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Original Article

Correlation of serum KLK1 and SOX6 levels with major adverse cardiovascular events in patients with ST-segment elevation myocardial infarction after percutaneous coronary intervention

Siliang Han[1], Xixi Tian[1], Fanchang Kong[2], Yichao Zhang[1], Junmin Xie[1], Zequn Zhao[1]

[1]*Department of Cardiology, Affiliated Hospital of Hebei University, Baoding 071000, Hebei, China;* [2]*Department of Vascular Surgery, Baoding Vasculitis Hospital, Baoding 071000, Hebei, China*

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Abstract: Objective: To investigate the relationship between serum kallikrein 1 (KLK1) and SRY-box transcription factor 6 (SOX6) levels and major adverse cardiovascular events (MACE) in patients with ST-segment elevation myocardial infarction (STEMI) following percutaneous coronary intervention (PCI). Methods: A total of 150 STEMI patients who underwent PCI from October 2021 to October 2022 were included in this study. Patients were divided into MACE and Non-MACE groups based on the occurrence of postoperative adverse cardiovascular events. General data, laboratory findings, and imaging results were compared between the two groups. Logistic regression analysis was used to identify factors influencing MACE, which were further used to develop a joint prediction model. ROC curves were plotted to assess the predictive values of the model. Results: MACE occurred in 20 patients (13.33%). The MACE group had significantly higher Killip grade ($P = 0.020$), elevated serum levels of cardiac troponin I (cTnI) ($P = 0.040$), creatine kinase (CK) ($P = 0.044$), KLK1 ($P < 0.001$), creatine kinase isoenzyme (CK-MB) ($P = 0.043$), and SOX6 ($P < 0.001$), as well as higher Gensini score ($P = 0.040$) and Grace score ($P = 0.045$). Logistic regression analysis identified KLK1 (OR = 1.015, $P = 0.016$) and SOX6 (OR = 1.823, $P < 0.001$) as independent risk factors for MACE. The combination of KLK1 and SOX6 showed excellent predictive value for MACE, with an AUC of 0.889. Conclusions: Elevated levels of KLK1 and SOX6 are associated with an increased risk of MACE. The combined detection of these biomarkers can effectively predict MACE, aiding in early identification and timely intervention for high-risk patients.

Keywords: ST-segment elevation myocardial infarction (STEMI), percutaneous coronary intervention (PCI), major adverse cardiovascular events (MACE), Kallikrein 1 (KLK1), SRY-box transcription factor 6 (SOX6), prediction model

Introduction

ST-segment elevation myocardial infarction (STEMI) is a severe form of coronary artery disease, characterized by acute ischemic necrosis of the myocardium due to reduced or interrupted blood flow in the coronary arteries [1-3]. This condition leads to prolonged ischemia, resulting in full-thickness or near-full-thickness myocardial necrosis, which can be life-threatening [4-6]. Percutaneous coronary intervention (PCI) is a critical treatment for STEMI, as it restores blood flow to the affected myocardium, thereby reducing myocardial damage and improving patient outcomes [7-9]. Despite its effectiveness, approximately 10% to 15% of STEMI patients still experience major adverse cardiovascular events (MACE) after PCI, increasing mortality risk [10].

Identifying reliable biomarkers to predict MACE is crucial for optimizing treatment strategies and improving patient survival and prognosis. Kallikrein 1 (KLK1) is a serine protease widely expressed in the cardiovascular system, particularly in renal and cardiac tissues. It plays a role in myocardial protection, vascular homeostasis, and the inhibition of cell apoptosis and fibrosis, potentially reducing myocardial hypertrophy and fibrosis associated with hyperten-

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sion [11]. SRY-box transcription factor 6 (SOX6) is involved in cardiomyocyte development and differentiation, promoting cell apoptosis during late-stage cardiomyocyte maturation, which can affect heart function recovery and prognosis [12].

This study is the first to systematically evaluate the combined application of KLK1 and SOX6 as biomarkers for predicting MACE. Our findings provide new tools for early identification of high-risk patients and lay the foundation for further exploration of their biological mechanisms and clinical applications.

Patient information

General information

A total of 150 STEMI patients who underwent PCI from October 2021 to October 2022 were retrospectively selected and divided into groups with and without MACE. The study was approved by the Institutional Review Board and Research Ethics Committee of the Affiliated Hospital of Hebei University.

Inclusion criteria: ① Patients met STEMI criteria as per relevant guidelines [13]; ② Patients were initially diagnosed with STEMI and received PCI within 12 hours after onset; ③ Preoperative angiography showed that myocardial infarction related artery stenosis ≥ 75% and postoperative thrombolytic flow grade ≥ 2; ④ Complete clinical data.

Exclusion criteria: ① Patients with history of thrombolysis or cardiopulmonary resuscitation; ② Complicated with other cardiac diseases; ③ Previous history of cardio-cerebrovascular diseases such as myocardial infarction or cerebral infarction; ④ Presence of autoimmune diseases; ⑤ Malignant tumors or hepatic and renal insufficiency; ⑥ Psychiatric disorders or coagulopathy.

