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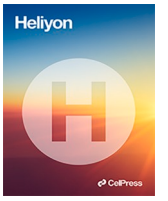

Research article

Relationship between serum glucose-potassium ratio and 90-day outcomes of patients with acute ischemic stroke

Xiaohui Yan [1], Dan Wu [1], Xinyu Xu [1], Aimei Zhang, Junqi Liao, Qiuhua He, Fantao Song, Yan Liu, Zhaoyao Chen, Minghua Wu, Li Li **, Wenlei Li *

Department of Neurology, Jiangsu Province Hospital of Chinese Medicine, Affiliated Hospital of Nanjing University of Chinese Medicine, No. 155 Hanzhong Road, 210029, Nanjing, China

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ABSTRACT

Background: Recent studies have shown that the serum glucose-potassium ratio (GPR) upon admission is correlated with the prognosis of cerebrovascular disorders. Herein, we investigated the relationship between GPR and 90-day functional outcomes in patients with acute ischaemic stroke (AIS).

Methods: Clinical data were collected from patients with AIS registered at the Stroke Center of Jiangsu Provincial Hospital of Chinese Medicine. The relationship between the GPR and 90-day outcomes was analysed using univariate and multivariate logistic regression analyses, linear regression analyses, and subgroup analyses.

Results: A total of 1826 patients met the enrolment requirements. The number of patients with a glucose-to-potassium ratio greater than the median value increased proportionally with increases in the NIHSS at admission and the 90-day modified Rankin scale (mRS). Univariate logistic regression analysis revealed a significant relationship between GPR and 90-day negative prognosis (OR 1.34 [95%Cl, 1.17–1.54], $P < 0.001$). After adjusting for all confounding variables, the relationship between GPR and 90-day adverse prognosis was shown to be nonlinearly U-shaped, with an inflection point of the curve for GPR of 1.347. Two linear regression analyses were performed on the basis of the inflection points of the curves. The results of this analysis revealed a negative correlation between GPR and 90-day adverse outcomes at GPR<1.347 (OR 0.86 [95% CI,0.09–7.86], $P = 0.897$), as well as a positive correlation between GPR and 90-day adverse outcomes at GPR≥1.347 (OR1.52 [95%CI, 1.19–1.93], $P = 0.001$). Subgroup analyses verified that the association between GPR and 90-day poor prognosis still existed, regardless of whether the patient had a history of diabetes mellitus (DM). (with DM: OR 1.39 [95%Cl, 1.05–1.83], $P = 0.001$); without DM: OR 0.93 [95%Cl,0.56–1.55], $P = 0.016$).

Conclusions: GPR significantly correlated with poor prognosis at 90-days in patients with AIS. Early intervention and control of GPR are expected to enhance functional outcomes in patients with AIS.

* Corresponding author.
** Corresponding author.
E-mail addresses: guaidaojide1222@163.com (L. Li), yfy120@njucm.edu.cn (W. Li).
[1] **Equal contribution and first authorship**:These authors contributed equally to this work and share first authorship.

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1. Introduction

Ischaemic stroke is not only the leading cause of death and disability among adults in China, but also the second leading cause of death worldwide [1]. Patients often experience severe neurological deficits, which can seriously endanger human health, reduce their quality of life, and even inflict a heavy economic and mental burden on society [2]. Therapeutic decisions and the management of various indicators related to disease prognosis in the early stages can have a significant impact on the prognosis of patients with ischemic stroke [3]. As such, to enhance the prognosis of patients with ischaemic stroke, it is crucial to identify predictive factors affecting stroke prognosis, and to perform reasonable management.

Serum potassium and glucose levels are common and easily accessible biochemical markers in the blood. Glucose, the primary energy source for cells, is essential for preserving cellular metabolism [4]. Potassium ions are the most prevalent cations in human cells, and play vital roles in numerous physiological functions, including muscle contraction, cardiac pulsation, neural conduction, and preservation of normal renal function [5]. Previous studies have demonstrated a strong connection between potassium and glucose metabolism in the human body [5]. The possible interaction between serum glucose and serum potassium led to the introduction of the glucose-potassium ratio (GPR). The GPR is calculated by dividing the blood glucose value by the blood potassium value after admission. The combined effect of GPR has previously been identified as an early predictor of prognosis in several diseases, including massive pulmonary embolism [6], blunt abdominal trauma [7], isolated thoracoabdominal blunt trauma [8], acute type A aortic dissection surgery [9], aneurysmal subarachnoid haemorrhage [10–13],and severe traumatic brain injury [14,15]. Additionally, this factor has been linked to intermediate syndrome following acute exposure to anticholinesterases and delayed neuropsychiatric syndrome in cases of carbon monoxide poisoning [16]. However, only a limited number of studies have been conducted to determine the possibility of using GPR to predict the prognosis of acute ischemic stroke (AIS) patients. Nevertheless, this factor has the potential to serve as a reference for more effectively identifying clinical markers that have a strong correlation with the long-term prognosis of patients with AIS, and are affordable and simple to identify. This study focused on the relationship between the GPR at admission and the 90-day prognosis of patients with AIS.

2. Materials and methods

2.1. Study population

This study enrolled 1914 patients from the Stroke Centre of Jiangsu Province Hospital between January 2017 and July 2021, all of whom received complete treatment in the stroke unit in accordance with international standards. The inclusion criteria were as follows: (1) at least 18 years of age; (2) Diagnosis of AIS based on the Chinese AIS diagnostic guidelines; and (3) Complete blood biochemical examination at admission. The exclusion criteria were as follows: (1) severe systemic disease; (2) An inability to evaluate the relevant scores (NIHSS or mRS) after hospitalization; (3) Loss to visit after 90 days; and (4) Severely ambiguous values. Fig. 1 shows the flowchart of this study.

