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ARTICLE

Relationship Between Stress Hyperglycemia Ratio and In-Stent Restenosis in Patients Receiving Drug-Eluting Stents

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Abstract

Aims/Background In-stent restenosis (ISR) is a major cause of long-term failure in coronary revascularization among patients undergoing percutaneous coronary intervention (PCI). Emerging evidence suggests that the stress hyperglycemia ratio (SHR) is a novel biomarker with potential predictive value for cardiovascular diseases. This study aimed to investigate the relationship between SHR and ISR in patients treated with drug-eluting stents (DES).

Methods This retrospective study included 410 patients who underwent DES implantation at the Cardiology Department of Yixing People's Hospital between January 2015 and December 2022. All participants underwent coronary angiography (CAG) to evaluate the incidence of ISR and were categorized into two groups based on CAG results: non-ISR (n = 346) and ISR (n = 64). Laboratory parameters were evaluated prior to CAG for all participants. A restricted cubic spline (RCS) analysis was performed to evaluate the potential nonlinear associations between SHR and ISR. Multivariate logistic regression was used to identify independent risk factors for ISR, while the predictive value of SHR for ISR was assessed using receiver operating characteristic (ROC) analysis.

Results RCS analysis revealed a nonlinear, J-shaped relationship between SHR and ISR ($p < 0.05$). Multivariate logistic regression identified SHR as an independent risk factor of ISR (odds ratio (OR) = 32.05, 95% confidence interval (CI): 6.827–150.450, $p < 0.05$). ROC analysis revealed that SHR had a high predictive value for ISR, with an area under the curve (AUC) of 0.81 (95% CI: 0.74–0.87, $p < 0.001$). The optimal SHR cutoff value was 0.87, with a sensitivity of 79.69% and a specificity of 73.41%.

Conclusion Our findings identified a significant association between SHR and the risk of ISR in patients with coronary heart disease (CHD) undergoing PCI with DES implantation. SHR may serve as a valuable biomarker for predicting ISR, enabling improved risk stratification and patient management.

Key words: hyperglycemia; physiological stress; percutaneous coronary intervention; coronary restenosis

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Introduction

In-stent restenosis (ISR) is a prevalent long-term complication that contributes to the failure of revascularization in patients undergoing percutaneous coronary intervention (PCI) (Giustino et al, 2022). During the era of bare-metal stents (BMS), the incidence of ISR was alarmingly high, reaching up to 44%. However, the widespread adoption of drug-eluting stents (DES) has significantly reduced ISR rates to 5%–20% (Aoki and Tanabe, 2021). Despite this progress, ISR remains a clinically significant challenge.

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Basic research suggests that ISR is driven by mechanisms such as chronic inflammation, proliferation and migration of inflammatory cells and smooth muscle cells, secretion of inflammatory factors and extracellular matrix components, and neo-atherosclerosis development. However, the precise pathophysiological mechanisms underlying ISR are not fully understood and warrant further investigation (Clare et al, 2022).

The management of ISR requires addressing clinical risk factors and identifying reliable predictive indicators. Established clinical risk factors for ISR include diabetes mellitus, smoking, and hypertension (Alexandrescu et al, 2021; Wang et al, 2020). Although various approaches have been proposed to minimize ISR incidence, a reliable, accurate, and easily measurable predictor remains elusive (Shimono et al, 2021; Ullrich et al, 2021).

The stress hyperglycemia ratio (SHR) is a novel metric that quantifies stress-induced hyperglycemia by reflecting relative changes in blood glucose levels more precisely (Roberts et al, 2015). Unlike absolute blood glucose levels, which are affected by factors such as diet and medication, SHR accounts for fluctuations over a defined period offering a more stable and reliable measure. Prior study has established a relationship between SHR and cardiovascular outcomes (Li et al, 2024). Research has also shown that blood glucose variability is closely associated with adverse cardiovascular events (An et al, 2021). These findings suggest that SHR may be a superior indicator compared to traditional blood glucose measurements.

Despite the potential clinical relevance of SHR, few studies have examined its relationship with ISR. This study aimed to evaluate the predictive value of SHR for ISR in patients treated with DES. By employing a retrospective approach, our findings will offer a novel clinical indicator for ISR and improve risk stratification in this patient population.

