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Analysis of Non-Cardiogenic Young Minor Ischemic Stroke Patients' Risk Factors in Chinese Han Population

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Manuscript Preparation E
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Background: Young adults with minor ischemic stroke (MIS) often experience early onset and mild symptoms but face a high recurrence rate. Research into risk factors and etiology of young adult MIS in developing countries is limited. We investigated these aspects in young non-cardiogenic MIS patients from the Chinese Han population and identified risk factors for initial stroke and long-term poor prognosis.

Material/Methods: Data from MIS patients aged 18 to 50 years and a healthy control group at The First Affiliated Hospital of Anhui Medical University and The Third People's Hospital of Hefei City from January 2019 to July 2023 were analyzed. Risk factors and stroke etiology were compared. ROC curves assessed the predictive ability of original and modified Essen Stroke Risk Scores (ESRS).

Results: Among 155 patients, 25 (16.1%) experienced recurrence within a year. Patients with MIS differed significantly from the control group in sex, hypertension history, diabetes, dyslipidemia, smoking, higher biomarkers (SBP, TG, VLDL-C, hs-CRP, WBC, RBC, NEUT, HB), and lower HDL-C. Univariate analysis found dyslipidemia, moderate to severe vascular stenosis, resting heart rate, and modified ESRS scores linked to recurrence. Multivariate analysis identified dyslipidemia, vascular stenosis, and resting heart rate as key risk factors. Large artery atherosclerosis was the most common stroke etiology (59.2%). ROC curves revealed areas under the curve for ESRS, modified ESRS-1, and modified ESRS-2 as 0.550, 0.660, and 0.937, respectively.

Conclusions: MIS was associated with a high recurrence rate and specific risk factors. Improved ESRS effectively predicted stroke recurrence within 1 year, with large artery atherosclerosis being the predominant etiology.

Keywords: Risk • Stroke

Abbreviations: **MRI DWI** – magnetic resonance imaging diffusion weighted imaging; **NIHSS** – National Institute of Health Stroke Scale; **ESRS** – Essen Stroke Risk Score; **SBP** – systolic blood pressure; **DBP** – diastolic blood pressure; **RHR** – resting heart rate; **BS** – blood glucose; **TG** – triglyceride; **TC** – total cholesterol; **LDL-C** – low-density lipoprotein cholesterol; **VLDL-C** – very low-density lipoprotein cholesterol; **HDL-C** – high-density lipoprotein cholesterol; **UA** – uric acid; **hs-CRP** – hypersensitive C-reactive protein; **FIB** – fibrinogen; **D-D** – D-dimer; **WBC** – white blood cells; **RBC** – red blood cells; **PLT** – platelets; **NEUT** – neutrophils; **HB** – hemoglobin

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Introduction

Minor ischemic stroke (MIS) in young adults is a specific subtype of ischemic stroke, defined by a National Institutes of Health Stroke Scale (NIHSS) score of 3 or less. Young adult MIS occurs in patients between the ages of 18 and 50 years and accounts for approximately 10% to 15% of all cerebrovascular diseases [1,2]. The incidence of MIS in young adults has been rising steadily in recent years, likely due to the increasing prevalence of risk factors in younger populations. This condition poses significant societal challenges, as it often affects individuals during a critical period of professional development and personal responsibility. The onset of young adult MIS can severely affect patients' quality of life, diminish work capacity, and result in substantial social and economic burdens.

MIS in young adults often presents with symptoms of localized neurological deficits, speech difficulties, vision problems, gait disturbances, and occasionally headache. Although these symptoms can be mild, failure to address them promptly can lead to worsening conditions and long-term sequelae. Early medical intervention and treatment, including pharmacotherapy and rehabilitation, can significantly improve outcomes. Lifestyle modifications, such as controlling hypertension, diabetes, and hypercholesterolemia, as well as smoking cessation, are crucial in reducing the risk of future strokes [3-5].

