “syndromes” is highly subjective and lacks objective criteria, resulting in significant uncertainty and variability among individuals. This presents challenges for standardization in clinical settings [8]. Therefore, identifying straightforward and accessible objective indicators can establish a reliable foundation for predicting types of AIS syndrome. This study employs a retrospective case-control design with real-world data to analyze the correlations between symptoms, signs, physical examinations, imaging, and laboratory indicators in patients with ischemic stroke characterized by “Zhong Jingluo” Qi deficiency and blood stasis syndrome, compared with other syndromes. The aim is to explore the diagnostic value of these indicators in AIS patients with Qi deficiency and blood stasis syndrome and provide new guidance for the rapid identification of this syndrome in clinical practice and for reducing misdiagnosis and missed diagnosis.

## 2 Data and methods

### 2.1 Participants

This study employed a retrospective case-control design. Patients were screened from The First Hospital of Hunan University of Chinese Medicine who were hospitalized in the Neurology Department between January 1, 2013 and December 31, 2022, with diagnoses of AIS, acute cerebral infarction, cerebral infarction, cerebellar infarction, brainstem infarction, acute phase of cerebral infarction,

or ischemic cerebral infarction. According to TCM syndrome differentiation criteria, patients who met the diagnostic criteria for Qi deficiency and blood stasis syndrome were assigned to case group, while patients with other syndrome types were assigned to control group. Clinical data for both groups were recorded in detail.

Sample size estimation was based on the methods described by GAO et al. [9]. Logistic regression was used to analyze the included variables. According to previous study [10], the Events per Variable (EPV) should be set to 10. Consequently, a total of 24 covariates were ultimately included in the logistic regression analysis. Therefore, the required sample size should be at least 240 cases per group.

This study protocol was approved by the Ethics Committee of The First Hospital of Hunan University of Chinese Medicine (HN-LL-GZR-2022-26).

**2.1.1 Diagnostic criteria** The diagnostic criteria for AIS were based on the Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke 2023 [11], requiring all the following conditions: (i) acute onset; (ii) focal neurological deficit (e.g., weakness or numbness of one side of the face or limbs, speech disorders), with a few cases presenting with global neurological deficit; (iii) imaging that shows a responsible lesion or symptoms/signs that persist for more than 24 h; (iv) exclusion of non-vascular causes; (v) brain computed tomography (CT)/magnetic resonance imaging (MRI) to exclude cerebral hemorrhage.

The diagnostic criteria for Zhong Jingluo with Qi deficiency and blood stasis syndrome are based on the Evidence-Based Practice Guidelines for the Integrated Traditional Chinese and Western Medicine Treatment of Stroke (2019) [12]. "Zhong Jingluo" does not involve changes in consciousness, and includes hemiplegia, facial and tongue deviation, difficulty in speech or muteness, numbness on one side of the body, dull complexion, shortness of breath and fatigue, spontaneous sweating, palpitations, swollen hands, loose stools, dark tongue color with thin white or white coating, and sinking and fine pulse.

**2.1.2 Inclusion criteria and exclusion criteria** Patients were included in the study if they met the following specific criteria: (i) diagnosis of AIS confirmed by at least two attending physicians or higher; (ii) presence of clear ischemic lesion on imaging examinations; (iii) the time interval from symptom onset to hospital admission did not exceed 4 d; (iv) with complete medical documentation.

Patients were excluded from study participation if they met any of the following criteria: (i) patients aged over 80 years at disease onset; (ii) delayed hospital admission (> 4 d post-onset); (iii) radiologically confirmed or suspected cerebral hemorrhage; (iv) presence of coma, severe cognitive impairment, or consciousness disturbances, differentiated as "Zhong Zangfu" syndrome in TCM terminology; (v) significant comorbidities including severe cardiovascular disorders (myocardial infarction, serious arrhythmias such as ventricular fibrillation and acute coronary syndrome), digestive disorders (including gastrointestinal ulcers), urinary diseases, hematopoietic diseases, or severe liver and kidney insufficiency [alanine aminotransferase (ALT)/aspartate aminotransferase (AST) > 1.5 times the upper limit of the normal reference value, creatinine value ⩾ 177 μmol/L]; (vi) pregnancy or lactation status; (vii) patients with incomplete biochemical indicator or physical sign information.

## 2.2 Data collection

Data collection was conducted using clinical medical records from the Electronic Medical Record (EMR) system at The First Hospital of Hunan University of Chinese Medicine. The authors manually transcribed the relevant information for documentation purposes.

**2.2.1 General information** The collected data included age, gender, onset time, National Institutes of Health Stroke Scale (NIHSS) score, systolic blood pressure (SBP) at admission, diastolic blood pressure (DBP), past medical history (including hypertension, diabetes mellitus, cardiovascular disease, and heart function).

**2.2.2 Symptoms and signs** The symptoms and signs recorded included the chief complaint, tongue diagnosis, pulse diagnosis, and physical signs such as limb numbness, limb weakness, limb pain, limited limb movement, headache, dizziness, visual vertigo, speech disturbance, aphasia, facial palsy, sialorrhea, sleep disturbance, unsteady gait, chest tightness, visual abnormalities, auditory abnormalities, choking when drinking water, nausea, vomiting, and consciousness disturbances.

**2.2.3 Abnormalities in limbs and sensation** The evaluation included the muscle strength of the limbs, muscle tone of the limbs, deep sensory disturbance (including proprioceptive deficit, vibration sense deficit, and kinesthetic sense deficit), and hypoesthesia (including amblyaphia, hypoesthesia to temperature, and hypalgesia).

