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Relationship between stress hyperglycemia ratio and progression of non target coronary lesions: a retrospective cohort study

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Abstract

Background Stress hyperglycemia ratio is a novel indicator of acute coronary synthesis (ACS), which is closely related to the severity and complications of ACS and other cardiovascular diseases. However, its relationship with the progression of non target coronary lesions remains unclear. The purpose of this paper is to explore the relationship between stress hyperglycemia ratio and the progression of non target coronary lesions.

Methods This study retrospectively enrolled patients diagnosed with acute coronary syndrome who underwent stent implantation and follow-up evaluations by coronary angiography at Zhongda Hospital between January 2019 and January 2024. Patients were classified into progression and non progression groups based on follow-up angiography findings. Logistic regression models, restricted cubic spline analysis, and machine learning algorithms (LightGBM, decision tree, and XGBoost) were utilized to analyse the relationship of stress hyperglycemia ratio and non target lesion progression.

Results A total of 1,234 ACS patients were included; 29.1% experienced non target lesions progression. Logistic regression analysis showed that stress hyperglycemia ratio (SHR) was a risk factor for non target disease progression ($P < 0.001$), and after adjusting for other variables, SHR was still independently associated with non target disease progression (OR = 2.12, 95% CI: 1.30–3.44, $p = 0.003$). RCS analysis revealed a near-linear relationship between SHR and nontarget lesions progression ($P = 0.14$). With the increase of SHR, the risk of non target lesions progression continued to increase, and the risk was significant when the SHR was greater than 0.96, but tended to be stable when the SHR was greater than 1.36 ($p = 0.0047$). A hybrid model combining logistic regression and XGBoost yielded the best predictive performance, with an AUC of 0.78 (95% CI: 0.72–0.85), incorporating SHR, number and stenosis severity of non target lesions (NTLs), hypertension and high-density lipoprotein cholesterol (HDL-c). Subgroup analysis showed that elevated SHR was a stronger predictor of NTL progression in non-diabetic patients (OR = 3.76, $p = 0.007$) compared with diabetic patients (OR = 1.69, $p = 0.083$).

Conclusion Stress hyperglycemia ratio is closely related to the progression of non target lesions. This study provides a novel insight for optimizing the long-term management of non target lesions after PCI.

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Keywords Non target lesion progression, Stress hyperglycemia ratio, Diabetic and non-diabetic, XGBoost predictive model

Background

Coronary atherosclerotic heart disease remains one of the leading cause of mortality and morbidity worldwide. In the era of drug-eluting stents (DES), the incidence of in-stent restenosis (ISR) has significantly declined, shifting attention to the progression of non target lesions (NTLs). NTL progression has emerged as a critical determinant of treatment outcomes and overall prognosis. Studies have reported that nearly half of recurrent ischemic cardiac events after percutaneous coronary intervention (PCI) originate from the progression of NTLs [1–3]. However, the underlying factors contributing to NTL progression remain unclear. Traditional cardiovascular risk factors, including hypertension, diabetes, smoking, and dyslipidemia, are thought to contribute to NTL progression [4–10]. With advancements in novel biomarker research, indicators related to glucose–lipid metabolism, insulin resistance, and inflammation have been increasingly recognized as important determinants of cardiovascular disease occurrence, progression, and prognosis. The stress hyperglycemia ratio (SHR), which reflects an individual's metabolic response to acute stress, is calculated by comparing blood glucose levels during stress to baseline levels. In patients undergoing stent implantation, follow-up coronary angiography is typically performed within two years, and SHR measured at follow-up serves as an indicator of recent stress states and glucose metabolism abnormalities. Elevated SHR has been associated with exacerbated oxidative stress, heightened inflammatory responses, and endothelial dysfunction, all of which contribute to an increased risk of complications. Evidence further suggests a significant correlation between SHR and cardiovascular mortality in patients with acute coronary syndrome (ACS) [11, 12]. Among critically ill patients with acute myocardial infarction (AMI), elevated SHR is strongly associated with both one-year and long-term all-cause mortality, particularly in nondiabetic populations [13].

This study aims to investigate the relationship between SHR and NTL progression. By integrating clinical factors, echocardiographic indicators, stent characteristics, and NTL-specific features, this study seeks to comprehensively evaluate the predictive factors associated with NTL progression.

Methods

Study population

This study consecutively enrolled patients diagnosed with acute coronary syndrome (ACS) at Zhongda Hospital between January 2019 and January 2024. Eligible patients underwent at least one stent implantation and follow-up coronary angiography (CAG). All patients received dual antiplatelet therapy in accordance with current guidelines following the procedure. Patients were excluded if they had: a history of prior percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG); without non target lesion; a diagnosis of malignancy, acute infection, inflammatory disease, or severe autoimmune disease; were receiving hemodialysis treatment; or had incomplete clinical data or unclear angiographic images. The study was approved by the Ethics Committee of Zhongda Hospital (Ethics ID: 2023ZDSYLL264-P01).

Clinical data

Demographic and clinical data collected included sex, age, and medical history, such as hypertension, diabetes, stroke, and smoking status. Laboratory parameters included glycated hemoglobin (HbA1c), admission glucose (ABG), fasting glucose, creatinine, uric acid, D-dimer, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), apolipoprotein A1, apolipoprotein B, lipoprotein (a), and left ventricular ejection fraction (LVEF). Patients with a prior diagnosis of diabetes or HbA1c > 6.5% were classified as diabetic. LVEF was assessed via echocardiography. The stress hyperglycemia ratio (SHR) was calculated as ABG (mmol/L) ÷ (1.59 × HbA1c [%] – 2.59).

