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Inflammation Biomarker-Driven Vertical Visualization Model for Predicting Long-Term Prognosis in Unstable Angina Pectoris Patients with Angiographically Intermediate Coronary Lesions

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Objective: Angina, a prevalent manifestation of coronary artery disease, is primarily associated with inflammation, an established contributor to the pathogenesis of atherosclerosis and acute coronary syndromes (ACS). Various inflammatory markers are employed in clinical practice to predict patient prognosis and optimize clinical decision-making in the management of ACS. This study investigated the prognostic significance of integrating commonly used, easily repeatable inflammatory biomarkers within a multimodal preoperative prediction model in patients presenting with unstable Angina Pectoris (UAP) and intermediate coronary lesions.

Methods: This retrospective analysis included patients diagnosed with UAP and intermediate coronary lesions (50%–70% stenosis) who underwent coronary angiography at our hospital between January 2019 and June 2021. The assessed outcome was the occurrence of major adverse cardiac and cerebrovascular events (MACCEs). The Boruta algorithm was applied to identify potential risk factors and develop a prognostic multimodal model.

Results: A total of 773 patients were enrolled and divided into a training cohort (n=463) and validation cohort (n=310). A nomogram was constructed to predict the probability of MACCE-free survival based on five clinical features: diabetes mellitus, current smoking, history of myocardial infarction, neutrophil-to-lymphocyte ratio, and fasting blood glucose. In the training cohort, the area under the curve values for the nomogram at 24, 32, and 40 months were 0.669, 0.707, and 0.718, respectively, while those in the validation cohort were 0.613, 0.612 and 0.630, respectively. The model demonstrated good calibration in both cohorts with predicted outcomes aligning well with actual results at all time points up to 40 months. Furthermore, decision curve analysis showed significant clinical utility of the model across the specified time intervals.

Conclusion: The developed preoperative prognostic model visually illustrates the association among inflammation, blood glucose level, established risk factors, and long-term MACCEs in UAP patients with intermediate coronary lesions.

Keywords: unstable angina pectoris, inflammatory, neutrophil-to-lymphocyte ratio, prediction nomogram, major adverse cardiac and cerebrovascular events

Introduction

Atherosclerosis is a chronic inflammatory disease affecting the arterial walls that serves as the pathophysiological basis for acute coronary syndrome (ACS).[1] ACS is a leading cause of death and disability globally.[2] Recent advancements in

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revascularization techniques and preventive strategies, including particularly effective lipid-lowering treatments such as statins, have significantly improved the clinical management of atherosclerosis and its complications.[2] Despite these advancements, the past three decades have seen an increase in the prevalence of cardiovascular diseases and acute events such as myocardial infarction, leading to higher mortality rates.[1,2] Accordingly, new targets need to be identified to reduce the residual risk and potential risk associated with cardiovascular events.[2–11]

Previous research has established that inflammation plays a crucial role in worsening unstable angina by promoting the rupture and erosion of vulnerable coronary plaques.[9,12] In ACS patients, clinical evidence has demonstrated that elevated levels of inflammation biomarkers are significant clinical features and prognostic indicators for adverse outcomes.[6,10,11,13] In patient management, laboratory indicators of inflammation, such as the neutrophil-to-lymphocyte ratio (NLR), can be obtained from routine blood tests and can provide valuable insight into the inflammatory response.[10,14] Although the NLR has shown promising predictive performance in ACS patients, a single variable is insufficient given that ACS results from the complex interplay of multiple risk factors.[15] Recent studies have demonstrated the potential of machine learning techniques to visualize relationships among a variety of independent predictors and adverse outcomes, enhancing our understanding of the clustering and diversity of patient risk factors.[16–19] Compared with traditional statistical methods, the Boruta algorithm can effectively identify and select features most relevant to the target variable, offering improved model performance and reducing the risk of overfitting.[20] Furthermore, this algorithm can identify all relevant features that will contribute significantly to a comprehensive predictive model, offering a comprehensive understanding of crucial information within the feature set.[20] It also assigns importance scores to each feature, allowing assessment of their relative significance.[20]

A limited amount of clinical data suggests the potential efficacy of incorporating inflammatory biomarkers into a predictive model for personalized risk stratification in patient with unstable angina pectoris (UAP) and intermediate coronary lesions. To better understand the contributions of such biomarkers to a prognostic model for these patients, in the present study, we applied the Boruta algorithm to integrate inflammatory markers across diverse data types in the development of a multimodal preoperative prediction model for long-term outcomes in patients with UAP and angiographically intermediate coronary lesions.

Methods

Patient Population

Consecutive patients diagnosed with UAP and exhibiting angiographically intermediate coronary lesions (50%–70% stenosis) at The Suzhou First People's Hospital from January 2019 to June 2021 were identified and included in this retrospective study. UAP was diagnosed according to contemporary international guidelines.[3] The exclusion criteria were: acute myocardial infarction, chronic coronary syndrome, acute infection, connective tissue disease, malignant tumor, previously proven systemic inflammatory disease, and recent surgery. Ethical approval for this study was granted by the local research ethics committee (No. SzTTLLKy2024015) at Suzhou First People's Hospital. Given the retrospective design and utilization of de-identified patient data, the requirement for patients' informed consent was waived. We ensured strict confidentiality of all patient information and adhered fully to the principles outlined in the Declaration of Helsinki throughout the research process.

Biochemical Tests

A comprehensive complete blood count, encompassing white blood cell count, neutrophil count, lymphocyte count, platelet count, monocyte count, NLR, platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), as well as electrolyte analysis and serum creatinine measurement, was systematically conducted for all patients prior to their scheduled coronary angiography. Blood samples for measurement of fasting blood glucose (FBG), total bilirubin, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transpeptidase, total protein, albumin, globulin, albumin/globulin ratio, and lipid profiles (including triglycerides, total cholesterol, high-density lipoprotein cholesterol [HDL-C], and low-density lipoprotein cholesterol [LDL-C]) were collected in the early morning after overnight fasting.

Coronary Angiography

Upon admission for UAP, the standard treatment protocol was initiated promptly for all patients and included coronary angiography examination by experienced senior cardiologists. Intermediate coronary lesions are characterized by a significant narrowing (stenosis) of the coronary artery, typically ranging from 50%–70%. This degree of stenosis is deemed critical, as it can markedly diminish blood flow to the myocardium, potentially inducing symptoms such as angina and increasing the risk of ACS.[21] The identification of coronary lesions and assessment of their severity are essential for effective management of coronary artery disease and for guiding appropriate therapeutic interventions.[21] After discharge, all patients received standard treatment per established guidelines, including antiplatelet therapy and statins.

Clinical Endpoint

All included patients underwent regular patient follow-up at our clinic, including additional appointments as needed. In case of missed follow-up visits, we proactively reached out to patients via telephone. The primary objective of follow-up evaluations was to detect the occurrence of major adverse cardiac and cerebrovascular events (MACCEs), which included cardiac mortality, acute myocardial infarction, revascularization procedures, and stroke. An impartial panel of clinical physicians supervised the monitoring process for all MACCE occurrences.

