

## Original Article

# Use of blood glucose level for predicting the degree of coronary artery disease and cardiovascular adverse events in diabetic patients with acute coronary syndrome

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Received November 27, 2024; Accepted April 3, 2025; Epub April 15, 2025; Published April 30, 2025

**Abstract:** Objective: To investigate the predictive value of blood glucose level in patients with type 2 diabetes mellitus (T2DM) and acute coronary syndrome (ACS) concerning the degree of coronary artery disease and major adverse cardiovascular events (MACE). Method: A retrospective study was conducted on 104 T2DM patients with ACS who visited West China Hospital, Sichuan University, from August 2020 to March 2024. Based on the Gensini score, patients were categorized into mild (0-30 points), moderate (31-59 points), and severe ( $\geq 60$  points) groups. Additionally, patients were divided into MACE and non-MACE groups based on the occurrence of MACE. General information, blood glucose levels, and coronary angiography results were collected, along with six-month follow-up data. The predictive value of blood glucose levels for the severity of coronary artery disease and cardiovascular adverse events was analyzed using receiver operating characteristic (ROC) curves. Results: There were significant differences in the levels of glycosylated serum protein (GSP), insulin-like growth factor-1 (IGF-1), and the triglyceride-glucose (TyG) index among patients with varying degrees of coronary artery disease ( $P < 0.05$ ), with levels increasing in line with disease severity. The MACE group exhibited generally higher levels of GSP, IGF-1, and TyG compared to the non-MACE group ( $P < 0.05$ ). ROC curve analysis revealed that the area under the curve (AUC) for GSP, IGF-1, and TyG for predicting severe coronary artery disease were 0.861, 0.936, and 0.896, respectively, and for predicting MACE occurrence were 0.738, 0.814, and 0.710, respectively ( $P < 0.05$ ). Conclusion: Blood glucose levels in T2DM patients with ACS have predictive value for both the severity of coronary artery disease and the occurrence of MACE. Measurement of GSP, IGF-1, and TyG is clinically significant for assessing prognosis and developing treatment strategies.

**Keywords:** Acute coronary syndrome, diabetes, glycosylated serum protein, insulin-like growth factor-1, TG-fasting blood glucose

## Introduction

Acute coronary syndrome (ACS) refers to a group of clinical syndromes resulting from acute myocardial ischemia, typically caused by thrombosis due to the rupture or erosion of unstable atherosclerotic plaque in a coronary artery. It represents the acute clinical presentation of coronary atherosclerotic heart disease (coronary heart disease) [1-3]. In recent years, the widespread application of reperfusion therapies, such as percutaneous coronary intervention (PCI) and coronary artery bypass graft-

ing (CABG), along with the establishment of chest pain centers, has significantly improved the management and rescue of ACS patients [4, 5]. Nevertheless, despite adherence to recommended diagnostic and therapeutic guidelines, some ACS patients remain at elevated risk for major adverse cardiovascular events (MACE), including recurrent myocardial infarction, recurrent angina, severe arrhythmia, and death [6-8]. This indicates that additional risk factors influencing the long-term prognosis of ACS patients may not yet be fully identified or controlled.

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Diabetes is a chronic metabolic disease characterized by elevated blood sugar levels, associated with an increased risk of cardiovascular complications [9]. Stress hyperglycemia is common in ACS patients, and significant fluctuations in blood sugar may exacerbate damage by vascular disease [10]. Yamamoto et al. [11] have shown that blood glucose fluctuations are an important factor affecting the prognosis of patients with coronary artery disease (CAD). Liu et al. [12] noted that the estimation of glucose disposal rate (eGDR) can predict the prognosis of non-diabetic patients following PCI to a certain extent. Additionally, the high prevalence of undiagnosed diabetes and prediabetes in ACS patients and their effect on clinical outcomes have also attracted extensive attention [13]. Specifically, hyperglycemia may exacerbate the severity of coronary artery lesions and increase the risk of MACE, such as recurrent myocardial infarction, recurrent angina, severe arrhythmias, and death. It is worth noting that in the context of ACS, the blood glucose characteristics of diabetic patients not only reflect the metabolic disorder under stress, but may also be closely related to the complexity of coronary artery lesions and the occurrence of cardiovascular events. In addition, the long-term effects of blood glucose fluctuations and hyperglycemia on the cardiovascular system may extend beyond the acute rise in blood glucose levels alone. Research by Wang et al. [14] showed that 26.28% of ACS patients had concurrent diabetes. Therefore, investigating the predictive value of blood glucose levels in diabetic patients with ACS for the degree of coronary artery disease and cardiovascular adverse events is of great significance.

