

Predictive value of carotid atherosclerotic plaques assesment, in combination with glycosylated hemoglobin A1c and C-reactive protein levels, for disease progression in young patients with acute ischemic stroke.

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Keywords: Ischemic Stroke; Plaque, Atherosclerotic; Carotid Arteries; C-Reactive Protein; Hemoglobin HA1c.

Abstract. This study evaluated the predictive significance of combining carotid atherosclerotic plaques assesment with glycosylated hemoglobin A1c (HbA1c) and C-reactive protein (CRP) levels for disease progression in young acute ischemic stroke (AIS) patients. A total of 130 subjects were evenly recruited, comprising young patients with AIS admitted between January 2015 and March 2025 (case group) and healthy individuals undergoing physical examinations during the same period (control group). Comparisons were conducted on the incidence rate of carotid atherosclerotic plaques and serum HbA1c and CRP levels. The case group was categorized into mild-moderate and severe groups according to the National Institute of Health Stroke Scale (NIHSS) score. Significant differences were observed between the severe and mild-moderate groups in NIHSS scores, carotid atherosclerotic plaque incidence, and serum levels of HbA1c and CRP ($p < 0.05$). Increased serum HbA1c levels, elevated CRP levels, and presence of carotid atherosclerotic plaques functioned as risk factors for AIS progression in young patients (odds ratio > 1 , $p < 0.05$).

Serum HbA1c and CRP levels, along with the presence of carotid atherosclerotic plaques, showed a positive correlation with NIHSS scores ($r > 0$, $p < 0.05$). The areas under the ROC curves of serum HbA1c and CRP levels, carotid atherosclerotic plaques and their combination for assessing AIS progression in young patients were 0.810, 0.823, 0.781, and 0.905, respectively. Elevated HbA1c, CRP, and the presence of carotid plaques are associated with AIS severity in young patients. Combined detection improves predictive accuracy, suggesting clinical utility for risk stratification.

Valor predictivo de la detección de placas ateroscleróticas carotídeas, en combinación con los niveles de hemoglobina glicosilada A1c y proteína C reactiva, para la progresión de la enfermedad en pacientes jóvenes con accidente cerebrovascular isquémico agudo.

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Palabras clave: Accidente Cerebrovascular Isquémico; Placa Aterosclerótica; Arterias Carótidas; Proteína C-Reactiva; Hemoglobina HA1c.

Resumen. Este estudio evaluó la significancia predictiva de combinar placas ateroscleróticas carotídeas con niveles de hemoglobina glicosilada A1c (HbA1c) y proteína C reactiva (PCR) para la progresión de la enfermedad en pacientes jóvenes con accidente cerebrovascular isquémico agudo (AIS). Se reclutó de manera uniforme un total de 130 sujetos, que comprendían pacientes jóvenes con AIS ingresados entre enero de 2015 y marzo de 2025 (grupo de casos) e individuos sanos sometidos a exámenes físicos durante el mismo período (grupo de control). Se realizaron comparaciones en la tasa de incidencia de placas ateroscleróticas carotídeas y los niveles séricos de HbA1c y PCR. El grupo de casos se categorizó en grupos leve-moderado y grave según la puntuación de la Escala de Accidente Cerebrovascular del Instituto Nacional de Salud (NIHSS). Se observaron diferencias significativas entre los grupos grave y leve-moderado en las puntuaciones NIHSS, la incidencia de placa aterosclerótica carotídea y los niveles séricos de HbA1c y PCR ($p < 0,05$). El aumento de los niveles séricos de HbA1c, los niveles elevados de PCR y la presencia de placas ateroscleróticas carotídeas funcionaron como factores de riesgo para la progresión del AIS en pacientes jóvenes (odds ratio > 1 , $p < 0,05$). Los niveles séricos de HbA1c y PCR, junto con la presencia de placas ateroscleróticas carotídeas, mostraron una correlación positiva con las puntuaciones NIHSS ($r > 0$, $p < 0,05$). Las áreas bajo las curvas ROC de los niveles séricos de HbA1c y PCR, las placas ateroscleróticas carotídeas y su combinación para evaluar la progresión del AIS en pacientes jóvenes fueron 0,810, 0,823, 0,781 y 0,905, respectivamente. Los niveles elevados de HbA1c, PCR y presencia de placas carotídeas se asocian con la gravedad del AIS en pacientes jóvenes. La detección combinada mejora la precisión predictiva, lo que sugiere utilidad clínica para la estratificación del riesgo.