Research methods

Assessment of postoperative MACE: Postoperative MACE in STEMI patients after PCI included acute myocardial infarction, recurrent angina pectoris, severe arrhythmia (e.g., ventricular fibrillation, ventricular tachycardia, third-degree atrioventricular block), acute heart failure, and stroke [14].

Data collection and routine index detection: (1) General information: Patient demographic and clinical information, including age, gender, medical history, and physical examination data, were collected. Upon admission, blood pressure and heart rate were measured in a quiet and peaceful environment. (2) Blood biochemical indicators: Peripheral venous blood (4-5 mL) was drawn from all patients at admission, placed in a sterile environment at room temperature for 1 hour, centrifuged at 3600 r/min for 15 minutes, and then stored in a refrigerator. Serum protein levels were detected using a double antibody sandwich method. Automatic blood biochemical analysis instrument (LH750, Beckman Coulter, USA) was used to detect blood biochemical indicators. Routine blood indexes included white blood cell (WBC), hemoglobin (Hb). Biochemical indicators included total cholesterol (TC) and SRY-box transcription factor 6 (SOX6) protein. Cardiac enzyme indexes included cardiac troponin I (cTnI), creatine kinase (CK), kallikrein 1 (KLK1), and creatine kinase isoenzyme (CK-MB). (3) Imaging data examination: All subjects underwent coronary angiography at admission, and the examination data included the number of diseased vessels, stent implantation, coronary Gensini score and Grace score.

According to the results of coronary angiography, the Gensini score was calculated blindly by two cardiologists [15]. The Gensini score is the sum of the stenosis degree score and the lesion location score for each diseased coronary artery vessel, with higher scores indicating more severe lesions. Stenosis degrees are scored as follows: ≤ 25% = 1 point, 26%-50% = 2 points, 51%-75% = 4 points, 76%-90% = 8 points, 91%-99% = 16 points, and complete occlusion = 32 points. The weighting factors for coronary artery segments are: left main coronary artery = 5, left anterior descending artery (proximal, mid, distal) = 2.5, 1.5, 1.0, respectively, circumflex artery (proximal = 2.5, mid-distal = 1.0), right coronary artery = 1.0, and minor branches = 0.5.

The Grace scoring system includes factors such as age, heart rate, systolic blood pressure, serum creatinine, elevated cardiac injury markers, electrocardiographic ST-segment deviation, pre-hospital cardiac arrest, and Killip class. The total score ranges from 1 to 375

Table 1. Comparison of general information between the non-MACE and MACE groups

Parameters	Non-MACE Group (n = 130)	MACE Group (n = 20)	t/χ^2	P
Age (years)	63.58 ± 5.31	64.44 ± 6.19	0.658	0.511
Gender [Male, %]	73 (56.15%)	11 (55.00%)	0.009	0.923
BMI (kg/m^2)	24.15 ± 3.24	24.26 ± 3.12	0.135	0.893
Hypertension [n (%)]	69 (53.08%)	10 (50.00%)	0.066	0.798
Diabetes [n (%)]	46 (35.38%)	7 (35.00%)	0.001	0.973
Hyperlipidemia [n (%)]	17 (13.08%)	2 (10.00%)	0.001	0.981
Stroke [n (%)]	12 (9.23%)	3 (15.00%)	0.160	0.689
Smoking history [n (%)]	48 (36.92%)	8 (40.00%)	0.070	0.791
Drinking history [n (%)]	28 (21.54%)	5 (25.00%)	0.003	0.954

Note: BMI: body mass index; MACE: Major Adverse Cardiovascular Events.

points, with a score < 109 indicating low risk, 109 to 140 indicating intermediate risk, and > 140 indicating high risk [16].

Observation indicators and test standards

For the post hoc analysis, G*Power 3.1.9.7 was utilized with the option "Means: Difference between two independent means (two groups)" selected under the t tests category. The analysis settings included a two-tailed test with an effect size of d = 0.7 and an alpha error probability of 0.05. After inputting the sample sizes for both groups, the test power (1 minus the beta error probability) was computed to be 0.825.

The data were analyzed using SPSS 26.0. Continuous data were presented as (Mean ± SD) and analyzed by t test. Categorical data were expressed as [n (%)] and analyzed using χ^2. Spearman's correlation was used to assess the relationship between indicators and MACE. Factors affecting MACE were examined using LASSO regression with R software (version 3.6.1) and the "glmnet" package (R Foundation for Statistical Computing, Vienna, Austria). The clinical value of blood biochemical indexes for predicting MACE was evaluated by Receiver Operating Characteristic (ROC). A *p*-value of < 0.05 was considered statistically significant.

Results

General information

A comparison of general information between the Non-MACE Group (n = 130) and the MACE Group (n = 20) revealed no significant differences in age, gender distribution, body mass index (BMI), prevalence of hypertension, diabetes, hyperlipidemia, stroke history, smoking history alcohol consumption ($P > 0.05$) (**Table 1**). This suggests that the differences in outcomes observed in this study are unlikely to be attributed to these baseline characteristics.