**2.2.4 Imaging examinations** Magnetic resonance imaging-diffusion weighted imaging (MRI-DWI) was performed to assess infarctions in various brain regions, including the centrum semiovale, cerebellum, hippocampal region, brainstem, midbrain, thalamus, hypothalamus, corpus callosum, lateral ventricles, frontal lobe, occipital lobe, parietal lobe, temporal lobe, insular lobe, basal ganglia region, corona radiata, pontine region, and lacunar regions, as well as signs of cerebral atrophy and old cerebral infarctions. Additionally, color Doppler ultrasonography of the carotid and vertebral arteries was employed to assess stenosis in the vertebral artery,

carotid artery, anterior cerebral artery, middle cerebral artery, posterior cerebral artery, and subclavian artery.

**2.2.5 Biochemical examination indicators** The biochemical indicators measured in this study included: white blood cell count (WBC), neutrophil count (N), lymphocyte count (L), red blood cell count (RBC), hemoglobin concentration (Hb), C-reactive protein level (CRP), prothrombin time (PT), fibrinogen level (FIB), thrombin time (TT), D-dimer levels (DD), total cholesterol (TCHO), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (GLU), and glycated hemoglobin (HbA1c).

### 2.3 Diagnostic model evaluation

In the analysis, WBC, N, L, RBC, Hb, CRP, PT, FIB, TT, DD, TCHO, TG, HDL-C, LDL-C, GLU, HbA1c, and other indicators were treated as categorical variables. Variables that exhibited statistical differences ($P < 0.05$) in group comparisons were included in multivariate logistic regression analysis, using the enter method to establish the regression model.

To evaluate the diagnostic value of the test, the relationship between sensitivity and specificity was illustrated using a receiver operating characteristic (ROC) curve. The area under the curve (AUC) was calculated to indicate the diagnostic value, with values ranging from 0.5 to 1.0, where a higher AUC indicates greater diagnostic accuracy. An ROC curve was plotted to comprehensively assess the predictive value of various indicators for Qi deficiency and blood stasis syndrome in AIS patients. The AUC and cutoff value were determined. The cutoff value represented the optimal balance between sensitivity and specificity, facilitating the accurate identification of case group to the greatest extent while minimizing the misclassification of negative samples as positive. Utilizing the cutoff value and the gold standard diagnostic results, patients were classified into true positives (TP), false positives (FP), false negatives (FN), and true negatives (TN). These classifications enabled the calculation of sensitivity, specificity, accuracy, and Youden's index using the corresponding formulas. We explored the diagnostic value of the model for AIS with Qi deficiency and blood stasis syndrome patients using the following indices:

$$\text{Sensitivity} = TP/(TP + FN) \times 100\%$$

$$\text{Specificity} = TN/(TN + FP) \times 100\%$$

$$\text{Accuracy} = (TP + TN)/(TP + TN + FP + FN) \times 100\%$$

$$\text{Youden's index} = (\text{sensitivity} + \text{specificity}) - 1.$$

### 2.4 Statistical analysis

Statistical analysis was conducted using SPSS 25.0 and R software v4.3.0. For quantitative data, the distribution was assessed, with normally distributed data presented as mean ± standard deviation (SD) and non-normally distributed data described by medians and ranges $M(P_{25}, P_{75})$. Comparisons between groups were performed using $t$ test for normally distributed data and Wilcoxon signed-rank test for non-normally distributed data. Categorical data were expressed as percentages (%) and compared using Chi-square tests. $P < 0.05$ was considered statistically significant.

## 3 Results

### 3.1 Case collection

We initially identified 6 179 AIS cases from the EMR system. After applying the diagnostic, inclusion, and exclusion criteria, a total of 1 035 patients with AIS with "Zhong Jingluo" syndrome were identified. Among them, 404 patients diagnosed with Qi deficiency and blood stasis syndrome according to TCM diagnostic criteria were included in case group, 631 patients that met the AIS diagnosis but did not fit the Qi deficiency and blood stasis syndrome diagnosis were included in control group. The screening process is illustrated in Figure 1.

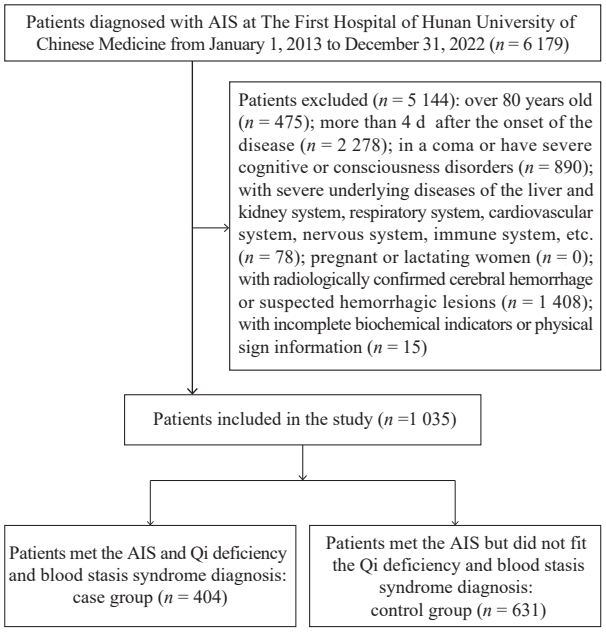


**Figure 1** Flowchart of patient selection process

### 3.2 Comparison of general clinical data between case group and control group

The general clinical data of patients in both case and control groups were compared, as presented in Table 1. Case group was significantly older than the control group, with an extended onset time, and exhibited reduced DBP and NIHSS scores ($P < 0.05$). Case group showed a lower history of hypertension compared with control group ($P < 0.05$). However, no statistically significant differences were found in SBP, history of diabetes, or heart function between the two groups ($P > 0.05$).

