BMC Neurology

RESEARCH

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Factors influencing the occurrence of ischemic stroke in elderly patients with hypertension and type 2 diabetes mellitus: a case-control study

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Abstract

Objective To investigate the risk factors for ischemic stroke in elderly patients with hypertension and type 2 diabetes mellitus.

Methods A total of 112 elderly patients with hypertension and type 2 diabetes, treated at Jiangmen Central Hospital from January 2023 to December 2023, were selected and categorized into a stroke group and a non-stroke group, each comprising 56 patients. The two groups were examined for demographic data, risk variables were evaluated by multifactorial logistic regression analysis, and the predictive value was determined using ROC curves.

Results The comparison of hyperhomocysteinemia (HHcy), fibrinogen (FIB), and high-density lipoprotein cholesterol (HDL-C) between the non-stroke and stroke groups revealed statistically significant differences ($P<0.05$). Logistic regression analysis indicated that HHcy (OR 16.936; 95% CI 1.946–146.071; $P=0.010$), FIB (OR 1.773; 95% CI 1.238–2.540; $P=0.002$), and HDL-C (OR 0.182; 95% CI 0.043–0.775; $P=0.021$) were significant factors in the onset of ischemic stroke among elderly patients with hypertension and type 2 diabetes. ROC curve analysis revealed that the area under the curve (AUC) for FIB, HDL-C, and HHcy in diagnosing stroke associated with hypertension and type 2 diabetes mellitus in the elderly were 0.704, 0.640, and 0.598, respectively, while the AUC for the combined diagnosis of all three was 0.784.

Conclusions HHcy, FIB, and HDL-C independently influence the occurrence of ischemic stroke in elderly patients with hypertension combined with type 2 diabetes mellitus, and their combined enhanced predictive capability for ischemic stroke occurrence.

Keywords Elderly, Hypertension and type 2 diabetes mellitus, Ischemic stroke, Influential factors

Ischemic stroke (IS) is a circulatory disorder of blood flow to the brain that results in local tissue ischemia and necrosis, manifesting as transient or permanent neurological deficits, and is mostly seen in the elderly population [1]. Hypertension (HTN) and diabetes mellitus (DM) are prevalent chronic conditions and significant risk factors for the onset of IS. According to epidemiology, the prevalence of diabetes mellitus in hypertensive individuals is 16.77 percent and the prevalence of hypertension

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in diabetic patients is 62.71 percent. Additionally, the prevalence of hypertension and diabetes mellitus (HTN-DM) ranges from 5.02 percent to 6.20 percent [2]. The prevalence of HTN and DM is steadily rising among the elderly as the population ages, and the two conditions are linked to a markedly increased risk of cardiovascular disease and damage to target organs compared to either condition alone [3]. Data show that stroke occurs in 5.5% of cases of HTN-DM, compared with 0.6% of strokes without HTN-DM; furthermore, the risk of stroke in HTN-DM increases with age [4]. The risk factors for the development of IS in older patients with hypertension and type 2 diabetes mellitus (HTN-T2DM) have not been examined in the majority of prior research, which has focused on the risk factors influencing the development of IS for a single disease. To lower the chance of developing IS, this study will screen for IS in high-risk individuals, examine risk factors for IS development in older patients with HTN-T2DM, and provide prompt intervention follow-up.

Methods

Study population

A case–control study was conducted involving 158 elderly IS patients with HTN-T2DM from the Department of Neurology and 61 elderly patients with HTN-T2DM from the Department of Endocrinology at Jiangmen Central Hospital, selected based on the inclusion and exclusion criteria from January 2023 to December 2023. The elderly IS patients with HTN-T2DM for the stroke group and elderly patients with HTN-T2DM for the non-stroke group each had 56 cases after controlling for age, sex, and BMI using propensity score matching and removing the impact of confounding variables. The hospital ethics committee approved the study protocol. (Jiangxin Medical Ethics Review [2024] 177A).

Inclusion criteria for the non-stroke group:

1. Age > 60 years.
2. Concurrent HTN and T2DM, with a medical history exceeding one year:
    1) HTN [5]: patients with a systolic blood pressure above140 mmHg and/or diastolic blood pressure above90 mmHg measured three times on non-simultaneous days without the use of antihypertensive medication, or patients who had a previous definitive diagnosis of hypertension and were being treated with antihypertensive medication.
    2) T2DM [6]: oral Glucose Tolerance Test Two-hour venous plasma glucose exceeding 200 mg/dL (greater than 11.1 mmol/L); fasting plasma glucose surpassing 126 mg/dL (more than 7.0 mmol/L); individuals exhibiting classic symptoms of hyperglycemia or hyperglycemic crises with random blood glucose levels over 200 mg/dL (greater than 11.1 mmol/L); glycated hemoglobin greater than 6.5 percent.