Feature Selection

Careful selection of suitable variables is critical for ensuring the performance of a prognostic model. Therefore, we utilized the Boruta algorithm, which employs a random forest classifier to perform feature selection across multiple datasets with a high number of dimensions and multivariate characteristics.[20] This approach is known to allow the identification of the most relevant variables that contribute to both accuracy and stability of the model. To assess the impact of the selected features on the developed model, we conducted an additional evaluation of prognostic factors using stepwise backward multivariate Cox regression analysis.

Model Performance

The dataset was split into training and validation cohorts in a 6:4 ratio. The methods employed to evaluate specific aspects of the predictive performance of the model were as follows. The predictive accuracy of the nomogram was evaluated by calculating the area under the curve (AUC) and 95% confidence interval (CI) by receiver operating characteristic (ROC) curve analysis. These metrics reflected the model's discriminatory power. Calibration plots were created to evaluate how closely the model's predicted probabilities of MACCEs at 24, 32, and 40 months matched to observed outcomes. Decision curve analysis (DCA) was performed to assess the net clinical benefit of the nomogram across a range of threshold probabilities.

Statistical Analysis

Study data were analyzed using SPSS version 26 and R software version 4.2.2. Categorical data were presented as frequencies and proportions, and continuous data were presented as medians with interquartile ranges (IQRs) or means plus standard deviations (SDs). For continuous variables that did not follow a normal distribution, the Mann–Whitney *U* test was employed for comparisons between the training and validation cohorts. Categorical variables were compared using Fisher's exact test or the chi-square test, as appropriate. A two-tailed P value <0.05 was taken as the level of statistical significance for all tests.

Results

Patient Characteristics

A total of 773 patients with UAP and intermediate coronary lesions observed by coronary angiography were included in this retrospective study. These patients had a median age (IQR) of 66 years (57–72 years), and 54.2% were male. The study population was divided in a 6:4 ratio into a training cohort (n=463) and a validation cohort (n=310) (Table 1). The baseline characteristics and frequency of the clinical endpoint (MACCE occurrence) were comparable between the cohorts.

Feature Selection for Prediction of MACCEs

The Boruta feature selection process identified five variables—diabetes mellitus, history of myocardial infarction, current smoking, NLR, FBG, and globulin—out of 46 clinical variables, as potential predictors of MACCEs, as detailed in Table 1 and illustrated in Figures 1 and 2. The subsequent multivariate Cox regression analysis, employing the backward

Table 1 Baseline Characteristics

Characteristic or Outcome	Total Cohort N=773	Training Cohort n=463	Verification Cohort n=310	P-value
Male, n (%)	419 (54.20%)	246 (53.13%)	173 (55.81%)	0.511
Age (years)	66.00 [57.00;72.00]	66.00 [57.00;71.50]	67.00 [58.00;72.00]	0.095
Hypertension, n (%)	465 (60.16%)	287 (61.99%)	178 (57.42%)	0.232
Diabetes mellitus, n (%)	168 (21.73%)	112 (24.19%)	56 (18.06%)	0.053
Current smoking, n (%)	109 (14.10%)	64 (13.82%)	45 (14.52%)	0.868
Current alcohol consumption, n (%)	46 (5.95%)	26 (5.62%)	20 (6.45%)	0.744
History of myocardial infarction, n (%)	42 (5.43%)	26 (5.62%)	16 (5.16%)	0.911
Previous percutaneous coronary intervention, n (%)	282 (36.48%)	162 (34.99%)	120 (38.71%)	0.329
Previous Stroke, n (%)	142 (18.37%)	93 (20.09%)	49 (15.81%)	0.158
Systolic blood pressure, mmHg	138.00 [123.00;152.00]	139.00 [124.00;152.50]	137.00 [122.00;152.00]	0.452
Diastolic blood pressure, mmHg	83.00 [74.00;91.00]	83.00 [75.00;92.00]	82.00 [74.00;90.00]	0.443
Heart rate, Times per minute	74.00 [67.00;84.00]	75.00 [68.00;84.00]	74.00 [66.00;84.00]	0.297
White blood cell count, $\times10^9$/L	6.11 [5.05;7.36]	5.97 [5.07;7.25]	6.24 [5.04;7.46]	0.287
Neutrophil count, $\times10^9$/L	3.79 [2.99;4.76]	3.74 [3.01;4.62]	3.95 [2.97;4.92]	0.211
Lymphocyte count, $\times10^9$/L	1.63 [1.30;2.04]	1.64 [1.29;2.03]	1.62 [1.31;2.04]	1.000
Monocyte count, $\times10^9$/L	0.40 [0.32;0.52]	0.40 [0.32;0.52]	0.40 [0.33;0.53]	0.693
NLR	2.33 [1.77;3.11]	2.30 [1.78;3.09]	2.40 [1.76;3.14]	0.715
PLR	125.86 [94.25;166.87]	128.14 [94.00;166.90]	122.97 [94.90;163.74]	0.591
LMR	4.04 [3.13;5.19]	4.00 [3.12;5.20]	4.11 [3.14;5.18]	0.883
Platelet count, $\times10^9$/L	206.00 [170.00;246.00]	208.00 [173.00;246.50]	202.50 [166.25;243.00]	0.308
Mean platelet volume	10.10 [9.40;11.00]	10.00 [9.40;10.80]	10.10 [9.40;11.10]	0.111
Thrombocytocrit, %	0.21 [0.18;0.25]	0.21 [0.18;0.25]	0.21 [0.18;0.25]	0.655
Platelet distribution width, %	16.10 [15.50;16.30]	16.10 [15.40;16.30]	16.10 [15.60;16.40]	0.489
Large platelet ratio, %	26.10 [21.40;32.50]	25.80 [21.30;31.55]	26.60 [21.72;33.85]	0.119
Hemoglobin, g/L	133.00 [122.00;145.00]	132.00 [122.00;144.00]	135.00 [123.00;145.00]	0.174
Red cell distribution width-CV	12.80 [12.50;13.30]	12.80 [12.50;13.30]	12.80 [12.43;13.30]	0.420
Red cell distribution width-SD	42.20 [40.60;43.90]	42.20 [40.70;44.00]	42.00 [40.40;43.90]	0.240
Creatinine, mmol/L	63.00 [55.00;74.00]	63.00 [56.00;75.00]	62.00 [55.00;73.00]	0.621
Fasting blood glucose, mmol/L	5.82 [5.34;7.11]	5.77 [5.31;7.04]	5.89 [5.36;7.18]	0.503
NT-proBNP, ng/L	101.00 [30.00;341.00]	96.00 [30.00;315.00]	111.00 [36.00;347.25]	0.209
Triglyceride, mmol/L	1.49 [0.99;2.07]	1.43 [0.94;2.02]	1.53 [1.07;2.10]	0.195
Total cholesterol, mmol/L	4.46 [3.79;5.09]	4.44 [3.76;5.08]	4.50 [3.84;5.09]	0.817
HDL-C, mmol/L	1.30 [1.10;1.51]	1.30 [1.10;1.54]	1.29 [1.10;1.50]	0.602
LDL-C, mmol/L	2.44 [1.92;3.04]	2.37 [1.92;3.02]	2.49 [1.94;3.09]	0.311
Total bilirubin, μmol/L	11.80 [8.70;15.30]	11.70 [8.70;15.55]	11.85 [9.22;15.07]	0.500
Alanine aminotransferase, U/L	22.00 [17.00;31.00]	22.00 [17.00;31.50]	23.00 [17.00;31.00]	0.712
Aspartate aminotransferase, U/L	21.00 [18.00;26.00]	21.00 [18.00;26.50]	21.00 [18.00;26.00]	0.979
Gamma-glutamyl transpeptidase, U/L	23.00 [17.00;35.00]	23.00 [17.00;34.00]	24.00 [17.00;37.00]	0.186
Total protein, g/L	66.90 [60.90;71.40]	67.10 [60.90;71.35]	66.40 [61.00;71.50]	0.695
Albumin, g/L	40.90 [38.10;43.30]	41.10 [38.20;43.40]	40.50 [38.10;43.30]	0.400
Globulin, g/L	26.20 [23.10;28.80]	26.20 [23.15;28.80]	26.05 [22.92;29.15]	0.591
Albumin/Globulin	1.58 [1.41;1.73]	1.58 [1.41;1.73]	1.58 [1.41;1.74]	0.853
Serum kalium, mmol/L	3.92 [3.68;4.14]	3.93 [3.69;4.17]	3.87 [3.66;4.11]	0.101
Serum natriumion, mmol/L	140.40 [139.00;141.80]	140.40 [139.00;141.80]	140.40 [138.90;141.70]	0.422
Chloridion, mmol/L	105.20 [103.30;107.10]	105.20 [103.30;107.10]	105.20 [103.20;106.90]	0.557

