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Analysis of Risk Factors in Patients with Cerebrovascular Disease Complicated by Chronic Coronary Syndrome

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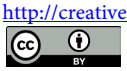

Abstract

Background: The number of patients with both cerebrovascular disease and chronic coronary syndrome (CCS) is rising, but shared risk factors are not well understood. This study identifies key risk factors by analyzing clinical data from these patients. **Methods:** We analyzed 403 patients (203 with intracranial aneurysms, 200 with intracranial stenosis) treated at the Second Affiliated Hospital of Kunming Medical University from June 1, 2022, to July 31, 2024. Data on demographics, medical history, and lab results were collected. Univariate and binary logistic regression analyses were used to identify significant risk factors. **Results:** Patients with intracranial stenosis and CCS were mostly male and had higher rates of diabetes, hyperhomocysteinemia, elevated NLR, troponin, and BNP. Those with aneurysms and CCS were also predominantly male and showed associations with older age, hypertension, diabetes, alcohol use, aneurysm rupture, and elevated uric acid, lipoprotein(a), homocysteine, and troponin. Logistic regression confirmed that male sex, older age, diabetes, and hyperlipoproteinemia. were independently linked to dual disease. **Conclusion:** Patients with both cerebrovascular disease and CCS are more likely to be male, older, and have diabetes or hyperlipidemia. These findings support routine cardiovascular risk assessment in this group.

Keywords

Intracranial Aneurysm, Intracranial Arterial Stenosis, Chronic Coronary Syndrome, Risk Factors

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1. Introduction

Intracranial atherosclerotic stenosis (ICAS) and intracranial aneurysms (IA) are major contributors to cerebrovascular disease. ICAS is characterized by the development and accumulation of atherosclerotic plaques within the arterial wall, leading to progressive narrowing or occlusion of the vascular lumen and representing the primary etiology of ischemic stroke [1]. IA refers to a localized dilation resulting from structural weakness in the arterial wall and is prevalent in the adult population. Based on rupture status, IAs are classified as unruptured intracranial aneurysms (UIAs) or ruptured aneurysms. The global prevalence of UIAs among individuals around 50 years of age is approximately 3% [2], while aneurysm rupture constitutes the leading cause of spontaneous subarachnoid hemorrhage (SAH). SAH incidence exhibits marked geographical variation, with notably higher rates observed in Japan and Finland [3]. Despite advances in medical and interventional therapies that have significantly reduced aneurysm-related mortality, a substantial proportion of survivors experience persistent neurological impairments, which profoundly impact post-event quality of life. In China, the prevalence of UIAs is reported at 7%, and the annual incidence of SAH is 2 per 100,000 person-years, with the majority of cases attributed to aneurysm rupture [2]. The term "chronic coronary syndrome (CCS)" was introduced by the European Society of Cardiology in 2019, replacing the previously used designation of stable coronary artery disease (CAD), to better reflect the dynamic nature of atherosclerotic cardiovascular disease [4]. These three conditions—ICAS, IA, and CCS—are closely linked to atherosclerosis and share overlapping pathophysiological mechanisms. In recent years, growing interest in the concept of the "heart-brain axis" and integrated cardiovascular-neurological management has highlighted the need to identify patient populations at increased risk for coexisting cerebrovascular and coronary disease. However, the risk factors associated with the concurrent presence of ICAS or IA and CCS remain poorly defined. This study therefore aims to investigate clinical risk factors in patients with both cerebrovascular disease and CCS, using routinely available clinical data, to compare them with those having isolated cerebrovascular disease and to inform strategies for early detection, prevention, and comprehensive management.

2. Material and Methods

This study was a retrospective case-control analysis of 403 patients admitted to the Department of Cerebrovascular Diseases at the Second Affiliated Hospital of Kunming Medical University between June 1, 2022, and July 31, 2024. The cohort included 203 patients with intracranial aneurysms and 200 with intracranial arterial stenosis. Of these, 43 patients in the aneurysm group and 44 in the stenosis group were diagnosed with CCS, based on criteria outlined in the Chinese Guidelines for the Diagnosis and Management of Chronic Coronary Syndrome: 1) Patients with suspected coronary artery disease and stable angina symptoms, regardless of whether they have dyspnea or not. 2) Patients with ischemic cardiomyopa-