Methods

Study Design and Population

This study was a retrospective case-control investigation that included a cohort of consecutive patients with coronary heart disease (CHD) who underwent coronary angiography (CAG) following DES implantation. The study was conducted in the Cardiology Department of Yixing People's Hospital between January 2015 and December 2022. Based on CAG findings, participants were classified into non-ISR (n = 346) and ISR (n = 64) groups. Clinical data and preoperative biochemical indicators were collected for all patients, including blood glucose, glycated hemoglobin (HbA1c), blood lipid levels, and echocardiogram. Inclusion criteria were as follows: (1) Patients who underwent DES implantation at least one year post-PCI; (2) Adherence to regular medication regimens; and (3) Availability of complete clinical and laboratory data. Exclusion criteria included: (1) Patients with acute cardiovascular or cerebrovascular conditions (e.g., acute myocardial infarction, acute cerebral infarction, acute heart failure); (2) Patients with acute infectious diseases (e.g., severe pneumonia, septicemia, acute cholecystitis); (3) Patients with severe hepatic or renal diseases with significant laboratory abnormalities (e.g., transam-

inase levels > three times the normal upper limit or serum creatinine clearance <30 mL/min); (4) Patients with autoimmune diseases, malignancies, or hemorrhagic disorders (e.g., severe gastrointestinal bleeding, intracerebral hemorrhage, or thrombocytopenia-induced bleeding).

This study was conducted following the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Yixing People's Hospital (approval number: 2024-004-01).

Laboratory Analysis

Two independent researchers conducted data collection, ensuring accuracy through a systematic data entry process, validation using SPSS software, and re-verification of extreme values during analysis. Laboratory data were obtained upon the admission of patients to the hospital. Routine blood tests, blood lipids, blood glucose, and glycated hemoglobin (HbA1c) were performed in the Department of Laboratory Medicine at Yixing People's Hospital. The SHR value was calculated using the following formula:

SHR = admission blood glucose (mmol/L)/(1.59 × HbA1c – 2.59) (Roberts et al, 2015).

Angiographic Assessment

CAG or PCI follows professional norms and standards. Two experienced attending physicians independently interpreted angiographic images. ISR was defined as ≥50% reduction in the diameter of the coronary artery, occurring within the stent or extending up to 5 mm beyond its edges.

Statistical Analysis

All statistical analyses and graphical representations were conducted using SPSS (version 26.0, SPSS Inc., Chicago, IL, USA) and R software (version 4.2.1, R Foundation for Statistical Computing, Vienna, Austria). Data normality was assessed using Levene's test. Quantitative data conforming to a normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$) and compared between groups using the independent *t*-test. For data that did not conform to a normal distribution, parametric tests were employed, and results were expressed as medians with interquartile ranges (median [25%, 75%]).

Qualitative data were analyzed using the Chi-square test or Fisher's exact test. Correlations were assessed using Pearson or Spearman correlation analysis, depending on the data type. Restricted cubic spline (RCS) analysis was utilized to evaluate the potential nonlinear relationship between SHR and ISR. RCS curves were constructed with 4 knots at the 5th, 35th, 65th, and 95th percentiles of SHR. Multivariate logistic regression analysis was conducted to identify independent risk factors associated with ISR. The predictive performance of SHR and other indicators for ISR was evaluated using receiver operating characteristic (ROC) curve analysis. Statistical significance was defined as $p < 0.05$.

Table 1. Baseline clinical characteristics and laboratory parameters of the study population.

