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# The association of triglyceride glucose index and postoperative outcome in patients with severe spontaneous intracerebral hemorrhage: a multiple-center cohort study

Haishuang Tang<sup>1,2,4</sup>, Kaiwen Wang<sup>3,4</sup>, Kaige Zheng<sup>1,2</sup>, Zheng Wen<sup>1,2</sup>, Yi Yang<sup>1,2</sup>, Shaohua Mo<sup>1,2</sup>, Xin Nie<sup>1,2</sup>, Chuanjin Lan<sup>1,2</sup>, Qingyuan Liu<sup>1,2</sup> & Shuo Wang<sup>1,2</sup> □

The triglyceride-glucose (TyG) index, a marker of insulin resistance, reflects combined lipid and glucose dysregulation, which may exacerbate severe spontaneous intracerebral hemorrhage (SSICH) outcomes. The association of TyG index and postoperative outcome of SSICH patients hasn't been extensively studied. This study aimed to investigate whether the high TyG index was associated with increased risk of poor outcomes in SSICH patients. This study included SSICH patients from a multicenter, prospective cohort study in China from September 2019 to December 2022. TyG index was calculated on admission and the 7th day after surgery and all patients were categorized as Q1 to Q4 according to the interquartile ranges (IQRs) of TyG index. The primary outcome was the incidence of major adverse cardiovascular and cerebrovascular events (MACCE) within 180 days after hemorrhage. This study included 761 SSICH patients receiving surgery with a median admission TyG index of 7.2 (IQR, 6.7-7.6). MACCE occurred in 131 (17.2%) patients within 180 days after SSICH. The results showed that a high TyG index is related to a high incidence of 180-day MACCE events (odds ratio, 2.36, per 1 unit; 95% CI: 1.82, 2.06; P < 0.001), and the risk of 180-day MACCE events significantly increased with the TyG index from Q1 to Q4 (P for trend < 0.001). The further analysis of TyG index on the 7th day after surgery reveal the similar results between TyG index and 180-day clinical outcomes (P < 0.001). This study revealed that high TyG index was associated with the risk of poor outcomes in SSICH patients after surgery, which may serve as an effective and stable indicator for clinical monitoring.

**Keywords** Triglyceride glucose index, Spontaneous intracerebral hemorrhage, Major adverse cardiovascular and cerebrovascular events, Surgery, Metabolism

Spontaneous intracerebral hemorrhage is the third most common subtype of stroke, contributing to 10–20% of all stroke cases and over 30% of stroke-related deaths<sup>1</sup>. SSICH is characterized by extensive hematoma and escalating intracranial pressure, which is the most perilous and fatal form of hemorrhagic stroke. As a potentially lethal disease, the outcomes of SSICH depend on many aspects, including timely surgical intervention and efficient site-specific critical care<sup>2</sup>. Currently, with the advancement of ongoing optimized treatment protocols, the long-term disability and complication, as well as the accompanying growing economic burden, cannot be neglected<sup>3</sup>. Thus, this situation underscores the need for the identification of prognostic indicators that can evaluate the adverse outcomes in a relatively accurate range. The selected indicator should also be convenient, stable, and cost-efficient in the clinical setting.

<sup>1</sup>Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, People's Republic of China. <sup>2</sup>China National Clinical Research Center for Neurological Diseases, Beijing, People's Republic of China. <sup>3</sup>Beijing Youyi Hospital, Capital Medical University, Beijing, People's Republic of China. <sup>4</sup>Haishuang Tang and Kaiwen Wang contributed equally. <sup>⊠</sup>email: 13260457220@163.com; captain9858@126.com

TyG index consists of triglycerides and fasting blood glucose, and patients with elevated TyG index were characterized by dysregulation of lipid metabolism and glucose metabolism<sup>4</sup>. The subsequent intertwined metabolic abnormalities constantly lead to severe disease complications in clinical<sup>5</sup>. While TyG index is linked to several cerebrovascular diseases including intracranial/extracranial atherosclerotic stenosis, ischemic stroke and cerebral small vessel disease<sup>6,7</sup>, its utility in SSICH—where acute metabolic derangements from hematoma and intracranial hypertension may synergize with chronic metabolic dysfunction—has not been investigated. Metabolic dysfunction after SSICH—characterized by insulin resistance, hypertriglyceridemia, and hyperglycemia—may impair hematoma clearance and exacerbate neuroinflammation, linking TyG index to clinical deterioration. We hypothesize that TyG index reflects both baseline metabolic dysregulation and acute stress responses, offering a dynamic prognostic tool in SSICH.