Disease-related characteristics

Disease-related characteristics are shown in **Table 2**. No significant differences were observed in systolic blood pressure, diastolic blood pressure, heart rate, or time from onset to PCI between the two groups ($P > 0.05$). Regarding in-hospital medication use, no significant differences were found in the use of aspirin, clopidogrel, nitrates, β-blockers, statins, or potassium-sparing diuretics ($P > 0.05$). However, a significant difference was observed in Killip grade distribution ($\chi^2 = 0.020$, $P = 0.020$). Specifically, a higher proportion of patients in the non-MACE group had Killip grade I, while the proportions of patients with Killip grades III and IV were higher in the MACE group compared to the non-MACE group. These results suggest that while most disease-related characteristics and in-hospital medication use were similar between the two groups, the MACE group presented with more severe heart failure at admission.

Blood biochemical indexes of the MACE group and non-MACE group

No significant differences were observed in WBC, Hb and TC levels ($P > 0.05$) (**Figure 1A-C**). However, significant differences were observed in several biomarkers. With levels of the following being significantly higher in the MACE group compared to the non-MACE group: SOX6 (856.34 ± 90.65 μg/L vs. 765.15 ± 60.38

Table 2. Comparison of disease-related characteristics between the two groups

Parameters	Non-MACE Group (n = 130)	MACE Group (n = 20)	t/χ^2	P
Systolic pressure (mmHg)	136.24 ± 23.15	136.48 ± 22.38	0.042	0.966
Diastolic pressures (mmHg)	80.15 ± 15.23	80.24 ± 13.46	0.026	0.979
Heart rate (bpm)	81.26 ± 16.34	80.23 ± 13.26	0.267	0.790
In-hospital medication use [n (%)]				
Aspirin	126 (96.92%)	18 (90.00%)	None	0.182
Clopidogrel	92 (70.77%)	14 (70.00%)	0.005	0.944
Nitrates	95 (73.08%)	13 (65.00%)	0.561	0.454
β-blockers	110 (84.62%)	18 (90.00%)	0.087	0.769
Statins	125 (96.15%)	19 (95.00%)	None	0.583
Potassium-sparing diuretics	65 (50.00%)	9 (45.00%)	0.173	0.677
Time from onset to PCI (hours)	6.69 ± 0.71	6.71 ± 0.72	0.129	0.898
Killip grade [n (%)]			None	0.020
I	109 (83.85%)	13 (65.00%)		
II	17 (13.08%)	3 (15.00%)		
III	3 (2.31%)	3 (15.00%)		
IV	1 (0.77%)	1 (5.00%)		

Note: MACE: Major Adverse Cardiovascular Events; PCI: percutaneous coronary intervention.

