Original Article

Correlation of blood lipids, glucose, and inflammatory indices with the occurrence and prognosis of lesion complexity in unstable angina, a retrospective cohort study

Yingkai Xu[1]^, Guiling Ma[1], Boqia Xie[1,2], Jing Zhao[3], Xingpeng Liu[1], Jianjun Zhang[1], Mulei Chen[1]^

[1]Department of Cardiology, Beijing Chaoyang Hospital, Heart Center and Beijing Key Laboratory of Hypertension, Capital Medical University, Beijing, China; [2]Department of Cardiovascular Imaging Center, Beijing Chaoyang Hospital, Heart Center and Beijing Key Laboratory of Hypertension, Capital Medical University, Beijing, China; [3]Department of Cardiac Surgery, Beijing Chaoyang Hospital, Heart Center and Beijing Key Laboratory of Hypertension, Capital Medical University, Beijing, China

Contributions: (I) Conception and design: Y Xu, G Ma, M Chen; (II) Administrative support: Y Xu, M Chen, G Ma, J Zhang, X Liu; (III) Provision of study materials or patients: Y Xu, J Zhao, B Xie, M Chen; (IV) Collection and assembly of data: Y Xu, M Chen, B Xie, G Ma; (V) Data analysis and interpretation: Y Xu, J Zhao, J Zhang, X Liu, M Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Mulei Chen, MD. Department of Cardiology, Beijing Chaoyang Hospital, Heart Center and Beijing Key Laboratory of Hypertension, Capital Medical University, No. 8 South Road of Beijing Workers' Stadium, Chaoyang District, Beijing 100020, China. Email: cyyycmlxn@126.com.

Background: In recent years, novel cardiometabolic biomarkers and related pathogenic genes and their heritability have been examined. However, no multitarget predictive evaluation models exist can identify and predict complex lesions in unstable angina (UA) in the early stages before coronary angiography (CAG) or evaluate the prognosis of patients with UA and complex lesions. In this study, we sought to investigate the correlation between blood lipid, glucose, and inflammatory indices and the occurrence and prognosis of UA with complex lesions, and also the risk factors for major adverse cardiocerebrovascular events (MACCEs).

Methods: Patients with UA who underwent percutaneous coronary intervention (PCI) at Chaoyang Hospital between March 2019 and December 2020 were included. Patients with UA who underwent PCI were divided into complex lesion group and noncomplex lesion group according to the CAG results. The blood lipid and glucose levels, inflammatory indices, Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) scores, and clinical outcome events after 3 years follow-up from both groups were calculated.

Results: A total of 523 patients were included, with 248 and 275 patients in the complex and noncomplex lesion groups, respectively. There were no significant differences between the two groups in terms of sex, age, medical history, or demographic characteristics. After 3 years of follow-up, compared with the noncomplex lesion group, the complex lesion group had a higher incidence of target vessel revascularization (TVR) (8.1% *vs.* 4.0%; P=0.049) and MACCEs (11.7% *vs.* 5.8%; P=0.02). High remnant lipoprotein cholesterol (RLP-C) level, high small dense low-density lipoprotein cholesterol (sLDL-C) level, high lipoprotein (a) [Lp(a)] level, high high-sensitivity C-reactive protein (hs-CRP) level, low lymphocyte level, low albumin level, and low hs-CRP:albumin ratio (CAR) were found to be risk factors for the occurrence of UA with complex lesions. High RLP-C level, high sLDL-C level, high Lp(a) level, and high neutrophil:lymphocyte ratio (NLR) were independent risk factors for MACCEs in the complex lesion group, from which a new prediction model was created. The area under the curve (AUC) of the new model for predicting MACCEs events after 3 years of follow-up [AUC =0.935; 95% confidence interval (CI): 0.881–0.989] in the complex lesion group was higher than that of the SYNTAX score (AUC =0.671; 95% CI: 0.584–0.757) (P<0.001).

^ ORCID: Yingkai Xu, 0000-0003-2945-2724; Mulei Chen, 0009-0009-3795-5912.

Conclusions: Blood lipid and glucose levels and inflammatory indices may be associated with the occurrence of UA with complex lesions. The new model for UA with complex lesions constructed using high RLP-C level, high sLDL-C level, high Lp(a) level, and high NLR level had a stronger ability to predicts MACCEs during follow-up than did the SYNTAX score. Our findings could enhance early detection of patients with UA and complex lesions, potentially improving prevention and treatment strategies for perioperative UA-PCI patients.

Keywords: Unstable angina (UA); complex lesions; blood lipids; glucose levels; inflammatory indices

Submitted Dec 05, 2024. Accepted for publication Jan 09, 2025. Published online Jan 22, 2025.
doi: 10.21037/jtd-2024-2122
View this article at: https://dx.doi.org/10.21037/jtd-2024-2122

Introduction

Unstable angina (UA) is a clinical type of non-ST segment elevation acute coronary syndrome (NSTE-ACS) that is characterized by a rapid onset and easily develops into myocardial infarction (MI) or sudden death (1). Owing to the negative serum cardiac markers of UA, these patients are often overlooked in clinical practice, which may lead to catastrophic clinical outcomes, especially for those patients with complex lesions. There are numerous evaluation indicators related to the grading and risk stratification of acute coronary syndrome (ACS), such as the Global Registry of Acute Coronary Events (GRACE) score, for predicting the risk level of patients with ACS. However, no multitarget predictive evaluation models exist that can identify and predict complex lesions in UA in the early stages before coronary angiography (CAG) or that can evaluate the prognosis of patients with UA and complex lesions (2). The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score can assess the complexity of coronary artery lesions, but it needs to be calculated after CAG, and the effectiveness of SYNTAX score and its derived score (SYNTAX II, etc.) on the long-term impact of clinical events in patients with UA and complex lesions is limited (3). Therefore, early attention to UA with complex lesions and the establishment of pre-CAG clinical prediction models can prevent further deterioration in patients and improve prognosis.