(*Continued*)

Table 1 (Continued).

Characteristic or Outcome	Total Cohort N=773	Training Cohort n=463	Verification Cohort n=310	P-value
Total calcium ion, mmol/L	2.33 [2.24;2.46]	2.32 [2.24;2.46]	2.33 [2.24;2.45]	0.970
Clinical endpoint				
MACCEs, n (%)	82 (10.61%)	50 (10.80%)	32 (10.32%)	0.927
Cardiac mortality, n (%)	13 (1.68%)	10 (2.16%)	3 (0.97%)	0.328
Revascularization, n (%)	16 (2.07%)	12 (2.59%)	4 (1.29%)	0.323
Acute myocardial infarction, n (%)	6 (0.78%)	4 (0.86%)	2 (0.65%)	1.000
Stroke, n (%)	52 (6.73%)	26 (5.62%)	26 (8.39%)	0.173

Notes: Values are given as n (%), mean ± SD, or median [IQR].
Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; NT-proBNP, N-terminal pro brain natriuretic peptide; CV, coefficient of variation; SD, standard deviation; MACCEs, major adverse cardiac and cerebrovascular events.

Wald method, identified diabetes mellitus (hazard ratio [HR]=2.587, 95% confidence interval [CI]: 1.467–4.563, P=0.001), current smoking (HR=3.177, 95% CI: 1.729–5.838, P<0.001), history of myocardial infarction (HR=3.246, 95% CI: 1.508–6.987, P=0.003), NLR (HR=1.159, 95% CI: 1.035–1.298, P=0.01), and FBG (HR=1.076, 95% CI: 1.009–1.147, P=0.026) as significant independent predictors of MACCEs within the training cohort (Figure 3).

