Journal of Inflammation Research

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ORIGINAL RESEARCH

Association Between Systemic Immune-Inflammatory Indices and Severity of Coronary Artery Lesions in Patients With Coronary Artery Disease in Different Glucose Metabolic States

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Video abstract

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Background: The systemic immune-inflammatory index (SII) serves as a comprehensive indication of systemic inflammation. However, the relationship between SII and the severity of coronary artery lesions in participants with coronary artery disease (CAD) in different glucose metabolic states has not been fully elucidated.

Methods: A total of 2727 patients with CAD were enrolled between January 2018 and April 2022. SII was calculated as (platelet count × neutrophil count)/lymphocyte count. Participants were grouped by SII quartiles. Glucose metabolic status was classified as normal glucose regulation (NGR), pre-diabetes mellitus (Pre-DM) and diabetes mellitus (DM) according to World Health Organization guidelines. Logistic regression and restricted cubic spline models were applied to estimate the relationship between SII and severity of coronary artery lesions in different glucose metabolic states with further adjustments for confounders.

Results: Logistic regression analysis indicated a significant association between SII and coronary lesion severity ($P < 0.05$). Regardless of glucose metabolic status, Participants in the highest SII quartile (Q4) had a markedly higher risk of severe coronary lesions than those in the lowest quartile (Q1). After adjusting for confounders, a significant association between SII and coronary lesion severity was observed in the Pre-DM and DM individuals ($P < 0.05$), whereas not in the NGR individuals ($P > 0.05$). Subgroup analyses revealed that the association between SII and coronary lesion severity was consistent across age, gender, hypertension, antihypertensive drugs, hyperlipidemia, antilipidemic drugs, smokingand drinking ($P > 0.05$). Furthermore, restricted cubic spline modeling indicated a significant linear correlation between SII and coronary artery lesion severity.

Conclusion: The SII is a relatively stable indicator of inflammation and is positively correlated with coronary lesion severity. This study highlights the potential of SII as a novel inflammatory biomarker for assessing the coronary lesion severity among patients in different glucose metabolic states.

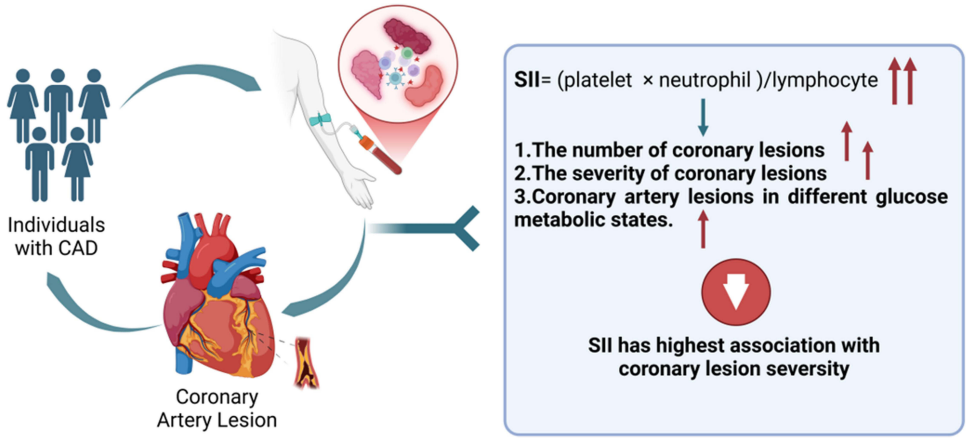
Keywords: systemic immune-inflammation index, SII, coronary heart disease, coronary artery disease severity, glucose metabolic status

Introduction

Coronary artery disease (CAD) is a chronic cardiac disorder resulting from varying degrees of coronary artery constriction. Globally, CAD is becoming a major public health concern due to rising incidence and fatality rates.[1,2]

Received: 29 November 2024
Accepted: 22 February 2025
Published: 6 March 2025

Graphical Abstract



Recent research indicates that individuals with diabetes mellitus (DM) have a substantially higher risk of developing CAD, compared to traditional CAD risk factors such as hypertension and hyperlipidemia,[3,4] Abnormal glucose metabolism, including diabetes and impaired glucose tolerance, is a major risk factor for coronary heart disease and is closely linked with the onset and progression of coronary artery lesions.[5,6] Clinically, timely identification and intervention for high-risk CAD individuals is essential to reduce CAD incidence and mortality, highlighting the importance of early detection and intervention in improving patient outcomes.

Inflammation contributes a significant role in the development and progression of atherosclerotic coronary artery disease (CAD)[7]. Various inflammatory indicators derived from whole blood counts, including neutrophils, lymphocytes, and C-reactive protein, effectively represent the body's inflammatory status and are instrumental in predicting the onset and prognosis of cardiovascular disease.[8,9] However, relying on a single marker or a limited set of inflammatory markers may be insufficient to evaluate the body's overall inflammatory state. When two or three interacting cellular ratios are combined, the overall predictive potential for determining the occurrence and prognosis of cardiovascular disease significantly increases.[10,11]

In recent years, a novel inflammatory marker known as the systemic immune-inflammatory index (SII), calculated as (neutrophils × platelets) / lymphocytes, has been demonstrated to play a significant role in predicting the occurrence, progression, and severity of coronary heart disease, as well as hyperlipidemia and stroke.[12–14] SII has also emerged as an independent risk factor for adverse cardiovascular events, including all-cause cardiovascular mortality, myocardial infarction incidence, heart failure onset, and rehospitalization due to heart failure.[15,16] Given the heightened inflammatory response linked with metabolic disorders, individuals with glucose metabolism dysregulation are at an increased risk of developing cardiovascular disease[17,18]. However, the association between SII and the severity of coronary artery lesions in CAD patients in different glucose metabolic states remains unclear. Therefore, this study aims to investigate the relationship between SII and coronary artery lesion severity in different glucose metabolic states.

Materials and Methods

Study Population

The inclusion criteria for study participants were as follows: (1) patients hospitalized in the Cardiology Department of Tianjin Union Medical Center between January 2018 and April 2022 due to typical symptoms of chest tightness and chest pain who subsequently underwent coronary angiography; (2) age ≥18 years; The exclusion criteria were as follows: (1) patients with incomplete data; (2) patients with severe liver or renal insufficiency, significant valvular disease, cardiomyopathy, rheumatic heart disease, or malignancy. A total of 27 27 individuals (1287 men and 1440 women) were included in the study. The study protocol was approved by the Human Research Committee of Tianjin Union Medical

Center (IRB number: 2021-C03). This study was conducted in accordance with the principles of the Declaration of Helsinki. As this was a retrospective study with no additional interventions, all patient data were anonymized to ensure confidentiality. Therefore, informed consent is not required.

Data Collection

Participant data were obtained from the digital medical record system, encompassing key demographic characteristics, clinical background, blood analysis results, and relevant medical imaging records. Demographic characteristics included age, gender, weight, height, blood pressure, smoking and drinking states. Clinical history covered diagnoses of hypertension and diabetes as well as Treatment status. Medication data included information on antihypertensive, antidiabetic, and antilipidemic therapies.

Blood samples were collected in the morning from fasting venous blood by skilled healthcare professionals. HDL-C, LDL-C, Blood glucose, HbA1c, TC, TG, WBC, RBC, PDW, MPV, NEUT, LYMP, MONO, PLT, TG, ALT and AST were analyzed using an automated blood analyzer. Catheter-based invasive coronary angiography (CAG) was performed via the percutaneous radial or femoral artery. The angiography equipment used was sufficiently versatile to allow accurate assessment of all manifestations of coronary artery conditions.

Coronary Angiography

All patients received 300 mg of aspirin and 300 mg of clopidogrel prior to undergoing coronary angiography or percutaneous coronary intervention, which were performed by specialized cardiologists. In this study, the transradial approach was used for coronary angiography in all patients. The standard clinical procedure involves using the Judkins technique to visualize both the left and right coronary arteries, with multiple projection views to provide a comprehensive and accurate assessment of the most severe coronary artery lesions.[19]

To ensure the objectivity and accuracy of angiography results, the location and severity of coronary lesions were jointly assessed and documented by 2–3 experienced clinicians. Coronary artery disease (CAD) was diagnosed according to the clinical guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA): CAD was defined as ≥30% stenosis of the left main coronary artery or ≥50% stenosis in any other major coronary artery branch[2.] The Gensini score was used to quantify the severity of coronary artery stenosis.[20,21]

Definition

The severity of CAD is determined by the number of diseased vessels and the Gensini score (GS), which takes into account the degree of luminal stenosis and the importance of its location in the following way: obstruction of less than 25% is scored as 1 point, 26–50% obstruction is scored as 2 points, 51–75% obstruction is scored as 4 points, 76–90% obstruction is scored as 8 points and 91–99% obstruction is scored as 16 points. Complete obstruction (100%) is given a score of 32. The score is then multiplied by a coefficient that depends on the functional importance of the area provided by the segment.5 for the left main coronary artery, 2.5 for the proximal segment of the left anterior descending or circumflex artery, and 1.5 for the middle segment of the left anterior descending branch.[11,22]

The systemic immunoinflammatory index (SII) was calculated by the formula = platelet count × neutrophil count/ lymphocyte count (10^{9} /L).[23,24.]

