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# Association of diabetes and white blood cell count with stroke in patients with carotid artery dissection

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## Abstract

**Background** Carotid artery dissection is an important cause of stroke. However, the predictors of ischemic stroke in patients with carotid artery dissection are controversial. The study aimed to analyze the predictors of ischemic stroke in patients with carotid artery dissection through retrospective medical records.

**Methods** Data of discharged patients diagnosed with carotid artery dissection during 2019–2023 were retrospectively collected. Based on the occurrence of ischemic stroke, the patients were divided into the ischemic stroke or non-ischemic stroke groups. Based on the results of univariate analyses, variables with an associated  $P$  value  $< 0.05$  were introduced into the multivariable logistic regression analysis.

**Results** A total of 165 patients were included in the study, with an average age of 55.00 (48.00, 66.00) years, including 86 patients with internal carotid artery dissection and 79 patients with vertebral artery dissection. Ischemic stroke occurred in 69 patients with carotid artery dissection. Multivariate logistic regression analysis indicated that diabetes (odds ratio [OR]: 3.144, 95% confidence interval [CI]: 1.552–6.508,  $P < 0.002$ ) and high white blood cells count (OR: 1.157, 95% CI: 1.02–1.327,  $P = 0.028$ ) were related to the incidence of ischemic stroke in patients with carotid artery dissection.

**Conclusion** Ischemic stroke caused by carotid artery dissection causes severe damage to the nervous system. This study found that diabetes and high white blood cells count were associated with the incidence of ischemic stroke in patients with carotid artery dissection. Therefore, monitoring and controlling blood glucose levels and infections is essential in patients with carotid artery dissection to reduce the incidence of stroke.

**Keywords** Carotid artery dissection, Ischemic stroke, Internal carotid artery dissection, Predictive factors, Vertebral artery dissection

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## Background

Cervical artery dissection (CAD) refers to intramural hematoma caused by tearing of the inner lining of the carotid artery, resulting in arterial stenosis, occlusion, or aneurysm-like changes. CAD includes internal carotid artery dissection (ICAD) and Vertebral artery dissection (VAD) [1, 2]. The incidence of CAD was observed to be (2.6–3.0)/100,000 person-years, among which the incidences of ICAD and VAD were (2.5–3.0)/100,000 and (1.0–1.5)/100,000 person-years, respectively. Additionally, roughly 13–16% of patients have multiple arterial dissection [3].

The clinical manifestations of CAD are diverse, with local symptoms primarily involving cranial nerve function. Secondary cerebrovascular disease can lead to severe neurological impairment. Ischemic stroke is the most common type of cerebrovascular disease in patients with CAD [3]. Nearly 67% of these patients reportedly have cerebral ischemia symptoms, most of which are ischemic stroke [4]. There is no consensus on the risk factors of ischemic stroke in patients with CAD, and some studies on CAD have small sample sizes [5]. This study analyzes the risk factors of ischemic stroke in patients with CAD in China via retrospective multicenter investigation and provides evidence for corresponding measures to reduce the incidence of ischemic stroke.

## Methods

### Study population

We included patients diagnosed with CAD who were hospitalized in Zhengzhou People's Hospital and the Second People's Hospital of Chengdu and the Second Affiliated Hospital of Chongqing Medical University from 2019 to 2023. The diagnosis was reviewed by two experienced neurologists and radiologists. We included patients with confirmed and suspected dissection and excluded those with atherosclerosis. Based on the occurrence of ischemic stroke, patients were divided into the ischemic stroke or non-ischemic stroke groups.

### Imaging diagnostic criteria for CAD [6–8]

Confirmed dissection (meets one of the following three criteria):

- A. Digital subtraction angiography (DSA) shows one of the intimal flaps or double lumen signs.
- B. Magnetic resonance angiography (MRA)/magnetic resonance imaging (MRI) shows one of the intimal flaps or double lumen signs, and experienced physicians can see clear intimal flaps and double lumen signs on ultrasound or CTA.
- C. Imaging shows any of D, E, and F, and clear changes can be seen during follow-up; other diagnoses are excluded.

Suspected dissection (meets one of the following three criteria):

- D. DSA shows nonspecific signs suggestive of dissection, including beading and conical occlusion, but no Class A signs.
- E. The beaded and linear signs and conical blocks can be seen on MRA.
- F. T1WI showed an enhanced signal indicating intramural hematoma.

**Imaging diagnostic criteria for atherosclerosis [8]** (one of the following three criteria needs to be met):

- (1) Carotid plaque as shown by color Doppler ultrasonography of the carotid artery.
- (2) Supra-aortic MRA, CTA, or DSA showing >30% stenosis at the common carotid artery bifurcation or at the beginning of the internal carotid artery.
- (3) Irregular or unevenly thick arterial wall.

