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Prognostic value of TIMI risk score combined with systemic immune-inflammation index and lipoprotein(a) in patients with ST-Segment elevation myocardial infarction after percutaneous coronary intervention

Yuankun Gu [a,b], Yu Zhang [a,b], Deshan Yao [a,b], Hui Shen [a,b], Xin Pan [a,b], Kaizheng Gong [a,b,1,*]

[a] Department of Cardiology, Affiliated Hospital of Yangzhou University, Yangzhou University, Yangzhou 225000, China
[b] Institute of Cardiovascular Disease, Yangzhou Key Lab of Innovation Frontiers in Cardiovascular Disease, Yangzhou 225001, China

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ABSTRACT

Background: Thrombolysis in Myocardial Infarction (TIMI) risk score in patients with ST-segment elevation myocardial infarction (STEMI) is associated with major adverse cardiovascular events (MACE). This study aimed to develop a prediction model based on the TIMI risk score for MACE in STEMI patients after percutaneous coronary intervention (PCI).

Methods: We conducted a retrospective data analysis on 290 acute STEMI patients admitted to the Affiliated Hospital of Yangzhou University from January 2022 to June 2023 and met the inclusion criteria. The primary endpoint was the occurrence of MACE. Multivariate logistic regression was used to identify independent predictors that could predict the likelihood of MACE, and R software was utilized to construct and validate the prediction model.

Results: Systemic immune-inflammation index (SII), lipoprotein(a) [Lp(a)], and TIMI risk score were identified as independent risk factors for MACE in STEMI patients ($p < 0.05$). A nomogram was constructed based on these factors. The area under the receiver operating characteristic curve values for the training and validation sets were 0.883 (95 % CI: 0.836–0.930) and 0.841 (95 % CI: 0.756–0.925), respectively. The calibration curves displayed a high consistency between prediction and observation in the training and validation sets. Additionally, decision curve analysis (DCA) demonstrated the clinical usefulness of the nomogram.

Conclusions: SII, Lp(a), and TIMI risk score are independent risk factors for MACE within one year in STEMI patients after PCI. Incorporating SII and Lp(a) into the TIMI risk score enhances the predictive value for adverse outcomes, thereby supporting healthcare professionals in clinical decision-making.

1. Introduction

Atherosclerotic cardiovascular disease (ASCVD) is a chronic metabolic disease characterized by chronic inflammation and lipid metabolism disorders [1,2]. As a fatal critical condition within ASCVD, acute ST-segment elevation myocardial infarction (STEMI) can be complicated by major adverse cardiovascular events (MACE), such as heart failure, cardiogenic shock, malignant arrhythmias, mechanical complications, and death, which are closely related to patient prognosis. Percutaneous coronary intervention (PCI) is the preferred treatment strategy for STEMI patients, as it can open the acute blocked coronary arteries and save ischemic cardiomyocytes. Although the treatment of STEMI patients has made great progress, the mortality remains high [3]. Therefore, early assessment and prediction of MACE incidence are crucial for improving patient prognosis [4].

The ST-elevation Thrombolysis in Myocardial Infarction (TIMI) risk score is an integer score derived from 8 differentially weighted indicators ascertained upon admission. TIMI risk score indicators (and

* Corresponding author at: Department of Cardiology, Affiliated Hospital of Yangzhou University, Yangzhou University. No. 368 Hanjiang Middle Rd, Yangzhou 225001, China.
E-mail address: yungkzh@163.com (K. Gong).
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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their associated point value) are age (2 points: 65–74 years, 3 points: 75 years and older), history of angina, diabetes, or hypertension (1 point), admission systolic blood pressure <100 mm Hg (3 points), admission heart rate >100 beat/min (2 points), admission Killip class II to IV (2 points), admission weight <67 kg (1 point), anterior infarction or left bundle-branch block (1 point), and time to reperfusion therapy >4 h among patients who received reperfusion therapy (1 point). Previous studies have shown that the TIMI risk score has a predictive value for the occurrence of MACE in STEMI patients [5]. However, the TIMI risk score excludes biomarkers reflecting inflammation and lipid metabolism, and its predictive efficacy remains controversial compared to other commonly used scores.

Recent studies on inflammation-related hematological markers as an indirect reflection of systemic inflammation reveal the significant association between the systemic immune-inflammation index (SII, platelet count × neutrophil count/lymphocyte count) and the prognosis of certain cardiovascular diseases [6,7]. SII was closely linked with increased cardiovascular mortality in the general population [8]. Moreover, a higher SII was significantly associated with an increased risk of cardiovascular diseases [9]. Lipoprotein(a)[Lp(a)] is a complex of apolipoprotein(a) and low-density lipoprotein, which is a strong independent cardiovascular risk factor [10], and its levels are closely related to the occurrence and development of coronary heart disease and myocardial infarction.

This study aims to incorporate SII and Lp(a) into the TIMI risk score to improve the predictive value of the TIMI risk score for MACE in STEMI patients, providing a reference for early identification, treatment plan optimization, and prognosis improvement of high-risk STEMI patients.

2. Methods

2.1. Study design and participants

Fig. 1 shows the flow diagram of our study. This study retrospectively analyzed 290 patients diagnosed with STEMI from the Cardiology Department of the Affiliated Hospital of Yangzhou University from January 2022 to June 2023. The inclusion criteria were as follows: (1) age ≥ 18 years; (2) symptoms of chest pain >30 min in the 24 h prior to admission; (3) ECG indicates ST-segment elevation and/or abnormal Q wave in two or more adjacent leads and new left bundle branch block; (4) serum myocardial markers cardiac troponin T (cTnT) and/or creatinine kinase-myocardial band isoenzyme (CK-MB) are positive within 24 h of the onset of chest pain symptoms; (5) received standardized treatment according to relevant clinical guidelines and underwent PCI within 12 h. The exclusion criteria were: (1) incomplete data; (2) presence of other serious heart diseases such as valvular heart disease, infectious endocarditis, or cardiomyopathy; (3) acute infectious diseases within the previous 3 months; (4) renal insufficiency (GFR<30 mL/min); (5) chronic inflammatory diseases, including hematologic disorders, tumors, and rheumatic immune system diseases; (6) history of glucocorticoid use; (7) previously undergone PCI; (8) pregnancy or breastfeeding. Finally, 290 patients met the inclusion criteria and were included in the study.

2.2. Clinical data collection and collation

Clinical basic information on patients was obtained through the hospital's electronic medical record system, and laboratory test data was collected through the clinical examination system. The clinical information specifically included gender, age, height, weight, body mass index (BMI), medical history, in-hospital conditions, laboratory tests, echocardiography, the occurrence of MACE within one year of onset, and the calculation of the patient's TIMI risk score. Laboratory tests were conducted immediately upon admission or the following morning with fasting peripheral venous blood samples being taken, and echocardiography results were completed and recorded within two days of admission. The outcome events of this study included the occurrence of MACE within one year of onset, including cardiac death, cardiogenic shock, arrhythmias (including ventricular tachycardia /ventricular fibrillation, atrial fibrillation), cardiac arrest, cardiac rupture, and bleeding events.