The WHO guidelines for diabetes mellitus define diabetes mellitus (DM) as FPG > 7.0 mmol/L, 2-hour plasma glucose level ≥ 11.1 mmol/L based on an oral glucose tolerance test, HbA1c ≥ 6.5%, or a history of T2DM. Normoglycemic regulation (NGR) is characterized by an FPG < 6.1 mmol/L and a 2-hour plasma glucose level < 7.8 mmol/L. Pre-diabetes mellitus (Pre-DM) should be examined in those who have high plasma glucose levels but fail to match the diagnostic categories as T2DM.[25,26]

Statistical Analysis

Statistical analyses were conducted with continuous variables expressed as mean ± standard deviation (SD) and compared using the *t*-test or Mann–Whitney *U*-test as appropriate. For comparisons involving more than two groups, one-way analysis of variance (ANOVA) or the Kruskal–Wallis test was applied. For continuous variables not following

a normal distribution, the data were presented as median (interquartile range, IQR), while categorical variables were expressed as percentages (%), with comparisons made using the chi-square test. Bonferroni corrections were applied to account for multiple comparisons. Correlation analyses utilized Pearson or Spearman correlation coefficients as appropriate. The systemic immune-inflammation index (SII) was divided into quartiles for group-based analysis. A multivariable logistic regression model was employed to examine the association between SII levels and the number and severity of coronary artery lesions in patients with coronary artery disease (CAD) after adjusting for covariates. Subgroup analyses were performed to evaluate the relationship between SII levels (as a continuous variable) and the severity of coronary lesions across various subgroups of CAD patients, and to calculate the P for the interaction. Multivariable logistic analysis was used to estimate odds ratios (ORs) in subgroup analyses.

Additionally, LASSO regression analyses were performed using the 'glmnet' package in R to identify factors associated with the severity of coronary artery disease. The discriminatory ability of the model to identify disease risk was assessed using the receiver operator characteristic curve (ROC). A restricted cubic spline (RCS) curve based on the multivariable logistic regression model was used to visualize the association between SII levels and CAD severity, with three knots chosen for the analysis. $P<0.05$ was considered statistically significant, All data analyses were performed using SPSS software version 26.0, GraphPad Prism 8, and R Studio version 4.2.3.

Results

Basic General Clinical Characteristics

The characteristics of the study participants are summarized in Table 1.A total of 2727 participants were included and divided into four groups based on quartiles of SII values: Q1 (SII ≤ 351.52), Q2 (351.52 < SII ≤ 485.77), Q3 (485.77 < SII ≤ 682.86), and Q4 (SII > 682.86). Significant differences were observed among the quartiles in terms of gender, SBP, hypertension, antihypertensive drugs, WBC, RBC, PDW, MPV, NEUT, LYMP, MONO, PLT, TG, and AST *(P* < 0.05);

Table 1 General Characteristics of Research Participants

	Quartile 1 (n=682)	Quartile 2 (n=682)	Quartile 3 (n=682)	Quartile 4 (n=681)	*P* value
Gender					0.001
Male (n,%)	285 (41.8%)	314 (46.0%)	328 (48.1%)	360 (52.9%)	
Female (n,%)	397 (58.2%)	368 (54.0%)	354 (51.9%)	321 (47.1%)	
Age (year)	63.20±8.46	62.96±7.80	62.98±8.53	63.28±8.14	0.849
BMI (Kg /M^2)	25.56 (23.44, 27.76)	25.39 (23.50, 27.84)	25.40 (23.44, 27.89)	25.39 (23.44, 27.68)	0.990
SBP (mmHg)	133.69±16.14	135.17±16.15	135.3±16.92	136.82±17.77[a]	0.008
DBP (mmHg)	78.32±10.68	78.01±10.78	78.18±11.31	79.38±11.80	0.462
History of smoking (n,%)	259 (38.0%)	273 (40.1%)	285 (41.9%)	286 (42.1%)	0.384
History of drinking (n,%)	182 (26.7%)	204 (30.0%)	198 (29.1%)	209 (30.7%)	0.394
Hypertension (n,%)	402 (58.9%)	441 (64.7%)	448 (65.7%)	486 (71.4%)	<0.001
Diabetes (n,%)	173 (25.4%)	194 (28.5%)	196 (28.7%)	196 (28.8%)	0.425
Hyperlipidaemia (n,%)	56 (8.2%)	62 (9.1%)	79 (11.6%)	56 (8.2%)	0.104
Stroke (n,%)	82 (12.0%)	87 (12.8%)	80 (11.7%)	85 (12.5%)	0.939
Drugs					
Antihypertensive drugs (n,%)	331 (48.7%)	384 (56.3%)	396 (58.1%)	426 (62.6%)	<0.001
Antidiabetes drugs (n,%)	142 (20.8%)	169 (24.8%)	171 (25.1%)	174 (25.6%)	0.149
Antilipidemic drugs (n,%)	60 (8.8%)	79 (11.6%)	82 (12.0%)	63 (9.3%)	0.121
Laboratory parameters					
WBC count (10^9/L)	5.57 (4.63, 6.66)	6.02 (5.13, 6.96)[a]	6.63 (5.67, 7.6)[ab]	7.43 (6.28, 8.8)[abc]	<0.001
RBC count (10^12/L)	4.30 (3.94, 4.63)	4.31 (4.02, 4.66)[a]	4.42 (4.124.73)[ab]	4.51 (4.17, 4.82)[abc]	<0.001
PDW (fL)	12.19±2.17[bc]	11.52±1.90[a]	11.379±1.78[a]	11.18±4.03[a]	<0.001
MPV (fL)	10.45±1.12[bc.]	10.15±0.89[a]	10.07±0.96[a.]	9.90±0.99[abc]	<0.001
NEUT (10^9/L)	3.10 (2.50, 3.87)	3.73 (3.18, 4.54)[a]	4.53 (3.80, 5.39)[ab]	5.67 (4.63, 7.20)[abc]	<0.001

(*Continued*)

Table 1 (Continued).

	Quartile 1 (n=682)	Quartile 2 (n=682)	Quartile 3 (n=682)	Quartile 4 (n=681)	*P* value
LYMP (10^9/L)	2.15 (1.72, 2.83)	1.87 (1.54, 2.42)[ab]	1.80 (1.41, 2.27)[a]	1.50 (1.12, 1.90)[abc]	<0.001
MONO (10^9/L)	0.40 (0.32, 0.54)	0.42 (0.32, 0.54)	0.45 (0.34, 0.6)[ab]	0.47 (0.34, 0.68)[ab]	<0.001
PLT (10^9/L)	185 (160, 214)	207 (180, 239)[a]	225 (196, 259)[ab]	243 (206, 281)[abc]	<0.001
Glucose (mol/L)	6.37±3.36	6.35±2.11	6.41±1.98	6.62±2.31[a]	0.161
HbA1c (%)	6.39±1.17	6.35±1.10	6.45±1.19	6.56±1.35	0.086
TC (mmol/L)	4.62±2.08	4.55±1.04	4.68±1.64	4.58±1.11	0.444
TG (mmol/L)	1.46 (1.04, 2.09)	1.37 (1.02, 1.87)	1.50 (1.08, 2.04) [b]	1.42 (1.04, 2.05)	0.033
HDL-C (mmol/L)	1.20±0.34	1.17±0.28	1.16±0.28	1.15±0.27	0.145
LDL-C (mmol/L)	2.86±0.93	2.87±0.87	2.95±0.90	2.90±0.89	0.253
TP (g/L)	64.89±8.09	64.89±7.57	65.87±8.69	65.50±7.03	0.586
ALB (g/L)	39.59±3.83	39.59±4.35	39.34±4.42	39.62±3.64	0.528
ALT (U/L)	18 (13, 28)	17 (13, 25)	18 (13, 26)	19 (13, 27)	0.210
AST (U/L)	19 (16, 25)	18 (15, 22) [a]	18 (15, 23)	18 (15, 24)[a]	0.014
The number of coronary lesions					0.001
Single-vessel (n,%)	199 (29.2%)	195 (28.6%)	173 (25.4%)	165 (24.2%)	
Double -vessels (n,%)	160 (23.5%)	146 (21.4%)	168 (24.6%)	162 (23.8%)	
Triple-Vessels (n,%)	143 (21.0%)	167 (24.5%)	178 (26.1%)	216 (31.7%)	
Severity of coronary stenosis					<0.001
Mild	523 (76.7%)	503 (73.8%)	462 (63.7%)	434 (63.7%)	
Moderate	85 (12.5%)	84 (12.3%)	101 (14.8%)	106 (15.6%)	
Severe	74 (10.9%)	95 (13.9%)	119 (17.4%)	141 (20.7%)	

Notes: Data are presented as mean ±SD, n (%), or median (quartile). Normally distributed variables were used for ANOVA test, abnormally distributed variables were used for nonparametric tests (Kruskal–Wallis test); χ^2 or Fisher test for categorical variables. Bonferroni corrections were applied to account for multiple comparisons; $P < 0.05$ was considered statistically significant; [a]$P < 0.05$ vs Q1. [b]$P < 0.05$ vs Q2. [c]$P < 0.05$ vs Q3.