**Diagnostic criteria for ischemic stroke associated with CAD [6–8]**

- (1) Acute onset.
- (2) Focal neurological deficit (weakness or numbness of one face side or limb, speech disorder, etc.), a few are comprehensive neurological deficit.
- (3) The duration of symptoms and signs is not limited (when imaging shows a responsible lesion) or it lasts for more than 24 h (when a responsible lesion is absent).
- (4) Excluded non-vascular causes.
- (5) Head CT/MRI dismissed cerebral hemorrhage.
- (6) Ischemic stroke is associated with CAD.

### Data collection

The detailed demographic and clinical parameters of the patients were recorded upon admission. The parameters included sex and age; disease-related information; smoking history (current or quit smoking ≤6 months prior); alcohol consumption (intake >80 g/day, or quit drinking ≤6 months prior); family history of dissection (a history of dissection in the immediate family); history of ischemic stroke; statin use history (current or quit ≤6 months prior); body mass index (BMI = weight [kg] ÷ height<sup>2</sup> [m]); diabetes status (receiving medicine for diabetes mellitus, fasting blood glucose ≥7.0 mmol/L, 2-hour postprandial blood glucose or random blood glucose ≥11.1 mmol/L); hypertension status (receiving antihypertensive treatment, or blood pressure ≥140/90 mmHg on repeated measurements); Laboratory parameters included alanine aminotransferase, aspartate aminotransferase, serum albumin, fasting blood glucose, hemoglobin Alc, triglyceride, cholesterol, high density lipoprotein (HDL), low density lipoprotein cholesterol (LDL-C), glucose-triglycerides, and homocysteine

levels; and white blood cell and neutrophil counts. Imaging parameters included dissection location (including ICAD and VAD).

### Statistical method

This study used the R 4.1.1 software (R Foundation for Statistical Computing, Vienna, Austria) for data processing and statistical analysis. The measurement data were represented by mean and standard deviation if normal distribution was followed, and median and quarterback distance if not. Counting data were represented by frequency and component ratio. The independent sample *t*-test and one-way ANOVA were used to compare

**Table 1** General patient information

Variable	Level	Overall
n		165
Stroke (%)	No	96 (58.2)
	Yes	69 (41.8)
Sex (%)	Male	123 (74.5)
	Female	42 (25.5)
Age (median [IQR]) years		55.00 [48.00–66.00]
Smoking (%)	No	94 (57.0)
	Yes	71 (43.0)
Drinking (%)	No	108 (65.5)
	Yes	57 (34.5)
Family history of carotid dissection (%)	No	165 (100.0)
History of ischemic stroke (%)	No	133 (80.6)
	Yes	32 (19.4)
Previous history of statin use (%)	No	128 (77.6)
	Yes	37 (22.4)
BMI (mean (SD))		24.56 (3.08)
Location (%)	ICAD	86 (52.1)
	VAD	79 (47.9)
ALT (mmol/L) (median [IQR])		22.00 [15.00–36.00]
AST (mmol/L) (median [IQR])		22.00 [17.00–29.00]
Serum albumin (mmol/L) (median [IQR])		41.00 [38.00–43.80]
FBG (mmol/L) (median [IQR])		5.70 [5.10–7.00]
Diabetes (%)	No	116 (70.3)
	Yes	49 (29.7)
HbA1c (%) (median [IQR])		5.80 [5.40–6.60]
Hypertension (%)	No	63 (38.2)
	Yes	102 (61.8)
Triglyceride (mmol/L) (median [IQR])		1.46 [1.10–2.38]
Cholesterol (mmol/L) (median [IQR])		4.70 [3.83–5.52]
HDL-C (mmol/L) (median [IQR])		1.06 [0.88–1.26]
LDL-C (mmol/L) (median [IQR])		2.88 [2.08–3.80]
TyG (median [IQR])		4.24 [2.64–5.74]
Homocysteine (μmol/L) (median [IQR])		12.87 [10.00–16.40]
WBC (×10 <sup>9</sup> /L) (median [IQR])		7.10 [5.53–8.69]
NEU (×10 <sup>9</sup> /L) (median [IQR])		61.30 [52.80–69.30]

Abbreviations: IQR, inter quartile range; BMI, body mass index; SD, standard deviation; AST, aspartate aminotransferase; ALT, alanine transaminase; FBG, fasting blood glucose; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride-glucose index; WBC, white blood cell; NEU, neutrophils

differences between groups of measurement data subject to normal distribution. The rank sum test was used to compare the difference between groups of measurement data not subject to normal distribution. Moreover, the Chi-squared test or Fisher's exact probability method was used to compare the difference between groups of count data. Based on the results of univariate analyses, variables with an associated *P* value < 0.05 were introduced into the multivariable logistic regression analysis.

