Correlation Between Triglyceride-Glucose Index and Early Neurological Deterioration in Patients with Recent Solitary Subcortical Infarction: Postprint

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Abstract

Background: Early neurological deterioration (END) is a common complication following acute ischemic stroke that leads to increased functional disability and mortality. The triglyceride-glucose index (TyG index) is an independent predictor of the severity of neurological deficit in acute ischemic stroke patients and is also associated with early recurrent ischemic lesions. However, studies investigating its correlation with END in recent single subcortical infarction (SSI) are rarely reported, and the relationship remains unclear.

Objective: To investigate the correlation between the TyG index and END in patients with recent SSI.

Methods: A total of 197 patients diagnosed with SSI and admitted to the Department of Neurology, The Third Hospital of Hebei Medical University within 72 hours of symptom onset from 2020 to 2021 were enrolled. Based on the occurrence of END, patients were divided into an END group (n=45) and a non-END group (n=152). Clinical data were collected, and multivariate Logistic regression analysis was used to explore the relationship between the TyG index and END in recent SSI patients. Receiver operating characteristic (ROC) curve analysis was employed to evaluate the predictive value of the TyG index for END in recent SSI patients.

Results: The proportions of diabetes mellitus, fasting blood glucose (FBG), triglycerides (TG), and TyG index were higher in the END group than in the non-END group ($P<0.05$). Multivariate Logistic regression analysis revealed that elevated TyG index was a risk factor for END in recent SSI patients [OR=1.726, 95%CI (1.008, 2.956), P=0.047]. Across different infarction locations, elevated TyG index was a risk factor for END in recent SSI patients

with infarction in the basal ganglia region [OR=3.164, 95%CI (1.290, 7.760), P=0.012]. Elevated TyG index was not associated with END in SSI patients with infarction in the centrum semiovale (P>0.05). The area under the ROC curve (AUC) for the TyG index in predicting END in recent SSI patients was 0.66 [95%CI (0.57, 0.75), P=0.001], with an optimal cutoff value of 8.61, sensitivity of 0.689, and specificity of 0.638. Based on the optimal cutoff value of the TyG index, patients were stratified into TyG index $ $8.61 and TyG index <8.61 groups. Compared with patients with TyG index <8.61, those with TyG index $ $8.61 exhibited higher proportions of hyperlipidemia, diabetes mellitus, and END, as well as elevated levels of FBG, total cholesterol (TC), TG, and low-density lipoprotein (LDL), and reduced age and high-density lipoprotein (HDL) levels (P<0.05).

Conclusion: The TyG index is associated with END in SSI patients, and increased TyG index is an independent risk factor for END in SSI patients. This association varies by lesion location.

Full Text

Abstract

Background: Early neurological deterioration (END) is common after acute ischemic stroke and contributes to increased functional impairment and mortality. The triglyceride glucose index (TyG index) is an independent predictor of neurological deficit severity in acute ischemic stroke patients and is associated with early recurrent ischemic lesions. However, its correlation with END in recent single subcortical infarction (SSI) has rarely been reported and remains unclear.

Objective: To investigate the correlation between TyG index and END in patients with recent SSI.

Methods: A total of 197 patients diagnosed with SSI and admitted within 72 hours of symptom onset to the Department of Neurology at the Third Hospital of Hebei Medical University between 2020 and 2021 were included. Patients were divided into an END group (n=45) and non-END group (n=152) based on END occurrence. Clinical data were collected, and multivariate logistic regression analysis was used to explore the relationship between TyG index and END in recent SSI patients. Receiver operating characteristic (ROC) curves were used to evaluate the predictive value of TyG index for END.