The predictive factors for these complex lesions have typically been traditional indicators, such as low-density lipoprotein cholesterol (LDL-C), age, N-terminal pro-B-type natriuretic peptide (NT-proBNP), and high-sensitivity C-reactive protein (hs-CRP), which lack specificity (4,5). While a recent study indicated that indicators, such as cystatin C levels, can influence the occurrence of major adverse cardiocerebrovascular events (MACCEs) in ACS patients after percutaneous coronary intervention (PCI), this study focused on single target and did not encompass the impact of multiple metabolic markers on outcomes (6). In recent years, with the development of metabolomics and genomics for cardiovascular diseases, novel cardiometabolic biomarkers and related pathogenic genes and their heritability have been examined (7,8). Although some novel biomarkers, such as microRNAs are closely linked to UA, their routine use in patients is limited due to the high cost and logistical challenges associated with their detection (9). In addition to novel cardiometabolic biomarkers, psychological and mental factors also influence the prognosis of ACS patients (10). Although a previous study on predictive models for MACCEs in AMI-PCI patients (11), further research is needed to determine the correlation between blood lipids, glucose, inflammatory indices, and the occurrence and prognosis of UA with complex lesions, as well as the management of patients with UA after PCI. In this context, we conducted this study to develop a multivariable prediction model which could predict the occurrence and prognosis of UA with complex lesions. We present this article in accordance with the TRIPOD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2024-2122/rc).

Methods

Study design and population

Patients who underwent PCI and were diagnosed with UA at the Heart Center of Beijing Chaoyang Hospital, Capital Medical University, from March 2019 to December 2020, were retrospectively included in this study. Complex lesions were those that met any of the following conditions: (I)

≥3 stents implanted; (II) ≥3 lesions treated; (III) 2 stent implantations for bifurcate lesions; (IV) total stent length ≥60 mm; and (V) chronic total-occlusion (CTO) lesions (12). Patients with UA who underwent PCI were divided into a complex lesion group and noncomplex lesion group according to the CAG results.

The inclusion criteria for patients were as follows: (I) new-onset or aggravated chest pain symptoms on exertion or angina without elevated serum cardiac markers diagnosed as UA (1); (II) UA and coronary artery stenosis confirmed via CAG and completion of PCI treatment; and (III) regular intake of medication according to the clinician's advice and completion of follow-up. Meanwhile, the exclusion criteria were as follows: (I) no PCI or medication being the sole treatment; (II) coronary artery bypass graft (CABG) treatment; (III) ACS with ST-segment elevation myocardial infarction (STEMI) or non-ST segment elevation myocardial infarction (NSTEMI); (IV) presence of terminal malignant tumors, uncontrolled infections, or severe autoimmune diseases that could seriously affect prognosis; (V) incomplete clinical data for blood lipid, glucose level, or inflammatory indices during admission; (VI) intolerance to anticoagulants; (VII) incomplete follow-up data; and (VIII) lack of consent to participate in the study.

The baseline data, laboratory results, imaging results, and follow-up period of the two groups were collected, and the blood lipid and glucose levels, inflammatory indices, SYNTAX scores, and clinical outcome events after 3 years of follow-up from both groups were calculated. This study was approved by the Ethics Committee of Beijing Chaoyang Hospital, Capital Medical University (No. 2024-345) and conformed to principles of the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from all the patients.

Highlight box

Key findings

- Blood lipid and glucose levels and inflammatory indices may be associated with the occurrence of unstable angina (UA) with complex lesions.
- The new model for UA with complex lesions was constructed using remnant lipoprotein cholesterol (RLP-C), small dense low-density lipoprotein cholesterol (sLDL-C), lipoprotein (a) [Lp(a)], and neutrophil:lymphocyte ratio (NLR) had a stronger ability to predict major adverse cardiocerebrovascular events (MACCEs) during follow-up than did the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score.

What is known and what is new?

- The predictive factors for these complex lesions have mostly consisted of traditional indicators, such as LDL-C, age, N-terminal pro-B-type natriuretic peptide, and high-sensitivity C-reactive protein, which lack specificity.
- In this study, blood lipid and glucose levels and inflammatory indices were found to be associated with the occurrence of complex lesions in UA. The new model constructed using RLP-C, sLDL-C, Lp(a), and NLR could more effectively predict MACCEs during follow-up than could the SYNTAX score in the patients with UA and complex lesions.

What is the implication, and what should change now?

- We created a multitarget and multisystem metabolic-related risk factor model to predict the occurrence and prognosis of UA with complex lesions. This can provide novel insights into the early identification of patients with UA and complex lesions and the prevention and treatment targets for cardiologists in the long-term clinical management of these patients after percutaneous coronary intervention.