Coronary angiographic data

Coronary angiograms were analyzed by two experienced interventional cardiologists. Vessel edges were delineated using an automated edge-detection algorithm applied to contrast-enhanced images. After identifying the start and end points of the enhanced images, coronary arteries were processed to create a vascular path, which was then used to outline the vessel contour. The path and contours were determined automatically based on contrast density but occasionally required manual adjustments by the analysts. Measured variables included minimal lumen diameter (MLD) and percentage stenosis [14]. Non-target lesions are defined as lesions located more than 10 mm from the edge of the target lesion stents, with lumen stenosis ranging from 50 to 80% or less than 50%, as identified during the initial intervention [15]. Definition of non target lesion (NTL) progression: 1) ≥ 10% diameter reduction in preexisting stenosis ≥ 50%. 2) ≥ 30% diameter reduction in preexisting stenosis < 50%. 3) Progression to total occlusion of a lesion [16]. Patients meeting these criteria were classified into the NTL progression

group. Variables recorded included the number, location, and percentage stenosis for non target lesions at both angiographic assessments, along with stent count, length, diameter, and drug coating.

Data analysis

All statistical analyses were conducted using R statistical software (version 4.2.2). Categorical variables were presented as counts (percentages) and compared using the chi-square test. Continuous variables were expressed as mean ± SD or median ± interquartile range and compared using the t-test or rank-sum test as appropriate. Multivariable logistic regression, restricted cubic spline (RCS) models, and LASSO regression were employed to identify significant variables. Machine learning models, including XGBoost, LightGBM, and decision trees, were constructed. Receiver operating characteristic (ROC) curves and decision curve analysis (DCA) were used to evaluate model performance. Subgroup and sensitivity analyses were conducted to explore the robustness of the models. A two-sided p-value of <0.05 was considered statistically significant.

Result

Baseline characteristics

A total of 1,234 patients diagnosed with acute coronary syndrome (ACS) who underwent stent implantation and completed regular follow-up at our hospital were included in the study (Fig. 1). The clinical and angiography characteristics are summarized in Table 1. Among the patients, 29.1% experienced non target lesion (NTL) progression. Compared with the non-progression group, patients in the progression group were more likely to be have a higher prevalence of hypertension, lower levels of HDL-c, elevated serum creatinine levels, and a greater number of non target lesions, smaller percentage stenosis. When quantitatively calculating the degree of stenosis of non target lesions by QCA, the progression group had significantly larger diameter changes and larger minimum lumen diameters (MLD) at the time of stent implantation.

Relationship between stress hyperglycemia ratio and NTL progression

To investigate the association between stress hyperglycemia ratio (SHR) and NTL progression, binary logistic regression analysis was performed. Both univariate

