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Research article

Nonlinear relationship between triglycerides and cognitive function after acute ischemic stroke among older adults

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ABSTRACT

Background: Although studies have explored the association between triglyceride levels and cognitive function after acute ischemic stroke (AIS), the results have been conflicting. Therefore, the purpose of this study was to investigate the relationship between triglyceride levels and cognitive function after AIS among older adults.

Methods: This is an observational cross-sectional study. From November 2022 to June 2023, we consecutively collected patients diagnosed with AIS in China. Triglyceride levels were measured within 24 h of admission. The Mini-Mental State Examination (MMSE) was used to assess cognitive function. Nonlinear associations between triglyceride levels and cognitive function were assessed using smooth curve fitting and threshold effect analysis.

Results: In this study, a total of 221 patients (mean ± SD: 70.64 ± 7.43 years) with AIS were consecutively recruited, among whom 144 (65.16%) were male. Among the 221 recruited patients, 102 (46.15%) had cognitive impairment. Triglyceride levels and cognitive impairment were found to have a nonlinear association after controlling for potential confounders, with an inflection point at 0.8 mmol/L. Below the inflection point, triglyceride levels were positively correlated with MMSE scores (β = 14.11, 95% confidence interval [CI] = 2.33–25.89, P = 0.020). However, above the inflection point, the correlation between MMSE score and triglyceride levels was not statistically significant (β = 1.04, 95% CI = −1.27 – 3.34, P = 0.380).

Conclusion: There is a nonlinear association between triglyceride levels and cognitive function after AIS in older adults. Triglyceride was positively connected with cognitive function when it was less than 0.8 mmol/L.

1. Introduction

Stroke ranks as the second most common cause of death and disability worldwide [1]. Acute ischemic stroke (AIS) is the

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predominant type, accounting for an estimated incidence rate of approximately 72% and a prevalence rate of around 84% [2]. AIS refers to a clinical syndrome characterized by sudden neurological dysfunction resulting from impaired blood supply to the brain. Two-thirds of stroke cases occur among older adults [3].

The prevalence of cognitive impairment after stroke varied widely, ranging from around 20%–80%, due to differences in national, ethnic, and diagnostic criteria [4,5]. Cognitive impairment represents a common complication of ischemic stroke and is characterized by impairments in language, executive functions, memory, calculation, and comprehension [6,7]. Severely, it may progress to dementia. Older individuals with cognitive impairment encounter challenges in their community reintegration, increasing the risks of stroke recurrence and mortality. This situation places a significant burden on both patients and caregivers [8,9].

Clinical blood lipid testing typically involves triglycerides, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Triglycerides are the primary form of dietary fat in the human body and are more susceptible to lifestyle habits, particularly diet and exercise [10]. Therefore, measuring triglyceride levels can serve as a more sensitive indicator to monitor changes in blood lipid levels and provide data for adjusting nursing strategies. Different lipids may have varying mechanisms and effects on cognitive function [11]. Triglycerides may impact cognition by disrupting leptin, causing dysfunction in the brain-blood barrier, or contributing to pathologies such as cerebral β-amyloid protein/tau [12,13]. HDL-C and LDL-C may potentially reduce vascular Aβ accumulation, leading to Aβ-induced endocarditis [14]. Furthermore, elevated triglyceride levels may alter lipid metabolism pathways and efficiency, leading to structural and functional changes in LDL-C and HDL-C. It may increase the levels of LDL and weaken the cholesterol transport reversal and antioxidant capacity associated with HDL [15].

Triglycerides are a common lipid component primarily stored in adipose tissue and the liver. It has been implicated in the development of various diseases, including vascular disorders. In recent years, there has been considerable interest in exploring the association between triglycerides and cognitive function in older adults. However, studies examining the connection between triglyceride levels and cognition showed inconsistent findings [13]. A previous study involving 8.6 thousand participants, the findings indicated that older adults with triglyceride levels in the normal to high-normal range were less likely to develop cognitive decline than those with lower triglyceride levels [16]. Conversely, some studies have indicated triglycerides are negatively correlated with cognitive function in nondemented aging adults [17]. The current research on the relationship between triglycerides and cognitive function is limited and unclear, indicating the need for further studies to explore this relationship.