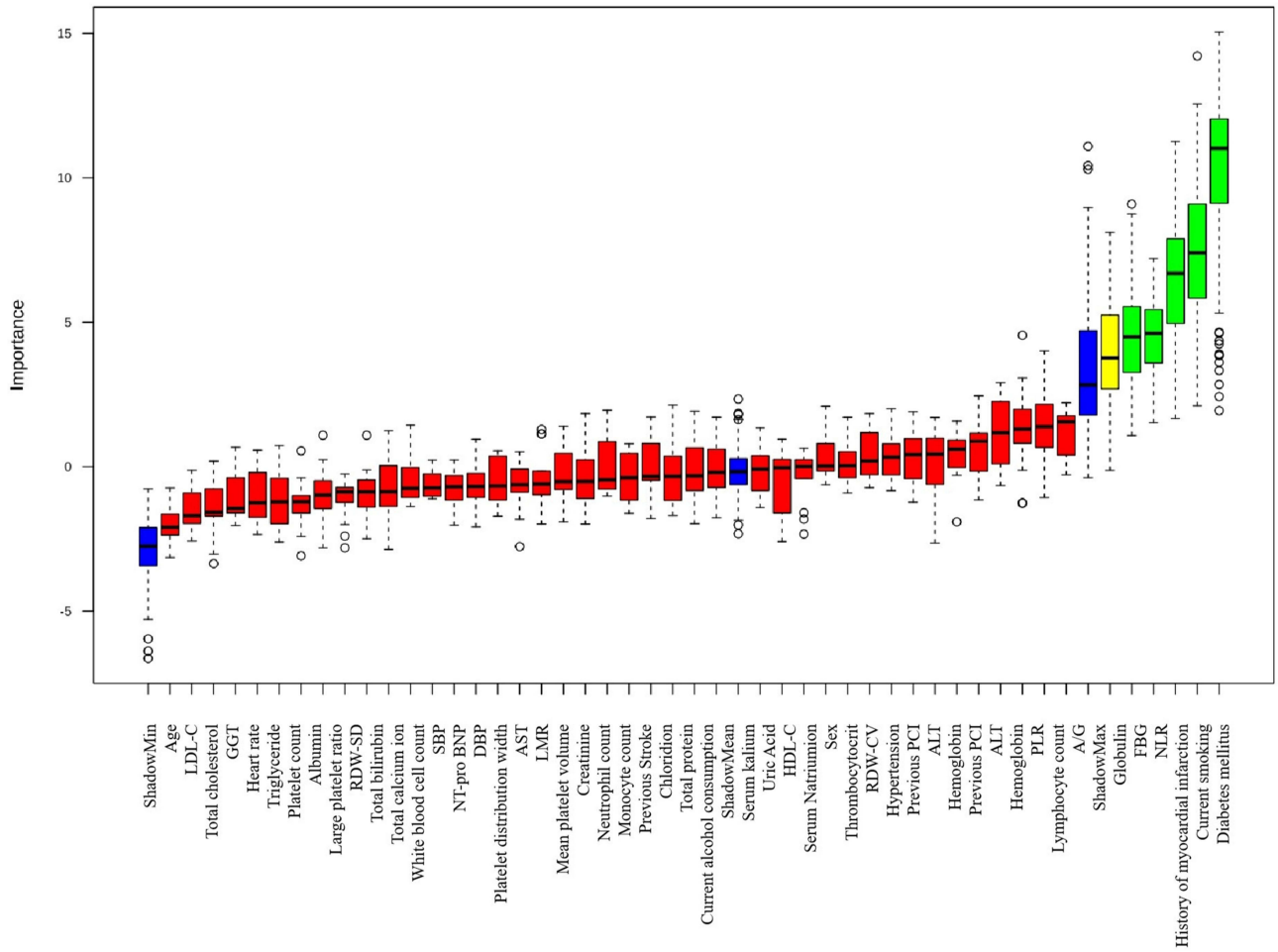

Figure 1 Forty-six clinical variables evaluated as potential predictors of MACCEs using the Boruta algorithm. The Boruta algorithm assesses how randomizing a specific feature affects classifier performance, thereby quantifying the unique information encapsulated by that feature. The minimum, mean, and maximum scores associated with a shadow attribute are represented by the blue boxplots. The yellow boxplots depict potential attributes such as loop length and large loops, while confirmed features are indicated by the green boxplots.

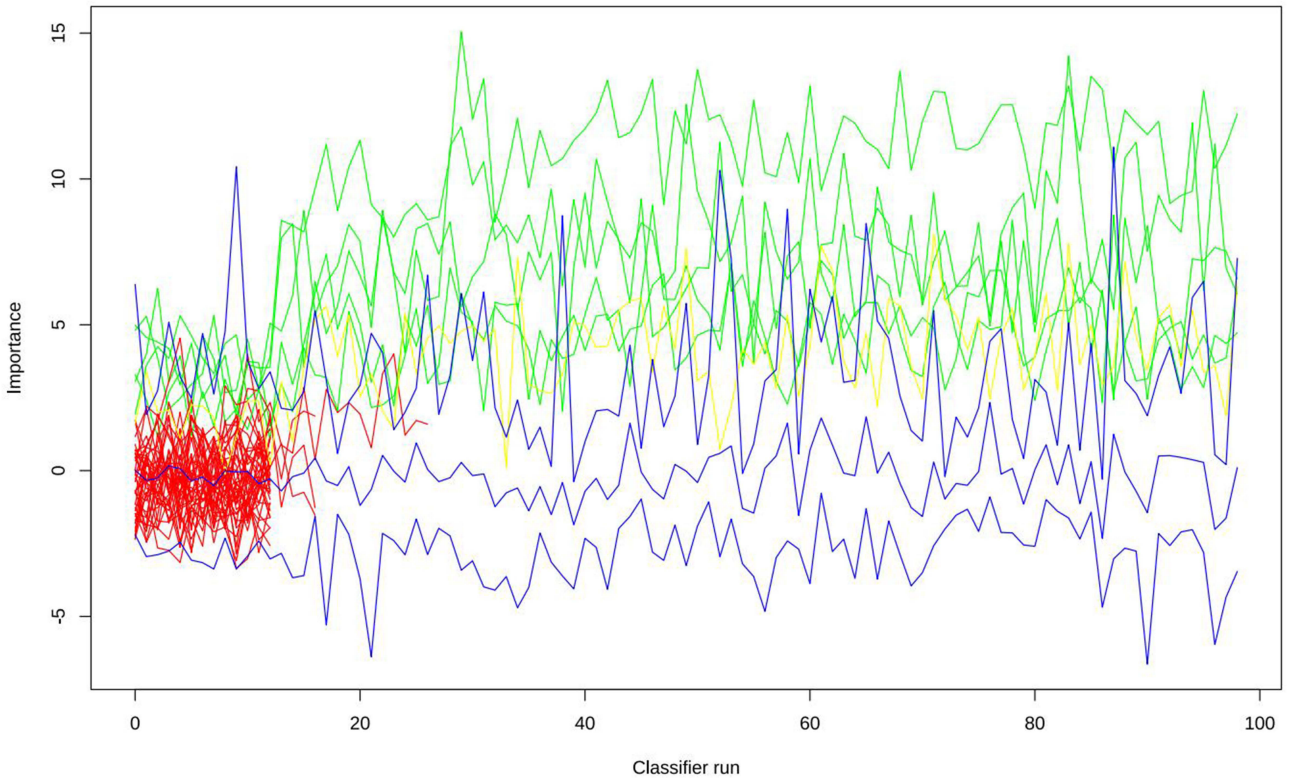

Figure 2 Variations in the significance of features across 100 iterations of the Boruta Algorithm. This visual representation demonstrates how importance scores for different features (represented by various colors) change throughout the feature selection process. The y-axis represents the "importance score" assigned by the Boruta algorithm, while the x-axis tracks sequential classifier runs. Confirmed variables are indicated by green boxes and lines; tentative attributes are denoted by yellow lines; and rejected variables are represented by red lines in model calculation.