Characteristics	Non-ISR (n = 346)	ISR (n = 64)	$\chi^2/t/Z$ value	*p*-value
Age (years)	60.09 ± 11.07	63.61 ± 9.25	–2.393	0.017
Gender (male) [n (%)]	302 (87.28)	58 (90.62)	0.563	0.453
Time after PCI (years)	1.05 (1.00, 1.20)	1.10 (1.01, 1.37)	–2.208	0.027
Hypertension [n (%)]	212 (61.27)	41 (64.06)	0.178	0.673
Diabetes mellitus [n (%)]	106 (30.64)	22 (34.38)	0.352	0.553
Smoking [n (%)]	157 (45.38)	27 (42.19)	0.222	0.638
Multi-vessel lesion [n (%)]	271 (78.32)	60 (93.75)	8.262	0.004
Number of stents (n)	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	–2.616	0.009
Total stent length (mm)	33 (28.00, 51.00)	38 (29.00, 65.50)	–2.705	0.007
Stent diameter (mm)	3.23 ± 0.41	3.11 ± 0.42	2.200	0.028
TC (mmol/L)	3.27 (2.85, 3.79)	3.39 (2.94, 3.81)	–0.901	0.368
TG (mmol/L)	1.80 ± 1.46	1.50 ± 0.82	1.623	0.105
HDL-C (mmol/L)	1.05 ± 0.27	1.07 ± 0.22	–0.380	0.704
LDL-C (mmol/L)	1.93 ± 0.65	1.93 ± 0.47	–0.002	0.998
Cr (μmol/L)	74.42 ± 17.45	74.13 ± 17.15	0.127	0.899
EF (%)	58.66 ± 7.46	59.71 ± 6.00	–1.206	0.231
Blood glucose (mmol/L)	5.56 (4.91, 6.71)	7.97 (6.44, 10.00)	–7.707	<0.001
HbA1c (%)	6.43 ± 1.22	6.27 ± 0.99	1.004	0.316
SHR	0.79 (0.70, 0.88)	1.09 (0.89, 1.30)	–7.811	<0.001

PCI, percutaneous coronary intervention; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Cr, creatinine; EF, ejection fraction; SHR, stress hyperglycemia ratio; HbA1c, glycated hemoglobin; ISR, in-stent restenosis.

Results

Clinical Characteristics of ISR

A total of 410 participants were included in this study, comprising 64 individuals in the ISR group and 346 individuals in the non-ISR group. No statistically significant differences were observed between the two groups in gender, history of hypertension, diabetes mellitus, smoking status, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC), creatinine levels, ejection fraction (EF), or glycosylated hemoglobin (all $p > 0.05$). However, significant differences were identified between the two groups in age, time since PCI, the presence of multi-vessel coronary disease, number of stents implanted, average stent diameter, total stent length, admission blood glucose levels, and SHR (all $p < 0.05$, Table 1).

Correlation Analysis of ISR

Correlation analysis revealed that ISR was positively associated with age (r = 0.118, $p < 0.05$) and time after PCI ($\rho = 0.109$, $p < 0.05$). Admission blood glucose levels ($\rho = 0.381$, $p < 0.05$) and SHR ($\rho = 0.386$, $p < 0.05$) also demonstrated significant positive correlations with ISR. Additionally, ISR was positively correlated

Table 2. Correlation analysis of ISR.

Characteristics	Correlation coefficient	*p*-value
Age	0.118	0.017
Time after PCI	0.109	0.027
Blood glucose	0.381	<0.001
SHR	0.386	<0.001
Number of stents	0.129	0.009
Total stent length	0.134	0.007
Stent diameter	–0.108	0.028

PCI, percutaneous coronary intervention; SHR, stress hyperglycemia ratio.

with the number of stents implanted ($\rho = 0.129$, $p < 0.05$) and total stent length ($\rho = 0.134$, $p < 0.05$). Conversely, ISR exhibited a negative correlation with average stent diameter (r = –0.108, $p < 0.05$) (Table 2).

Nonlinear Relationship Between the SHR and ISR

Using a logistic regression model, adjustments were made for confounding variables, including age, gender, smoking status, hypertension, diabetes, and stent implantation duration. RCS analysis with 4 knots at the 5th, 35th, 65th, and 95th percentiles of SHR was employed to explore the dose-response relationships. The x-axis represents the continuous variation of SHR, while the y-axis displays the odds ratio (OR), with the optimal cutoff value of SHR serving as a reference.

The analysis revealed a nonlinear dose-response relationship between SHR and ISR ($p < 0.05$). Initially, the curve exhibited a relatively flat trend. However, as SHR approached approximately 0.81, an upward trajectory was observed, indicating a stronger association and tendency toward a linear correlation. These findings underscore the intricate and vital role of SHR in predicting ISR risk (Fig. 1).

Risk Factors for In-Stent Restenosis

Logistic regression analysis was conducted to evaluate the risk factors associated with ISR. Univariate logistic regression revealed that several variables were significantly correlated with the incidence of ISR, including age (OR = 1.031, $p < 0.05$), stent implantation duration (OR = 1.001, $p < 0.05$), presence of multiple lesions (OR = 4.151, $p < 0.05$), number of stents (OR = 2.030, $p < 0.05$), total stent length (OR = 1.024, $p < 0.05$), average stent diameter (OR = 0.488, $p < 0.05$), admission blood glucose levels (OR = 1.621, $p < 0.05$), and SHR (OR = 82.160, $p < 0.05$).