Inclusion criteria for the stroke group:

1. Fulfilment of inclusion criteria for the non-stroke group.
2. Confirmation of IS. IS was diagnosed as follows [7]:
    1) Neuroimaging or other techniques in clinically relevant areas of the brain.
    2) If there is no evidence of an imaging responsible lesion, the presence of a focal neurological deficit or a global neurological deficit resulting in clinical. Signs/symptoms such as weakness or numbness of one side of the face or limb, speech disorders, and other clinical signs/symptoms lasting longer than 24 h.

Exclusion criteria:

1. CT/MR of the brain reveals intracranial hemorrhage (including parenchymal hemorrhage, intraventricular hemorrhage, subarachnoid hemorrhage and subdural/extracranial hematoma.) and an intracranial tumor.
2. Stroke caused by arteritis, migraine, vasospasm, or substance abuse.
3. Myocardial infarction or unstable angina within the past three months.
4. Prior diagnosis of transient ischemic attack (TIA) or cranial trauma.
5. Severe hepatic and renal insufficiency, autoimmune diseases, and hematological diseases.
6. Self-reported failure to adhere to the doctor's regimen and medication dose over time. According to the definition of self-reported medication adherence, the last prescription, at least 80% or more of the medication was consumed [8].
7. Patients with more than 20% missing data were included.

Data collection

Demographic data and laboratory indicators of the patients were collected.

1. Demographic data: age, gender, height body mass index (BMI (weight/height^2)), education, marital sta-

tus, residential location, smoking, drinking, duration of HTN, and duration of T2DM.
2. Comorbidities: atrial fibrillation (AF), hyperhomocysteinemia (HHcy), hyperlipidemia (HLP), and coronary heart disease (CHD).
3. Blood indices:

    1) Blood routine examination: platelet count (PLT), hemoglobin (Hb), thrombocytocrit (PCT), hematocrit (HCT), platelet distribution width (PDW), and platelet mean volume (MPV).
    2) Blood coagulation function: plasminogen time (PT), fibrinogen (FIB), activated partial thromboplastin time (APTT), thromboplastin time (TT), and D-Dimer.
    3) Serum biochemical indexes: blood uric acid (UA), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C).
    4) Liver function tests: albumin (ALB).
    5) Glycosylated hemoglobin (HbA1c).

Equipment and methods for blood index testing

Blood specimens were collected from the patients within 24 h of admission and after 8 h of fasting. Blood specimens were dispatched to the Laboratory of Jiangmen Central Hospital for testing, where qualified personnel completed the necessary chemical tests and analyses. The following are many test indicators and instruments:

1) Blood routine examination required the collection of whole blood samples, which were evaluated using the Shenzhen Mindray BC-6800 automatic blood cell analyzer. HCT, PDW, and MPV were determined using instrumental methods, PLT was assessed using sheath flow impedance, and Hb was quantified using colorimetric methods.
2) Liver function and biochemical indices: Serum samples were collected and analyzed using the HITACHI 7600 automatic biochemical analyzer from Japan. The bromocresol green method was employed to quantify ALB; the direct antibody inhibition method was utilized for LDL-C and HDL-C analysis; the GPO-PAP method was applied for TG measurement; the CHOD-PAP method was used for TC analysis; and the uric acid enzyme method was implemented for UA assessment.
3) Blood coagulation function indices: plasma samples were collected and analyzed using the Sysmex CS-5100 automatic coagulation analyzer from Japan; D-Dimer was assessed via the immunoturbidimetric method; PT, FIB, APTT and TT were evaluated using coagulation techniques.
4) HbA1c: measured using chromatographic technique utilizing the Japanese ARKRAY HA-8180 fully automated glycated protein analyzer.

Therapeutic regimen

Physicians at the study hospital tailored the treatment based on the medication regimen administered to the enrolled patients, considering their specific blood pressure and blood sugar management.

HTN treatment regimen [9]: in individuals with HTN-T2DM, angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) are advised as the optimal choice for blood pressure management.

DM treatment regimen [10]: oral α-glucosidase inhibitors, metformin (MET), oral SGLT-2 inhibitors (sodium-dependent glucose transporters 2 inhibitors), and glucagon-like peptide-1 receptor agonists (GLP-1RAs) were taken either singularly or in combination, contingent upon the patient's glycemic profile. glucagon-like peptide-1 receptor agonist (GLP-1RA). Subcutaneous insulin was used when the medicine proved ineffective.