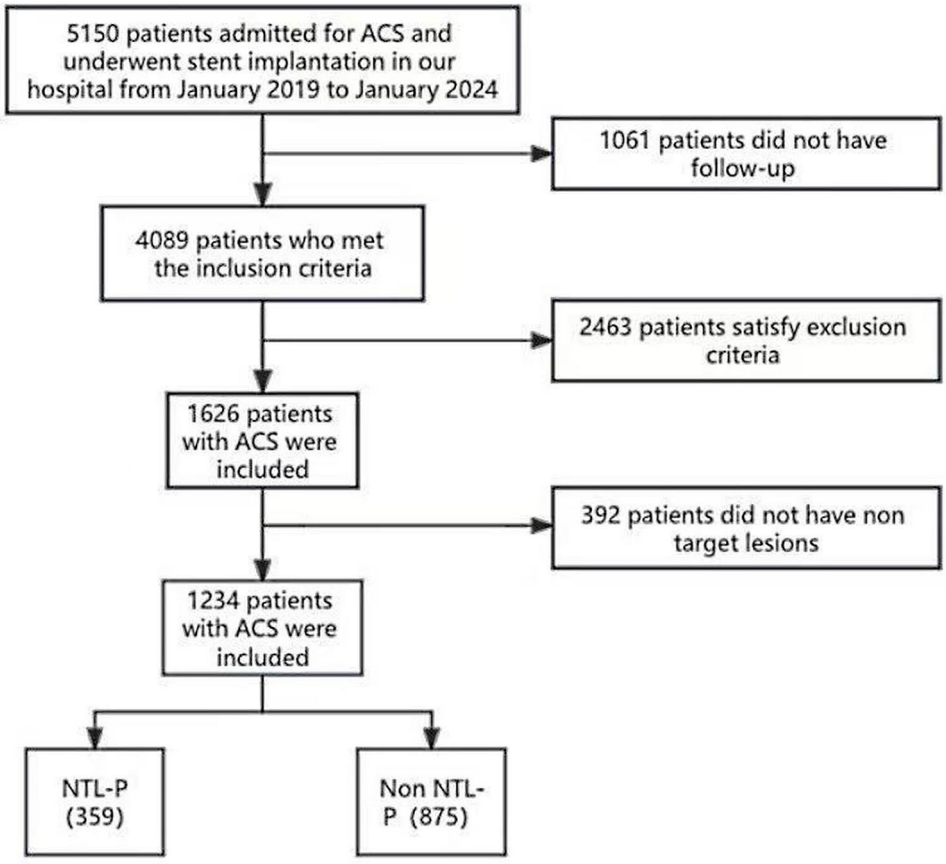

Fig. 1 Enrollment flow chart

Table 1 The difference of two groups of characteristics

	NTLP ($n=359$)	non-NTLP ($n=875$)	*P*
Male, n (%)	261 (72.70)	608 (69.50)	0.303
Age, y	65.97 (10.64)	65.07 (10.44)	0.224
Smoker, n (%)	132 (36.80)	317 (36.20)	0.827
Diabetes Mellitus, n (%)	194 (54.00)	436 (49.80)	0.229
Hypertension, n (%)	286 (79.70)	636 (72.70)	0.019
Myocardial Infarction, n (%)	146 (40.70)	303(34.60)	0.069
Unstable angina pectoris	235(65.4)	597(68.2)	
STEMI	25(7.0)	60(6.9)	
non STEMI	99(27.5)	218(24.9)	
Stroke, n (%)	85 (23.70)	186 (21.30)	0.414
LVEF,%	65.12 (9.91)	66.65 (10.22)	0.329
TG, mmol/L	1.51 (1.22)	1.49 (1.14)	0.882
TC, mmol/L	3.28 (1.01)	3.26 (0.94)	0.733
HDL, mmol/L	1.07 (0.28)	1.11 (0.28)	0.024
LDL, mmol/L	1.69 (0.78)	1.64 (0.69)	0.275
LPA, mg/L	251.69 (272.31)	269.56 (302.85)	0.421
D-dimer, mg/L	358.56 (904.58)	269.54 (585.22)	0.088
Uric Acid, umol/L	351.93 (105.35)	340.88 (93.59)	0.061
Serum Creatinine, mg/L	89.55 (79.48)	81.52 (38.89)	0.034
Number of Stents, n	1.79 (1.00)	1.83 (1.09)	0.571
Part of Stents, n (%)			0.229
LAD	173 (48.20)	477 (54.50)	
LCX	70 (19.50)	140 (16.00)	
RCA	116 (32.30)	258 (29.50)	
Stent Style, n (%)			0.557
Sirolimus eluting stents	241 (67.10)	535 (61.14)	
Everolimus eluting stents	54 (15.10)	134 (15.32)	
Zotamus eluting stents	64 (17.80)	206 (23.54)	
Number of NTL, n	3.68 (1.66)	2.94 (1.64)	< 0.001
Part of NTL, n (%)			0.158
LAD	138 (38.44)	377 (43.10)	
LCX	101 (28.13)	258 (29.50)	
RCA	120 (33.43)	240 (27.40)	
Revascularization of NTL, n	161 (44.8%)	63 (7.2)	< 0.001
ISR, n (%)	47 (13.10)	126 (14.40)	0.278
Percentage stenosis of NTL (%)	59.23 (13.6)	67.17 (11.4)	< 0.001
MLD (mm)	2.1 (0.64)	1.66 (0.56)	< 0.001
Diameter Change (cm) of NTL	0.58 (0.41)	0.02 (0.05)	< 0.001
SHR	1.08 (0.30)	1.00 (0.29)	< 0.001

Values are mean ± SD, mean (25th-75th quantiles), or n (%). LVEF left ventricular ejection fraction, TC Total cholesterol, TG Triglycerides, LDL-c Low-density lipoprotein cholesterol, HDL-c High-density lipoprotein cholesterol, LPA apolipoprotein a, ISR in-stent restenosis, LAD left anterior descending branch, LCX left circumflex artery, RCA right coronary artery, NTL non target lesion, MLD minimum lumen diameter, STEMI ST segment Elevation Myocardial Infarction, SHR stress hyperglycemia ratio

and multivariate regression analyses identified SHR as a significant risk factor for NTL progression ($p<0.001$), and an increase in SHR was associated with a 2.12-fold increase in the odds of NTL progression ($p=0.003$, Table 2). We applied restricted cubic splines(RCS) to assess the potential nonlinear relationship between between SHR and NTL progression. After adjusting for confounders, there was an approximately linear relationship (nonlinear $p=0.14$) between stress hyperglycemia ratio(SHR) and the risk of NTL progression, as shown in Fig. 2, with the increase of SHR, the risk of non target lesions progression continued to increase ($P<0.01$), the Odds Ratio was significant when SHR was greater than 0.96, but the tendency tended to be stable when SHR was greater than 1.36 (Fig. 2). In addition, the stress hyperglycemia ratio is correlated with the diameter change of NTL by Spearman Correlation Analysis ($P=0.01$). Furthermore, we documented 286 cases of non target revascularization, 165 cases of in-stent restenosis, and 328 cases of recurrent revascularization, showing that SHR was significantly associated with adverse events ($P=0.002$, $P=0.001$, and $P=0.005$, respectively).

Table 2 Logistic regression of influence factors of nontarget lesions progression

	OR (univariable)	OR (multivariable)
Male, n (%)	1.16 (0.89–1.51, $p=0.281$)	-
Age, y	1.01 (1.00–1.02, $p=0.244$)	-
Diabetes mellitus, n (%)	1.13 (0.89–1.43, $p=0.332$)	-
Hypertension, n (%)	1.48 (1.06–2.07, $p=0.020$)	1.58(1.10–2.28,$p=0.014$)
Stroke, n (%)	0.86 (0.65–1.15, $p=0.310$)	-
Smoker, n (%)	1.02 (0.80–1.31, $p=0.856$)	-
Myocardial Infarction, n (%)	1.132 (0.88–1.45, $p=0.325$)	-
LVEF,%	0.990 (0.98,1.00, $p=0.099$)	-
HbAlc,%	1.03 (0.95–1.12, $p=0.421$)	-
SHR	2.50 (1.67–3.75, $p<0.001$)	2.12 (1.30–3.44, $p=0.003$)
TG, mmol/L	1.00 (0.90–1.11, $p=0.934$)	-
TC, mmol/L	1.00 (0.89–1.14, $p=0.956$)	-
HDL, mmol/L	0.56 (0.35–0.88, $p=0.011$)	0.52 (0.30–0.91, $p=0.021$)
LDL, mmol/L	1.05 (0.89–1.25, $p=0.547$)	-
D-dimer, mg/L	1.00 (1.00–1.001, $p=0.077$)	-
Uric Acid, umol/L	1.00 (1.00–1.002, $p=0.213$)	-
Serum Creatinine, mg/L	1.00 (1.00–1.00, $p=0.056$)	-
Number of Stents, n	0.93 (0.83–1.04, $p=0.220$)	-
Part of Stents, n (%)		
LAD	reference	
LCX	1.03 (0.74–1.44, $p=0.847$)	-
RCA	0.84 (0.64–1.11, $p=0.230$)	-
Stent Style, n (%)		
Sirolimus eluting stents	reference	
Everolimus eluting stents	1.06 (0.76–1.48, $p=0.743$)	-
Zotamus eluting stents	0.74 (0.55–1.00, $p=0.054$)	-
Number of NTL, n	1.26 (1.17–1.36, $p<0.001$)	1.51 (1.37–1.65, $p<0.001$)
Part of NTL, n (%)		
LAD	reference	
LCX	1.05 (0.79–1.39,$p=0.730$)	-
RCA	1.26 (0.95–1.19,$p=0.109$)	-
percentage stenosis of NTL(%)	0.94 (0.94–0.95,$p<0.001$)	0.93 (0.92,0.94,$p<0.001$)

