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ORIGINAL ARTICLE

Serum TG/HDL-C level at the acute phase of ischemic stroke is associated with post-stroke cognitive impairment

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Abstract

Background The ratio of triglycerides (TG) to high-density lipoprotein cholesterol (HDL-C) bears a relation with poor outcomes of acute ischemic stroke (AIS), but the impact of serum TG/HDL-C level on post-stroke cognitive impairment (PSCI) remains unknown. We conducted this prospective study to explore the association between TG/HDL-C and PSCI.

Methods Consecutive AIS patients from the Stroke Units of our hospital were prospectively enrolled between July 1, 2020, and June 30, 2021. Blood samples were collected within 24 h after admission. Cognition function was evaluated by the Montreal Cognitive Assessment (MoCA) at 3 months after stroke. We used logistic regression analyses to explore the relationship between TG/HDL-C and PSCI, and then used a receiver operating characteristic (ROC) analysis to assess the ability of acute TG/HDL-C for predicting PSCI.

Results A total of 227 AIS patients were recruited. Compared with patients without PSCI, those with PSCI had a higher level of TG/HDL-C at admission ($P < 0.01$). The multivariate logistic regression analyses showed that TG/HDL-C level was independently associated with PSCI ($P < 0.01$). The area under the curve of the ROC for TG/HDL-C as predictor of PSCI was 0.701 (95%CI 0.635–0.768). The optimal cutoff value of TG/HDL-C to indicate PSCI was 1.564, which gave a sensitivity of 55.2% and specificity of 80.6%.

Conclusions Our study demonstrated that a higher level of TG/HDL-C at the acute phase of ischemic stroke predicted the presence of PSCI at 3 months after stroke.

Keywords Post-stroke cognitive impairment · TG/HDL-C · Acute ischemic stroke · Serum lipids

Introduction

Ischemic stroke is a leading cause of death and disability in China [1]. Previous studies and interventions have generally focused on physical disability after stroke, but neglected from consideration post-stroke cognitive impairment (PSCI) [2], which affects about two-thirds of stroke survivors [3]. PSCI not only affects quality of life, but also leads to poorer prognosis and increased mortality in AIS patients [4]. Consequently, there is an important clinical need for neurologists to identify diagnostic biomarkers and related risk factors of PSCI, which might support timely interventions. In recent years, an increasing number of studies have indicated that certain biomarkers of inflammation and oxidative damage might be associated with PSCI [5–7]. Besides, plasma lipid levels have also been reported to be associated with ischemic stroke and subsequent cognitive impairment [8–10]. However, no clear consensus has yet emerged on these issues.

The TG/HDL-C ratio was first reported to be significantly correlated with insulin resistance [11], and subsequently was widely acknowledged as a major risk factor of cardiovascular events [12]. More recently, a population-based study in Japan has shown that an elevated TG/HDL-C ratio can predict chronic kidney disease [13]. Besides, recent research has

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found the level of TG/HDL-C to be independently associated with mortality, poor outcome, and hemorrhagic transformation after AIS [14, 15]. However, the possible relationship between TG/HDL-C and PSCI is not well-established.

Therefore, in the current study, we explored the relationship between TG/HDL-C level at admission and PSCI, with an aim to establish a predictive value of TG/HDL-C for PSCI.

Methods

Patients' recruitment

The present study was approved by the Medical Ethics Committee of the First People's Hospital of Yancheng and complied with the Declaration of Helsinki. All participants or their relatives provided written informed consent. This study was conducted between July 1, 2020, and June 30, 2021. All the study subjects were recruited from the Stroke Unit of the First People's Hospital of Yancheng, consecutively. All eligible patients were included in the present analysis.

