Stress hyperglycemia predicts early neurological deterioration and poor outcomes in patients with single subcortical infarct

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Research Article

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Abstract

Aim: The goal of this study was to determine whether the stress hyperglycemia ratio (SHR) is associated with early neurological deterioration (END) and poor outcomes in patients with single subcortical infarct (SSI).

Methods: This study prospectively enrolled patients with SSI admitted between 2015 and 2021. END was defined as an increase of ≥ 2 points in the National Institutes of Health Stroke Scale (NIHSS) or ≥ 1 point in the motor items of the NIHSS within seven days of hospital admission. The modified Rankin Scale (mRS) was used to evaluate patient prognosis. Good and poor outcomes were defined as mRS scores ≤ 2 and > 2, respectively. The relationships between SHR and risk of END as well as outcomes were analyzed using multivariate logistic regression models.

Results: A total of 1049 patients with SSI and an average age of 59.49 years met the inclusion criteria for the analysis. The incidence of END markedly increased with increasing SHR. Multivariate logistic regression analysis showed that a higher SHR was independently associated with END (OR 4.04, 95% CI, 2.43-6.69, $P < 0.001$) and 3-month poor outcomes (OR 2.34, 95% CI, 1.44-3.82, $P = 0.003$). A receiver operating characteristic analysis of the SHR based on the area under the curve showed a diagnostic accuracy equal or greater than other well-known predictors. **Conclusion:** SHR is a reliable predictor of END and poor outcomes in patients with SSI.

Introduction

A single subcortical infarct (SSI) is defined as an infarction within the perforating artery, and is usually associated with favorable outcomes[1, 2]. However, between 20 and 43% of patients may suffer from early neurological deterioration (END), which has deleterious effects on long-term functional outcomes[3]. Increasing interest has focused on the identification of new markers to better classify patients who are at a higher risk for END[4]. Many demographic, clinical, and laboratory variables have been used to identify the risk for END, such as age, sex, homocysteine, and inflammatory factors[5–7]; however, the predictive value of these indicators remains limited.

Stress hyperglycemia is the relative temporary increase in glucose, secondary to inflammation during neurohormonal disturbances and critical illnesses, such as stroke[8]. Previous human and animal studies have shown that stress hyperglycemia is associated with a high risk of cardiovascular diseases[9–11]. However, few studies have investigated the association between stress hyperglycemia and the risk of END in patients with SSI. Furthermore, although previous studies have analyzed the status of diabetes, most of them defined stress hyperglycemia as the index of the glucose/HbA1c ratio[12, 13]. Nathan et al. created an equation to convert HbA1c into estimated average glucose values 'Estimated average glucose = ((1.59 × HbA1c) − 2.59)[14]. Glycemic control can be assessed more accurately using this estimate instead of measuring HbA1c. Additionally, the stress-induced hyperglycemia ratio (SHR), which is

calculated as admission blood glucose divided by estimated average glucose, was developed to define stress hyperglycemia.

In this study, we aimed to investigate whether the SHR is associated with END and poor outcomes in patients with SSI.

Patients And Methods

Study participants were obtained from the Henan Province Stroke Registry[15, 16] at the First Affiliated Hospital of Zhengzhou University. Patients with SSI admitted within 72 h after onset of symptoms were examined between January 2015 and January 2022. Brain magnetic resonance imaging (MRI), electrocardiography, and laboratory examinations were performed on all patients. SSI was diagnosed when there was a single subcortical infarction in a perforating artery (lenticulostriate artery, posterior cerebral artery, or territories basilar artery) on diffusion-weighted imaging. The ethics committee of the First Affiliated Hospital of Zhengzhou University approved this study (Approval No. 2021-KY-0067-001), and all patients signed written informed consent forms.

The inclusion criteria were as follows: (1) patients admitted within 72 h after symptom onset with SSI confirmed by diffusion-weighted imaging, (2) aged ≥ 18 years, (3) who provided signed informed consent.

The exclusion criteria were as follows: (1) suspected cardioaortic embolism or ipsilateral carotid artery stenosis (50% of cases); (2) glucose-lowering use; (3) END occurred before the first brain MRI after admission; (4) cancer, surgery, or severe renal or hepatic disease; (5) incomplete National Institutes of Health Stroke Scale (NIHSS) score or other baseline data; (6) loss to follow-up.

Data Collection

Patient demographics, clinical characteristics, and cardiovascular risk factors were assessed at baseline, including sex, age, diastolic blood pressure, systolic blood pressure, drinking, and smoking. Risk factors included a coronary heart disease (CHD), history of hypertension, diabetes mellitus, atrial fibrillation, stroke/transient ischemic attacks (TIA), and dyslipidemia. Laboratory examinations, including blood routine examination, fasting plasma glucose (FPG), HbAlc, total cholesterol, and LDL-C, were routinely performed within 24 h of admission. SHR was calculated using the following formula: SHR = admission FPG / [1.59 × HbA1c (%) − 2.59].