thy. 3) Patients with asymptomatic coronary artery disease detected during screening. 4) Patients with suspected vasospasm or microvascular disease presenting with angina pectoris. 5) Patients who were hospitalized due to ACS or coronary revascularization and were discharged after their condition stabilized. Comprehensive clinical data were collected, including demographic characteristics (sex, age), lifestyle factors (smoking and alcohol use), medical history (hypertension and diabetes), disease-specific features (aneurysm rupture status, aneurysm location, presence and location of stenosis), and laboratory markers such as total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), lipoprotein-a (Lp-a), uric acid (UA), homocysteine (HCY), neutrophil-to-lymphocyte ratio (NLR), fibrinogen (FIB), D-dimer (DD), interleukin-6 (IL-6), high-sensitivity C-reactive protein (Hs-CRP), cardiac troponin I (CTnI), and B-type natriuretic peptide (BNP). To enable comparative analysis, patients were stratified into four groups: Group 1 (intracranial aneurysm + CCS), Group 2 (intracranial aneurysm only), Group 3 (intracranial stenosis + CCS), and Group 4 (intracranial stenosis only). This classification allowed for direct comparison between patients with dual pathology and those with isolated cerebrovascular disease. The study protocol was approved by the Ethics Committee of the Second Affiliated Hospital of Kunming Medical University, and all procedures adhered to ethical standards for research involving human subjects.

2.1. Inclusion Criteria

1) Digital Subtraction Angiography (DSA) examination results show that the patient has an intracranial segment aneurysm, regardless of the size, location, and whether it has ruptured or not.

2) Computed tomography angiography (CTA)/DSA angiography clearly diagnoses an intracranial segment artery stenosis rate of ≥50% (or diagnoses moderate to severe intracranial artery stenosis).

2.2. Exclusion Criteria

1) Complete occlusion of the stenotic vessel as confirmed by CTA or DSA angiography.

2) Patients with intracranial aneurysms who have undergone prior surgical or endovascular intervention;

3) Patients diagnosed with CCS in the presence of concomitant cardiac conditions, including valvular heart disease or arrhythmia;

4) Patients with intracranial arterial stenosis who have received revascularization therapy or surgical treatment;

5) Patients with a history of gout, uric acid stones, or use of uric acid-lowering medications within the past three months;

6) Patients who have used folic acid or other agents known to reduce homocysteine levels during the study period;

7) Patients with active systemic conditions that may influence inflammatory markers, such as recent infections or malignancy.

2.3. Statistical Analysis

Normally distributed continuous variables are presented as mean ± standard deviation, and intergroup comparisons were performed using the independent samples t-test. Non-normally distributed continuous variables are reported as median (interquartile range), and group differences were assessed using the Mann-Whitney U test. Categorical variables are expressed as frequency (percentage), with comparisons conducted via the chi-square test or Fisher's exact test when appropriate. Variables showing statistically significant differences in univariate analyses were subsequently included in multivariate logistic regression models to identify independent predictors of coexisting chronic coronary syndrome. All statistical analyses were carried out using SPSS software, and a two-tailed P value < 0.05 was considered statistically significant.

3. Results

A total of 203 patients with intracranial aneurysms were enrolled in this study. Univariate analysis comparing clinical characteristics between double-disease group 1 and control group 1 revealed statistically significant differences in gender, age, alcohol consumption history, hypertension history, diabetes history, aneurysm rupture status, uric acid, lipoprotein(a), homocysteine, and troponin levels (all P < 0.05) (Table 1). To identify independent predictors of chronic coronary syndrome, binary logistic regression analysis was performed with the presence of chronic coronary syndrome as the dependent variable and all significantly associated variables from univariate analysis included as covariates (Table 2). The results demonstrated that age, male gender, and elevated lipoprotein(a) levels were independent risk factors for coexisting chronic coronary syndrome (P < 0.05). Gender-based subgroup analysis was subsequently conducted (Table 3). Among males, those with chronic coronary syndrome were significantly older and exhibited higher prevalences of hypertension and aneurysm rupture, as well as increased levels of lipoprotein(a), homocysteine, NLR, D-dimer, and troponin. Among females, patients with chronic coronary syndrome were older and had higher levels of uric acid and total cholesterol compared to their counterparts without the condition.