Further multivariate logistic regression analysis identified age and SHR as independent predictors of ISR, with ORs of 1.037 and 32.050, respectively (Table 3).

Predictive Value of SHR for ISR: ROC Analysis

ROC curve analysis was conducted to assess the predictive value of SHR for ISR. The area under the curve (AUC) for SHR was 0.81 (95% confidence interval (CI): 0.74–0.87; $p < 0.001$), indicating a robust predictive capacity. The optimal

Table 3. Results of univariate and multivariate logistic regression.

Variable	Univariate logistic regression					Multivariate logistic regression				
	β	S.E.	Wald	*p*	OR (95% CI)	*β*	S.E.	Wald	*p*	OR (95% CI)
Gender (male)	0.342	0.458	0.559	0.455	1.408 (0.574–3.457)					
Age	0.031	0.013	5.582	0.018	1.031 (1.005–1.058)	0.036	0.016	5.078	0.024	1.037 (1.005–1.070)
Smoking	–0.130	0.275	0.222	0.638	0.878 (0.512–1.506)					
Hypertension	0.119	0.283	0.178	0.673	1.127 (0.647–1.962)					
Diabetes mellitus	0.171	0.288	0.351	0.553	1.186 (0.675–2.085)					
Time after PCI	0.001	<0.001	4.292	0.038	1.001 (1.001–1.002)	0.001	0.001	2.351	0.125	1.00 (1.001–1.002)
Multi-vessel lesion	1.423	0.533	7.142	0.008	4.151 (1.462–11.791)	0.898	0.609	2.177	0.140	2.455 (0.745–8.098)
Number of stents	0.708	0.211	11.268	<0.001	2.030 (1.343–3.069)	–0.130	0.606	0.046	0.830	0.878 (0.268–2.880)
Stent total length	0.024	0.007	13.131	<0.001	1.024 (1.011–1.038)	0.022	0.019	1.335	0.248	1.022 (0.985–1.062)
Stent diameter	–0.72	0.330	4.740	0.029	0.488 (0.255–0.931)	–0.293	0.401	0.534	0.465	0.746 (0.340–1.637)
Blood glucose	0.483	0.068	50.042	<0.001	1.621 (1.418–1.853)	0.170	0.095	3.183	0.074	1.185 (0.983–1.428)
HbA1c	–0.129	0.128	0.100	0.316	0.879 (0.684–1.131)					
SHR	4.409	0.583	57.166	<0.001	82.160 (26.202–257.625)	3.467	0.789	19.314	<0.001	32.050 (6.827–150.450)

PCI, percutaneous coronary intervention; SHR, stress hyperglycemia ratio; OR, odds ratio; CI, confidence interval; S.E., Standard Error.