This study can help identify risk factors that influence the long-term prognosis of patients and provide more accurate treatment strategies to reduce the risk of cardiovascular events in diabetic patients. By examining the relationship between blood glucose levels and cardiovascular events, we can offer a more solid scientific basis for the management of patients with diabetes and ACS, ultimately improving their outcome.

### Materials and methods

#### General information

A total of 104 patients with type 2 diabetes mellitus (T2DM) and ACS who visited West

China Hospital, Sichuan University from August 2020 to March 2024 were selected as the study subjects. Inclusion criteria: (1) meeting the diagnostic criteria for T2DM [15], which included typical diabetes symptoms plus fasting blood glucose  $>7.0$  mmol/L, a 2-hour blood glucose level  $>11.1$  mmol/L following an oral glucose tolerance test (OGTT), random blood glucose  $>11.1$  mmol/L with potential hyperglycemic crisis or typical hyperglycemia symptoms, or glycated hemoglobin (HbA1c)  $>6.5\%$ ; (2) fulfilling the diagnostic criteria for ACS as indicated by electrocardiogram [16-18] (Supplementary Table 1); (3) age  $\leq 80$  years old. Exclusion criteria: (1) individuals with severe infections in the past two months; (2) individuals with severe organ dysfunction; (3) patients with incomplete clinical data records necessary for this study; (4) patients with concurrent malignant tumors. This study was approved by the Ethics Committee of West China Hospital, Sichuan University.