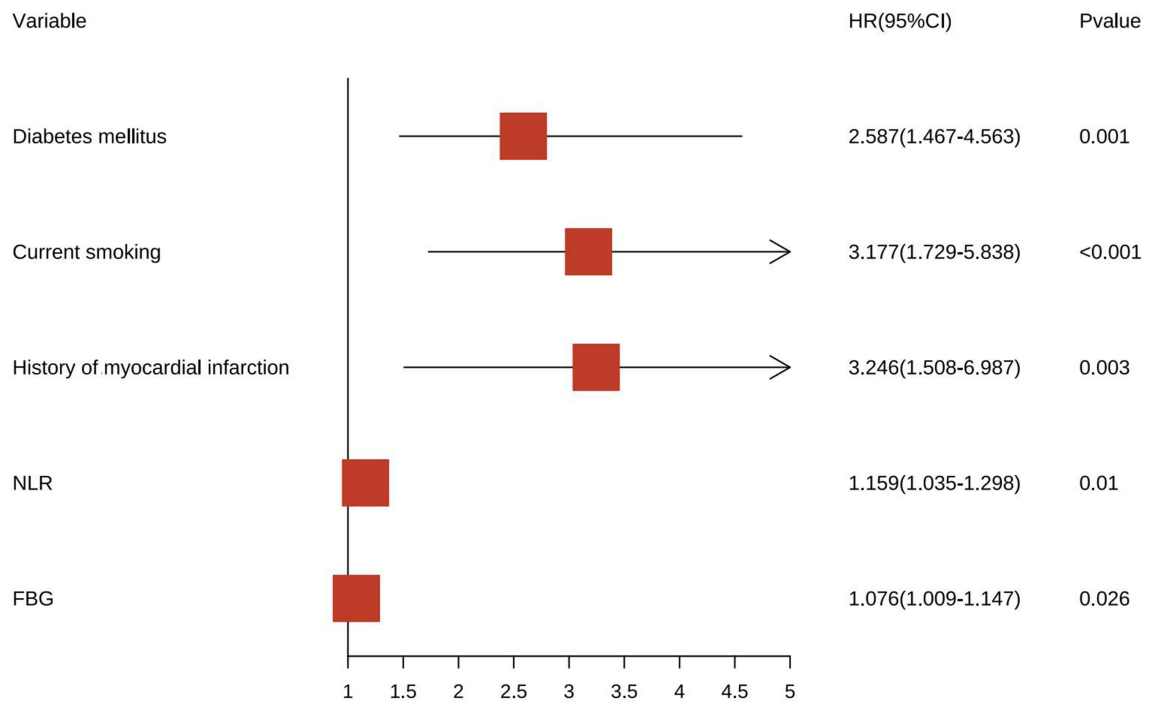

Figure 3 Forest plot illustrating the hazard ratios (HRs) for prognostic variables identified as independent factors through multivariate Cox regression analysis with backward Wald method in the training cohort.

Construction of the Prediction Model

The variables identified by the multivariate Cox regression analysis with stepwise backward selection as predictive of the risk of MACCEs were subsequently utilized to construct a predictive nomogram (Figure 4). In the training cohort, diabetes mellitus, current smoking, history of myocardial infarction, elevated NLR, and FBG were significantly associated with an increased risk of MACCEs. These associations were consistently observed in the validation cohort.

In clinical application of the prediction model, vertical lines are drawn for each of the five variables until they intersect with the "Points" line positioned at the apex of the nomogram model. This procedural approach facilitates the determination of the corresponding point totals associated with each variable. By then summing these point totals, the cumulative score ranging from 0–200 is calculated. Finally, to ascertain the risk probability of MACCEs within durations of 24, 32, and 40 months, a vertical line is drawn on the scale that appears below the "Total Points" line.

Performance of the Prediction Model

In the training cohort, ROC curve analysis revealed AUC values of 0.669 (95% CI: 0.553–0.784), 0.707 (95% CI: 0.618–0.796), and 0.718 (95% CI: 0.637–0.798) for the ability of the model to predict MACCEs at 24, 32, and 40 months, respectively (Figure 5A). In the validation cohort, the corresponding AUC values were 0.613 (95% CI: 0.458–0.769), 0.612 (95% CI: 0.479–0.744), and 0.630 (95% CI: 0.504–0.756), respectively (Figure 5B).

Calibration plots were created to evaluate the observed and predicted probabilities of MACCEs during the 24-, 32-, and 40-month intervals for both the training and validation groups (Figure 6A and B). The accuracy of the prediction nomogram was assessed using bootstrapping with 200 replications. Furthermore, DCA was performed to determine the overall benefit of the clinical prediction model (Figure 7A–E). In the training group, DCA analysis revealed threshold probability ranges of 5%–55%, 5%–70%, and 7%–73% for predicting MACCE risk over durations of 24, 32, and 40 months, respectively (Figure 7A–E). In the validation group, DCA produced threshold probability ranges of 5%–25%, 10%–40%, and 5%–53% for the respective follow-up durations (Figure 7B–F). The net benefit rate of using the

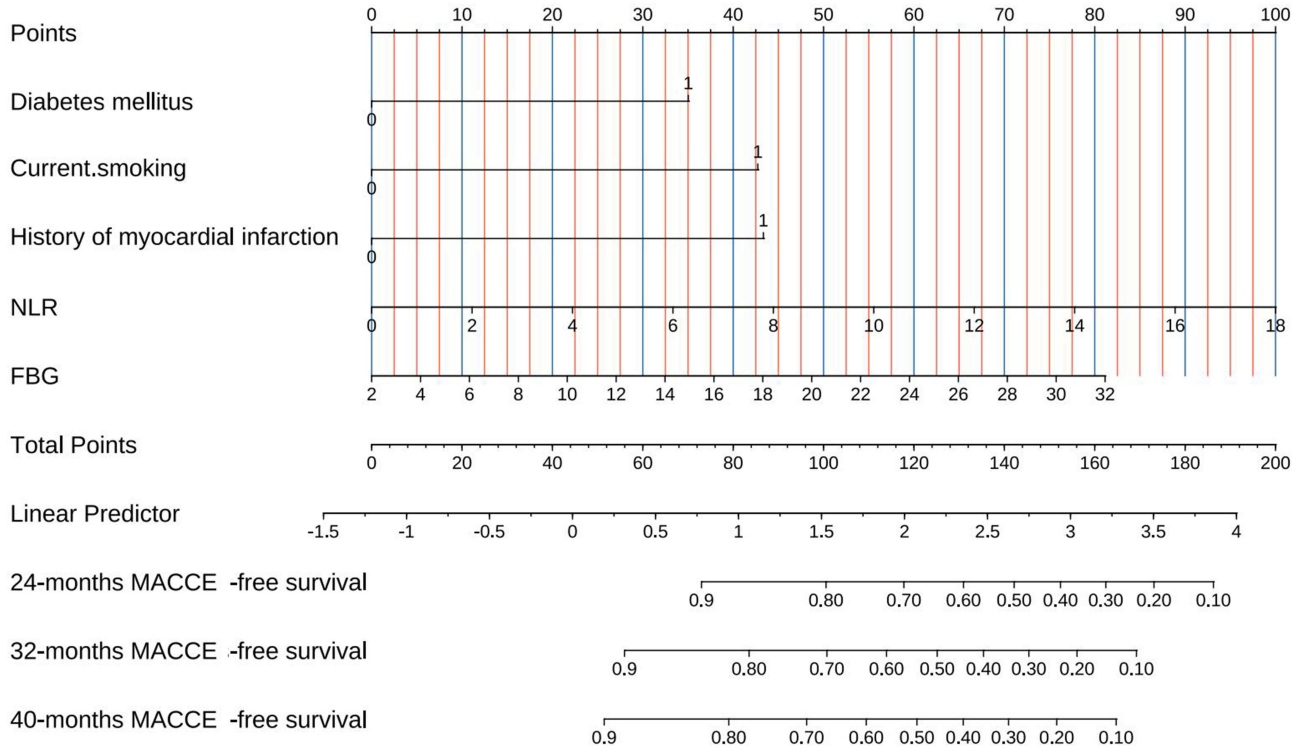

Figure 4 Prediction nomogram constructed based on variables identified by multivariate Cox regression analysis (diabetes mellitus, current smoking, history of myocardial infarction, neutrophil-to-lymphocyte ratio, and fasting blood glucose).