## Results

### General information

A total of 334 patients with CAD (ICAD or VAD) were included in our study. After a careful review of medical records and imaging data, 165 patients with cervical atherosclerosis were excluded, and four patients were excluded for other reasons. The study ultimately included 165 patients; the mean age was 55 (range: 48–66) years, and 123 patients were male. Eighty-six and 79 patients had ICAD and VAD, respectively (Table 1). No family history of dissection was found among the patients included in the study.

### Related factors for ischemic stroke caused by CAD

Ischemic stroke occurred in 69 of 169 patients with CAD. Univariate analysis showed that diabetes and white blood cell count were associated with ischemic stroke in CAD. Multivariate logistic regression analysis indicated that diabetes (OR: 3.144, 95% CI: 1.552–6.508, *P* < 0.002) and high white blood cell count (OR: 1.157, 95% CI: 1.02–1.327, *P* = 0.028) were associated factors for ischemic stroke in patients with CAD (Table 2).

## Discussion

The etiology and pathogenesis of CAD are still unclear; however, it is known to be associated with infection, trauma, inflammation, and connective tissue diseases [9–13]. The risk factors for ischemic stroke in patients with CAD are also unclear [5]. This study found that diabetes and a high infection index may be related factors for ischemic stroke in patients with ICAD.

The mean age of patients with ICAD in our study was 55.00 years, which is consistent with the average age of 54.2 years in the study by Janquli et al. [14]. Based on some previous studies, ICAD occurs between the average age of 43–54 years [15–18]. Another study with a small sample size found that the average age of patients was 60.7 ± 14.2 years [19]. Due to the small sample size of studies on ischemic stroke caused by CAD, selection bias is possible. In this study, 69 (41.8%) patients with CAD had ischemic stroke, which was basically consistent with the 39.6% reported by Christoph Lichy et al. [20]. However, this percentage is lower than the results of another study involving 149 patients with CAD wherein

**Table 2** Univariate analysis of associated factors of ischemic stroke in patients with CAD

variable		Non- ischemic stroke group	ischemic stroke group	p
n		96	69	
Sex (%)	Male	70 (72.9)	53 (76.8)	0.7
	Female	26 (27.1)	16 (23.2)	
Age (median [IQR]) years		54.50 [46.00, 64.00]	56.00 [48.00, 67.00]	0.916
Smoking (%)	NO	54 (56.2)	40 (58.0)	0.951
	Yes	42 (43.8)	29 (42.0)	
Drinking (%)	No	64 (66.7)	44 (63.8)	0.826
	Yes	32 (33.3)	25 (36.2)	
Family history of carotid dissection (%)	No	96 (100.0)	69 (100.0)	-
Trauma (%)	No	94 (97.9)	68 (98.6)	1
	Yes	2 (2.1)	1 (1.4)	
History of ischemic stroke (%)	No	80 (83.3)	53 (76.8)	0.398
	Yes	16 (16.7)	16 (23.2)	
Previous history of statin use (%)	No	75 (78.1)	53 (76.8)	0.992
	Yes	21 (21.9)	16 (23.2)	
BMI (mean (SD))		24.30 (3.26)	24.93 (2.79)	0.194
Location (%)	ICAD	47 (49.0)	39 (56.5)	0.423
	VAD	49 (51.0)	30 (43.5)	
ALT (mmol/L) (median [IQR])		22.00 [15.00, 37.00]	20.00 [15.00, 34.00]	0.709
AST (mmol/L) (median [IQR])		21.50 [17.00, 29.25]	23.00 [17.00, 29.00]	0.695
Serum albumin (mmol/L) (median [IQR])		41.00 [38.67, 43.85]	41.00 [36.70, 43.80]	0.774
FBG (mmol/L) (median [IQR])		5.59 [5.00, 6.89]	5.90 [5.11, 7.20]	0.12
Diabetes (%)	No	78 (81.2)	38 (55.1)	0.001
	Yes	18 (18.8)	31 (44.9)	
HbA1c (%) (median [IQR])		5.80 [5.40, 6.50]	5.90 [5.60, 6.70]	0.058
Hypertension (%)	No	33 (34.4)	30 (43.5)	0.682
	Yes	63 (63.6)	39 (56.5)	
Triglyceride (mmol/L) (median [IQR])		1.42 [1.06, 2.05]	1.51 [1.12, 2.68]	0.154
Cholesterol (mmol/L) (median [IQR])		4.53 [3.82, 5.49]	4.97 [3.90, 5.66]	0.242
HDL-C (mmol/L) (median [IQR])		1.01 [0.86, 1.23]	1.11 [0.92, 1.27]	0.159
LDL-C (mmol/L) (median [IQR])		2.99 [2.08, 4.04]	2.84 [2.10, 3.70]	0.465
TyG (median [IQR])		4.24 [2.81, 5.63]	4.24 [2.38, 5.74]	0.561
Homocysteine ( $\mu\text{mol/L}$ ) (median [IQR])		12.60 [10.17, 16.92]	13.30 [10.00, 16.30]	0.886
WBC ( $\times 10^9/\text{L}$ ) (median [IQR])		6.64 [5.19, 8.24]	7.76 [6.17, 9.47]	0.005
NEU ( $\times 10^9/\text{L}$ ) (median [IQR])		59.90 [52.88, 68.32]	62.70 [52.50, 72.80]	0.2