SHR stress hyperglycemia ratio, EF left ventricular ejection fraction, TC Total cholesterol, TG Triglycerides, LDL-c Low-density lipoprotein cholesterol, HDL-c High-density lipoprotein cholesterol, LAD left anterior descending branch, LCX left circumflex artery, RCA right coronary artery, NTL non target lesion

Predictive model for NTL progression

To identify predictive factors for NTL progression, logistic regression analysis and machine learning algorithms were employed. Model performance was evaluated using the area under the receiver operating characteristic curve (AUC), accuracy, and decision curve analysis (DCA). In multivariate binary logistic regression, forward and backward stepwise methods (LR and Wald) identified hypertension, SHR, the number and percentage stenosis of non target lesions, and HDL as significant variables. A heatmap revealed no significant correlations between these variables (Supplementary Fig. 1). Supplementary Fig. 2 presents the Lasso regression path plot for variable selection, and Supplementary Fig. 3 shows the AUCs for individual variables.

Among the machine learning algorithms, the XGBoost model demonstrated superior performance with an AUC of 0.74 (95% CI: 0.68–0.80), compared to 0.69 for the Decision Tree and 0.64 for LightGBM (Fig. 3). The Binomial Deviance Curve of XGBoost suggested that 4–10 variables were optimal for prediction (Supplementary Fig. 4). Lasso regression results identified six key variables, achieving an AUC of 0.70 and an accuracy of 0.73 in the test set. To address potential overfitting, we incorporated five variables selected by the Wald method into the model. This yielded an AUC of 0.90 (95% CI: 0.87–0.92) with an accuracy of 0.83 in the training set, and an AUC of 0.74 (95% CI: 0.68–0.80) with an accuracy of 0.71 in the test set. The decision and calibration curves of the model are illustrated in Figs. 4 and 5. A hybrid model combining logistic regression and XGBoost achieved the best predictive performance, with an AUC of 0.78 (95% CI: 0.72–0.85), surpassing the predictive value of each individual model. The hybrid model included variables such as hypertension, SHR, the number and percentage stenosis of NTLs, and HDL-c levels. The variable

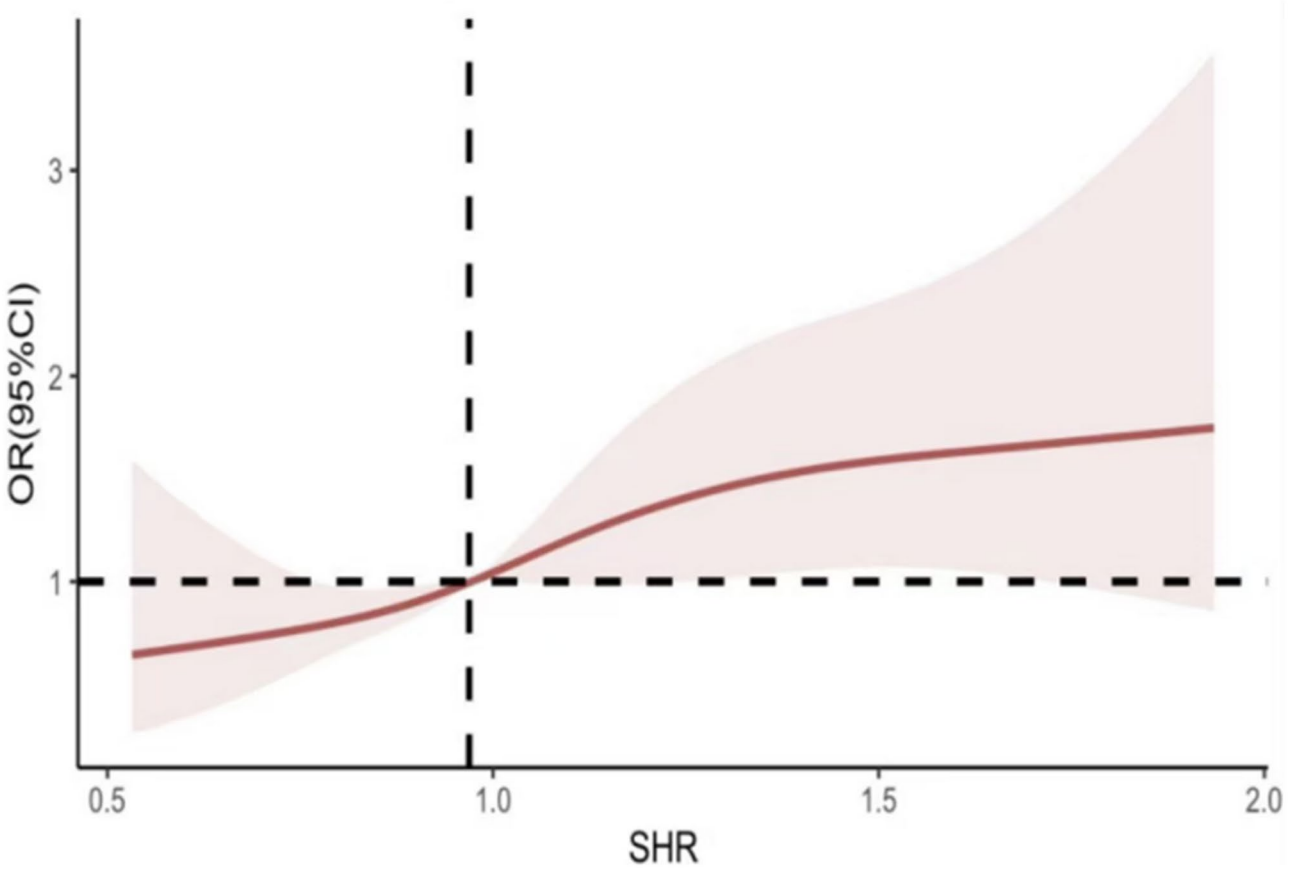

Fig. 2 Restricted cubic spline regression analysis of SHR and nontarget lesion progression