Statistical analysis

Statistical analyses were performed using R Studio; SPSS 27.0 and GraphPad Prism 8.0. Continuous variables were tested for normality using the Kolmogorov–Smirnov test, with data conforming to a normal distribution described as mean (mean ± standard deviation (SD)), and non-normally distributed data described as median (interquartile range, IQR) using the independent samples t-test and the Mann–Whitney test for nonnormally distributed variables. Categorical variables were shown as frequencies and percentages using the χ^2 test. The diagnostic efficacy of the indicators was assessed by ROC curves using multivariate logistic regression analyses. $P < 0.05$ was statistically significant. Statistical significance was set at $P < 0.05$ In this study, missing continuous variables were entered using the mean value method and missing categorical variables were entered using the random interpolation fill method.

Results

Profile of the study

The investigators were recruited from January 2023 to December 2023 from the Department of Neurology and Endocrinology of Jiangmen Central Hospital. The flow of patients in the stroke and non-stroke groups, as shown in Fig. 1.

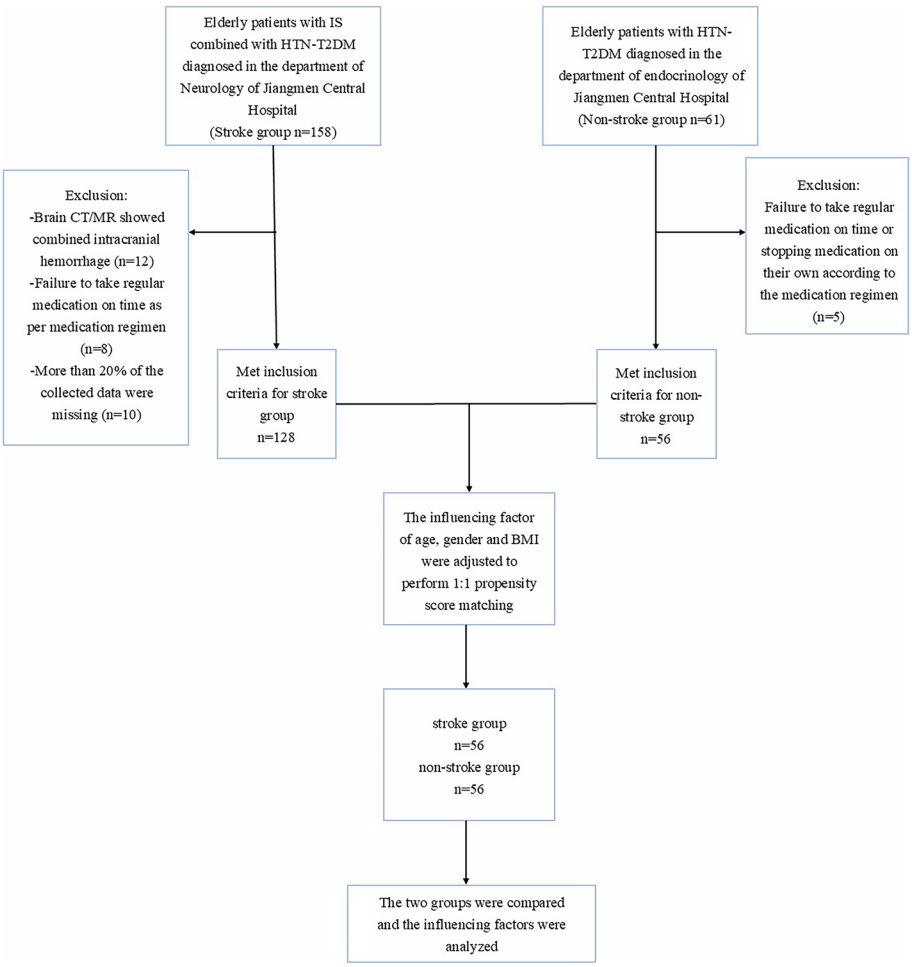

Fig. 1 Flow diagram showing study recruitment

Comparison of general clinical data between stroke and non-stroke groups

A comparative analysis of the two sets of information showed that there were 12 cases (21.43%) of HHcy in the stroke group and 1 case (1.79%) of HHcy in the non-stroke group, and the difference between the two groups was statistically significant ($P<0.05$). The FIB in the stroke group (3.25 (2.77,3.73)) was higher than that in the non-stroke group (4.91 (3.35,5.58)) ($P<0.001$). HDL-C was lower in the stroke group than in the non-stroke group (1.06 (0.89,1.39) vs 0.95(0.80,1.13), $P=0.010$). The difference between the two groups was statistically significant ($P<0.05$). There was no significant difference in other clinical data between the stroke group and the non-stroke group ($P>0.05$). Comparison of general clinical data between the two groups is shown in Table 1.