**Table 1** Comparison of general clinical data between case and control groups

| Group | Age (year) | Onset time (d) | SBP (mmHg) | DBP (mmHg) | NIHSS | History of hypertension [*n* (%)] | History of diabetes [*n* (%)] |
|---|---|---|---|---|---|---|---|
| Control | 65.99 ± 12.02 | 2.00 (1.00-4.50) | 155.87 ± 23.57 | 90.97 ± 13.25 | 0.00 (0.00 – 3.00) | 538 (85.26%) | 208 (32.96%) |
| Case | 68.24 ± 11.36 | 3.00 (2.00-6.00) | 154.81 ± 24.20 | 89.40 ± 12.34 | 0.00 (0.00 – 1.00) | 316 (78.22%) | 123 (30.45%) |
| *P* value | 0.003 | 0.013 | 0.483 | 0.049 | < 0.001 | 0.004 | 0.397 |

| Group | Heart function [*n* (%)] | | | Gender [*n* (%)] | | Atherosclerosis [*n* (%)] |
|---|---|---|---|---|---|---|
| | NYHA Class I | NYHA Class II | NYHA Class III | Female | Male | |
| Control | 47 (7.45%) | 30 (4.75%) | 42 (6.66%) | 197 (31.22%) | 434 (68.78%) | 82 (13.00%) |
| Case | 45 (11.14%) | 19 (4.70%) | 21 (5.20%) | 201 (49.75%) | 203 (50.25%) | 37 (9.16%) |
| *P* value | 0.189 | | | < 0.001 | | 0.059 |

### 3.3 Comparison of symptoms and signs between case group and control group

Table 2 revealed that case group exhibited dark and pale tongue colors more frequently than control group in the comparison of tongue color between the two groups ($P < 0.001$). In terms of tongue coating, case group had a higher prevalence of white coating compared with control group ($P < 0.001$). Similarly, the comparison of pulse characteristics showed that fine, astringent, and sinking pulses were more frequently observed in case group ($P < 0.05$). Concerning symptoms, case group only showed a reduction in speech impairment compared with control group ($P < 0.05$). No significant differences were observed in other symptoms and signs, including limb numbness, limb weakness, limb pain, limb movement disorders, headache, dizziness, visual vertigo, speech impairment aphasia, facial palsy, sialorrhea, sleep disturbances, unsteady gait, chest tightness, visual abnormalities, nausea and vomiting, choking when drinking water, altered mental status, and hearing impairment between two groups ($P > 0.05$).

### 3.4 Comparison of muscle strength and sensory abnormalities between case group and control group

Table 3 indicated no statistically significant differences in muscle strength, muscle tone, or deep sensory disturbance between case group and control group ($P > 0.05$). However, hypoesthesia was significantly more prevalent in case group compared with control group ($P < 0.05$).

### 3.5 Comparison of imaging findings between case group and control group

Table 4 revealed that brain MRI findings showed a significantly higher prevalence of centrum semiovale infarction, cerebral atrophy, and vertebral artery stenosis in case group compared with control group ($P < 0.05$). However, no significant differences were observed in other infarction locations, including the cerebellar, hippocampal region, brainstem, midbrain, thalamic, corpus callosum, and various cerebral lobes, or other vascular stenoses, including the carotid, anterior cerebral, middle cerebral, posterior cerebral, and subclavian arteries, between the two groups ($P > 0.05$).

### 3.6 Comparison of biochemical indicators between case group and control group

Table 5 revealed a significantly higher prevalence of elevated GLU, HbA1c, and reduced WBC, TG, Hb, and HDL-C in case group compared with control group ($P < 0.05$). However, no significant differences were observed in other indicators, such as N, RBC, CRP, PT, TT, FIB, DD, TCHO, and LDL-C, between the two groups ($P > 0.05$).

### 3.7 Multivariate logistic regression analysis of factors associated with AIS with Qi deficiency and blood stasis syndrome

Indicators that exhibited statistically significant differences in the univariate group comparisons presented in Table 1 to 5 were incorporated into the multivariate logistic regression analysis. These indicators included gender, dark tongue, purple tongue, red tongue, pale tongue, white tongue coating, yellow coating, greasy and yellow coating, string pulse, slippery pulse, fine pulse, astringent pulse, rapid pulse, irregular pulse, sinking pulse, speech impairment, hypoesthesia, history of hypertension, centrum semiovale infarction, cerebral atrophy, vertebral artery stenosis, WBC, Hb, TCHO, HDL-C, GLU, and HbA1c. In this analysis, the tongue color of dark and the tongue coating of white were randomly selected as the reference categories for tongue color and tongue coating, respectively. The dependent variable for this analysis was the diagnosis of AIS with Qi deficiency and blood stasis syndrome, with the independent variable displayed in Table 6. Age, onset time, DBP, and NIHSS score were used as measured values. The analysis revealed that the presence of fine pulse, astringent pulse, hypoesthesia, centrum semiovale infarction, cerebral atrophy,