Table 1. Analysis of risk factors in patients with intracranial aneurysm and chronic coronary syndrome.

Factor	Group 1 (n = 43), n (%)	Group 2 (n = 160), n (%)	T/Z/χ^2	P
Male	30 (69.8%)	57 (35.6%)	16.1	<0.01
Age/Years	65.95 ± 9.68	59.6 ± 10.64	−4.17	<0.01
Smoking history	6 (14%)	11 (7%)	2.21	0.14

Continued

Alcohol consumption history	5 (11.6%)	6 (3.7%)	4.1	0.04
Hypertension	36 (83.7%)	89 (55.6%)	11.3	<0.01
Diabetes	10 (23.3%)	16 (10%)	5.33	0.02
Rupture of aneurysms	4 (9.3%)	48 (30%)	7.62	0.006
UA μmol/L	389.1 ± 93.46	315.19 ± 117.79	3.8	<0.01
TC mmol/L	4.14 ± 1.29	4.56 ± 1.28	−1.92	0.06
TG mmol/L	0.93 (0.5)	1.45 (0.42)	−1.72	0.08
LDL-C mmol/L	2.54 ± 0.97	2.84 ± 0.85	−1.97	0.051
HDL-C mmol/L	1.18 ± 0.28	1.18 ± 0.32	−0.02	0.98
LP-a mg/dL	12.6 (20.22)	8.7 (5.77)	−2.18	0.03
HCY μmol/L	27.41 (3.22)	12.33 (1.17)	−2.44	0.015
Neutrophile Granulocyte109/L	4.14 (1.71)	4.26 (0.89)	−0.88	0.38
Lymphocyte 109/L	1.62 (0.43)	1.58 (0.2)	−1.37	0.17
NLR	2.36 (2.03)	2.77 (1.63)	−1.54	0.12
Anterior Circulation	38 (88.4%)	146 (91.3%)	0.33	0.57
FIB g/L	3.12 ± 0.51	3.24 ± 0.32	−0.74	0.46
DD μg/mL	0.53 (0.76)	0.45 (0.75)	−0.73	0.94
IL-6 pg/ml	4.16 (5.05)	4.35 (5.67)	−0.42	0.67
Hs-CRP mg/L	1.4 (7.4)	1.9 (5.4)	−1.03	0.31
CTnI ng/ml	0.01 (0.25)	0.007 (0.021)	−3.09	0.002
BNP pg/ml	136 (204)	66 (169)	−1.48	0.14

Table 2. Binary logistic regression analysis.

Factor	Partial regression coefficient	SE	wald	P	OR	95% confidence interval
Male	−0.07	0.024	8.23	0.004	0.93	0.89 - 0.98
Age	1.46	0.47	9.47	0.002	4.31	1.7 - 10.91
Hypertension	0.8	0.5	2.63	0.11	2.23	0.85 - 5.88
Diabetes	0.73	0.52	1.95	0.16	2.07	0.75 - 5.74
Alcohol consumption history	0.19	0.77	0.06	0.81	1.21	0.27 - 5.49
Rupture of aneurysms	−1.13	0.65	2.98	0.08	0.32	0.09 - 1.17
UA	−0.003	0.002	2.13	0.14	1	0.993 - 1.001
LP-a	−0.024	0.009	6.47	0.01	0.98	0.958 - 0.994
HCY	0.026	0.054	0.23	0.63	1.03	0.92 - 1.14
CTnI	−1.2	1.69	0.5	0.48	0.3	0.01 - 8.24

Table 3. Analysis of risk factors in patients with intracranial aneurysms of different genders complicated by coronary heart disease.