This study focused on the relationship between the TyG index and the relevant clinical outcomes in SSICH patients. And we paid further attention to whether TyG index was reliable enough to provide an underlying hint of long-term outcomes on both admission time and on 7 th day after surgery. Thus, in this research, we aim to evaluate whether TyG index can serve as an effective and stable indicator in SSICH and to promote the critical care protocol in those SSICH patients.

# Materials and methods Study population

The patients involved in this study were enrolled by a multicenter, prospective cohort (SAP-ICH cohort, unique identifier: ChiCTR1900024406) and the patients were diagnosed with SSICH from September 2019 to December 2022 in seven medical institutions. The ethical approval was obtained in our study. This study was performed in accordance with the Declaration of Helsinki. Guardians of all patients provided written informed consent.

The inclusion criteria were listed in the following: (1) age between 18 and 75 years; (2) non-traumatic severe intracerebral hemorrhage, which was confirmed by radiological examinations (supratentorial hematoma volume > 30 ml, infratentorial hematoma volume > 10 ml, midline shift > 1 cm, or severe intraventricular hemorrhage). (3) patients with complete data of TyG index both in preoperative and postoperative time of the surgical group. The exclusion criteria were listed in the following: (1) patients received conservative treatment; (2) hemorrhagic transformation of cerebral infarction; (3) intracranial tumors (such as meningioma, glioma, etc.); (4) cerebrovascular diseases (such as intracranial aneurysms, cerebrovascular malformations, etc.); (5) severe coagulation disorders such as hemophilia, or coagulation dysfunction; (6) intracerebral hemorrhage precipitated by venous thrombosis; (7) death within a short period (6 h) postadmission; (8) lacking crucial or follow-up data; (9) antithrombotic medication (vitamin K antagonist and et al.) before hemorrhage. The diagram of included patients is displayed in Fig. 1.

## Clinical data extraction and data processing

Demographic and clinical data were collected from electronic medical records, consisting of age, sex, comorbidities (i.e., hypertension, diabetes mellitus, dyslipidemia, coronary heart disease and ischemic stroke), alcohol and tobacco consumption history, treatment strategy and hematoma site. Laboratory indicators included triglyceride, and glucose both from preoperative and postoperative periods. Patients' neurological function was evaluated by virtue of a modified Rankin Scale (mRS)<sup>8</sup>.

Alcohol consumption history was classified as regular drinkers (one drink or more per week) and non-regular drinkers (less than one drink per week, or no drinking)<sup>9</sup>. Tobacco consumption history was classified as current smokers (patients never quit smoking or have smoking cessation less than 1 year)<sup>10</sup>. Hematoma sites were categorized as infratentorial and supratentorial<sup>11</sup>.

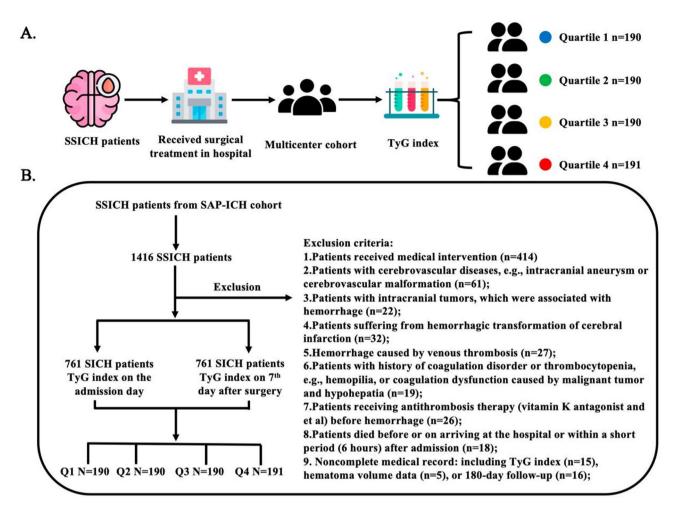
Radiological features were measured by two investigators (who worked as vascular neurosurgeons for >5 years, and were blinded to the patients' clinical information), according to the CT results on admission. The discrepancy was properly solved by a senior neurosurgeon (who worked as vascular neurosurgeon for >15 years). Radiological features included hematoma location and volume, and intraventricular bleeding. The ABC/2 method was employed to measure hematoma volume.