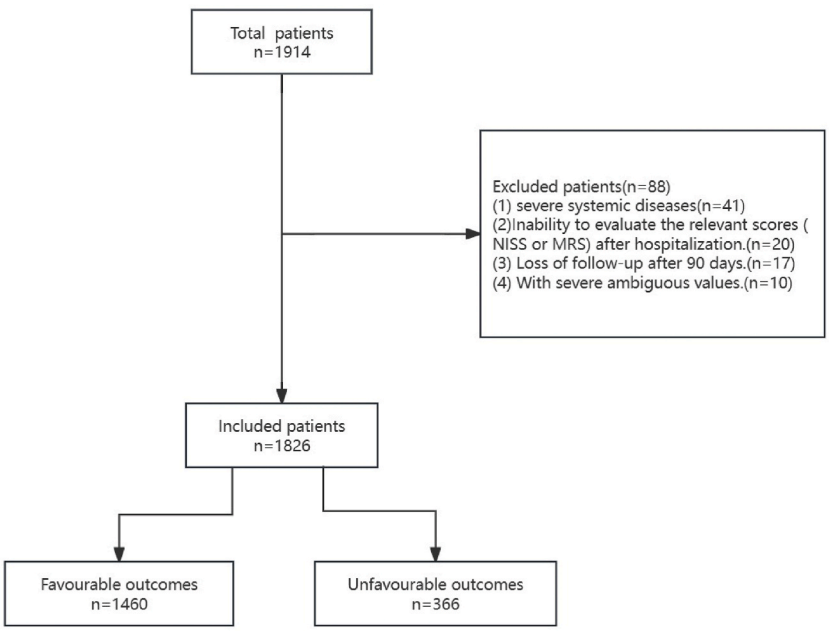

Fig. 1. Flow chart.

2.2. Clinical data collection

On the day of admission, standardized information was collected from all individuals, including demographic characteristics (age, sex), vascular risk factors (hypertension, diabetes mellitus, dyslipidaemia, atrial fibrillation, neoplasia, current smoking, current alcohol use, previous stroke, peripheral arterial disease, and coronary artery disease), medication history (antihypertensive, hypoglycaemic, anticoagulant, antiplatelet, and statin medications), clinical assessment (admission and follow-up NIHSS and mRS assessed by a trained and qualified clinical neurologist), vital signs (blood pressure), stroke classification and specific treatment (classification by stroke site and aetiology, thrombolysis, or thrombectomy), treatment history (onset to treatment time, complications during hospitalization, and death), and laboratory data. Vital signs were measured immediately after admission, and demographic information was collected, followed by evaluation of the lesion site (OCSP score), stroke subtype (TOAST score), hypertension, and arterial pressure by electron computed tomography, magnetic resonance imaging, electrocardiography, echocardiography, arterial ultrasound, and transcranial multispectral examination.

Table 1
Clinical and biochemical characteristics of the favourable and unfavourable outcome groups.

Variables	Total (n = 1826)	Favourable (n = 1460)	Unfavourable (n = 366)	p
Demographic characteristic				
Age,years	68.9 ± 11.4	67.6 ± 11.1	74.0 ± 11.0	<0.001
Male, n (%)	1220 (66.8)	1002 (68.6)	218 (59.6)	<0.001
Vascular risk factors,%				
Hypertension, n (%)	1438 (78.8)	1153 (79)	285 (77.9)	0.644
Diabetes mellitus, n (%)	726 (39.8)	566 (38.8)	160 (43.7)	0.084
TIA or stroke, n (%)	570 (31.2)	429 (29.4)	141 (38.5)	<0.001
Atrial fibrillation, n (%)	143 (7.8)	84 (5.8)	59 (16.1)	<0.001
Coronary heart disease, n (%)	267 (14.6)	194 (13.3)	73 (19.9)	0.001
Heart failure, n (%)	13 (0.7)	6 (0.4)	7 (1.9)	0.007
Hyperlipidaemia, n (%)	101 (5.5)	87 (6)	14 (3.8)	0.11
Chronic renal insufficiency, n (%)	60 (3.3)	39 (2.7)	21 (5.7)	0.003
Cancer, n (%)	81 (4.4)	61 (4.2)	20 (5.5)	0.285
Smoking, n (%)	515 (28.2)	437 (29.9)	78 (21.3)	0.001
Drinking, n (%)	340 (18.6)	290 (19.9)	50 (13.7)	0.006
Clinical data				
Antihypertensive drug, n (%)	1338 (73.3)	1081 (74)	257 (70.2)	0.139
Antihyperglycemic drug, n (%)	679 (37.2)	534 (36.6)	145 (39.6)	0.282
Antiplatelet drug, n (%)	1699 (93.0)	1365 (93.5)	334 (91.3)	0.133
Anticoagulant drug, n (%)	496 (27.2)	383 (26.2)	113 (30.9)	0.074
Statin, n (%)	1764 (96.6)	1420 (97.3)	344 (94)	0.002
TOAST, n (%)				<0.001
LAA	599 (32.8)	431 (29.5)	168 (45.9)	
CE	1166 (63.9)	993 (68)	173 (47.3)	
SAO	56 (3.1)	31 (2.1)	25 (6.8)	
ODC	5 (0.3)	5 (0.3)	0 (0)	
OCSP, n (%)				<0.001
TACI	83 (4.5)	25 (1.7)	58 (15.8)	
PACI	540 (29.6)	404 (27.7)	136 (37.2)	
POCI	518 (28.4)	427 (29.2)	91 (24.9)	
LACI	685 (37.5)	604 (41.4)	81 (22.1)	
Admission NIHSS, Mean ± SD	3.8 ± 4.4	2.7 ± 2.5	8.1 ± 6.9	<0.001
Admission mRS, Mean ± SD	2.4 ± 1.4	2.0 ± 1.2	3.7 ± 1.3	<0.001
Laboratory data				
WBC, Mean ± SD	7.0 ± 2.4	6.9 ± 2.1	7.6 ± 3.1	<0.001
HDL, Mean ± SD	1.2 ± 0.3	1.2 ± 0.3	1.3 ± 0.3	0.494
TC, Mean ± SD	4.3 ± 1.1	4.3 ± 1.1	4.3 ± 1.2	0.191
TG, Mean ± SD	1.6 ± 1.3	1.6 ± 1.4	1.4 ± 0.8	0.002
LDL, Mean ± SD	2.7 ± 0.9	2.7 ± 0.9	2.7 ± 1.0	0.313
HbA1c, Mean ± SD	6.9 ± 1.6	6.9 ± 1.6	7.1 ± 1.8	0.077
ALB, Mean ± SD	38.1 ± 4.4	38.5 ± 4.2	36.5 ± 4.5	<0.001
HB, Mean ± SD	134.6 ± 18.5	135.9 ± 17.8	129.7 ± 20.3	<0.001
FBG, Mean ± SD	6.6 ± 2.9	6.5 ± 2.7	7.2 ± 3.3	<0.001
K, Mean ± SD	3.8 ± 0.4	3.8 ± 0.4	3.8 ± 0.4	0.033
GPR, Mean ± SD	1.8 ± 0.7	1.7 ± 0.7	1.9 ± 0.8	<0.001