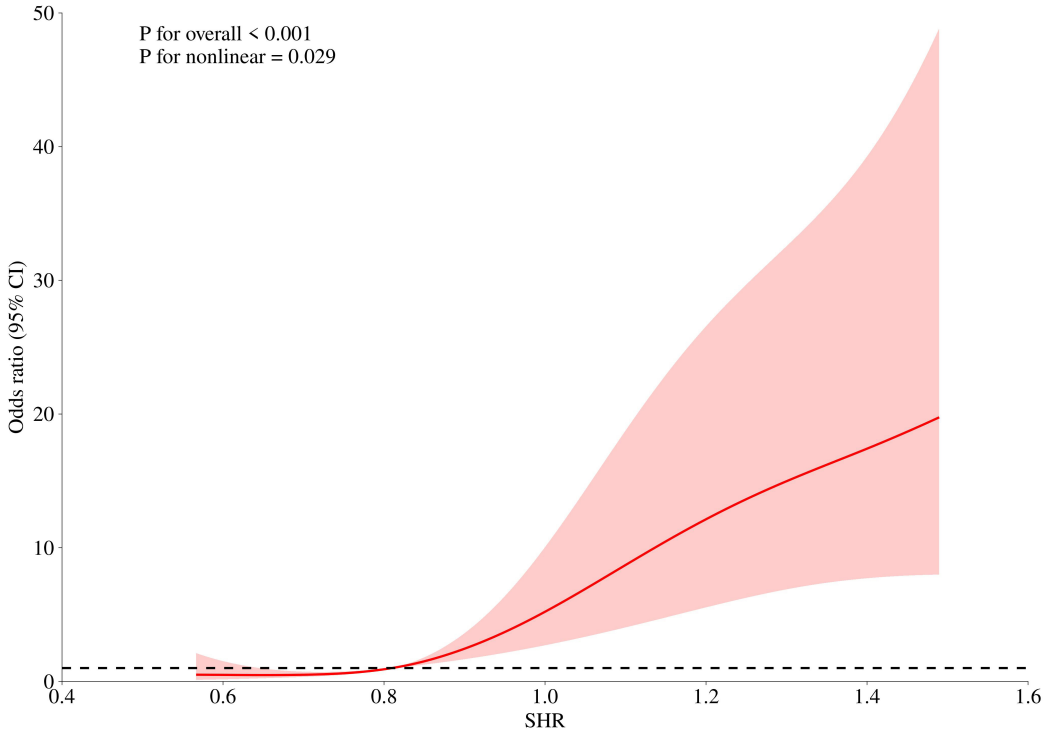

Fig. 1. RCS curve showing the relationship between SHR and ISR. SHR, stress hyperglycemia ratio; RCS, restricted cubic spline; CI, confidence interval.

SHR cutoff value, determined using the Youden index, was 0.87, yielding a sensitivity of 79.69% and a specificity of 73.41% (Fig. 2).

Discussion

This study is the first to evaluate the association between SHR and ISR in patients undergoing DES implantation. Our findings revealed that patients in the ISR group exhibited significantly higher SHR levels compared to the non-ISR group. Additionally, a significant relationship between elevated SHR and the incidence of ISR was identified. RCS analysis highlighted a nonlinear association between SHR and ISR, showing a sharp increase in ISR incidence when SHR exceeded 0.81. ROC analysis further confirmed the predictive utility of SHR, highlighting its potential as a valid biomarker for ISR risk stratification.

The pathophysiology of ISR is a multifaceted process influenced by biological and mechanical factors. Central to this process are local inflammatory responses, the accumulation of extracellular matrix components, and the development of intimal hyperplasia (Li et al, 2021). Research has shown that in-stent restenosis is a complex pathophysiological process involving multiple inflammatory cells. Early stages of ISR involve the recruitment and activation of inflammatory cells, especially neutrophils and macrophages, at the site of stent implantation. These cells subsequently infiltrate the surrounding tissues, amplifying the inflammatory response (Liu et al, 2023b). Under certain circumstances, the adaptive immune system also contributes to ISR development (Liu et al, 2019).