Multifactorial logistic regression analysis

Multifactorial logistic regression analyses were performed with the presence of IS as the independent variable HHcy, FIB, and HDL-C as the dependent variables, adjusted for related factors. The results showed that HHcy (OR 16.936; 95% CI 1.946–146.071; $P=0.010$), FIB (OR 1.773; 95% CI 1.238–2.540; $P=0.002$), and HDL-C (OR 0.182; 95% CI 0.043–0.775; $P=0.021$) were the main factors for the elderly risk factors for the development of IS in patients with HTN-T2DM, as shown in Table 2 and Fig. 2.

Diagnostic value of independent risk factors for the occurrence of IS in HTN-T2DM in the elderly

The factors with significance in multifactorial logistic regression analysis were analyzed by ROC curves. The results in Table 3 showed that the areas under the ROC curve (AUC) of FIB, HDL-C and HHcy alone for diagnosing elderly stroke combined with HTN-T2DM occurring IS were 0.704 (0.604–0.803), 0.640 (0.538–0.743) and 0.598 (0.541–0.655). Combined diagnosis of the three risk factors gives an area under the ROC curve (AUC) of 0.784 (0.700–0.868), which is significantly higher than the

Table 1 General clinical data of the study population

Characteristics	Non-stroke group ($n = 56$)	Stroke group ($n = 56$)	*P* values
Demographic characteristics			
Age, years, (mean (SD))	71.50 ± 7.18	71.21 ± 6.23	0.822
BMI, kg/m^2, (mean (SD))	24.78 ± 2.80	24.83 ± 2.94	0.924
Gender, n (%)			
Female	26 (46.43%)	22 (39.29%)	0.445
Male	30 (53.57%)	34 (60.71%)	
Marital status, n (%)			
Single	9 (16.07%)	9 (16.07%)	1.000
Married	47 (83.93%)	47 (83.93%)	
Residential location, n (%)			0.127
Countryside	20 (35.71%)	28 (50.00%)	
Downtown	36 (64.29%)	28 (50.00%)	
Educational background, n(%)			0.576
Below primary education	33 (58.93%)	32 (57.14%)	
Junior high school education	14 (25.00%)	11 (19.64%)	
High school education or above	9 (16.07%)	13 (23.21%)	
Smoking, n (%)			0.102
No smoking	48 (85.71%)	41 (73.21%)	
Smoking	8 (14.29%)	15 (26.79%)	
Drinking, n (%)			0.051
No drinking	55 (98.21%)	50 (89.29%)	
Drinking	1 (1.79%)	6 (10.71%)	
Disease duration			
Duration of HTN, years, (median [IQR])	8.00 (3.00,10.00)	5.00 (5.00,8.00)	0.739
Duration of T2DM, years, (median [IQR])	8.00 (4.75,10.00)	8.00 (4.75,10.00)	0.097
Vascular risk factors, n (%)			
HLP, n (%)	15 (26.79%)	20 (35.71%)	0.308
AF, n (%)	3 (5.36%)	4 (7.14%)	0.696
HHcy, n (%)	1 (1.79%)	12 (21.43%)	< 0.001
CHD, n (%)	10 (17.86%)	5 (8.93%)	0.165
Laboratory parameters			
PLT, 10^9/L, (mean (SD))	231.11 ± 69.16	232.75 ± 54.88	0.890
Hb, g/L, (median [IQR])	133.00 (123.75,142.25)	129.50 (123.00,145.00)	0.511
PCT, %, (median [IQR])	0.20 (0.18,0.24)	0.20 (0.18,0.23)	0.919
D-dimer, mg/L, (median [IQR])	0.66 (0.33,0.94)	0.58 (0.28,1.32)	0.696
UA, μmol/L, (median [IQR])	377.40 (318.95,446.50)	378.66 (313.32,395.00)	0.340
HCT, %, (median [IQR])	0.40 (0.38,0.43)	0.39 (0.37,0.43)	0.448
PDW, fL, (mean (SD))	16.13 ± 0.41	16.06 ± 0.41	0.411
MPV, fL, (mean (SD))	9.34 ± 1.26	9.04 ± 1.03	0.180
PT, s, (median [IQR])	10.90 (10.40,11.43)	10.80 (10.40,11.10)	0.269
INR, (median [IQR])	0.95 (0.90,0.99)	0.93 (0.90,0.96)	0.165
FIB, mg/L, (median [IQR])	3.25 (2.77,3.73)	4.91 (3.35,5.58)	< 0.001
APTT, s, (median [IQR])	25.70 (24.48,26.52)	25.50 (24.48,26.00)	0.400
TT, s, (median [IQR])	18.10 (17.40,18.72)	17.95 (17.25,18.30)	0.349
HbA1c, %, (median [IQR])	8.05 (6.90,10.45)	8.25 (7.20,8.60)	0.588
ALB, g/L, (median [IQR])	38.60 (36.45,41.15)	38.85 (37.18,41.12)	0.703
TC, mmol/L, (mean (SD))	4.65 ± 1.19	4.74 ± 1.41	0.736
TG, mmol/L, (median [IQR])	1.60 (1.15,2.45)	1.64 (1.26,2.62)	0.274
HDL-C, mmol/L, (median [IQR])	1.06 (0.89,1.39)	0.95 (0.80,1.13)	0.010
LDL-C, mmol/L, (median [IQR])	3.03 (2.27,3.74)	3.08 (2.40,3.92)	0.841