Abbreviations: TIA:Transient ischemic attack; LAA: Large artery atherosclerosis; CE: Cardioembolism; SAO: Small artery occlusion; ODC: Stroke of other determined cause; TACI: Total anterior circulation infarcts; PACI: Partial anterior circulation infarcts; POCI: Posterior circulation infarcts; LACI: Lacunar infarcts; NIHSS: National institutes of health stroke scale; mRS: Modified Rankin scale; WBC: White blood cell; HDL: High density lipoprotein; TC: Total cholesterol; TG: Triglyceride; LDL: Low density lipoprotein; HbAlc: Glycosylated hemoglobin; ALB: Albumin; HB: Hemoglobin; FBG: Fast blood glucose; K: Potassium; GPR: Glucose-potassium ratio.

2.3. Laboratory testing and glucose-potassium ratio definition

Laboratory data included routine blood counts, liver and kidney functions, lipid levels, blood homocysteine, cytokines, immune factors, and thyroid function. The glucose-potassium ratio can be derived after the first blood draw on admission. Blood samples were collected at approximately 07:30 on the first day of admission, following a fast of at least 8-h, to reduce the impact of food on the level of test results. The blood samples were tested at a standard serological testing facility.

2.4. Follow-up and outcomes

Follow-up information of patients with AIS was collected via telephone interviews 90 days after disease onset. The interview assignment was conducted by two postgraduates who had received training and certification in data collection. When the patients died or were unable to assist with the investigation, their guardians were questioned instead. The patients' functional outcomes were assessed and classified as either good or poor based on the modified Rankin scale (mRS). mRS <3 indicates a good outcome, and mRS$\geq$3 indicates a poor outcome (including haemorrhage, recurrence, and death within 90 days after stroke).

2.5. Statistical analysis

This study included 1914 patients with acute ischaemic stroke. Blood glucose and serum potassium levels were measured and added to the database for all trial participants. Data are expressed as mean $\pm$ SD, IQR. The study employed logistic regression analysis to ascertain the correlation between GPR parameters (mean $\pm$ GPR, IQR of GPR) and unfavourable functional outcomes. A smooth curve provided the best fit for the relationship between the baseline GPR and functional prognosis, and the odds ratios (OR) and corresponding 95 % confidence intervals (CIs) of the main results were therefore assessed using reverse stepwise logistic regression analysis. All data were analysed using Free Statistics software version 1.8. The mRS at 90 days after onset is the most important indicator of AIS prognosis. We used the mRS to assess functional outcomes following stroke, with scores ranging from 0 (asymptomatic) to 6 (death). A score of $\geq$3 was defined as an unfavourable outcome.

The following variables were adjusted based on clinical significance and previous study findings: age, sex, hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, antihypertensive medications, hypoglycaemic medications, hyperlipidaemia, history of alcohol consumption, history of smoking, antiplatelet medications, statins, low-density lipoprotein cholesterol, total cholesterol, triglycerides, glycosylated haemoglobin, albumin, TOAST, and NIHSS at admission.