Recent studies have focused on MIS in young adults, but differences in research standards have led to variability in reports regarding the rates of neurological deterioration and recurrence. In clinical treatment, we should pay more attention to the progression and deterioration of the patient's disease; therefore, it is particularly important to assess the risk of this population and take appropriate management measures [6,7]. The etiology and risk factors of MIS in young adults can vary depending on geographic location and ethnicity. In China, the Anhui region has a notably high incidence of acute minor ischemic stroke, yet there is limited research on the specific risk factors associated with the first onset and recurrence of young adult MIS in this region. Ischemic patients with mild clinical symptoms and few neurological deficits can often obtain better therapeutic effect after treatment. Therefore, if risk factors can be found and early prevention can reduce the risk of recurrence in this population, the prognosis of patients will be greatly improved. Therefore, this article mainly focuses on the risk factors and etiology of MIS in young adults in Anhui Han population, in order to reduce the incidence of MIS in this population.

Material and Methods

Data Collection

This study was approved by the Ethics Committee of the First Affiliated Hospital of Anhui Medical University and The Third People's Hospital of Hefei. The 221 young adult patients with acute MIS were hospitalized in the Department of Neurology of the hospital. MIS diagnosis met the standards of the Chinese Acute Minor Ischemic Stroke Diagnosis and Treatment Guide 2018 [8] and the definition of young stroke [4]. After rigorous screening by 2 experienced clinicians, patients with cardiogenic stroke, previous history of acute cerebral infarction (including symptomatic and asymptomatic stroke), severe liver and kidney insufficiency, and malignant tumors, and those not undergoing computed tomography angiography (CTA) and magnetic resonance imaging diffusion weighted imaging (MRI DWI) were excluded. Also, patients who were lost to follow-up and had incomplete data were excluded. In all, 145 patients were excluded. Seventy-six patients were followed up in outpatient visits or by telephone at 1 year. According to whether they had recurrent stroke or not, they were divided into a stroke recurrent group and a non-recurrent group. At the same time, 18 hospitalized patients with dizziness and headache were selected as the healthy control group, in whom no acute infarction was seen on the cranial MRI DWI (**Figure 1**).

Survey of Risk Factors

The double entry method was used to record related risk factors, including sex, age, history of hypertension, history of diabetes, history of dyslipidemia, history of smoking, history of alcohol consumption, moderate to severe vascular stenosis, National Institute of Health Stroke Scale (NIHSS) score, original Essen Stroke Risk Score (ESRS), SPAN-100 score at the time of admission, systolic blood pressure (SBP), diastolic blood pressure (DBP), resting heart rate (RHR) on admission, laboratory testing of fasting blood glucose (BS), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), high-density lipoprotein cholesterol (HDL-C), uric acid (UA), hypersensitive C-reactive protein (hs-CRP), fibrinogen (FIB), D-dimer (D-D), white blood cells (WBC), red blood cells (RBC), platelets (PLT), neutrophils (NEUT), and hemoglobin (HB). The above data were inputted and checked again by 2 other staff members.

Risk Score Scale

After admission, the NIHSS score, original ESRS, modified ESRS-1, modified ESRS-2, and SPAN-100 scores were evaluated. The original ESRS included age, hypertension, diabetes, previous myocardial infarction, other heart diseases (except for myocardial infarction and atrial fibrillation), peripheral artery

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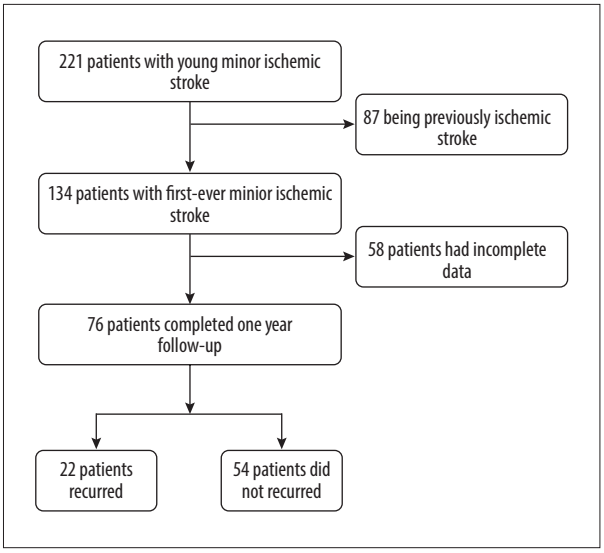

Figure 1. Flow chart of the participants included in this study.

disease, smoking, and previous history of transient ischemic attack (TIA) or ischemic stroke [9]. The modified ESRS-1 included age, hypertension, diabetes, previous myocardial infarction, other heart diseases (except for myocardial infarction and atrial fibrillation), peripheral artery disease, smoking, previous TIA or ischemic stroke history, LDL cholesterol, and intracranial and extracranial large vessel stenosis [10-12]. The modified ESRS-2 included hypertension over 15 years, diabetes over 10 years, large artery atherosclerosis cerebral infarction by TOAST criteria, and a history of TIA or ischemic stroke [13]. The SPAN-100 score was the sum of age and NIHSS score.