We hypothesized that both high and low triglyceride levels are associated with an increased risk of cognitive impairment in AIS patients. Therefore, the objective of this study was to investigate the relationship between triglyceride levels and cognitive function among older adults following an acute ischemic stroke. Furthermore, this study may provide a scientific reference for clinical practice for clinically delaying cognitive function decline in AIS patients by controlling triglyceride levels.

2. Materials and methods

2.1. Study design and participants

This observational cross-sectional study was conducted at Shenzhen Second People's Hospital. From November 2022 to June 2023, consecutive collection of inpatients with AIS was performed. Following were the inclusion criteria for this study: (1) age ≥60 years; (2) admission within 7 days following the occurrence of AIS symptoms; and (3) a confirmed diagnosis of AIS based on CT or MRI brain scans. The following criteria were used for exclusion: (1) presence of aphasia that impeded the assessment of cognitive function; (2) without education information; (3) history of mental disorders. The Ethics Committee of Shenzhen Second People's Hospital has granted approval for this study. All participants or their legal guardians or family members have provided informed consent. This was registered in the Clinical Trials (Registration no: NCT05465980) and Chinese Clinical Trial Registry (Registration no: ChiCTR2200064375).

2.2. Data collection

2.2.1. Covariates

On admission, demographic and clinical data, including age, gender, body mass index (BMI), education, smoking status, alcohol use, as well as medical history of hypertension, diabetes, hyperlipemia, atrial fibrillation, and stroke were documented. Within 24 h after admission, measurements including systolic blood pressure (SBP), triglyceride (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), homocysteine (HCY), high-sensitivity C-reactive protein (hs-CRP) were obtained. Within 24 h of admission, the National Institutes of Health Stroke Scale (NIHSS) was used to determine the severity of the stroke, and the modified Rankin scale (mRS) was used to assess functional outcomes. Both doctors and examiners were blinded so that they did not know whether the patient was a participant.

2.2.2. Cognitive assessment

Cognitive assessment was performed during the enrollment phase through face-to-face interviews conducted by well-trained senior postgraduate medical students. We used The Mini-Mental State Examination (MMSE) to assess cognitive function after 24 h within 7 days after admission. The MMSE was utilized as the standardized tool for evaluating cognitive function. It consists of six cognitive domains including orientation, immediate memory, attention and calculation, recall, language (language repetition, three-step instruction, reading comprehension, writing), and copying (visuospatial). The scale comprises a total of 30 items, with a maximum score of 30. Subsequently, cognitive impairment was identified when stroke survivors obtained an MMSE score below 27 [18].

2.3. Statistical analysis

For normally distributed data, continuous variables were reported as mean ± standard deviation (SD), or as median (range) for skewed distribution. We divided triglyceride into 3 group based on tertiles. To compare the variables between different triglyceride groups, categorical variables were analyzed using the chi-square test, normally distributed variables were assessed using one-way ANOVA, and skewed distribution variables were evaluated using the Kruskal-Wallis H test. To explore the linear relationship between triglycerides and cognitive function, three models were developed by multiple regressions: Model 1 (no adjustment for covariates), Model 2(adjustment for sociodemographic variables), and Model 3 (adjustment for all potential confounders variables, including age, gender, BMI, education, alcohol, admission NIHSS, admission mRS, TC, HDL, LDL and previous diabetes.). Effect sizes were reported with β coefficients (β), 95% confidence interval (CI), and P value. Potential nonlinearity between triglycerides and cognitive function was addressed using smooth curve fitting with the penalized spline method and the generalized additive model (GAM). Furthermore, a two-piecewise binary linear regression model was employed to examine potential nonlinearity. Using exploratory analysis, which involve moving the trial turning point along the pre-defined interval and selecting the one that generated the greatest model likelihood, the turning point for the triglyceride was identified. The one-line linear regression model and the two-piece-wise linear model were contrasted using a log-likelihood ratio test. Data were analyzed with the use of the statistical packages R (The R Foundation; http://www.r-project.org; version 4.2.0) and EmpowerStats (www.empowerstats.net, X&Y solutions, Inc. Boston, Massachusetts). P-value less than 0.05 (two-sided) was considered statistically significant.