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INTRODUCTION

Acute ischemic stroke (AIS) is defined as a cerebrovascular disease attributed to blood supply disorders to brain tissues, which displays high mortality and disability rates. Besides, AIS exhibits a significantly increasing incidence rate in young people in recent years along with improved living standards and changed dietary patterns of people, which has become a major disease jeopardizing the health of young adults. Through extensive and in-depth research on the pathogenesis of AIS in young patients, it is discovered that atherosclerosis acts as the underlying cause. Hence, clarifying the predictors of atherosclerosis and implementing early interventions after accurately predicting the development and progression risk of AIS are of great clinical significance for reducing the incidence, mortality and disability rates of AIS in young adults. Atherosclerotic plaques are a product of atherosclerosis, and the presence of carotid atherosclerotic plaques gives rise to narrowed inner diameter of the carotid artery, leading to artery stenosis, which, when reaching a certain degree, can cause blood shortage to the brain. Once unstable plaques rupture, the dislodged plaques can result in thrombosis in distal intracranial vessels and eventually AIS^{1,2}. Abnormal glucose metabolism is able to not only induce damage to vascular endothelial cells, but also facilitate smooth muscle hyperplasia and inflammatory responses, thereby triggering atherosclerosis, which serves as a crucial cause of the development and progression of cerebrovascular diseases³. Glycosylated hemoglobin A1c (HbA1c), formed by the binding of hemoglobin to blood glucose in red blood cells, is a frequently measured biomarker in patients with abnormal glucose metabolism. Therefore, the glucose metabolism status in the body can be effectively mastered by measuring serum HbA1c level. C-reactive protein (CRP)-mediated inflammatory responses participate in the whole process of athero-

sclerosis development and progression, serving as a risk factor inducing cerebrovascular diseases⁴. Research has shown that atherosclerotic plaques and levels of serum HbA1c and CRP are correlated with the onset and advancement of AIS, potentially serving as reliable indicators of the condition.

Given this, in the present study, analyses were carried out on the distribution of carotid atherosclerotic plaques and expressions of HbA1c and CRP in young patients with AIS, as well as their correlations with and predictive value for the progression of AIS.

MATERIALS AND METHODS

Subjects

A total of 65 young AIS patients admitted to our hospital between January 2015 and March 2025 were consecutively enrolled as the case group, including 59 males and 6 females, aged 23-45 years (mean age, 39.11 ± 5.61 years). The body mass index (BMI) of the case group ranged from 21 to 26 kg/m², with a mean value of 23.46 ± 0.45 kg/m². During the same period, 65 age- and sex-matched healthy individuals undergoing routine physical examinations at our hospital were recruited as the control group, comprising 57 males and 8 females, aged 23-46 years (mean age, 38.86 ± 5.46 years), with a BMI ranging from 21 to 26 kg/m² (mean, 23.42 ± 0.48 kg/m²).

Inclusion and exclusion criteria

Inclusion criteria for the case group were: 1) patients diagnosed with AIS via cranial Computed Tomography (CT) images⁵, 2) ischemia duration of less than 72 hours, 3) informed consent obtained from family members, and 4) first episode of the disease.

The exclusion criteria were listed below: 1) patients with such diseases as brain tumors and brain traumas, 2) those with severe insufficiency of the heart, liver, kidneys or other organs, 3) those with a history of cardiogenic AIS or AIS induced by rheumatic

heart disease, atrial fibrillation, or other factors, 4) those with a history of administration of such drugs as propranolol, morphine and hydrochlorothiazide, or 5) those with a history of surgery or traumas or a history of nosocomial infection with obvious signs and clinical evidence in the past 1 week.

Blood sample collection

A 5 mL fasting venous blood sample was collected from the median cubital vein of participants in the health group during their physical examination and from the case group on the morning before treatment, then allowed to stand at room temperature for 30 minutes. After that, centrifugation was conducted (centrifugal radius: 10 cm, centrifugation speed: 2500 r/min, and centrifugation time: 10 min). The upper serum was transferred to a centrifuge tube and stored at -80°C for future analysis.