For inclusion, subjects must meet all following criteria: (1) ≥ 18 years of age, (2) admission within 72 h of onset, (3) first stroke, (4) subjects were willing and able to provide their disease history and informed consents. The exclusion criteria included the following: (1) severe aphasia or dysarthria or hearing impairment that might influence cognitive examination; (2) any history of stroke; (3) Alzheimer's disease (AD), depression, dementia with Lewy bodies (DLB), frontotemporal dementia (FTD), or dementia caused by other diseases such as malignant tumors, intracranial infection, neurodegenerative diseases, and craniocerebral trauma; (4) history of mental diseases or behavior disorders; and (5) use of nootropics, antipsychotic, antilipemic drugs within 3 months.

Clinical and laboratory assessments

The baseline characteristics collected on admission included demographic data (gender, age, body mass index (BMI), years of education), past medical history (hypertension, diabetes mellitus, heart diseases, atrial fibrillation, smoking habit, and alcohol use), clinical assessment (baseline National Institutes of Health Stroke Score (NIHSS), cerebral infarct volume, infarction location, carotid plaque, artery stenosis, Fazekas score, stroke etiology), and blood laboratory data (homocysteine (Hcy), uric acid (UA), glycosylated hemoglobin A1 (HbA1c), total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL)). MRI was performed on patients within 72 h after admission. An infarction impinging upon any part of the cerebral cortex was defined as a cortical infarction. The infarct volume was evaluated using the initial DWI lesion volume and calculated as the sum of the infarction area of every slice multiplied by the slice thickness. The degree of cerebral vascular damage was assessed on MRI by applying the Fazekas score. The Fazekas score is a validated diagnostic tool for assessing the severity of white matter hyperintensities in periventricular regions and deep white matter, with a possible score from 0 to 6. All patients underwent carotid ultrasound or carotid artery CTA to assess plaque and stenosis. Stroke etiology was categorized according to Trial of Org 10,172 in Acute Stroke Treatment (TOAST) criteria.

Blood samples were collected after at least 8 h of fasting within 24 h of hospital admission and the plasma was separated and frozen at − 80 °C before being assayed. A laboratory technician blinded to all clinical data processed all the samples. The levels of serum lipids including TG, TC, HDL-C, and LDL-C were measured in the clinical laboratory of the hospital with an automated biochemical analyzer. The levels of Hcy, UA, and HbA1c were also analyzed and recorded by staff who were blinded to the clinical data of the patients.

Definition of PSCI

The cognitive dysfunction was assessed by trained neurologists at 3 months after stroke onset through the Chinese version of the Montreal Cognitive Assessment (MoCA). MoCA is a well-known questionnaire to assess the severity of cognitive impairment. PSCI was defined by a MoCA score < 26. We add one point to scores of those with education less than 12 years [16, 17].

Statistical analysis

Statistical analyses were performed by SPSS version 23.0 (IBM SPSS Inc.). Continuous variables, which followed normal or skewed distributions, were respectively presented as the mean ± standard deviation or the median (25% and 75% interquartile). Categorical variables were presented as frequency (percentages). Differences in baseline characteristics among TG/HDL-C quartiles were conducted using analysis of variance or the Kruskal–Wallis test for continuous variables, and chi-square test for categorical variables. Differences in baseline characteristics among PSCI and non-PSCI groups were conducted using analysis of one-way ANOVA or the Mann–Whitney test for continuous variables, and chi-square test for categorical variables. Univariable logistic regression analysis was applied to screen risk factors. All variables with a significant relationship at $P < 0.15$ in univariate analysis entered multivariable analysis. Multivariate logistic regression analysis was then applied to evaluate the independent impact of TG/HDL-C on the occurrence of PSCI, and the corresponding odds ratios (ORs) and 95%CIs were calculated. Furthermore, we conducted receiver operating characteristic (ROC) analysis to evaluate the predictive

ability of TG/HDL-C to PSCI, and then calculated the area under the curve (AUC) of the ROC and best cutoff point. A value of $P < 0.05$ was considered to be statistically significant.