A 3.0-T MR scanner was used to perform brain MRI and MR angiography within 24 hours of admission for all participants. Proximal SSI refers to an infarction located adjacent to the parent artery and extending towards the basal surface of the parent artery. Distal SSI was defined as an infarction that exists only in the distal area which does not meet the basal surface of the parent artery[17]. Anterior and

posterior circulations were involved in the involved vascular territory. Two trained neuroradiologists reviewed all the imaging procedures and performed the analysis.

The NIHSS score was used to evaluate SSI severity on the day of admission. After admission, NIHSS scores were assessed by two certified neurologists 1–2 times per day. END was defined as an increase of ≥ 2 points in the total NIHSS score or ≥ 1 point in the motor items of the NIHSS within seven days of admission[18]. Most patients were subsequently followed up via telephone. Patient prognosis was evaluated using the modified Rankin Scale (mRS). Good and poor prognosis were defined as mRS scores ≤ 2 and > 2, respectively.

Statistical analysis

SPSS (version 24.0; IBM Corp, Armonk, NY, USA) was used to conduct statistical analyses. Mann-Whitney U tests or independent Student's t-tests were used to analyze continuous variables described as mean ± SD. Categorical variables were presented as proportions and analyzed using $\chi 2$ tests. The associations between SHR and END, as well as the 3-month outcomes were evaluated using multivariate logistic regression analysis. SHR was divided into quartiles (Q1, < 0.89; Q2, ≥ 0.89 and < 0.95; Q3, ≥ 0.95 and < 1.11; and Q4, ≥ 1.11). Two models corresponding to the different endpoint outcomes were used. The baseline variables were adjusted for in the models, except for those that were collinear. Receiver operating characteristic (ROC) analysis was used to determine the critical values of SHR for predicting END, 3-month mortality, and 3-month poor outcome. We calculated the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy accordingly. Area under the curve (AUC) tests were performed using MedCalc's DeLong test package to compare diagnostic accuracy. All probability values were two-tailed. A threshold of $P < 0.05$ was used for statistical significance.

Results

Baseline characteristics

A total of 1049 patients with SSI (743 males and 306 females) with an average age of 59.49 ± 12.19 years met the inclusion criteria for analysis (Table 1). The baseline NIHSS score was 3 (IQR: 1–5); the admission FPG and HbA1c were 6.40 ± 2.58 mmol/l and 6.96 ± 1.91 mmol/l, respectively, and the average SHR was 1.01 ± 0.23. END was observed in 206 (19.6%) patients. Poor outcomes were as follows: 3-month mortality (23 patients, 2.2%) and 3-month poor mRS (3–6; 195 patients, 18.6%). A total of 361 patients were excluded from the study (Fig. 1). There was a good balance between the baseline characteristics of the excluded and included patients ($P > 0.05$).

Table 1
The baseline characteristics of the included and excluded patients.

Characteristics	Enrolled (n = 1049)	Excluded (n = 361)	*P* Value
Age (years)	59.49 ± 12.19	59.01 ± 12.29	0.591
Male, n (%)	743 (70.8)	265 (73.4)	0.282
SBP (mmHg)	148.64 ± 23.96	146.62 ± 23.86	0.877
DBP (mmHg)	88.45 ± 13.91	88.23 ± 13.89	0.776
Smoking	337 (32.1)	115 (31.9)	0.818
Drinking	264 (25.2)	92 (25.6)	0.824
Baseline NIHSS	3 (1–5)	3 (1–4)	0.625
Reperfusion therapy	103 (9.8)	33361 (9.2)	0.184
Medical history, n (%)			
Hypertension	624 (59.4)	208 (57.5)	0.636
CHD	97 (9.2)	34 (9.4)	0.892
Atrial fibrillation	49 (4.7)	18 (5.1)	0.652
Diabetes mellitus	253 (24.2)	80 (22.2)	0.710
Stroke/TIA	251 (23.9)	92 (25.5)	0.539
Dyslipidemia	85 (8.1)	25 (6.8)	0.125
SSI type n (%)			0.548
Proximal SSI	519 (49.5)	172 (47.6)	
Distal SSI	530 (50.5)	189 (52.4)	
Involved vascular territory, n (%)			0.585
Anterior SSI	628 (59.9)	222 (61.5)	
Posterior SSI	412 (40.1)	139 (38.5)	
Laboratory			
WBC (10^9/L)	6.77 ± 1.97	6.85 ± 2.18	0.529

SBP, systolic blood pressure; DBP, diastolic blood pressure; NIHSS, national institutes of health stroke scale; CHD, coronary heart disease; TIA, transient ischemic attack; WBC, white blood cell; TC, total cholesterol; LDL-C, low-density lipoprotein; FPG, fasting plasma glucose; SHR, stress-induced hyperglycemia ratio; SSI, single subcortical infarct