Biochemical analysis and definitions

All patients underwent fasting serum sample collection and laboratory tests (hemogram and lipid profiles) after fasting overnight (>12 h). The concentrations of high-density lipoprotein cholesterol (HDL-C), LDL-C, total cholesterol (TC), and triglycerides (TGs) were measured via standard laboratory procedures with a fully automatic biochemical analyzer (ADVIA 2400 Clinical Chemistry System, Siemens Healthineers, Erlangen, Germany). Lipoprotein (a) [Lp(a)] was assayed via immunoturbidimetry with a fully automatic biochemical analyzer (ADVIA 2400 Clinical Chemistry System). Glycosylated hemoglobin A1c (HbA1c) was measured via high-performance liquid chromatography with an automated glycohemoglobin analyzer (Tosoh Corporation, Tokyo, Japan). hs-CRP levels were measured via Ultrasensitive CRP Kit (Aidian Oy, Jyväskylä, Finland). Small dense low-density lipoprotein cholesterol (sLDL-C) levels were measured using a commercial kit (McBioengineering, Beijing, China). RLP-C was calculated as follows: RLP-C (mmol/L) = TC (mmol/L) – HDL (mmol/L) – LDL (mmol/L) (13). The TG-glucose (TyG) index was calculated as follows: Napierian logarithm (ln) [TG (mg/dL) × fasting plasma glucose (FPG) (mg/dL)/2] (14). The neutrophil:lymphocyte ratio (NLR) was calculated based on the ratio of absolute neutrophil (NE) and lymphocyte (LYN) counts (15). The hs-CRP:albumin ratio (CAR) was defined as the ratio of hs-CRP to albumin

(ALB) (16).

PCI procedure and SYNTAX score

All patients who underwent PCI were given 300 mg of aspirin (Bayer AG, Leverkusen, Germany) and 300 mg of clopidogrel bisulfate (Sanofi Winthrop Industrie, Paris, France) or 180 mg of ticagrelor (AstraZeneca, Cambridge, UK). All patients were administered 3,000 IU of heparin (Shanghai No. 1 Biochemical Pharmaceutical Co., Ltd., Shanghai, China) intrathecally at the beginning of angiography, and additional heparin was provided during PCI if required (100 IU/kg of body weight). The surgeon determined the use of tirofiban during PCI. The SYNTAX score was calculated using the SYNTAX score online calculator (https://m.medsci.cn/scale/show.do?id=f1f22922dc) with reference to the algorithm of a previous study (3). The results were assessed by two interventional cardiologists with at least 5 years of interventional experience based on the angiography results. Cardiologists were blinded to the patients' blood lipid, glucose, and inflammatory indices and to the patients' grouping. If there were any discrepancies in the results of patients' SYNTAX score calculations, the final decision was made through discussion among all cardiologists at the heart center. All patients routinely received 100 mg of aspirin (Bayer AG) once daily and 75 mg of clopidogrel bisulfate (Sanofi Winthrop Industrie) once daily or 90 mg of ticagrelor (AstraZeneca) twice daily after PCI unless contraindications (such as bleeding) were present.

Medication and follow-up

All patients were followed-up through outpatient visits, telephone calls, or readmissions for CAG (patients with recurrent UA symptoms). Routine outpatient or telephone follow-ups were conducted at 3 months, 6 months, 1 year, 2 years, and 3 years. The endpoint events of follow-up were MACCEs, MI, target vessel revascularization (TVR), death, and stroke. MACCEs included death, MI, TVR, and stroke. Death was considered cardiogenic unless there was clear evidence to prove that it was not correlated with cardiogenic factors (17). MI was considered to be a cardiac troponin I (cTnI) level > the upper reference limit (URL), symptoms of myocardial ischemia, and a patient meeting any of the following requirements: (I) recent pathological Q-wave or newly occurring ischemic electrocardiogram change; (II) coronary artery occlusion or severe stenosis with thrombus confirmed by angiography; and (III) new-onset myocardial activity reduction or ventricular wall motion abnormalities consistent with the cause of ischemia confirmed by imaging (18). During the follow-up period, outpatient cardiovascular physicians determined the use of β-blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs), and proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitor.

Statistical analysis

To estimate sample size, we made assumptions based on two previous studies (19,20) and the average incidence of MACCEs reported therein was selected for the sample size calculation. The sample size was calculated based on an expected prevalence rate (π) of 9.5%, an allowable error (δ) of 0.03, and a two-tailed standard normal variate value with $u_{\alpha/2}$ set at 1.96. The initial calculation yielded a sample size of 367. To account for a potential 20% loss to follow-up, the sample size was adjusted to 440.

For quantitative data, normally distributed data are expressed as the mean ± standard deviation (SD), and *t*-tests were used for two-group comparisons. Variables with skewed distribution data are shown as the median and interquartile range (IQR), and the Wilcoxon rank-sum test was used for intergroup comparisons. Categorical variables are expressed as percentages and were analyzed using the Chi-squared test or Fisher exact test. The cumulative incidence rate of endpoint events in the two groups of patients was determined using Kaplan-Meier survival analysis and evaluated using the log-rank test. Multivariate logistic regression analysis was used to determine the risk factors affecting the incidence of complex lesions in patients with UA, and the results are presented in a forest plot. Univariate and multivariate logistic regression analyses were used to determine the risk factors for MACCEs in the complex lesion group. Statistically significant factors in the univariate logistic regression analysis were included in the final multivariate logistic regression model. Based on the final results of the multivariate logistic regression model in the UA complex lesion group, a nomogram was established using the R (The R Foundation of Statistical Computing) to identify the risk factors for MACCEs in the complex lesion group during the follow-up period. The area under the curve (AUC) was then calculated to evaluate the predictive accuracy of the nomogram. The receiver operating characteristic (ROC) curve was used to evaluate the ability of the new predictive model based on the nomogram and SYNTAX score to predict the incidence