2.3. Sample size evaluation and statistical analysis

A sample size of at least 34 cases (17 MACE and 17 non-MACE) was required in the training and validation sets according to the following hypothesis: power, 90 %; two-sided significance level, 0.05; alternative hypothesis of the area under the curve (AUC), 0.8 compared with the null hypothesis of the AUC, 0.5, and the allocation of the positive group was equal to that of negative group. Therefore, the sample size of 203 cases (78 MACE and 125 non-MACE) in the training set and 87 cases (37 MACE and 50 non-MACE) in the validation set were sufficient to detect an AUC difference of 0.5 with 90 % power if the true AUC was >0.8.

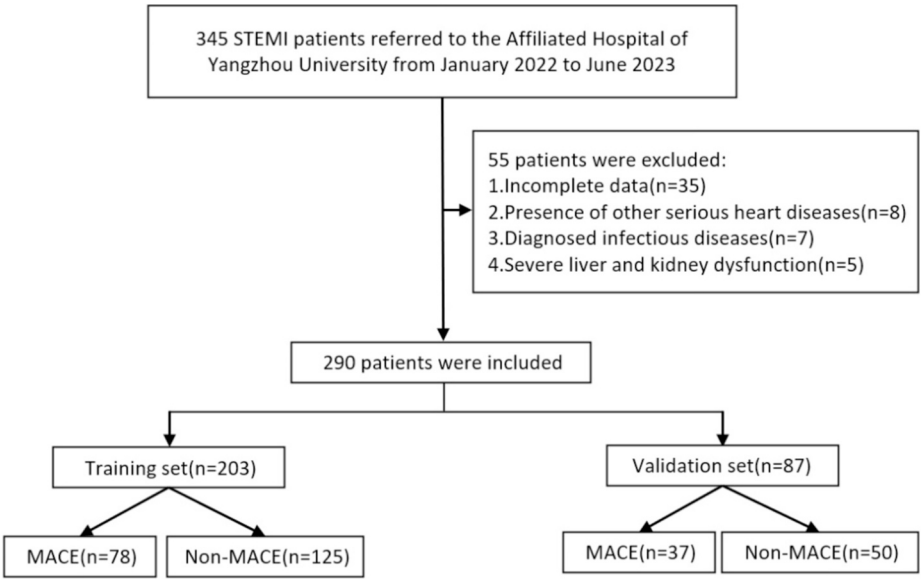

Fig. 1. Study flow diagram.

Statistical analyses were performed using PASS (version 2021). Consequently, patients were randomly divided into a training set (203 cases, used to build the model) and a validation set (87 cases, used for internal model validation) in a ratio of 7:3.

Statistical analyses of the study results were carried out using R 4.3.1 and SPSS 26.0 software. The normal distribution of continuous variables was expressed as mean ± standard deviation ($\bar{x} \pm s$), and comparisons between two groups were conducted using an independent sample *t*-test. The skewed distribution of continuous variables was expressed as median (25th percentile, 75th percentile) and was analyzed by the Mann–Whitney *U* test. Categorical variables were expressed as frequencies (%), and two groups were compared using the $\chi 2$ test or Fisher's exact test. Univariate and multivariate logistic regression models were used to analyze the influencing factors of MACE. A predictive model was constructed based on the results of multivariate logistic regression, and a nomogram for individualized prediction of MACE risk was drawn using the "rms" package. In both the training and validation sets, the area under the receiver operating characteristic (ROC) curve, calibration curves, and decision curve analysis (DCA) were used to evaluate the discrimination, calibration, and clinical utility of the nomogram. DeLong's test was used for comparisons between ROC curves, and the maximum Youden index (Youden index = sensitivity + specificity − 1) was employed to determine the optimal positive cutoff value. P-value < 0.05 was considered statistically significant.

3. Results

3.1. Baseline patient characteristics

According to the inclusion and exclusion criteria, 290 STEMI patients were included in this study, with 203 forming the training set and 87 forming the validation set. The training set consisted of 167 patients (82.3 % males), and the median TIMI score was 4. Among the set, 78 (38.4 %) patients experienced MACE. Similarly, in the validation set, there were 74 (85.1 %) male patients, 37 (42.5 %) of whom experienced MACE, and the median TIMI score was 5. The past medical history and in-hospital conditions are shown in Table 1. Statistical analysis of baseline data revealed no significant differences between the training and validation sets ($p > 0.05$) (Table 1).

3.2. Clinical characteristics

In the training set, there were 78 cases in the MACE group and 125 cases in the non-MACE group. The age, Killip classification, WBC, NEUT, hs-CRP, Lp(a), SII, and TIMI scores of the MACE group were significantly higher than those of the non-MACE group, while LVEF, LYMPH, and Hb were significantly lower ($p < 0.05$). In the validation set, there were 37 cases in the MACE group and 50 cases in the non-MACE group. Similarly, the age, systolic blood pressure, WBC, NEUT, creatinine, hs-CRP, Lp(a), SII, and TIMI scores of the MACE group were significantly higher than those of the non-MACE group, while LVEF and TG were significantly lower ($p < 0.05$). These findings consistently underscore the distinct clinical and biochemical profile of the MACE group compared to the non-MACE group (Table 2).

Table 1
Baseline Patient Characteristics.

Characteristics	Training Set (N = 203)	Validation Set (N = 87)	P-value
Sex, N(%)			0.682
Male	167(82.3)	74(85.1)	
Female	36(17.7)	13(14.9)	
Age, years	63.0(53.0–72.0)	63.0(53.0–73.0)	0.960
BMI, kg/m^2	24.7 ± 3.32	24.2 ± 3.61	0.238
Medical history			
Hypertension, N(%)	126(62.1)	57(65.5)	0.671
Diabetes, N(%)	69(34.0)	21(24.1)	0.128
Cerebral infarction, N(%)	19(9.36)	3(3.45)	0.134
In-hospital conditions			
SBP, mmHg	127(112–146)	125(117–138)	0.447
DBP, mmHg	79.0(71.0–90.0)	80.0(73.0–88.0)	0.763
Heart rate, bpm	78.0(68.0–88.5)	80.0(69.5–89.0)	0.224
LVEF (%)	62.0(55.0–65.0)	60.0(55.0–63.0)	0.063
Killip class ≥ 2, N(%)	46(22.7)	22(25.3)	0.739
TIMI	4.0(3.0–6.0)	5.0(3.0–6.0)	0.416
MACE, N(%)	78(38.4)	37(42.5)	0.600

3.3. Independent predictors of MACE

After excluding WBC, NEUT, and LYMPH according to collinearity, the remaining indicators were included in univariate and multivariate logistic regression analyses, and the occurrence of MACE was considered the dependent variable. The results of univariate logistic regression analysis showed that age, Killip classification, hs-CRP, LVEF, Hb, Lp(a), SII, and TIMI score were significantly associated with MACE ($p < 0.05$). Multivariate logistic regression analysis demonstrated that SII, Lp(a), and TIMI score were independent risk factors for MACE in STEMI patients ($p < 0.05$) (Table 3).