3. Results

3.1. Characteristics between triglyceride tertiles

We consecutively recruited 221 inpatients with AIS (Fig. 1), aged 60–96 years old (mean ± SD: 70.64 ± 7.43 years), including 144 (65.16%) men. The triglyceride was divided into 3 tertiles, low (0.33–0.97 mmol/L), middle (1.00–1.32 mmol/L), and high (1.33–7.04 mmol/L), respectively. Statistically significant differences were found in TC, HDL, LDL, and previous diabetes among different triglyceride tertiles ($P < 0.05$) (Table 1).

3.2. Characteristics of the cognitive impairment groups and non-cognitive impairment groups

Among the 221 AIS participants, 102 (46.15%) of them had cognitive impairment. The two groups showed significant differences in NIHSS score, education, and admission mRS between the two groups ($P < 0.05$) (Table 2).

3.3. Relationships between triglycerides and cognitive function

To explore the association between triglyceride and cognitive function, a binary logistic regression analysis was conducted. In Model 1, triglyceride showed no relationship with cognitive function ($\beta = 0.71$, 95% CI: −0.26 to 1.68, $P = 0.156$). The findings remained consistent in Model 2, which adjusted for age, gender, and BMI ($\beta = 0.58$, 95% CI: −0.93 to 1.56, $P = 0.243$). Similarly, in Model 3, included adjustments for all potential factors, no significant association was found ($\beta = 0.51$, 95% CI: −0.57 to 1.60, $P = 0.354$). Additionally, sensitivity analysis using triglyceride as a categorical variable (tertiles) also found no significant results after adjusting for other factors ($P > 0.05$) (Table 3).

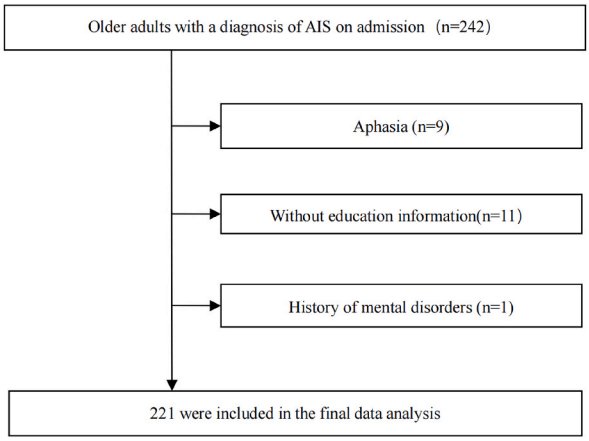

Fig. 1. Flow chart of study population.

Table 1
Baseline characteristics of participants.