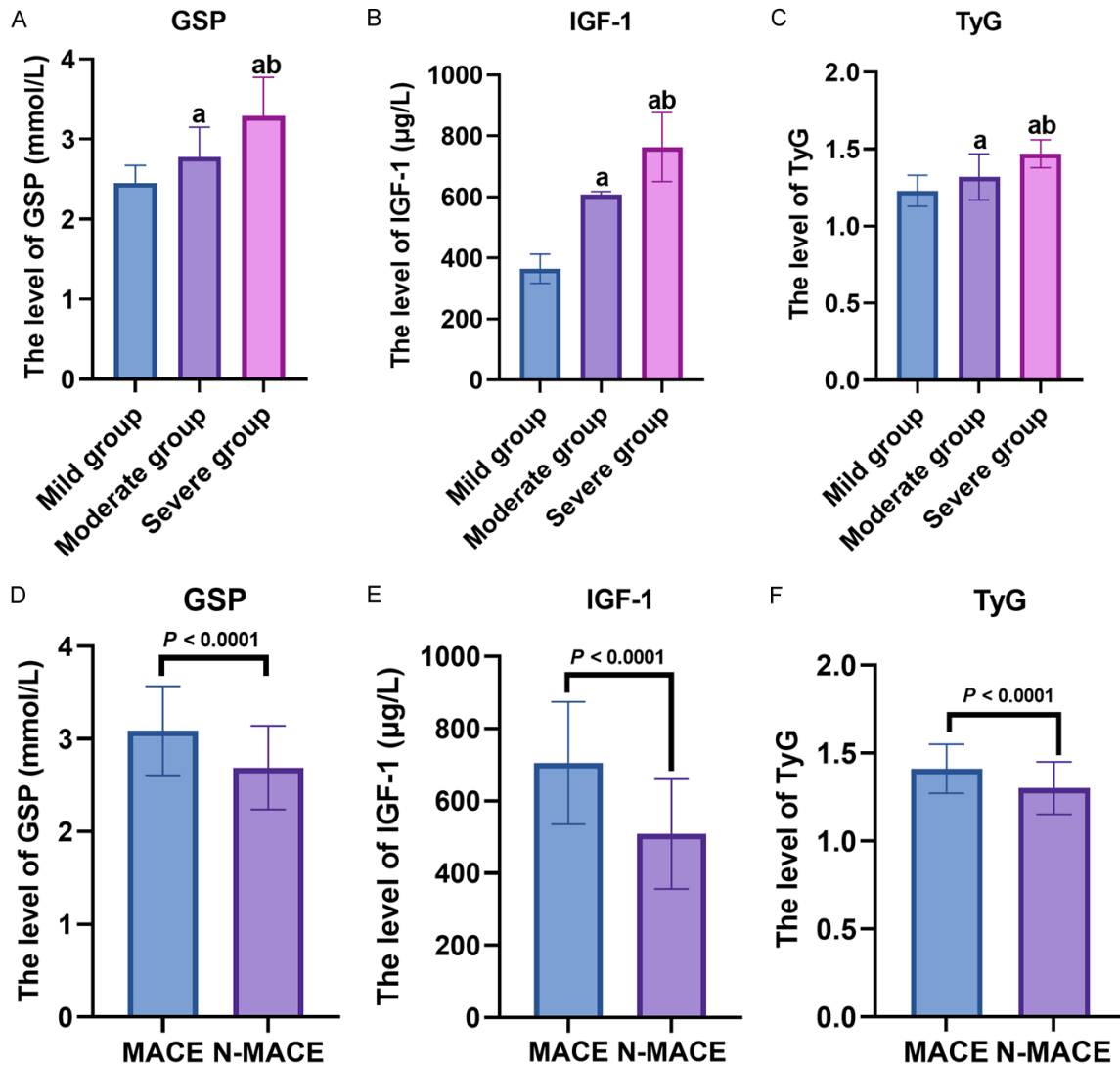
#### Sample size calculation method

This study was a single-sample diagnostic test designed to evaluate the accuracy of blood glucose level in predicting coronary artery disease severity or MACE occurrence. The minimum sensitivity and specificity were both set at 60%. Based on the pilot study, sensitivity and specificity were both 85%, the tolerance errors were both 0.1, and the prevalence rate was 30%. A two-sided test was used, with an alpha of 0.05 and a power of 90% ( $1-\beta$ ). The sample size was calculated to be 91 using PASS software. Considering a 10%-20% invalid sample rate, the final sample size was adjusted to 104.

#### Data collection methods

The clinical data of the study subjects were collected through our hospital's electronic medical record system, and the research process is shown in **Figure 1**. The clinical data collected in this study included: (1) General information including gender, age, duration of T2DM, body mass index (BMI), history of hypertension, smoking history, alcohol consumption history, and history of cardiovascular and cerebrovascular diseases; (2) Clinical indicators: blood sample results, blood glucose levels, and coronary angiography results; (3) Follow-up: After discharge, the researchers conducted a six-month follow-up by telephone, outpatient

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**Figure 1.** Comparison of GSP, IGF-1, and TyG levels among patients with different degrees of coronary artery disease (A-C), as well as between patients with and without MACE (D-F). Notes: GSP: glycosylated serum protein; IGF-1: insulin-like growth factor-1; TyG: triglyceride fasting blood glucose; MACE: major adverse cardiovascular events. Compared to the mild group, <sup>a</sup> $P < 0.0001$ ; compared to the moderate group, <sup>b</sup> $P < 0.0001$ .

visits, or readmission to record the occurrence of MACE [6], including arrhythmia, heart failure, unstable angina, recurrent myocardial infarction, and all-cause mortality. Patients who experienced MACE during the follow-up period were classified as the MACE group, while the remaining patients were classified as the non-MACE group.