**Table 2** Comparison of symptoms and physical signs between case and control groups [*n* (%)]

| Group | Chief complaint | | | | | Limb numbness | | |
|---|---|---|---|---|---|---|---|---|
| | Speech impairment | Limb weakness | Abnormal limb sensation | Limited limb movement | Dizziness | Left side | Right side | Both side |
| Control | 218 (34.55%) | 189 (29.95%) | 65 (10.30%) | 74 (11.73%) | 85 (13.47%) | 78 (12.36%) | 92 (14.58%) | 25 (3.96%) |
| Case | 124 (30.69%) | 125 (30.94%) | 50 (12.38%) | 58 (14.36%) | 47 (11.63%) | 66 (16.34%) | 44 (10.89%) | 13 (3.22%) |
| *P* value | | | 0.389 | | | | 0.126 | |

| Group | Tongue coating | | | Cracked tongue [case (%)] | String pulse | Slippery pulse | Fine pulse | Astringent pulse |
|---|---|---|---|---|---|---|---|---|
| | White | Yellow | Yellow and greasy | | | | | |
| Control | 76 (12.04%) | 122 (19.33%) | 225 (35.66%) | 11 (1.74%) | 491 (77.81%) | 293 (46.43%) | 59 (9.35%) | 17 (2.69%) |
| Case | 227 (56.19%) | 49 (12.13%) | 57 (14.11%) | 7 (1.73%) | 173 (42.82%) | 52 (12.87%) | 146 (36.14%) | 35 (8.66%) |
| *P* value | | < 0.001 | | 0.990 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |

| Group | Rapid pulse | Irregular pulse | Sinking pulse | Floating pulse | Slow pulse | Limb weakness | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Left side | Right side | Both side |
| Control | 52 (8.24%) | 12 (1.90%) | 23 (3.65%) | 1 (0.16%) | 1 (0.16%) | 162 (25.67%) | 175 (27.73%) | 50 (7.92%) |
| Case | 11 (2.72%) | 1 (0.25%) | 30 (7.43%) | 1 (0.25%) | 2 (0.50%) | 111 (27.48%) | 92 (22.77%) | 46 (11.39%) |
| *P* value | < 0.001 | 0.020 | 0.007 | 1.000 | 0.564 | | 0.120 | |

| Group | Limb movement disorder | | | Tongue color | | | | Limb pain |
|---|---|---|---|---|---|---|---|---|
| | Left side | Right side | Both side | Dark | Purplish | Red | Pale | |
| Control | 86 (13.63%) | 104 (16.48%) | 2 (0.32%) | 67 (10.62%) | 9 (1.43%) | 385 (61.01%) | 170 (26.94%) | 10 (1.58%) |
| Case | 57 (14.11%) | 49 (12.13%) | 4 (0.99%) | 51 (12.62%) | 12 (2.97%) | 123 (30.45%) | 218 (53.96%) | 8 (1.98%) |
| *P* value | | 0.140 | | | | < 0.001 | | 0.635 |

| Group | Headache | Dizziness | Visual vertigo | Speech impairment | Aphasia | Facial paralysis | Sialorrhea | Sleep disturbance |
|---|---|---|---|---|---|---|---|---|
| Control | 71 (11.25%) | 211 (33.44%) | 24 (3.80%) | 349 (55.31%) | 11 (1.74%) | 132 (20.92%) | 62 (9.83%) | 64 (10.14%) |
| Case | 40 (9.90%) | 130 (32.18%) | 15 (3.71%) | 194 (48.02%) | 9 (2.23%) | 91 (22.52%) | 43 (10.64%) | 44 (10.89%) |
| *P* value | 0.493 | 0.674 | 0.940 | 0.022 | 0.581 | 0.540 | 0.671 | 0.701 |

| Group | Unsteady gait | Chest tightness | Visual abnormality | Nausea and vomiting | Choking | Hearing impairment | Altered mental status |
|---|---|---|---|---|---|---|---|
| Control | 222 (35.18%) | 67 (10.62%) | 58 (9.19%) | 50 (7.92%) | 84 (13.31%) | 20 (3.17%) | 38 (6.02%) |
| Case | 148 (36.63%) | 47 (11.63%) | 34 (8.42%) | 29 (7.18%) | 50 (12.38%) | 17 (4.21%) | 31 (7.67%) |
| *P* value | 0.635 | 0.611 | 0.669 | 0.659 | 0.662 | 0.380 | 0.299 |

**Table 3** Comparison of muscle strength, muscle tone, and sensory abnormalities between case and control groups [*n* (%)]

| Group | Left upper extremity muscle strength | | | | |
|---|---|---|---|---|---|
| | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
| Control | 9 (1.43%) | 11 (1.74%) | 38 (6.02%) | 97 (15.37%) | 456 (72.27%) |
| Case | 7 (1.73%) | 9 (2.23%) | 33 (8.17%) | 68 (16.83%) | 279 (69.06%) |
| *P* value | | | 0.539 | | |
| **Group** | **Left lower extremity muscle strength** | | | | |
| | **Grade 1** | **Grade 2** | **Grade 3** | **Grade 4** | **Grade 5** |
| Control | 14 (2.22%) | 14 (2.22%) | 55 (8.72%) | 109 (17.27%) | 432 (68.46%) |
| Case | 4 (0.99%) | 7 (1.73%) | 46 (11.39%) | 90 (22.28%) | 253 (62.62%) |
| *P* value | | | 0.120 | | |
| **Group** | **Right upper extremity muscle strength** | | | | |
| | **Grade 1** | **Grade 2** | **Grade 3** | **Grade 4** | **Grade 5** |
| Control | 15 (2.38%) | 5 (0.79%) | 48 (7.61%) | 96 (15.21%) | 453 (71.79%) |
| Case | 6 (1.49%) | 3 (0.74%) | 31 (7.67%) | 71 (17.57%) | 284 (70.30%) |
| *P* value | | | 0.862 | | |
| **Group** | **Right lower extremity muscle strength** | | | | |
| | **Grade 1** | **Grade 2** | **Grade 3** | **Grade 4** | **Grade 5** |
| Control | 12 (1.90%) | 10 (1.58%) | 61 (9.67%) | 104 (16.48%) | 435 (68.94%) |
| Case | 3 (0.74%) | 9 (2.23%) | 35 (8.66%) | 84 (20.79%) | 268 (66.34%) |
| *P* value | | | 0.313 | | |