3. Results

3.1. Patient characteristics

This study enrolled 1826 patients with AIS (1220 males, 606 females), with a median age of 69 (IQR 61–78) years. The median GPR value was 1.52 (IQR 1.28–1.96) mmol/L. Table 1 presents a comparison of the clinical and biochemical characteristics of the good and

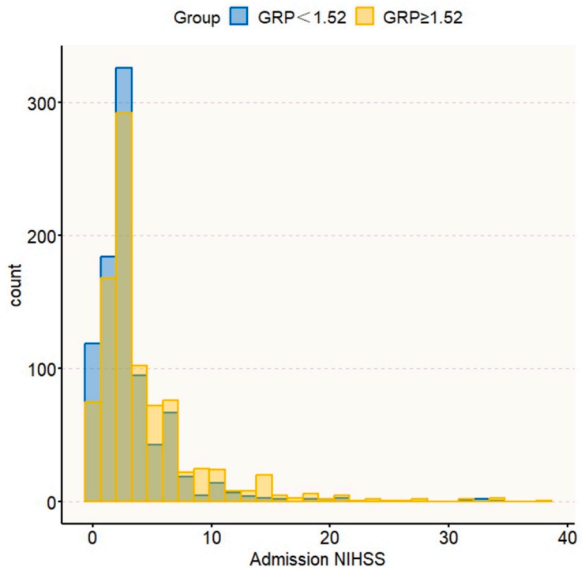

Fig. 2. Association between serum glucose and potassium ratio and NIHSS on admission. A strong correlation was retained whether serum glucose and potassium ratios or admission NIHSS were identified as categorical or continuous variables.

poor prognosis groups. There were many notable differences between the two groups in terms of age, sex, smoking, drinking, coronary heart disease (CHD), atrial fibrillation (AF), transient ischaemic attack (TIA), chronic renal insufficiency (CRI), TOAST classification, hypoglycaemic drugs (HGD), antiplatelet drugs (APD), admission NIHSS, admission mRS, and GPR level. There were no significant differences between the two groups in terms of hypertension, diabetes, tumours, hyperlipidaemia, HbA1c, antihypertensive drugs, or hypoglycaemic drugs.

3.2. The relationship between GPR and AIS severity

Our research showed that the median blood glucose concentration was 5.66 mmol/l with a range of 3.1–25.46 mmol/l and an interquartile spacing of 2.47 mmol/l; the median serum potassium concentration was 3.78 mmol/l with a range of 2.46–5.97 mmol/l (interquartile spacing, 0.47 mmol/l). As such, the range of blood glucose-potassium ratio was 0.64–6.35 (median, 1.52; interquartile spacing, 0.68). Both the NIHSS at admission and the 90-day mRS revealed a strong correlation between AIS severity and glucose-to-potassium ratio. To validate this correlation, some minor changes were made: (1) the serum glucose-potassium ratios were alternately treated as quantitative or qualitative variables; (2) The NIHSS and mRS were alternately recognised as continuous or categorical variables; and (3) patients were divided into two groups according to the median glucose-potassium ratio (values less than or greater than the median of 1.52). The number of patients with a glucose-to-potassium ratio greater than the median value was proportionally higher as the NIHSS and mRS increased, as shown in Figs. 2 and 3.

3.3. Association between GPR and unfavourable functional outcomes

Univariate logistic regression analysis identified a significant relationship between GPR and 90-day negative prognosis using the GPR level as a continuous variable (OR 1.34 [95%Cl, 1.17–1.54], $P < 0.001$). After adjusting for age and sex, the correlation between GPR and 90-day adverse prognosis was still statistically significant (OR 1.41 [95%Cl, 1.22–1.64], $P < 0.001$; Table 2). After adjusting for hypertension, coronary heart disease, atrial fibrillation, antihypertensive drugs, hyperlipidaemia, history of alcohol use, history of smoking, antiplatelet drugs, statin drugs, low-density lipoprotein cholesterol, total cholesterol, triglycerides, urea, creatinine, albumin, TOAST, and NIHSS at admission. The statistical significance of the relationship between GPR and the 90-day adverse prognosis persisted (OR 1.29 [95%Cl, 1.05–1.58], $P = 0.016$; Table 2).

3.4. Smooth curve-fitting analysis for relationship between GPR and unfavourable functional outcomes

Three models (models 1, 2, and 3) were considered when adjusting the curve fitting analysis. Model 1 exhibits a continuously increasing curve (Fig. 4). To explore possible non-linear links, we used linear regression analysis models (Models 2 and 3) with various confounders. Model 2, adjusted for sex and age, showed that the association between GPR and 90-day adverse prognosis was still linear. The risk of 90-day unfavourable functional outcomes increased as the GPR increases (Fig. 5). According to Model 3 (adjusting for age, sex, hypertension, diabetes mellitus, coronary heart disease, atrial fibrillation, antihypertensive drugs, antihyperglycemic drugs, hyperlipidaemia, history of alcohol use, history of smoking, antiplatelet drugs, statin drugs, low-density lipoprotein cholesterol,

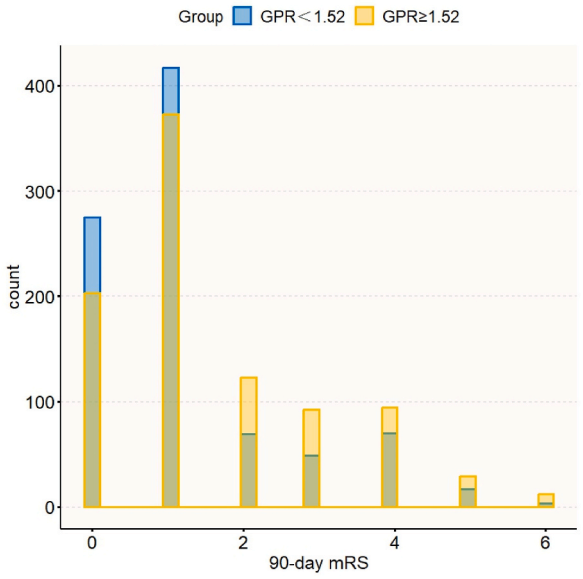

Fig. 3. Association between serum glucose and potassium ratio and mRS 90 days after AIS. A strong correlation was retained whether serum glucose and potassium ratios or mRS 90 days after AIS were identified as categorical or continuous variables.