Judgment Criteria for Intracranial and Extracranial Artery Stenosis

Head and neck computed tomography angiography was performed immediately after admission. According to computed tomography angiography, young adult MIS patients were divided into 2 groups, with and without moderate to severe cerebral artery stenosis. The intracranial arteries included the intracranial C6-7 of the internal carotid artery, A1 segment of the anterior cerebral artery, M1 segment of the middle cerebral artery, P1 segment of posterior cerebral artery, and V4 segment of the vertebral artery and basilar artery. Extracranial arteries included the internal carotid artery extracranial C1-5 segment and vertebral artery extracranial V1-3 segment. The vascular stenosis rate was calculated according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria and the vascular stenosis rate, calculated as vascular stenosis rate = (the diameter of the normal vessel at the distal end of the stenosis - the narrowest diameter of the stenosis segment) / the shortest normal diameter of the distal end of the stenosis ×100%. A vessel stenosis rate ≤49% was mild stenosis, 50-69% was moderate stenosis, and 70-100% was severe stenosis or occlusion. If there were 2 or more arterial stenoses in the statistical process, the highest stenosis rate was taken [14].

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 17. The measurement data are expressed as $\bar{\chi}\pm s$, and the count data are expressed as a percentage or median (interquartile range). The *t* test was used to analyze quantitative data conforming to a normal distribution, the nonparametric test was used for quantitative data not conforming to the normal distribution, and the chi-square test was performed to compare qualitative data. Univariate and multivariate analyses were conducted using a logistic regression model to identify risk factors for first-time onset and stroke recurrence within 1 year in young adult patients with MIS. Multivariate analysis used a stepwise regression approach. The results are presented as odds ratios (OR) with 95% CI. The ratio of the healthy control group and MIS patients was approximately 1: 4, to meet the minimum sample size in statistics. The level of significance was set at 0.05.

Results

Baseline Data of MIS Patients and Healthy Control Group

Among 221 young adult patients with MIS, 65 were lost to follow-up, 25 had recurrent stroke, and 130 did not have recurrent stroke. In addition, 87 of the 221 patients had previous ischemic stroke, and 58 patients had incomplete data. In total, 76 patients completed follow-up. According to the recurrence of stroke after 1 year, 76 patients were divided into a recurrent group (22 patients) and a non-recurrent group (54 patients). Among them, there were 57 men, 19 women, 37 cases of hypertension, 17 cases of diabetes, 37 cases of dyslipidemia, 12 cases of hyperuricemia, 34 cases of smoking, 25 cases of alcohol consumption, and 19 cases of moderate to severe vascular stenosis. TOAST classification suggested there were 45 cases of large atherosclerosis, 28 cases of small artery occlusion, 1 case of unknown cause, and 2 cases of other causes. In addition, the control group included 8 men, 10 women, 3 cases of hypertension, 0 cases of diabetes, 3 cases of dyslipidemia, 2 cases of hyperuricemia, 3 cases of smoking, 2 cases of drinking, and 1 case of moderate to severe vascular stenosis.

Statistical Analysis of Different Risk Factors Between MIS and Control Groups

As shown in **Table 1**, there were no significant differences in age, hyperuricemia, history of alcohol consumption, moderate to severe vascular stenosis, DBP, BS, TC, LDL-C, UA, FIB, DD, PLT, and RHR (all $P>0.05$). Compared with the control group, sex,

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Table 1. Analysis of risk factors for the first-ever young MIS patients.