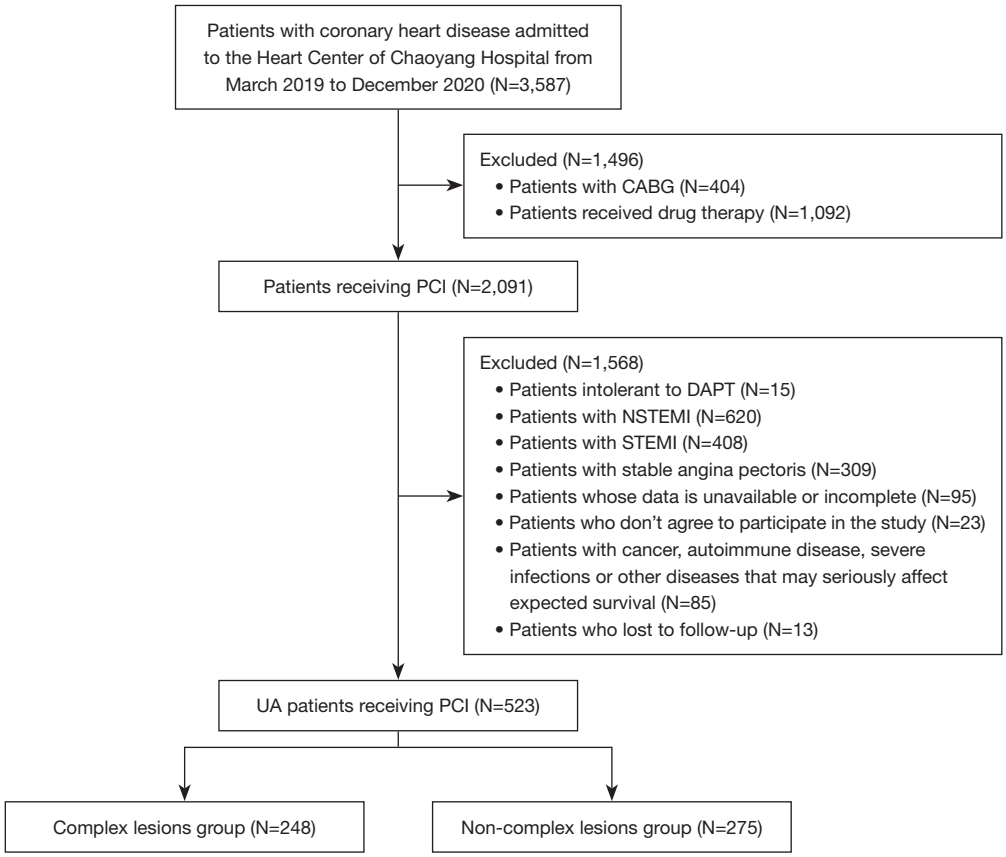

Figure 1 Study flowchart. CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; DAPT, dual antiplatelet therapy; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina.

of MACCEs in the complex lesion group. A two-tailed P value <0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS 26 (IBM Corp., Armonk, NY, USA) and R version 3.6.1.

Results

Laboratory metabolic indices and demographic characteristics

A total of 523 patients were included, with 248 and 275 patients in the complex and noncomplex lesion groups, respectively (*Figure 1*). In the complex lesion group, 29 (11.7%) patients experienced MACCEs, while 16 (5.8%) experienced MACCEs in the noncomplex lesion group. There were no significant differences between the two groups in terms of sex, age, medical history, or demographic characteristics (*Table 1*).

The mean first blood glucose (FBG) levels in the complex lesion group were significantly higher than those in the noncomplex lesion group (6.51±2.76 *vs.* 5.67±2.16 mmol/L; P<0.001), but there was no statistically significant difference in LDL or TC levels between the two groups. The mean HDL-C level (0.99±0.24 mmol/L) in the noncomplex lesion group was higher than that in the complex lesion group (0.92±0.25 mmol/L) (P=0.001). The mean level of sLDL-C in the complex lesion group was higher than that in noncomplex lesion group (0.94±0.47 *vs.* 0.78±0.40 mmol/L; P<0.001), and the median level of Lp(a) in the complex lesion group (median: 31.25 mg/dL, IQR: 11.93–67.48 mg/dL) was also higher than that in noncomplex lesion group (median: 15.00 mg/dL, IQR: 8.50–28.70 mg/dL) (P<0.001). No significant difference was found between the two groups for other laboratory indicators such as left ventricular ejection fraction or BNP level. In terms of metabolic indicators, the TyG index in the complex lesion group was higher than that in the noncomplex lesion group (8.95±0.65 *vs.* 8.72±0.68) (P<0.001), and the RLP-C level

Table 1 Medical history and demographic characteristics of the patients

Indexes	Noncomplex lesions (n=275)	Complex lesions (n=248)	P value
Male	183 (66.5)	180 (72.6)	0.14
Age (years)	63.99±9.77	64.04±10.04	0.95
BMI (kg/m^2)	25.47±3.00	25.57±2.88	0.70
Medical history			
Hypertension	192 (69.8)	184 (74.2)	0.27
Diabetes mellitus	107 (38.9)	115 (46.4)	0.09
Dyslipidemia	198 (72.0)	184 (74.2)	0.57
Previous stroke	32 (11.6)	33 (13.3)	0.56
Previous MI	54 (19.6)	58 (23.4)	0.30
Previous CABG	10 (3.6)	16 (6.5)	0.14
Peripheral artery disease	17 (6.2)	25 (10.1)	0.10
Smoking	93 (33.8)	96 (38.7)	0.25

Data are presented as n (%) or mean ± standard deviation. BMI, body mass index; MI, myocardial infarction; CABG, coronary artery bypass graft.