Factor	Male (n = 87)			Female (n = 116)		
	Group 1 (n = 30), n (%)	Group 1 (n = 57), n (%)	P	Group 1 (n = 13), n (%)	Group 1 (n = 103), n (%)	P
Age/Years	64.93 ± 5.78	58.7 ± 11.22	0.006	68.31 ± 10.82	60.1 ± 10.32	0.008
Smoking history	6 (20%)	11 (19.3%)	0.94	0	0	-
Alcohol consumption history	5 (16.7%)	6 (10.5%)	0.41	0	0	-
Hypertension	26 (86.7%)	31 (54.4%)	0.003	10 (76.9%)	58 (56.3%)	0.15
Diabetes	7 (23.3%)	6 (10.5%)	0.11	3 (23.1%)	10 (9.7%)	0.15
Rupture of aneurysms	2 (6.7%)	17 (29.8%)	0.01	2 (15.4%)	31 (30.1%)	0.27
UA μmol/L	397 (60)	378 (68)	0.09	331 (133)	272 (39)	0.03
TC mmol/L	4.23 ± 1.39	4.33 ± 1.28	0.74	3.94 ± 1.06	4.69 ± 1.27	0.04
TG mmol/L	1.36 ± 0.53	2.06 ± 2.02	0.06	1.95 ± 1.52	1.61 ± 0.75	0.18
LDL-C mmol/L	1.17 ± 0.28	1.08 ± 0.27	0.15	1.2 ± 0.27	1.23 ± 0.33	0.69
HDL-C mmol/L	2.54 ± 0.99	2.69 ± 0.85	0.48	2.54 ± 0.98	2.92 ± 0.84	0.14
LP-a mg/dL	16.1 (25.3)	8.1 (6.8)	0.002	8.1 (36.7)	9 (8.14)	0.52
HCY μmol/L	14.91 (4.19)	12.36 (2.28)	0.02	10.99 (4.5)	11.97 (1.32)	0.8
Neutrophile Granulocyte 10^9/L	4.06 (1.7)	5.09 (1.44)	0.04	4.29 (4.55)	3.96 (1.15)	0.91
Lymphocyte 10^9/L	1.67 (0.51)	1.58 (0.33)	0.08	1.51 (0.85)	1.54 (0.23)	0.73
NLR	2.25 (1.45)	2.96 (3.55)	0.02	2.61 (6.22)	2.43 (1.6)	0.84
Anterior Circulation	27 (90%)	50 (87.7%)	0.75	11 (84.6%)	96 (93.2%)	0.28
FIB g/L	2.85 (0.53)	3.95 (0.59)	0.55	3.12 (1.19)	3.06 (0.38)	0.5
DD μg/mL	0.58 (0.89)	0.33 (1.47)	0.04	0.26 (1.66)	0.6 (0.85)	0.1
IL-6 pg/ml	3.69 (5.95)	3.22 (13.16)	0.5	4.78 (10.94)	4.74 (5.19)	0.5
Hs-CRP mg/L	1.04 (9.92)	1.46 (12.78)	0.5	1.86 (10.14)	2.08 (4.73)	0.79
CTnI ng/ml	0.01 (0.37)	0.008 (0.036)	0.002	0.009 (0.007)	0.006 (0.027)	0.73
BNP pg/ml	73 (269)	67 (147)	0.4	189 (316)	65 (249)	0.06

A total of 200 patients with moderate to severe intracranial artery stenosis were enrolled in this study, including 44 patients with coexisting chronic coronary syndrome. Compared with those who had isolated intracranial stenosis, patients with both conditions were more likely to be male and had a significantly higher prevalence of diabetes mellitus, as well as elevated levels of homocysteine, NLR, troponin, and BNP (all $P < 0.05$) (Table 4). Among patients with anterior circulation stenosis, those with chronic coronary syndrome exhibited significantly higher concentrations of troponin and BNP ($P < 0.05$). In patients with posterior circulation stenosis, the presence of chronic coronary syndrome was associated with higher levels of total cholesterol, triglycerides, and troponin ($P < 0.05$) (Table 5). To identify independent risk factors for the coexistence of chronic coronary syndrome, multivariate logistic regression analysis was performed using variables

that showed statistical significance in univariate analyses. The results revealed that older age, male sex, and a history of diabetes mellitus were independently associated with an increased risk of chronic coronary syndrome in patients with moderate to severe intracranial artery stenosis ($P < 0.05$) (Table 6).

Table 4. Analysis of risk factors in patients with intracranial artery stenosis combined with chronic coronary syndrome.