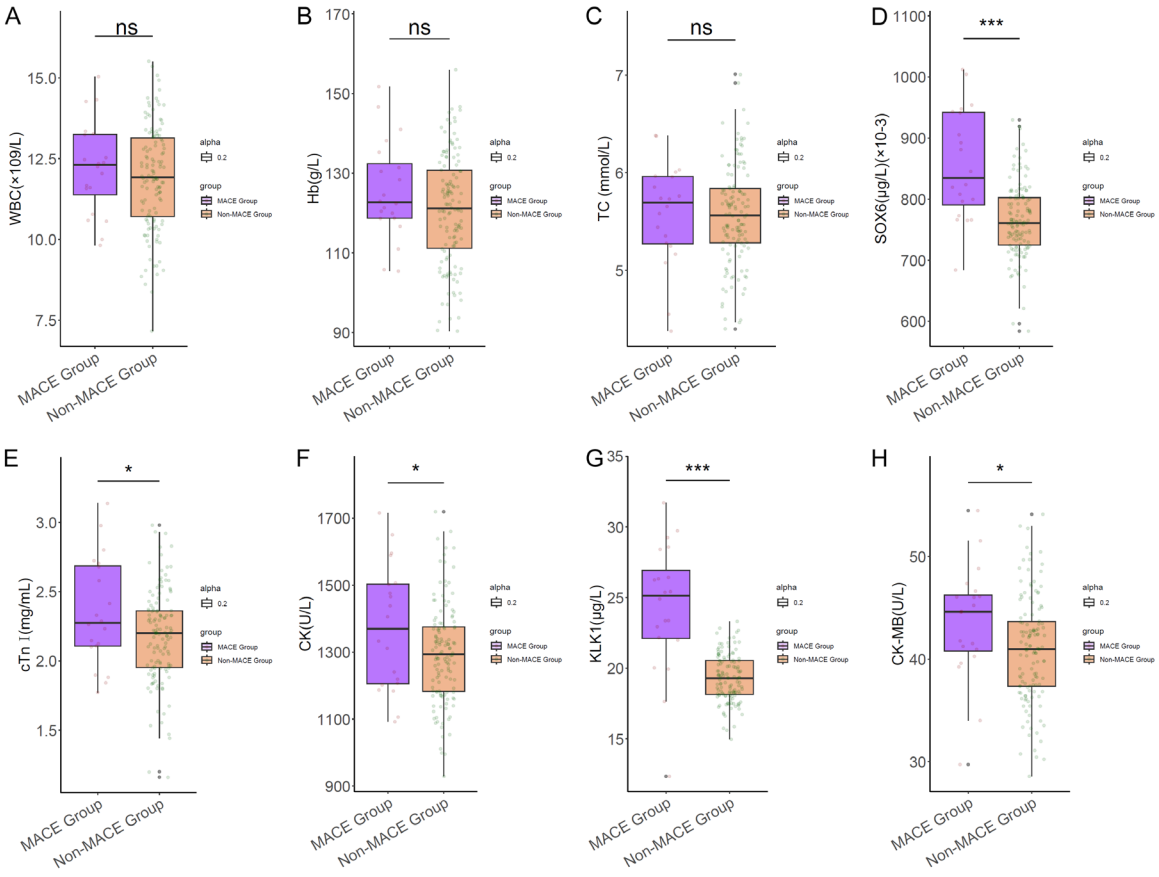

Figure 1. Comparison of blood biochemical indicators between the two groups. A. WBC; B. Hb; C. TC; D. SOX6; E. cTnI; F. CK; G. KLK1; H. CK-MB. *: P < 0.05, ***P < 0.001, ns: no significant difference. Note: WBC: white blood cell; Hb: hemoglobin; TC: total cholesterol; SOX6: SRY-box transcription factor 6; cTnI: cardiac troponin I; CK: creatine kinase; KLK1: kallikrein 1; CK-MB: creatine kinase isoenzyme.

Table 3. Comparison of imaging data between the two groups

Parameters	Non-MACE Group (n = 130)	MACE Group (n = 20)	t/χ^2	P
Number of diseased vessels [n (%)]	3 (2.31%)	2 (10.00%)	1.243	0.265
Number of stents implanted [n (%)]	3 (2.31%)	2 (10.00%)	1.243	0.265
Gensini score	43.52 ± 5.99	46.54 ± 6.61	2.072	0.040
Grace score	116.44 ± 14.68	123.84 ± 18.57	2.021	0.045

Note: MACE: Major Adverse Cardiovascular Events.

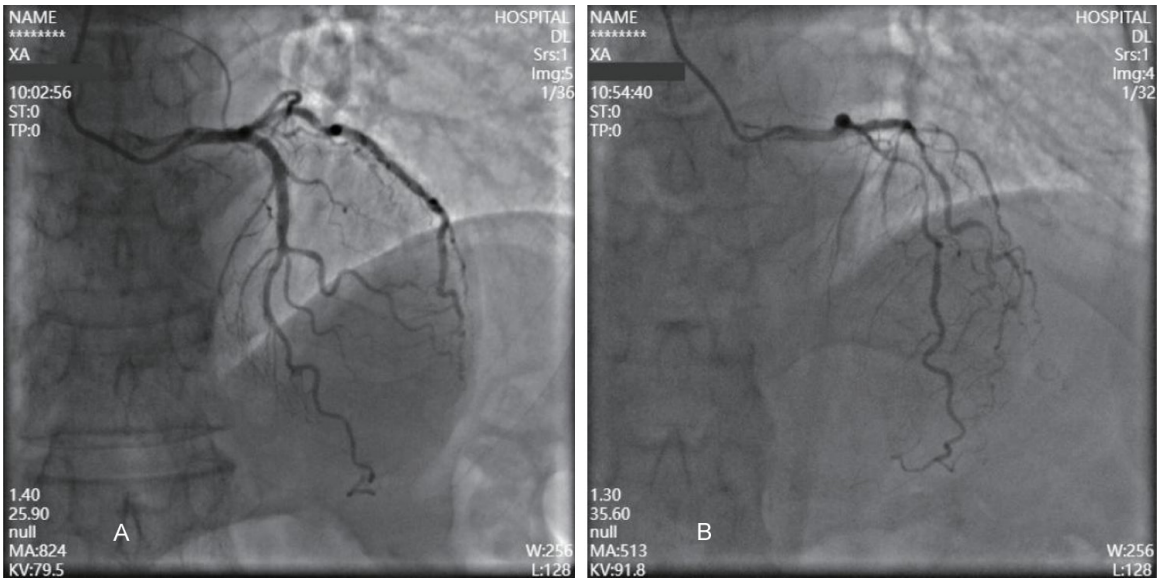

Figure 2. Coronary angiography images. A. Coronary angiography image of a patient in the non-MACE group, showing mild coronary artery stenosis. B. Coronary angiography image of a patient in the MACE group, showing severe coronary artery stenosis.

μg/L, t = 4.352, P < 0.001) (**Figure 1D**), cTnI (2.35 ± 0.39 mg/mL vs. 2.18 ± 0.33 mg/mL, t = 2.076, P = 0.04) (**Figure 1E**), CK (1371.19 ± 188.28 U/L vs. 1296.02 ± 148.13 U/L, t = 2.034, P = 0.044) (**Figure 1F**), KLK1 (24.31 ± 4.57 μg/L vs. 19.29 ± 1.67 μg/L, t = 4.857, P < 0.001) (**Figure 1G**) and CK-MB (43.49 ± 5.65 U/L vs. 40.92 ± 5.18 U/L, t = 2.041, P = 0.043) (**Figure 1H**). These results highlight the potential utility of these biomarkers in predicting and monitoring the risk of major adverse cardiac events.