Measurement of serum HbA1c and CRP levels

The serum was removed from refrigeration, thawed at room temperature, and analyzed for HbA1c using a latex agglutination test (RB, USA) with a reference range of 3.8-5.8%, and for CRP levels using a double-antibody sandwich ELISA [Pointe Biotechnology (Nanjing) Co., Ltd.] with a reference range of 0-5 mg/L.

Detection of carotid atherosclerotic plaques

Color Doppler ultrasonic diagnostic apparatus (produced by Aloka, Japan) was employed to detect the distribution of carotid atherosclerotic plaques in both groups. During examination, the subjects were instructed should be instructed to lie in a relaxed position, with the shoulders elevated with the help of soft pads and the head turning to the opposite side to fully extend the neck. Next, a linear array probe was selected, with the frequency set at 3-11 MHz, and evenly applied with the couplant on the surface. Ultrasonic scans were performed on the common carot-

id artery, its bifurcation, and the carotid bulb (typically 4.0-6.0 cm above the bifurcation). The carotid intima-media thickness (IMT) was measured three times, and the results were averaged. Presence of carotid atherosclerotic plaques was considered in case of IMT ≥ 1.5 mm or localized thickening exceeding 50% of the surrounding intimal thickness.

Evaluation of AIS progression

The severity of AIS in the case group was evaluated using the NIHSS score (National Institutes of Health Stroke Scale) ⁶. Patients with a score of ≤ 15 were categorized as mild-moderate, while those scoring >15 were classified as severe.

Collection of general data

The collected data included gender, age, BMI, allergic constitution (yes/no), smoking history (≥ 5 years, >10 cigarettes/day), drinking history (≥ 5 years, >1 liang/day), hypertension (yes/no), NIHSS score, and laboratory indicators such as white blood cell count (WBC), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), and low-density lipoprotein (LDL).

Statistical analysis

Statistical analysis was completed with SPSS 23.0 software. Measurement data underwent normality testing. Normally distributed data were expressed as mean $\pm$ standard deviation ($\bar{X} \pm SD$) and analyzed using independent-samples t-tests for intergroup comparisons and paired-samples t-tests for intragroup comparisons. A logistic regression analysis was conducted to determine risk factors influencing AIS progression in young patients. Kendall's Tau-b and Pearson correlation analyses were used to examine the relationships between NIHSS scores and carotid atherosclerotic plaques, as well as serum HbA1c and CRP levels. ROC curves were utilized to evaluate the predictive values of carotid atherosclerotic plaques, serum HbA1c levels, serum CRP levels, and their combination for AIS progression, and the optimal cut-

off values were determined using the Youden index. AUCs >0.90 indicate high predictive value, 0.71-0.90 suggest fair value, 0.50-0.70 denote low value, and <0.50 reflect no predictive value. A p-value less than 0.05 was considered statistically significant.

RESULTS

Baseline and key characteristics

Baseline demographic, clinical, and laboratory characteristics of the case and control groups are presented in Table 1. No significant differences were observed between the two groups in age, sex, BMI, allergic constitution, smoking or drinking history, hypertension status, WBC count, or lipid profiles (TG, TC, HDL-C, and LDL-C) (all $p>0.05$). In contrast, serum HbA1c and CRP levels were significantly higher in the case group, and carotid atherosclerotic plaques were more frequently detected in the case group, whereas no plaques were observed in the control group (all $p<0.001$).

Relevant data in case and health groups

The case group exhibited significantly higher serum HbA1c levels ($6.05\pm1.84\%$ vs. $4.26\pm0.50\%$) and serum CRP levels (3.08 ± 2.98 mg/L vs. 0.55 ± 0.30 mg/L) compared with the healthy group (both $p<0.001$). In addition, carotid atherosclerotic plaques were detected in 19 patients (29.23%) in the case group, whereas no plaques were observed in the control group ($p<0.001$) (Table 2).

Disease progression in case group

Among the 65 patients in the case group, 50 patients (76.92%) were classified as having mild-moderate AIS, and 15 patients (23.08%) were classified as having severe AIS based on NIHSS scores.