Characteristics	Enrolled (n = 1049)	Excluded (n = 361)	*P* Value
TC (mmol/L)	4.27 ± 1.17	4.23 ± 1.12	0.621
LDL-C (mmol/L)	2.71 ± 1.04	2.62 ± 0.95	0.182
FPG (mmol/L)	6.40 ± 2.58	6.13 ± 2.38	0.307
HbAlc (mmolL)	6.96 ± 1.91	6.87 ± 1.75	0.298
SHR	1.01 ± 0.23	0.99 ± 0.22	0.603

SBP, systolic blood pressure; DBP, diastolic blood pressure; NIHSS, national institutes of health stroke scale; CHD, coronary heart disease; TIA, transient ischemic attack; WBC, white blood cell; TC, total cholesterol; LDL-C, low-density lipoprotein; FPG, fasting plasma glucose; SHR, stress-induced hyperglycemia ratio; SSI, single subcortical infarct

A quartile system was used to divide SHR values from small to large (Q1, < 0.89; Q2, ≥ 0.89 and < 0.95; Q3, ≥ 0.95, and < 1.11; and Q4, ≥ 1.11). Based on the quartile groups, baseline characteristics of the patients were compared (Q1–Q4). As shown in Table 2, a history of diabetes was more common among patients in the highest quartile of SHR. In contrast, the higher the SHR, the smaller was the number of distal SSI. Patients in the fourth SHR quartile had higher age, WBC, FPG, and HbA1c values than those in the other three groups. Moreover, neurological impairment, as measured by the NIHSS score at admission, was more severe in patients in the fourth SHR quartile than in those in the other groups. Other characteristics were not statistically significant.

Table 2
Comparison of the clinical, and laboratory testing characteristics between patients with different values of SHR.

Characteristic	SHR				*P* Value
	Q1 (n = 262)	Q2 (N = 262)	Q3 (N = 262)	Q4 (N = 263)	
Age (years)	58.81 ± 12.31	57.28 ± 11.52	59.91 ± 12.95	60.22 ± 12.29	0.027
Male, n (%)	179 (68.1)	186 (71.1)	182 (68.9)	196 (74.8)	0.331
SBP (mmHg)	144.62 ± 24.27	146.95 ± 24.25	147.71 ± 23.84	147.23 ± 23.11	0.456
DBP (mmHg)	87.12 ± 12.42	88.87 ± 13.96	88.60 ± 14.14	88.32 ± 14.88	0.495
Smoking	71 (27.1)	83 (31.4)	93 (35.5)	90 (34.4)	0.158
Drinking	57 (21.7)	59 (22.4)	77 (29.5)	71 (27.2)	0.115
Baseline NIHSS	2 (1–4)	3 (1–4)	4 (2–5)	4 (2–7)	0.015
Reperfusion therapy	24 (9.3)	24 (9.3)	21 (8.0)	34 (12.9)	0.249
Medical history, n (%)					
Hypertension	148 (56.3)	149 (57.1)	163 (62.4)	164 (62.6)	0.296
CHD	24 (9.2)	22 (8.4)	25 (9.5)	26 (9.9)	0.899
Atrial fibrillation	12 (4.6)	12 (4.6)	10 (3.8)	15 (5.7)	0.452
Diabetes mellitus	47 (18.1)	60 (22.9)	63 (24.0)	82 (31.2)	0.006
Stroke/TIA	60 (23.1)	66 (25.2)	58 (22.1)	67 (25.5)	0.751
Dyslipidemia	20 (7.7)	22 (8.4)	26 (9.9)	17 (6.5)	0.538
SSSI type n (%)					0.009
Proximal SSI	115 (44.2)	116 (44.3)	142 (53.8)	146 (55.5)	
Distal SSI	145 (55.8)	146 (55.7)	122 (46.2)	117 (44.5)	
Involved vascular territory, n (%)					0.152
Anterior SSI	171 (65.8)	149 (56.9)	156 (59.1)	152 (57.8)	
Posterior SSI	89 (34.2)	113 (43.1)	108 (40.9)	111 (42.2)	
Laboratory					

SBP, systolic blood pressure; DBP, diastolic blood pressure; NIHSS, national institutes of health stroke scale; CHD, coronary heart disease; TIA, transient ischemic attack; WBC, white blood cell; TC, total cholesterol; LDL-C, low-density lipoprotein; FPG, fasting plasma glucose; SHR, stress-induced hyperglycemia ratio; SSI, single subcortical infarct