Imaging data

A comparison of imaging data between the non-MACE and the MACE groups is shown in **Table 3** and **Figure 2**. No significant differences were observed in the number of diseased vessels or stents implanted (P > 0.05). However, the Gensini score (46.54 ± 6.61 vs. 43.52 ± 5.99, t = 2.072, P = 0.040) and the Grace score (123.84 ± 18.57 vs. 116.44 ± 14.68, t = 2.021, P = 0.045) were significantly higher in the MACE group compared to the non-MACE group. These findings suggest that patients in the MACE group had more severe coronary artery disease and a higher risk of adverse outcomes.

Correlation between indicators and MACE

Table 4 presents the correlation between various indicators and MACE. Killip grade was positively correlated with MACE (rho = 0.182, P = 0.025). SOX6 levels showed a strong positive correlation with MACE (rho = 0.358, P < 0.001), as did KLK1 levels (rho = 0.434, P < 0.001). CK-MB levels showed a positive correlation with MACE (rho = 0.172, P = 0.035). Additionally, the Gensini score exhibited a positive correlation with MACE (rho = 0.198, P = 0.015). In contrast, no significant correlations were observed between MACE and cTnI, CK or Grace score.

Table 4. Correlation between indicators and MACE

Parameters	rho	P
Killip grade [n (%)]	0.182	0.025
SOX6 (μg/L) (×10^{-3})	0.358	< 0.001
cTnI (mg/mL)	0.125	0.127
CK (U/L)	0.132	0.108
KLK1 (μg/L)	0.434	< 0.001
CK-MB (U/L)	0.172	0.035
Gensini score	0.198	0.015
Grace score	0.128	0.118

Note: MACE: Major Adverse Cardiovascular Events; SOX6: SRY-box transcription factor 6; cTnI: cardiac troponin I; CK: creatine kinase; KLK1: kallikrein 1; CK-MB: creatine kinase isoenzyme.

LASSO regression analysis

To analyze the predictive power of various parameters for MACE, LASSO regression analysis was conducted using MACE as the dependent variable and Killip grade, SOX6, KLK1, CK-MB, and Gensini score as independent variables (**Figure 3**). The analysis, which plotted the log(λ) on the x-axis and the prediction error on the y-axis, identified that the prediction error was minimized with two selected variables. The optimal predictors identified were SOX6 and KLK1, indicating that SOX6 and KLK1 are the most effective predictors for the occurrence of MACE.

Logistic regression analysis of influencing factors

The results of the logistic regression analysis for factors influencing MACE are presented in **Table 5**. Both SOX6 (OR = 1.015, P = 0.016) and KLK1 (OR = 1.823, P < 0.001) were identified as risk factors for the occurrence of MACE. These findings underscore the potential utility of SOX6 and KLK1 as valuable biomarkers for risk stratification and early intervention in patients at risk of MACE.

Clinical value of combined KLK1 and SOX6 indexes in predicting MACE

ROC analysis showed that the area under the curve (AUC) for predicting MACE were 0.804 for SOX6 and 0.868 for KLK1 when assessed individually (**Table 6**). When combined, the AUC increased to 0.889 (**Figure 4**), indicating that the combined diagnosis has a better predictive value.

Discussion

STEMI is one of the most severe conditions of acute coronary syndrome and represents the most critical clinical presentation of coronary heart disease. With the extension of life expectancy, the mortality of cardiovascular diseases in the elderly is gradually increasing [17]. PCI remains the most common and effective treatment for STEMI patients. However, STEMI patients have a risk of MACE after PCI, contributing to higher patient mortality [18, 19]. In clinical practice, timely and accurate screening can help mitigate the risk of MACE, providing valuable time for developing individualized prevention and treatment measures for high-risk patients. Studies have shown that changes in serum biomarkers reflect acute events such as vascular endothelial injury, platelet activation, aggregation, and thrombosis, which are integral to the progression of coronary atherosclerosis. These biomarkers can effectively predict the occurrence of postoperative MACE [20]. Therefore, identifying objective and reliable markers for predicting MACE risk is crucial for improving patient outcomes.

Some studies have shown that the incidence of STEMI is increasing with the aging of society and population [21, 22], and primary PCI has been recognized as the first choice for the treatment of STEMI. However, STEMI can result in a substantial thrombus load at the site of vascular injury, leading to slow flow or no-reflow phenomenon and increased perfusion malperfusion after primary PCI [23], which in turn heightens the risk of major adverse cardiovascular events. In this study, among the 150 STEMI patients, 20 experienced MACE after PCI, yielding an incidence of 13.33%, which is consistent with the 10%-15% incidence observed in other studies [18]. Analysis of blood biochemical indicators revealed that SOX6, cTnI, CK, KLK1, CK-MB, Gensini score and Grace score were significantly higher in the MACE group. Spearman correlation analysis showed that Killip grade, SOX6, KLK1, CK-MB and Gensini score were positively correlated with MACE. The Logistic analysis further indicated that KLK1 and SOX6 were the influencing factors of MACE. Additionally, LASSO regression analysis identi-