Results

Baseline characteristics among TG/HDL-C quartiles

In this study, a total of 452 consecutively admitted patients with AIS were screened. A total of 177 AIS patients were excluded for various reasons, including aphasia (24, 13.6%). Among the 275 patients who met entry criteria, 48 patients had dropped out of the study during follow-up. Ultimately, 227 patients were included in our study (Fig. 1).

The range of TG/HDL-C in all participants was 0.33–8.37. The 227 patients included were stratified into three groups according to TG/HDL-C ratio quartile. The cutoff values of the TG/HDL-C quartiles were ≤ 1.07, 1.07–1.70, and ≥ 1.70. Comparisons of baseline characteristics among the three groups are shown in Table 1. Among the three groups, BMI ($P = 0.014$), Hcy level ($P = 0.03$), proportion of PSCI ($P < 0.01$), HbA1c level ($P = 0.029$), TG level ($P < 0.01$), HDL-C level ($P < 0.01$), LDL-C level ($P = 0.02$), and MoCA score ($P = 0.001$) showed significant differences, while other variables did not show any difference.

Characteristics between PSCI group and non-PSCI group

Of the 227 patients in the study, 134 (59.0%) were diagnosed with PSCI 3 months after stroke. Compared with patients without PSCI, patients with PSCI had greater age ($P = 0.003$), higher education level ($P < 0.001$), higher levels of TG ($P < 0.001$) and TG/HDL ($P < 0.001$), higher NIHSS score ($P < 0.001$), higher proportion of cortical infarct ($P = 0.006$), larger infarct volume ($P < 0.001$), and lower level of HDL ($P = 0.001$). However, no significant differences were found in gender, BMI, and other vascular risk factors (Table 2).

Risk factors associated with PSCI

The results of logistic regression analyses for the risk factors associated with PSCI are shown in Table 3. The univariate logistic regression analyses presented that age, education level, NIHSS scores, infarct volume, cortical infarction, stroke etiology, TG, HDL-C, and TG/HDL-C were all associated with PSCI ($P < 0.05$). All variables with a significant relationship at $P < 0.15$ in univariate analysis were entered into multivariate regression analysis, which showed that age (OR = 1.032, 95%CI = 1.003–1.062, $P = 0.028$), education level (OR = 0.151, 95%CI = 0.061–0.374, $P < 0.001$), cortical infarction (OR = 2.243, 95%CI = 1.086–4.633, $P = 0.029$), baseline NIHSS (OR = 1.312, 95%CI = 1.184–1.454, $P < 0.001$), and TG/HDL (OR = 3.940, 95%CI = 2.337–6.664, $P < 0.001$) were independently associated with PSCI.