Characteristic	SHR				*P* Value
	Q1 (n = 262)	Q2 (N = 262)	Q3 (N = 262)	Q4 (N = 263)	
WBC (10^9/L)	6.91 ± 2.19	6.69 ± 2.20	6.62 ± 1.93	7.18 ± 2.34	0.016
TC (mmol/L)	4.12 ± 1.16	4.15 ± 0.94	4.32 ± 1.14	4.34 ± 1.21	0.054
LDL-C (mmol/L)	2.55 ± 1.01	2.57 ± 0.83	2.71 ± 1.03	2.67 ± 0.91	0.167
FPG (mmol/L)	5.30 ± 1.39	5.38 ± 1.06	5.98 ± 1.73	7.87 ± 3.49	0.001
HbAlc (mmolL)	8.08 ± 2.03	6.75 ± 1.39	6.32 ± 1.33	6.33 ± 1.57	0.001

SBP, systolic blood pressure; DBP, diastolic blood pressure; NIHSS, national institutes of health stroke scale; CHD, coronary heart disease; TIA, transient ischemic attack; WBC, white blood cell; TC, total cholesterol; LDL-C, low-density lipoprotein; FPG, fasting plasma glucose; SHR, stress-induced hyperglycemia ratio; SSI, single subcortical infarct

Association Between Shr And Outcomes After Ssi

The incidence of END markedly increased with increasing SHR (Table 3). As shown in Fig. 2, compared with the lowest quartile of SHR, univariate analysis revealed OR (95% CI) with the highest quartile were 3.96 (2.21–6.89) for END, 2.95 (0.32–11.95) for mortality, and 2.52 (1.31–3.95) for poor outcome. After adjusting for age, sex, reperfusion therapy, baseline NIHSS score, history of ischemic stroke/TIA, hypertension, CHD, atrial fibrillation, diabetes mellitus, dyslipidemia, SSI type and WBC count, the multivariate logistic regression analysis showed that higher SHR was independently associated with END (OR 4.04, 95% CI, 2.43–6.69, $P < 0.001$) and 3-month poor mRS (OR 2.34, 95% CI, 1.44–3.82, $P = 0.001$). Similar results were observed for each end point when the sensitivity analyses were further adjusted for SHR (Table 3, **Model 2).**

Table 3
Risk of Outcomes After A SSI by SHR

Outcomes	SHR	n	Events, n (%)	Model 1*	*P* Value	Model 2**	*P* Value
END	Q1 (0. 89)	262	23 (8.8)	1		1	
	Q2 (0.89–0.95)	262	50 (19.1)	2.43 (1.43–4.12)	0.001	2.73 (1.53–4.87)	0.001
	Q3 (0.95–1.11)	262	59 (22.3)	2.97 (1.77–4.97)	0.001	3.48 (1.87–6.43)	0.001
	Q4 (1.11)	263	74 (28.1)	4.04 (2.43–6.69)	0.001	4.43 (2.22–8.89)	0.001
	P for trend				0.001		0.001
3-month mortality	Q1 (0. 89)	262	3 (1.2)	1		1	
	Q2 (0.89–0.95)	262	4 (1.5)	1.33 (0.29–5.99)	0.712	1.11 (0.24–5.19)	0.895
	Q3 (0.95–1.11)	262	7 (2.7)	2.33 (0.59–9.12)	0.223	1.91 (0.45–8.12)	0.385
	Q4 (1.11)	263	9 (3.4)	3.04 (0.81–11.34)	0.099	1.14 (0.23–5.74)	0.877
	P for trend				0.294		0.727
3-month poor mRS (3–6)	Q1 (0. 89)	262	28 (10.7)	1		1	
	Q2 (0.89–0.95)	262	55 (21.1)	2.20 (1.35–3.60)	0.002	2.27 (1.37–3.77)	0.001
	Q3 (0.95–1.11)	262	54 (20.5)	2.13 (1.31–3.49)	0.003	2.08 (1.25–3.46)	0.005

*Model 1: adjusted for age, sex, baseline NIHSS, reperfusion therapy, history of ischemic stroke/TIA, hypertension, CHD, atrial fibrillation, diabetes mellitus, dyslipidemia, SSI type, WBC

**Model 2: adjusted for model 1 + glucose, HbAlc

Outcomes	SHR	n	Events, n (%)	Model 1*	*P* Value	Model 2**	*P* Value
	Q4 (1.11)	263	58 (22.1)	2.34 (1.44–3.82)	0.001	2.32 (1.14–3.86)	0.001
	P for trend				0.003		0.005
*Model 1: adjusted for age, sex, baseline NIHSS, reperfusion therapy, history of ischemic stroke/TIA, hypertension, CHD, atrial fibrillation, diabetes mellitus, dyslipidemia, SSI type, WBC							
**Model 2: adjusted for model 1 + glucose, HbAlc							

Results Of Subgroup Analysis For The Outcomes

In the subgroup analysis, our results showed that particular groups might alter the correlation between SHR and outcomes (Fig. 3). There was an independent association between SHR and END in older patients (OR 6.73, 95% CI, 3.12–8.95), thrombolysis patients (OR 5.31, 95% CI, 3.01–8.41), non-diabetic patients (OR 6.73, 95% CI, 1.89–10.98), and proximal type SSI (OR 4.39, 95% CI, 2.32–6.22). Furthermore, the association between SHR and 3-month poor mRS was attenuated in young (OR 1.67, 95% CI, 0.86–3.23) and distal type SSI (OR 1.05, 95% CI, 0.45–2.44).