Triglyceride tertile , mmol/L	Low (0.33–0.97)	Middle (1.00–1.32)	High (1.33–7.04)	P value
No. of subjects	63	61	66	
Age, mean (SD), year	72.4 (8.1)	71.0 (7.1)	70.2 (7.6)	0.264
SBP, mean (SD), mmHg	135.2 (20.7)	136.6 (21.1)	139.5 (18.1)	0.462
TC, mean (SD), mmol/L	3.6 (0.8)	4.0 (1.1)	4.5 (1.3)	<0.001
HDL, mean (SD), mmol/L	1.3 (0.3)	1.2 (0.2)	1.0 (0.2)	<0.001
LDL, mean (SD), mmol/L	2.1 (0.6)	2.5 (1.0)	2.9 (1.2)	<0.001
HCY, mean (SD), umol/L	14.3 (4.3)	14.8 (7.7)	13.4 (4.4)	0.462
hs-CRP, median (min–max), mg/L	1.4 (0.2–185.1)	2.3 (0.5–172.1)	1.4 (0.4–155.8)	0.372
BMI, mean (SD), kg/㎡	23.6 (3.3)	24.0 (2.9)	24.8 (3.0)	0.103
NIHSS score, median (min-max)	1.0 (0–20.0)	2.0 (0–11.0)	1.0 (0–14.0)	0.284
MMSE score, median (min-max)	27.0 (5.0–30.0)	27.0 (6.0–30.0)	28.0 (12.0–30.0)	0.256
Gender, n (%)				0.193
Female	16 (25.4%)	23 (37.7%)	26 (39.4%)	
Male	47 (74.6%)	38 (62.3%)	40 (60.6%)	
Smoke, n (%)				0.505
No	33 (52.4%)	38 (62.3%)	36 (54.5%)	
Yes	30 (47.6%)	23 (37.7%)	30 (45.5%)	
Alcohol, n (%)				0.898
No	37 (58.7%)	38 (62.3%)	41 (62.1%)	
Yes	26 (41.3%)	23 (37.7%)	25 (37.9%)	
Previous hypertension, n (%)				0.567
No	19 (30.2%)	21 (34.4%)	17 (25.8%)	
Yes	44 (69.8%)	40 (65.6%)	49 (74.2%)	
Previous diabetes, n (%)				0.039
No	51 (81.0%)	47 (77.0%)	41 (62.1%)	
Yes	12 (19.0%)	14 (23.0%)	25 (37.9%)	
Previous hyperlipemia, n (%)				0.894
No	57 (90.5%)	54 (88.5%)	60 (90.9%)	
Yes	6 (9.5%)	7 (11.5%)	6 (9.1%)	
Previous atrial fibrillation, n (%)				0.320
No	60 (95.2%)	57 (93.4%)	65 (98.5%)	
Yes	3 (4.8%)	4 (6.6%)	1 (1.5%)	
Previous stroke, n (%)				0.075
No	36 (57.1%)	42 (68.9%)	50 (75.8%)	
Yes	27 (42.9%)	19 (31.1%)	16 (24.2%)	
Education, n (%)				0.579
Primary or below	19 (30.2%)	20 (32.8%)	19 (28.8%)	
Junior high	18 (28.6%)	8 (13.1%)	13 (19.7%)	
Vocational or high	18 (28.6%)	16 (26.2%)	18 (27.3%)	
Junior college	3 (4.8%)	10 (16.4%)	8 (12.1%)	
Undergraduate	4 (6.3%)	6 (9.8%)	7 (10.6%)	
Master or above	1 (1.6%)	1 (1.6%)	1 (1.5%)	
Admission mRS score, n (%)				0.266
0	9 (14.3%)	9 (14.8%)	15 (22.7%)	
1	30 (47.6%)	26 (42.6%)	30 (45.5%)	
2	7 (11.1%)	15 (24.6%)	8 (12.1%)	
3	7 (11.1%)	4 (6.6%)	4 (6.1%)	
4	10 (15.9%)	6 (9.8%)	6 (9.1%)	
5	0 (0)	1 (1.6%)	3 (4.5%)	

Continuous variables are presented as mean ± standard deviation or median (quartile). Categorical data are presented as numbers (percentages). Abbreviations: *SBP* Systolic blood pressure, *TC* total cholesterol, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *HCY* homocysteine, *hs-CRP* high-sensitivity C-reactive protein, *BMI* body mass index, *NIHSS* National Institutes of Health Stroke Scale, *mRS* modified Rankin Scale, *MMSE* Mini-mental state examination.

3.4. Nonlinear connection studies

We explored the nonlinear connection between triglyceride levels and cognitive function (Fig. 2). Triglyceride levels and cognitive impairment were found to have a nonlinear connection after controlling for potential variables($P = 0.029$). We determined the inflection point to be at 0.8 mol/L by utilizing a two-piecewise linear regression model. Below the inflection point, triglyceride levels were positively correlated with MMSE scores ($\beta = 14.11$, 95% confidence interval [CI] = 2.33–25.89, $P = 0.020$). However, above the inflection point, the correlation between MMSE score and triglyceride levels was not statistically significant ($\beta = 1.04$, 95% CI = −1.27-3.34, $P = 0.380$). (Table 4).