Abbreviations: Quartile 1, the first SII quartile; Quartile 4, the fourth SII quartile; SBP, systolic blood pressure, DBP, diastolic blood pressure, BMI, Weight (kg) /Height (m)^2; WBC, white blood cell; RBC, red blood cell; MPV, average platelet volume, PDW, Platelet volume distribution width, NEUT, neutrophils; LYMP, lymphocytes; MONO, monocytes; PLT, platelet count; HbA1c, glycosylated hemoglobin; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TP, total protein; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SII, systemic immune-inflammatory index.

Moreover, the number and severity of coronary artery lesions differed significantly across the SII groups ($P < 0.05$). Participants in Q4 had a higher likelihood of presenting with more numerous and severe coronary artery lesions compared with those in Q1. Additionally, Q4 participants were more likely to be male and to have higher levels of SBP, WBC, RBC, NEUT, MONO, PLT, hypertension and lower levels of PDW, MPV, LYMP, TG, AST.

Correlation of SII With Risk Factors for Coronary Artery Disease

Pearson and Spearman correlation analyses demonstrated that SII was negatively correlated with Gender (rho = −0.054), PDW (rho = −0.085), and MPV (rho = −0.140) (all $P < 0.05$). However, SII demonstrated positive correlations with Hypertension (rho = 0.097), WBC (rho =0.423), RBC (rho = 0.169), HbA1c (rho =0.054), The number of coronary lesions (rho =0.101), and Gensini scores (rho =0.110), (all $P < 0.05$) as in Table 2 and Figure 1.

Factors Associated With Coronary Lesion Severity and Their Risk Prediction Models Based on LASSO Regression Screening

LASSO regression was employed to identify factors associated with the severity of coronary artery lesions, including laboratory markers and demographic variables (gender, age, and BMI). To determine the optimal penalty parameter λ, we applied 10-fold cross-validation with 100 iterations to ensure model accuracy. A critical and suitable number of variables were selected at λ = 0.000217, as shown in Figure 2A; By examining the regression coefficients at this optimal λ, we explicitly identified the variables associated with coronary lesion severity, which include: gender, age, BMI hypertension, diabetes, hyperlipidaemia, smoking, drinking, SBP, DBP, WBC, NEUT. LYMP, MONO, RBC, PDW, TP, ALB, ALT, AST, TC, TG, HDL-C, LDL-C, Glucose, HbA1c and SII as shown in Figure 2B; Subsequently,

Table 2 The Correlation Between SII and CAD Risk Factors

Var	SII		
	rho	*P*	
Gender	−0.054*	0.005	Pearson
Age	0.017	0.371	Pearson
BMI	0.004	0.816	Spearman
SBP	0.048*	0.012	Pearson
DBP	0.018	0.353	Pearson
History of smoking	0.035	0.067	Spearman
History of drinking	0.029	0.134	Spearman
Hypertension	0.097**	<0.001	Spearman
Diabetes	0.025	0.193	Spearman
Hyperlipidaemia	0.015	0.433	Spearman
WBC	0.423**	<0.001	Spearman
RBC	0.169**	<0.001	Spearman
PDW	−0.085**	<0.001	Pearson
MPV	−0.140**	<0.001	Pearson
Glucose	0.037	0.054	Pearson
HbA1c	0.054**	0.010	Pearson
TC	−0.016	0.417	Pearson
TG	0.006	0.754	Spearman
HDL-C	−0.023*	0.234	Pearson
LDL-C	−0.006	0.747	Pearson
TP	0.011	0.578	Pearson
ALB	−0.003	0.863	Pearson
ALT	0.003	0.874	Spearman
AST	−0.034	0.072	Spearman
The number of coronary lesions	0.101**	<0.001	Spearman
Gensini scores	0.110**	<0.001	Spearman

Notes: $P < 0.05$ was considered statistically significant,

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, Weight (kg) /Height (m) ^{2}; WBC, white blood cell; RBC, red blood cell; MPV, average platelet volume; PDW, platelet volume distribution width; NEUT, neutrophils; LYMP, lymphocytes; MONO, monocytes; PLT, platelet count; HbA1c, glycosylated hemoglobin; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TP, total protein; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SII, systemic immune-inflammatory index.

we performed logistic regression analysis to further refine the model by selecting variables with statistically significant associations which include: gender, hypertension, PDW, ALT, AST, HDL-C, LDL-C, HbA1c and SII; ROC curve analysis was performed on these variables, and the area under the curve (AUC) of the model's working characteristics of the subjects was calculated, with a value of 80.45%, indicating that the model had good predictive accuracy, as shown in Figure 2C.

Multiple Logistic Regression Analysis of SII Levels and the Number of Coronary Lesions in Patients With Coronary Artery Disease

The results of the multiple logistic regression analysis indicated that SII levels in the highest quartile (Q4) were significantly associated with a higher risk of the number of coronary lesions in patients with coronary artery disease ($P < 0.05$), as presented in Table 3. Even after adjusting for these variables, including age, gender, diabetes, antilipidemic drugs, smoking, drinking, RBC, PDW, ALT, AST, TG, HDL-C, and HbA1c levels. SII levels remained significantly associated with coronary lesion risk, Q4 was 1.175 times higher in the number of coronary lesions compared to those in Q1 (95% CI: 1.044–1.324, $P < 0.05$), as shown in Table 3.

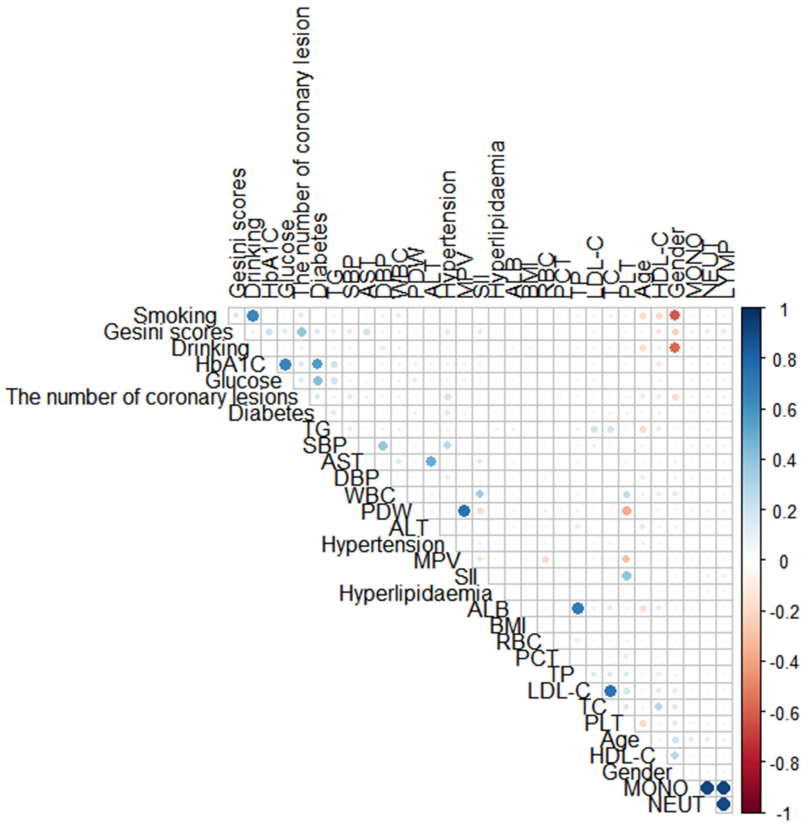


Figure 1 The correlation between SII and CAD risk factors. $P < 0.05$ was considered statistically significant.