Table 2
Relationship between GPR and 90-day unfavourable outcome in AIS patients.

Variable	Total	Event (%)	Non-adjusted OR (95%CI)	P	Adjusted OR (95%CI)	P
Model1	1826	366 (20)	1.34 (1.17–1.54)	<0.001	1.34 (1.17–1.54)	<0.001
Model2	1826	366 (20)	1.34 (1.17–1.54)	<0.001	1.41 (1.22–1.64)	<0.001
Model3	1826	366 (20)	1.34 (1.17–1.54)	<0.001	1.29 (1.05–1.58)	0.016

Model1 Unadjusted.
Model2 Adjusted for age, and gender.
Model3 Adjusted for age, sex, hypertension, diabetes mellitus, coronary heart disease, atrial fibrillation, antihypertensive drugs, antihyperglycemic drugs, hyperlipidaemia, history of alcohol use, history of smoking, antiplatelet drugs, statin drugs, low-density lipoprotein cholesterol, total cholesterol, triglycerides, glycated haemoglobin, albumin, TOAST, and admission NIHSS.

total cholesterol, triglycerides, glycated haemoglobin, albumin, TOAST classification, and admission NIHSS), the GPR and 90-day unfavourable functioning outcomes were correlated in a U-shaped curve. The results of the inflection point analysis of the fitted curve demonstrated that the confidence interval ranged from 1.347 to 1.75, with an inflection point of 1.347. A positive correlation was subsequently observed between GPR and unfavourable functional outcomes at GPR≥1.347, which is located on the right side of the inflection point. Conversely, a negative correlation was found on the left of the inflection point (Fig. 6). An analysis of the GPR and 90-day adverse prognosis was conducted using two linear regression analyses, based on the inflection point of the GPR (1.347). Crude and adjusted models were used to explore the non-linear relationships. GPR<1.347 (OR 1.21 [95%CI,0.18–8.28], P = 0.848); After adjustment, OR 0.86 [95%CI,0.09–7.86], P = 0.897). And GPR≥1.347 (OR 1.26 [95%CI, 1.07–1.49], P = 0.006); After adjustment, OR1.52 [95%CI, 1.19–1.93], P = 0.001) (Table 3). As such, the relationship between the GPR and 90-day unfavourable functional outcomes was determined to be non-linear U-shaped.

The potential cut-off point was set as 1.347 based on the smoothed spline plot.

3.5. Subgroup analyses

Subgroup analyses were performed to evaluate the effect of GPR on the 90-day adverse outcomes in a particular population. Strong and consistent correlations were found across various subgroups (Fig. 7). However, no significant interaction was found between GPR and the 90-day unfavourable outcome in any of the subgroups analysed (age ≥69 years or not, sex, AF, HGD) (Table 4). Based on the subgroup analysis, after excluding the effect of diabetes mellitus, it was possible to verify the significance of the relationship between GPR and 90-day adverse prognosis (with DM: OR 1.39 [95%Cl, 1.05–1.83], P = 0.001); without DM: OR 0.93 [95%Cl,0.56–1.55], P = 0.016).

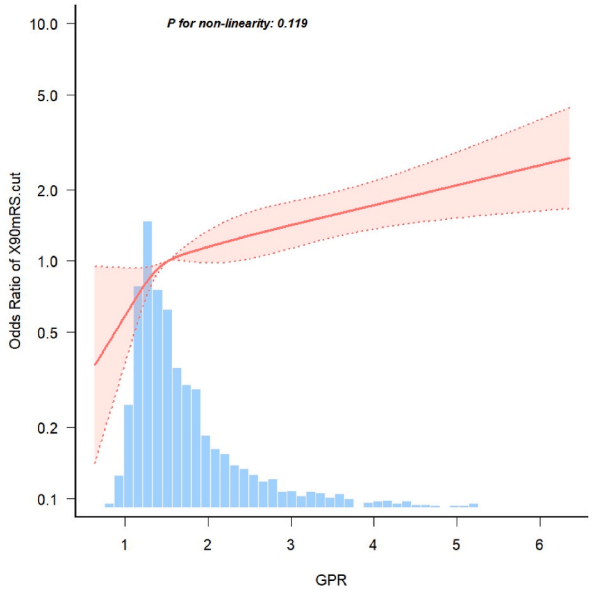

Fig. 4. Relationship between serum glucose-potassium and unfavourable functional outcomes according to the smooth fitting curve (non-adjusted variables).

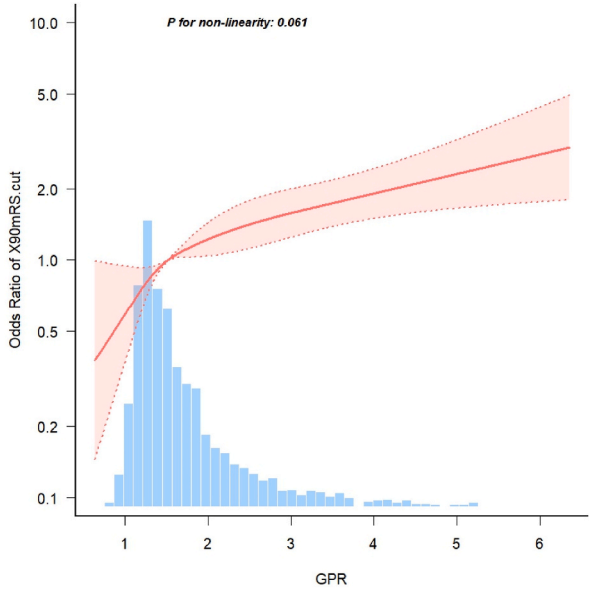

Fig. 5. Relationship between serum glucose-potassium and unfavourable functional outcomes according to smooth fitting curve (adjusted for age and gender).