Relevant data of patients in mild-moderate and severe groups

No significant differences were found between the mild-moderate and severe

groups in terms of sex distribution, age, BMI, allergic constitution, smoking history, drinking history, hypertension, WBC or serum lipid profiles, including TG, TC, HDL-C, and LDL-C (all $p>0.05$). In contrast, the severe group exhibited significantly higher NIHSS scores, as well as a higher prevalence of carotid atherosclerotic plaques and significantly elevated serum HbA1c and CRP levels, compared with the mild-moderate group ($p<0.001$) (Table 3).

Results of logistic regression analysis on AIS progression in young patients

Logistic regression analysis was carried out with AIS progression in young patients as the dependent variable (1=severe, 0=mild-moderate) and variables showing statistically significant differences in univariate analyses (except NIHSS score) as the independent variables. Serum HbA1c level (OR=17.583, 95% CI: 2.545-121.500, $p=0.004$), serum CRP level (OR=14.391, 95% CI: 2.852-72.625, $p=0.001$), and the presence of carotid atherosclerotic plaques (OR=12.667, 95% CI: 2.361-67.958, $p=0.003$) were independently associated with an increased risk of AIS progression in young patients (Table 4 and Fig. 1).

Results of correlation analyses

Correlation analyses demonstrated that NIHSS scores were positively correlated with serum HbA1c levels ($r=0.401$, $p=0.001$), serum CRP levels ($r=0.430$, $p<0.001$), and the presence of carotid atherosclerotic plaques ($r=0.522$, $p=0.004$) in young patients with AIS (Table 5).

Value of serum HbA1c levels, serum CRP levels, carotid atherosclerotic plaques and their combination for assessing AIS progression in young patients

ROC curves analyses were performed to evaluate the ability of serum HbA1c levels, serum CRP levels, presence of carotid atherosclerotic plaques, and their combination to discriminate severe AIS from mild-mod-

erate AIS (Fig. 2). As shown in Table 6, the AUCs were 0.810 for serum HbA1c levels, 0.823 for serum CRP levels, and 0.781 for carotid atherosclerotic plaques. The combined model demonstrated the highest discriminative performance, with an AUC of 0.905 ($p < 0.001$).

DISCUSSION

In the pathogenetic process of AIS, a range of extremely complex pathophysiological variations are triggered owing to ischemia and hypoxia at lesion sites, involving multiple factors.

Table 1. Baseline characteristics and key study parameters of the case and control groups.

Variable	Case group (n=65)	Control group (n=65)	Statistical test	p value
Age (years)	39.11±5.61	38.86±5.46	t=0.258	0.797
Gender, n (%)			$\chi^2=0.080$	0.777
Male	59 (90.77)	57 (87.69)		
Female	6 (9.23)	8 (12.31)		
Body mass index (kg/m ²)	23.46±0.45	23.42±0.48	t=0.490	0.625
Allergic constitution, n (%)			$\chi^2=0.301$	0.583
Yes	9 (13.85)	6 (9.23)		
No	56 (86.15)	59 (90.77)		
Smoking history, n (%)			$\chi^2=0.040$	0.841
Yes	18 (27.69)	16 (24.62)		
No	47 (72.31)	49 (75.38)		
Drinking history, n (%)			$\chi^2=0.037$	0.847
Yes	20 (30.77)	18 (27.69)		
No	45 (69.23)	47 (72.31)		
Hypertension, n (%)			$\chi^2=0.035$	0.851
Yes	22 (33.85)	20 (30.77)		
No	43 (66.15)	45 (69.23)		
WBC ($\times 10^9/L$)	6.78±1.52	6.62±1.47	t=0.610	0.543
Serum TG (mmol/L)	1.54±0.46	1.48±0.42	t=0.777	0.439
Serum TC (mmol/L)	4.62±0.71	4.58±0.69	t=0.326	0.745
Serum HDL-C (mmol/L)	1.12±0.24	1.15±0.22	t=-0.743	0.459
Serum LDL-C (mmol/L)	2.76±0.58	2.69±0.55	t=0.706	0.481
Serum HbA1c (%)	6.05±1.84	4.26±0.50	t=7.569	<0.001
Serum CRP (mg/L)	3.08±2.98	0.55±0.30	t=6.810	<0.001
Carotid atherosclerotic plaque, n (%)			Fisher's exact test	<0.001
Present	19 (29.23)	0 (0.00)		
Absent	46 (70.77)	65 (100.00)		

Data are presented as mean $\pm$ standard deviation for continuous variables and number (percentage) for categorical variables. WBC: white blood cell count; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; HbA1c: glycated hemoglobin A1c; CRP: C-reactive protein. Comparisons between the case and control groups were performed using the independent-samples t test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate.