Abbreviations: CAD, coronary artery disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index (Weight (kg)/Height (m)^2); WBC, white blood cell; RBC, red blood cell; MPV, mean platelet volume; PDW, platelet distribution width; HbA1c, glycosylated hemoglobin; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TP, total protein; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SII, systemic immune-inflammatory index.

Multiple Logistic Regression Analysis of SII Levels and Coronary Stenosis Severity in Patients With Coronary Artery Disease

Gensini scores were adopted to evaluate the severity of coronary artery stenosis: Mild (Gensini scores ≤ 24), Moderate (24 < Gensini scores ≤ 45), and Severity (Gensini scores > 45). The study results indicated SII was significantly associated with the severity of coronary artery stenosis ($P < 0.05$), as shown in Table 4. In addition, after adjusting for confounders such as hypertension, antihypertensive drugs, diabetes, antidiabetes drugs, hyperlipidemia, antilipidemic drugs, smoking, drinking, BMI, SBP, TC, TG, HDL-C, LDL-C, Glucose and HbA1c in the multivariate regression analysis, SII levels remained significantly associated with the level of CAD severity, the highest SII quartile (Q4) exhibited a 1.430 times higher in coronary stenosis severity compared to those in Q1 (95% CI 1.209–1.691, $P < 0.05$), as shown in Table 4.

Association Between SII Levels and the Number and Severity of Coronary Lesions in Patients With Coronary Artery Disease

To further investigate the relationship between SII and the number and severity of coronary artery lesions in patients with coronary artery disease. Participants were grouped according to SII quartiles to assess the number and severity of coronary artery lesions. The study results indicated that the number of coronary artery lesions vessels and severity were significantly higher in Q4 compared with Q1 and Q2 ($P < 0.05$) as shown in Figures 3A and B. Additionally, participants were grouped according to the number of coronary vascular lesions and stenosis severity grouping to assess SII levels. SII levels were significantly higher in those with three coronary vessel lesions than in those with single- and two-vessel lesions; and SII levels were significantly higher in those with severe coronary stenosis than in those with mild coronary stenosis ($P < 0.05$) as shown in Figures 3C and D.

https://doi.org/10.2147/JIR.S507696

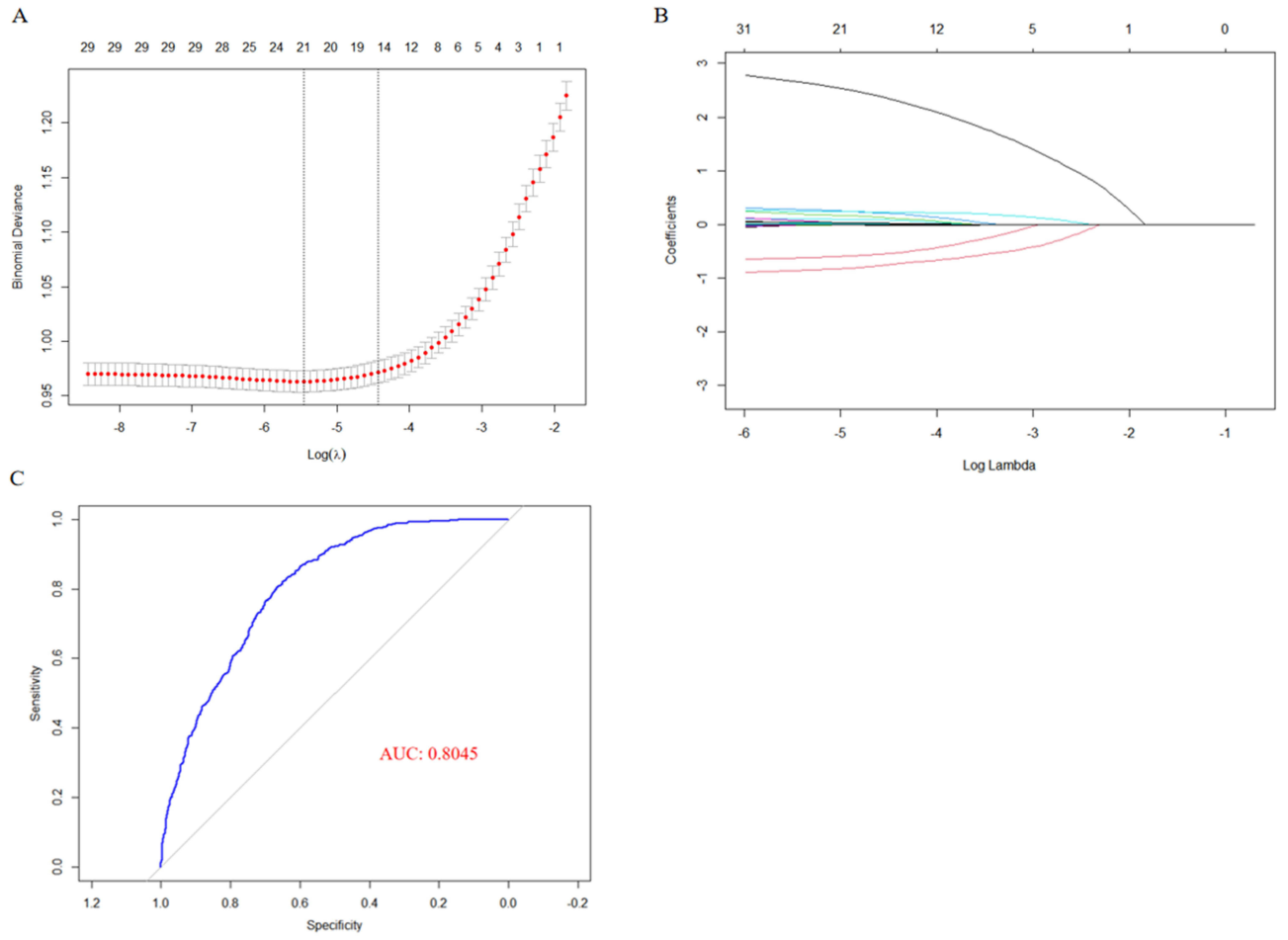


Figure 2 Coronary artery lesion severity correlates and their risk prediction models based on LASSO regression screening, (**A**) Cross-validation plots; (**B**) LASSO regression coefficient plots; (**C**) ROC curves of the predictive power of variables in the estimation model for the severity of coronary artery lesions.
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, Weight (kg) /Height (m) ^{2}; WBC, white blood cell; RBC, red blood cell; PDW, Platelet volume distribution width; NEUT, neutrophils; LYMP, lymphocytes; MONO, monocytes; HbA1c, glycosylated hemoglobin; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TP, total protein; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SII, systemic immune-inflammatory index; LASSO, least absolute shrinkage; and selection operator; ROC, receiver operator characteristic curve.

Relationship Between SII Levels and Severity of Coronary Artery Lesions in Patients With Coronary Artery Disease in Different Glucose Metabolic States

As shown in Table 5, without adjustment for confounders, the risk of developing coronary artery lesions was higher in Q4 than in Q1 regardless of glucose metabolism status (P<0.05). After adjusting for confounders, A significant

Table 3 Multiple Logistic Regression Analysis of SII Levels and the Number of Coronary Lesions

Variable	Number of Coronary Lesions					
	Model 1 OR (95% CI)	*p*	Model 2 OR (95% CI)	*p*	Model 3 OR (95% CI)	*p*
SII						
Quartile 1	Reference		Reference		Reference	
Quartile 2	1.049(0.953–1.154)	0.330	1.035(0.937–1.143)	0.499	1.044(0.931–1.172)	0.461
Quartile 3	1.119(1.017–1.231)	0.021	1.098(0.994–1.213)	0.065	1.043(0.929–1.171)	0.472
Quartile 4	1.253(1.138–1.379)	<0.001	1.205(1.091–1.332)	<0.001	1.175(1.044–1.324)	0.008

Notes: Data are odd ratios (95% CI) of multiple logistic regression; Model 1: unadjusted; Model 2: adjusted for age, gender, Model 3: adjusted for diabetes, antilipidemic drugs, smoking, drinking, RBC, PDW, ALT, AST, TG, HDL-C, and HbA1c on the basis of model 2; P < 0.05 was considered statistically significant.
Abbreviations: OR, odds ratios; CI, confidence intervals; Quartile 1, the first SII quartile; Quartile 4, the fourth SII quartile; SII, systemic immune-inflammatory index.