Risk factors	YMIS (n=76)	HC (n=18)	Test value	P value
Male gender, n (%)	57 (75.00)	8 (44.44)	6.369[b]	0.012
Age, years, M (P25, P75)	45 (40.00, 48.00)	46 (38.75, 48.25)	-0.135[c]	0.893
Hypertension, n (%)	37 (48.68)	3 (16.67)	6.103[b]	0.013
Diabetes mellitus, n (%)	17 (22.37)	0 (0.00)	4.915[b]	0.027
Dyslipidemia, n (%)	33 (43.42)	3 (16.67)	4.408[b]	0.036
Hyperuricemia, n (%)	12 (15.79)	2 (11.11)	0.251[b]	0.616
Smoking, n (%)	34 (44.74)	3 (16.67)	4.804[b]	0.028
Alcohol consumption, n (%)	25 (32.89)	2 (11.11)	3.271[b]	0.071
Moderate to severe vascular stenosis, n (%)	19 (25.00)	1 (5.56)	3.285[b]	0.070
SBP [mmHg, $\bar{\chi}$±s]	136.84±22.15	124.17±15.76	2.290[a]	0.024
DBP [mmHg, $\bar{\chi}$±s]	83.76±16.30	80.50±12.19	0.797[a]	0.428
BS [mmol/L, M(P25, P75)]	5.49 (4.87, 7.71)	5.27 (5.06,5.50)	-1.432[c]	0.152
TG [mmol/L, M(P25, P75)]	1.46 (1.22, 2.15)	0.94 (0.71, 1.37)	-3.123[c]	0.002
TC [mmol/L, $\bar{\chi}$±s]	3.86±1.19	3.70 (1.35)	0.500[a]	0.619
LDL-C [mmol/L, M(P25, P75)]	2.18 (1.65, 2.78)	2.00 (1.37, 2.85)	-0.668[c]	0.504
VLDL-C [mmol/L ,M(P25 ,P75)]	0.55 (0.43, 0.79)	0.35 (0.24, 0.51)	-2.970[c]	0.003
HDL-C [mmol/L, $\bar{\chi}$±s]	0.97±0.23	1.09±0.23	-2.045[a]	0.044
UA (umol/L, $\bar{\chi}$±s]	313.18±95.87	298.06±96.94	0.601[a]	0.549
hs-CRP [mg/L, M(P25, P75)]	0.58 (0.36, 2.64)	0.37 (0.21, 1.58)	-2.309[c]	0.021
FIB [g/L, $\bar{\chi}$±s]	3.06±0.85	3.16±1.22	-0.427[a]	0.670
D-D [ug/ML, M(P25, P75)]	0.22 (0.16, 0.51)	0.18 (0.14, 0.44)	-1.438[c]	0.150
WBC [$\times 10^9$/L, $\bar{\chi}$±s]	7.82±2.28	6.17±1.77	2.865[a]	0.005
RBC [$\times 10^{12}$/L, $\bar{\chi}$±s]	4.65±0.47	4.40±0.54	2.015[a]	0.047
PLT [$\times 10^9$/L, $\bar{\chi}$±s]	225.25±65.94	248.61±81.97	-1.288[a]	0.210
NEUT [$\times 10^9$/L, M(P25, P75)]	4.76 (3.63, 6.42)	3.65 (2.77, 4.70)	-3.017[c]	0.003
HB[g/l, $\bar{\chi}$±s]	138.57±17.06	127.11±17.64	2.545[a]	0.013
RHR[n/min, $\bar{\chi}$±s]	73.86±11.46	75.94±12.59	-0.682[a]	0.497

1 mmHg=0.133 kPa; [a] is the t value of t test, [b] is the χ^2 value of χ^2 test, and [c] is the Z value of Mann-Whitney U test.

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Table 2. Univariate Logistic regression analysis for risk factors of recurrent ischemic stroke at 1 year.