Table 3 Feature variables of hybrid model screening

	OR(CI)	*P*
Hypertension	1.58 (1.10,2.28)	0.01
HDL	0.52 (0.29,0.90)	0.02
Number of NTL	1.50 (1.36,1.66)	< 0.001
Percentage stenosis of NTL (%)	0.93 (0.92,0.94)	< 0.001
SHR	2.07 (1.26, 3.42)	0.004

HDL-c: High-density lipoprotein cholesterol, SHR: stress hyperglycemia ratio, NTL: non target lesion

importance diagram is shown in Fig. 6, and the SHAP diagram is provided in Supplementary Fig. 5. To explore the interaction between variables, interaction terms were established for the number and the percentage stenosis of non target lesions, and the stress hyperglycemia ratio (SHR). Regression analysis revealed a significant interaction effect between the number and percentage stenosis of non target lesions ($p < 0.01$). This finding indicates that the number and percentage stenosis of non target lesions jointly influence NTL progression, with a higher number of lesions and a lower percentage stenosis synergistically increasing the likelihood of lesion progression.

Subgroup analysis

To assess the robustness of the association between SHR and NTL progression, subgroup analyses were conducted based on diabetes status, history of myocardial infarction, revascularization of non-target lesions, and follow-up interval. While the interaction effect was not statistically significant ($p = 0.107$), elevated SHR was significantly associated with an increased risk of NTL progression in non-diabetic patients (OR = 3.76, $p = 0.007$), but not in diabetic patients (OR = 1.69, $p = 0.083$). Regarding the follow-up interval, a significant difference in the effect was observed between durations of ≤ 24 months and > 24 months ($p = 0.018$). For patients with a follow-up interval of ≤ 24 months, elevated SHR was a significant predictor of NTL progression (OR = 2.84, $p = 0.001$), whereas no significant association was detected in those with a follow-up duration > 24 months. Furthermore, the relationship between SHR and NTL progression remained consistent regardless of a history of myocardial infarction or prior revascularization procedures (Table 4).