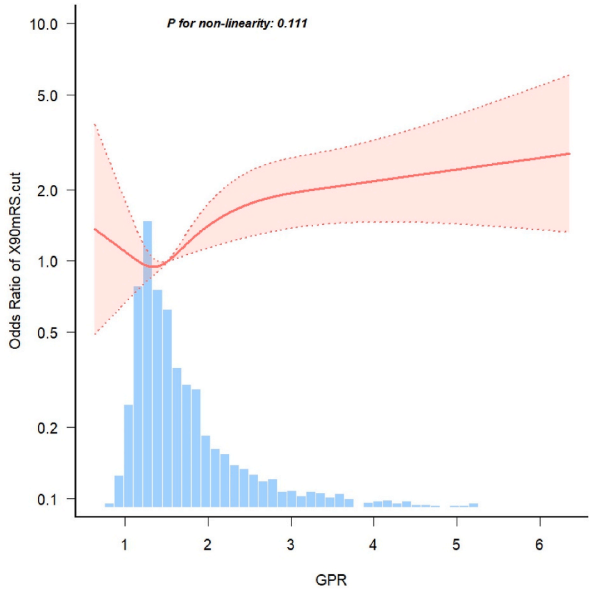

Fig. 6. Relationship between serum glucose-potassium and unfavourable functional outcomes according to smooth fitting curve (adjusted for age, gender, hypertension, diabetes mellitus, coronary heart disease, atrial fibrillation, antihypertensive drugs, antihyperglycemic drug, hyperlipidaemia, history of alcohol use, history of smoking, antiplatelet drugs, statin drugs, low-density lipoprotein cholesterol, total cholesterol, triglyceride, glycated haemoglobin, albumin, TOAST, and admission NIHSS).

4. Discussion

In the present study, we verified identified a close correlation between the severity of AIS and GPR, as indicated by the NIHSS at admission and the 90-day mRS. Moreover, GPR was separately correlated with 90-day poor outcomes after AIS, an effect which was retained after adjusting for potentially confounding factors. Curve-fitting analysis revealed that the relationship between GPR and 90-day unfavourable outcomes was U-shaped, and that the curve inflection point of GPR was approximately 1.347. Two linear regression analyses were conducted based on the inflection point, for which the results showed that on the left side of the inflection point, the GPR was negatively correlated with 90-day unfavourable functional outcomes, whereas a positive correlation existed on the right side of the

Table 3
Results of two-piecewise linear regression analysis for GPR and 90-day unfavourable outcomes.

GPR	Crude model	Crude.P-value	Adj model	Adj.P-value
GPR < 1.347	1.21 (0.18–8.28)	0.848	0.86 (0.09–7.86)	0.897
GPR≥1.347	1.26 (1.07–1.49)	0.006	1.52 (1.19–1.93)	0.001

Data are expressed as the OR (95 % CI). GPR serum glucose to potassium ratio. Crude model: not adjusted.
Adjusted for age, sex, hypertension, diabetes mellitus, coronary heart disease, atrial fibrillation, antihypertensive drugs, antihyperglycaemic drugs, hyperlipidaemia, history of alcohol use, history of smoking, antiplatelet drugs, statin drugs, low-density lipoprotein cholesterol, total cholesterol, triglycerides, glycated haemoglobin, albumin, TOAST, and admission NIHSS.

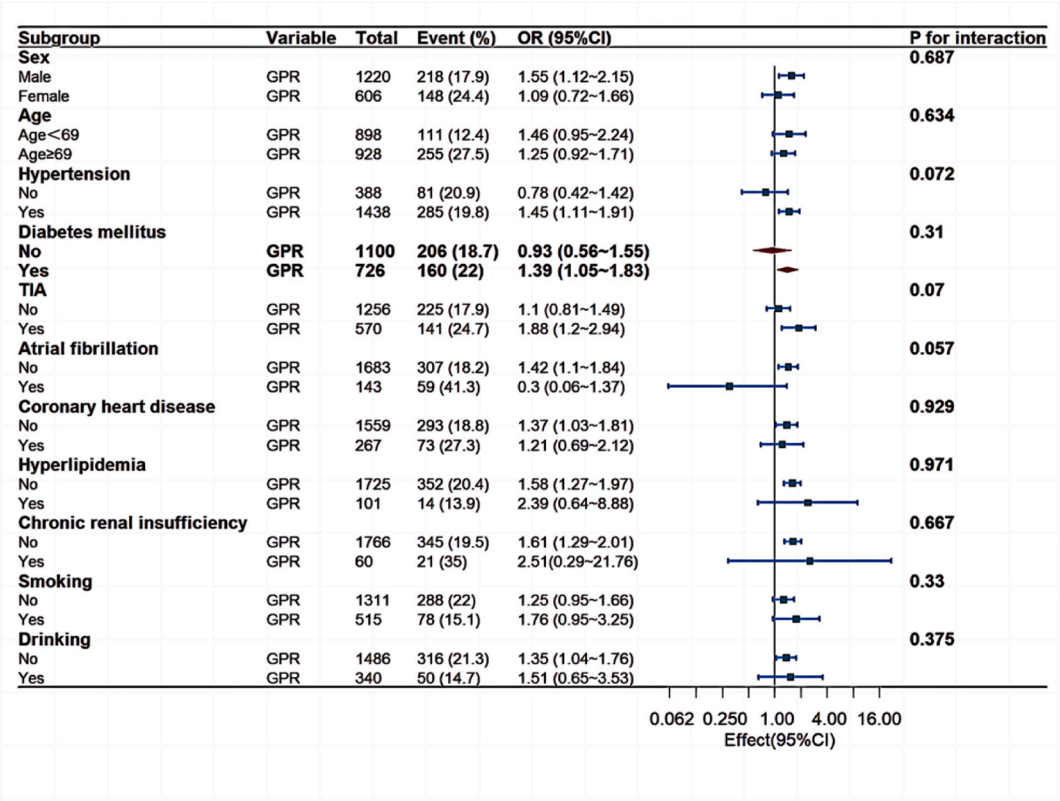

Fig. 7. Subgroup analyses for the risk of 90-day adverse prognosis.