Factors	OR	95% CI	P value
Male gender	0.840	0.261-2.703	0.770
Age	0.980	0.911-1.055	0.980
Hypertension	0.929	0.344-2.503	0.884
Diabetes mellitus	0.487	0.157-1.507	0.212
Dyslipidemia	5.220	1.559-17.475	0.007
Hyperuricemia	2.273	0.455-11.342	0.317
Smoking	1.625	0.586-4.504	0.351
Alcohol consumption	2.000	0.640-6.253	0.233
Moderate to severe vascular stenosis	0.173	0.055-0.541	0.003
SBP	1.017	0.993-1.043	0.172
DBP	1.015	0.983-1.048	0.354
BS	1.017	0.838-1.235	0.863
TG	1.924	0.971-3.812	0.061
TC	1.505	0.910-2.487	0.111
LDL-C	1.167	0.663-2.053	0.592
VLDL-C	3.583	0.747-17.185	0.111
HDL-C	2.003	0.220-18.243	0.538
UA	1.005	0.999-1.011	0.105
hs-CRP	1.114	0.994-1.249	0.063
FIB	0.685	0.383-1.225	0.202
D-D	0.446	0.188-1.060	0.068
WBC	1.028	0.824-1.281	0.809
RBC	2.351	0.778-7.099	0.130
PLT	1.003	0.996-1.011	0.404
NEUT	0.981	0.795-1.211	0.857
HB	1.015	0.986-1.045	0.372
RHR	0.928	0.883-0.976	0.003
NIHSS score	0.951	0.868-1.041	0.276
ESRS	0.844	0.497-1.435	0.531
Modified ESRS-one	0.770	0.599-0.989	0.040
Modified ESRS-two	0.441	0.231-0.842	0.013
SPAN-100 score	0.965	0.909-1.024	0.244

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Table 3. Multivariate Logistic regression analysis of recurrent ischemic stroke at 1 year.

Factors	OR	95% CI	P value
Dyslipidemia	6.403	1.487-27.572	0.013
Moderate to severe vascular stenosis	0.171	0.037-0.802	0.025
RHR	0.919	0.863-0.979	0.009
Modified ESRS-one	1.018	0.718-1.710	0.643
Modified ESRS-two	0.465	0.163-1.321	0.151

history of hypertension, diabetes, dyslipidemia, and smoking, and SBP, TG, VLDL-C, hs-CRP, WBC, RBC, NEUT, and HB were significantly higher in the MIS group, and HDL-C was significantly lower (all $P<0.05$).

Univariate Logistic Regression Analysis of the Risk Factors of the Recurrent Group and the Non-Recurrent Group After 1 Year

As shown in **Table 2**, age, history of high blood pressure, history of diabetes, hyperuricemia, history of smoking, history of drinking, SBP, DBP, BS, TG, TC, LDL-C, VLDL-C, HDL-C, UA, hs-CRP, FIB, DD, WBC, RBC, PLT, NEUT, HB, admission NIHSS score, ESRS score, and SPAN-100 score were not statistically significant between the recurrent and non-recurrent groups (all $P>0.05$). Compared with the non-recurrent group, history of dyslipidemia, moderate to severe vascular stenosis, RHR, modified ESRS-1 score, and modified ESRS-2 score were significantly higher in the recurring group (all $P<0.05$).

Multivariate Logistic Regression Analysis of the Risk Factors of the Recurrent Group and the Non-Recurrent Group After 1 Year

As shown in **Table 3**, compared with the non-recurrent group, the recurrent group had significantly higher dyslipidemia, moderate to severe vascular stenosis, and RHR. The differences were statistically significant (OR=6.796, 95%CI: 1.600-28.873, $P=0.009$; OR=0.953, 95%CI: 0.035-0.679, $P=0.014$; OR=0.929, 95%CI: 0.878-0.984, $P=0.012$, respectively).

Receiver Operating Characteristic Curve Analyses

To evaluate the prediction accuracy of the modified ESRS compared with the original, we calculated total scores for each patient and generated receiver operating characteristic (ROC) curves (**Figure 2**). The modified ESRS showed better performance in predicting recurrent ischemic stroke. The original ESRS had an area under the ROC curve (AUC) of 0.550 ($P>0.05$, 95% CI: 0.399-0.700). In contrast, the modified ESRS-1 had an AUC of 0.660 ($P<0.05$, 95% CI: 0.526-0.794), and the modified ESRS-2 had an AUC of 0.937 ($P<0.001$, 95% CI: 0.000-1.000). The cut-off points were 6 for the ESRS-1 and 2 for the ESRS-2. Sensitivity was 54.5% for the ESRS-1 and 90.9% for the ESRS-2, while specificity was 75.9% for the ESRS-1 and 96.3% for the ESRS-2. The highest Youden index was 30.4 for the ESRS-1 and 87.2 for the ESRS-2.