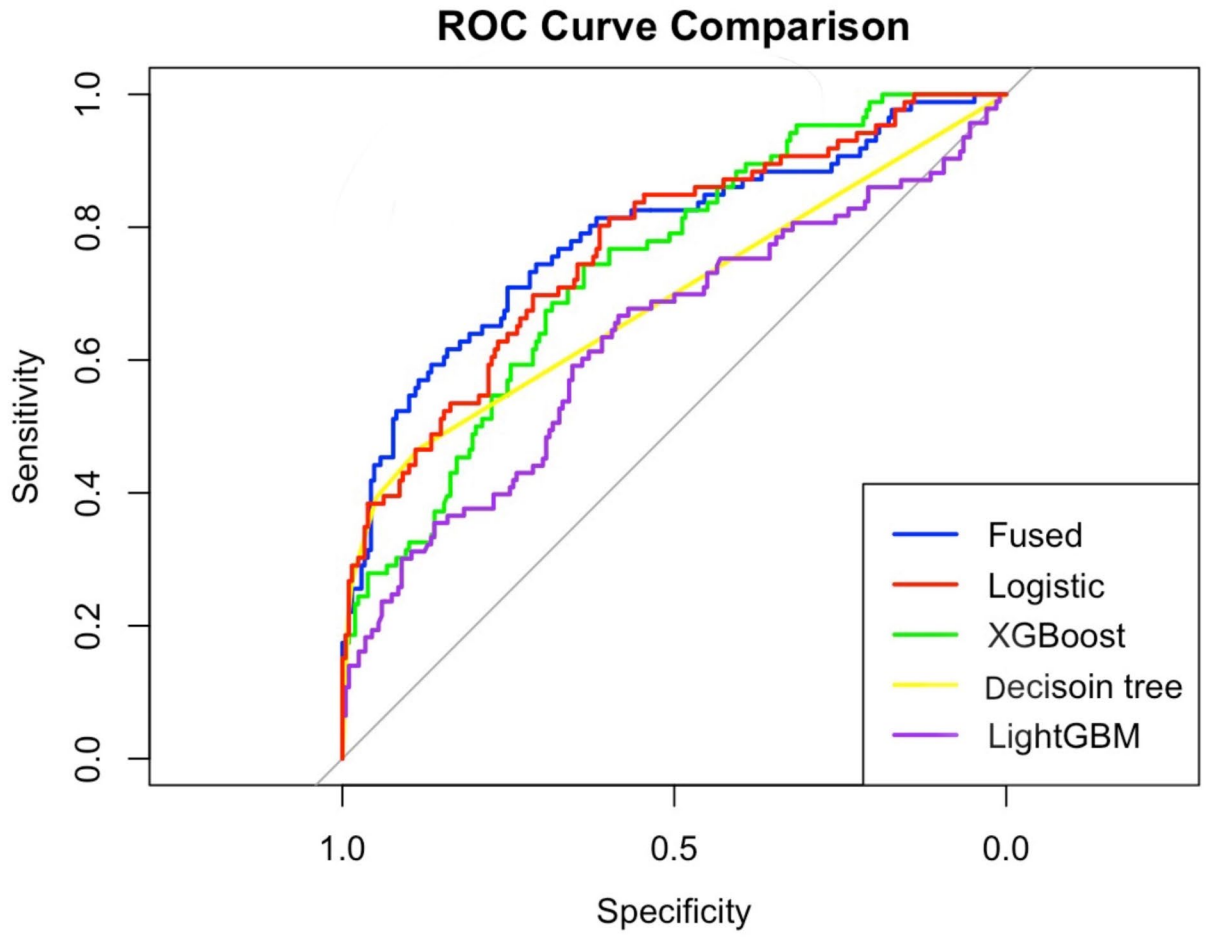

Fig. 3 Receiver operating characteristic curve comparison of different model

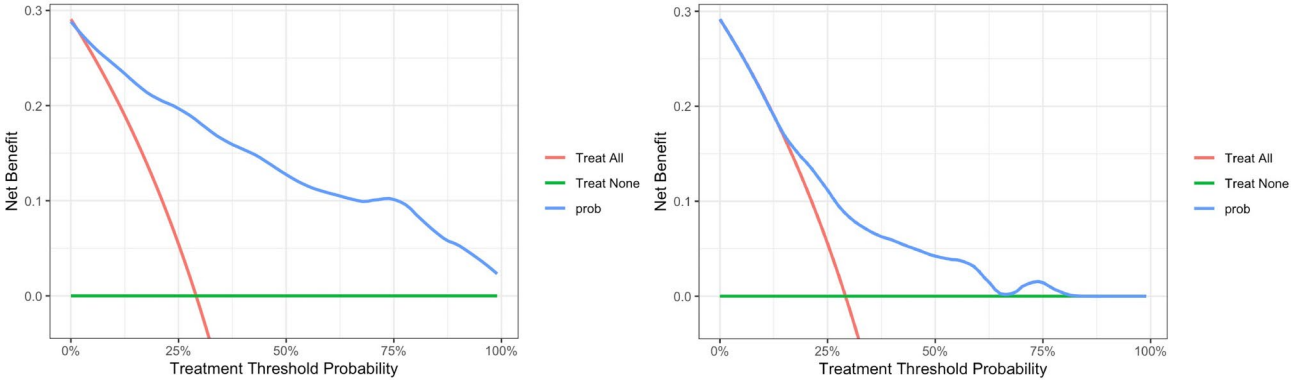

Fig. 4 Decision curve of training set and test set of XGBoost model

Discussion

This study demonstrates a strong relationship between SHR and the progression of nontarget lesions (OR = 2.12, 95% CI: 1.30–3.44, $p = 0.003$). The RCS curve demonstrates a rising risk of non target disease progression with SHR > 0.96. Additionally, a hybrid predictive model combining logistic regression and XGBoost machine learning algorithms was developed, incorporating hypertension (OR = 1.58, 95% CI: 1.10–2.28, $p = 0.01$), SHR (OR = 2.07, 95% CI: 1.26–3.42, $p = 0.004$), the number (OR = 1.50, 95% CI: 1.36–1.66, $p < 0.001$) and percentage stenosis (OR = 0.93, 95% CI: 0.92–0.94, $p < 0.001$) of NTLs, and HDL-c (OR = 0.52, 95% CI: 0.29–0.90, $p = 0.02$). The factors influencing coronary NTL progression remain