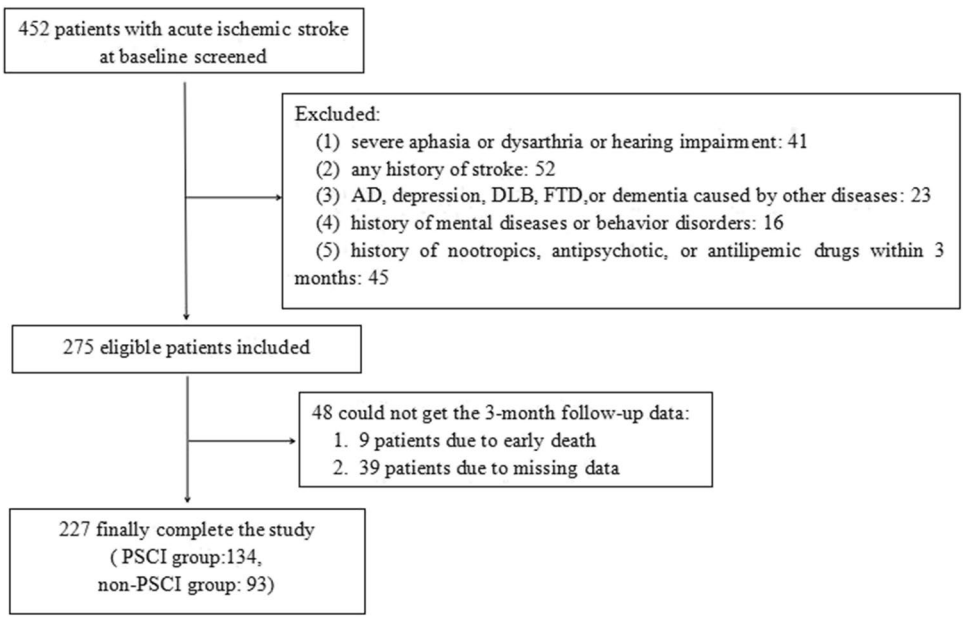

Fig. 1 Study recruitment profile

Table 1 Baseline characteristics of groups according to TG/HDL-C quartiles

Baseline characteristics	Quartile 1 ($n=75$)	Quartile 2 ($n=77$)	Quartile 3 ($n=75$)	P value
Demographics				
Male (%)	50 (66.7)	42 (54.5)	43 (57.3)	0.287
Age (years)	67.0 ± 11.3	67.2 ± 14.4	64.8 ± 12.9	0.457
BMI, kg/m^2	23.8 ± 3.3	24.8 ± 3.1	25.2 ± 2.8	0.014
Education level (%)				0.282
Illiterate	10 (13.3)	16 (20.8)	14 (18.7)	
Primary school	24 (32.0)	30 (39.0)	32 (42.7)	
Secondary school or above	41 (54.7)	31 (40.3)	29 (38.7)	
Medical history (%)				
Hypertension	44 (58.7)	45 (58.4)	50 (66.7)	0.498
Diabetes mellitus	15 (20.0)	24 (31.2)	25 (33.3)	0.149
Coronary artery disease	10 (13.3)	11 (14.3)	11 (14.7)	0.971
Atrial fibrillation	11 (14.7)	18 (23.4)	9 (12.0)	0.144
Smoking (%)	22 (29.3)	26 (33.8)	24 (32.0)	0.84
Drinking (%)	28 (37.3)	23 (29.9)	27 (36.0)	0.585
Clinical characteristics				
NIHSS on admission	5 (2, 10)	5 (2, 8)	4 (2, 8)	0.749
Cerebral infarct volume (cm^3)	1.0 (0.5, 4.4)	1.5 (0.6, 4.9)	2.0 (0.6, 5.3)	0.493
Cortical infarction (%)	25 (33.3)	29 (37.7)	36 (48.0)	0.168
Carotid plaque (%)	67 (89.3)	65 (84.4)	60 (80)	0.285
Carotid artery stenosis (%)	15 (20.0)	17 (22.1)	19 (25.3)	0.733
Fazekas score	4 (3,4)	3 (3,4)	3 (3,4)	0.106
Stroke etiology (%)				0.498
LAA	48 (64.0)	43 (55.8)	44 (58.7)	
Cardioembolism	9 (12.0)	11 (14.3)	4 (5.3)	
Small vessel occlusion	15 (20.0)	19 (24.7)	22 (29.3)	
Undetermined/unclassified	3 (4.0)	4 (5.2)	5 (6.7)	
PSCI (%)	33 (44.0)	39 (50.6)	62 (82.7)	< 0.01
Laboratory characteristics				
Hcy (μmol/L)	11.4 (8.7, 17.0)	7.6 (6.7, 15.0)	11.6 (9.0, 17.4)	0.03
Uric acid (μmol/L)	320.1 ± 89.2	336.0 ± 86.2	342.2 ± 91.6	0.294
HbA1c (%)	5.6 (5.3, 5.8)	5.9 (5.4, 6.7)	5.8 (5.3, 6.7)	0.029
TG (mmol/L)	0.9 (0.8, 1.2)	1.4 (1.1, 1.6)	2.4 (2.0, 3.0)	< 0.01
TC (mmol/L)	4.3 ± 1.1	4.4 ± 1.3	4.7 ± 1.3	0.207
HDL-C (mmol/L)	1.2 (1.0, 1.5)	1.0 (0.9, 1.2)	0.9 (0.8, 1.0)	< 0.01
LDL-C (mmol/L)	2.5 ± 0.8	2.7 ± 0.9	2.8 ± 0.9	0.02
MoCA	26 (20, 27)	25 (21.5, 27)	22 (19, 25)	0.001