3.4. Predictive nomogram development

Based on the results of the multivariate logistic regression analysis, SII, Lp(a), and TIMI scores were utilized to construct a nomogram, which provided an individualized prediction of the risk of MACE in STEMI patients. Each of these independent predictors was projected upward to the value of the "points" at the top level of the nomogram to obtain a score within the range of 0 to 100. The scores for all variables were then summed to obtain the total score, and a vertical line was projected downward from that value on the "total points" row to the "risk" row to indicate the risk of MACE. The total score of the nomogram ranged from 32 to 70 points, corresponding to a 10 % to 90 % risk of MACE in STEMI patients. Therefore, the nomogram can predict MACE for individual patients based on their medical condition (Fig. 2).

3.5. Validation of the nomogram

The AUC of the nomogram was 0.883 (95 % CI: 0.836–0.930), with the maximum Youden index being 0.640. This resulted in the optimal cut-off value for the nomogram at 37.1 %. At this cut-off value, the prediction accuracy of the nomogram was the best, with a diagnostic sensitivity of 80.8 % and a specificity of 83.2 %. Furthermore, it is noteworthy that the AUC of the model for predicting MACE was significantly higher than that of the TIMI score (0.883 vs. 0.797, $p < 0.05$) (Fig. 3a). Internal validation using the validation set showed an AUC of 0.841 (95 % CI: 0.756–0.925) for the nomogram. These findings indicated that the nomogram had good discriminative ability and distinction in both the training and validation sets. Furthermore, there was no statistically significant difference in the predictive performance between the training and validation sets (0.883 vs. 0.841, $p > 0.05$) (Fig. 3b).

The calibration curve was plotted to evaluate the calibration of the model after 1000 bootstrap resamples. For the training set, the Brier score of the calibration curve was 0.135, while the Brier score was 0.156 in the validation cohort, indicating that the model's calibration was satisfactory in both groups. Specifically, the predicted probability of MACE occurrence in STEMI patients is highly consistent with the actual occurrence probability. Overall, the calibration of this nomogram is strong (Fig. 4).

Using high-risk threshold probabilities as the horizontal axis and clinical net benefit as the vertical axis, DCA was plotted. The net benefit threshold probability intervals in the training and validation sets were 3–1 % and 4–100 %, which suggested that when the risk probability of MACE in STEMI patients fell within the net benefit threshold probability

Table 2
Clinical Characteristics in the training and validation set.

ariables	Training Set (n = 203)			Validation Set (n = 87)		
	MACE (n = 78)	Non-MACE (n = 125)	P value	MACE (n = 37)	Non-MACE (n = 50)	P value
Age, years	65.4 ± 13.7	61.5 ± 11.6	0.036	68.6 ± 14.1	58.7 ± 13.3	0.001
Male	63(80.8)	104(83.2)	0.801	30(81.1)	44(88.0)	0.555
BMI, kg/m^2	24.6 ± 3.70	24.8(3.07)	0.652	23.6 ± 3.92	24.6 ± 3.34	0.197
SBP, mmHg	125(114–146)	128(112–146)	0.473	126(122–142)	122(111–130)	0.049
DBP, mmHg	78.0(68.2–89.8)	80.0(72.0–90.0)	0.374	80.0(74.0–90.0)	79.5(72.2–86.0)	0.478
Heart rate, bpm	78.5(69.0–88.2)	77.0(68.0–88.0)	0.289	83.8(18.2)	79.5(14.1)	0.240
Hypertension	53(67.9)	73(58.4)	0.224	24(64.9)	33(66.0)	1.000
Diabetes	26(33.3)	43(34.4)	0.997	8(21.6)	13(26.0)	0.827
Cerebral infarction	9(11.5)	10(8.00)	0.552	3(8.11)	0(0.00)	0.073
LVEF (%)	60.0(49.2–64.0)	63.0(57.0–66.0)	0.005	58.0(48.0–62.0)	61.0(57.2–63.0)	0.046
Killip class ≥ 2	26(33.3)	20(16.0)	0.007	13(35.1)	9(18.0)	0.117
WBC,×10^9/L	10.9(8.85–12.4)	9.00(7.61–10.7)	<0.001	11.2(9.71–12.0)	8.86(8.05–10.7)	0.001
NEUT,×10^9/L	8.63(6.82–10.3)	6.78(5.24–8.00)	<0.001	8.85(7.62–10.0)	6.62(5.70–7.80)	<0.001
LYMPH,×10^9/L	1.36(0.97–1.69)	1.57(1.27–1.94)	0.001	1.52(1.24–1.82)	1.67(1.29–2.50)	0.089
Hb, g/L	134(117–150)	143(132–152)	0.002	142(114–149)	148(133–156)	0.059
PLT,×10^9/L	222(176–280)	216(175–247)	0.130	203(180–234)	220(196–251)	0.226
hs-CRP, mg/L	5.24(2.31–26.3)	2.69(0.82–6.66)	0.001	5.10(2.21–14.9)	1.74(0.84–5.64)	0.010
Glu, mmol/L	7.53(6.32–11.4)	8.04(6.37–10.5)	0.575	8.07(6.32–10.2)	8.55(6.67–10.4)	0.628
Cr, μmol/L	77.6(64.7–100)	72.0(58.2–83.2)	0.010	88.4(73.2–103)	72.8(58.6–87.1)	0.001
UA, mmol/L	350(288–422)	347(287–406)	0.763	388(95.2)	359(99.5)	0.174
TC, mmol/L	4.43(3.79–5.24)	4.42(3.69–4.95)	0.471	4.43(1.30)	4.52(0.99)	0.734
TG, mmol/L	1.32(1.02–1.83)	1.57(1.08–2.21)	0.082	1.22(0.85–1.86)	1.65(1.15–2.49)	0.018
HDL, mmol/L	1.07(0.86–1.21)	1.02(0.86–1.19)	0.433	0.98(0.25)	1.01(0.25)	0.571
LDL, mmol/L	2.84 ± 0.87	2.74 ± 0.84	0.426	2.70 ± 1.00	2.58 ± 0.80	0.554
Lp(a), mg/L	241(101–397)	97.2(46.7–208)	<0.001	190(131–295)	101(46.5–208)	0.001
hsTnT, pg/ml	8475.9(3576.1–26673)	8056.7(3005.0–22604.5)	0.130	10135.5(3215.6–26673.0)	7732.4(910.37–25609.5)	0.379
NT-proBNP, pg/ml	3479.1(553.7–22546.5)	1368.0(160.9–17355.5)	0.101	3500(1941.5–25822)	2122.3(658.6–24998.0)	0.095
SII	1397(1100–1844)	905(587–1192)	<0.001	1236(902–1702)	822(672–953)	<0.001
TIMI	6.0(5.0–7.0)	3.0(2.0–5.0)	<0.001	6.0(5.0–7.0)	4.0(2.0–5.0)	<0.001

Table 3
Univariate and multivariate logistic regression analysis of the result of MACE incidence in the training set.