### Observation indicators

(1) Blood glucose levels: On the second day of admission, continuous blood glucose testing was performed for each patient. A 4 mL fasting

venous blood sample was collected, centrifuged at 3000/min for 10 minutes, and the supernatant was used for testing. Glycosylated serum protein (GSP) levels were detected using an automated biochemical analyzer, insulin-like growth factor-1 (IGF-1) levels were measured using enzyme-linked immunosorbent assay (ELISA), triglyceride (TG) levels were determined using the colorimetric method, and the triglyceride-glucose index (TyG) was calculated as:  $\text{TyG index} = \text{TG} \times \text{fasting blood glucose}$ . (2) Severity of coronary artery disease: The Gensini score was used to assess the severity of coronary artery disease based on the location of

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**Table 1.** General information of included patients

Index	Specific data	
Gender		
Male	67	64.42
Female	37	35.58
Age (years)	63.95±5.44	
Duration of T2DM (years)	6 (5.00, 6.75)	
BMI (kg/m <sup>2</sup> )	23.48 (22.66, 24.17)	
History of hypertension		
Yes	73	70.19
No	31	29.81
Smoking history		
Yes	34	32.69
No	70	67.31
Alcohol consumption history		
Yes	59	56.73
No	45	43.27
History of cardiovascular and cerebrovascular diseases		
Yes	27	25.96
No	77	74.04
MACE		
Yes	32	30.77
No	72	69.23

Notes: T2DM: type 2 diabetes mellitus; BMI: body mass index; MACE: major adverse cardiovascular events.

coronary artery involvement and the degree of stenosis [18] (Supplementary Table 2). The Gensini score is the product of the degree of stenosis and the lesion site coefficient. ACS patients were divided into a mild group (0-30 points), moderate group (31-59 points), and severe group ( $\geq 60$  points) based on Gensini score. (3) MACE occurrence [6]: During the six-month follow-up period, all patients who experienced arrhythmia, heart failure, unstable angina, recurrent myocardial infarction, or all-cause death were recorded.

### Statistical analysis

Data were analyzed using SPSS 26.0 statistical software. Counted data were expressed as n (%), and the chi-square test was used to compare differences between groups. Measured data were expressed as mean  $\pm$  standard deviation, and analysis of variance was used for comparison among multiple groups, while independent sample t-test was used for comparison between two groups. Pearson's correlation test was used to examine the correlation

between blood glucose levels and Gensini score, while Spearman's correlation test was used to analyze the correlation between blood glucose levels and the occurrence of MACE. Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive value of blood glucose levels for the severity of coronary artery disease and the occurrence of MACE in ACS patients.  $P < 0.05$  was considered significant.

### Results

#### General information of patients

According to the Gensini score, the 104 patients were divided into a mild group (36 cases), moderate group (38 cases), and severe group (30 cases).

The Gensini scores for mild group, moderate group and severe group were (17.22 $\pm$ 3.63), (41.11 $\pm$ 6.64), and (67.83 $\pm$ 4.62), respectively. During the six-month follow-up period, 32 out of 104 ACS patients developed MACE, accounting for 30.78%. As shown in **Table 1**, the study population consisted of 67 males and 37 females, with an average age of (63.95 $\pm$ 5.44) years. Additionally, 73 patients had a history of hypertension, 34 had a history of smoking, and 59 had a history of alcohol consumption.