#### TyG index calculation

TyG index was selected over individual parameters due to its superior representation of insulin resistance, a key mechanistic link to vascular outcomes. The TyG index, the main indicator in the study, was calculated by the following formula: Ln (triglycerides  $[mg/dL] \times fasting$  blood glucose [mg/dL]/2). TyG index was measured on the day of admission and on the 7th day after surgery. Day 7 was selected to balance surgical recovery and metabolic stabilization, avoiding acute postoperative fluctuations while capturing persistent stress response.

#### Outcome assessment and follow-up protocol

The primary outcome was the MACCE (including myocardial infarction and ischemic stroke) rate of SSICH patients on the 180 th day after hemorrhage<sup>12</sup>. The secondary outcome was the mortality rate on the 180 th day after hemorrhage and the neurological function outcome of SSICH patients on the 180 th day after hemorrhage, evaluated using the mRS score<sup>8</sup>. A 180-day mRS of 4–6 was defined as a poor outcome, while an mRS of 0–3 was deemed as good outcome. The mRS is a globally recognized measure of neurological function, ranging from 0 to 6, with 0–3 indicating no or mild/moderate disability and 4–6 indicating severe disability or death. To circumvent evaluation bias, in-hospital and follow-up records were collected and independently assessed by two experienced neurosurgeons (with more than 10 years of work experience and blinded to patients' information). Any disagreements were resolved through consultation with a senior neurosurgeon (with more than 20 years of work experience).



**Fig. 1.** Diagram of TyG index study design of study. The summary of data generation in the study. The flowchart and design of enrolled patients in the TyG index study. This study prospectively included SSICH patients receiving surgery from the hospital. SSICH, spontaneous intracerebral hemorrhage; TyG index, triglyceride glucose index.

All included SSICH patients were monitored through clinical and radiological follow-up. Clinical follow-up includes outpatient visits and telephonic consultations every 3 months until either death or 180 days after discharge. During each follow-up, investigators recorded survival status, and causes of death (if applicable), and assessed functional state using the mRS score<sup>8</sup>. Radiological follow-up includes head CT examination, and/or head MRI examination, on the 30 th day and 180 th day after discharge.

#### Statistical analysis

All statistical analyses were carried out by using SPSS (version 27.0) and GraphPad Prism 10 software. A two-tailed P< 0.05 was considered to be of statistical significance. Normally distributed continuous variables were represented as means and SD, and medians and inter-quartile range for non-normally distributed data. Categorical variables were presented as numbers (n) and percentages (%). Differences between continuous variables were compared using Student's t-tests or Wilcoxon rank sum tests, and differences in categorical variables using  $\chi^2$  tests or Fisher's exact tests. To identify the factors related to poor outcomes of SSICH patients, univariate and multivariate logistic regression analyses were performed. The result was presented as an odds ratio (OR) and 95% CI. The performance of TyG index for predicting the risk of outcome events was evaluated by using the C-index and receiver operating characteristic curve. AUCs were validated via bootstrap and calibrated using Hosmer-Lemeshow tests (p > 0.05 for all models). Subgroup analysis was performed based on sex, age (> 60 and  $\leq$  60 years), smoking, drinking, diabetes mellitus, dyslipidemia, coronary heart disease, and ischemic stroke.

#### Results

#### **Baseline** information

In this study, 761 SSICH patients receiving surgical treatment were enrolled according to the stringent inclusion and exclusion criteria (Fig. 1).