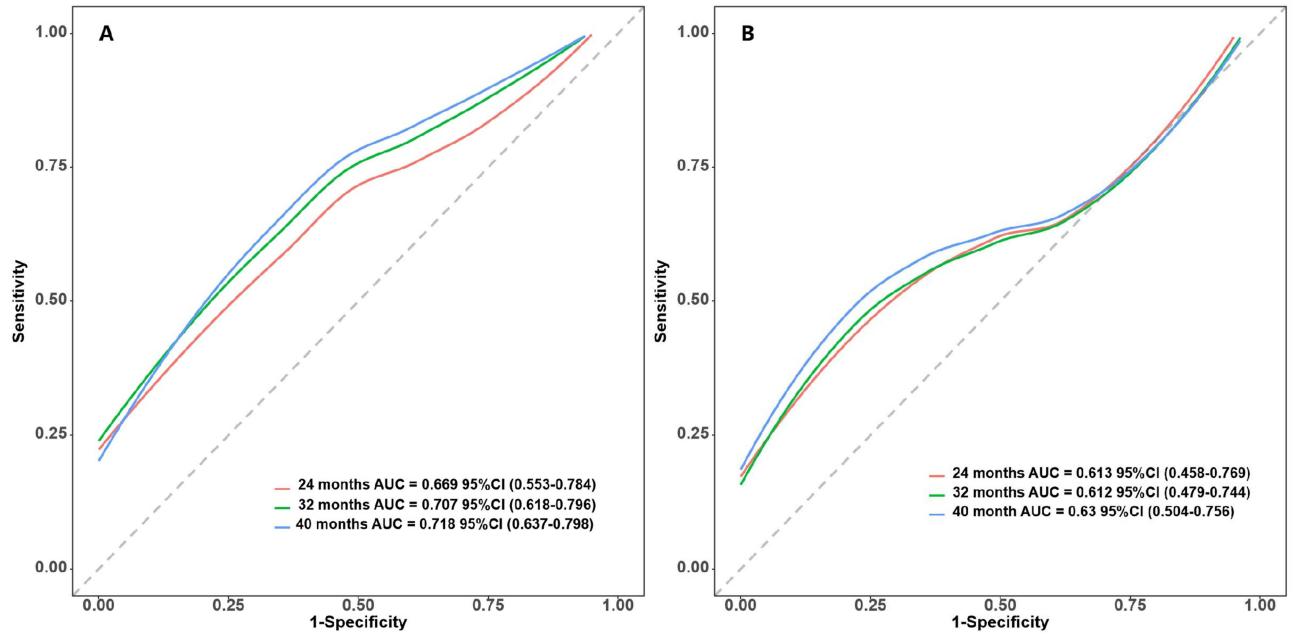

Figure 5 Receiver operating characteristic (ROC) curve analysis of the predictive accuracy of the nomogram for 24-, 32- and 40-month MACCE risk in the (**A**) training and (**B**) validation cohorts.

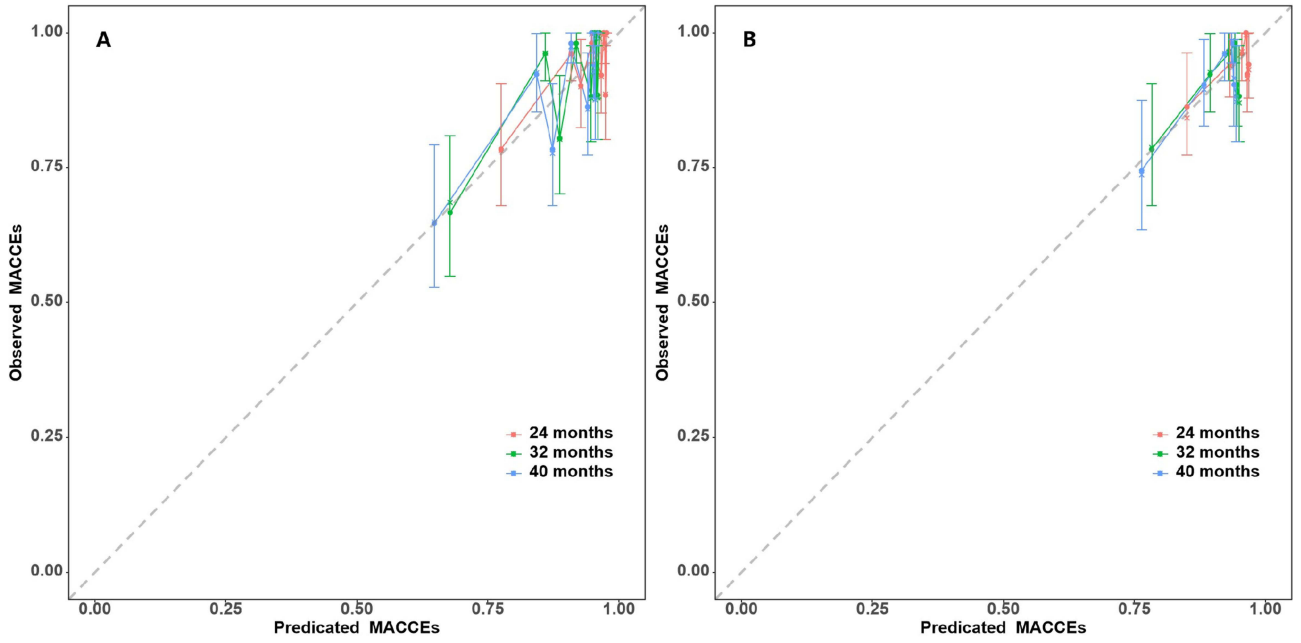

Figure 6 Calibration plots generated using 200 bootstrap replications to demonstrate the effectiveness of the nomogram for predicting MACCE risk during 24-, 32- and 40-month intervals for both the (**A**) training and (**B**) validation cohorts.

prediction nomogram was found to be superior than that of running separate models for each of the five dependent variables (diabetes mellitus, current smoking, history of myocardial infarction, elevated NLR, and FBG) in both the training and validation cohorts for all three follow-up intervals (Supplemental Figure 1A–F).