| Group | Left upper extremity muscle tone | | Left lower extremity muscle tone | | Deep sensory disturbance |
|---|---|---|---|---|---|
| | Increased | Decreased | Increased | Decreased | |
| Control | 19 (3.01%) | 6 (0.95%) | 17 (2.69%) | 7 (1.11%) | 16 (2.54%) |
| Case | 18 (4.46%) | 4 (0.99%) | 17 (4.21%) | 5 (1.24%) | 12 (2.97%) |
| *P* value | 0.473 | | 0.402 | | 0.674 |
| **Group** | **Right upper extremity muscle tone** | | **Right lower extremity muscle tone** | | **Hypoesthesia** |
| | **Increased** | **Decreased** | **Increased** | **Decreased** | |
| Control | 24 (3.80%) | 5 (0.79%) | 20 (3.17%) | 5 (0.79%) | 37 (5.86%) |
| Case | 14 (3.47%) | 2 (0.50%) | 14 (3.47%) | 4 (0.99%) | 44 (10.89%) |
| *P* value | 0.852 | | 0.894 | | 0.003 |

vertebral artery stenosis, GLU, HbAlc, pale, purple, red, dark tongue, and white tongue coating were significant factors influencing the diagnosis of Qi deficiency and blood stasis syndrome in AIS patients ($P < 0.05$, Table 7).

### 3.8 Predictive value of related factors for AIS with Qi deficiency and blood stasis syndrome differentiation

The logistic regression equation for predicting AIS with Qi deficiency and blood stasis syndrome is as follows: logit (AIS with Qi deficiency and blood stasis syndrome) = 1.441 12 – 1.882 09 × string pulse – 1.838 39 × slippery pulse + 1.560 99 × fine pulse + 1.278 59 × astringent pulse – 1.640 23 × rapid pulse + 0.474 13 × vertebral artery stenosis – 0.491 37 × history of hypertension + 1.352 77 × HbA1c – 1.054 79 × WBC + 0.477 69 × cerebral atrophy + 1.045 37 × purple tongue – 1.055 23 × red tongue + 0.256 17 × pale tongue – 0.099 78 × NIHSS – 3.127 89 × irregular pulse – 1.073 50 × sinking pulse. Based on the multivariate logistic regression analysis, ROC curves were plotted for each indicator to predict the differentiation of AIS as Qi deficiency and blood stasis syndrome. The AUC was 0.878 (95% CI = 0.855 – 0.900), with a sensitivity of 0.760 (0.716, 0.800), specificity of 0.884 (0.857, 0.907), accuracy of 0.836, and Youden's index of 0.644. These results indicate that using tongue and pulse diagnosis as the primary predictive factors, in conjunction with other indicators such as physical signs, superficial sensory abnormalities, history of hypertension, cerebral atrophy, location of infarction, responsible vessels, and biochemical blood indicators, can effectively predict AIS with Qi deficiency and blood stasis syndrome. This demonstrates that the predictive model has a high diagnostic value for AIS with Qi deficiency and blood stasis syndrome (Figure 2).

**Table 4** Comparison of imaging between case and control groups [*n* (%)]

| Group | Stroke location based on MRI-DWI | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cerebral hemispher | Cerebellar | hippocampal region | Brainstem | Midbrain | Thalamic | Superior colliculus | Hypothalamus | Corpus callosum | Ventricle | Lateral ventricle | Ventricle body |
| Control | 14 (2.22%) | 22 (3.49%) | 12 (1.90%) | 24 (3.80%) | 3 (0.48%) | 41 (6.50%) | 9 (1.43%) | 0 (0.00%) | 12 (1.90%) | 1 (0.16%) | 28 (4.44%) | 0 (0.00%) |
| Case | 11 (2.72%) | 22 (5.45%) | 9 (2.23%) | 16 (3.96%) | 4 (0.99%) | 24 (5.94%) | 9 (2.23%) | 2 (0.50%) | 14 (3.47%) | 4 (0.99%) | 17 (4.21%) | 2 (0.50%) |
| *P* value | 0.606 | 0.128 | 0.717 | 0.898 | 0.441 | 0.719 | 0.336 | 0.152 | 0.117 | 0.079 | 0.860 | 0.152 |