PSCI, post-stroke cognitive impairment; *BMI*, body mass index; *NIHSS*, National Institutes of Health Stroke Scale; *LAA*, large artery atherosclerosis; *Hcy*, homocysteine; *HbA1c*, glycosylated hemoglobin A1c; *TG*, triglyceride; *TC*, total cholesterol; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *TG/HDL-C*, TG to HDL-C ratio

ROC analysis to explore the predictive ability of TG/HDL-C to PSCI

ROC analysis was further conducted to explore the ability of TG/HDL-C to predict the subsequent development of PSCI. The results showed that the corresponding area under the curve (AUC) to indicate PSCI was 0.701 (95%CI = 0.635–0.768). The optimal cutoff value of TG/HDL-C for the diagnosis of PSCI was 1.564 with a sensitivity of 55.2% and a specificity of 80.6% (Fig. 2).

Discussion

We conducted this prospective study to explore the relationship between TG/HDL-C upon admission of AIS patients and PSCI at 3 months later. Results from the current study showed that patients in the third TG/HDL-C tertile had lower MoCA score ($P = 0.001$) and higher proportion of PSCI ($P < 0.001$) than those in the first and second tertiles. Further analysis indicated that higher TG/HDL-C

Table 2 Characteristics between PSCI group and non-PSCI group

Baseline characteristics	PSCI ($n=134$)	Non-PSCI ($n=93$)	P value
Demographics			
Male (%)	73 (54.5)	62 (66.7)	0.066
Age (years)	68.4 ± 12.2	63.3 ± 13.5	0.003
BMI, kg/m^2	24.44 ± 3.10	24.78 ± 3.07	0.405
Education level, *n* (%)			< 0.001
Illiterate	33 (24.6)	7 (7.5)	
Primary school	59 (44.0)	27 (29.0)	
Secondary school or above	42 (31.3)	59 (63.4)	
Medical history, *n* (%)			
Hypertension	88 (65.7)	51 (54.8)	0.099
Diabetes mellitus	42 (31.3)	22 (23.7)	0.206
Coronary artery disease	17 (12.7)	15 (16.1)	0.464
Atrial fibrillation	25 (18.7)	13 (14.0)	0.353
Smoking	44 (32.8)	28 (30.1)	0.664
Drinking	50 (37.3)	28 (30.1)	0.261
Clinical characteristics			
NIHSS on admission	7 (3, 12)	3 (2, 5)	< 0.001
Cerebral infarct volume (cm^3)	2.50 (0.84, 6.94)	0.76 (0.38, 1.45)	< 0.001
Cortical infarction (%)	63 (47.0)	27 (29.0)	0.006
Carotid atherosclerosis	117 (87.3)	75 (80.6)	0.171
Carotid artery stenosis	31 (23.1)	20 (21.5)	0.772
Fazekas score	3.5 (3, 4)	3 (3, 4)	0.124
Stroke etiology			0.102
LAA	83 (61.9)	52 (55.9)	
Cardioembolism	15 (11.2)	9 (9.7)	
Small vessel occlusion	33 (24.6)	23 (24.7)	
Undetermined/unclassified	3 (2.2)	9 (9.7)	
Laboratory characteristics			
Hcy (μmol/L)	11.04 (8.68, 16.93)	10.70 (8.20, 16.40)	0.4
Uric acid (μmol/L)	330.71 ± 93.06	335.87 ± 83.43	0.669
HbA1c (%)	5.70 (5.30, 6.53)	5.70 (5.33, 6.28)	0.587
TG (mmol/L)	1.64 (1.13, 2.49)	1.29 (0.97, 1.67)	< 0.001
TC (mmol/L)	4.57 ± 1.28	4.35 ± 1.13	0.174
HDL-C (mmol/L)	0.99 (0.86, 1.14)	1.08 (0.92, 1.29)	0.001
LDL-C (mmol/L)	2.76 ± 0.87	2.57 ± 0.89	0.102
TG/HDL	1.65 (1.07, 2.81)	1.14 (0.82, 1.50)	< 0.001