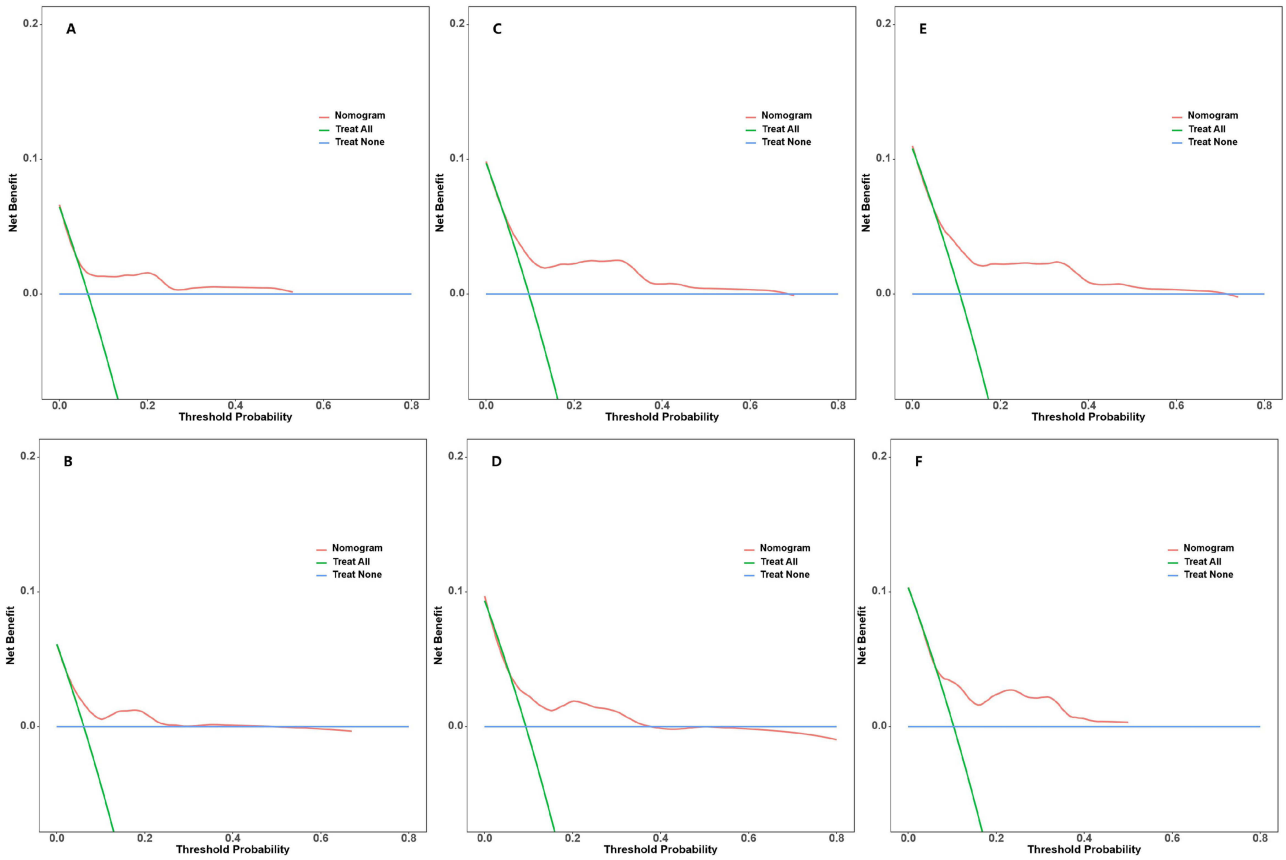

Figure 7 Decision curve analysis of the predictive accuracy of the nomogram for MACCE risk across different time intervals in each cohort: (**A** and **B**) 24-month MACCE risk in the training and validation cohorts, respectively; (**C** and **D**) 32-month MACCE risk in the training and validation cohorts, respectively; and (**E** and **F**) 40-month MACCE risk in the training and validation cohorts, respectively.

Discussion

This study introduces an innovative preoperative predictive model that effectively integrates inflammatory markers with traditional cardiovascular risk factors to enhance prognostic assessments in UAP patients with angiographically intermediate coronary lesions (Figure 8). By applying the Boruta method, this study identified critical clinical features that significantly predict MACCEs in these patients, showcasing the pivotal role of inflammation in their condition. The developed nomogram provides a valuable tool for visualizing the complex interactions among inflammation, metabolic parameters, and established risk factors, thereby facilitating more precise risk stratification and personalized treatment planning. The model's robust performance, demonstrated by its AUC values, calibration and DCA, demonstrates its potential clinical utility for improving patient outcomes through targeted coronary interventions.

Currently, coronary heart disease, particularly when accompanied by intermediate coronary lesions, presents a unique and complex challenge in the field of cardiovascular medicine.[22–24] Clinically, such cases, characterized by the instability of angina symptoms and the ambiguity posed by intermediate coronary lesions (50%–70% stenosis), require a nuanced approach to risk stratification and management. Therefore, the critical nature of addressing this subset of coronary heart disease lies in the delicate balance between progression to ACS and the indeterminate threshold of coronary revascularization benefits. Our study focused on this sensitivity, aiming to enhance prognostic assessments by integrating inflammatory markers with traditional risk factors in an advanced predictive modeling approach for UAP patients with angiographically intermediate coronary lesions.

The main pathophysiological processes associated with ACS are related to the rupture of an atherosclerotic plaque that is unstable, which leads to the formation of a blood clot. The involvement of inflammation in these mechanisms has been supported by pathological examinations and further confirmed by optical coherence tomography studies.[9,25,26]

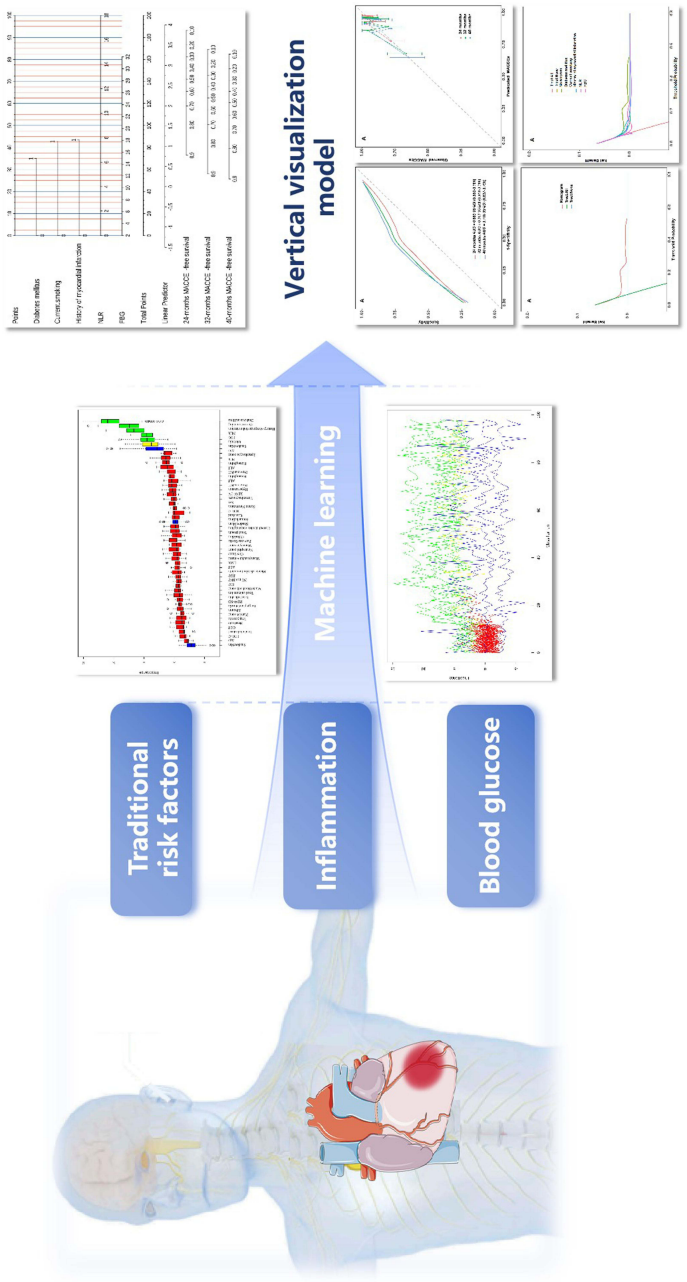

Figure 8 Identifcation of MACCEs risk predictors using machine learning. Our study presents a biomarker-driven vertical visualization model for predicting long-term prognosis in patients with unstable angina pectoris and angiographically intermediate coronary lesions, emphasizing the crucial role of inflammation in their clinical condition.