#### Blood glucose levels of patients

The GSP levels of mild, moderate, and severe groups were (2.45 $\pm$ 0.22) mmol/L, (2.78 $\pm$ 0.37) mmol/L, and (3.29 $\pm$ 0.48) mmol/L, respectively. The IGF-1 levels for the mild, moderate, and severe groups were (365.02 $\pm$ 48.01)  $\mu$ g/L, (608.19 $\pm$ 79.52)  $\mu$ g/L and (763.78 $\pm$ 113.53)  $\mu$ g/L, respectively. The TYG levels for the mild, moderate, and severe groups were (1.23 $\pm$ 0.10), (1.32 $\pm$ 0.15) and (1.47 $\pm$ 0.09), respectively. Analysis of variance revealed significant differences in GSP, IGF-1, and TyG levels among

**Table 2.** Correlation between blood glucose levels and severity of CAS and occurrence of MACE in patients

Index	Gensini	MACE
GSP	0.657**	0.462**
IGF-1	0.861**	0.356**
TyG	0.650**	0.302**

Notes: \*\* $P < 0.01$ ; MACE: major adverse cardiovascular event. CAS: coronary artery stenosis.

patients with different degrees of coronary artery disease (all  $P < 0.0001$ ). Bonferroni's post-hoc analysis showed that patients with more severe lesions had higher levels of GSP, IGF-1, and TyG (all  $P < 0.0001$ ), as shown in **Figure 1A-C**. The levels of GSP, IGF-1 and TYG in the MACE group were  $(3.09 \pm 0.48)$  mmol/L,  $(704.93 \pm 169.56)$   $\mu\text{g/L}$ , and  $(1.41 \pm 0.14)$   $\mu\text{g/L}$ , respectively, and those levels in the non-MACE group were  $(2.69 \pm 0.45)$  mmol/L,  $(508.44 \pm 151.81)$   $\mu\text{g/L}$  and  $(1.30 \pm 0.15)$   $\mu\text{g/L}$ , respectively. Significantly higher levels of GSP, IGF-1, and TyG were found in patients with MACE compared to those without MACE ( $P < 0.001$ ), as shown in **Figure 1D-F**.

#### Correlation analysis

As shown in **Table 2**, Pearson correlation analysis showed that the Gensini score of ACS patients was positively correlated with their GSP, IGF-1, and TyG levels ( $r = 0.657, 0.861$ , and  $0.650$ , all  $P < 0.001$ ). Spearman correlation analysis showed that the occurrence of MACE in ACS patients was positively correlated with GSP, IGF-1, and TyG levels ( $r = 0.462, 0.356$ , and  $0.302$ , and  $P < 0.001$ ).

#### Predictive value analysis

The ROC curve analysis results showed that with cutoff values of 3.27, 698.33, and 1.35, the AUCs of GSP, TGF-1, and TyG for predicting severe coronary artery disease in ACS patients were 0.861, 0.936, and 0.896, respectively (all  $P < 0.001$ ) (**Figure 2A; Table 3**). For predicting MACE in ACS patients, ROC curve analysis results showed that the cutoff values were 2.84, 631.12, and 1.30, and the AUCs were 0.738, 0.814, and 0.710 for GSP, TGF-1, and TyG, respectively (all  $P < 0.001$ ) (**Figure 2B; Table 3**).