in complex lesion group (0.87±0.62 mmol/L) was higher than that in noncomplex lesion group (0.67±0.39 mmol/L) (P<0.001). Among the inflammatory indicators, the NE count in complex lesion group [(4.96±2.20)×10^9] was higher than that in noncomplex lesion group [(4.39±1.69)×10^9] (P=0.001), the LYN count in the complex lesion group [(1.72±0.61)×10^9] was lower than that in the noncomplex lesion group [(1.97±0.68)×10^9] (P<0.001), and the NLR in complex lesion group was higher than that in noncomplex lesion group (3.36±2.27 *vs.* 2.58±1.86; P<0.001). The erythrocyte sedimentation rate (ESR) in the complex lesion group (median: 8.00 mm/h, IQR: 4.00–12.00 mm/h) was higher than that in noncomplex lesion group (median: 6.00 mm/h, IQR: 2.00–10.00 mm/h) (P<0.001), and the CAR in the complex lesion group (median: 0.06, IQR: 0.02–0.10) was higher than that in noncomplex lesion group (median: 0.03, IQR: 0.01–0.06) (P<0.001) (*Table 2*). Multivariate logistic regression analysis was conducted on indicators that showed significant differences, and it was found that high RLP-C level, high Lp(a) level, high sLDL-C level, high hs-CRP level, low LYN level, low ALB level, and low CAR were associated with a risk of complex lesions forming in patients with UA (*Figure 2*).

PCI characteristics and follow-up results

The SYNTAX score in the noncomplex lesion group (15.81±6.84) was lower than that in complex lesion group (30.10±8.14) (P<0.001), while the number and total length of stents implanted in the left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA) in patients in the complex lesion group were significantly higher than those in the noncomplex lesion group (P<0.001). The use of coronary rotational atherectomy/excimer laser coronary atherectomy (ELCA) and cutting balloon was more frequent in patients with complex lesions than in those with noncomplex lesions (*Table 3*). During the follow-up period, no significant differences were found in the use of β-blockers, ACEI/ARB, PCSK-9 inhibitors, or other drugs between the two groups. At the 1-year follow-up, there was no significant difference in the incidence of adverse events between the two groups. However, after 3 years of follow-up, the incidence of TVR and MACCEs in the complex lesion group was significantly higher than that in the noncomplex lesion group (TVR: 8.1% *vs.* 4.0%, P=0.049; MACCE: 11.7% *vs.* 5.8%; P=0.02) (*Table 4* and *Figure 3*).

Subgroup analysis of complex lesions

Univariate logistic regression analysis showed that the high TyG index, high RLP-C level, high sLDL-C level, high Lp(a) level, high NLR level, high BNP level and high SYNTAX score were risk factors for MACCEs in the

Table 2 Comparison of laboratory examination and lipid metabolism indices between the two groups

Indexes	Noncomplex lesions (n=275)	Complex lesions (n=248)	P value
HDL-C (mmol/L)	0.99±0.24	0.92±0.25	0.001
LDL-C (mmol/L)	2.17±0.72	2.14±0.77	0.65
TC (mmol/L)	3.83±0.87	3.93±0.95	0.19
TGs (mmol/L)	1.65±1.02	1.80±0.12	0.11
FBG (mmol/L)	5.67±2.16	6.51±2.76	<0.001
TyG index	8.72±0.68	8.95±0.65	<0.001
RLP-C (mmol/L)	0.67±0.39	0.87±0.62	<0.001
sLDL-C (mmol/L)	0.78±0.40	0.94±0.47	<0.001
Lp(a) (mg/dL)	15.00 (8.50–28.70)	31.25 (11.93–67.48)	<0.001
WBC ($\times10^9$)	7.06±1.93	7.31±1.27	0.19
NE ($\times10^9$)	4.39±1.69	4.96±2.20	0.001
LYN ($\times10^9$)	1.97±0.68	1.72±0.61	<0.001
NLR	2.58±1.86	3.36±2.27	<0.001
HGB (g/L)	133.26±14.17	133.53±18.21	0.85
PLT ($\times10^9$)	222.50±86.36	214.07±54.72	0.19
Hcy (μmol/L)	15.72±7.08	16.52±7.29	0.20
HbA1c (%)	6.62±1.35	6.96±1.56	0.01
hs-CRP (mg/L)	1.24 (0.53–2.27)	2.4 (0.72–3.73)	<0.001
ALB (g/L)	41.02±3.30	39.96±3.37	<0.001
CAR	0.03 (0.01–0.06)	0.06 (0.02–0.10)	<0.001
ESR (mm/h)	6.00 (2.00–10.00)	8.00 (4.00–12.00)	<0.001
Creatinine (μmol/L)	71.62±33.27	79.27±60.84	0.08
eGFR (mL/min/1.73 m^2)	83.12±25.54	81.83±25.02	0.56
Uric acid (μmol/L)	359.57±84.59	363.49±91.37	0.61
BNP (pg/mL)	42.00 (20.00–87.00)	49.50 (25.00–89.75)	0.12
LVEF (%)	64.94±4.51	64.17±6.83	0.19

Data are presented as mean ± standard deviation or median (interquartile range). HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TGs, triglycerides; FBG, first blood glucose; TyG, triglyceride-glucose; RLP-C, remnant lipoproteins cholesterol; sLDL-C, small dense low- density lipoprotein cholesterol; Lp(a), lipoprotein (a); WBC, white blood cell; NE, neutrophil; LYN, lymphocyte; NLR, neutrophil:lymphocyte ratio; HGB, hemoglobin; PLT, platelet; Hcy, homocysteine; HbA1c, glycosylated hemoglobin A1c; hs-CRP, high-sensitivity C-reactive protein; ALB, albumin; CAR, high-sensitivity C-reactive protein:albumin ratio; ESR, erythrocyte sedimentation rate; eGFR, epidermal growth factor receptor; BNP, B-type natriuretic peptide; LVEF, left ventricular ejection fraction.