| Group | Stroke location based on MRI-DWI | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Centrum semiovale | Frontal lobe | Parietal lobe | Temporal lobe | Occipital lobe | Insular lobe | Basal ganglia | Corona radiata | Pontine | Cerebral atrophy | Old infarction | Lacunar infarction |
| Control | 34 (5.39%) | 66 (10.46%) | 66 (10.46%) | 37 (5.86%) | 50 (7.92%) | 9 (1.43%) | 116 (18.38%) | 84 (13.31%) | 66 (10.46%) | 326 (51.66%) | 169 (26.78%) | 131 (20.76%) |
| Case | 39 (9.65%) | 53 (13.12%) | 46 (11.39%) | 29 (7.18%) | 32 (7.92%) | 11 (2.72%) | 91 (22.52%) | 52 (12.87%) | 52 (12.87%) | 253 (62.62%) | 127 (31.44%) | 94 (23.27%) |
| *P* value | 0.009 | 0.191 | 0.640 | 0.398 | 0.999 | 0.139 | 0.104 | 0.838 | 0.234 | < 0.001 | 0.106 | 0.340 |

| Group | The responsible vessels based on color Doppler ultrasonography finding | | | | | |
|---|---|---|---|---|---|---|
| | Carotid artery stenosis | Vertebral artery stenosis | Anterior cerebral artery stenosis | Middle cerebral artery stenosis | Posterior cerebral artery stenosis | Subclavian artery stenosis |
| Control | 396 (62.76%) | 185 (29.32%) | 5 (0.79%) | 7 (1.11%) | 7 (1.11%) | 86 (13.63%) |
| Case | 257 (63.61%) | 155 (38.37%) | 1 (0.25%) | 1 (0.25%) | 1 (0.25%) | 51 (12.62%) |
| *P* value | 0.781 | 0.003 | 0.413 | 0.159 | 0.159 | 0.642 |

**Table 5** Comparison of abnormal blood biochemical test indicators between case and control groups [*n* (%)]

| Group | WBC | N | L | RBC | Hb | CRP | PT | FIB |
|---|---|---|---|---|---|---|---|---|
| Control | 43 (6.81%) | 99 (15.69%) | 42 (6.66%) | 45 (7.13%) | 79 (12.52%) | 15 (2.38%) | 84 (13.31%) | 79 (12.52%) |
| Case | 15 (3.71%) | 57 (14.11%) | 17 (4.21%) | 27 (6.68%) | 16 (3.96%) | 12 (2.97%) | 57 (14.11%) | 56 (13.86%) |
| *P* value | 0.034 | 0.488 | 0.097 | 0.782 | < 0.001 | 0.559 | 0.715 | 0.532 |
| **Group** | **TT** | **DD** | **TCHO** | **TG** | **HDL-C** | **LDL-C** | **GLU** | **HbA1c** |
| Control | 32 (5.07%) | 21 (3.33%) | 129 (20.44%) | 96 (15.21%) | 91 (14.42%) | 174 (27.58%) | 95 (15.06%) | 23 (3.65%) |
| Case | 22 (5.45%) | 16 (3.96%) | 85 (21.04%) | 42 (10.40%) | 33 (8.17%) | 100 (24.75%) | 84 (20.79%) | 52 (12.87%) |
| *P* value | 0.792 | 0.593 | 0.817 | 0.026 | 0.003 | 0.315 | 0.017 | < 0.001 |

**Table 6** Logistic regression analysis assignment of related factors

| Variable | Assignment |
|---|---|
| Gender | 0 = female, 1 = male |
| Syndrome | Without Qi deficiency and blood stasis syndrome = 0, Qi deficiency and blood stasis syndrome = 1 |
| Tongue color | Dark = 1, purple = 2, red = 3, pale = 4 |
| Tongue coating | White = 1, yellow = 2, greasy and yellow = 3 |
| String pulse | No = 0, Yes = 1 |
| Slippery pulse | No = 0, Yes = 1 |
| Fine pulse | No = 0, Yes = 1 |
| Astringent pulse | No = 0, Yes = 1 |
| Rapid pulse | No = 0, Yes = 1 |
| Irregular pulse | No = 0, Yes = 1 |
| Sinking pulse | No = 0, Yes = 1 |
| Speech impairment | No = 0, Yes = 1 |
| hypoesthesia | No = 0, Yes = 1 |
| History of hypertension | No = 0, Yes = 1 |
| History of atherosclerosis | No = 0, Yes = 1 |
| Centrum semiovale infarction | No = 0, Yes = 1 |
| Cerebral atrophy | No = 0, Yes = 1 |
| Abnormal WBC count | No = 0, Yes = 1 |
| Abnormal Hb levels | No = 0, Yes = 1 |
| Abnormal TCHO levels | No = 0, Yes = 1 |
| Abnormal HDL-C levels | No = 0, Yes = 1 |
| Elevated fasting blood glucose | No = 0, Yes = 1 |
| Abnormal glycated hemoglobin | No = 0, Yes = 1 |

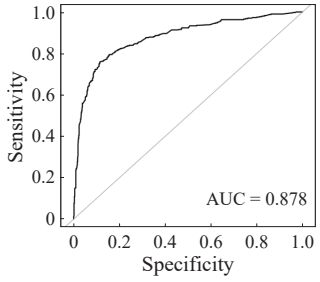


**Figure 2** ROC curve for predicting Qi deficiency and blood stasis syndrome in patients with AIS

## 4 Discussion

Clinically, AIS with "Zhong Jingluo" syndrome is categorized into five syndrome types: Qi deficiency and blood stasis, wind-phlegm obstructing the collaterals, wind-fire disturbing the upper body, Yin deficiency with wind movement, and liver-kidney deficiency syndrome. However, TCM primarily relies on subjective judgment based on symptoms and signs. This diagnostic method is significantly influenced by subjective factors and lacks objective standards, making it challenging to meet the needs of integrated TCM and western medicine diagnosis and treatment. Therefore, the objective of this research was to compare symptoms, signs, physical examinations, imaging findings, and biochemical indices to objectify the subjective syndrome differentiation method.