Table 4 Multiple Logistic Regression Analysis of SII Levels and the Severity of Coronary Lesions

Variable	Severity of Coronary Stenosis					
	Model 1OR (95% CI)	***p***	**Model 2 OR (95% CI)**	***p***	**Model 3 OR (95% CI)**	***p***
SII						
Quartile 1	Reference		Reference		Reference	
Quartile 2	1.134(0.972–1.323)	0.109	1.112(0.950–1.301)	0.187	1.148(0.963–1.369)	0.124
Quartile 3	1.346(1.160–1.562)	<0.001	1.314(1.129–1.530)	<0.001	1.259(1.059–1.495)	0.009
Quartile 4	1.510(1.305–1.747)	<0.001	1.436(1.237–1.668)	<0.001	1.430(1.209–1.691)	<0.001

Notes: Data are odd ratios (95% CI) of multiple logistic regression; Model 1: unadjusted; Model 2: adjusted for age, gender; Model 3: adjusted for hypertension, antihypertensive drugs, diabetes, antidiabetes drugs, hyperlipidemia, antilipidemic drugs, smoking, drinking, BMI, SBP, TC, TG, HDL-C, LDL-C, Glucose and HbA1c on the basis of model 2; $P < 0.05$ was considered statistically significant.
Abbreviations: OR, odds ratios; CI, confidence intervals; Quartile 1, the first SII quartile; Quartile 4, the fourth SII quartile; SII, systemic immune-inflammatory index.

relationship was observed between SII and the severity of coronary artery lesions in the Pre-DM and DM states (Pre-DM: OR 1.610, 95% CI: 1.055–2.457; DM: OR 1.749, 95% CI: 1.275–2.398; $P < 0.05$), however, there was no statistical significance in the NGR state ($P > 0.05$).

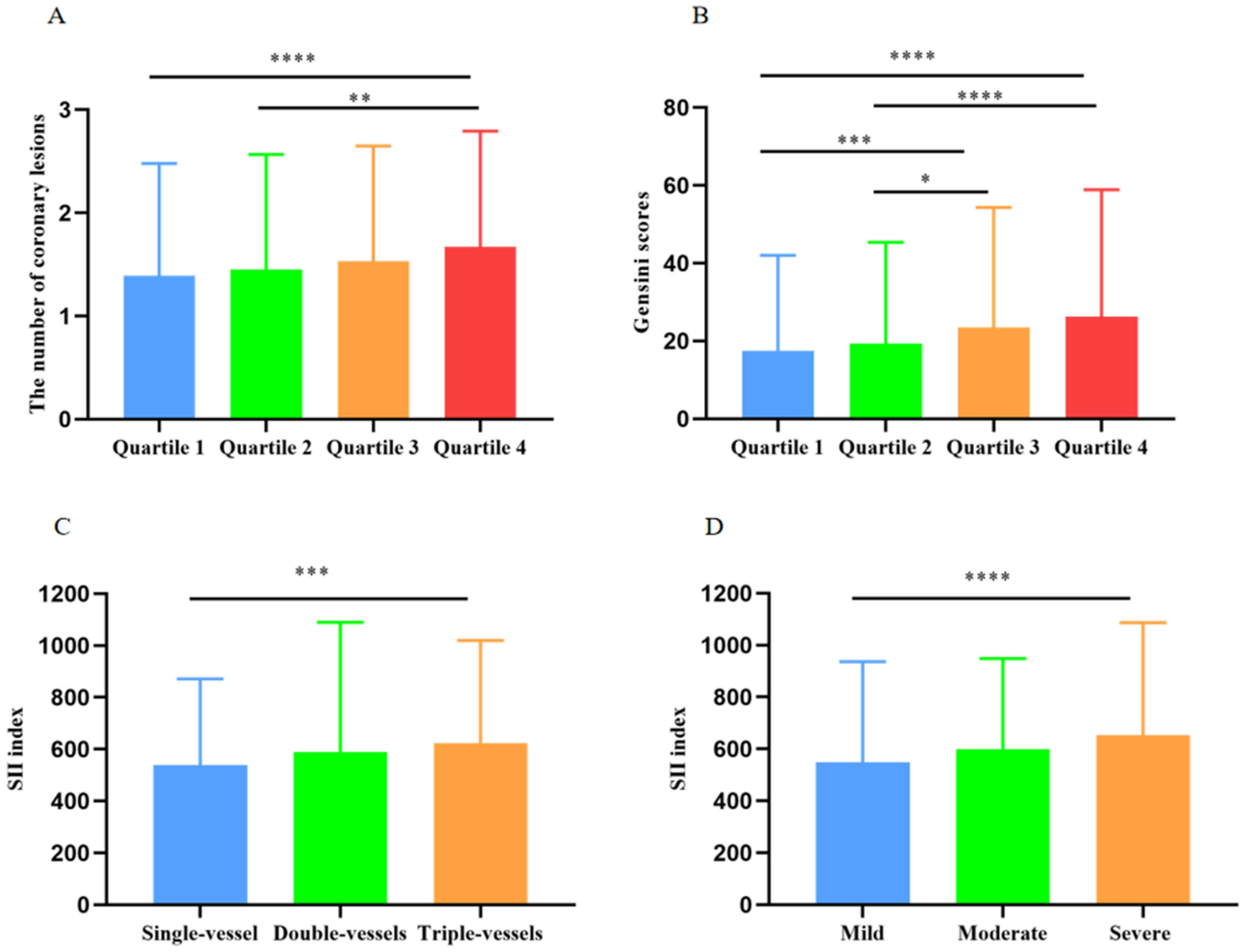


Figure 3 Association Between SII Levels and the Number and Severity of Coronary artery diseased in Patients With Coronary Artery Disease; (**A**) Number of diseased coronary artery vessels across SII quartiles. (**B**) Severity of coronary artery stenosis across SII quartiles. (**C**) SII levels by the number of coronary vessel lesions. (**D**) SII levels by the severity of coronary artery stenosis.
Note: Statistical differences were assessed using ANOVA; Bonferroni corrections were applied to account for multiple comparisons; The whiskers in the bar chart represent the mean ± SD of the data. $P < 0.05$ was considered statistically significant, *: $P<0.05$; **: $P<0.005$; ***: $P<0.0005$,****: $P<0.0001$.
Abbreviations: Quartile 1, the first SII quartile; Quartile 4, the fourth SII quartile; SII, systemic immune-inflammatory index.

https://doi.org/10.2147/JIR.S507696

Table 5 Relationship Between SII Levels and Severity of Coronary Artery Lesions in Patients With Coronary Artery Disease in Different Glucose Metabolic States

Glucose Metabolic State	Severity of Coronary Lesions					
	Model 1 OR (95% CI)	*p*	Model 2 OR (95% CI)	*p*	Model 3 OR (95% CI)	*p*
NGR						
SII						
Quartile 1	Reference		Reference		Reference	
Quartile 2	1.122(0.915–1.376)	0.267	1.077(0.873–1.329)	0.487	1.085(0.868–1.357)	0.475
Quartile 3	1.234(1.010–1.509)	0.040	1.160(0.943–1.426)	0.160	1.148(0.920–1.432)	0.223
Quartile 4	1.276(1.042–1.563)	0.018	1.164(0.944–1.435)	0.155	1.109(0.881–1.397)	0.380
Pre-DM						
Quartile 1	Reference		Reference		Reference	
Quartile 2	1.124(0.759–1.664)	0.560	1.165(0.778–1.744)	0.458	1.361(0.869–2.130)	0.178
Quartile 3	1.083(0.729–1.609)	0.692	1.177(0.783–1.770)	0.434	1.356(0.864–2.130)	0.186
Quartile 4	1.586(1.105–2.275)	0.012	1.555(1.070–2.260)	0.020	1.610(1.055–2.457)	0.027
DM						
Quartile 1	Reference		Reference		Reference	
Quartile 2	1.136(0.840–1.536)	0.409	1.122(0.825–1.525)	0.463	1.153(0.828–1.607)	0.399
Quartile 3	1.680(1.265–2.233)	<0.001	1.668(1.249–2.227)	0.001	1.582(1.152–2.173)	0.005
Quartile 4	1.785(1.350–2.361)	<0.001	1.795(1.351–2.385)	<0.001	1.749(1.275–2.398)	0.001

Notes: Data are odd ratios (95% CI) of multiple logistic regression. Model 1: unadjusted; Model 2: adjusted for age, gender; Model 3: adjusted for hypertension, antihypertensive drugs, diabetes, antidiabetes drugs, hyperlipidaemia, antilipidemic drugs, smoking, drinking, MPV BMI, ALB, ALT, AST, TC, TG, HDL-C, LDL-C on the basis of model 2; $P < 0.05$ was considered statistically significant.