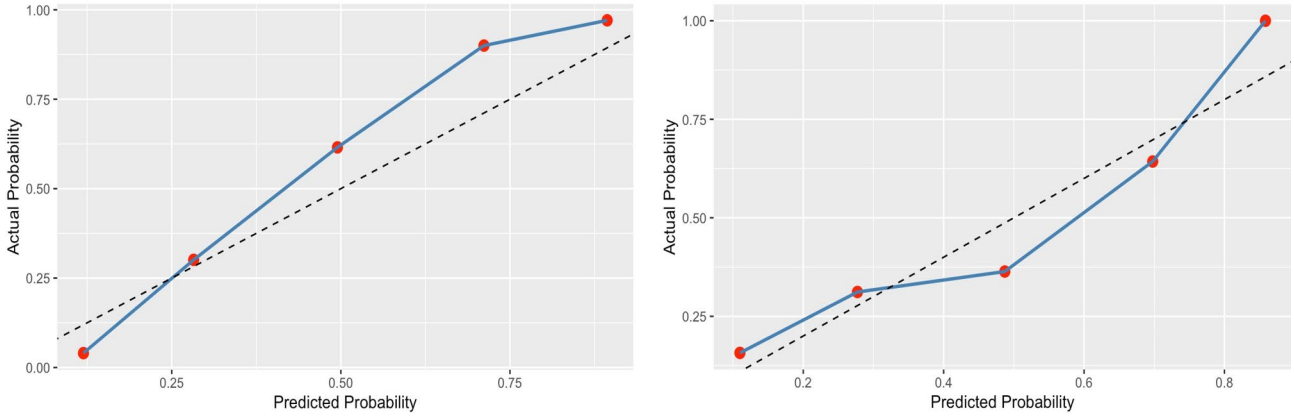

Fig. 5 Calibration curve of training set and test set of XGBoost model

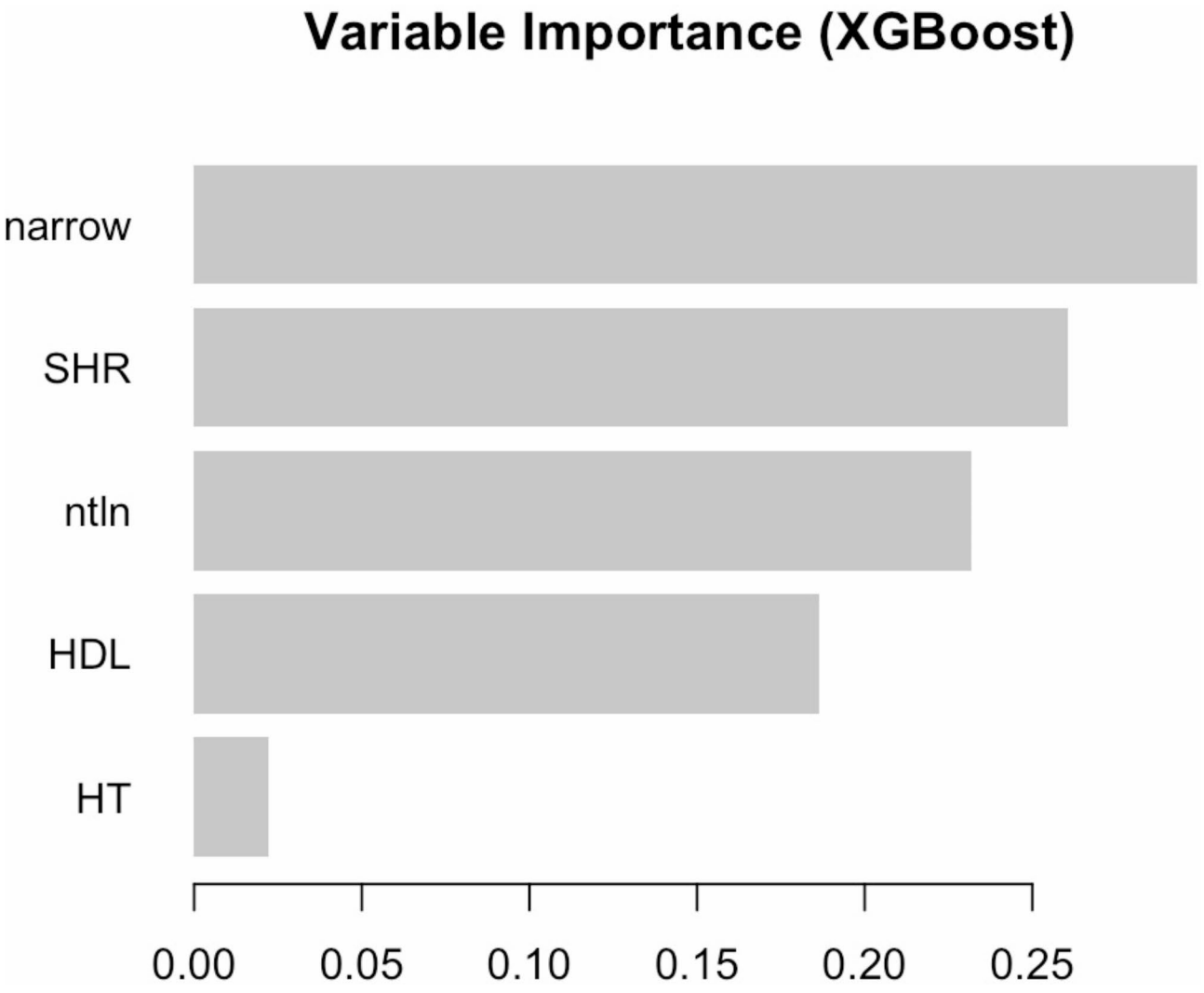

Fig. 6 Variable importance of XGBoost model

Table 4 Subgroup analysis of the relationship between nontarget lesion progression and SHR

	OR (CI)	*P*	*p* for interaction
Diabetes mellitus			0.107
No	3.76 (1.45–9.87)	0.007	
Yes	1.69 (0.94–3.08)	0.083	
Myocardial Infarction			0.313
No	2.07 (1.09–3.93)	0.026	
Yes	2.34 (1.04–5.39)	0.041	
Interval of CAG			0.018
≤ 24months	2.84 (1.60–5.08)	< 0.001	
>24months	1.13 (0.42-3.00)	0.812	
Revascularization			0.652
No	2.30 (1.40–3.80)	0.001	
Yes	3.00 (1.25–7.82)	0.019	

incompletely understood, it is likely that inflammation, oxidative stress, coronary vascular conditions, and plaque characteristics all play a role in NTL progression. Notably, this study is the first to include SHR as a novel biomarker in the predictive model, demonstrating that its incorporation improves predictive performance for NTL progression. Subgroup analyses revealed that elevated SHR was a stronger predictor of NTL progression in non-diabetic patients compared to diabetic patients (OR = 3.76 vs. 1.69, $p = 0.007$ vs. 0.083). This finding aligns with previous studies, such as Liu et al., who reported that elevated SHR was more strongly associated with long-term mortality in non-diabetic acute myocardial infarction (AMI) patients than in diabetic patients [13], Zhang et al. observed that among over 3,800 intensive care unit (ICU) patients, SHR was significantly associated with in-hospital and 1-year all-cause mortality in non-diabetic patients, but not in diabetic patients [17]. Furthermore, SHR was shown to exhibit a U-shaped relationship with adverse cardiovascular and cerebrovascular events in non-diabetic patients undergoing non-cardiac surgery [18]. These findings suggest that acute hyperglycemia or glucose variability may be a stronger indicator of severe stress in individuals with normal glucose metabolism. In our study revealed that while the detection rate of NTL progression was higher after two years post-stenting, the significant association between SHR and NTL progression was observed only within the first two years, with no correlation beyond this period. This suggests that NTL progression may occur early after stent implantation, with elevated SHR playing a role in its early development, whereas this correlation may weaken with longer follow-up. SHR not only reflects disease severity, our findings indicate that SHR was significantly associated with NTL progression regardless of whether recurrent revascularization was required. This highlights that SHR might indirectly reflect coronary disease progression and systemic inflammatory and oxidative stress state rather than simply representing disease severity.