#### Influencing factor analysis

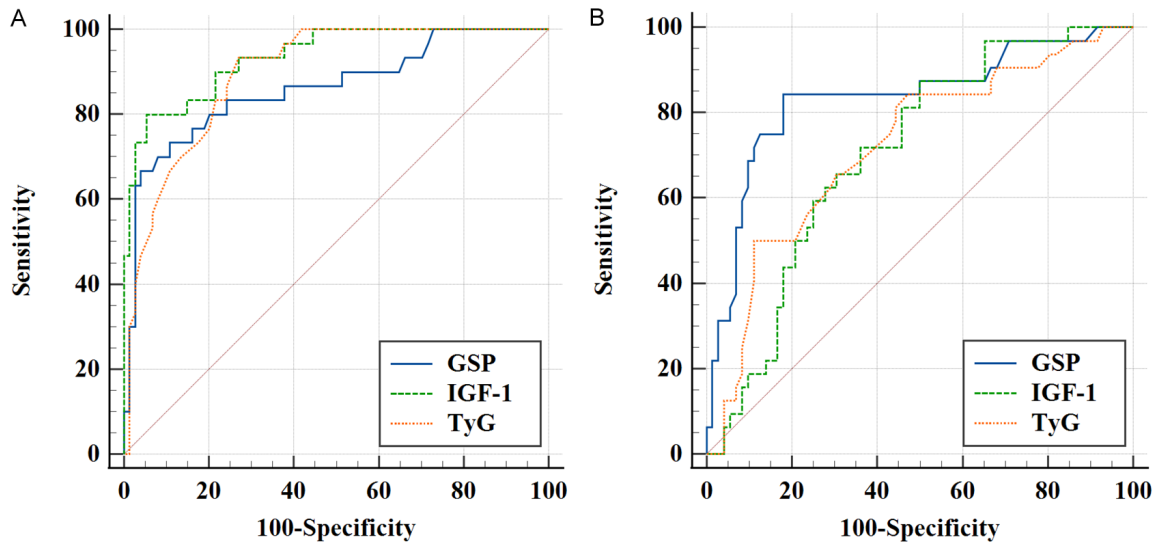
As shown in **Table 4**, linear regression analysis with GSP, TGF-1, and TyG as independent variables and Gensini score as the dependent variable demonstrated significant correlations between GSP, TGF-1, TyG and Gensini score ( $F = 135.732, P < 0.001, P < 0.001$ , and  $P = 0.022$ , respectively). The results indicated that the levels of GSP, TGF-1 and TyG significantly influenced the severity of coronary artery lesions. As shown in **Table 5**, logistic regression analysis was conducted with GSP, TGF-1, and TyG as independent variables and MACE occurrence as the dependent variable. The results showed that GSP significantly affected MACE occurrence ( $P = 0.001$ ).

#### Discussion

##### Research background and significance

With the aging population and changes in lifestyle in China, the incidence of ACS continues to rise, and the age of onset is trending younger. This health issue not only threatens the safety and quality of life of the population but also presents significant challenges to medical resource allocation and disease prevention and control, placing a heavy burden on China's healthcare system. Among various chronic diseases, T2DM is particularly prevalent and is closely associated with cardiovascular diseases [19, 20]. T2DM can accelerate atherosclerosis and thrombosis, thereby increasing the risk of cardiovascular and cerebrovascular diseases in affected patients. Studies [21, 22] indicate that the risk of cardiovascular and cerebrovascular diseases in patients with T2DM is higher than in those without T2DM. Therefore, patients with T2DM and ACS may confront a more severe health crisis. In clinical practice, blood glucose levels are key indicators for evaluating the condition of T2DM patients, with markers such as GSP, TGF-1 and TyG reflecting blood glucose levels [23-25]. Changes in these indicators may be associated with the extent of coronary artery lesions and the occurrence of adverse cardiovascular events. Therefore, exploring the predictive value of blood glucose levels for coronary artery lesions and MACE in T2DM patients with ACS is of great clinical significance. The aim of this study is to investigate the predictive value of blood glucose level on

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**Figure 2.** ROC curves of GSP, IGF-1, and TyG for predicting severe ACS (A) and MACE incidence (B). Notes: ROC: receiver operation characteristic; ACS: acute coronary syndrome; MACE: major adverse cardiovascular event.

**Table 3.** Predictive value of serum GSP, TGF-1, and TyG levels for severe coronary artery disease and the occurrence of MACE

Index	Criterion	AUC	P	Sensitivity (%)	Specificity (%)
GSP <sup>1</sup>	3.27	0.861	<0.001	66.67	95.95
TGF-1 <sup>1</sup>	698.33	0.936	<0.001	80.00	94.59
TyG <sup>1</sup>	1.35	0.896	<0.001	93.33	72.97
GSP <sup>2</sup>	2.84	0.738	<0.001	75.00	77.78
TGF-1 <sup>2</sup>	631.12	0.814	<0.001	75.00	77.78
TyG <sup>2</sup>	1.30	0.710	<0.001	84.37	52.78

Notes: <sup>1</sup>the prediction of severe coronary artery disease; <sup>2</sup>the prediction of the occurrence of MACE; AUC: area under the curve; GSP: glycosylated serum protein; IGF-1: insulin-like growth factor-1; TyG: triglyceride fasting blood glucose; MACE: major adverse cardiovascular event.