Variable	Univariate Logistic Regression			Multivariate Logistic Regression		
	OR	95 %CI	P value	OR	95 %CI	P value
Age	1.026	1.002–1.050	0.031	0.981	0.947–1.017	0.302
LVEF	0.950	0.918–0.984	0.004	0.963	0.919–1.009	0.112
Killip class ≥ 2	2.625	1.342–5.135	0.005	1.866	0.733–4.753	0.191
Hb	0.980	0.966–0.995	0.009	1.008	0.988–1.028	0.445
hs-CRP	1.012	1.001–1.022	0.026	1.000	0.989–1.012	0.949
Lp(a)	1.002	1.000–1.003	0.008	1.002	1.001–1.004	0.003
SII	1.002	1.001–1.002	< 0.001	1.002	1.001–1.002	< 0.001
TIMI	1.771	1.481–2.119	< 0.001	1.997	1.530–2.607	< 0.001

interval, the clinical net benefit level of using this nomogram is remarkably better than the “no intervention” and “full intervention” treatment strategies. Therefore, the wide range of alternative threshold probability intervals indicated decent clinical utility of this nomogram (Fig. 5).

4. Discussion

STEMI is a critical cardiovascular emergency with high mortality rates both in-hospital and out-of-hospital, imposing a serious burden on families and society. Over the past few decades, the in-hospital mortality rate of STEMI has significantly decreased. This improvement is mainly attributed to the widespread use of early PCI, the establishment of coronary care units, and advances in modern medicine [11–13]. Despite these advancements, STEMI still exhibits a high mortality rate, and the survival rates remain suboptimal [14]. Current statistics indicate that the one-year mortality rate for STEMI patients is as high as 10 % [15]. The prevention and treatment of complications related to STEMI patients remain key focus areas in the cardiovascular field. With the advent of precision medicine strategies, gaining a comprehensive understanding of the likelihood of cardiovascular events in patients is essential for optimizing treatment strategies. The scoring items of the TIMI risk score are based on easily accessible in-hospital data, allowing for quick completion after admission, which are simple to calculate and widely used in extremely high-risk cardiovascular diseases like STEMI [16,17]. Additionally, the TIMI risk score can accurately predict short-term and long-term mortality, as well as the incidence of MACE in acute coronary syndrome (ACS) patients [17]. Consequently, this study aims to construct a clinical prediction model based on the TIMI risk score.

Inflammation and platelet activation are critical in the onset and prognosis of STEMI. ASCVD is a chronic inflammatory condition in which inflammatory responses permeate the entire pathological process of atherosclerosis, from fatty streak formation to plaque rupture during STEMI onset [18]. Moderate inflammatory responses are essential for the repair of damaged myocardial tissue, whereas excessive inflammatory responses can accelerate apoptosis and necrosis of myocardial cells [19]. Inflammatory cells play a crucial role in this process. Specifically, leukocytes and their subtypes are widely applied as inflammatory markers to predict cardiovascular outcomes in patients with myocardial infarction. Neutrophils play a critical role in the immune-inflammatory response leading to atherosclerosis, and their concentration is closely related to the incidence of adverse cardiac events [20]. Studies have shown that lymphocytes have pro-atherosclerotic and anti-atherosclerotic protective effects [21]. As a result, lymphopenia is

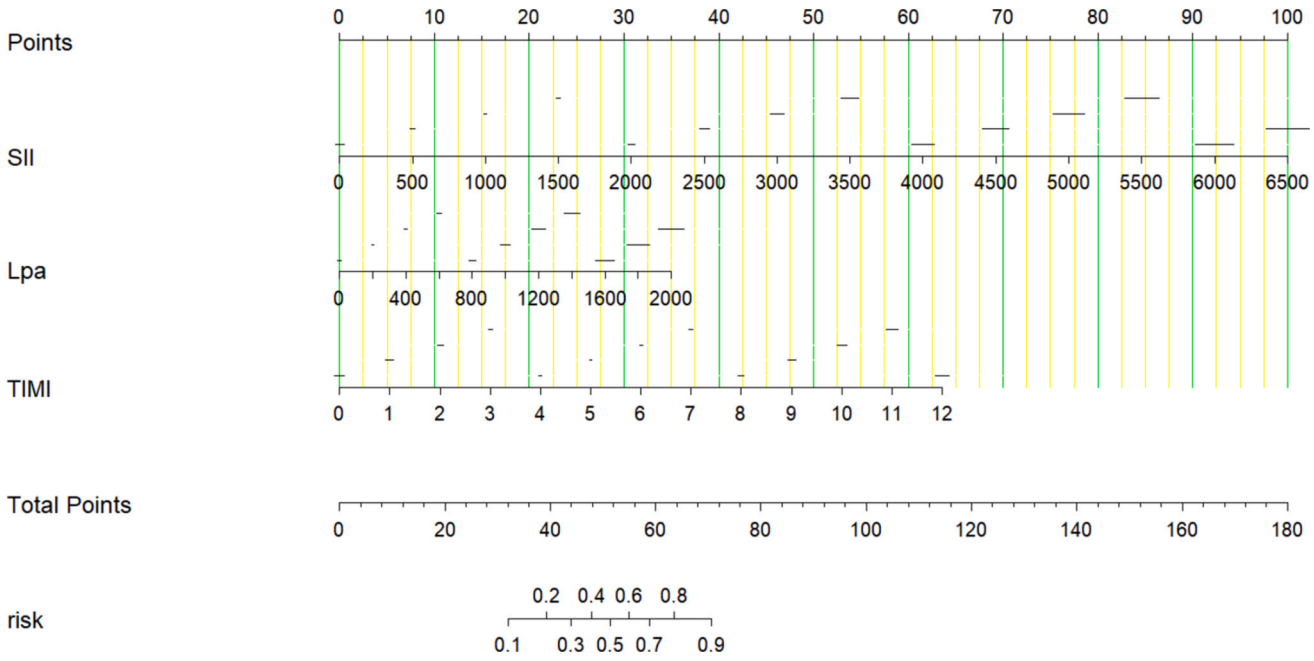

Fig. 2. Nomogram used for predicting MACE in STEMI patients. The final score (total points) is calculated as the sum of the individual scores of each of the three variables included in the nomogram. Abbreviations: SII, Systemic immune-inflammation index; Lp(a), Lipoprotein-a; TIMI, Thrombolysis in Myocardial Infarction.