The demographic and clinical characteristics of the included patients were summarized in Table 1. Of them, the median age was 52 (IQR: 43-62) years, and 582 (76.5%) patients were male. 97 (12.7%) patients had a

Categories	Overall (N= 761)	Q1 (N= 190)	Q2 (N= 190)	Q3 (N=190)	Q4 (N= 191)	P value
TyG index, m (IQR)	7.2 (6.7–7.6)	6.5 (6.4-6.6)	6.9(6.8-7.0)	7.3 (7.1–7.3)	8.1 (7.8-8.3)	< 0.001*
Age, m (IQR), years	52 (43-62)	52 (44, 62)	54(46, 63)	53 (42, 62)	51 (40, 62)	0.590
Male, n (%)	582 (76.5)	140 (73.7)	137 (72.1)	156 (82.1)	149 (78.0)	0.092
BMI	31.4 (27.3-35.5)	29.7 (25.4–32.9)	31.2 (27.1–35.6)	31.5 (27.1–35.8)	32.3 (28.3–36.)	< 0.001*
Comorbidities, n (%)						
Hypertension	655 (86.1)	162 (85.3)	159 (83.7)	172 (90.5)	162 (84.8)	0.221
Diabetes mellitus	97 (12.7)	21 (11.1)	11 (5.8)	28 (14.7))	37 (19.4)	< 0.001*
Dyslipidemia	54 (7.1)	4 (2.1)	8 (4.2)	18 (9.4))	24 (12.6)	< 0.001*
Coronary heart disease	60 (7.9)	10 (5.3)	13 (6.8)	17 (8.9)	20 (10.5)	0.247
Ischemic stroke	114 (15.0)	22 (11.6)	35 (18.4)	32 (16.8)	25 (13.1)	0.208
Regular alcohol drink, n (%)	244 (32.1)	48 (25.3)	55 (28.9)	74 (38.9)	67 (35.1)	0.020*
Current-or-ever tobacco, n (%)	214 (28.1)	48 (25.3)	51 (26.8)	52 (27.4)	63 (33.0)	0.360
mRS score (4-6) on admission	430 (56.5)	101 (53.2)	113 (59.5)	111 (58.4)	105 (54.9)	0.108
Hematoma volume (ml)	38 (25–47)	36 (20-45)	39 (25–48)	35 (21–46)	38 (24-46)	0.538
Hematoma location, n (%)						0.061
Infratentorial	56 (7.4)	19 (10.0)	8 (4.2)	19 (10.0)	10 (5.2)	
Supratentorial (Deep and superficial)	705 (93.6)	171 (90.0)	182 (95.8)	171 (90.0)	181 (94.8)	

**Table 1**. Characteristics and outcomes of patients, categorized by the interquartile range of TyG index. \*, significant difference. All patients were categorized by the interquartile range of TyG index, as Q1-Q4. TyG index, triglyceride glucose index; mRS: modified Rankin scale, BMI: body mass index.

180-day outcomes	Overall ( <i>N</i> = 761)	Q1 (N= 190)	Q2 (N=190)	Q3 (N= 190)	Q4 (N= 191)	P value
mRS score, n (%)						< 0.001*
0-3	533 (70.0)	165 (86.8))	157 (82.6)	125 (65.8)	86 (45.0)	
4-6	228 (30.0)	25 (13.2)	33 (17.4)	65 (34.2)	105 (55.0)	
MACCE, n (%)	131 (17.2)	11 (5.8)	22 (11.6)	35 (18.4)	63 (33.0)	< 0.001*
Mortality, n (%)	114(15.0)	9 (4.7)	15 (7.9)	16 (8.4)	74 (38.7)	< 0.001*

**Table 2.** 180-day clinical outcomes and TyG index in SSICH patients. \*, significant difference. All patients were categorized by the interquartile range of TyG index, as Q1-Q4. mRS, modified rankin scale; MACCE, major adverse cardiovascular and cerebrovascular events.

history of diabetes mellitus and 54 (7.1%) dyslipidemia. 184 (24.2%) patients received antiplatelet therapy before hemorrhage. 56 (7.4%) hematomas were infratentorial and 705 (92.6%) supratentorial.

The median TyG index was 7.2 (IQR: 6.7–7.6) (Figure S1). Based on the IQR of the TyG index, 761 SSICH patients were categorized into four groups (Fig. 1; Table 1). The specific TyG index for Q1 was 6.5 (6.4–6.6), Q2 was 6.9(6.8–7.0), Q3 was 7.3 (7.1–7.3) and Q4 was 8.1 (7.8–8.3). Comparing the differences among the four groups, significance was found in alcohol abuse, diabetes mellitus, and dyslipidemia (all P < 0.05).