PSCI, post-stroke cognitive impairment; *BMI*, body mass index; *NIHSS*, National Institutes of Health Stroke Scale; *LAA*, large artery atherosclerosis; *Hcy*, homocysteine; *HbA1c*, glycosylated hemoglobin A1c; *TG*, triglyceride; *TC*, total cholesterol; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *TG/HDL-C*, TG to HDL-C ratio

was independently associated with increased risk of PSCI (OR = 3.940, 95%CI = 2.337–6.664, $P < 0.001$). The optimal cutoff value of TG/HDL-C to predict the appearance of PSCI was 1.564, and its corresponding sensitivity and specificity were 55.2% and 80.6%, respectively. Our results revealed that TG/HDL-C was an effective indicator of PSCI.

Our study showed that the prevalence of PSCI was 59.0% in our study group, which is in line with the previous research [18]. Similar to the results of previous reports [18–22], we also found that certain indicators like age, NIHSS score, education level, cerebral infarct volume, and proportion of cortical infarction differed significantly between the PSCI and non-PSCI groups. Meanwhile, patients in the PSCI group had lower TG and higher HDL-C and TG/HDL-C. Further analysis showed that age, education level, baseline NIHSS, cortical infarction, and TG/HDL were independently associated with PSCI.

Previous studies have found that dyslipidemia might be a risk factor of ischemic stroke and cognitive impairment or AD [19–21]. However, the prognostic significance of serum

Table 3 Univariate and multivariate analyses for the potential prognostic factors associated with PSCI by logistic regression model

Baseline characteristics	Univariate analysis		Multivariate analysis	
	OR (95%CI)	*P* value	Adjusted OR (95%CI)	*P* value
Demographics				
Male (%)	1.672 (0.965–2.894)	0.067	1.265 (0.558–2.871)	0.573
Age (years)	1.032 (1.010–1.054)	0.004	1.032 (1.003–1.062)	0.028
BMI, kg/m^2	0.964 (0.884–1.051)	0.404		
Education level, *n* (%)				
Illiterate	Reference		Reference	
Primary school	0.464 (0.182–1.180)	0.107	0.933 (0.298–2.917)	0.905
Secondary school or above	0.151 (0.061–0.374)	<0.001	0.347 (0.109–1.104)	0.073
Medical history, *n* (%)				
Hypertension	1.575 (0.916–2.709)	0.1	1.174 (0.551–2.503)	0.678
Diabetes mellitus	1.473 (0.807–2.689)	0.207		
Coronary artery disease	0.756 (0.357–1.601)	0.465		
Atrial fibrillation	1.394 (0.672–2.892)	0.373		
Smoking	1.135 (0.641–2.009)	0.664		
Drinking	1.434 (0.831–2.475)	0.195		
Clinical characteristics				
NIHSS on admission	1.242 (1.144–1.349)	<0.001	1.312 (1.184–1.454)	<0.001
Cerebral infarct volume (cm^3)	1.066 (1.018–1.116)	0.006	1.035 (0.983–1.090)	0.190
Cortical infarction (%)	2.169 (1.237–3.804)	0.007	2.243 (1.086–4.633)	0.029
Carotid atherosclerosis	1.652 (0.801–3.405)	0.174		
Carotid artery stenosis	1.099 (0.581–2.077)	0.772		
Fazekas score	1.218 (0.945–1.568)	0.128	1.040 (0.700–1.545)	0.846
Stroke etiology				
LAA	Reference		Reference	
Cardioembolism	1.044 (0.426–2.558)	0.925	0.441 (0.131–1.486)	0.168
Small vessel occlusion	0.899 (0.476–1.697)	0.742	1.723 (0.698–4.250)	0.238
Undetermined/unclassified	0.209 (0.054–0.807)	0.023	0.347 (0.062–1.930)	0.227
Laboratory characteristics				
Hcy (μmol/L)	1.023 (0.975–1.075)	0.353		
Uric acid (μmol/L)	0.999 (0.996–1.002)	0.667		
HbA1c (%)	1.123 (0.916–1.376)	0.264		
TG (mmol/L)	2.247 (1.516–3.329)	<0.001	0.389 (0.061–2.459)	0.315
TC (mmol/L)	1.165 (0.935–1.453)	0.174		
HDL-C (mmol/L)	0.261 (0.107–0.633)	0.003	1.848 (0.188–18.177)	0.598
LDL-C (mmol/L)	1.292 (0.949–1.758)	0.104	1.368 (0.845–2.216)	0.202
TG/HDL	2.781 (1.849–4.185)	<0.001	3.940 (2.337–6.644)	<0.001