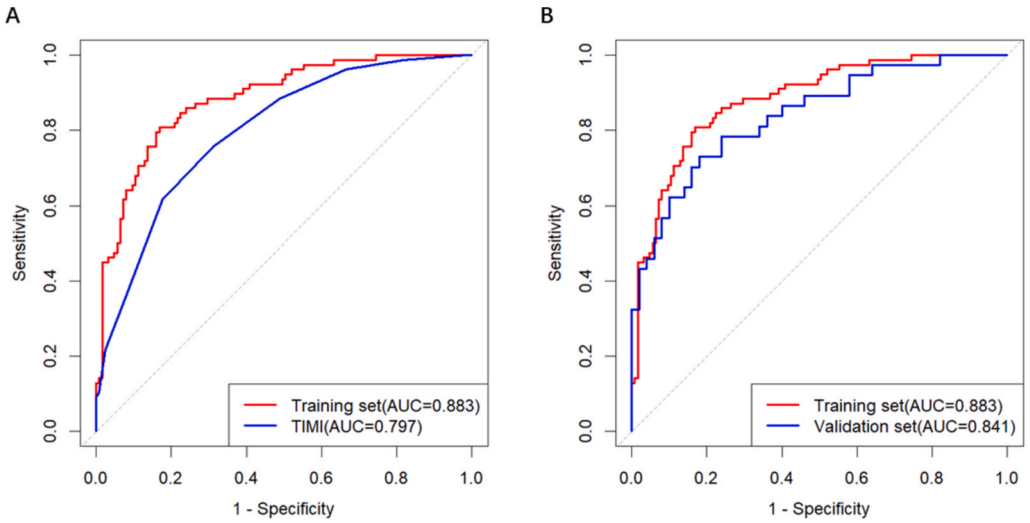

Fig. 3. (A) ROC curves of the nomogram and TIMI score for predicting the risk of MACE in STEMI patients; (B) ROC curves of the training set and validation set for predicting the risk of MACE in STEMI patients. Abbreviations: AUC, the area under the ROC curve; ROC, receiver operating characteristic.

considered a risk factor for cardiovascular events to some extent. Additionally, platelets are not only involved in acute thrombotic vascular occlusion but also in chronic inflammation present in the early vascular wall, which may contribute to the instability of late-stage atherosclerotic lesions [22]. Consequently, SII is one of the new inflammatory markers that combine platelets with other inflammatory indicators. Research has indicated that elevated levels of SII are independently linked to cardiovascular incidents after STEMI [23].

Furthermore, SII serves as a more effective predictor of serious cardiovascular events compared to conventional indicators [24] and has shown identified application value in both acute and chronic cardiovascular diseases. Dziedzic et al. [25] reported that SII levels were higher in patients with ACS than in those with stable coronary artery disease. Additionally, compared to patients with single-vessel disease, those with multivessel disease had higher SII levels. This study concluded the linear relationship of SII with the severity of ACS. A recent survey conducted by Ozan Tezen et al. [26] examined the relationship between contrast-induced nephropathy (CIN) development and SII in non-ST-segment elevation myocardial infarction patients, which confirmed that high SII levels were associated with an increased risk of CIN. SII is involved in various aspects of the development of coronary artery disease. In heart failure (HF), SII has predictive value for both the occurrence and prognosis of HF. A retrospective study involving 4606 patients with congestive heart failure (CHF) found that high SII levels in CHF patients were associated with higher short-term mortality and the occurrence of MACE [27]. Mert İlker Hayıroğlu et al.'s study further confirmed that SII may be an independent predictive marker for long-term mortality and appropriate implantable cardioverter defibrillator therapy in patients with heart failure with reduced ejection fraction [28]. In the future, SII is expected to play a role in evaluating drug efficacy and guiding individualized treatment strategies.

Lp[a] is a low-density lipoprotein (LDL) cholesterol-like particle that

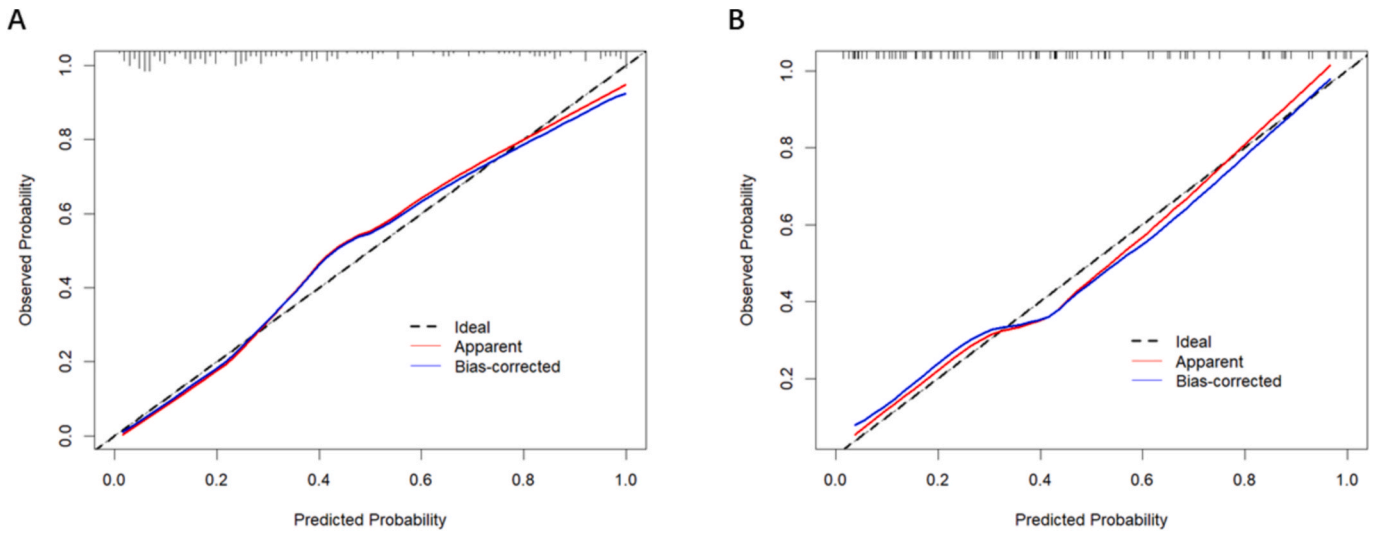

Fig. 4. Calibration curve of the nomogram for the training set (A) and the validation set (B). The X-axis represents the overall predicted probability of MACE and the Y-axis represents the actual probability. Model calibration is indicated by the degree of fitting of the curve and the diagonal.