Abbreviations: *BMI* Body mass index, *HLP* Hyperlipidemia, *AF* Atrial fibrillation, *HHcy* Hyperhomocysteinemia, *CHD* Coronary heart disease, *PLT* Blood platelet, *UA* Blood uric acid, *HCT* Hematocrit, *PDW* Platelet distribution width, *MPV* Mean platelet volume, *PT* Prothrombin time, *INR* International normalized ratio, *FIB* Fibrinogen, *APTT* Activated partial thromboplastin time, *TT* Thrombin time, *HbA1c* Glycosylated hemoglobin, *ALB* Albumin, *TC* Total cholesterol, *TG* Triglyceride, *HDL-C* High-density lipoprotein cholesterol, *LDL-C* Low-density lipoprotein cholesterol

Table 2 Multifactorial analysis of elderly patients with HTN-T2DM

	B	SE	Wald	OR	95%CI	P
HHcy	2.829	1.099	6.625	16.936	1.946–146.071	0.010
FIB	0.573	0.183	9.763	1.773	1.238–2.540	0.002
HDL-C	-1.706	0.740	5.313	0.182	0.043–0.775	0.021

Abbreviations: *HHcy* Hyperhomocysteinemia, *FIB* Fibrinogen, *HDL-C* High-density lipoprotein cholesterol

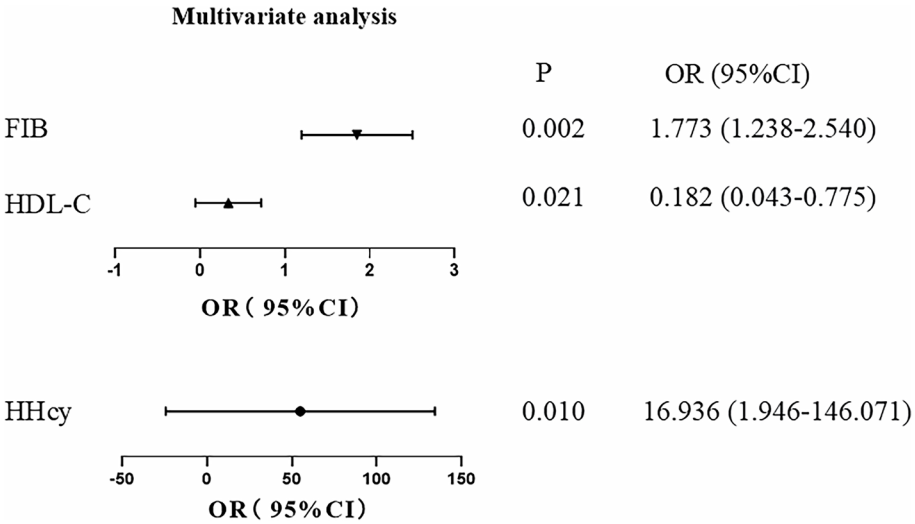

Fig. 2 Multifactorial analysis. Abbreviations: HHcy hyperhomocysteinemia; FIB fibrinogen; HDL-C high-density lipoprotein cholesterol

diagnosis of FIB, HDL-C, and HHcy alone and has a better diagnostic value. The ROC curve is shown in Fig. 3.

Discussion

This study aimed to examine the risk variables that influence the onset of is in older adults with HTN-T2DM. The results of this study indicated that FIB, HDL-C, and HHcy were independent factors influencing the onset of IS in older individuals with HTN-T2DM ($P < 0.05$) and were predictive of IS development. The predictive capacities of FIB, HDL-C, and HHcy for IS onset in older individuals with documented HTN-T2DM were 0.704, 0.640, and 0.598, respectively. The three risk factors together exhibited a greater predictive value than diagnosis alone, with a total diagnostic predictive ability of 0.784.