**Table 7** Multivariate logistic regression analysis of factors associated with AIS with Qi deficiency and blood stasis syndrome

| Variable | OR | 95%CI low | 95%CI up | *P* value |
|---|---|---|---|---|
| Age | 1.00 | 0.98 | 1.01 | 0.58 |
| NIHSS | 0.91 | 0.86 | 0.97 | < 0.01 |
| Gender | 0.74 | 0.51 | 1.06 | 0.10 |
| String pulse | 0.16 | 0.10 | 0.24 | < 0.01 |
| Slippery pulse | 0.16 | 0.11 | 0.25 | < 0.01 |
| Fine pulse | 4.38 | 2.86 | 6.70 | < 0.01 |
| Astringent pulse | 3.67 | 1.72 | 7.82 | < 0.01 |
| Rapid pulse | 0.19 | 0.08 | 0.44 | < 0.01 |
| Irregular pulse | 0.05 | < 0.01 | 0.50 | 0.01 |
| Sinking pulse | 0.36 | 0.17 | 0.77 | < 0.01 |
| Speech impairment | 0.88 | 0.62 | 1.25 | 0.49 |
| Hypoesthesia | 1.86 | 0.99 | 3.51 | 0.05 |
| History of hypertension | 0.58 | 0.37 | 0.91 | 0.02 |
| Centrum semiovale infarction | 1.57 | 0.80 | 3.09 | 0.19 |
| Cerebral atrophy | 1.55 | 1.08 | 2.23 | 0.02 |
| Vertebral artery stenosis | 1.62 | 1.13 | 2.34 | < 0.01 |
| WBC | 0.32 | 0.14 | 0.75 | < 0.01 |
| Hb | 0.56 | 0.29 | 1.07 | 0.07 |
| TG | 0.67 | 0.38 | 1.18 | 0.16 |
| HDL-C | 0.68 | 0.38 | 1.20 | 0.18 |
| GLU | 1.17 | 0.72 | 1.90 | 0.52 |
| HbA1c | 3.52 | 1.71 | 7.24 | < 0.01 |
| Purple tongue color | 2.86 | 0.80 | 10.17 | 0.10 |
| Red tongue color | 0.36 | 0.21 | 0.61 | < 0.01 |
| Pale tongue color | 1.32 | 0.75 | 2.30 | 0.33 |
| Yellow tongue coating | 0.27 | 0.15 | 0.47 | < 0.01 |
| Yellow and greasy tongue coating | 0.34 | 0.19 | 0.59 | < 0.01 |
| Onset time | 1.02 | 0.99 | 1.06 | 0.23 |

### 4.1 Distribution of TCM syndrome types and etiological analysis of AIS

Through our preliminary statistics of the distribution of the five syndrome types in patients with AIS "Zhong Jingluo" (affecting the meridians), we found that wind-phlegm obstructing the collaterals and Qi deficiency with blood stasis were the most common types of AIS, which is consistent with conclusions from other studies [13, 14]. These studies indicate that Qi deficiency and blood stasis syndrome is one of the main syndrome types of AIS and represents an important disease pathogenesis.

In our research, the onset time of AIS patients is far beyond the optimal time window for thrombolysis and mechanical thrombectomy. Additionally, various contraindications limit the actual benefits for most patients [15, 16]. More than 80% of AIS patients were suffering from hypertension, and nearly 10% of them had coagulation abnormalities. Therefore, the rehabilitation treatment of AIS still relies on comprehensive internal medicine approaches.

Through age, onset time, NIHSS, past medical history, and symptoms, this study aligns with previous research findings [17-19], which suggests that patients with Qi deficiency and blood stasis syndrome experience milder conditions and less severe neurological deficits. This may be related to the progressive weakness in the elderly, with gradual deficiency of Qi, blood, Yin, and Yang. Insufficient Qi to promote blood circulation can lead to blood stasis [20]. In addition, elderly patients often have underlying diseases, and milder symptoms may not be taken seriously by the patients. Coupled with the inconvenience of seeking medical treatment, they may only seek hospital care when significant discomfort occurs post-onset, potentially missing the optimal treatment window. Due to the milder symptoms of this syndrome type, many AIS with Qi deficiency and blood stasis syndrome patients only seek outpatient care and do not undergo systematic hospital treatment, delaying comprehensive treatment. Therefore, it is crucial in medical practice to pay sufficient attention to the diagnosis and treatment of these patients to avoid exacerbating their condition due to delayed diagnosis and treatment.

The analysis of tongue and pulse in this study is in accordance with the fundamental diagnostic tenets of TCM. These characteristics are consistent with AIS with Qi deficiency and blood stasis syndrome. There is still a diversity of clinical opinions regarding their accurate judgment, necessitating more objective indicators for assessment.

The analysis of hematological indicators is consistent with previous studies on the differences in blood sugar and lipids among patients with different syndrome types of AIS [20]. This further supports the notion that patients with Qi deficiency and blood stasis syndrome have relatively mild conditions, with onset likely related to abnormalities in sugar and lipid metabolism. In terms of imaging diagnosis, while some studies have reported that AIS with Qi deficiency and blood stasis syndrome predominantly occurs in the anterior or posterior circulation, with the responsible vessels mostly being the carotid arteries [21], our study found that the infarction sites for this syndrome type are more likely to occur in the centrum semiovale area, with the responsible vessels often being the vertebral arteries. This discrepancy may be related to the geographical location of the patients' onset. Additionally, some studies have shown that the location of AIS onset in patients can vary due to regional, climatic, and other factors [22, 23].