Factor	Group 3 (n= 44), n (%)	Group 4 (n= 156), n (%)	T/Z/χ^2	P
Male	35 (79.5%)	95 (61%)	5.25	0.022
Age/Years	67.91 ± 9.72	61.83 ± 10.63	3.41	0.037
Smoking history	12 (27.3%)	36 (23%)	0.33	0.57
Alcohol consumption history	8 (18.2%)	26 (16.7%)	0.056	0.81
Hypertension	37 (84.1%)	119 (76.3%)	1.22	0.27
Diabetes	21 (47.7%)	46 (29.5%)	5.13	0.024
History of stroke	13 (29.5%)	28 (17.9%)	2.83	0.092
UA μmol/L	364.34 ± 119.81	345.54 ± 101.21	1.04	0.3
TC mmol/L	3.93 ± 1.01	4.13 ± 1.18	−1.05	0.29
TG mmol/L	1.29 (0.5)	1.36 (0.36)	−0.79	0.43
LDL-C mmol/L	2.38 ± 0.77	2.51 ± 0.81	−0.98	0.33
LP-a mg/dL	10.95 (12.11)	12.1 (8.84)	−0.6	0.55
HCY μmol/L	15.51 (2.6)	15.35 (3.51)	−2.07	0.039
NLR	3.05 (1.79)	2.3 (0.65)	−2.06	0.04
Anterior Circulation	26 (59.1%)	113 (72.4%)	2.88	0.089
FIB g/L	3.27 ± 0.71	3.17 ± 1.11	0.56	0.58
DD μg/mL	0.34 (0.42)	0.3 (0.18)	−1.9	0.06
IL-6 pg/ml	5.34 (10.84)	4.62 (7.06)	−1.87	0.06
Hs-CRP mg/L	1.1 (11.8)	1.55 (5.73)	−1.16	0.25
CTnI ng/ml	0.015 (0.12)	0.01 (0.01)	−4.25	<0.001
BNP pg/ml	115 (469)	59 (68)	−3.9	<0.001
Narrowing symptoms	40 (91%)	149 (96%)	1.4	0.24

Table 5. Binary logistic regression analysis.

Factor	Partial regression coefficient	SE	wald	P	OR	95% confidence interval
Male	0.98	0.44	4.92	0.026	2.66	1.12 - 6.32
Age	−0.06	0.02	8.8	0.003	0.94	0.91 - 0.98
Diabetes	0.88	0.39	5.16	0.023	2.4	1.13 - 5.1
HCY	−0.003	0.02	0.02	0.89	1	0.96 - 1
NLR	−0.03	0.09	0.09	0.76	0.97	0.83 - 1.15
CTnI	−5.29	3.92	1.81	0.18	0.005	0.001 - 11.12
BNP	−0.001	−0.001	2.03	0.16	1	0.99 - 1

Table 6. Risk factors for intracranial artery stenosis in different regions (proximal and distal circulation) combined with chronic coronary syndrome.

Factor	Anterior Circulation (n = 139)			Posterior Circulation (n = 61)		
	Group 3 (n = 26), n (%)	Group 4 (n = 113), n (%)	P	Group 3 (n = 18), n (%)	Group 4 (n = 43), n (%)	P
Male	19 (73%)	69 (61%)	0.25	16 (89%)	26 (60%)	0.03
Age/Years	66.73 ± 9	60.5 ± 10.4	0.006	69.61 ± 10.68	65.3 ± 10.63	0.16
Smoking history	5 (19%)	26 (23%)	0.68	6 (33%)	10 (23%)	0.21
Alcohol consumption history	3 (12%)	19 (17%)	0.51	5 (27%)	8 (18%)	0.3
Hypertension	20 (77%)	82 (72%)	0.65	17 (94%)	37 (86%)	0.35
Diabetes	11 (42%)	28 (25%)	0.07	10 (55%)	18 (41%)	0.33
History of stroke	8 (31%)	19 (17%)	0.11	5 (27%)	9 (21%)	0.56
UA μmol/L	369.24 ± 112.8	343.03 ± 93.1	0.21	356.44 ± 132.2	352.16 ± 120.88	0.9
TC mmol/L	4.14 ± 1.1	4.1 ± 1.26	0.96	3.62 ± 0.82	4.15 ± 0.98	0.049
TG mmol/L	1.42 (0.7)	1.26 (0.48)	0.58	1.07 (0.69)	1.44 (0.36)	0.03
LDL-C mmol/L	2.51 ± 0.85	2.51 ± 0.7	0.98	2.18 ± 0.62	2.52 ± 0.72	0.09
LP-a mg/dL	11.65 (14.3)	13.1 (11)	0.85	8.8 (23)	10.6 (15.7)	0.31
HCY μmol/L	15.1 (3.2)	13.85 (2.1)	0.11	16.7 (4.7)	14.2 (11.8)	0.26
NLR	2.78 (2.8)	2.35 (0.77)	0.29	3.18 (2.1)	2.3 (1.3)	0.06
FIB g/L	3.21 ± 0.72	3.14 ± 1	0.76	3.36 ± 0.7	3.24 ± 1.39	0.73
DD μg/mL	0.31 (0.56)	0.28 (0.19)	0.2	0.46 (0.71)	0.36 (0.41)	0.26
IL-6 pg/ml	5.79 (45.6)	4.29 (4.01)	0.057	4.7 (4.95)	4.64 (23.9)	0.86
Hs-CRP mg/L	1.01 (15.6)	1.55 (5.9)	0.29	1.36 (3.55)	1.54 (13.8)	0.55
CTnI ng/ml	0.013 (0.168)	0.008 (0.007)	<0.001	0.016 (0.01)	0.01 (0.003)	0.01
BNP pg/ml	143 (793)	51 (89)	<0.001	109 (112)	92 (85)	0.33
Narrowing symptoms	24 (92%)	107 (95%)	0.64	16 (89%)	42 (97%)	0.15