Significant risk factors for IS development include age, HTN, and T2DM [4]. As age increases, the body's resistance and function decline, rendering them more vulnerable to various illnesses and complications that lead to a poor prognosis. Research indicates that the presence of HTN increases the likelihood of developing T2DM and vice versa. T2DM is more likely to arise in people with HTN, and the incidence of HTN in T2DM is double that of non- T2DM individuals [11].

HTN and T2DM share an analogous pathophysiology, interact mutually, and their coexistence elevates the likelihood of developing IS. Peripheral vascular resistance increases owing to endothelial dysfunction,

Table 3 ROC curve analysis of risk of IS in elderly patients with HTN-T2DM

	Sensitivity	Specificity	Cutoff Point	AUC	95%CI
FIB	0.696	0.714	3.525	0.704	0.604–0.803
HDL-C	0.857	0.393	1.185	0.640	0.538–0.743
HHcy	0.214	0.982	0.684	0.598	0.541–0.655
FIB + HDL-C + HHcy	0.643	0.821	0.533	0.784	0.700–0.868

Abbreviations: *HHcy* Hyperhomocysteinemia, *FIB* Fibrinogen, *HDL-C* High-density lipoprotein cholesterol

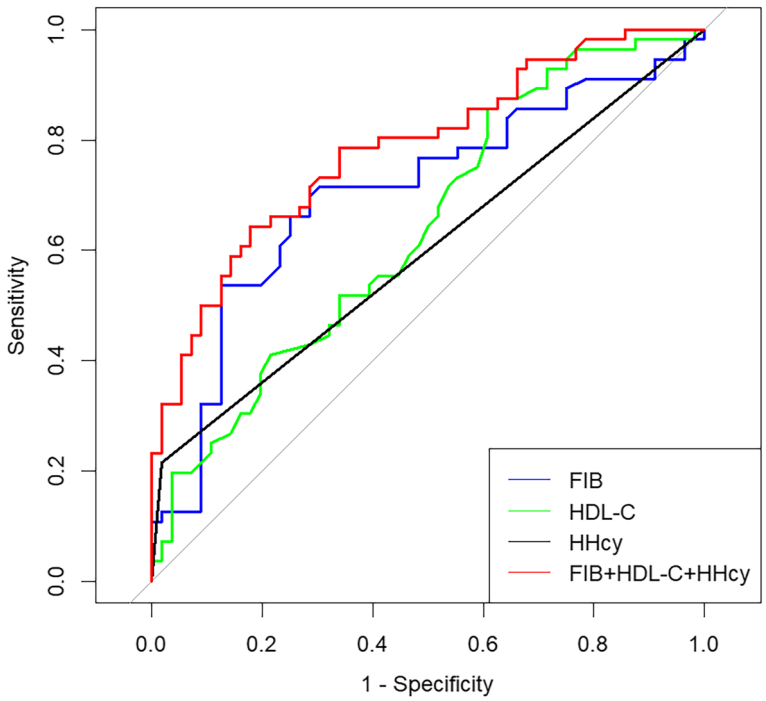

Fig. 3 Receiver operating characteristic curve of HTN-T2DM in elderly patients with stroke. The AUC was 0.704 (0.604–0.803) in blue line for FIB, 0.640 (0.538–0.743) in green line for HDL-C, 0.598 (0.541–0.655) in black line for HHcy, 0.784 (0.700–0.868) in red line for combined diagnosis (FIB, HDL-C, and HHcy)

atherosclerosis, vascular remodeling, and elevated blood volume. This subsequently affects the fluctuations in blood pressure. Hyperinsulinemia is the initial symptom of early-onset DM, which later develops into hyperglycemia. Resistance to vascular remodeling and increased blood volume are affected by DM. Early in the onset of diabetes, sodium reabsorption capacity increases and blood volume increases [12]. Hyperinsulinemia and hyperglycemia enhance the activity of the renin–angiotensin–aldosterone system and the development of angiotensin type I receptors in vascular tissues, contributing to vascular remodeling and leading to atherosclerosis of the arteries [13, 14]. Endothelial dysfunction complicated by hyperglycemia increases vasoconstrictor secretion, leading to a decrease in vascular smooth muscle cell tone, which further promotes leukocyte adherence, smooth muscle cell proliferation, and ultimately leads to resistance vascular remodeling and elevated blood pressure [15, 16]. HTN in conjunction with DM exacerbates endothelial cell dysfunction and impairs smooth muscle function [17]. Endothelial cell dysfunction compromises the barrier integrity of the blood and arterial walls, resulting in the progression of vasculopathy and atherosclerosis. Consequently, older adults with HTN-T2DM exhibit an elevated risk of developing IS.