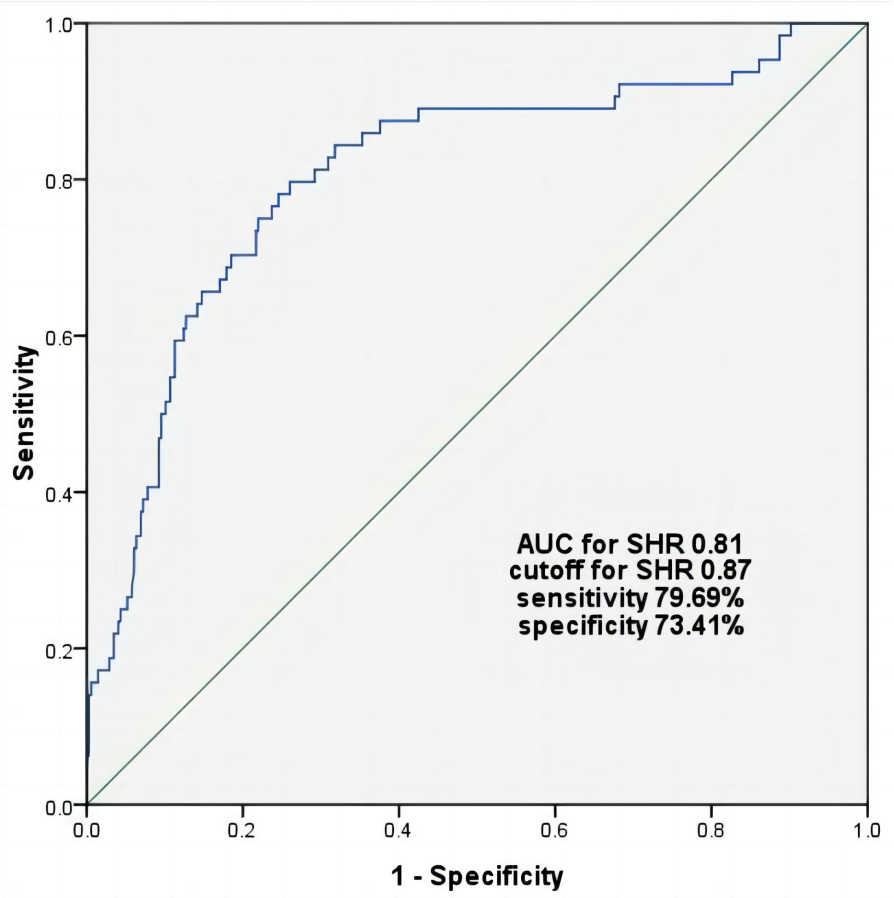

Fig. 2. ROC curve for SHR in predicting ISR. ROC, receiver operating characteristic; SHR, stress hyperglycemia ratio; AUC, area under the curve.

Endothelial cell injury and dysfunction, along with smooth muscle cell (SMC) proliferation and migration, form the pathological foundation for ISR and other vascular proliferative diseases such as atherosclerosis and hypertension (Ebert et al, 2021). Cytokines and extracellular matrix proteins released during vascular healing promote endothelial hyperplasia and lipid plaque formation. Additionally, key signaling pathways, including Nuclear Factor kappa-B, Transforming Growth Factor-β/small mothers against decapentaplegic (Smad), and Notch, regulate SMC phenotypic transformation, proliferation, and migration (Tang et al, 2022). These pathways form a complex regulatory network, underscoring the intricate vascular response to PCI.

Clinical studies have identified numerous factors that significantly contribute to the development of ISR (Alexandrescu et al, 2021; Zhao et al, 2020). Conditions such as hypertension, hyperlipidemia, and diabetes mellitus are strongly linked to the occurrence of coronary ISR (Wang et al, 2020). Among these, diabetes is a significantly critical risk factor. Diabetic patients commonly experience impaired endothelial function, abnormal platelet activity, and coagulation irregularities, leading to an increased risk of ISR. Studies report that the incidence of ISR following PCI is 2–4 times higher in diabetic patients compared to non-diabetic individuals (Jakubiak et al, 2021; Wang et al, 2018). Santos-Pardo et al (2024) demonstrated

that poor glycemic control significantly increases the risk of stent failure driven by ISR. Similarly, Chen et al (2023) identified a significant correlation between elevated fasting blood glucose (FBG) levels and ISR in non-diabetic patients with CHD. Additional studies have revealed that blood glucose levels and insulin resistance are intricately linked to ISR development, with FBG levels exceeding 6.1 mmol/L associated with a heightened risk of ISR (Xue et al, 2022; Zhu et al, 2021).

Moderate hyperglycemia serves as a protective mechanism, supplying adequate energy during periods of stress. However, excessive stress-induced hyperglycemia can have detrimental effects which were driven by various mechanisms (Li et al, 2022; Vedantam et al, 2022). Stress-induced hyperglycemia enhances immune-inflammatory responses, leading to increased secretion of pro-inflammatory cytokines such as interleukin-1, interleukin-6, and tumor necrosis factor. Additionally, it promotes thrombotic activity by enhancing platelet aggregation and increasing fibrinogen levels, further contributing to vascular complications (Vedantam et al, 2022).

Admission glucose levels alone may not effectively represent the extent of stress-induced hyperglycemia due to the influence of baseline glycemic status. Therefore, SHR, which incorporates admission glucose and estimated chronic blood glucose levels, provides a more accurate measure of relative hyperglycemia (Roberts et al, 2015). Growing evidence underscores the significance of SHR in various cardiovascular conditions, including its potential role in predicting adverse outcomes (Huang et al, 2022, 2023; Wang et al, 2024).

The SHR effectively captures fluctuations in blood glucose levels, offering insights beyond the static measurement of blood glucose levels alone. Research has shown that variations in blood glucose are closely associated with cardiovascular events (An et al, 2021). Compared to blood glucose levels, SHR is considered a superior prognostic indicator. For instance, a cohort study identified SHR as a significant risk factor for one-year long-term all-cause mortality in patients with acute myocardial infarction across Chinese and U.S. populations (Liu et al, 2023a).