Table 2
Characteristics of the cognitive impairment and non-cognitive impairment groups.

Characteristic	Non-PSCI	PSCI	Standardize diff.	P value
No. of subjects	119	102		
Age, mean (SD), year	70.1 (7.3)	71.3 (7.6)	0.2 (−0.1, 0.4)	0.239
SBP, mean (SD), mmHg	136.7 (20.6)	138.6 (19.2)	0.1 (−0.2, 0.4)	0.483
Triglyceride, mean (SD), mmol/L	1.3 (0.7)	1.3 (0.9)	0 (−0.2, 0.3)	0.766
TC, mean (SD), mmol/L	4.1 (1.2)	4.0 (1.1)	0.1 (−0.2, 0.3)	0.703
HDL, mean (SD), mmol/L	1.1 (0.2)	1.2 (0.3)	0.2 (−0.1, 0.5)	0.107
LDL, mean (SD), mmol/L	2.6 (1.1)	2.4 (0.9)	0.1 (−0.2, 0.4)	0.405
HCY, mean (SD), umol/L	14.0 (6.1)	14.8 (8.7)	0.1 (−0.2, 0.4)	0.492
hs-CRP, median (min–max), mg/L	1.4 (0.2–185.1)	2.2 (0.4–80.4)	0.2 (−0.2, 0.5)	0.143
BMI, mean (SD), kg/m^2	24.3 (2.8)	24.3 (3.4)	0 (−0.3, 0.3)	0.983
NIHSS score, median (min-max)	1.0 (0–20.0)	2.0 (0–14.0)	0.3 (0.1, 0.6)	0.008
Gender, n (%)			0.1 (−0.1, 0.4)	0.327
Female	38 (31.9%)	39 (38.2%)		
Male	81 (68.1%)	63 (61.8%)		
Smoke, n (%)			0 (−0.3, 0.3)	0.967
No	68 (57.1%)	58 (56.9%)		
Yes	51 (42.9%)	44 (43.1%)		
Alcohol, n (%)			0.1 (−0.2, 0.3)	0.623
No	72 (60.5%)	65 (63.7%)		
Yes	47 (39.5%)	37 (36.3%)		
Previous hypertension, n (%)			0(-0.2, 0.3)	0.841
No	37 (31.1%)	33 (32.4%)		
Yes	82 (68.9%)	69 (67.6%)		
Previous diabetes, n (%)			0.1 (−0.2, 0.4)	0.516
No	84 (70.6%)	76 (74.5%)		
Yes	35 (29.4%)	26 (25.5%)		
Previous hyperlipemia, n (%)			0.2 (0, 0.5)	0.089
No	104 (87.4%)	96 (94.1%)		
Yes	15 (12.6%)	6 (5.9%)		
Previous atrial fibrillation, n (%)			0.3 (0, 0.5)	0.084
No	117 (98.3%)	95 (93.1%)		
Yes	2 (1.7%)	7 (6.9%)		
Previous stroke, n (%)			0.1 (−0.1, 0.4)	0.351
No	84 (70.6%)	66 (64.7%)		
Yes	35 (29.4%)	36 (35.3%)		
Education, n (%)			0.6 (0.3, 0.9)	0.002
Primary or below	24 (20.2%)	42 (41.2%)		
Junior high	20 (16.8%)	23 (22.5%)		
Vocational or high	40 (33.6%)	23 (22.5%)		
J unior college	18 (15.1%)	7 (6.9%)		
Undergraduate	14 (11.8%)	7 (6.9%)		
Master or above	3 (2.5%)	0 (0%)		
Admission mRS score, n (%)			0.5 (0.2, 0.7)	0.039
0	24 (20.2%)	14 (13.7%)		
1	61 (51.3%)	40 (39.2%)		
2	18 (15.1%)	17 (16.7%)		
3	7 (5.9%)	9 (8.8%)		
4	8 (6.7%)	18 (17.6%)		
5	1 (0.8%)	4 (3.9%)		