### Elevated TyG index as a risk factor of 180-day MACCE events

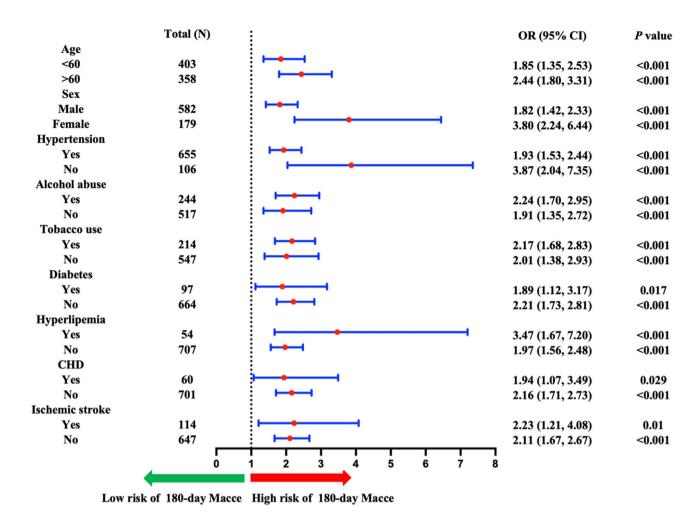
After a median follow-up time of 390 (IQR, 192–588) days, MACCE events occurred in 131 (17.2%) patients within 180 days after surgery, with a mortality as 114 (15.0%) (Table S1). 228 (30.0%) patients were with the 180-day mRS score of 4–6. From the low level to the high level of the TyG index, the incidence of MACCE events, mortality and mRS score of 4–6 had an increasing trend (P< 0.001, Table 2).

As shown in Table 3, the logistic model analysis showed that increasing the TyG index was related to increasing the risk of 180-day MACCE events (OR 2.36, per 1 unit; 95% CI, 1.82, 2.06; P < 0.001), and the risk of 180-day MACCE events significantly increased with the TyG index from Q1 to Q4 (P for trend < 0.001). After being adjusted for age, sex, hypertension, diabetes mellitus, dyslipidemia, ischemic stroke, and coronary heart disease, the result remained consistent. For the secondary outcomes, the increasing TyG index was also associated with an increasing risk of 180-day mortality and a 180-day mRS score of 4–6 (Tables S2 and S3).

As shown in Fig. 2, subgroup analysis showed that the increasing TyG index was related to the increasing incidence of 180-day MACCE events in all subgroups (all P < 0.05). Subgroups with hyperlipidemia (OR 3.47, p = 0.002) showed stronger associations, likely due to amplified metabolic dysfunction, suggesting synergistic effects. A similar result was also observed in the TyG index for 180-day mortality and 180-day mRS score of 4–6 (Figure S2 and Figure S3).

	Model 1			Model 2			Model 3		
Parameters	OR (95% CI)	P value	P for trend	OR (95% CI)	P value	P for trend	OR (95% CI)	P value	P for trend
Continuous variable per 1 unit of TyG index	2.36 (1.82, 2.06)	< 0.001 ∗		2.37 (1.82, 3.08)	< 0.001*		2.34 (1.79, 3.08)	< 0.001*	
Interquartile range			< 0.001*			< 0.001∗			< 0.001*
Q1 $(n = 190)$	Reference			Reference			Reference		
Q2 $(n = 190)$	2.13 (1.00, 4.53)	0.049*		2.12 (0.99, 4.50)	0.051		2.03 (0.95, 4.35)	690.0	
Q3 $(n = 190)$	3.67 (1.81, 7.48)	< 0.001*		3.76 (1.85, 7.68)	< 0.001*		3.30 (1.59, 6.81)	0.001	
Q4 (n = 191)	8.01 (4.06, 15.80)	< 0.001 ∗		8.13 (4.11, 16.05)	< 0.001*		7.72 (3.87, 15.43)	< 0.001*	

Table 3. The risk of TyG index at admission for 180-day MACCEs. \*, significant difference. All patients were categorized by the interquartile range of TyG index, as Q1-Q4. Model 1, unadjusted model 2: model adjusted for age and sex. Model 3: model adjusted for age, sex, hydel 2: model adjusted for age, sex, hydel 3: modified Rankin scale; MACCE, major adverse cardiovascular and cerebrovascular events; OR, odds ratio.