Predictive Values Of Fpg And Shr For Outcomes In Ssi

As shown in Table 4 and Fig. 4, FPG and SHR were analyzed using ROC curves to determine their predictive value for SSI outcome. SHR showed a higher AUC value than FPG ($P < 0.001$) in END (AUC = 0.798, 95% CI, 0.773–0.822) and poor mRS (AUC = 0.720, 95% CI, 0.692–0.747). There were no statistically significant differences in the mortality rates. The best predictive cut-off values of SHR were 1.035 for END (sensitivity 58.7% and specificity 71.2%), 1.085 for 3-month mortality (sensitivity 65.2% and specificity 74.1%), and 1.075 for 3-month poor mRS (sensitivity 42.6% and specificity 74.6%). Table 4 shows the positive and negative likelihood ratios and accuracies of each predictive marker.

Table 4
The cut-off points and accuracy of SHR to predict END and poor outcomes.

Variable	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
END	1.035	58.7	71.2	33.2	87.6	69.7
3-month mortality	1.085	65.2	74.1	5.4	98.9	65.2
3-month poor mRS (3–6)	1.075	42.6	74.6	27.7	85.1	64.6
mRS, modified Rankin Scale; NPV, negative predictive value; PPV, positive predictive value.						

Discussion

Our results revealed that a high SHR was associated with the risk of END and poor outcomes in patients with SSI. This association was more pronounced in the groups with older age, thrombolysis, non-diabetes, and proximal type SSI. Furthermore, SHR was a clinically available predictor and had a better predictive value than FPG levels in the current analysis.

SHR is a new quantitative expression of stress blood glucose levels, which considers the condition of previous diabetes mellitus or previous diabetes mellitus with poor blood glucose control[19]. SHR can reflect the real increase in blood glucose levels when the body has an acute disease by correcting for the basal blood glucose level, which has been proven to be related to the prognosis of diseases such as stroke and myocardial infarction[20, 21]. Previous studies have shown that SHR, measured by blood glucose/glycated hemoglobin, was independently associated with poor prognosis after acute ischemic stroke in patients with diabetes[22, 23]. Furthermore, results from the Clopidogrel in High-risk patients with Acute Non-disabling Cerebrovascular Events (CHANCE) study showed that stress hyperglycemia (glucose/glycated albumin) was associated with an increased risk of recurrent stroke in patients with mild ischemic stroke and a high-risk of TIA, and that it was independent of hyperglycemia at admission[24]. Nevertheless, the calculation method of SHR in previous studies was difficult to understand and may have limited their acceptance. Nathan et al. created an equation to translate HbA1c into estimated average glucose values (Estimated average glucose = (1.59 × HbA1c) − 2.59)[14]. This estimate can more accurately reflect the actual status of glycemic control than HbA1c[19]. Additionally, the SHR, which is calculated as admission blood glucose divided by estimated average glucose, was developed to define stress hyperglycemia.

Our study showed that high SHR values were associated with END and 3-month poor mRS in patients with SSI. At present, the pathophysiology of SHR and stroke severity and prognosis in patients with SSI remain unclear. Several hypotheses may explain this phenomenon. Previous studies have demonstrated that oxidative stress-induced endothelial dysfunction plays an important role in the development of cerebrovascular diseases[25, 26]. Rapid fluctuations in blood glucose levels produce more oxidative stress and reactive oxygen species, which promote micro- and macrovascular damage[27]. Oxidative stress is thought to be a potential pathogenic mechanism that links insulin resistance to β-cell dysfunction and ultimately leads to diabetes and cerebrovascular diseases[28, 29]. Available evidence suggests that hyperglycemia induces microglial and astrocyte activation, which is associated with increased expression of markers of inflammation and oxidative stress, such as TNF-α, iNOS, and other pro-inflammatory factors[30]. Elevated biomarkers of inflammation and hyperglycemia are associated with a higher risk of poor outcomes in patients with SSI. These findings suggest that oxidative stress and inflammatory responses may be involved in the pathophysiological process of END and its prognosis[31]. However, the underlying mechanisms require further investigation.