complex lesion group at 3 years of follow-up. Multivariate logistic regression analysis indicated that high RLP-C level, high sLDL-C level, high Lp(a) level, and high NLR level were independent risk factors for MACCE in the complex lesion group at 3 years of follow-up (*Table 5*). A nomogram was then generated to predict MACCEs in the complex lesion group at the 3-year follow-up (*Table 6* and *Figure 4*). The AUC of this model for predicting MACCEs in the complex lesion group at the 3-year follow-up [AUC =0.935; 95% confidence interval (CI): 0.881–0.989] was higher than

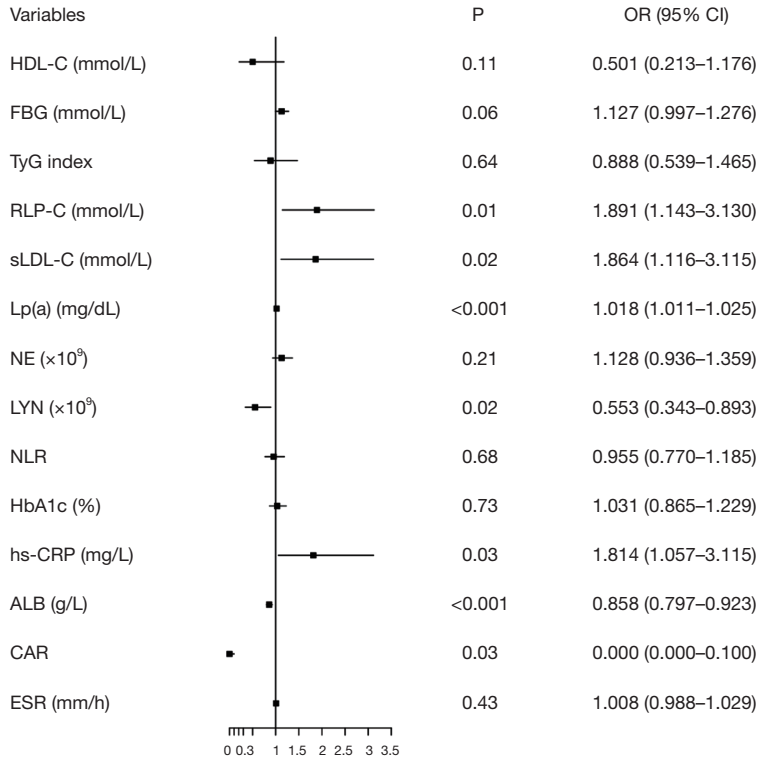

Figure 2 Multivariate logistic regression analysis of risk factors associated with lesion complexity in patients with UA. OR, odds ratio; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; FBG, first blood glucose; TyG, triglyceride-glucose; RLP-C, remnant lipoproteins cholesterol; sLDL-C, small dense low- density lipoprotein cholesterol; Lp(a), lipoprotein (a); NE, neutrophil; LYN, lymphocyte; NLR, neutrophil:lymphocyte ratio; HbA1c, glycosylated hemoglobin A1c; hs-CRP, high-sensitivity C-reactive protein; ALB, albumin; CAR, high-sensitivity C-reactive protein:albumin ratio; ESR, erythrocyte sedimentation rate; UA, unstable angina.

that of the SYNTAX score (AUC =0.671; 95% CI: 0.584–0.757) (P<0.001) (*Figure 5*).

Discussion

In this study, we found that high RLP-C level, high Lp(a) level, high sLDL-C level, high hs-CRP level, low LYN level, low ALB level, and low CAR were independent risk factors for complex lesions in patients with UA. Even if optimal drug treatment was administered to both groups, the incidence of MACCEs was higher in the complex lesion group during follow-up than in the noncomplex lesion group. Additionally, the nomogram plot showed that high RLP-C level, high sLDL-C level, high Lp(a) level, and high NLR level were independent risk factors for MACCEs in the complex lesion group at follow-up. Moreover, the new model constructed via nomogram prediction had a stronger predictive ability for MACCEs than did the SYNTAX score in the complex lesion group.

The prognosis of patients with complex lesions was found to be worse than that of those with noncomplex lesions, with a 3-year follow-up MACCE incidence rate of 11.7%, which is in line with Kawashima *et al.*'s study (21). UA lesions involve a complex coronary anatomical morphology and multivessel stenosis. Once an STEMI or NSTEMI develops, the condition becomes critical. Therefore, early identification and effective management of patients with complex UA lesions during follow-up is critical. CAG is the gold-standard examination method but is invasive, often requires hospitalization, lacks convenience, and does not reduce the risk of death in patients with coronary artery disease (22). Novel biomarkers, such as long noncoding RNA and some peptides, can predict the prognosis and genesis of coronary artery disease (23,24), but these specific biomarkers have certain weaknesses, such as inconvenience and the inability to be routinely performed in hospitalized patients due to cost. Although some studies have shown that traditional biomarkers, such as hs-CRP, BNP, and LDL-C,