**Table 4.** Linear regression analysis of factors associated with coronary artery disease severity (Gensini score)

Index	B	SE	$\beta$	t	P	95% CI
GSP	10.658	2.243	0.253	4.752	<0.001	6.208-15.107
IGF-1	0.073	0.007	0.637	10.241	<0.001	0.059-0.087
TyG	18.576	7.963	0.135	2.333	0.022	2.778-34.375
Constant	-55.531	9.292	-	-	-	-

**Table 5.** Logistic regression analysis of influencing factors for MACE

Index	B	SE	Wald $\chi^2$	P	OR	95% CI
GSP	2.068	0.616	11.276	0.001	7.911	2.366-26.457
IGF-1	0.001	0.002	0.323	0.570	1.001	0.997-1.005
TyG	0.993	2.195	0.205	0.651	2.699	0.037-199.263
Constant	-8.805	2.623	11.269	-	-	-

Note: MACE: major adverse cardiovascular event.

the degree of coronary artery disease and MACE in T2DM patients with ACS, providing a more accurate tool for clinical assessment, optimizing treatment plans, and improving patient prognosis.

### *Relationship between blood glucose levels, coronary artery disease, and MACE*

The results of this study demonstrated that as the Gensini score increased, reflecting the severity of coronary artery disease, there was a significant increase in the levels of GSP, IGF-1, and TyG in patients. This indicates that these blood glucose indicators are closely associated with the severity of coronary artery disease. Additionally, the levels of GSP, IGF-1, and TyG were generally higher in the MACE group compared to the non-MACE group, further confirming the significant role of blood glucose levels in predicting the occurrence of MACE. Hyperglycemia is not only a clinical manifestation of diabetes but also a crucial predictor of cardiovascular

disease progress and poor prognosis [26-28]. The study's results show that, in patients with diabetes and ACS, elevated blood glucose levels may worsen coronary artery disease and raise the risk of MACE. This aligns with previous research indicating that poor blood glucose control is linked to an increased risk of cardiovascular events [9]. In a hyperglycemic state, various biological pathways are activated, leading to vascular endothelial dysfunction and the progression of atherosclerosis. The heightened oxidative stress caused by high blood sugar results in endothelial cell damage, which promotes the adhesion and migration of inflammatory cells, thereby intensifying the inflammatory response in the vascular wall [28, 29]. Additionally, high blood sugar can induce insulin resistance, which then activates the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS), both of which promote vasoconstriction, increase blood pressure, and exacerbate coronary artery disease [30].

### *Mechanism and predictive value of blood glucose indicators for coronary artery disease and MACE*

IGF-1, an important growth factor, plays a key role in the proliferation and migration of vascular smooth muscle cells and the synthesis of extracellular matrix, contributing significantly to the formation and development of atherosclerosis [31]. An increase in IGF-1 levels may reflect the activity of vascular damage and repair processes or may directly participate in the progression of coronary artery disease [32]. Additionally, the TyG index, a marker of blood glucose fluctuations and lipid metabolism disorders, is elevated in response to insulin resistance and  $\beta$ -cell dysfunction [33]. In insulin resistance, triglyceride production by the liver increases, while the inhibition of lipolysis in adipose tissue by insulin decreases, leading to an accumulation of free fatty acids in the blood. This further aggravates lipid metabolism and inflammatory reactions, further advancing progression of atherosclerosis [34]. This study evaluated the predictive value of GSP, IGF-1, and TyG for severe coronary artery disease and MACE occurrence using ROC curve analysis. The results showed that these blood glucose indicators had high AUC values, indicating

their strong predictive power for the severity of coronary artery disease and the occurrence of MACE in ACS patients. Notably, IGF-1 demonstrated high sensitivity and specificity in predicting severe coronary artery disease, potentially related to its role in vascular injury repair and inflammatory response. These findings provide new blood glucose monitoring indicators for clinical evaluation and prediction of cardiovascular risk in ACS patients.