In this study, subgroup analysis revealed that particular groups might alter the correlation between SHR and END. Compared with the diabetes group, the SHR group showed the highest OR value in the untreated diabetes group. Similar results have been found in previous studies related to brain injury and pneumonia. We speculate that acute hyperglycemia promotes oxidative stress, whereas chronic hyperglycemia induces antioxidant defenses in tissues and cells[32]. Thus, acute hyperglycemia may increase antioxidant defenses in diabetes patients, thus protecting tissues from oxidative stress, and thereby reducing the inflammatory response caused by oxidative stress[33]. Another key point was that SHR appeared to have greater significance for proximal than for distal SSI. The two SSI locations may have different underlying pathophysiological mechanisms. Previous studies have shown that SSI lesions closer to the opening of the perforating artery show more evidence of other atherosclerosis, and that the smaller proportion of SSI with leukopenia and cerebral micro-hemorrhage mostly present as proximal SSI[34]. It is well known that hyperglycemia is closely related to the instability of atherosclerotic plaques[35]. Stress hyperglycemia is also a factor that affects plaque stability. Nevertheless, distal SSI lesions are often relatively close to the perforating opening and likely to be associated with small distal vascular lesions[36]. These pathologies are long term and stable. Therefore, stress hyperglycemia is less involved in the occurrence of END in patients with distal SSI.

This study has several limitations. First, only Chinese patients were enrolled in the study, limiting the generalizability of the findings to Western populations. Second, it was not possible to observe dynamic changes in SHR during follow-up. Finally, although we minimized the time between onset and admission, detailed information on the pre-hospital course was not available, and we could not exclude potential effects of pre-hospital management on outcomes.

Conclusion

The current study, which used SHR for measuring stress hyperglycemia, suggests that SHR is independently associated with END and poor outcomes in patients with SSI, especially in older patients and proximal type SSI. In the medical practice, SHR levels may be useful to distinguish END, and provide a novel target for neuroprotection in patients with SSI.

Declarations

Author Contribution

Research design: Dr. Yuming Xu and Dr. Yuan Gao; Writing: Dr. Hongbing Liu and Dr. Kai Liu; Data analysis and arrangement: Dr. Shen Li and Xin Wang; English editing help: Dr. Bo Song; Data collection: Ke Zhang, Ce Zong, and Ying Yao; Tables and Figures: Dr. Hongxun Yang

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Data availability statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The ethics committee of the First Affiliated Hospital of Zhengzhou University approved this study (Approval No. 2021-KY-0067-001), and all patients signed written informed consent forms.

Consent for publication

Not applicable.

Declaration of conflicting interests

All authors declared that no potential conflicts of interest with respect to the research, authorship, and/or publication in this study.