Table 2. Relevant data in case and health groups.

Group	n	Serum HbA1c level (%)	Serum CRP level (mg/L)	Carotid atherosclerotic plaque, n (%)	
				Yes	No
Control	65	4.26±0.50	0.55±0.30	0 (0.00)	65 (100.00)
Case	65	6.05±1.84	3.08±2.98	19 (29.23)	46 (70.77)
<i>t</i>		7.569	6.810	22.252	
<i>p</i>		<0.001	<0.001	<0.001	

Data are presented as mean ± standard deviation or number (percentage). HbA1c: glycated hemoglobin A1c; CRP: C-reactive protein. Comparisons between the case and control groups were performed using the independent-samples *t* test for continuous variables and the chi-square test for categorical variables.

Table 3. Relevant indicators of patients in mild-moderate and severe groups

Indicator		Mild-moderate group (n=50)	Severe group (n=15)	Statistical value	<i>p</i>
Gender, n (%)	Male	28 (56.00)	6 (40.00)	1.184	0.277
	Female	22 (44.00)	9 (60.00)		
Allergic constitution, n (%)	Yes	3 (6.00)	0 (0.00)	0.073	0.787
	No	47 (94.00)	15 (100.00)		
Smoking history, n (%)	Yes	6 (12.00)	3 (20.00)	0.130	0.718
	No	44 (88.00)	12 (80.00)		
Drinking history, n (%)	Yes	8 (16.00)	2 (13.33)	0.025	0.875
	No	42 (84.00)	13 (86.67)		
Carotid atherosclerotic plaque, n (%)	Yes	6 (12.00)	13 (86.67)	27.592	<0.001
	No	44 (88.00)	2 (13.33)		
Hypertension, n (%)	Yes	22 (44.00)	4 (26.67)	1.444	0.229
	No	28 (56.00)	11 (73.33)		
Age (year)		39.11±5.61	40.13±5.23	0.627	0.533
BMI (kg/m ²)		23.46±0.44	23.43±0.43	0.233	0.817
WBC (×10 ⁹ /L)		3.95±0.28	3.89±0.27	0.734	0.466
Serum TG (nmol/L)		2.03±0.25	2.05±0.26	0.269	0.789
Serum TC (nmol/L)		6.85±0.16	6.88±0.18	0.619	0.538
Serum HDL-C (nmol/L)		0.84±0.17	0.82±0.16	0.405	0.687
Serum LDL-C (nmol/L)		4.87±0.13	4.85±0.15	0.504	0.616
Serum HbA1c (%)		5.50±0.55	7.88±0.62	14.276	<0.001
Serum CRP (mg/L)		2.84±0.25	3.88±0.36	12.697	<0.001
NIHSS score (points)		22.15±4.24	38.24±5.12	12.282	<0.001

Data are presented as mean ± standard deviation for continuous variables and number (percentage) for categorical variables. BMI: body mass index; WBC: white blood cell count; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; HbA1c: glycated hemoglobin A1c; CRP: C-reactive protein; NIHSS: National Institutes of Health Stroke Scale; AIS: acute ischemic stroke. Comparisons between mild-moderate and severe AIS groups were conducted using the independent-samples *t* test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate.

Table 4. Results of logistic regression analysis on acute ischemic stroke progression in young patients.

Variable	B	Standard error	Wals	p	Odds ratio	95% confidence interval
Serum HbA1c level	2.776	0.975	7.340	0.004	17.583	2.545-121.500
Serum CRP level	2.556	0.715	9.444	0.001	14.391	2.852-72.625
Presence of carotid atherosclerotic plaques	2.428	0.656	7.764	0.003	12.667	2.361-67.958

B represents the regression coefficient. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using multivariable logistic regression. Serum HbA1c and serum CRP levels were entered into the model as continuous variables (per 1% increase in HbA1c and per 1 mg/L increase in CRP). Presence of carotid atherosclerotic plaques was entered as a binary variable (present vs. absent). HbA1c: glycated hemoglobin; CRP: C- reactive protein.