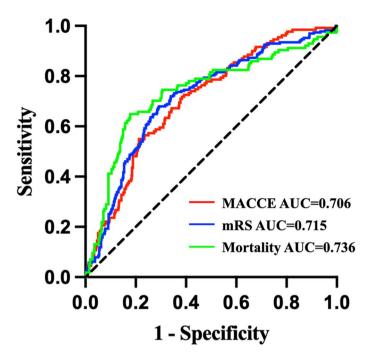
**Fig. 2**. Subgroup analysis of TyG index for 180-day MACCE. TyG index, triglyceride glucose index; MACCE, major adverse cardiovascular and cerebrovascular events; CHD, coronary heart disease.

For sensitivity analysis, since antihyperglycemic and antihyperlipidemic drugs affect glucose and glyceride metabolism, further affecting TyG index. We performed sensitivity analyses after excluding patients on antihyperglycemic/antihyperlipidemic therapy, and similar results were evidenced both when the TyG index was treated as a continuous and categorical variable. SSICH can trigger significant metabolic stress, influencing glucose and lipid metabolism, we also perform sensitivity analyses excluding patients with extreme TyG index outliers (>95 th percentile). Further, we perform sensitivity analysis filling missing values via multiple imputation using chained equations (MICE), the consistent conclusion was evidenced (Tables S4-S7).

In addition, we evaluated the performance of the TyG index to predict the 180-day clinical outcome of SSICH patients. The results showed that the C-index of the TyG index to predict the 180-day MACCE events was 0.706 (95% CI: 0.696–0.713), and the cut-off value for TyG index was 7.3. The C-index predicting 180-day mortality was 0.736 (95% CI: 0.725–0.745) and the C-index predicting 180-day mRS score of 4–6 was 0.715 (95% CI: 0.706–0.723) (Fig. 3). The performance of TyG index on predicting the incidence of 180-day MACCE, 180-day mortality and 180-day mRS was superior when compared with individual triglycerides/glucose (Tables S8).

# TyG index serves as a stable indicator for 180-day poor clinical events

To investigate whether the TyG index can serve as a stable indicator for 180-day poor clinical events, the TyG index on the 7 th day after surgery was further acquired. The median TyG index on the 7 th day after surgery was 7.2 (IQR: 6.6–7.8), and there was no significant difference between TyG index on admission and on the 7 th day (p = 0.328). The TyG index trajectories showed persistent elevation in MACCE patients compared to non-MACCE (median increase 0.12 in MACCE vs. decrease 0.08 in non-MACCE). The logistic model analysis showed that increasing TyG index on 7 th day after surgery, both treated as continuous and categorical variable, was related to increasing risk of 180-day MACCE events (P < 0.001). The further logistic model analysis showed that increasing TyG index on the 7 th day after surgery was also related to increasing risk of 180-day mortality and 180-day mRS score of 4–6 (P < 0.001), indicating the role of TyG index serving as stable indicator of 180-day clinical outcomes in SSICH patients. (**Table S9-11**).



**Fig. 3.** Performance of TyG index on predicting the incidence of 180-day MACCE, 180-day mortality and 180-day mRS of 4–6. TyG index, triglyceride glucose index; MACCE, major adverse cardiovascular and cerebrovascular events.

#### Discussion

Patients with increasing TyG index were characterized by dysregulation of lipid metabolism and glucose metabolism. Based on a cohort including 761 SSICH patients receiving surgical treatment, we found that the increasing TyG index was associated with an increased incidence of 180-day MACCE events, 180-day mortality and 180-day mRS score of 4–6. Elevated TyG index at admission in SSICH patients was highly related to the risk of MACCE events. Further analysis of the TyG index on the 7th day after surgery suggested its stability in revealing poor outcomes. This study revealed that a high TyG index was associated with the risk of poor outcomes in SSICH patients after surgery, which may serve as an effective and stable marker for clinical monitoring.

SSICH, characterized by extensive hematoma and escalating intracranial pressure, was the most perilous and fatal form of hemorrhagic stroke, thus the proper management of SSCIH is critical in reducing the risk of poor clinical outcomes. The metabolic disorder after intracerebral hemorrhage was commonly presented in SSCIH patients, but the detailed relationship between metabolic disorder and SSCIH has not yet been completely understood. And study strongly suggested maintaining appropriate levels of blood glucose level and triglyceride level when treating SSCIH patients<sup>13</sup>.