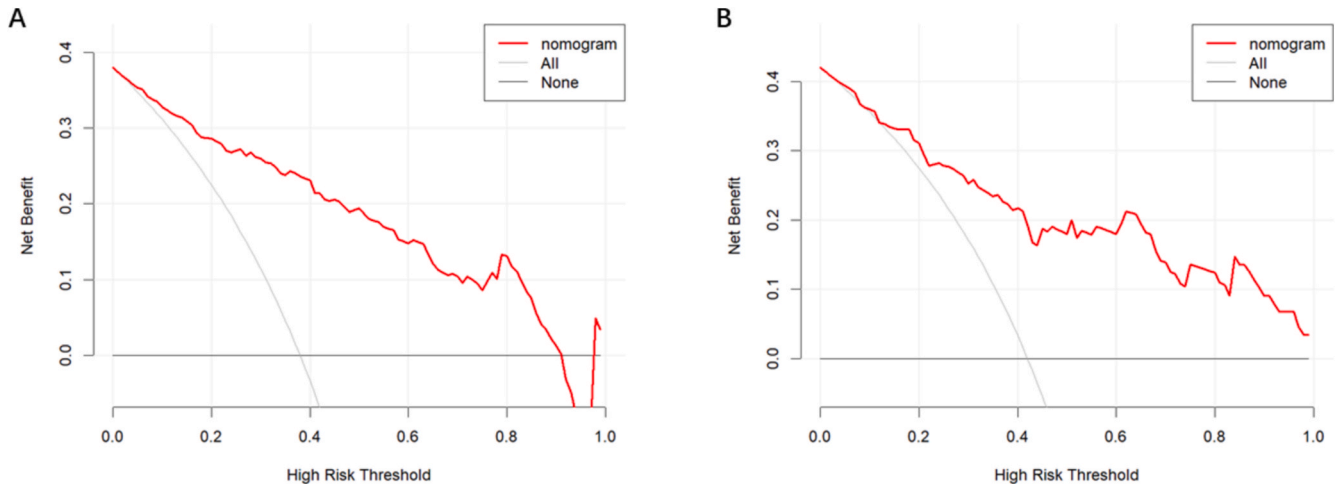

Fig. 5. Decision curve analysis for the training set (A) and the validation set (B). A horizontal line indicates that all samples are negative and not treated, with a net benefit of zero. An oblique line indicates that all samples are positive. The net benefit has a negative slope.

binds to apolipoprotein(a) [29], functioning as a pathogenic lipoprotein in the body [30]. Its concentration is largely determined by genetics and shows significant variation among different populations [31]. The oxidized LDL-C (oxLDL-C) component of Lp(a) has multiple pro-atherosclerotic effects, including vascular smooth muscle cell proliferation and foam cell formation [32,33]. Furthermore, some studies have shown that Lp(a) promotes platelet activation and aggregation and the progression of vulnerable plaques, ultimately leading to atherothrombotic events [34,35]. In particular, the predictive value of plasma Lp(a) levels, independent of other lipoproteins (such as LDL-C), has attracted considerable attention from researchers in recent years [36]. Many studies have indicated that higher plasma concentrations of Lp(a) are associated with an increased risk of myocardial infarction [37,38].

Currently, several risk scores are available for assessing the prognosis of ACS patients, including TIMI risk score, GRACE risk score, SYNTAX score, and Intermountain Risk Score (IMRS). The TIMI risk score is straightforward, easy to use, and allows for rapid risk assessment, which has been widely validated and applied in clinical practice. However, it eliminates key prognostic indicators, such as inflammatory status and metabolic conditions. The GRACE score has broad applicability and can be used for various types of acute coronary syndromes, including STEMI and Non-ST-Elevation Acute Coronary Syndrome. Nevertheless, it is relatively complex to calculate and involves tests like blood creatinine and myocardial enzymes, which may delay the acquisition of results [39]. Compared to the first two scores, the IMRS predicts mortality risk by incorporating routine biochemistry and complete blood count data with the patient's age and sex. Previous studies demonstrate that the predictive value of the IMRS for overall mortality in patients with STEMI is comparable to the first two scores [40], and it also has prognostic significance for both short- and long-term mortality in patients with cardiogenic shock [41]. The SYNTAX score mainly evaluates factors such as the number, type, location, and length of coronary artery lesions, reflecting the complexity of coronary artery disease and closely correlating with patient prognosis [42]. Each of these scores shows collinearity and has a distinct focus. These scores have been paired with others in several studies to increase predictive efficacy [43,44]. It is anticipated that future studies will further improve their forecast accuracy by combining these scores to capitalize on their advantages and minimize their disadvantages.

This study enhanced the predictive value for the occurrence of MACE in patients with acute myocardial infarction by incorporating SII and Lp (a) into the TIMI score to construct a clinical prediction model. This

approach allows for a more effective assessment of STEMI patients' condition and enables prompt treatment adjustment, thereby guiding improvements in prognosis. Our analysis found that SII, Lp(a), and TIMI scores are independent risk factors for MACE. Based on these findings, a nomogram predicting the risk of MACE in STEMI patients was successfully constructed. The nomogram can quantify the scores of various factors in the regression model, thereby enabling individualized prediction of the risk of target events in different patients [45]. The AUC values in the two sets were 0.883 (95 % CI: 0.836–0.930) and 0.841 (95 % CI: 0.756–0.925), sensitivity was 80.8 % and 73.0 %, specificity was 83.2 % and 82.0 %, respectively. These results indicate that the prediction model has high clinical application value, in which case it can perform risk analysis for each patient individually, rather than broadly categorizing patients into risk groups. Additionally, the data required to construct the nomogram are simple and easily accessible, without the need for complex calculations, and the model offers high accuracy. Clinicians can take targeted measures to reduce the incidence of mortality in STEMI patients.

In conclusion, SII, Lp(a), and TIMI risk score are independent risk factors for the occurrence of MACE within one year in STEMI patients. Both SII and Lp(a) have significant predictive value for MACE within this period. By incorporating these two factors into the TIMI risk score, the predictive value for adverse prognosis can be improved.

Limitations

(1) This study of 290 clinical cases is retrospective and single-center, which has a small sample size. Such limitations may lead to certain selection biases and confounding factors, making it challenging to ensure that the study subjects fully represent the general population. Therefore, the research results still need to be confirmed by large-scale, multicenter prospective studies. (2) The model was only internally validated, which means it lacked external validation with prospective and multicenter samples. As a result, the extrapolation and stability of the model are unknown. (3) This study did not conduct a dynamic analysis of the SII and Lp(a) levels of the study subjects, only evaluating clinical indicators at the time of admission. Future research needs to incorporate dynamic monitoring.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Medical College of Yangzhou University (protocol code YXYLL-2023-157). The study protocol conforms to the ethical guidelines of the 1957 Declaration of Helsinki. On account of this retrospective observational study, informed consent was waived, which was approved by the Ethics Committee of the Medical College of Yangzhou University.