Table 3 Comparison of PCI surgical characteristics between the two groups

Indexes	Noncomplex lesions (n=275)	Complex lesions (n=248)	P value
SYNTAX score	15.81±6.84	30.10±8.14	<0.001
PCI target vessel			
LM	17 (6.2)	40 (16.1)	<0.001
LAD	151 (54.9)	174 (70.2)	<0.001
LCX	68 (24.7)	127 (51.2)	<0.001
RCA	93 (33.8)	152 (61.3)	<0.001
Maximum stent diameter in LM (mm)	3.68±0.43	3.71±0.39	0.76
Total stent length in LM (mm)	20.29±4.77	22.58±6.18	0.18
Stent implantation number (LAD)	1.18±0.38	1.61±0.69	<0.001
Maximum stent diameter in LAD (mm)	3.17±0.43	3.21±0.39	0.36
Total stent length in LAD (mm)	26.49±10.77	39.50±18.63	<0.001
Stent implantation number (LCX)	1.09±0.29	1.33±0.58	<0.001
Maximum stent diameter in LCX (mm)	2.83±0.46	2.95±0.44	0.09
Total stent length in LCX (mm)	22.93±7.41	30.50±16.27	<0.001
Stent implantation number (RCA)	1.15±0.36	1.91±0.86	<0.001
Maximum stent diameter in RCA (mm)	3.33±0.51	3.43±0.48	0.13
Total stent length in RCA (mm)	26.55±11.13	49.68±25.44	<0.001
PCI technique			
Coronary rotational atherectomy/ELCA	9 (3.3)	22 (8.9)	0.007
Cutting balloon	24 (8.7)	37 (14.9)	0.03
Drug balloon	98 (35.6)	86 (34.7)	0.82
IVUS/OCT	37 (13.5)	46 (18.5)	0.11
IABP	4 (1.5)	8 (3.2)	0.18

Data are presented as mean ± standard deviation or n (%). PCI, percutaneous coronary intervention; SYNTAX, Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery; LM, left main artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; ELCA, excimer laser coronary atherectomy; IVUS, intravenous ultrasound; OCT, optical coherence tomography; IABP, intra-aortic balloon pump.

can predict the prognosis of patients with multivessel lesions, their predictive ability for the prognosis of other complex lesions remains unclear (25,26). Thus, establishing a novel multitarget, convenient biomarker prediction model that incorporates blood lipid, glucose, and inflammatory indices for the predicting the genesis and prognosis of complex lesions in UA is essential.

There were no differences in BNP levels between the two groups, which differs from the findings of Kotecha *et al.* (27). This is because the levels of myocardial injury markers, including BNP, are not elevated in patients with UA, and the cardiac function might have been similar between the two groups, regardless of lesion complexity. Similarly, there were no differences in lipid indicators including TC, LDL-C, and TGs between the two groups, and LDL-C was not a risk factor for complex lesions, which may be related to the high proportion of statin use (95.41%) during follow-up. LDL-C level has been widely recognized as a risk factor for the occurrence and prognosis of coronary artery disease. Even with optimal statin therapy, some patients may still experience MACCEs despite their LDL-C being controlled within the normal scope recommended by the relevant

Table 4 Comparison of results during the follow-up between the two groups

Indexes	Noncomplex lesions (n=275)	Complex lesions (n=248)	P value
Drug used during follow-up period, n (%)			
β-blocker	194 (70.5)	179 (72.2)	0.68
ACEI/ARB	118 (42.9)	105 (42.3)	0.90
CCB	99 (36.0)	107 (43.1)	0.10
Statins	262 (95.3)	237 (95.6)	0.87
Hypoglycemic drugs or insulin	90 (32.7)	83 (33.5)	0.86
PCSK-9 inhibitor	23 (8.4)	24 (9.7)	0.60
ARNI	29 (10.5)	26 (10.5)	0.98
1-year follow-up, n (%)			
Target vessel MI[†]	3 (1.1)	6 (2.4)	0.32
Target vessel revascularization	5 (1.8)	7 (2.8)	0.44
Cardiac death[†]	2 (0.7)	4 (1.6)	0.43
MACCE	7 (2.5)	11 (4.4)	0.24
3-year follow-up, n (%)			
Target vessel MI	7 (2.5)	12 (4.8)	0.16
Target vessel revascularization	11 (4.0)	20 (8.1)	0.049
Cardiac death	5 (1.8)	9 (3.6)	0.20
MACCE	16 (5.8)	29 (11.7)	0.02

[†], using Fisher's exact test. ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; CCB, calcium channel blocker; PCSK-9, proprotein convertase subtilisin/kexin type 9; ARNI, angiotensin receptor neprilysin inhibitor; MI, myocardial infarction; MACCE, major adverse cardiocerebrovascular event.

guidelines.

Lp(a) was found to be a risk factor for the occurrence of complex UA lesions and MACCEs, which is consistent with the findings of Xu *et al.* (28), who reported that Lp(a) was related to the complexity of lesions, but not to long-term prognosis, in patients with coronary artery disease undergoing PCI. Chieng *et al.* (29) also found that a simultaneous increase in Lp(a) and LDL-C level is an independent predictor of high SYNTAX scores and lesion complexity in patients with early-onset coronary heart disease. These findings may be attributable to Lp(a) being associated with the accelerated progression of low-density coronary atherosclerotic plaque (necrotic core), which in turn hastens the process of atherosclerosis (30). Nurmohamed *et al.* using coronary computed tomography angiography scans, reported that higher levels of Lp(a) were correlated with the progression of plaque burden and increased inflammation of pericoronary adipose tissue, which may also help explain our results (31). In our study, sLDL-C was identified as another risk factor for the occurrence of complex lesions and poor prognosis in UA, which is in line with previous research (32,33). As a subgroup of LDL-C, sLDL-C is considered the main pathogenic component of LDL-C because of its high content of apolipoprotein B (Apo B), which facilitates its penetration into the arterial wall and leads to atherosclerosis. sLDL-C can also promote endothelial cell dysfunction and induce platelet aggregation in endothelial cells (34). In short, an increase in sLDL-C level leads to the occurrence of complex UA lesions, resulting in severe damage to the coronary artery. RLP-C was also found to be a risk factor associated with the occurrence and prognosis of complex UA lesions and may increase the risk of MACCEs in patients with UA and complex lesions. This finding is consistent with previous reports (35,36), which indicated that high RLP-C levels can lead to the