Neutrophils are known to be key players in acute inflammation, but growing research highlights their critical role in sustaining chronic inflammation as well.[27] Elevated neutrophil levels contribute to the release of inflammatory mediators, such as serine proteases and neutrophil extracellular traps, and promote interactions among immune cells.[28] In chronic inflammation, changes in immune cell numbers and functions have significant prognostic implications.[27,28] Previous studies have shown that an elevated neutrophil count, alongside a reduced lymphocyte count, correlates with increased mortality in multiple cardiovascular diseases.[29] The NLR is a recent addition to the extensive list of inflammatory markers. Derived from a complete blood count with normalization, the NLR serves as an inexpensive and easily obtainable marker for inflammation.[29,30] Previous research has demonstrated its wide utility and ability to assist in risk stratification for patients with various cardiovascular conditions, alongside conventional markers.[29] Furthermore, it has been linked to arterial stiffness and elevated coronary calcium scores, both significant indicators of cardiovascular disease.[29] The NLR has been identified as an independent prognostic factor for outcomes in stable coronary artery disease and as a predictor of both short- and long-term mortality in individuals experiencing ACS.[29] A recent meta-analysis evaluated the diagnostic and prognostic value of the NLR in ACS, utilizing data from 90 studies involving 45,990 participants, and the findings revealed significant differences in NLR values among various types of ACS their correlation with mortality.[31] Specifically, lower NLR values are observed in survivors, while elevated NLR values are found in ACS patients who experience adverse cardiovascular events.[31] Furthermore, evidence in the literature also indicates that the NLR, as a biomarker of inflammation, exhibits a strong correlation with the occurrence of plaque rupture in ACS patients with only an intermediate coronary artery lesion.[32] Therefore, prior clinical studies underscore the efficacy of the NLR as a valuable diagnostic tool for differentiating various types of ACS and for prognosticating the risks of adverse outcomes.[31,32] However, current evidence is limited regarding a possible link between the NLR and the occurrence of long-term MACCEs in UAP patients with angiographically intermediate coronary lesions.

The primary innovation of our study was the integration of the NLR with established cardiovascular risk factors to construct a predictive model for MACCEs. The Boruta method was employed to ensure that the most relevant and impactful clinical features were included in the model, ultimately enhancing its predictive accuracy. This integrated approach not only underscores the interplay between the NLR and traditional risk factors but also offers a more comprehensive tool for clinicians in assessing patient risk profiles. In our previous research endeavors, we employed machine learning techniques to analyze intricate datasets and identify significant predictive variables. The resultant visualizations revealed patterns and interactions among predictors, providing essential insights into the influences of various factors on the risks of adverse outcomes. This approach enhances the comprehension of risk profiles and aids in the effective dissemination of findings to healthcare professionals, thereby supporting the development of personalized treatment strategies.[5,6,16–19] The present study identified diabetes mellitus, current smoking, a history of myocardial infarction, the NLR, and fasting blood glucose as significant predictors of long-term MACCEs in our patient population. These results align with existing literature highlighting the relevance of metabolic control and lifestyle factors to cardiovascular outcomes. However, the inclusion of the NLR, an inflammatory marker, as a significant predictor emphasizes the need for clinicians to consider inflammation as a crucial component of coronary heart disease pathogenesis. Moreover, our findings emphasize the significance of considering patient demographics when applying the nomogram in clinical practice, highlighting its relevance to personalized medicine. For instance, it is crucial to acknowledge that the prognostic value of inflammatory markers may vary according to the presence of specific comorbid conditions. Additionally, by bridging the gap between innovative research methodologies and practical clinical applications, this study contributes to the evolving landscape of coronary artery disease management, highlighting the pivotal role of personalized medicine in optimizing long-term health outcomes. This visualization model facilitates risk factor evaluation and provides valuable insights for identifying patients who are likely to benefit from coronary interventions. Furthermore, our aim is to contribute to the development of more personalized and efficacious management strategies for this high-risk population by enhancing comprehension of the intricate interplay between inflammation and adverse outcomes, drawing upon data from large-scale, multi-center studies.

Study Limitations

First, the retrospective design of the present study inherently limits the causal inferences that can be drawn from the findings. The reliance on medical records for data collection may introduce potential biases and inaccuracies, particularly

concerning historical and clinical variables. Second, the study cohort was restricted to a single-center population, which may limit the generalizability of the results to broader, more diverse populations. Multicenter studies are needed to confirm the applicability of the predictive model in different demographic and clinical settings. Third, while the model incorporates several key inflammatory and traditional risk markers, other potentially significant variables may not have been captured or included, potentially impacting the model's comprehensiveness and predictive accuracy. Fourth, additional evaluations via endovascular imaging and coronary functional techniques are lacking. Finally, the follow-up duration, although significant, was limited to 40 months, which may not fully capture long-term cardiovascular outcomes and risks. Future research with extended follow-up periods and larger, more diverse cohorts is needed to validate and refine the model further.

Conclusions

This study presents a novel preoperative prediction model that combines an inflammatory marker, the NLR, with traditional risk factors for assessing the long-term risks of MACCEs in patients with UAP and intermediate coronary lesions. Our model offers a clear visualization of the complex interactions between inflammatory factors, metabolic factors, and traditional cardiovascular risks, which can facilitate more precise risk stratification and decision-making in clinical settings.

Abbreviations

ACS, acute coronary syndromes; MACCEs, major adverse cardiac and cerebrovascular events; UAP, unstable angina pectoris; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic; DCA, decision curve analysis; IQRs, interquartile ranges; SDs, standard deviations; CI, confidence interval.

Data Sharing Statement

Individual participant data that underlie the results reported in this article, after de-identification can be obtained from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

Ethical approval for this study was granted by the local research ethics committee (The Suzhou First People's Hospital, No.SzTTLLKy2024015). Because of the retrospective design of the study, the need to obtain informed consent from eligible patients was waived by the ethics committee. We ensured strict confidentiality of all patient information and adhered fully to the principles outlined in the Declaration of Helsinki throughout the research process.

Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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