CRediT authorship contribution statement

Yuankun Gu: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Yu Zhang:** Investigation, Data curation. **Deshan Yao:** Supervision, Investigation. **Hui Shen:** Resources, Funding acquisition. **Xin Pan:** Supervision. **Kaizheng Gong:** Writing – review & editing, Validation, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] X. Xiong, J. Zhou, Q. Fu, et al., The associations between TMAO-related metabolites and blood lipids and the potential impact of rosuvastatin therapy, Lipids Health Dis. 21 (2022) 60, https://doi.org/10.1186/s12944-022-01673-3.
[2] M. Karakayali, M. Altunova, T. Yakışan, et al., Relationship between nonobstructive coronary arteries and metabolic parameters, Kafkas J. Med. Sci. 14 (2) (2024) 138–143.
[3] M. Karakayali, T. Omar, I. Artac, et al., The prognostic value of HALP score in predicting in-hospital mortality in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention, Coron. Artery Dis. 34 (2023) 483–488, https://doi.org/10.1097/MCA.0000000000001271.
[4] H.L. Nguyen, J. Yarzebski, D. Lessard, et al., Ten-year (2001–2011) trends in the incidence rates and short-term outcomes of early versus late onset cardiogenic shock after hospitalization for acute myocardial infarction, JAHA 6 (2017) e005566, https://doi.org/10.1161/JAHA.117.005566.
[5] D.A. Morrow, E.M. Antman, A. Charlesworth, et al., TIMI risk score for ST-elevation myocardial infarction: A convenient, bedside, clinical score for risk assessment at presentation: An intravenous nPA for treatment of infarcting myocardium early II trial substudy, Circulation 102 (2000) 2031–2037, https://doi.org/10.1161/01.cir.102.17.2031.
[6] Y. Li, M. Liu, Y. Cui, et al., Increased risk of testosterone deficiency is associated with the systemic immune-inflammation index: a population-based cohort study, Front. Endocrinol. (lausanne) 13 (2022) 974773, https://doi.org/10.3389/fendo.2022.974773.
[7] L. Fani, K.D. van der Willik, D. Bos, et al., The association of innate and adaptive immunity, subclinical atherosclerosis, and cardiovascular disease in the Rotterdam Study: A prospective cohort study, PLoS Med. 17 (2020) e1003115, https://doi.org/10.1371/journal.pmed.1003115.
[8] Y. Xia, C. Xia, L. Wu, et al., Systemic immune inflammation index (SII), system inflammation response index (SIRI) and risk of all-cause mortality and cardiovascular mortality: A 20-year follow-up cohort study of 42,875 US adults, J. Clin. Med. 12 (2023) 1128, https://doi.org/10.3390/jcm12031128.
[9] Z. Ye, T. Hu, J. Wang, et al., Systemic immune-inflammation index as a potential biomarker of cardiovascular diseases: A systematic review and meta-analysis, Front. Cardiovasc. Med. 9 (2022) 933913, https://doi.org/10.3389/fcvm.2022.933913.
[10] R. Verbeek, R.M. Hoogeveen, A. Langsted, et al., Cardiovascular disease risk associated with elevated lipoprotein(a) attenuates at low low-density lipoprotein cholesterol levels in a primary prevention setting, Eur. Heart J. 39 (2018) 2589–2596, https://doi.org/10.1093/eurheartj/ehy334.
[11] S.-C. Chung, J. Sundström, C.P. Gale, et al., Comparison of hospital variation in acute myocardial infarction care and outcome between Sweden and United Kingdom: Population based cohort study using nationwide clinical registries, BMJ 351 (2015) h3913, https://doi.org/10.1136/bmj.h3913.
[12] D.S. Menees, E.D. Peterson, Y. Wang, et al., Door-to-balloon time and mortality among patients undergoing primary PCI, N. Engl. J. Med. 369 (2013) 901–909, https://doi.org/10.1056/NEJMoa1208200.
[13] G. Giustino, U. Baber, G.G. Stefanini, et al., Impact of clinical presentation (Stable Angina pectoris vs unstable angina pectoris or non-ST-elevation myocardial infarction vs ST-elevation myocardial infarction) on long-term outcomes in women undergoing percutaneous Coronary Intervention with drug-eluting stents, Am. J. Cardiol. 116 (2015) 845–852, https://doi.org/10.1016/j.amjcard.2015.06.010.
[14] Y. Karabağ, M. Çağdaş, I. Rencuzogullari, et al., Comparison of SYNTAX score II efficacy with SYNTAX score and TIMI risk score for predicting in-hospital and long-term mortality in patients with ST segment elevation myocardial infarction, Int. J. Cardiovasc. Imaging 34 (2018) 1165–1175, https://doi.org/10.1007/s10554-018-1333-1.
[15] B. Ibanez, S. James, S. Agewall, et al., 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC), Eur. Heart J. 39 (2018) 119–177, https://doi.org/10.1093/eurheartj/ehx393.
[16] The Ratio of Circulating Endothelin-1 to Endothelin-3 Associated with TIMI Risk and Dynamic TIMI Risk Score in ST Elevation Acute Myocardial Infarction - PubMed. https://pubmed.ncbi.nlm.nih.gov/32315546/. Accessed 31 Jul 2024.
[17] E.M. Antman, M. Cohen, P.J. Bernink, et al., The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making, JAMA 284 (2000) 835–842, https://doi.org/10.1001/jama.284.7.835.
[18] P. Libby, Inflammation in Atherosclerosis-No Longer a Theory, Clin. Chem. 67 (2021) 131–142, https://doi.org/10.1093/clinchem/hvaa275.
[19] Inflammation in Cardiac Injury, Repair and Regeneration - PubMed. https://pubmed.ncbi.nlm.nih.gov/25807226/. Accessed 31 Jul 2024.
[20] C. Silvestre-Roig, Q. Braster, A. Ortega-Gomez, O. Soehnlein, Neutrophils as regulators of cardiovascular inflammation, Nat. Rev. Cardiol. 17 (2020) 327–340, https://doi.org/10.1038/s41569-019-0326-7.