Continuous variables are presented as mean ± standard deviation or median (quartile). Categorical data are presented as numbers (percentages).
Abbreviations: *SBP* Systolic blood pressure, *TC* total cholesterol, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *HCY* homocysteine, *hs-CRP* high-sensitivity C-reactive protein, *BMI* body mass index, *NIHSS* National Institutes of Health Stroke Scale, *mRS* modified Rankin Scale, *MMSE* Mini-mental state examination, *PSCI* post-stroke cognitive impairment.

4. Discussion

This study utilized smooth curve fitting and threshold effect analysis to examine the association between triglyceride levels and cognitive function among older adults after AIS. After controlling for potential variables, it did not appear to be significantly correlated between triglyceride levels and cognitive function. Similarly, when considering triglyceride levels as a categorical variable, no substantial findings were observed. However, a nonlinear relationship was discovered between triglyceride levels and cognitive function, with distinct correlations on either side of the inflection point (triglyceride = 0.8 mmol/L). Specifically, below the inflection point, a positive association was observed between triglyceride levels and MMSE score, whereas, above the inflection point, no statistically significant relationship was found.

Previous studies have shown that the association between triglyceride levels and cognitive function has been a topic of ongoing debate. Some studies showed that there was no significant relationship between triglyceride levels and cognitive function [19–21],

Table 3
Relationships between triglyceride and MMSE.

Exposure	Model 1 β (95%CI) P value	Model 2 β(95%CI) P value	Model 3 β (95%CI) P value
Triglyceride, mmol/L	0.71 (−0.26, 1.68) 0.156	0.58 (−0.39, 1.56) 0.243	0.51 (−0.57, 1.60) 0.354
Triglyceride tertile, mmol/L			
Low	Ref	Ref	Ref
Middle	1.34 (−0.60, 3.27) 0.178	1.19 (−0.75, 3.14) 0.229	0.63 (−1.36, 2.62) 0.534
High	2.36 (0.46, 4.26) 0.016	2.10 (0.17, 4.04) 0.034	1.79 (−0.55, 4.14) 0.136
P for trend	1.18 (0.23, 2.13) 0.016	1.05 (0.09, 2.01) 0.034	0.87 (−0.31, 2.05) 0.151

Model 1: Non-adjusted model.
Model 2: Adjusted for age, gender and BMI.
Model 3: Adjusted for age, gender, BMI, education, alcohol, admission NIHSS, admission mRS, TC, HDL, LDL, and previous diabetes.
Abbreviations: *BMI* body mass index, *TC* total cholesterol, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *NIHSS* National Institutes of Health Stroke Scale, *mRS* modified Rankin Scale, *MMSE* Mini-mental state examination, *CI* Confidence, *Ref* Reference.

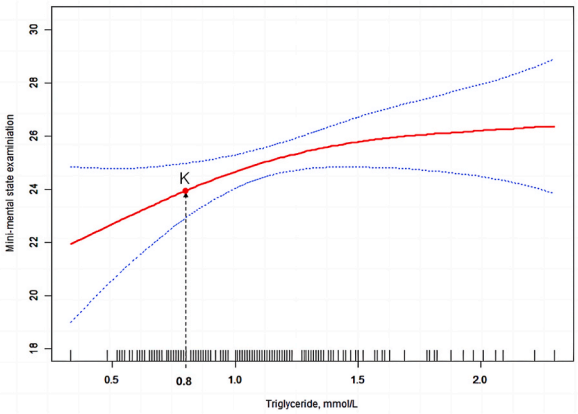

Fig. 2. Nonlinear association between the triglyceride and MMSE.
The solid red line represents the smooth curve fit between variables. Blue bands represent the 95% confidence interval from the fit. K: Infection point of triglyceride (0.8 mmol/L). Adjusted for age, gender, BMI, education, alcohol, admission NIHSS, admission mRS, TC, HDL, LDL, and previous diabetes. Abbreviations:*BMI* body mass index, *TC* total cholesterol, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *NIHSS* National Institutes of Health Stroke Scale, *mRS* modified Rankin Scale, *MMSE* Mini-mental state examination.