TyG index consists of triglyceride and blood glucose, and patients with elevated TyG index were characterized by dysregulation of lipid metabolism and glucose metabolism<sup>4</sup>. The previous study suggested a positive association between high triglyceride levels and intracerebral hemorrhage<sup>14</sup>. Meanwhile, research revealed that the hyperglycemia level could independently increase the risk of early death and poor clinical outcomes among SSCIH patients<sup>15</sup>. All these studies provide a strong basis for the further exploration of TyG index significance in SSCIH patients. In our study, the TyG index, treated both as continuous and categorical variables, showed a positive relation to increasing risk of 180-day MACCE events. In logistic regression analysis, results revealed that diabetes mellitus and dyslipidemia were related to MACCE events. After modifying these confusing factors, the TyG index still presented with a positive association with poor clinical outcomes.

The application of the TyG index in clinical settings derives from its convenience in representing insulin resistance, which is usually accompanied by disrupted glucose metabolism and subsequent disrupted lipid metabolism<sup>4</sup>. Currently, guidelines recommend incorporating insulin resistance markers in patients with metabolic syndrome and advocating for metabolic optimization<sup>16,17</sup>. While TyG index is not yet explicitly mentioned, its role as a surrogate for insulin resistance aligns with these recommendations. The advantage of TyG index utility is that it can be obtained without participants of fasting insulin level, providing a more intuitive and stable method for insulin resistance detection. The manifestations of patients who are diagnosed with insulin resistance are increased insulin levels arising from insulin insensitivity and high triglyceride levels<sup>18</sup>. The regulation of glucose by insulin mainly includes promoting the uptake of glucose by skeletal muscle, myocardium, and adipose tissue and restraining glycogen breakdown and gluconeogenesis in the liver. Elevated triglycerides level further contributes to the dysregulation of hepatic glucose production and muscle glucose metabolism. Thus, early detection of insulin resistance among at-risk populations is crucial for early management.

TyG index has been suggested as a convincing surrogate marker of insulin resistance, which provides a convenient way to measure the metabolism status of glucose and lipid<sup>19</sup>. Currently, the TyG index has been

reported to be associated with atherosclerotic disease, cardiovascular disease and cerebrovascular diseases. For cerebrovascular diseases, Wang et al. reported elevated TyG index could provide an incremental effect on the predictive value for extra-cranial artery stenosis<sup>20</sup>. Another study found high TyG index was the key risk factor for symptomatic intracranial atherosclerosis. Meanwhile, there was a synergistic effect of symptomatic intracranial atherosclerosis and higher TyG on ischemic stroke<sup>21</sup>. As for ischemic stroke, study has suggested the independent association between the TyG index and ischemic stroke occurrence<sup>22,23</sup>. Not only for the occurrence of ischemic stroke, the neurological deterioration outcomes and high recurrence rate in stroke patients with higher TyG index were also reported in recent studies<sup>24</sup>.

Of particular note, current literature on the relationship between the TyG index and hemorrhagic stroke patients was few. Huang et al. performed a retrospective analysis of hemorrhagic stroke patients in MIMIC-IV database and they aim to investigate the linkage between the TyG index and all-cause mortality<sup>25</sup>. Their study exhibited a significant correlation with all-cause mortality among hemorrhagic stroke patients. Chen et al. found the TyG index was a significant predictor of the severity of impaired consciousness and in-hospital mortality in patients with traumatic cerebral hemorrhage cerebrovascular disease<sup>26</sup>. Yang et al. also evidenced that TyG index could serve as a potential predictor for in-hospital mortality in critically ill patients with intracerebral hemorrhage<sup>27</sup>. In our study, we primarily revealed the positive association between the TyG index and poor clinical outcomes. C-index for TyG index in prediction of MACCE was 0.706, which is higher than individual glucose/triglyceride and is also higher by using ICH score (c-index = 0.673) in Chen et al. study<sup>28</sup>. TyG index also predicted functional disability (mRS 4-6: OR 2.73), highlighting its multidimensional prognostic value. While acute metabolic stress may transiently elevate TyG index, sensitivity analyses excluding outliers confirmed the association's stability, supporting TyG index as a stable marker despite acute perturbations. Besides, the evaluation of the TyG index's significance between two different times was particularly mentioned in the limitation part in the studies of Jiang et al., and Huang et al.<sup>25,29</sup>. In our study, in order to explore the stability of the TyG index, we further collected the TyG index on the 7th day after surgery, the additional analysis suggested a similar conclusion between the TyG index and poor clinical outcomes. The consistency of conclusions can helpfully provide a meaningful hint in clinical management of critically intracerebral hemorrhage patients.