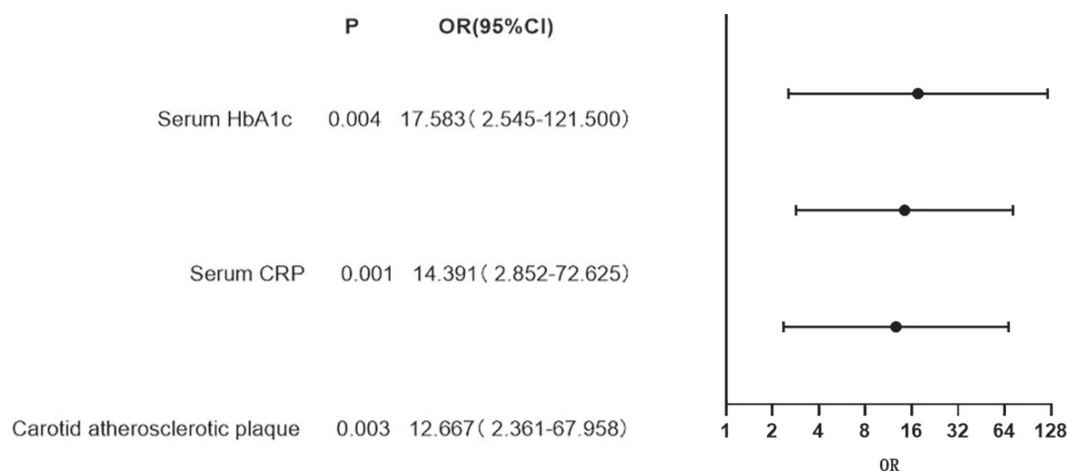


Fig. 1. Forest plot of clinical characteristics based on multivariate logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) are presented for each variable. Serum HbA1c was analyzed as a continuous variable per 1% increase, and serum CRP was analyzed per 1 mg/L increase. Presence of carotid atherosclerotic plaque was treated as a binary variable (present vs. absent). The horizontal lines represent 95% CIs, and the solid circles indicate the corresponding ORs. The x-axis is displayed on a logarithmic scale.

Table 5. Correlations of serum HbA1c and CRP levels and carotid atherosclerotic plaques with acute ischemic stroke progression in young patients.

Coefficient	Serum HbA1c level	Serum CRP level	Carotid atherosclerotic plaque
r	0.401	0.430	0.522
p	0.001	<0.001	0.004

Correlation coefficients (r) were calculated using Pearson or Kendall's Tau-b correlation analysis, as appropriate. Serum HbA1c (%) and serum CRP (mg/L) were analyzed as continuous variables. Presence of carotid atherosclerotic plaques was treated as a binary variable. p values <0.05 were considered statistically significant. HbA1c: glycated hemoglobin; CRP: C- reactive protein.