Abbreviations: IQR, inter quartile range; BMI, body mass index; SD, standard deviation; AST, aspartate aminotransferase; ALT, alanine transaminase; FBG, fasting blood glucose; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride-glucose index; WBC, white blood cell; NEU, neutrophils

54.4% had experienced ischemic stroke or transient ischemic attack (TIA) at baseline [21]. Another study with a smaller sample size found that 70% of patients had a stroke and among these, higher severity was observed in those with internal carotid artery dissection [22]. The difference in ischemic stroke caused by dissection may be related to the small sample size of the current studies on CAD.

The association of vascular risk factors with CAD remains controversial. Although most patients with CAD do not have common cerebrovascular risk factors, some cerebrovascular risk factors are still risk factors for CAD [5, 23], such as smoking [24, 25], male sex [26, 27], and advanced age [5]. We found that diabetes is a risk factor for ischemic stroke in patients with CAD. Consistent

with our findings, McNally et al. [28] found that male sex, smoking, hypertension, diabetes, and hyperlipidemia were risk factors for ischemic stroke due to CAD.

Growing evidence shows that inflammation and immunity are related to a variety of vascular diseases. White blood cells play an important role in the occurrence and development of vascular wall damage, thrombosis, and ischemic stroke [29, 30]. This connection is associated with a poor prognosis of ischemic stroke caused by CAD [31–35]. We found that patients with CAD with high white blood cell counts were prone to ischemic stroke. Similarly, Putaala et al. [36] identified recent infection as a predictor of ischemic stroke in patients with CAD. Additionally, a study on patients with acute posterior circulation ischemic stroke caused by vertebrobasilar

dissection also found significantly higher levels of peripheral neutrophils than normal controls and atherosclerotic-associated ischemic stroke [37]. Our results provide supporting evidence for an association between inflammation and ischemic stroke due to CAD; however, large experimental studies are needed to clarify the role of inflammatory factors in this process.

### Limitations

This study has some limitations; first, as some patients with CAD were asymptomatic or did not present with mild symptoms, the inclusion of patients may be subject to error. Second, the risk predictors included in our study focused more on demographic and clinical predictors and lacked imaging predictors. There was no further statistical classification of the imaging findings of the patients. Third, this study was a retrospective multicenter study, and we were unable to obtain more diagnosis and treatment information for patients with cerebral infarction. Fourth, because this is a multicenter retrospective study, more consistent infection indicators including C-reactive protein, procalcitonin and other indicators have not been collected. It is expected that the relationship between infection-related indicators and cerebral infarction caused by dissection can be further studied in the following studies. In the future, multicenter studies in China are needed to provide a basis for the prediction of risk factors for ICAD.

### Conclusion

This study revealed that diabetes, along with high white blood cell counts, may serve as risk factors for ischemic stroke in patients with CAD. Therefore, timely control of blood glucose and infection is crucial in patients with CAD, which may reduce the risk of ischemic stroke.

### Abbreviations

CAD	cervical artery dissection
DISH	diffuse idiopathic skeletal hyperostosis
DSA	digital subtraction angiography
HDL	high-density lipoprotein
ICAD	internal carotid artery dissection
LDL	low-density lipoprotein
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
VAD	vertebral artery dissection

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### Author contributions

MZ was responsible for the concept and design of the study, data collection and analysis, and the first and final drafts of the paper. XZ was responsible for the concept and design of the study, data collection and analysis, and the first and final drafts of the paper. HW was responsible for the concept and design of the study, and the first and final drafts of the paper. JD was responsible for the data collection and analysis. LL was responsible for the data collection and analysis. All authors read and approved the final manuscript for publication.

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### Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Declarations

#### Ethics approval and consent to participate

The study design was approved by the Medical and Health Research Ethics Committee of the Second People's Hospital of Chengdu, China. Ethics approval number is 2024115. All methods were carried out in accordance with relevant guidelines and regulations.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

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