4. Discussion

Our study demonstrates that male patients with intracranial aneurysms are at increased risk of coexisting chronic coronary syndrome, particularly in the presence of advanced age and hyperlipidemia. Furthermore, the combination of intracranial arterial stenosis and chronic coronary syndrome is more commonly observed in males and older individuals, especially those with diabetes mellitus. While the pathogenesis and management of cerebrovascular diseases and chronic coronary syndrome exhibit both overlapping and distinct features, the development of intracranial arterial stenosis, intracranial aneurysms, and chronic coronary syndrome is closely linked to atherosclerosis. Established risk factors for atherosclerosis include advanced age, hyperlipidemia, diabetes mellitus, alcohol consumption, and obesity [5] [6]. Notably, this study also identifies hyperuricemia and elevated homocysteine levels as potentially contributing factors in the pathogenesis

of these conditions.

Uric acid is the end product of purine nucleotide catabolism in humans and is sparingly soluble in water. It serves as a major endogenous antioxidant; however, elevated uric acid levels are closely associated with an increased risk of cardiovascular diseases [7]. In healthy individuals, serum uric acid levels are maintained within a delicate physiological equilibrium. Disruption of this balance may lead to cellular dysfunction and contribute to disease development [8]. Although the relationship between hyperuricemia and other coronary heart disease risk factors remains controversial, accumulating evidence indicates that uric acid levels exceeding 309 μmol/L are linked to a significantly higher incidence of coronary heart disease and other cardiovascular events. Specifically, each 60 μmol/L increase in uric acid concentration is associated with a 5% rise in coronary heart disease risk [8]. The pathophysiological mechanisms by which uric acid contributes to coronary heart disease include: 1) impairment of the endothelial cell system; 2) promotion of systemic inflammation; and 3) modulation of neurohormonal activity. Uric acid has been shown to induce inflammatory responses in endothelial and smooth muscle cells, leading to endothelial dysfunction. Recent studies have demonstrated that hyperuricemia reduces nitric oxide (NO) bioavailability by impairing NO synthesis and accelerating its degradation, primarily through oxidative stress and inflammatory activation in vascular endothelial cells [9]. During uric acid metabolism, activated xanthine oxidase generates reactive oxygen species, promoting a pro-inflammatory vascular state and thereby increasing cardiovascular risk [10]. Furthermore, uric acid stimulates vascular smooth muscle cells to produce pro-inflammatory mediators such as monocyte chemoattractant protein-1 (MCP-1), interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) [11]. Elevated uric acid levels can also enhance inflammasome activation and propagate inflammatory processes within atherosclerotic plaques, potentially influencing intracranial aneurysm instability and rupture. Collectively, hyperuricemia appears to be significantly associated with the development of cardiovascular diseases and is considered an important independent risk factor, although the precise underlying mechanisms remain incompletely understood.