Discussion

Studies have shown that male patients can be more likely to acquire ischemic stroke, due to high social pressure and unhealthy habits, including eating habits, smoking, staying up late, and obesity [15]. In addition, because young women have relatively more estrogen than older women, there is a protective effect on cerebral blood vessels, which may explain the lower incidence of ischemic stroke in women [16]. We found that male sex and smoking were risk factors for the first onset of young adult MIS. Because the two have a synergistic and additive effect, it is recommended that young male patients actively quit smoking. Scholars such as Perry et al and Ton et al [15,17] found that the most common risk factors for young adult MIS were hypertension, dyslipidemia, smoking, and drinking. In addition to the above reported risk factors, we found that diabetes history, elevated SBP, TG, VLDL-C, hs-CRP, WBC, RBC, NEUT, and HB, and low HDL-C are risk factors for its onset.

Hypertension not only caused atherosclerosis and vascular stenosis or occlusion, but also damaged the blood-brain barrier and eventually led to ischemia, with SBP, especially, having a greater impact on the brain barrier [18,19]. Therefore, young adult patients with MIS must pay attention to the management of blood pressure, especially to control SBP within the normal range. It is well known that chronic hyperglycemia can lead to endothelial dysfunction, inflammation, and accelerated atherosclerosis, resulting in large vessel stenosis or occlusion [20-22]. Long-term hyperglycemia could also accelerate the aging process of red blood cells and cause nerve cell permeability and edema, while increasing the incidence of irreversible neuronal damage, and ultimately promote its accumulation

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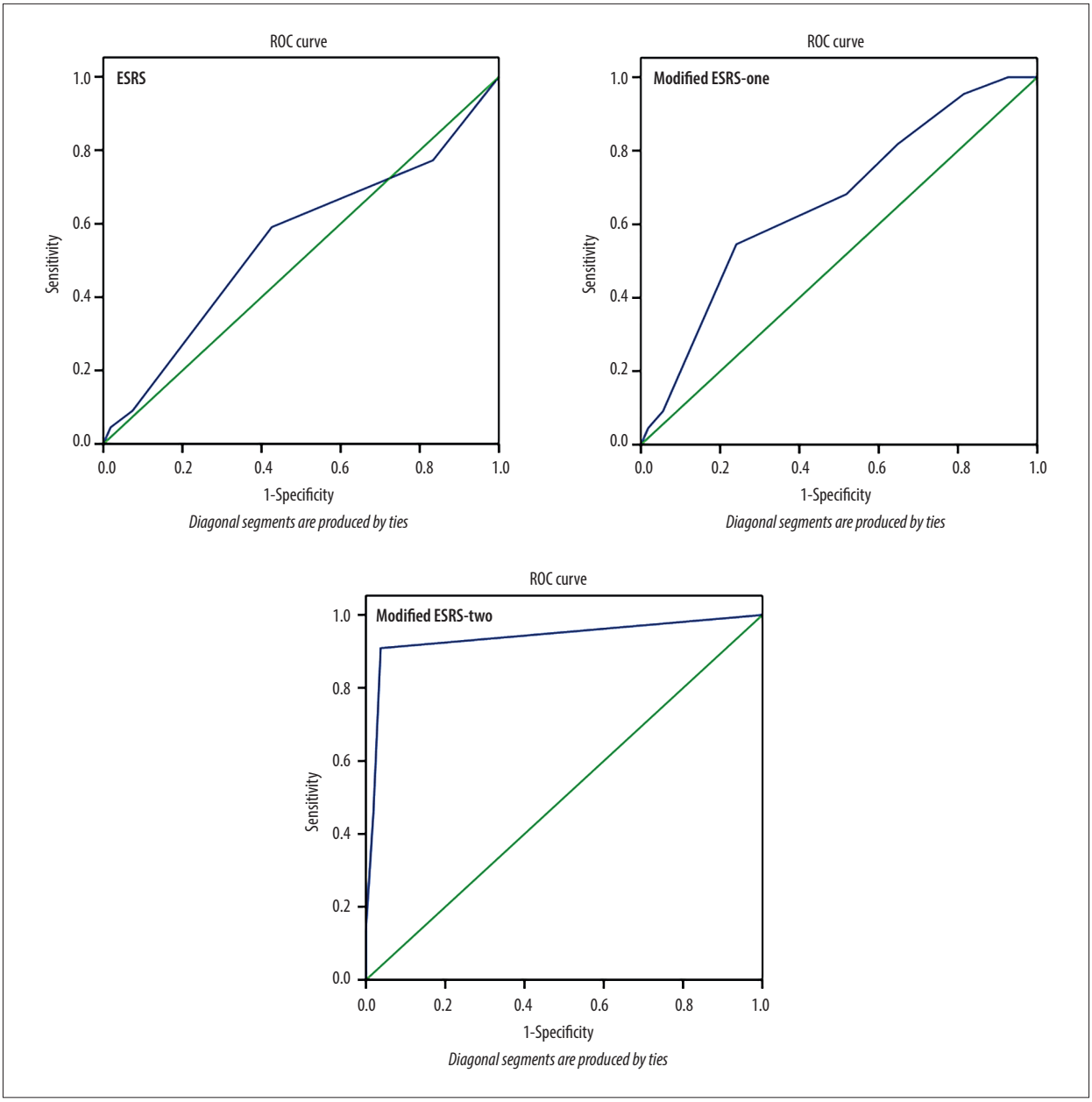