Abbreviations: NGR, normoglycemic regulation; Pre-DM, pre-diabetes mellitus; DM, diabetes mellitus OR, odds ratios; CI, confidence intervals; Quartile 1, the first SII quartile; Quartile 4, the fourth SII quartile; SII, systemic immune-inflammatory index.

Further subgroup analyses were conducted to evaluate whether the relationship between SII and coronary artery lesion severity was influenced by other covariates, as shown in Figure 4. The results indicated that there was no significant interaction between SII and age, gender, hypertension, antihypertensive drugs, hyperlipidaemia, antilipidemic drugs, smoking, drinking (all P for interaction > 0.05). Subgroup analyses determined the robustness of the association between SII and coronary artery lesion severity. The correlation between SII and severity of coronary artery lesions was further determined.

Linear Correlation Between SII and Severity of Coronary Artery Lesions

The relationship between SII and the severity of coronary artery lesions was assessed using the RCS model analysis (Figure 5), and there was a significant linear correlation between SII and the severity of coronary artery lesions. The results showed a positive correlation between SII and the severity of coronary lesions after adjustment for potential confounders in the model. In particular, a one-unit increase in SII was associated with a 41.6% in the severity of coronary lesions.

Discussion

In this retrospective cohort study of patients hospitalised with coronary artery disease in northern China, the present study first appraised the relationship between SII and coronary artery lesion severity, and the results indicated that there was a significant correlation between SII and the severity of coronary artery disease in patients with coronary artery disease and that there was a positive correlation. In addition, the severity of coronary lesions was significantly increased in patients in the highest quartile of SII (Q4) compared with the lowest quartile of SII (Q1). Next, the relationship between SII and coronary artery lesion severity was further evaluated in different glucose metabolic states in this study, Unadjusted for confounders, the relationship between SII and coronary artery lesion severity was statistically significant regardless of glucose metabolism states. After adjusting for confounders, a significant correlation between SII and

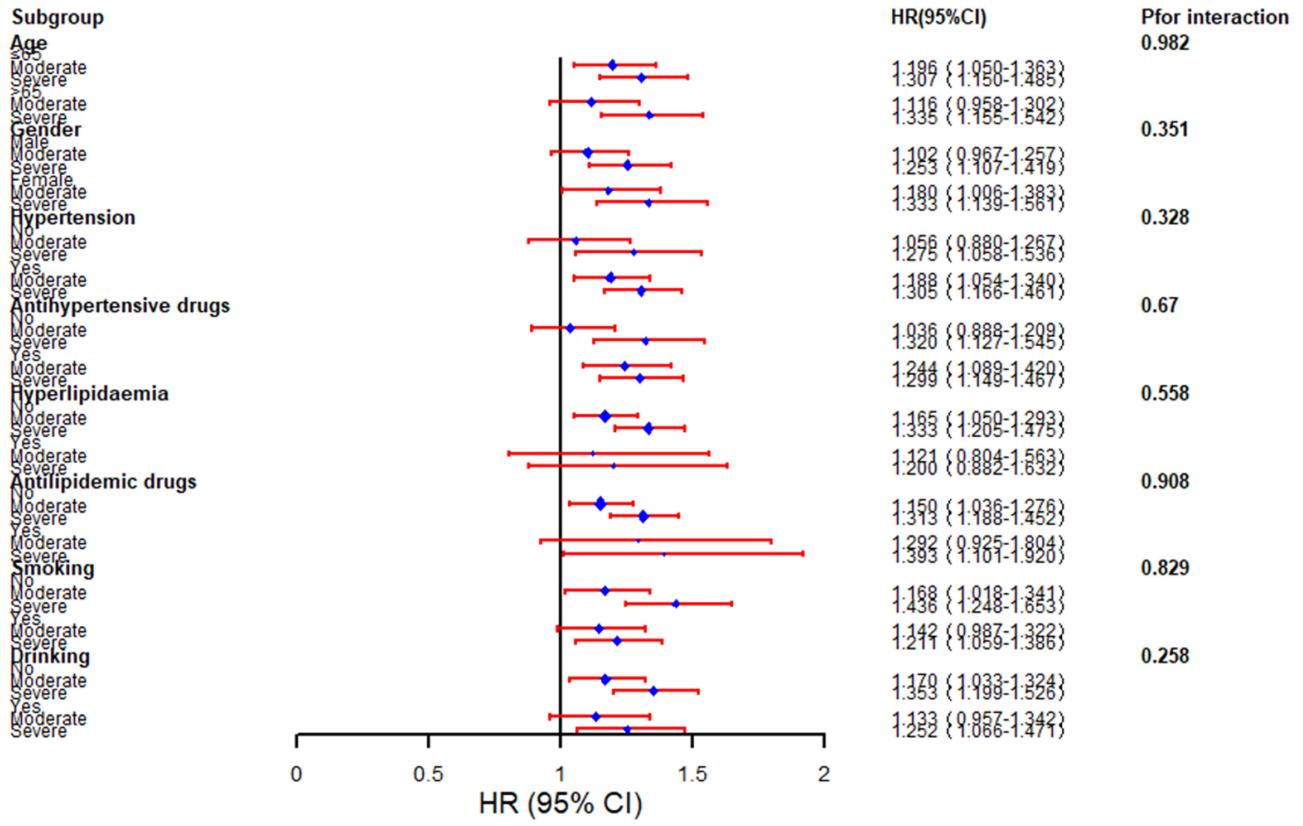


Figure 4 Subgroup analysis for the association between SII and Severity of coronary stenosis.

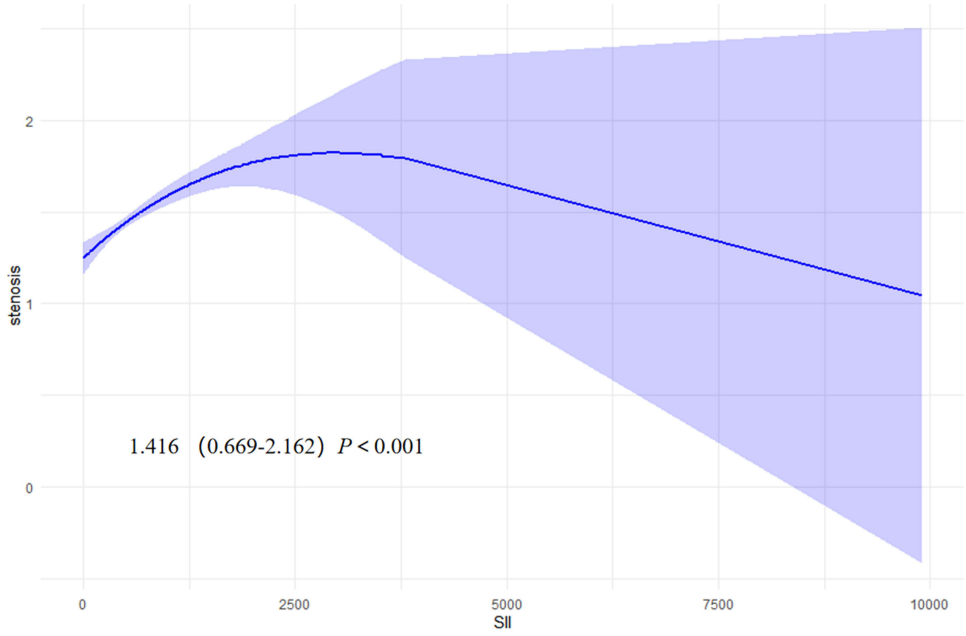


Figure 5 RCS model showing the association between the SII and severity of coronary artery lesions.
Notes: Restricted cubic spline (RCS) analysis was applied to analyze the data; Blue lines and shaded areas represent the odds ratios and 95% confidence intervals; P < 0.05 was considered statistically significant.
Abbreviation: SII, systemic immune-inflammatory index.

https://doi.org/10.2147/JIR.S507696

coronary lesion severity remained in the Pre-DM and DM states; however, there was no statistical significance in the NGR state. The results of subgroup analyses showed that this association was consistent across populations, further validating the robustness of the findings; the study also found a linear relationship between SII and coronary lesion severity, increasing coronary lesion severity by 41.6% for each unit increase in SII.