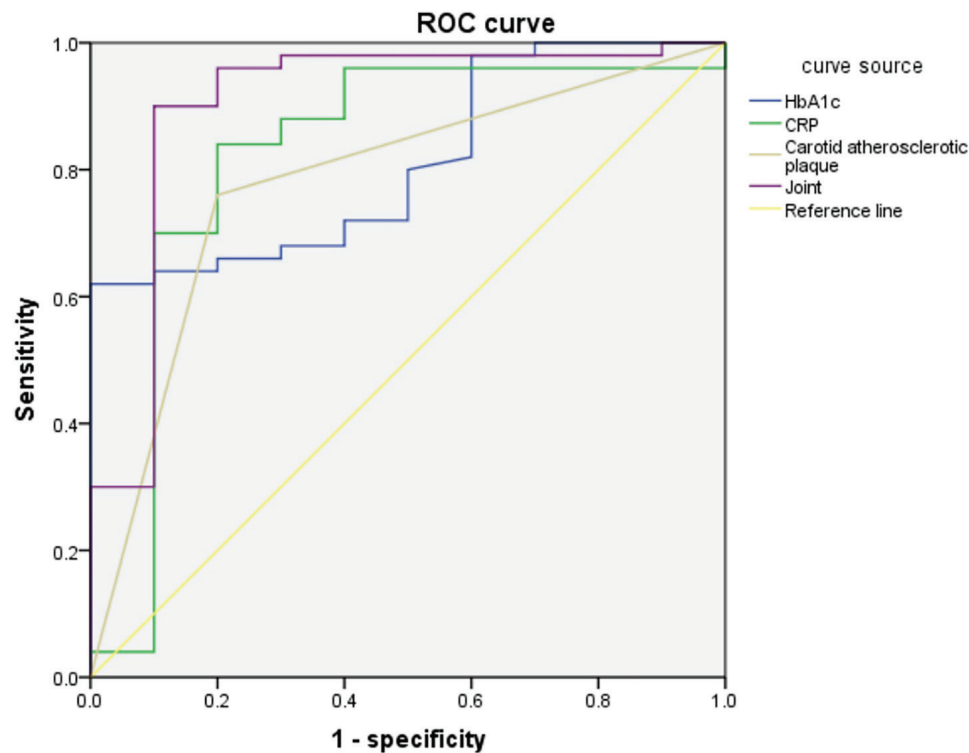


Fig. 2. ROC curves showing the predictive performance of serum HbA1c, serum CRP, carotid atherosclerotic plaque, and their combination for AIS progression in young patients. Serum HbA1c (%) and serum CRP (mg/L) were analyzed as continuous variables, and optimal cut-off values were determined using the Youden index. Presence of carotid atherosclerotic plaque was treated as a binary variable. The combined model demonstrated the highest discriminative performance, with an AUC of 0.905 ($p < 0.001$).

Table 6. Value of serum HbA1c levels, serum CRP levels, carotid atherosclerotic plaques and their combination for assessing acute ischemic stroke progression in young patients.

Item	Optimal cut-off value	Area under the curve	Standard error	p	95% confidence interval	Sensitivity	Specificity	Youden index
Serum HbA1c level	7.565 %	0.810	0.063	0.002	0.688-0.934	0.640	0.900	0.540
Serum CRP level	3.015 mg/L	0.823	0.091	0.001	0.644-0.998	0.840	0.800	0.640
Carotid atherosclerotic plaque	-	0.781	0.082	0.005	0.620-0.940	0.760	0.800	0.560
Combination	-	0.905	0.067	<0.001	0.772-0.999	0.900	0.900	0.800

Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive value of each parameter for AIS progression. Serum HbA1c (%) and serum CRP (mg/L) were analyzed as continuous variables, and the optimal cut-off values were determined using the Youden index. Presence of carotid atherosclerotic plaques was treated as a binary variable. The combined model was derived from multivariable logistic regression and represents the predicted probability of AIS progression. AIS: acute ischemic stroke; HbA1c: glycated hemoglobin; CRP: C- reactive protein.

A recent study reported that atherosclerotic changes in the brain and neck serve as the initiating factors for the development and progression of AIS⁷. Therefore, risk stratification of patients by identifying predictors directly associated with atherogenesis or susceptibility to atherosclerosis is conducive to more accurate implementation of interventions, and is of great clinical significance for hindering the progression of atherosclerosis to AIS.

In the present study, carotid atherosclerotic plaques were more frequently detected in the case group than in the control group, and their prevalence was significantly higher in patients with severe AIS than in those with mild-moderate AIS. Moreover, carotid atherosclerotic plaques were positively correlated with NIHSS scores and were independently associated with AIS progression in logistic regression analysis. These findings indicate that the presence of carotid atherosclerotic plaques is closely associated with disease severity and progression in young patients with AIS. Rather than establishing causality, these associations suggest that carotid atherosclerotic plaques may reflect a higher vascular risk burden in this population. It is speculated to be attributable to the following fact: Healthy arteries are elastic, but local lipid accumulation, fibrous tissue proliferation, and calcinosis of the arterial wall occur over time, starting from the intima of arteries, which gives rise to gradual hardening of arterial vessels and thus results in atherosclerosis^{8,9}. As atherosclerosis progresses, atherosclerotic plaques will form in blood vessels and then gradually enlarge over time. When the plaques erode and migrate to the small blood vessels in the brain, narrowing and blockage of the arterial lumen will be induced, affecting blood flow and normal nutrient delivery and thereby arousing various symptoms and diseases associated with AIS^{10,11}.