Elevated TyG index levels in SSICH patients may warrant enhanced metabolic surveillance and individualized preoperative optimization. Postoperatively, this index functions as a prognostic biomarker for evaluating metabolic restoration and forecasting long-term clinical trajectories. Surgical stress frequently aggravates IR, precipitating hyperglycemia and dyslipidemia, both of which may hinder recovery and elevate the likelihood of complications. Routine TyG index monitoring enables clinicians to identify sustained metabolic disturbances and tailor therapeutic strategies accordingly. Patients with TyG index beyond cut-off values might necessitate lifestyle modifications or pharmacotherapy to attenuate secondary complication risks. Integrating the TyG index into clinical protocols can refine surgical risk stratification and perioperative management, thereby improving patient prognoses. Its utility in preoperative risk assessment and postoperative care may substantially mitigate metabolic morbidity and facilitate targeted therapeutic approaches.

The underlying pathophysiological mechanism between the TyG index and the cerebrovascular progression remains elusive. The abnormal metabolism of glucose and lipids contributed to the clinical outcome deterioration, which was also hypothesized in recent studies. Hyperglycemia and the subsequent production of glycosylated products trigger endothelium impairment. This process not only causes the downstream inflammation cascade but also causes vasodilation dysfunction<sup>30</sup>. Besides, systemic lipid disturbances provoked elevated triglyceride, elevated low-density lipoprotein levels, and reduced high-density lipoprotein levels, which promoted oxidative stress and foam cell formation<sup>31</sup>. Additionally, the imbalance metabolism of glucose and lipids may synergistically exacerbate the platelet function<sup>32</sup>. Hematoma-induced inflammation and oxidative stress may synergize with TyG-related metabolic dysfunction to impair cerebrovascular autoregulation and neuronal survival, and all these mechanisms described above contribute to the aggravation of cerebrovascular diseases including hemorrhage stroke.

In this study, we conducted the association of the TyG index and clinical outcome among SSICH patients, providing insightful evidence in this field. Yet limitations should also be noted. Firstly, due to its observational design, the residual confounding cannot be excluded through multivariate adjustment and subgroup analyses performed in this study. Secondly, only adults (> 18 years old) and exclusively Chinese were recruited in our study, and uncertain whether our results can be generalized to younger or other country patients since it is recognized that the Chinese population has a higher incidence of MACCE<sup>33</sup>. And exclusion of antithrombotic users may limit generalizability to patients with pre-existing cardiovascular conditions. Thirdly, all analyzed clinical outcomes were acquired in 180 days, thus the exact temporal relation between the TyG index and the SSICH may be blurred. Fourthly, sensitivity analyses did not account for medication duration/type, which may influence TyG index interpretation and future studies are needed to stratify by medication classes.

#### Conclusion

In summary, our results broaden the TyG index application in patients with SSICH and the results showed that the TyG index can serve as an intuitive and stable method for evaluating clinical outcome risk.

#### Data availability

The datasets used and analyzed in the current study are available from the corresponding author upon reasonable request.

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# **Author contributions**

Haishuang Tang, Qingyuan Liu, and Shuo Wang design and concept the article; Haishuang Tang, Kaiwen Wang and Kaige Zheng prepare and write the article; Zheng Wen, Yi Yang, Shaohua Mo, Xin Nie and Chuanjin Lan review this study and provide the suggestions for revision.

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#### **Declarations**

# **Competing interest**

The authors declare no competing interests.

# Ethics approval and consent to participate

This study was granted approval from the Institutional Review Board of Beijing Tiantan Hospital (KY 2021–053 – 02), the patient's family sign the written informed consent before beginning.

#### Additional information

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Correspondence and requests for materials should be addressed to Q.L. or S.W.

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