Results: The END group had higher proportions of diabetes, as well as higher fasting blood glucose (FBG), triglyceride (TG), and TyG index levels compared to the non-END group (P<0.05). Multivariate logistic regression analysis showed that elevated TyG index was a risk factor for END in recent SSI patients (OR=1.726, 95%CI: 1.008–2.956, P=0.047). When stratified by infarct location, elevated TyG index was a risk factor for END in SSI patients with basal ganglia infarction (OR=3.164, 95%CI: 1.290–7.760, P=0.012) but was not

associated with END in patients with centrum semiovale infarction (P>0.05). The area under the ROC curve (AUC) of TyG index for predicting END in recent SSI patients was 0.66 (95%CI: 0.57–0.75, P=0.001), with an optimal cutoff value of 8.61, sensitivity of 0.689, and specificity of 0.638. Using this cutoff, patients with TyG index $ $8.61 showed higher proportions of hyperlipidemia and diabetes, higher levels of FBG, total cholesterol (TC), TG, and low-density lipoprotein (LDL), and a higher END rate, but lower age and high-density lipoprotein (HDL) levels compared to those with TyG index <8.61 (P<0.05).

Conclusion: TyG index is correlated with END in SSI patients, and increased TyG index is an independent risk factor for END. This association varies depending on lesion location.

Keywords: Ischemic stroke; Single subcortical infarction; Triglyceride glucose index; Insulin resistance; Early neurological deterioration; Correlation analysis

Introduction

Early neurological deterioration (END) refers to the worsening of neurological function within hours or days after acute ischemic stroke, leading to poor outcomes, and is a common complication in adult acute ischemic stroke patients [1]. The incidence of END in acute stroke ranges from 2.2% to 37.5% [1]. The etiology and pathogenesis of END are complex, influenced by multiple factors and mechanisms including hyperglycemia, hypoperfusion, collateral circulation impairment, in-situ thrombus progression, free radical damage, cerebral edema, and hemorrhagic transformation. Currently, there are no reliable early predictive indicators or effective prevention and treatment strategies.

Single subcortical infarction (SSI) is a stroke type associated with perforating arteries and is generally considered to have a good prognosis. However, current studies show that 20%–30% of SSI patients develop END [2]. Metabolic syndrome is a potential predictor of END after ischemic stroke [3]. Insulin resistance (IR), as a main characteristic of metabolic syndrome [4], has been shown by meta-analysis to be associated with increased risk of poor functional outcomes and neurological deterioration in acute stroke patients [5]. The triglyceride glucose index (TyG index) is a simple and reliable surrogate marker for IR [6]. High TyG index is associated with new-onset ischemic stroke in the general population [7-8], and ischemic stroke patients with high TyG index have higher stroke recurrence risk and increased mortality compared to those with low TyG index [8]. Triglyceride (TG) and fasting blood glucose (FBG), components of the TyG index formula, are known predictors of END in ischemic stroke patients [9-10]. However, the relationship between TyG index and END in recent SSI remains unclear. Therefore, this study aimed to analyze the correlation between TyG index and END in recent SSI patients to provide a reference basis for clinical research on SSI.

Methods

Study Subjects

We included 197 patients diagnosed with recent SSI and admitted within 72 hours of symptom onset to the Department of Neurology at the Third Hospital of Hebei Medical University between 2021 and 2022. Inclusion criteria were: (1) age >30 years; (2) imaging characteristics consistent with recent SSI [11]. Exclusion criteria were: (1) large-area cerebral infarction (axial infarct area >20 mm), multiple infarct locations, or cortical infarction; (2) intracranial or extracranial large artery stenosis $ $50%; (3) history of atrial fibrillation, infective endocarditis, valvular heart disease, or congenital heart disease; (4) thrombolytic therapy; (5) other head abnormalities such as trauma, hemorrhage, or space-occupying lesions; (6) incomplete clinical data. This study was approved by the Ethics Committee of the Third Hospital of Hebei Medical University (Approval No: 科 2022-011-1).