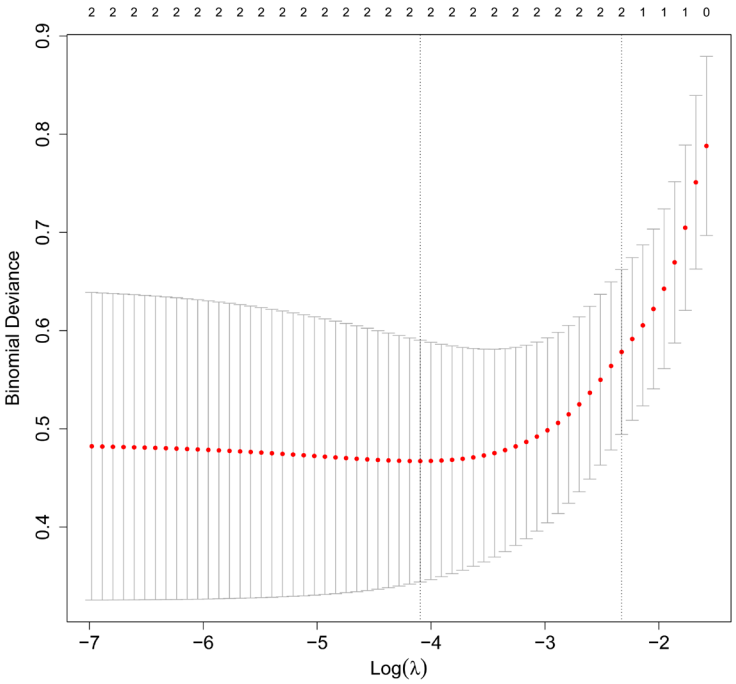

Figure 3. LASSO regression analysis. Note: LASSO: Least Absolute Shrinkage and Selection Operator.

Table 5. Logistic regression analysis of influencing factors

Factors	Std. Error	Wald χ^2	P	OR	95% CI
SOX6 (μg/L) (×10^{-3})	0.006	2.412	0.016	1.015	1.003-1.027
KLK1 (μg/L)	0.163	3.679	< 0.001	1.823	1.324-2.511

Note: SOX6: SRY-box transcription factor 6; KLK1: kallikrein 1; OR: odd ratio; CI: confidence interval.

Table 6. Diagnostic value of SOX6 and KLK1 for MACE

Indicators	AUC	Sensitivity	Specificity
SOX6 (μg/L) (×10^{-3})	0.804	0.950	0.562
KLK1 (μg/L)	0.868	0.800	0.946

Note: MACE: Major Adverse Cardiovascular Events; AUC: Area Under the Curve; SOX6: SRY-box transcription factor 6; KLK1: kallikrein 1.

fied SOX6 and KLK1 as key biomarkers for predicting MACE occurrence, with the prediction error minimized when only two variables were selected, indicating that these two biomarkers are the most effective predictors of MACE. The strength of LASSO regression lies in its ability to mitigate overfitting, thus providing a more robust predictive model. In our study, LASSO regression not only validated the results of the logistic regression analysis but also further emphasized the critical role of SOX6 and KLK1 in predicting MACE. Moreover, it helped eliminate variables that might seem significant in univariate analysis but contribute minimally to the model, thereby enhancing the simplicity and interpretability. These findings suggest that when the serum KLK1 and SOX6 levels are significantly increased in STEMI patients after PCI, timely preventive measures should be taken to reduce the risk of MACE, which could help in the recovery of myocardial function.

KLK1 is a serine protease presented in various tissues, including the kidneys and cardiovascular system. Previous studies have shown that KLK1 can generate bradykinin by catalyzing the conversion of kininogens, thereby performing multiple physiological functions [24]. Bradykinin has effects such as vasodilation, increased vascular permeability, inhibition of cell apoptosis, and anti-fibrosis, playing a crucial role in myocardial protection and angiogenesis. For example, a study demonstrated that KLK1 can promote the release of nitric oxide (NO) from endothelial cells by activating B2 receptors, thereby improving vascular endothelial function [25]. These findings are consistent with our study, suggesting a protective role for KLK1 in the occurrence of MACE.

SOX6, a member of the SOX transcription factor family, is primarily involved in the development and differentiation of cardiomyocytes. During the later stages of cardiomyocyte differentiation, SOX6 can promote cardiomyocyte apoptosis, affecting the recovery and prognosis of heart function. Existing studies have shown that SOX6 plays an important role in myocardial remodeling after myocardial infarction. For instance, one study found that overexpression of SOX6 leads to increased cardiomyocyte apoptosis, thereby exacerbating myocardial injury [26]. Another study indicated that SOX6