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Figures

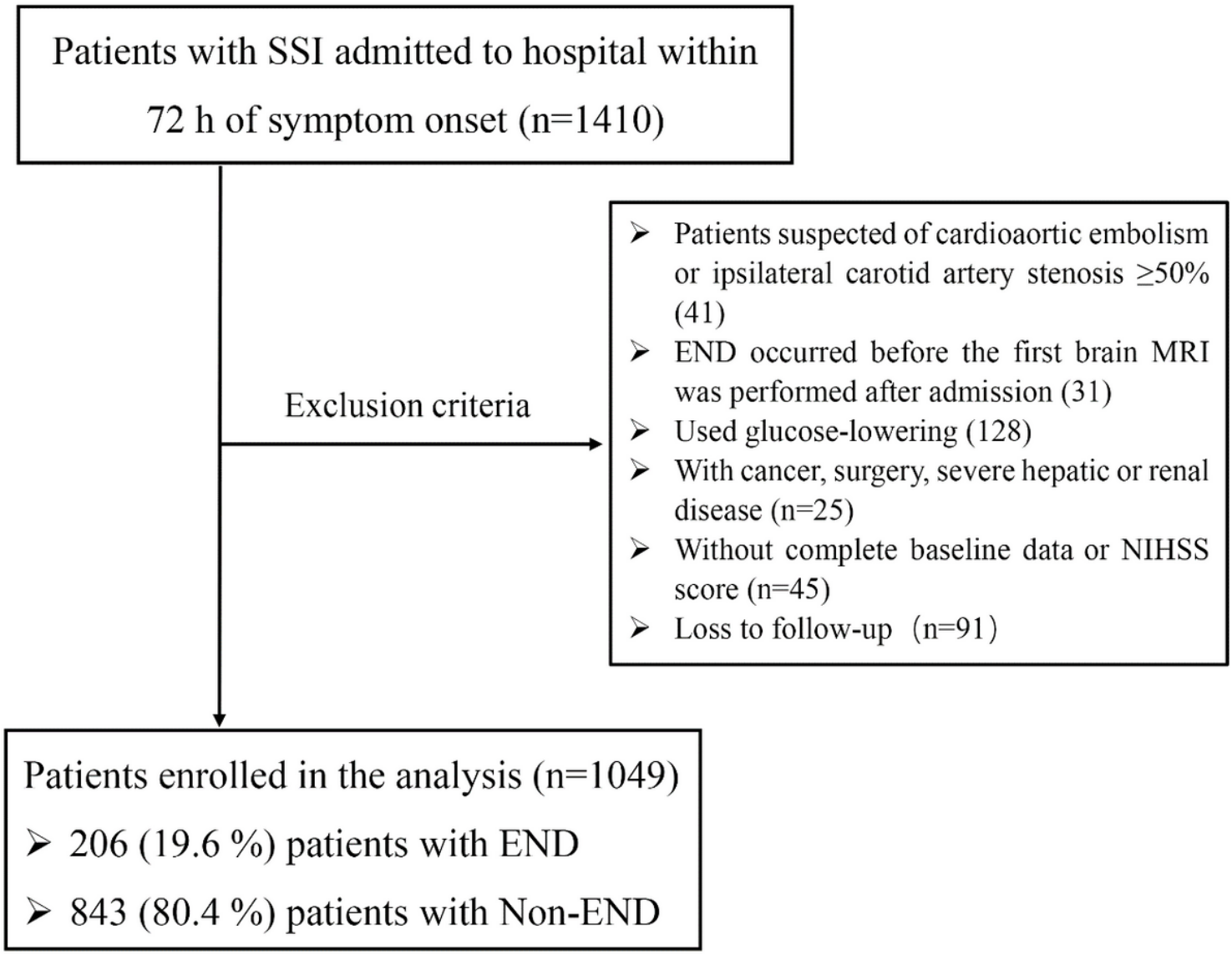

Figure 1

Patient flowchart of the cohort.

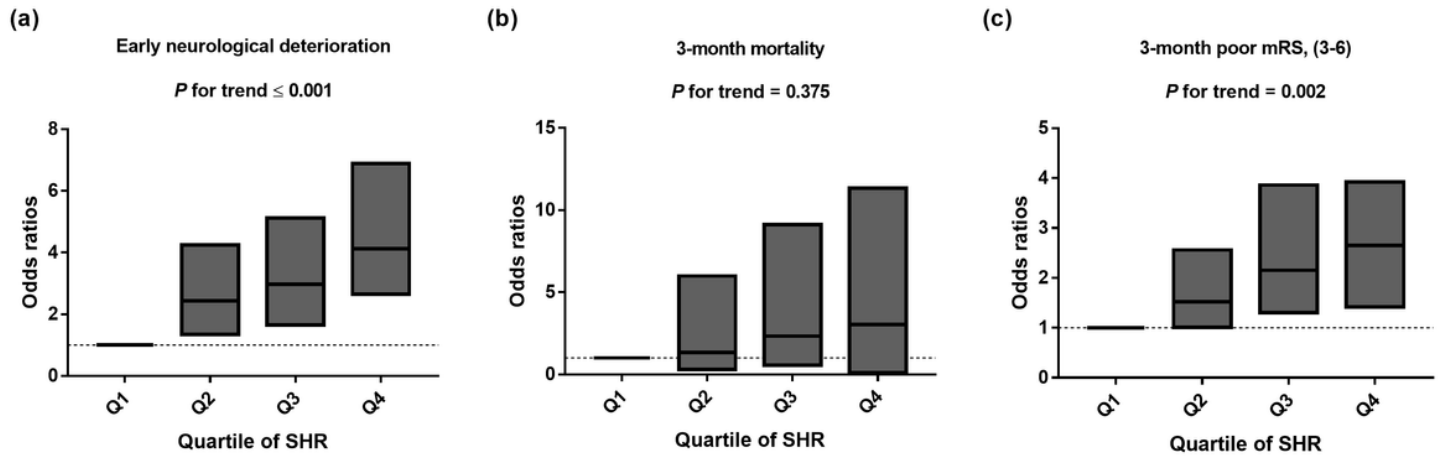

Figure 2

Multivariable adjusted odds ratios for functional outcomes, grouped by SHR quartile in patients with SSI.