Homocysteine is a sulfur-containing amino acid produced during methionine metabolism in the human body. Accumulating evidence indicates that elevated plasma homocysteine levels contribute to the pathogenesis and progression of intracranial aneurysms [12]. Furthermore, hyperhomocysteinemia is closely associated with the development of coronary heart disease through several potential mechanisms: 1) Homocysteine impairs endothelial function by reducing the synthesis of NO and prostacyclin (PGI_2) in damaged vascular endothelial cells—both critical mediators of vasodilation—thereby promoting endothelial dysfunction [13]; 2) it induces endothelial inflammation by stimulating the release of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor α (TNF-α), which exacerbate vascular injury; and 3) it directly promotes atherosclerotic changes in the vascular adventitia [13]. However, whether elevated homo-

cysteine levels represent a primary causal factor or merely a secondary biomarker of vascular events such as stroke remains controversial. Current evidence suggests that lowering homocysteine levels does not confer a significant causal benefit in the early stages of atherosclerosis [14].

Age and sex are established non-modifiable risk factors for coronary heart disease and frequently act as confounding variables in epidemiological studies. The incidence of coronary heart disease rises with advancing age, and disease severity tends to increase concurrently. Among individuals aged 50 years and older for men and 55 years and older for women, the risks of coronary atherosclerosis and myocardial infarction escalate progressively with age. Epidemiological evidence indicates that men have a higher mortality rate from coronary heart disease compared to women. This disparity may be attributed to greater exposure of men to modifiable risk factors such as smoking, alcohol consumption, poor dietary habits, chronic stress, and physical inactivity [15]. In contrast, premenopausal women benefit from the cardioprotective effects of estrogen, which helps lower triglyceride and low-density lipoprotein (LDL) levels while increasing high-density lipoprotein (HDL) concentrations, thereby reducing atherogenic risk [16]. Furthermore, studies suggest that women tend to adopt healthier lifestyle behaviors, including greater health awareness, preventive care, and engagement in health-promoting practices, which may collectively contribute to a lower incidence of coronary heart disease [17].

Diabetes mellitus is a prevalent metabolic disorder and a well-established risk factor for cardiovascular and cerebrovascular diseases. Atherosclerosis represents a primary pathological mechanism underlying diabetes-related vascular complications. The pathogenesis of atherosclerosis in diabetic patients involves multiple interrelated mechanisms: 1) insulin resistance and systemic metabolic dysregulation; 2) vascular injury induced by disturbances in glucose and lipid metabolism; 3) enhanced production and activation of pro-inflammatory cytokines; and 4) increased oxidative stress. In a study by Matthäus Metz *et al.* on insulin resistance, insulin was shown to play a critical role in regulating lipolysis in white adipose tissue (WAT). Conditions such as obesity impair insulin-mediated suppression of WAT lipolysis, leading to elevated free fatty acid levels, which subsequently activate the mitogen-activated protein kinase (MAPK) signaling pathway in the hypothalamus. This cascade contributes to endothelial dysfunction and promotes structural damage to the vascular wall, accelerating atherosclerotic progression [18]. Moreover, both sustained and fluctuating hyperglycemia exert detrimental effects on the vasculature. Accumulating evidence indicates that glycemic variability is strongly associated with atherosclerosis. For instance, Chen Shaomin *et al.* demonstrated in their study on blood glucose fluctuations and carotid atherosclerosis that greater glycemic variability is significantly correlated with atherosclerotic vascular disease and thrombosis, and constitutes an independent risk factor for atherosclerosis. Diabetes has been proven by many studies to be a risk factor for intracranial arterial stenosis. However, in contrast, there is still considera-

ble disagreement in the academic community regarding the relationship between diabetes and the occurrence and rupture of intracranial aneurysms. The main viewpoints can be classified into three categories: 1) Diabetes is closely related to the formation and rupture of aneurysms; 2) Diabetes is a protective factor for the formation and rupture of aneurysms, as it may stabilize aneurysms through vascular remodeling and hardening; 3) There is no relationship between diabetes and aneurysms.

In conclusion, advanced age, male sex, a history of diabetes mellitus, and hyperlipoproteinemia are independent risk factors for patients with cerebrovascular disease coexisting with chronic coronary syndrome. Furthermore, conditions such as hyperuricemia and hyperhomocysteinemia should also be considered potential risk factors contributing to the development of both disorders. Recognizing these factors can help guide clinical decision-making by enabling earlier risk stratification, more targeted diagnostic evaluation, and personalized therapeutic strategies, thereby improving patient outcomes.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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