PSCI, post-stroke cognitive impairment; *BMI*, body mass index; *NIHSS*, National Institutes of Health Stroke Scale; *LAA*, large artery atherosclerosis; *Hcy*, homocysteine; *HbA1c*, glycosylated hemoglobin A1c; *TG*, triglyceride; *TC*, total cholesterol; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *TG/HDL-C*, TG to HDL-C ratio

lipid levels remains conflicted, which may result from the clinically heterogeneous features of ischemic stroke. Several studies have reported that lower HDL-C or elevated TG could increase the risk of cognitive impairment in later life [21]. High serum TC and LDL-C have also been reported to be risk factors of cognitive impairment in elderly subjects respectively [10, 18, 22]. However, some other studies found conflicting results [23, 24].

Meanwhile, the close association of apolipoprotein E (ApoE) and cognitive impairment has been explicitly established. ApoE is a multifunctional protein that plays a crucial role in the transport of lipid and the mediation of dynamic lipid levels and lipid metabolism [25]. ApoE can not only directly modulate Aβ metabolism, but also affect cognitive function through Aβ-independent pathways by regulating neuronal function, lipid metabolism, or other related

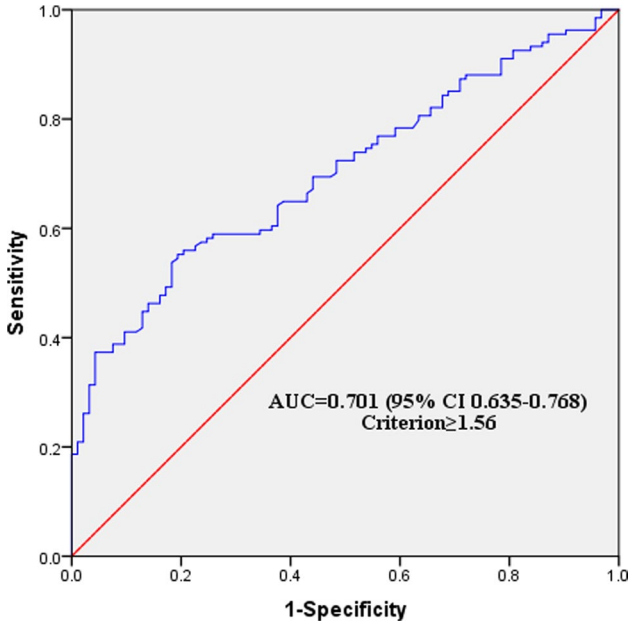

Fig. 2 ROC analysis to analyze the predictive value of TG/HDL-C for PSCI. The corresponding area under the curve (AUC) to indicate PSCI was 0.701 (95%CI 0.635–0.768, $P < 0.001$). The optimal cutoff value of TG/HDL-C for the diagnosis of PSCI was 1.564 with a sensitivity of 55.2% and a specificity of 80.6%

pathways [25, 26]. The APOE gene has been reported to be an important genetic risk factor for AD [26, 27]. Indeed, Farrer et al. [28] had reported that individuals who carry one ε4 allele bear a 2–fourfold higher AD risk, and those with two copies of ε4 have an 8–12-fold increased AD risk.