Figure 2. ROC curve analyses of the original Essen Stroke Risk Scores and modified Essen Stroke Risk Scores.

in the infarct area [23,24]. This shows that diabetes is a key predictor of the onset of a first stroke. Peters et al found that the influence of TC on the occurrence of acute ischemic stroke might be weaker than that of TG [25]. This study found that the levels of TG and VLDL of young adults with MIS were significantly higher than those of the healthy control group, indicating that TG and VLDL might have a more significant impact on the pathogenesis of young adult MIS. Studies had shown that HDL-C can not only resist LDL-C oxidation and reduce endothelial cell damage, but can also promote endothelial cells to produce nitric oxide, thereby exerting anti-apoptosis and anti-inflammatory actions and inhibiting vascular smooth muscle proliferation [26]. Therefore, loss of HDL-C was found to be a risk factor for young adult MIS, which is consistent with the results of this article. Studies have shown that hs-CRP is an independent risk factor for atherosclerotic plaque formation and can directly reflect the development of carotid atherosclerosis [27]. Elevated WBC and NEUT indicated that there was an inflammatory response in the body and rapid activation in the body's immune system, which might damage the vascular endothelium, cause platelet aggregation, and ultimately promote the formation of infarcts and even cause cognitive impairment [28-30]. In the present study, we found that hs-CRP, WBC, and NEUT were risk factors for the onset of young adult

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MIS, suggesting that the inflammatory mechanism might play an important role in its first onset, which is worthy of further exploration. Another study [31] demonstrated that the increase in the number of RBC could be related to the occurrence and development of carotid atherosclerosis. The connection between HB concentration and ischemic stroke continues to be a subject of debate; however, many studies have concluded that HB has a U-shaped relationship with ischemic stroke, that is, too high or too low HB increases the risk of stroke [32-34]. In the present study, we found that increases in RBC and HB were risk factors for young adult MIS, suggesting that the increase in RBC and HB can promote the occurrence of infarction by changing hemodynamics; however, this needs to be verified in additional high-quality studies.

We did not find that drinking was a high-risk factor for young adult MIS in the Han population in Anhui. We found that the above-mentioned study included people from the northeast region; therefore, the difference can be related to regional factors. A retrospective study report in Taiwan pointed out that the main subtype of ischemic stroke was arteriolar occlusive disease (37.7%), followed by arteriosclerosis (27.7%) [35]. In Jordan (36%) and Japan (54.1%) [36], arteriole occlusive disease was also the most common stroke subtype. In addition, the latest study conducted by Zafar et al showed that small artery occlusive disease was the most common etiological subtype of ischemic stroke (32.1%), followed by large atherosclerosis (14.6%) [36]. However, we found that the proportion of large atherosclerosis (59.2%) in young adult patients with MIS was higher than that of small artery occlusion (36.8%), which was similar to the results of Harris et al [37]. On one hand, this etiological difference could be caused by a different risk factor distribution, regional distribution, or ethnic groups. On the other hand, the difference might be due to asymptomatic young patients with MIS having acute small artery infarction or deep perforating infarction. Because they had no obvious clinical symptoms or only mild sensory disturbances, such as acute punctate thalamus or brainstem infarction, they had not been hospitalized. Reduced hospitalization rates would lead to the proportional decrease of small artery occlusion-type cerebral infarction. However, additional larger sample studies are needed to confirm.