Table 4
Nonlinear association between the triglyceride and MMSE.

Outcome	β, (95%CI) P value
Model I	1.89 (−0.29, 4.07) 0.092
Model II	
Infection point of triglyceride, mmol/L	0.8
<0.8	14.11 (2.33, 25.89) 0.020
>0.8	1.04 (−1.27, 3.34) 0.380
P for log likelihood ratio test	0.029

Model I: Fitting model by standard linear regression.
Model II: Fitting model by two-piecewise linear regression.
Model I and Model II are adjusted for age, gender, BMI, education, alcohol, admission NIHSS, admission mRS, TC, HDL, LDL, and previous diabetes.
Abbreviations: *BMI* body mass index, *TC* total cholesterol, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *NIHSS* National Institutes of Health Stroke Scale, *mRS* modified Rankin Scale, *MMSE* Mini-mental state examination, *CI* Confidence.

even in meta-analyses [20]. This finding may have been due to the small sample size, as just two references were included in the investigations. However, other studies have found higher levels of triglycerides are associated with better cognitive function. Yin et al. [22]. revealed a significant reduction in cognitive impairment when comparing the highest quartile of plasma triglyceride concentration to the lowest quartile (OR: 0.52, 95% CI: 0.33–0.84). He et al. [23] investigated a large cohort from the UK Biobank (n = 407, 190) and discovered that lower baseline triglyceride concentrations were associated with an increased risk of cognitive impairment (HR 0.924, 95% CI: 0.882–0.967, p = 0.019). Conversely, Deng et al. [24] and Yang et al. observed significantly higher mean

triglyceride levels in the Parkinson's disease mild cognitive impairment patients compared to those without cognitive impairment. Furthermore, dose-response analysis revealed that for every 3 mmol/L increase in triglyceride levels, the pooled relative risk (RR) for cognitive impairment was 1.12 (95% CI: 1.05–1.21) [25].

Previous studies have predominantly focused on investigating the linear relationship between triglyceride levels and cognitive function. However, the association may not simply follow a linear pattern but rather a nonlinear relationship. Our findings suggested a non-linear association. Zhu et al. has explored the presence of a U-shaped relationship, which, although statistically significant, has shown a small effect size, indicating limited clinical relevance (RR 0.97,95% CI 0.96–0.99) [26]. In contrast, Gong et al. found that the relationship is linear rather than curvilinear [27].

The divergent findings in this study may be attributed to multiple factors. Firstly, heterogeneity within the study populations plays a role. For example, in a study conducted by Robert S. Rosenson et al. [28], no association between triglycerides and incident cognitive impairment was found among White or Black men. However, among White women, triglycerides $\geq$150 mg/dL, compared to $<$100 mg/dL, were associated with a relative risk of 1.50 (95% CI 1.09–2.06). Among Black women, the relative risk was 1.21 (95% CI 0.93–1.57). Secondly, inconsistent assessment criteria may lead to significant variations in cognitive impairment prevalence, even resulting in a tenfold difference [29]. Additionally, the presence of confounding factors might obscure the observed relationships [30].

The mechanism of triglycerides in cognitive function has been studied. According to recent research, lipids are crucial to several physiological processes, including oxidative stress, lysosomal dysfunction, endoplasmic reticulum stress, and immunological response [31]. Lipids may operate as underlying mechanisms for neuroprotection by contributing to oxidative stress, chronic inflammation, and cytotoxic interactions with a-synuclein [24]. Moreover, elevated levels of triglycerides may disrupt the blood-brain barrier and correlate with increased amyloid-beta and tau protein pathology in the brain [32,33]. Triglycerides are prevalent in human cerebro-spinal fluid, readily penetrate the blood-brain barrier, and cause central leptin and insulin receptor resistance, which lowers cognition [34,35]. However, triglycerides can store excess calories and provide energy during necessary metabolic stress. Low levels of triglycerides may potentially influence neural repair [36].