### *Limitations and prospects*

The results of this study suggest that monitoring and controlling blood glucose levels, particularly GSP, IGF-1 and TyG, can help doctors more accurately assess the degree of coronary artery disease and the risk of MACE in diabetes patients, facilitating the development of personalized treatment strategies. However, this study has several limitations. First, it was a single-center study with a relatively small sample size, which may limit the generalizability and statistical power of the results. Second, the follow-up period was only six months, which is relatively short. Longer-term follow-up is necessary to evaluate the relationship between blood glucose levels and long-term cardiovascular events. Additionally, this study did not thoroughly evaluate other possible confounding factors, such as genetics, lifestyle, and dietary habits, all of which may influence blood glucose levels and the risk of cardiovascular events. Future prospective studies with multiple centers and larger sample size may enhance the external validity and robustness of these findings. Moreover, exploring the interaction between blood glucose levels and other cardiovascular risk factors (e.g., blood lipids, blood pressure, inflammatory markers) will aid in a more comprehensive understanding of the pathophysiologic mechanisms in diabetic patients with ACS.

### **Conclusion**

This study demonstrates the predictive value of blood glucose levels in diabetic patients with ACS regarding the severity of coronary artery disease and the incidence of MACE. It underscores the significance of blood glucose control in improving the prognosis of ACS patients and introduces a novel tool for monitoring and

assessing blood glucose levels in clinical practice. Future research should investigate the application of these blood glucose markers across various populations and disease stages, as well as their interactions with other cardiovascular risk factors.

### Disclosure of conflict of interest

None.

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## Blood glucose in coronary artery disease and MACE

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## Blood glucose in coronary artery disease and MACE

**Supplementary Table 1.** Diagnostic criteria for ACS

Type	Diagnostic criteria
STEMI	The myocardial injury marker cTnI is greater than 0.04 ng/ml, and the electrocardiogram shows ST arch upward elevation, accompanied by one or more of the following conditions: persistent ischemic chest pain; Echocardiography shows segmental wall activity abnormalities; Abnormal coronary angiography.
NSTEMI	Myocardial injury marker cTnI >0.04 ng/ml, accompanied by one or more of the following conditions: persistent ischemic chest pain; The electrocardiogram shows newly developed ST segment depression or low flat or inverted T waves; Echocardiography shows segmental wall activity abnormalities; Abnormal coronary angiography.
UA	cTnI is within the normal range (0.0-0.04 ng/ml), with ischemic chest pain. The electrocardiogram shows transient ST segment depression or T wave depression and inversion, with rare ST segment elevation (vasospastic angina).

Notes: STEMI: ST-segment Elevation Myocardial Infarction, NSTEMI: Non-ST-segment Elevation Myocardial Infarction, UA: Unstable Angina, ACS: acute coronary syndrome.

**Supplementary Table 2.** Gensini score and involvement coefficient of coronary artery stenosis degree in ACS patients

Narrowness	Score	Disease Site	Coefficient
1%-25%	1	Left main trunk	5
26%-50%	2	Near left anterior descending branch and left circumflex branch	2.5
51%-75%	4	Middle section of left anterior descending branch and left circumflex branch	1.5
76%-90%	8	Left anterior descending branch and left circumflex branch distal segment	1
91%-99%	16	First diagonal branch, first blunt edge branch	1
Complete occlusion	32	Right coronary artery, posterior descending artery, intermediate artery	1
		Second diagonal branch, second blunt edge branch	0.5

Note: ACS, acute coronary syndrome.