Previous studies have revealed that inflammatory and immune responses are continuously active during the development and progression of coronary atherosclerosis.[27,28] Neutrophil aggregation and release of various pro-inflammatory factors at the area of inflammation exacerbate vascular endothelial cell damage and promote the progression of atherosclerotic lesions, ultimately leading to atherosclerosis and cardiovascular disease.[29] In addition, platelet activation can promote inflammatory responses and participate in the formation and progression of atherosclerotic plaques.[30,31] And lymphocytes have also been shown to be involved in atherosclerotic plaque formation.[32,33] Abnormal glucose metabolism leads to enhanced levels of oxidative stress, which further triggers vascular endothelial damage. High inflammation and high oxidative stress states are key factors contributing to the progression of coronary artery disease,[34,35] Studies have also indicated that abnormal glucose metabolism not only accelerates the development of coronary atherosclerosis, but also leads to long-term activation and accumulation of inflammatory factors, which makes coronary artery lesions more severe.[36]

A large cohort study indicated that neutrophil counts were strongly associated with the prevalence of CVD, and high neutrophil counts were associated with a higher prevalence of CVD.[37] Comparatively, lymphocytes play a different role in regulating the inflammatory response of the body. Clinical studies have indicated that low lymphocyte counts are associated with a poorer prognosis in patients with CVD.[38] As SII is a combination of three inflammatory markers, namely neutrophils, lymphocytes and platelets, it can more fully reflect the balance between inflammation and immunity. SII components represent key pathophysiological mechanisms in coronary artery disease. In patients with coronary artery disease, the increasing number of neutrophils and platelets and decreasing number of lymphocytes indicate that the body is in a state of high inflammation and low immunosuppression, which contributes to the progression of atherosclerosis. This finding further supports that SII levels can, to a certain extent, reflect the stability of coronary plaques, thereby contributing to the assessment of lesion progression and prognostic evaluation.[15]

SII, which consists of neutrophils, lymphocytes and platelets, was first proposed by HU B et al in order to predict the prognosis of patients suffering from hepatocellular carcinoma after radical resection.[39] SII has been extensively investigated in a multitude of medical fields in diseases such as oncology, acute and critical illnesses and cerebrovascular diseases.[40–42] In recent years SII has also been used in the diagnosis and prognosis of various cardiovascular diseases.[43,44] Studies have indicated that higher SII is an independent risk factor for the development of CVD.[45] A recent study demonstrated that SII is a useful target for risk stratification and prognostic assessment of patients with acute decompensated heart failure, providing important prognostic information.[16] Furthermore, another study demonstrated that SII was an independent predictor of lesion severity in patients with acute coronary syndrome (ACS).[46] In the present study, we identified a significant association between SII and the severity of coronary artery lesions. Meanwhile, we observed that SII levels were significantly elevated in patients with abnormal glucose metabolism (including diabetes mellitus and impaired glucose tolerance) and positively correlated with the severity of coronary artery lesions. This finding indicates that SII may not only serve as an independent predictor of coronary artery disease risk in patients with glucose metabolism abnormalities, but may also provide a convenient indicator for assessing the inflammatory status of these patients, and further subgroup analyses also reinforced the robustness of our findings.

The innovation of this study is that it is the first time to combine the analysis of inflammatory indicators of glucose metabolism status and severity of coronary artery disease, proposing the potential clinical value of SII as a joint assessment tool, and providing a new perspective for the development of individualised diagnostic and therapeutic strategies. At the same time, the group analysis based on different glucose metabolism status reveals more precisely the interactive effects of glucose metabolism on inflammation level and coronary artery disease.

Despite this study provides useful valuable in exploring the relationship between SII and the severity of coronary artery lesions, some limitations remain. Firstly, the present study was a single-centre retrospective study with a limited sample size, which may affect the generalisability of the results; secondly, the present study was a cross-sectional study, which only provided an association between SII and the severity of coronary artery lesions, and not revealed a causal

relationship between the two. Future longitudinal studies could further explore the predictive value of SII on disease progression and clinical prognosis in patients with coronary artery disease. Additionally, CRP was not included as an analytical marker in this study. Although CRP is an important marker of inflammation and may have a correlation with the SII index, it was not included in the data, and thus we were unable to analyze it further. Future research should consider including CRP to comprehensively assess its relationship with the SII index. Finally, although some of the confounders were adjusted for in the analyses of this study, there were other possible influences (lifestyle factors, etc.) That were not included in the analyses. Future studies should consider controlling for additional confounders to enhance the explanatory power of the findings.

Conclusion

SII has a significant relationship with the severity of coronary artery disease; even in different states of glucose metabolism, SII remains correlated with the severity of coronary artery disease. Therefore, SII has potential application as a combined evaluation tool in clinical practice, providing a new perspective of individualised diagnostic and treatment strategies for coronary artery disease patients with abnormal glucose metabolism.

Ethics Approval

The study protocol was approved by the Ethics Committee of Tianjin Union Medical Center (IRB number:2021-C03), As this was a retrospective study with no additional interventions, all patient data were anonymized to ensure confidentiality. Therefore, informed consent is not required. This study was conducted in compliance with the Declaration of Helsinki.

Acknowledgments

Xiandu Jin and Yue Liu are co-first authors for this study. Graphical abstract is created in BioRender. Jin, X. (2025) https://BioRender.com/f52i642.

Funding

Supported by Tianjin administration of traditional Chinese medicine (grant no.2021155), Tianjin Science and Technology Project (grant no.23JCYBJC01470) and Foundation of Tianjin Union Medical Center (grant no. 2020YJ014).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Ma LY, Chen WW, Gao RL, et al. China cardiovascular diseases report 2018: an updated summary. *J Geriatr Cardiol*. 2020;17(1):1–8. doi:10.11909/j.issn.1671-5411.2020.01.001
2. Bergmark BA, Mathenge N, Merlini PA, et al. Acute coronary syndromes. *Lancet*. 2022;399(10332):1347–1358. doi:10.1016/S0140-6736(21)02391-6
3. Avis SR, Vernon ST, Hagström E, Figtree GA. Coronary artery disease in the absence of traditional risk factors: a call for action *Eur Heart J*. 2021;42(37):3822–3824
4. Xu X, Xie Y, Gu X, et al. Association between systemic immune inflammation level and poor prognosis across different glucose metabolism status in coronary artery disease patients. *J Inflamm Res*. 2023;16:4031–4042. doi:10.2147/JIR.S425189
5. Li H, Chen M, Wang Y, et al. The predictive value of TyG index and NLR for risk of CHD and the severity of coronary artery lesions in patients with type 2 diabetes mellitus. *J Inflamm Res*. 2024;17:11813–11828. doi:10.2147/JIR.S496419
6. Cai X, Zhang Y, Li M, et al. Association between prediabetes and risk of all cause mortality and cardiovascular disease: updated meta-analysis. *BMJ*. 2020;370:m2297. doi:10.1136/bmj.m2297
7. Jebari-Benslaiman S, Galicia-García U, Larrea-Sebal A, et al. Pathophysiology of atherosclerosis. *Int J Mol Sci*. 2022;23(6):3346. doi:10.3390/ijms23063346
8. Ma M, Liu Y, Wang L, et al. Relationship between monocyte-to-lymphocyte ratio as well as other leukocyte-derived ratios and carotid plaques in patients with coronary heart disease: a RCSCD-TCM study. *J Inflamm Res*. 2022;15:5141. doi:10.2147/JIR.S375759
9. Stewart JL, Burrows K, May AC, et al. C-reactive protein concentrations diverge as a function of substance use disorder: a pre-registered replication in a clinical sample. *Drug Alcohol Depend*. 2024;260:111323. doi:10.1016/j.drugalcdep.2024.111323
10. Adamstein NH, MacFadyen JG, Rose LM, et al. The neutrophil–lymphocyte ratio and incident atherosclerotic events: analyses from five contemporary randomized trials. *Eur Heart J*. 2021;42(9):896–903. doi:10.1093/eurheartj/ehaa1034
11. Chen K, Liu Y, Xu B, et al. Relationship between the lymphocyte to C-reactive protein ratio and coronary artery disease severity. *Exp Ther Med*. 2023;27(2):60. doi:10.3892/etm.2023.12348