inflection point. Simultaneously, subgroup analyses demonstrated that the GPR was independently linked to functional prognosis, regardless of whether the patient had a history of diabetes. Therefore, the serum glucose-to-potassium ratio is expected to predict unfavourable outcomes in patients with AIS.

Furthermore, it has been reported that high GPR is closely associated with an increased disease severity. In addition to massive pulmonary embolism [6], blunt abdominal trauma [7], isolated thoracoabdominal blunt trauma [8], and acute type A aortic dissection [9], these changes have also been observed in some pathological neurological diseases, including spinal cord and brain trauma. Two prior reports from Japanese scholars on aneurysmal subarachnoid haemorrhage (aSAH) showed that GPR was an independent predictor of poor prognosis, and that an increase in the GPR ratio indicated a higher level of disease severity [12,13]. The increase in this ratio significantly correlated with the incidence of cerebral vasospasm following aSAH [12]. In addition, serum GPR on admission has potential as a predictor of rebleeding and mortality in patients 3 months after aSAH [10,11]. Moreover, research on various forms of brain damage, such as traumatic brain injury and acute intracerebral haemorrhage, has consistently demonstrated a robust association between high GPR and adverse prognoses or 30-day mortality [14,15,17]. More recently, Zhou et al. [18] reported a substantial correlation between serum GPR and the severity of injury on admission as well as prognosis at 6 months in patients with acute traumatic spinal cord injury. These results indicate that GPR is a potential biomarker of stress damage that reflects the systemic condition of severe diseases and is closely linked to disease severity and poor outcomes.

AIS is a serious disease that can cause brain damage and complete stress response. To date, only one study has previously reported an association between the GPR and 30-day mortality in patients with ischaemic stroke [5]. This study included 784 patients with ischaemic stroke from a large emergency Norwegian cohort, and the results showed that 30-day mortality and GPR were positively

Table 4
Results of further subgroup analysis in diabetic and non-diabetic patients.

Subgroup	Variable	n.total	n.event_%	adj.OR_95CI	adj.P_value	P.for.interaction
Sex						0.687
Male	GPR	1220	218 (17.9)	1.55 (1.12–2.15)	0.008	
Female	GPR	606	148 (24.4)	1.09 (0.72–1.66)	0.672	
Age						0.634
Age < 69	GPR	898	111 (12.4)	1.46 (0.95–2.24)	0.081	
Age≥69	GPR	928	255 (27.5)	1.25 (0.92–1.71)	0.16	
Hypertension						0.072
No	GPR	388	81 (20.9)	0.78 (0.42–1.42)	0.413	
Yes	GPR	1438	285 (19.8)	1.45 (1.11–1.91)	0.007	
Diabetes mellitus						0.31
No	GPR	1100	206 (18.7)	0.93 (0.56–1.55)	0.785	
Yes	GPR	726	160 (22)	1.39 (1.05–1.83)	0.023	
TIA						0.07
No	GPR	1256	225 (17.9)	1.1 (0.81–1.49)	0.55	
Yes	GPR	570	141 (24.7)	1.88 (1.2–2.94)	0.006	
Atrial fibrillation						0.057
No	GPR	1683	307 (18.2)	1.42 (1.1–1.84)	0.007	
Yes	GPR	143	59 (41.3)	0.3 (0.06–1.37)	0.121	
Coronary heart disease						0.929
No	GPR	1559	293 (18.8)	1.37 (1.03–1.81)	0.028	
Yes	GPR	267	73 (27.3)	1.21 (0.69–2.12)	0.512	
Hyperlipidaemia						0.971
No	GPR	1725	352 (20.4)	1.58 (1.27–1.97)	<0.001	
Yes	GPR	101	14 (13.9)	2.39 (0.64–8.88)	0.194	
Chronic renal insufficiency						0.667
No	GPR	1766	345 (19.5)	1.61 (1.29–2.01)	<0.001	
Yes	GPR	60	21 (35)	2.51 (0.29–21.76)	0.404	
Smoking						0.33
No	GPR	1311	288 (22)	1.25 (0.95–1.66)	0.117	
Yes	GPR	515	78 (15.1)	1.76 (0.95–3.25)	0.071	
Drinking						0.375
No	GPR	1486	316 (21.3)	1.35 (1.04–1.76)	0.025	
Yes	GPR	340	50 (14.7)	1.51 (0.65–3.53)	0.34	

correlated, showing a linear relationship. As such, the GPR at admission might be a potential indicator of how patients with AIS will fare in the near future. Nevertheless, it is unknown how GPR is related to the long-term results of AIS. Thus, we examined the association between GPR at admission and AIS severity and explored its predictive value for 90-day prognosis. Our study included more patients with acute ischaemic stroke and retrospectively analysed data from 2786 patients. The results showed that the number of patients with a GPR greater than the median value was proportionally higher as the NIHSS and mRS increased, and the GPR was independently correlated with 90-day unfavourable outcomes in patients with AIS. This indicates that GPR may serve as an indicator of AIS severity, with a higher ratio indicating a more serious condition and a more unfavourable outcome.