Serum HbA1c and CRP levels were significantly higher in the case group than in the control group and were elevated in pa-

tients with severe AIS compared with those with mild-moderate AIS. Both biomarkers showed positive correlations with NIHSS scores and were independently associated with AIS progression in multivariable logistic regression analysis.

These results suggest that higher serum HbA1c and CRP levels are associated with greater neurological impairment and increased risk of disease progression in young AIS patients. This is ascribed to the under-mentioned facts. Elevated HbA1c levels cause a leftward shift in the oxygen dissociation curve, reducing the dissociation rate of oxyhemoglobin and increasing the affinity of red blood cells for oxygen. This results in a significant decrease in 2,3-diphosphoglycerate levels within red blood cells. If uncorrected over time, these changes can disrupt blood and oxygen supply to the brain, potentially inducing AIS^{12,13}. Secondly, hypoxia-ischemia brain damage exacerbates progressively as HbA1c levels continuously increase, together with constant AIS progression in young patients. Thirdly, an elevation in HbA1c levels enhances endothelial activity, activates smooth muscle endothelin-A receptors, and stimulates the renin-angiotensin system, leading to vasoconstriction. Additionally, it enhances protein glycosylation and oxidation, with the resulting glycosylation end products stimulating LDL-C cytophagy and oxidation by lymphocytes and monocytes on the arterial wall. This process leads to foam cell formation, advancing atherosclerosis and contributing to the development and progression of AIS¹⁴⁻¹⁶. CRP is a highly sensitive inflammatory marker, typically present at very low levels in the blood, but it significantly increases during acute inflammation, trauma, or necrosis. If CRP levels increase, nuclear factor-kB is continuously activated, resulting in abnormalities in hemorheology and making the blood in the arterial blood vessels hyperviscous and hypercoagulable and flow slowly. Consequently, thrombosis is readily triggered, leading to the onset

and advancement of AIS¹⁷⁻¹⁹. Fifthly, CRP may stimulate nerve cells and glial cells to release various inflammatory factors like tumor necrosis factor- α and interleukin by activating autoreceptors and the complement system. These inflammatory factors further induce peripheral immune cells to enter the brain, exacerbating inflammatory responses, which not only aggravate brain tissue damage, but also affect the recovery of neurological function, and thus boosting the progression of AIS^{20,21}.

ROC curve analyses further demonstrated that serum HbA1c levels, serum CRP levels, and carotid atherosclerotic plaques each exhibited moderate discriminative ability for AIS progression, whereas their combined assessment achieved the highest predictive performance. This finding suggests that integrating metabolic, inflammatory, and vascular indicators may improve risk stratification for AIS progression in young patients. Physicians can also better understand AIS progression in young patients based on the above indicators, and thus develop more effective treatment plans. The present study clarified the correlations of carotid atherosclerotic plaques and varying serum HbA1c and CRP levels with AIS in young adults, which, however, had some shortcomings. For instance, the sample size was small, and subjects were all from the same hospital, which may result in some degree of selection bias. Besides, only univariate logistic regression analysis was conducted in data statistics, and no investigation was carried out on independent risk factors for the development and progression of AIS in young adults, which may have a certain impact on research results. Future research should increase sample sizes for multicenter prospective studies and utilize univariate and multivariate logistic regression analyses to examine the impact of independent risk factors on AIS development and progression.

In conclusion, elevated serum HbA1c and CRP levels and the presence of carotid

atherosclerotic plaques were associated with increased disease severity and progression in young patients with AIS. The combined evaluation of these indicators demonstrated improved predictive performance and may provide additional value for clinical risk assessment.

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Conflict of interest

The authors report no conflicts of interest.

Author's contributions

SJ and MF designed the study, HL and CZ conceived and supervised the study, JY, YQ and YL performed and analyzed the experiments, SJ and MF drafted the paper. All authors read and approved the final manuscript.

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