### 4.2 Multivariate regression analysis and prediction model construction

In this study, we conducted a multivariate logistic regression analysis, which identified several factors significantly associated with the differentiation of AIS with Qi deficiency and blood stasis syndrome. It indicates a high diagnostic value of the predictive model for determining AIS with Qi deficiency and blood stasis syndrome.

Our study demonstrates innovation in the following aspects. First, we have integrated TCM diagnosis and western medicine diagnosis to provide a more comprehensive and objective basis for the diagnosis of Qi deficiency and blood stasis syndrome. Second, our results emphasize the importance of glycemic control and lipid metabolism in the pathogenesis of Qi deficiency and blood stasis syndrome, which may align with the current research trend on the relationship between metabolic syndrome and cerebrovascular disease.

### 4.3 Research limitations and future prospects

While our study is illuminating, it still has limitations. As a single-center investigation, our cohort may not be fully representative of the entire population of patients with AIS, potentially constraining the generalizability of our findings. Consequently, future research should consider multicenter studies with larger sample sizes to validate our observations and further explore disparities among different populations and regions. Moreover, our research suggests directions for future studies, including an in-depth exploration of the biological mechanisms underlying Qi deficiency and blood stasis syndrome, as well as the development of more precise diagnostic tools and therapeutic strategies. The integrated use of multiple indicators can significantly enhance the predictive accuracy of Qi deficiency and blood stasis syndrome, offering possibilities for personalized medicine in the future.

## 5 Conclusion

This study has substantiated that Qi deficiency and blood stasis syndrome is a predominant syndrome in AIS. We have developed a prediction model for the expedited recognition and precise diagnosis of Qi deficiency and blood stasis syndrome in the context of AIS, by integrating diagnostic techniques of TCM with advanced medical technologies. This diagnostic model facilitates the rapid identification of AIS with Qi deficiency and blood stasis syndrome patients and can mitigate the risks of misdiagnosis and missed diagnosis. Furthermore, this holds great significance for improving the predictive diagnosis of TCM syndromes.

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## Competing interests

The authors declare no conflict of interest.

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# 急性缺血性脑卒中气虚血瘀证临床特征分析及辨证预测的研究

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**【摘要】目的** 探讨急性缺血性脑卒中（AIS）的临床特点及辨证预测方法，构建AIS气虚血瘀证的预测模型。**方法** 本研究采用回顾性病例对照设计，分析2013年1月1日至2022年12月31日期间在湖南中医药大学第一附属医院神经内科接受住院治疗的AIS患者。将符合气虚血瘀证诊断标准的AIS患者纳入病例组，将非气虚血瘀证AIS患者纳入对照组。收集并比较两组患者的人口学特征（年龄、性别）、临床参数[发病至入院时间、美国国立卫生研究院卒中量表（NIHSS）评分、血压]、既往病史、中医诊断特征（舌象、脉象）、神经系统症状体征、影像学表现[磁共振弥散加权成像（MRI-DWI）]以及生化指标。将单因素分析中具有统计学差异（$P < 0.05$）的指标纳入多因素逻辑回归分析，评估其对气虚血瘀证诊断的预测价值，并通过受试者工作特征（ROC）曲线分析构建预测模型。**结果** 研究共纳入1 035例AIS患者，其中病例组404例，对照组631例。与对照组相比，病例组患者年龄显著较大，发病至入院时间延长，舒张压较低，NIHSS评分较低（$P < 0.05$）。病例组患者高血压史发生率较低（$P < 0.05$）。在舌脉特征方面，病例组更常见舌淡、舌暗、苔白、细脉、涩脉和沉脉。在影像学检查中，病例组半卵圆中心梗死、脑萎缩和椎动脉狭窄比例更高（$P < 0.05$）。在生化指标方面，病例组升高的空腹血糖和糖化血红蛋白（HbA1c）比例更高，而白细胞计数升高、血红蛋白降低和高密度脂蛋白胆固醇（HDL-C）降低的比例更低（$P < 0.05$）。多因素逻辑回归分析确定气虚血瘀证的显著预测因素包括：细脉[比值比（OR）= 4.38]、涩脉（OR = 3.67）、浅感觉异常（OR = 1.86）、半卵圆中心梗死（OR = 1.57）、脑萎缩（OR = 1.55）、椎动脉狭窄（OR = 1.62）和HbA1c升高（OR = 3.52）。综合预测模型的ROC曲线分析显示曲线下面积（AUC）为0.878 [95%置信区间（CI）= 0.855 – 0.900]。**结论** 本研究发现气虚血瘀证是AIS的主要类型之一。细脉、涩脉、浅感觉异常、半卵圆中心梗死、脑萎缩、椎动脉狭窄、血糖升高、HbA1c升高、舌淡、舌暗、苔白是AIS伴QBS辨证的关键客观诊断指标。基于这些指标，建立了辨证预测模型，为临床诊断提供了更客观的依据，有助于临床实践中快速识别该证型以及减少误诊和漏诊。

**【关键词】**缺血性脑卒中；病例对照研究；气虚血瘀证；辨证预测模型；逻辑回归分析