FIB is a coagulation factor integral to the coagulation cascade, platelet aggregation, inflammatory response, tissue healing, and is a principal determinant of blood viscosity [18]. Augmented platelet aggregation, elevated blood concentration, heightened occurrence of arterial thrombosis, and facilitation of atherosclerotic plaque advancement. Increasing data suggests that fibrinogen may serve as a biomarker for thrombosis and inflammation [19]. FIB has been recognized as a risk factor for IS in population-based research [20, 21]. Previous research conducted by Indian researchers shown that plasma fibrinogen levels were significantly higher in individuals with acute ischemic stroke (AIS) in comparison to control subjects [22]. While it has been established that FIB functions as an acute phase protein inside the cerebral vasculature during inflammation, the precise mechanism of FIB's influence on IS remains uncertain [23]. Peycheva et al. evaluated FIB levels in 153 individuals, comparing stroke group with non-stroke group, and found a positive connection between FIB levels and the occurrence of IS [24]. Consistent with the findings of the current study, a cross-sectional analysis included 55 hypertensive patients with IS compared with 110 hypertensive patients without IS. The sensitivity of FIB for diagnosing IS in hypertensive patients was determined to be 70.0%, with a specificity of 57.1%, yielding a diagnostic power (AUC = 0.694)

[25]. Following the start of IS, blood viscosity increases as fibrin levels diminish; nevertheless, fibrin levels increase during an inflammatory response, rendering FIB less selective and infrequently used in isolation as a diagnostic predictor of IS [26].

High-density lipoprotein (HDL) is a complex mixture of proteins, lipids, hormones, vitamins, and microRNAs that exhibits anti-inflammatory, anti-thrombotic, antioxidant, and immunomodulatory properties [27]. HDL-C is a general term for the concentration of various cholesterol and cholesteryl esters in HDL. One of the main causes and risk factors of IS is large-artery atherosclerosis. HDL is resistant to large artery atherosclerosis. As HDL enters macrophages and smooth muscle cells through the bloodstream and crosses the endothelium, it facilitates the efflux of cholesterol, functions as an antioxidant and an anti-inflammatory, and reduces the severity of atherosclerosis [28]. Another defensive function of HDL-C is its role in transporting cholesterol from cells, such as macrophages or smooth muscle cells within the artery wall, back to the liver for processing, exhibiting oxidative and anti-inflammatory properties [29]. A national survey with 4422 adults aged 40 years and older revealed that HDL-C exhibited a negative correlation with IS when HDL-C were below 1.55 mmol/L, suggesting that maintaining an optimal HDL-C range may mitigate the risk of IS [30]. A hypertensive population was chosen as the study population in a study by Zhang et al. [31] and it was found that low HDL-C increased the incidence of IS, that HDL-C was negatively connected with first-time IS, and that HDL-C demonstrated a protective effect against the first occurrence of IS. Similar to the results of this study, HDL-C was lower in the stroke group than in the non-stroke group, and the difference between the two groups was significant. The conclusion of a cohort analysis indicates that lower HDL-C are substantially correlated with the onset of IS [32]. However, the correlation between HDL-C and IS remains controversial. Jun et al. [33] stated in their study that there was no significant correlation between HDL-C and the incidence of IS. It is possible that there are differences in the studies in terms of factors, such as the selection of study subjects, sample size, or research methods, and it is not yet consistent whether HDL-C and IS produce a relationship. Therefore, the relationship between HDL-C and IS requires further research.