[21] F.K. Swirski, M. Nahrendorf, Leukocyte behavior in atherosclerosis, myocardial infarction, and heart failure, Science 339 (2013) 161–166, https://doi.org/10.1126/science.1230719.
[22] T.J. Barrett, M. Schlegel, F. Zhou, et al., Platelet regulation of myeloid suppressor of cytokine signaling 3 accelerates atherosclerosis, Sci. Transl. Med. 11 (2019) eaax0481, https://doi.org/10.1126/scitranslmed.aax0481.
[23] M. Karakayali, M. Altunova, T. Yakisan, et al., A Relação entre o Índice de Imuno-Inflamação Sistêmica e Isquemia com Artérias Coronárias Não Obstrutivas em Pacientes Submetidos à Angiografia Coronária, Arq. Bras. Cardiol. 121 (2024) e20230540, https://doi.org/10.36660/abc.20230540.
[24] Y.-L. Yang, C.-H. Wu, P.-F. Hsu, et al., Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease, Eur. J. Clin. Invest. 50 (2020) e13230, https://doi.org/10.1111/eci.13230.
[25] E.A. Dziedzic, J.S. Gąsior, A. Tuzimek, et al., investigation of the associations of novel inflammatory biomarkers-systemic inflammatory index (SII) and systemic inflammatory response index (SIRI)-with the severity of coronary artery disease and acute coronary syndrome occurrence, Int. J. Mol. Sci. 23 (2022), https://doi.org/10.3390/ijms23179553.
[26] O. Tezen, M.İ. Hayıroğlu, L. Pay, et al., The role of systemic immune-inflammatory index in predicting contrast-induced nephropathy in non-ST-segment elevation myocardial infarction cases, Biomark. Med. 1–8 (2024), https://doi.org/10.1080/17520363.2024.2415284.
[27] Y. Tang, X. Zeng, Y. Feng, et al., Association of systemic immune-inflammation index with short-term mortality of congestive heart failure: A retrospective cohort study, Front. Cardiovasc. Med. 8 (2021) 753133, https://doi.org/10.3389/fcvm.2021.753133.
[28] Hayırog I, Assoc TÇ, Çinier G Evaluating systemic immune-inflammation index in patients with implantable cardioverter defibrillator for heart failure with reduced ejection fraction.
[29] F. Duarte Lau, R.P. Giugliano, Lipoprotein(a) and its significance in cardiovascular disease: A review, JAMA Cardiol. 7 (2022) 760–769, https://doi.org/10.1001/jamacardio.2022.0987.
[30] R.C. Maranhão, P.O. Carvalho, C.C. Strunz, F. Pileggi, Lipoprotein (a): Structure, pathophysiology and clinical implications, Arq Bras Cardiol 103 (2014) 76–84, https://doi.org/10.5935/abc.20140101.
[31] S. Varvel, J.P. McConnell, S. Tsimikas, Prevalence of elevated Lp(a) mass levels and patient thresholds in 532 359 patients in the United States, Arterioscler. Thromb. Vasc. Biol. 36 (2016) 2239–2245, https://doi.org/10.1161/ATVBAHA.116.308011.
[32] G. Reyes-Soffer, H.N. Ginsberg, L. Berglund, et al., Lipoprotein(a): A genetically determined, causal, and prevalent risk factor for atherosclerotic cardiovascular disease: A scientific statement from the american heart association, Arterioscler. Thromb. Vasc. Biol. 42 (2022) e48–e60, https://doi.org/10.1161/ATV.0000000000000147.
[33] D. Saleheen, P.C. Haycock, W. Zhao, et al., Apolipoprotein(a) isoform size, lipoprotein(a) concentration, and coronary artery disease: a mendelian randomisation analysis, Lancet Diabetes Endocrinol. 5 (2017) 524–533, https://doi.org/10.1016/S2213-8587(17)30088-8.
[34] M.J.E. Kuijpers, K. Gilio, S. Reitsma, et al., Complementary roles of platelets and coagulation in thrombus formation on plaques acutely ruptured by targeted ultrasound treatment: a novel intravital model, J. Thromb. Haemost. 7 (2009) 152–161, https://doi.org/10.1111/j.1538-7836.2008.03186.x.
[35] M.B. Boffa, T.T. Marar, C. Yeang, et al., Potent reduction of plasma lipoprotein (a) with an antisense oligonucleotide in human subjects does not affect ex vivo fibrinolysis, J. Lipid Res. 60 (2019) 2082–2089, https://doi.org/10.1194/jlr.P094763.
[36] B.G. Nordestgaard, M.J. Chapman, K. Ray, et al., Lipoprotein(a) as a cardiovascular risk factor: current status, Eur. Heart J. 31 (2010) 2844–2853, https://doi.org/10.1093/eurheartj/ehq386.
[37] P.R. Kamstrup, M. Benn, A. Tybjaerg-Hansen, B.G. Nordestgaard, Extreme lipoprotein(a) levels and risk of myocardial infarction in the general population: The Copenhagen City Heart Study, Circulation 117 (2008) 176–184, https://doi.org/10.1161/CIRCULATIONAHA.107.715698.
[38] G. Goliasch, F. Wiesbauer, H. Blessberger, et al., Variation of lipoprotein(a) plasma levels after premature myocardial infarction, Int. J. Cardiol. 186 (2015) 5–6, https://doi.org/10.1016/j.ijcard.2015.03.211.
[39] D. Corcoran, P. Grant, C. Berry, Risk stratification in non-ST elevation acute coronary syndromes: Risk scores, biomarkers and clinical judgment, Int. J. Cardiol. Heart Vasc. 8 (2015) 131–137.
[40] T. Çınar, F. Şaylık, T. Akbulut, et al., Evaluation of Intermountain risk score for short- and long-term mortality in ST elevation myocardial infarction patients, Angiology 74 (2023) 357–364, https://doi.org/10.1177/00033197221105753.
[41] H. Mert İlker, S. Faysal, Y. Ahmet Çağdaş, et al., Prognostic value of Intermountain Risk Score for short- and long-term mortality in patients with cardiogenic shock, Coron. Artery Dis. 34 (2023) 154–159, https://doi.org/10.1097/MCA.0000000000001219.
[42] A.K. Chakrabarti, C.M. Gibson, The SYNTAX score: Usefulness, limitations, and future directions, J. Invasive Cardiol. 23 (2011) 511–512.
[43] A. Cordero, M. Rodriguez-Manero, J.M. García-Acuña, et al., Additive value of the CRUSADE score to the GRACE score for mortality risk prediction in patients with acute coronary syndromes, Int. J. Cardiol. 245 (2017) 1–5, https://doi.org/10.1016/j.ijcard.2017.07.095.
[44] M. Shuvy, E. Klein, T. Cohen, et al., Value of adding the CHA2DS2-VASc score to the GRACE score for mortality risk prediction in patients with acute coronary syndrome, Am. J. Cardiol. 123 (2019) 1751–1756, https://doi.org/10.1016/j.amjcard.2019.02.045.
[45] G.S. Collins, J.B. Reitsma, D.G. Altman, K.G.M. Moons, Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement, BMJ 350 (2015) g7594, https://doi.org/10.1136/bmj.g7594.