The mechanisms underlying NTL progression is consistent closely with those of coronary atherosclerosis, including elevated inflammatory markers and oxidative stress. This is evident from the lipid-rich composition of coronary plaques, increased macrophage and smooth muscle cell content, reduced collagen content, and upregulated expression of inflammatory mediators such as TNF-α, IL-6, MCP-1, and VCAM-1 [19]. Stent implantation triggers innate nonspecific inflammatory responses due to tissue injury. Plaque rupture releases large amounts of inflammatory factors and chemokines, exposing the vascular intima to injury and inflammatory stimuli. This disrupts the endothelial barrier's permeability, enhancing endothelial uptake of circulating lipoproteins, particularly LDL-c, which in turn reactivates atherogenesis. This process leads to increased coronary lipid deposition, higher plaque burden, and reduced plaque stability in NTLs [20]. Simultaneously, inflammatory mediators are released into circulation, raising the expression of systemic inflammatory proteins [18]. This cascade promotes the release of hyperglycemic hormones, such as catecholamines and glucagon, further exacerbating systemic inflammation and oxidative stress [21]. Hyperglycemia has been shown to induce mitochondrial electron transport chain overproduction of superoxides, triggering various DNA damage pathways. This activates PARP-1 and promotes downstream expression of NF-kB, IL-6, IL-1β, TNF-α, iNOS, and TGF-β [22]. While restenosis represents a robust but self-limiting acute inflammatory response, NTL progression reflects a chronic, systemic lipid accumulation, oxidative stress, and smooth muscle proliferation driven by diffuse inflammation. Research indicates that plaques associated with NTL progression are characterized by thin-cap fibroatheromas, lipid-rich plaques, unstable plaques, and plaque ruptures, all of which correlate with an increased risk of future major adverse cardiovascular events [23, 24]. Additionally, studies have shown that heterogeneous neointima is more prevalent with NTL progression than in those without, and this heterogeneous neointima has been identified as a predictive factor for rapid NTL progression [15]. On the other hand, hemodynamic changes following stent implantation also contribute to NTL progression. It has been proposed that stent implantation alters coronary blood flow, generating low wall shear stress vortices around stent struts. These low-shear regions prolong blood flow residence time and endothelial contact, promoting plaque formation [25]. Animal studies in pigs have demonstrated that after acute myocardial infarction, significant endothelial dysfunction occurs in both target and nontarget vessels [21].

In clinical research, SHR has been shown to predict in-hospital heart failure, recurrent AMI, and mortality in patients with AMI. Moreover, SHR exhibits a U-shaped relationship with the complexity of coronary artery disease [17]. Beyond coronary artery disease, SHR is also associated with adverse outcomes in other cardiovascular conditions, including all-cause mortality, cardiovascular mortality, and major adverse cardiovascular events (MACE) in critically ill patients with atrial fibrillation and those undergoing transcatheter aortic valve replacement (TAVR) for severe aortic stenosis [26–28]. The progression of NTLs has traditionally been linked to risk factors such as myocardial infarction, hypertension, and diabetes. Recent studies have highlighted the association between NTL progression and inflammatory markers such as CRP and IL-6 [5, 7, 29–31], as well as lipid metabolism indicators like LDL-c [6–8]. Although the precise mechanisms linking SHR to NTL progression remain unclear, it is reasonable to hypothesize that fluctuations in blood glucose levels and dysregulated glucose metabolism may influence the development and progression of NTLs.

Incorporating SHR and clinical prediction models into routine risk assessments could enhance the early identification of high-risk patients and guide personalized interventions. Targeted strategies to modulate stress-induced hyperglycemia, such as glucose control or anti-inflammatory therapies, may help mitigate NTL progression and reduce the incidence of MACE. However, further studies are required to determine whether interventions targeting SHR can translate into improved long-term outcomes.

This study has several limitations that should be acknowledged. First, as a single-center study, the findings may not be generalizable to broader populations. Second, the observational design precludes establishing causality between SHR and NTL progression. Third, this study did not evaluate the impact of specific glucose-lowering or anti-inflammatory therapies on SHR or NTL progression. Finally, the relatively short follow-up period limits the ability to assess long-term trends, and extended studies are needed to confirm our findings.

Conclusion

Our study highlights the close relationship between SHR and NTL progression. Higher SHR levels were associated with an increased risk of NTL progression, independent of traditional cardiovascular risk factors and making it possible as a novel biomarker to delineate risk stratification. These findings underscore the role of systemic inflammation and glucose metabolism in NTL progression, suggesting that managing stress-induced hyperglycemia could be a promising strategy to mitigate adverse outcomes. Integrating SHR into routine clinical risk assessment could enhance personalized treatment strategies, ultimately improving patient outcomes.

Abbreviations

SHR	Stress hyperglycaemic ratio
DM	Diabetes mellitus
PCI	Percutaneous coronary interventio
RCS	Restricted cubic spline
ROC	Receiver operating characteristic
AUC	Area under the receiver operating characteristic curve
DCA	Decision curve analysis
DES	Drug-eluting stents
ISR	In-stent restenosis
NTL	Nontarget lesions
CRP	C-reactive protein
IL-8	Interleukin-8
IL-6	Interleukin-6
IL-1β	Interleukin-1β
ACS	Acute coronary syndrome
AMI	Acute myocardial infarction
CAG	Coronary angiography
CABG	Coronary artery bypass grafting
LVEF	Left ventricular ejection fraction
TC	Total cholesterol
TG	Triglycerides
LDL-c	Low-density lipoprotein cholesterol
HDL-c	High-density lipoprotein cholesterol
LPA	Apolipoprotein a
ISR	In-stent restenosis
LAD	Left anterior descending branch
LCX	Left circumflex artery
RCA	Right coronary artery
HbA1c	Glycated hemoglobin
ICU	Intensive care unit
TNF-α	Tumor necrosis factor-α
MCP-1	Monocytechemoattractantprotein-1
VCAM-1	Vascular cell adhesion molecule-1
PARP-1	Poly (ADP-ribose) polymerase 1
NF-	κB Nuclear factor kappa B
iNOS	Inducible Nitric Oxide Synthase
TGF-β	Transforming Growth Factor- β
MACE	Major adverse cardiovascular events

Supplementary Information

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Supplementary Material 1

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Author contributions

Shiqi Liu, Dong Wang and Chengchun Tang designed the study, analysed the data, and wrote the manuscript; Shiqi Liu and Ziyang Wu collected and interpreted the data; Gaoliang Yan, Yong Qiao and Yuhan Qin critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript. Dong Wang and Chengchun Tang contributed equally to this work.

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Data availability

Due to privacy and ethical constraints, the datasets generated and analysed in this study are not publicly available but can be obtained from the corresponding author.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Zhongda Hospital. Written informed consent was obtained from all patients.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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