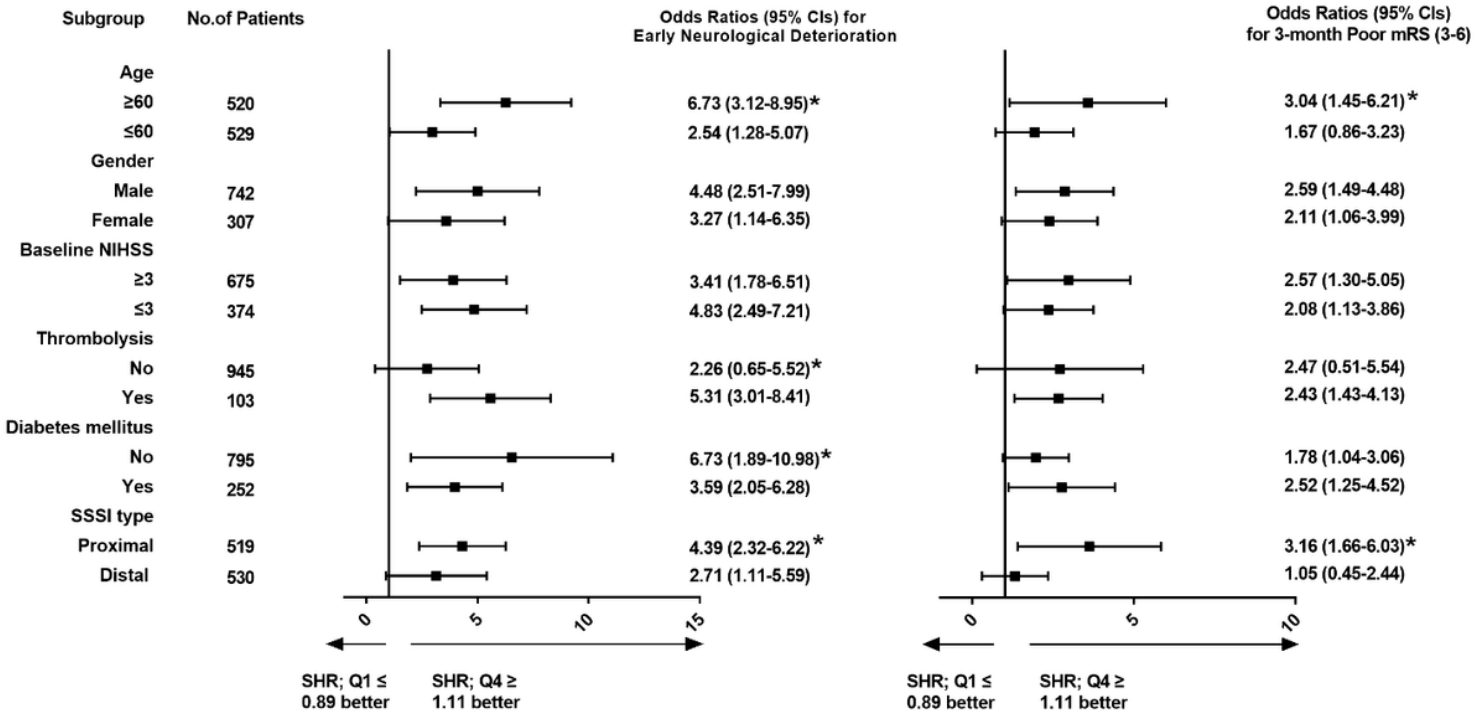

Figure 3

All odds ratios were calculated with SHR. Quartile < 0.89 as the reference groups, with models adjusted for age, sex, reperfusion therapy, baseline NIHSS score, history of ischemic stroke/TIA, hypertension, CHD, atrial fibrillation, diabetes mellitus, dyslipidemia, SSI type, and WBC count. Each group adjusted for the other covariates except itself.

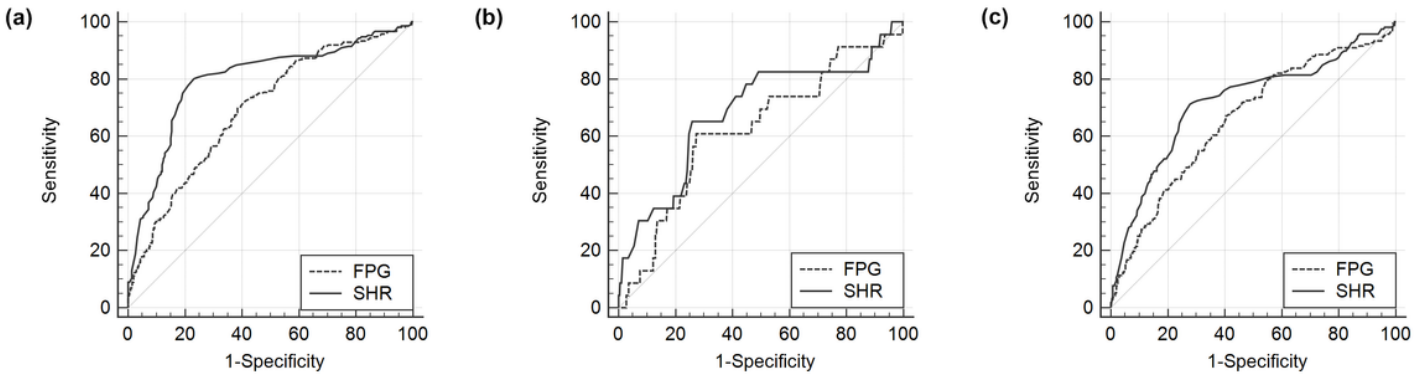

Figure 4

Predictive values of FPG and SHR for the outcomes. Receiver operating characteristic curves for outcomes. (a) Areas under the curves for END: 0.696 for FPG and 0.798 for SHR. (b) Areas under the curves for death: 0.623 for FPG and 0.683 for SHR. (c) Areas under the curves for poor mRS: 0.660 for FPG and 0.720 for SHR.