Data Collection

Baseline clinical data were collected at admission, including age, sex, smoking (at least one cigarette per day on average in the past year), alcohol consumption (defined as daily intake of $ $100 ml of alcohol$ ($50 \times$ FBG(mg/dL)/2]. All patients underwent brain MRI scanning using a 3.0 T MRI system (Philips, Netherlands), and infarct location was recorded.

Grouping

Neurological deficit severity was assessed using NIHSS at admission and daily at the same time for 3 days by neurologists. END was defined as an increase in NIHSS score $ $2 points from admission or a $ $1 point increase in the motor subscore [12]. Patients were divided into an END group (n=45) and non-END group (n=152) based on neurological deterioration within 3 days of admission.

Statistical Analysis

Normally distributed continuous variables were expressed as mean±standard deviation and compared using two-sample t-tests. Non-normally distributed continuous variables were expressed as median (P25, P75) and compared using rank-sum tests. Categorical variables were expressed as percentages and compared using chi-square tests. Multivariate logistic regression analysis was used to identify factors influencing END in recent SSI patients, with further analysis by infarct location. ROC curve analysis was used to evaluate the predictive value of TyG index for END. Statistical significance was set at $P<0.05$.

Results

Baseline Characteristics

Among 197 SSI patients, 124 (62.9%) were male and 73 (37.1%) were female, with a mean age of 63.6$±$11.8 years. The END group had significantly higher proportions of diabetes and higher levels of FBG, TG, and TyG index compared to the non-END group (P<0.05). There were no significant differences between groups in age, sex, smoking history, alcohol consumption, stroke history, hypertension, hyperlipidemia, coronary artery disease, admission NIHSS score, TC, HDL, LDL, Hcy, or infarct location (P>0.05) .

Multivariate Logistic Regression Analysis

Using END occurrence (yes=1, no=0) as the dependent variable and variables with statistical significance in univariate analysis [TyG index (actual value), diabetes (no=0, yes=1) (note: considering TyG index composition, FBG and TG were not included simultaneously with TyG index in the analysis)] and clinically meaningful variables [age (actual value), sex (female=0, male=1)] as independent variables, multivariate logistic regression showed that elevated TyG index was a risk factor for END in recent SSI patients (OR=1.726, 95%CI: 1.008–2.956, P=0.047) .

Analysis by Infarct Location

Multivariate logistic regression analysis stratified by infarct location (basal ganglia and centrum semiovale) showed that elevated TyG index was a risk factor for END in recent SSI patients with basal ganglia infarction (OR=3.164, 95%CI: 1.290–7.760, P=0.012) but was not associated with END in patients with centrum semiovale infarction (P>0.05) .

Predictive Value of TyG Index

ROC curve analysis showed that the AUC of TyG index for predicting END in recent SSI patients was 0.66 (95%CI: 0.57–0.75, P=0.001), with an optimal cutoff value of 8.61, sensitivity of 0.689, and specificity of 0.638 [Figure 1: see original paper].

Comparison by TyG Index Cutoff

Among 197 patients, 86 had TyG index $ $8.61 and 111 had TyG index <8.61. Compared to patients with TyG index <8.61, those with TyG index $ $8.61 had higher proportions of hyperlipidemia and diabetes, higher levels of FBG, TC, TG, and LDL, and a higher END rate, but lower age and HDL levels (P<0.05). Other clinical characteristics showed no significant differences (P>0.05) .

Discussion

This study found that IR, represented by high TyG index, is an independent risk factor for END in recent SSI patients. This association was more pronounced in patients with basal ganglia infarction (proximal SSI), supporting the hypothesis that SSI pathogenesis may differ by location.

Metabolic abnormalities associated with metabolic syndrome are closely related to acute ischemic stroke progression. These changes include impaired endogenous fibrinolysis, endothelial dysfunction, and pro-inflammatory states, all of which can lead to neurological deterioration. IR is the main pathological feature of metabolic syndrome. A large prospective cohort study of 16,310 acute ischemic stroke patients using TyG index as an IR marker found that high TyG index was associated with increased END risk, 12-month stroke recurrence, and all-cause mortality [13]. High TyG index also predicted poor 3-month functional outcomes in acute ischemic stroke patients after reperfusion therapy [14].