12. Ma J, Li K. Systemic immune-inflammation index is associated with coronary heart disease: a cross-sectional study of NHANES 2009–2018. *Front Cardiovasc Med*. 2023;10:1199433. doi:10.3389/fcvm.2023.1199433
13. Mahemuti N, Jing X, Zhang N, et al. Association between systemic immunity-inflammation index and hyperlipidemia: a population-based study from the NHANES (2015–2020). *Nutrients*. 2023;15(5):1177. doi:10.3390/nu15051177
14. Liu Y, Ye T, Chen L, et al. Systemic immune-inflammation index predicts the severity of coronary stenosis in patients with coronary heart disease. *Coron Artery Dis*. 2021;32(8):715–720. doi:10.1097/MCA.0000000000001037
15. Saylik F, Akbulut T. Systemic immune-inflammation index predicts major cardiovascular adverse events in patients with ST-segment elevated myocardial infarction. *Arq Bras Cardiol*. 2022;119(1):14–22. doi:10.36660/abc.20210412
16. Qiu J, Huang X, Kuang M, et al. Evaluating the prognostic value of systemic immune-inflammatory index in patients with acute decompensated heart failure. *ESC Heart Failure*. 2024;11(5):3133. doi:10.1002/ehf2.14904
17. Qiu Y, Fan S, Liu J, et al. Association between overweight/obesity metabolic phenotypes defined by two criteria of metabolic abnormality and cardiovascular diseases: a cross-sectional analysis in a Chinese population. *Clin Cardiol*. 2024;47(10):e70020. doi:10.1002/clc.70020
18. Neeland IJ, Lim S, Tchernof A, et al. Metabolic syndrome. *Nat Rev Dis Primers*. 2024;10(1):77. doi:10.1038/s41572-024-00563-5
19. Ryan TJ, Bauman WB, Kennedy JW, et al. Guidelines for percutaneous transluminal coronary angioplasty. A report of the American heart association/American college of cardiology task force on assessment of diagnostic and therapeutic cardiovascular procedures (committee on percutaneous transluminal coronary angioplasty). *Circulation*. 1993;88(6):2987–3007. doi:10.1161/01.cir.88.6.2987
20. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. *Am J Cardiol*. 1983;51(3):606. doi:10.1016/s0002-9149(83)80105-2
21. Aksu F, Ahmed SA. Gensini score's severity and its relationship with risk factors for coronary artery disease among patients who underwent angiography in Somalia's largest PCI centre. *Int J Gen Med*. 2024;17:187–192. doi:10.2147/IJGM.S384626
22. Guo J, Chen M, Hong Y, et al. Comparison of the predicting value of neutrophil to high-density lipoprotein cholesterol ratio and monocyte to high-density lipoprotein cholesterol ratio for in-hospital prognosis and severe coronary artery stenosis in patients with ST-segment elevation acute myocardial infarction following percutaneous coronary intervention: a retrospective study. *J Inflamm Res*. 2023;16:4541–4557. doi:10.2147/JIR.S425663
23. Wang H, Yang Y, Zeng P, et al. Association between systemic immune-inflammation index (SII) and new-onset in-hospital heart failure in patients with STEMI after primary PCI. *Rev Cardiovasc Med*. 2024;25(10):382. doi:10.31083/j.rcm2510382
24. Tuzimek A, Dziedzic EA, Beck J, Kochman W. Correlations between acute coronary syndrome and novel inflammatory markers (systemic immune-inflammation index, systemic inflammation response index, and aggregate index of systemic inflammation) in patients with and without diabetes or prediabetes. *J Inflamm Res*. 2024;17:2623. doi:10.2147/JIR.S454117
25. Wu X, Qiu W, Yang H, Chen Y-J, Liu J, Zhao G. Associations of the triglyceride-glucose index and atherogenic index of plasma with the severity of new-onset coronary artery disease in different glucose metabolic states. *Cardiovasc Diabetol*. 2024;23:76. doi:10.1186/s12933-024-02163-9
26. American Diabetes Association Professional Practice Committee. 2. classification and diagnosis of diabetes: standards of medical care in diabetes-2022. *Diabetes Care*. 2022;45(Suppl 1):S17–S38. doi:10.2337/dc22-S002.
27. Marcuzzi A, Melloni E, Zauli G, et al. Autoinflammatory diseases and cytokine storms-imbalances of innate and adaptative immunity. *Int J Mol Sci*. 2021;22(20):11241. doi:10.3390/ijms222011241
28. Wolf D, Ley K. Immunity and inflammation in atherosclerosis. *Circ Res*. 2019;124(2):315–327. doi:10.1161/CIRCRESAHA.118.313591
29. Flores-Gomez D, Bekkering S, Netea MG, Riksen NP. Trained immunity in atherosclerotic cardiovascular disease. *Arterioscler Thromb Vasc Biol*. 2021;41(1):62–69. doi:10.1161/ATVBAHA.120.314216
30. Cheng MD, Zheng YY, Zhang XY, et al. The simplified thrombo-inflammatory score as a novel predictor of all-cause mortality in patients with heart failure: a retrospective cohort study. *J Inflamm Res*. 2024;17:1845–1855. doi:10.2147/JIR.S452544
31. Berger JS, Cornwell MG, Xia Y, et al. J. A platelet reactivity expression score derived from patients with peripheral artery disease predicts cardiovascular risk. *Nat Commun*. 2024;15(1):6902. doi:10.1038/s41467-024-50994-7
32. Liu T, Chen Y, Hou L, et al. Immune cell-mediated features of atherosclerosis. *Front Cardiovasc Med*. 2024;11:1450737. doi:10.3389/fcvm.2024.1450737
33. Annink ME, Kraaijenhof JM, Stroes ESG, Kroon J. Moving from lipids to leukocytes: inflammation and immune cells in atherosclerosis. *Front Cell Dev Biol*. 2024;12:1446758. doi:10.3389/fcell.2024.1446758
34. Tejada B, Joehanes R, Hwang S-J, et al. Systemic inflammation is associated with cardiometabolic risk factors and clinical outcomes. *J Inflamm Res*. 2022;15:6891–6903. doi:10.2147/JIR.S382620
35. Poznyak A, Grechko AV, Poggio P, et al. The diabetes mellitus-atherosclerosis connection: the role of lipid and glucose metabolism and chronic inflammation. *Int J Mol Sci*. 2020;21(5):1835. doi:10.3390/ijms21051835
36. Kaze AD, Santhanam P, Musani SK, Ahima R, Echouffo-Tcheugui JB. Metabolic dyslipidemia and cardiovascular outcomes in type 2 diabetes mellitus: findings from the look AHEAD study. *J Am Heart Assoc*. 2021;10(7):e016947. doi:10.1161/JAHA.120.016947
37. Wu Z, Wu D, Chen S, et al. Resting heart rate mediates the association between circulating neutrophil count and arterial stiffness progression: the Kailuan study. *J Inflamm Res*. 2024;17:11347–11356. doi:10.2147/JIR.S488928
38. Pan Y, Wu TT, Deng CJ, et al. Association between the C-REACTIVE PROTEIN-ALBUMIN-LYMPHOCYTE (CALLY) index and adverse clinical outcomes in CAD Patients after PCI: findings of a real-world study. *Rev Cardiovasc Med*. 2024;25(4):111. doi:10.31083/j.rcm2504111
39. Hu B, Yang XR, Xu Y, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res*. 2014;20(23):6212–6222. doi:10.1158/1078-0432.CCR-14-0442
40. Li Y, Bai G, Gao Y, et al. The systemic immune inflammatory response index can predict the clinical prognosis of patients with initially diagnosed coronary artery disease. *J Inflamm Res*. 2023;16:5069. doi:10.2147/JIR.S432506
41. Aydogan S, Dilli D, Soysal C, et al. Role of systemic immune-inflammatory index in early diagnosis of sepsis in newborns with CHD. *Cardiol Young*. 2022;32(11):1826–1832. doi:10.1017/S1047951122001202
42. Wang M, Peng C, Jiang T, Wu Q, Li D, Lu M. Association between systemic immune-inflammation index and post-stroke depression: a cross-sectional study of the national health and nutrition examination survey 2005–2020. *Front Neurol*. 2024;15:1330338. doi:10.3389/fneur.2024.1330338
43. Xu M, Chen R, Liu L, et al. Systemic immune-inflammation index and incident cardiovascular diseases among middle-aged and elderly Chinese adults: the Dongfeng-Tongji cohort study. *Atherosclerosis*. 2021;323:20–29. doi:10.1016/j.atherosclerosis.2021.02.012

44. Nascimento MAL, Ferreira LGR, Alves TVG, Rios DRA. Inflammatory hematological indices, cardiovascular disease and mortality: a narrative review. *Arq Bras Cardiol*. 2024;121(7):e20230752. doi:10.36660/abc.20230752
45. Ye Z, Hu T, Wang J, et al. Systemic immune-inflammation index as a potential biomarker of cardiovascular diseases: a systematic review and meta-analysis. *Front Cardiovasc Med*. 2022;9:933913. doi:10.3389/fcvm.2022.933913
46. Qu C, Li X, Gao H. The impact of systemic inflammation response index on the prognosis of patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention. *Rev cardiovasc med*. 2023;24(5):153. doi:10.31083/j.rcm2405153