In AIS patients, there is an inflection point region in the relationship between triglycerides and cognitive impairment, which has important clinical implications. Within the Chinese population, triglyceride level ranging from 1.7 to 2.3 mmol/L is regarded as marginally elevated [37]. Some studies have also demonstrated that maintaining high levels of normal blood lipids is associated with better cognitive function [38]. Nevertheless, the precise threshold for triglyceride intervention in the management of AIS patients with cognitive impairments remains uncertain. Our study aimed to addresses this question. Our results showed that the inflection point of the relationship between triglycerides and cognitive function is 0.8 mmol/L. This implies that when triglyceride levels are below the inflection point, cognitive function deteriorates as the levels decrease. However, when triglyceride levels are above the inflection point, cognitive function does not significantly change even if the levels increase. Therefore, it is suggested that maintaining triglyceride levels between 0.8 and 1.7 mmol/L.

These findings hold great significance for the formulation of nursing strategies aimed at managing AIS patients with cognitive impairments. Triglycerides are a prominent dietary lipid involved in energy metabolism [39]. While most pharmaceutical treatments primarily offer symptomatic relief or delay disease progression, there is currently no pharmacological therapy exists to enhance the cognitive abilities of patients with cognitive impairments. Consequently, there has been a shift in focus towards exploring the potential of nutritional interventions particularly medium-chain triglycerides [40]. When triglycerides are below 0.8 mmol/L, it is recommended that patients with AIS receive active nutritional interventions and other measures to prevent cognitive decline. When patients maintain triglycerides between 0.8 and 1.7 mmol/L, the risk of adverse outcomes was lower. When triglycerides exceed 1.7 mmol/L, we need to prevent patients from developing hyperlipidemia, and use statin therapy to reduce triglyceride levels.

This study presents a novel contribution in our findings of the relationship between triglyceride levels and cognitive impairment after AIS among older adults. Notably, our findings reveal a distinct curvilinear relationship, highlighting the association of lower triglyceride levels on cognitive function. Specifically, lower triglyceride levels may serve as a vascular risk factor for cognitive impairments. Therefore, our study emphasizes the importance of effectively managing pre-stroke triglyceride levels to mitigate the occurrence of cognitive impairments and their subsequent consequences.

Our study had several limitations. Firstly, the cross-sectional design prevents us from establishing a causal relationship between exposure and outcome. Participants possibly had suffered from cognitive decline before the onset of AIS, although we excluded those may have cognitive impairment. Additionally, the estimation of disease incidence may be influenced by disease duration. Secondly, we did not account for potential population differences, which could affect the results. Thirdly, information regarding the use of lipid-lowering medications or other interventions that may impact cognitive function in participants, potentially confounding the study findings. Moreover, neuroimaging factors, were not assessed in this study. The relationship between TG and cognitive function cannot be extended to other blood lipids. These limitations should be considered when interpreting our study's findings.

5. Conclusion

In conclusion, we found a nonlinear relationship between triglyceride and cognitive impairment after AIS among older adults. Triglyceride was positively connected with cognitive function when it was less than 0.8 mmol/L.

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Data availability statement

All data used in this study in this article are available upon reasonable request to the corresponding author.

Ethics statement

This study was approved (Ethics approval number 2022015) by the Ethics Committee of Shenzhen Second People's Hospital on 14th June 2022. All participants or their legal guardians or family members have provided informed consent to participate in the study.

CRediT authorship contribution statement

Simin Cao: Writing – original draft, Investigation, Formal analysis. **Liting Teng:** Investigation, Formal analysis. **Maofeng Gao:** Investigation, Data curation. **Shoudi Hu:** Investigation, Data curation. **Shiyan Xiao:** Validation, Data curation. **Chen Chen:** Writing – review & editing, Methodology. **Yu He:** Investigation. **Shouzhen Cheng:** Supervision. **Xiaohua Xie:** Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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