HHcy is a metabolic disorder characterized by disturbances in the methionine cycle that results in elevated levels of homocysteine (Hcy) in vivo. Hcy exerts effects on endothelial cells, stimulates the proliferation of smooth muscle cells, promotes the oxidation of low-density lipoproteins, and enhances collagen synthesis as well as procoagulant factor activity. These processes contribute to impaired homeostasis of the vascular endothelium [34]. HHcy has been linked to atherosclerotic thrombosis and identified as a risk factor for stroke. By boosting the expression of IL-8, T-lymphocyte and neutrophil chemotactic chemicals in endothelial cells, and activating factors like cytokines, chemokines, and leukocyte adhesion molecules, hcy promotes inflammation and sclerosis in the vasculature [35]. In the second mechanism, HHcy can influence the development of atherosclerosis by inducing intracellular production of superoxide through oxidative stress. This process leads to the generation of lipid peroxides, which in turn cause an abnormal vasodilatory response [36]. Another mechanism involves endoplasmic reticulum (ER) stress. Elevated concentrations of homocysteine activate ER stress, which plays a significant role in atherogenesis and the progression of atherosclerosis through dysregulation of lipid metabolism, apoptotic cell death, and inflammation [37]. A cohort study with a 17-year follow-up demonstrated that the risk of IS was elevated with Hcy levels between 10 and 15 μmol/L compared with Hcy levels below 10 μmol/L. In the hypertensive subgroup, the risk of IS markedly increased with Hcy levels exceeding 15 μmol/L, and Hcy significantly enhanced the predictive capability of conventional stroke risk factors. A further investigation found that greater levels of Hcy enhanced the likelihood of recurrent IS [38]. Generally, Hcy levels beyond 10 to 15 μmol/L are classified as HHcy [39]. A study of typological subgroups in IS revealed that elevated Hcy levels correlated with an increased risk of small-artery occlusive stroke; however, this association was not observed in large-artery atherosclerotic stroke or cardiogenic embolic stroke [40]. The results of this study obtained that HHcy can influence the occurrence of IS, similar to the results of other researchers [41]. Some studies have included young patients without diabetes and hypertension as research subjects, concluding that elevated Hcy levels are closely associated with an increased risk of IS [42]. Therefore, we can infer that the impact of Hcy on IS risk is not influenced by age, hypertension, or diabetes. Furthermore, raises the risk of death, disability, bleeding, and functional impairment [43].

This study utilized propensity score matching to mitigate the influence of confounding factors and to enhance the accuracy of the findings. Nonetheless, it is crucial to recognize the specific limitations intrinsic to this research. As this was a retrospective study, future investigations should incorporate follow-up assessments and consider lifestyle factors to comprehensively explore the risk factors for IS in patients with HTN-T2DM. This approach aimed to further refine the accuracy of our results. Additionally, extending the duration of the study and increasing the sample size are essential steps toward bolstering the credibility of our conclusions.

In conclusion, FIB, HHcy, and HDL-C serve as valuable indicators for screening and identifying ischemic stroke risk in elderly patients with HTN-T2DM. It facilitates the screening and identification of high-risk target populations, providing them with pertinent treatments, such as illness education, healthy lifestyle coaching, and standardized management of chronic conditions.

Conclusion

This study demonstrated that FIB, HDL-C, and HHcy are independent risk factors for stroke in elderly patients with HTN-T2DM. The combination of FIB, HDL-C, and HHcy has predictive value for the occurrence of stroke in elderly patients with HTN-T2DM.

Abbreviations

AF	Atrial fibrillation
ALB	Albumin
APTT	Activated partial thromboplastin time
BMI	Body mass index
CHD	Coronary heart disease
DM	Diabetes mellitus
HTN-DM	Hypertension with diabetes mellitus
HTN-T2DM	Hypertension and type 2 diabetes mellitus
FIB	Fibrinogen
HbA1c	Glycosylated hemoglobin
HCT	Hematocrit
Hcy	Homocysteine
HDL-C	High-density lipoprotein cholesterol
HHcy	Hyperhomocysteinemia
HLP	Hyperlipidemia
HTN	Hypertension
INR	International normalized ratio
IS	Ischemic stroke
LDL-C	Low-density lipoprotein cholesterol
MPV	Mean platelet volume
PCT	Thrombocytocrit
PDW	Platelet distribution width
PLT	Blood platelet
PT	Prothrombin time
TC	Total cholesterol
TG	Triglyceride
TT	Thrombin time
T2DM	Type 2 diabetes mellitus
UA	Blood uric acid

Acknowledgements
The author would like to thank the neurology Department and endocrinology Department of Jiangmen Central Hospital for providing data support, and the chief nurse Gao Juanbi, the chief nurse Wang Haiqin, Zhu Minfang, doctor Liu Huazhao and the other medical staff for their support. Thank you for the help of the medical staff of the third district of the Department of Neurology Medicine.

Disclosure of conflict of interest
The authors declared that there was no conflict of interest associated with the manuscript.

Authors' contributions
LCJ wrote the study concept, data acquisition, writing the manuscript. OXL and CYZ were involved in study concept,critical revision of manuscript. LCJ, OXL and CYZ analysis and interpretation of data. YTH reviewed and finalized the manuscript.

Funding
This study was not supported by any sponsor or funding.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was approved by the Ethics Committee of Jiangmen Central Hospital (Approval No.: Jiangxin Medical Ethics Review [2024] 177A). All methods were performed in accordance with the Declaration of Helsinki, and written informed consent was obtained from the patients after explaining the purpose of the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 24 October 2024 Accepted: 3 January 2025
Published online: 24 January 2025

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