The study found that dyslipidemia, moderate to severe vascular stenosis, RHR, modified ESRS-1 scores, and modified ESRS-2 scores were significantly increased in the recurrent group. Dyslipidemia was not only a risk factor for the first onset of young adult MIS, but also a key predictor of its recurrence. This suggested that dyslipidemia might be more important for young adult MIS; therefore, it must be actively controlled. There were many mechanisms for the poor prognosis of YMIS, including vascular changes caused by atherosclerosis, hemodynamic changes (hypoperfusion mechanisms), and vascular inflammation mechanisms. However, the results of this study showed that moderate to severe vascular stenosis occupied an important position in the long-term recurrence of young adult MIS, which suggests that MIS recurrence could be related to the ischemic penumbra of a persistent hypoperfusion state. Finally, moderate to severe cerebral arteries led to the inability to establish effective collateral circulation and caused continuous ischemia and hypoxia, which ultimately resulted in the occurrence of adverse outcomes in young adult patients with MIS [38]. Therefore, we recommended routinely screening the degree of cerebrovascular stenosis of young adult patients with MIS. After strict evaluation, endovascular stent placement or carotid endarterectomy can be used for patients with surgical indications, to reduce the recurrence rate of stroke. The high RHR of patients in the MIS recurrent group can lead to a decrease in the effective ejection fraction of the heart, which can cause insufficient blood supply to the brain to cause an ischemic stroke [39]. Combining the results of univariate factor analysis and ROC analysis, we concluded that the ESRS had no predictive effect on the recurrence of young ischemic stroke, the modified ESRS-1 had limited predictive effect, and the modified ESRS-2 had a better predictive effect. In addition to the many risk factors in the original ESRS, the modified ESRS-1 also added a vascular stenosis scoring item. This result was similar to the independent predictive effect of moderate to severe vascular stenosis on the recurrence of MIS in the multivariate regression analysis. Compared with the ESRS, the modified ESRS-2 changed a simple history of hypertension to a history of more than 15 years, changed a history of diabetes to one of over 10 years, and added the type of aortic atherosclerosis. It can be seen that simply including the presence of risk factors, such as hypertension and diabetes history, into the scale for scoring was limited in predicting stroke recurrence. Therefore, we speculated that hypertension and diabetes must reach a certain critical point or inflection point before they have long-term cumulative effects on MIS recurrence. This is also a direction worthy of further exploration.

There are some limitations to this study. First, we did not discuss whether interventions targeting specific risk factors, such as dyslipidemia, are effective in reducing the incidence of young adult MIS, a limitation that suggests future studies should focus on assessing the effect of such interventions. Second, the relatively small sample size, especially the number of healthy control participants, limited the statistical power and generalizability of the findings. The sample size should be increased in the future, to obtain more robust data. In addition, the follow-up period of only 1 year may not have been sufficient to capture the long-term recurrence risk and disease progression of young adult MIS, and an extended follow-up period can help to more fully understand the long-term prognosis of these patients with MIS. The research object of this study was limited to the Chinese Han population in a specific region, which is

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not be fully representative of other ethnic groups or regions; therefore, the universality of the research results is limited. Finally, some risk factor data rely on self-reporting, which can introduce recall bias and thus affect the accuracy of the results. Future studies should consider using more objective measures to reduce potential bias. Future research plans include expanding the sample size to include more diverse populations and improve the generalizability of the findings. We also intend to extend the follow-up to better understand the long-term outcomes and recurrences of young adult MIS. In addition, we plan to investigate the effectiveness of targeted interventions, such as lipid management and blood pressure control, in reducing the incidence and recurrence of young adult MIS. Finally, we will adopt a more objective and standardized approach to collecting risk factor data, to minimize bias and improve the reliability of our findings.

Conclusions

In summary, the mechanisms of atherosclerosis and inflammation may play an important role in the first onset of young adult MIS, and the mechanisms of hypoperfusion might play a key role in stroke recurrence. We need to actively intervene in traditional risk factors and to pay attention to new risk factors. Also, we can use various modified ESRS scales to predict the probability of stroke recurrence after 1 year, so as to reduce the recurrence rate of stroke as much as possible and avoid serious disadvantages, such as disability.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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