Similarly, a cohort study in an Asian population revealed a U-shaped correlation between SHR and the incidence of adverse cardiovascular events over a two-year follow-up in patients with acute coronary syndrome undergoing drug-eluting stent implantation. Additionally, the relationship between SHR and specific outcomes, such as cardiac death and myocardial infarction, exhibited a J-shaped curve, with a critical threshold for adverse prognosis set at 0.78 (Yang et al, 2022). In another recent study, SHR was strongly associated with poor prognosis in patients with moderate-to-severe coronary artery calcification, with a threshold value of 0.83 serving as a predictor of unfavorable outcomes (Lin et al, 2024). Collectively, these findings suggest that SHR is a novel serological marker for predicting coronary lesions and overall clinical prognosis.

Numerous studies have highlighted the role of SHR in predicting risk and assessing prognosis in cardiovascular diseases (Zeng et al, 2023; Zhao et al, 2024). However, the relationship between SHR and ISR following PCI has not been previously explored. Our study bridges this gap and demonstrates a significant correlation between ISR and factors such as age and diabetes. Notably, blood glucose

levels were identified as a significant risk factor for ISR, alongside diabetes, multivessel coronary artery disease, and SHR. Through multivariate logistic regression analysis, we confirmed that age and SHR are independent risk factors for ISR. To further characterize the relationship between SHR and ISR, we used RCS analysis, which revealed a nonlinear association. The RCS curve initially displayed a flat trajectory, followed by a sharp increase at an SHR value of approximately 0.81, eventually approaching linearity. Additionally, ROC analysis demonstrated an AUC of 0.81 for SHR. The optimal cutoff value of SHR was determined to be 0.87, yielding sensitivity and specificity rates of 79.69% and 73.41%, respectively. These findings provide preliminary evidence that SHR may serve as a reliable predictive marker for ISR, offering valuable insights into its clinical application.

Despite its contributions, this study has several limitations. First, the retrospective nature of the investigation and its single-center design necessitate validation through multi-center prospective studies. Second, limitations in sample size and the completeness of clinical data restricted the inclusion of potentially relevant variables that might influence ISR. Third, although conventional risk factors, including lipid profiles, were accounted for, our analysis did not detect significant differences between the ISR and non-ISR groups. This finding may be attributed to the suboptimal lipid profiles observed in both groups, potentially affecting the analysis of ISR risk factors.

Despite these limitations, our study provides novel insights into the relationship between SHR and ISR, contributing to the growing evidence on SHR as a prognostic marker. Future research efforts will focus on refining study designs, incorporating larger sample sizes, and conducting multi-center studies to validate our findings and further explore the complex interplay between SHR and ISR.

Conclusion

The SHR is significantly associated with the occurrence of ISR following PCI. Compared to conventional blood glucose monitoring, SHR is more sensitive to relative fluctuations in blood glucose levels and demonstrates superior predictive performance for ISR. These findings highlight the potential of SHR as a valuable screening tool for the early detection of individuals at heightened risk of ISR, enabling timely clinical intervention and improved patient outcomes.

Key Points

- The stress hyperglycemia ratio (SHR) is significantly correlated with the occurrence of in-stent restenosis (ISR).
- Restricted cubic spline (RCS) analysis revealed a nonlinear J-shaped relationship between SHR and ISR incidence.
- Receiver operating characteristic (ROC) analysis revealed that the area under the curve (AUC) for SHR was 0.81 (95% CI: 0.74–0.87, $p < 0.001$). The optimal cutoff value for SHR was 0.87, with a sensitivity of 79.69% and a specificity of 73.41%.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding authors upon request.

Author Contributions

LX, MZ, JXS, YCC, CX and YJY conceived and designed the study. JXS and MZ collected materials from the patients for the manuscript. YJY and CX were responsible for the collection and assembly of data. MZ, YJY, YCC, JXS and LX conducted data analysis and interpretation. MZ and JXS drafted the manuscript. All authors contributed to revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Yixing People's Hospital (NO. 2024-004-01) and strictly complied with the principles of the Declaration of Helsinki. The informed consent for all patients was exempted by the Ethics Committee of Yixing People's Hospital.

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Conflict of Interest

The authors declare no conflict of interest.

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