Multiple pathological mechanisms have been proposed for the relationship between IR and stroke progression. First, IR may lead to a pro-thrombotic and pro-inflammatory state by increasing platelet activation and inhibiting endogenous fibrinolysis. Second, IR patients have endothelial dysfunction with upregulated plasminogen activator inhibitor-1 and reduced adiponectin, impairing vascular remodeling and growth [15]. The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) is widely used to evaluate IR, but TyG index has shown better predictive value than HOMA-IR in specific populations, as validated in multiple studies [16-17]. TyG index is easily measured, low-cost, and modifiable, ensuring its broad research and clinical applicability.

Previous predictive studies on END have identified obesity and waist-to-hip ratio as predictors of stroke progression [18]. A meta-analysis by MARTIN et al. [9] showed TG was associated with increased END rates. YU et al. [10] demonstrated that high FBG was an independent risk factor for progressive infarction within 48 hours of acute ischemic stroke, with potential mechanisms including endothelial injury, increased oxidative stress, lactate accumulation, and blood-brain barrier damage. TyG index is calculated from TG and FBG levels. Elevated plasma TG promotes endothelial dysfunction, plaque rupture, and arterial inflammation, while elevated FBG may induce oxidative stress by interfering with insulin signaling. Studies report that IR acts as a "trigger" for hypertension development, including inducing sodium retention, increasing circulating fluid volume, and activating the sympathetic nervous system [19].

SSI is a heterogeneous disease with varying clinical features and pathogenesis depending on lesion location. This study found that high TyG index was more predictive of END in basal ganglia infarction than centrum semiovale infarction. TG and FBG are closely related to atherosclerotic plaque instability, and TyG index is considered a promising atherosclerosis marker [20]. As an SSI in the middle cerebral artery territory, proximal SSI-related END is thought to be associated with atherosclerosis and prone to symptom deterioration and fluctu-

ation. The pathogenesis involves: (1) plaque growth or intraplaque hemorrhage progressing from near-occlusion to complete occlusion after the parent artery plaque blocks the perforating artery opening; and (2) emboli detaching from unstable atherosclerotic plaques and flowing distally into perforating arteries, causing infarct expansion or new infarcts [21]. Distal SSI is mainly associated with fibrinoid degeneration and lipohyalinosis [22]. Proximal SSI is considered more related to perforating artery atherosclerosis, consistent with findings from the Third China National Stroke Registry (CNSR3) [23]. Additionally, infarct location can predict in-hospital END occurrence. A prospective study similarly concluded that infarctions in deep lenticulostriate artery regions and cerebral watershed areas can predict END [24].

This study has several limitations. First, patients were admitted within 72 hours of stroke onset, and END typically occurs within 72 hours, especially within the first 24 hours, potentially underestimating END incidence. Second, this was a single-center retrospective study with a relatively small sample size, limiting generalizability. Finally, selection bias may have occurred, as patients may have taken glucose-lowering or lipid-lowering medications before admission that directly affect TyG index values.

Conclusion

TyG index is associated with END in SSI patients, and increased TyG index is an independent risk factor for END. This association varies by lesion location. Future multicenter, large-sample prospective studies are needed to further confirm the relationship between TyG index and END in SSI patients.

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Author Contributions

LUO Weigang was responsible for study design, data analysis, and manuscript drafting. LUO Weigang, YIN Yuanyuan, LIU Wanhu, and XU Yuzhu were responsible for data collection and literature review. CAO Xiaoyun and BU Wei revised the manuscript. ZHANG Lingyan and REN Huiling were responsible for quality control, review, and overall supervision.

Conflict of Interest

The authors declare no conflict of interest.

Note: Figure translations are in progress. See original paper for figures.