Elevated TG/HDL-C is acknowledged as a marker of insulin resistance and an independent predictor of cardiovascular risk [15, 29]. On the other hand, recent research found that lower levels of TG/HDL-C were associated with greater risk of hemorrhagic transformation and worse short-term outcomes after AIS [14, 15]. Nevertheless, that finding was limited to patients with large artery atherosclerosis stroke and the potential relationship between TG/HDL-C and PSCI was not explored. To our knowledge, the present study is the first research study to prospectively explore the possible correlation between TG/HDL-C and PSCI in AIS patients. We find that higher levels of TG/HDL-C at admission could increase the risk of PSCI. Therefore, TG/HDL-C ratio in the acute phase of ischemic stroke can be used as an indicator to predict the later occurrence of PSCI, which might guide the selection of timely rehabilitative interventions such as cognitive training, or efforts to rectify hyperlipidemia. The underlying mechanisms on the observed relationship between TG/HDL-C and PSCI remain unclear, but several potential pathways have been proposed. Previous research has reported that hypercholesterolemia might increase the production and deposition of amyloid beta peptides (Aβ) in the brain and promote the formation of neurotoxic fibrils and neuritis [10, 30, 31]. Some investigators have reported that HDL-C could prevent aggregation of Aβ and inflammation caused by neurodegenerative processes [32, 33]. Lower HDL-C levels have been previously reported to be associated with more severe white matter lesion changes, leading to AD and mild cognitive impairment [33]. The TG level has also been reported to be correlated with atherogenic and pro-inflammatory triglyceride-rich lipoproteins that may directly promote cognitive impairment [34]. We hypothesized that high TG concentration and low HDL concentration may contribute to cognitive sequelae, such that the TG/HDL-C ratio could be a sensitive predictor.

Our findings provide epidemiological evidence supporting the proposal that TG/HDL-C is a potential predictor of PSCI. However, some limitations should be pointed out in this study. First, our study was a single-center study, and the sample size was not large enough to support generalization, such that our findings should be further verified by a multi-center study with large samples. Second, several potential risk factors that may be associated with PSCI were not examined, notably among these the ApoE status, hypersensitive C-reactive protein, and 8-hydroxydeoxyguanosine. Third, due to the limited sample size, we did not make a more detailed classification of infarction location, but only considered cortical involvement as a factor. Fourth, we only investigated the baseline level of TG/HDL-C and did not conduct dynamic measures of TG/HDL-C over time after stroke, which may have sacrificed information about treatment effects on cognitive outcome. In addition, according to the strict exclusion criteria, quite a few AIS patients with massive infarction ($n=17$) or severe aphasia ($n=24$) or dysarthria ($n=11$) were excluded, which might have resulted in bias.

Conclusion

This study demonstrated that higher levels of TG/HDL-C at admission in AIS patients could serve as a predictor for PSCI 3 months later. The underlying molecular mechanisms are not clear, which calls for further studies in large populations. Results imply that early intervention against hyperlipidemia might have a preventive effect on the development of PSCI.

Author contribution DMS, YG, and YQC designed the study. HHZ, YQC, JC, LL, and CXL conducted the research. YQC and HHZ wrote the paper and analyzed the data. All authors reviewed and approved the final version of the manuscript.

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Data availability The data that support the findings of this study are available from Dingming Sun upon reasonable request.

Declarations

Ethical approval This study was conducted according to the protocol approved by the Human Subjects Research Ethics Board of The First People's Hospital of Yancheng.

Informed consent Written informed consent was obtained from all participants.

Conflict of Interest The authors declare no competing interests.

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