Overall, our results are consistent with those of previous studies, demonstrating a strong correlation between the severity of acute brain injury and increased serum GPR. The underlying mechanism may be related to stress hyperglycaemia and hypokalaemia because in our univariate analysis, both blood glucose and potassium levels on admission were independently associated with poor prognosis at 90 days. Several studies have previously shown that abnormalities in blood glucose and potassium metabolisms are independently associated with stroke. According to a recent meta-analysis, hyperglycaemia is significantly linked to worse clinical outcomes and increased 90-day mortality in patients with acute ischemic stroke [19]. Furthermore, several clinical studies have demonstrated that fasting blood glucose (FBG) could be used as an independent predictive factor for poor outcomes after stroke [20–22]. In addition, Linda et al. found that serum potassium levels are clearly correlated with both the prevalence and mortality of ischaemic stroke [23].

According to research reports, hyperglycaemia is a common occurrence during the acute stage of IS, as well as in non-diabetic IS patients [24]. Several prior studies have indicated that stress response may be the cause of hyperglycaemia following stroke [25]. Other studies have shown that individuals with stress hyperglycaemia tend to experience more severe strokes than those with diabetes mellitus type 2 [26]. In addition, Guo et al. found that IS patients with stress hyperglycaemia were more likely than those with type 2 diabetes to experience a 90-day stroke recurrence [27]. Catecholamines, glucagon, and corticosteroids are the primary hormones regulating blood sugar levels and are associated with hyperglycaemic response [28,29]. Catecholamines play a crucial role in the response to trauma and stress as they directly and indirectly increase blood glucose levels by stimulating glucagon release and blocking insulin [30]. Potassium is predominantly stored in cells, where it is actively taken up through the sodium/potassium adenosine triphosphatase pump (Na+/K + -ATPase) and the cell membrane. Peripheral blood potassium concentrations may decrease as a result of B2 adrenergic hormones, catecholamines, and insulin regulation of Na+/K + -ATPase [31]. Following ischaemic stroke, excessive catecholamine secretion leads to an increase in serum glucose concentration and enhancement of insulin secretion. Insulin can transport serum potassium into cells, resulting in a decrease in the circulating potassium concentration. In summary, given the comprehensive interaction between serum glucose and potassium, the GPR level could be a marker of stress injury, which indicates

how ischaemic stroke will develop.

In the present, after controlling for all variables such as sex, age, hypertension, alcohol consumption, smoking, FPG at enrolment, LDL, neutrophils, TOAST classification, NIHSS at enrolment, and END, the relationship between GPR and 90-day unfavourable prognosis was found to be U-shaped, with an inflection point of the curve for GPR of 1.347. The left side of the inflection point showed a negative correlation between GPR and 90-day adverse outcomes, whereas the right side showed a positive correlation. From the graph, it can be seen that at a GPR of 1.347, the patient had the least adverse outcomes, indicating that the patient had the best prognosis. Therefore, in clinical practice, it is suggested that controlling the GPR of patients around 1.347 may result in better functional outcomes. As such, early intervention and control of the glucose-potassium ratio are expected to improve functional outcomes in patients with AIS.

This study has some limitations. Initially, the original data contained no information about the levels of serum hormones, including corticosteroids, glucagon, and catecholamines. As such, the actual role of serum GPR in patients with severe AIS remains unclear. Second, the single-centre retrospective design of this study with a relatively small sample size may have resulted in selection bias and an inability to fully control for confounding factors. As such, multicentre prospective clinical studies are required to further validate our findings. In addition, we did not consider the possibility that other factors could influence serum glucose and potassium levels, such as the duration of food intake and the use of certain drugs prior to injury. Finally, rather than depending solely on the assessments made at admission, future studies should focus on dynamically tracking indices during the entire course of treatment.

5. Conclusion

To the best of our knowledge, this is the first study to demonstrate a close correlation between serum GPR and severity and 90-day prognosis of AIS. Serum GPR is a useful clinical risk factor as it can be used to predict the severity and 90-day prognosis of patients with AIS. In addition, it is possible to intervene in and control these indicators early in the course of the disease, resulting in a better prognosis. Large-scale studies will be conducted in the near future to validate our findings.

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Data availability statement

The data associated with this study have not been deposited in a publicly available repository, but can be made available upon request.

Ethics declaration

This study was reviewed and approved by the Institutional Research Review Board of the Affiliated Hospital of the Nanjing University of Chinese Medicine (2017NL-012-01, 3/30/2017, 9/30/2023). The board waived the need for signing consent for patients included in the study.

CRediT authorship contribution statement

Xiaohui Yan: Writing – original draft, Validation, Formal analysis, Data curation, Conceptualization. **Dan Wu:** Writing – original draft, Validation, Formal analysis, Data curation. **Xinyu Xu:** Validation, Software, Data curation. **Aimei Zhang:** Resources, Data curation. **Junqi Liao:** Resources, Data curation. **Qiuhua He:** Data curation. **Fantao Song:** Resources, Data curation. **Yan Liu:** Resources, Data curation. **Zhaoyao Chen:** Methodology, Data curation. **Minghua Wu:** Validation, Methodology. **Li Li:** Writing – review & editing, Validation, Project administration. **Wenlei Li:** Writing – review & editing, Validation, Supervision, Project administration.

Declaration of competing interest

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

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e36911.

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