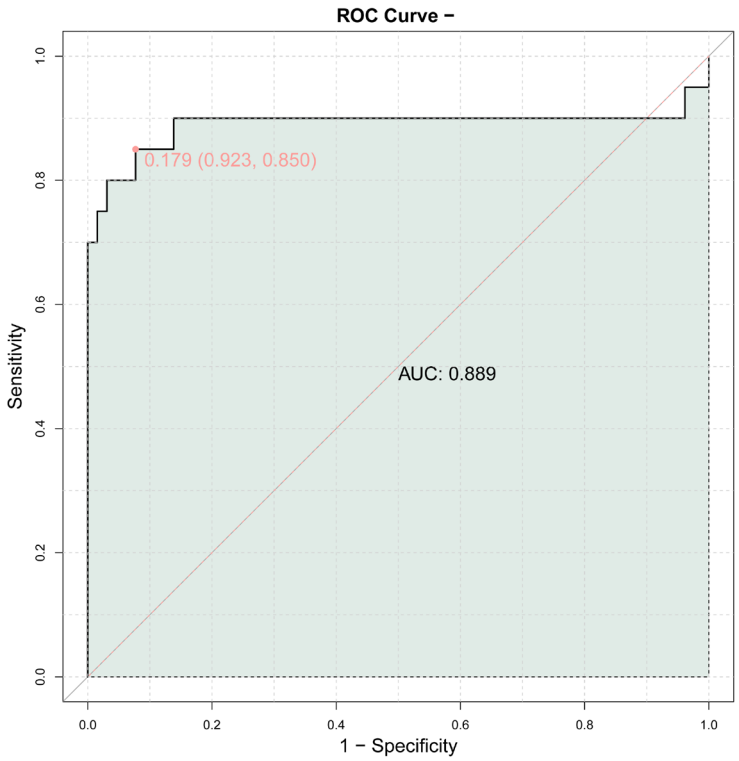

Figure 4. ROC curve of KLK1 combined with SOX6 in predicting the occurrence of MACE. Note: ROC: Receiver Operating Characteristic; MACE: Major Adverse Cardiovascular Events; SOX6: SRY-box transcription factor 6; KLK1: kallikrein 1; AUC: Area Under the Curve.

can influence cardiomyocyte proliferation and survival [27]. These findings align with our study, suggesting that SOX6 can serve as an effective predictive biomarker and therapeutic target for MACE.

Although previous studies have explored the roles of KLK1 and SOX6 in cardiovascular diseases, this study systematically evaluated the combined application of these two biomarkers in predicting MACE. In contrast, most existing studies focus on single markers and overlook their interactions. In this study, the AUC of KLK1 and SOX6 alone in predicting MACE was 0.868 and 0.804, respectively, and this value increased to 0.889 after their combination, indicating better predictive performance.

However, this study still has some limitations. First, the sample size was relatively small, especially for the MACE group. Larger sample sizes are needed in future studies to validate these findings. Additionally, the follow-up period was limited to the hospital stay. Long-term follow-up data will further verify the long-term validity of these biomarkers in predicting MACE. Furthermore, this study was a single-center study, which may introduce certain biases. Multi-center studies would enhance the generalizability and reliability of the results. Finally, this study primarily focused on SOX6 and KLK1. Future research could explore additional potential biomarkers to further improve the accuracy of predictions.

Conclusion

This study demonstrates that serum KLK1 and SOX6 levels are positively correlated with the occurrence of MACE in STEMI patients after PCI. The combined detection of these biomarkers offers a reliable and effective method for predicting MACE, providing clinicians with valuable tools for early identification and timely intervention in high-risk patients.

Disclosure of conflict of interest

None.

Address correspondence to: Yichao Zhang, Department of Cardiology, Affiliated Hospital of Hebei University, Baoding 071000, Hebei, China. E-mail: keaimao_123@yeah.net

References

[1] Frampton J, Devries JT, Welch TD and Gersh BJ. Modern management of ST-segment elevation myocardial infarction. Curr Probl Cardiol 2020; 45: 100393.
[2] Jolly SS and Nolan J. Radial first in ST-segment-elevation myocardial infarction. Circ Cardiovasc Interv 2021; 14: e010595.
[3] Shah T, Kapadia S, Lansky AJ and Grines CL. ST-segment elevation myocardial infarction: sex differences in incidence, etiology, treatment, and outcomes. Curr Cardiol Rep 2022; 24: 529-540.
[4] Birnbaum Y and Alam M. Is it ST-segment-elevation myocardial infarction? Tex Heart Inst J 2022; 49: e207545.

[5] Elendu C, Amaechi DC, Elendu TC, Omeludike EK, Alakwe-Ojimba CE, Obidigbo B, Akpovona OL, Oros Sucari YP, Saggi SK, Dang K and Chinedu CP. Comprehensive review of ST-segment elevation myocardial infarction: understanding pathophysiology, diagnostic strategies, and current treatment approaches. Medicine (Baltimore) 2023; 102: e35687.
[6] Mitsis A and Gragnano F. Myocardial infarction with and without ST-segment elevation: a contemporary reappraisal of similarities and differences. Curr Cardiol Rev 2021; 17: e230421189013.
[7] Davis MG and Blankenship JC. PCI for late STEMI: better late than never? Catheter Cardiovasc Interv 2023; 101: 11-12.
[8] Feistritzer HJ, Jobs A, de Waha-Thiele S, Eitel I, Freund A, Abdel-Wahab M, Desch S and Thiele H. Multivessel versus culprit-only PCI in STEMI patients with multivessel disease: meta-analysis of randomized controlled trials. Clin Res Cardiol 2020; 109: 1381-1391.
[9] Kastrati A, Coughlan JJ and Ndrepepa G. Primary PCI, late presenting STEMI, and the limits of time. J Am Coll Cardiol 2021; 78: 1306-1308.
[10] Yao W and Li J. Risk factors and prediction nomogram model for 1-year readmission for major adverse cardiovascular events in patients with STEMI after PCI. Clin Appl Thromb Hemost 2022; 28: 10760296221137847.
[11] Dai S, Yin B, Wang H and Zhang X. Imbalance between angiotensin II and Kallikrein in patients with ST-segment elevation myocardial infarction: a case-control emergency room study. Angiology 2024; 33197241232165.
[12] Wenxue J and Xiulan Q. Reducing heart failure in acute myocardial infarctionby downregulating SOX6 expression via nuclear Factor-κB. Altern Ther Health Med 2024; [Epub ahead of print].
[13] Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, Dendale P, Dorobantu M, Edvardsen T, Folliguet T, Gale CP, Gilard M, Jobs A, Jüni P, Lambrinou E, Lewis BS, Mehilli J, Meliga E, Merkely B, Mueller C, Roffi M, Rutten FH, Sibbing D and Siontis GCM; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2021; 42: 1289-1367.
[14] Huang L, Zhang J, Huang Q, Cui R and Chen J. In-hospital major adverse cardiovascular events after primary percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction: a retrospective study under the China chest pain center (standard center) treatment system. BMC Cardiovasc Disord 2023; 23: 198.
[15] Charach L, Blatt A, Jonas M, Teodorovitz N, Haberman D, Gendelman G, Grosskopf I, George J and Charach G. Using the Gensini score to estimate severity of STEMI, NSTEMI, unstable angina, and anginal syndrome. Medicine (Baltimore) 2021; 100: e27331.
[16] Chotechuang Y, Phrommintikul A, Kuanprasert S, Muenpa R, Ruengorn C, Patumanond J, Chaichuen T, Thanachaikun N, Benjanuwatra T and Sukonthasarn A. GRACE score and cardiovascular outcomes prediction among the delayed coronary intervention after post-fibrinolytic STEMI patients in a limited PCI-capable hospital. Open Heart 2020; 7: e001133.
[17] Terzian Z and Slama M. ST-elevation myocardial infarction (STEMI) in the elderly. Ann Cardiol Angeiol (Paris) 2018; 67: 417-421.
[18] Zhang Y, Yang Y, Xiao J, Sun Y, Yang S and Fu X. Effect of multidimensional comprehensive intervention on medication compliance, social function and incidence of MACE in patients undergoing PCI. Am J Transl Res 2021; 13: 8058-8066.
[19] Zhu XY, Yang DD, Zhang KJ, Zhu HJ, Su FF and Tian JW. Comparative analysis of four nutritional scores predicting the incidence of MACE in older adults with acute coronary syndromes after PCI. Sci Rep 2023; 13: 20333.
[20] Frank M, Sanders C and Berry BP. Evaluation and management of ST-segment elevation myocardial infarction in the emergency department. Emerg Med Pract 2021; 23: 1-28.
[21] Del Turco S, Basta G and Mazzone A. Different inflammatory profile in young and elderly STEMI patients undergoing primary percutaneous coronary intervention (PPCI): Its influence on no-reflow and mortality. Int J Cardiol 2020; 298: 17.
[22] Sheldon M and Blankenship JC. STEMI in nonagenarians: never too old. Catheter Cardiovasc Interv 2022; 100: 17-18.
[23] Suliman AA, Naseer N and Gersh B. Multivessel disease in STEMI patients: a perspective from limited-resource settings. Cardiovasc J Afr 2018; 29: 260-261.
[24] Tang L, Zhong X, Gong H, Tuerxun M, Ma T, Ren J, Xie C, Zheng A, Abudureheman Z, Abudukadeer A, Aini P, Yilamujiang S and Li L. Analysis of the association of ANO3/MUC15, COL4A4, RRBP1, and KLK1 polymorphisms with COPD susceptibility in the Kashi population. BMC Pulm Med 2022; 22: 178.
[25] Zhang M, Lin D, Luo C, Wei P, Cui K and Chen Z. Tissue kallikrein protects rat prostate against the inflammatory damage in a chronic autoimmune prostatitis model via restoring endothelial function in a bradykinin receptor B2-

dependent way. Oxid Med Cell Longev 2022; 2022: 1247806.
[26] Long R, Gao L, Li Y, Li G, Qin P, Wei Z, Li D, Qian C, Li J and Yang G. M2 macrophage-derived exosomes carry miR-1271-5p to alleviate cardiac injury in acute myocardial infarction through down-regulating SOX6. Mol Immunol 2021; 136: 26-35.
[27] Huang L, Yang L, Ding Y, Jiang X, Xia Z and You Z. Human umbilical cord mesenchymal stem cells-derived exosomes transfers microRNA-19a to protect cardiomyocytes from acute myocardial infarction by targeting SOX6. Cell Cycle 2020; 19: 339-353.