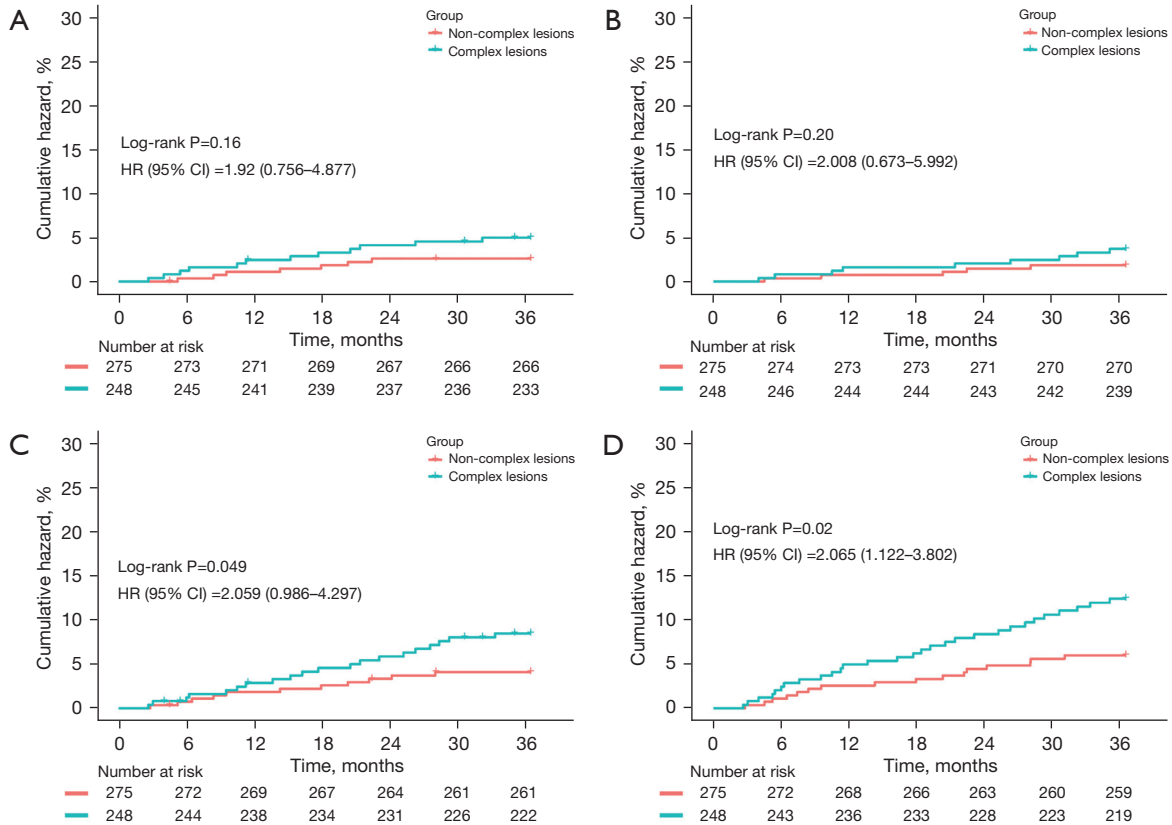

Figure 3 Kaplan-Meier curves for the comparison of (A) 3-year MI incidence, (B) 3-year mortality, (C) 3-year target reconstruction incidence, and (D) 3-year incidence of MACCEs between the noncomplex lesion group and complex lesion group. HR, hazard ratio; CI, confidence interval; MI, myocardial infarction; MACCEs, major adverse cardiocerebrovascular events.

occurrence of coronary artery disease and increase the risk of coronary artery disease in patients with type 2 diabetes mellitus. RLP-C includes intermediate-density lipoprotein cholesterol and very LDL-C, which have been shown to be associated with increased residual cardiovascular risk as derived lipid metabolism indices (37). RLP-C is more likely to penetrate the artery wall and accumulate in the vascular endothelium, which is absorbed by macrophages, thus accelerating the development of atherosclerosis and increasing the residual risk of cardiovascular disease. Delialis *et al.* (38) also confirmed that RLP-C is associated with a residual risk of atherosclerosis, which supports the findings of our study.

In terms of glucose metabolism, the TyG index in the complex lesion group was higher than that in the noncomplex lesion group. Univariate logistic regression analysis suggested that the TyG index was a risk factor for MACCEs in the complex lesion group, but in the multivariate logistic regression analysis, the TyG index was not a risk factor, which differs slightly from the study by Wang *et al.* (39). In their study, a higher average TyG index and TyG index variability were closely associated with the incidence of MACCEs. Another study proposed that the TyG index may be an important indicator for evaluating the occurrence and prognosis of cardiovascular disease and may predict MACCEs in patients with premature coronary artery disease (40). Wang *et al.* (41) reported that a higher TyG index was associated with multivessel coronary artery disease and predictive coronary artery disease severity of coronary artery disease in patients with early diabetes mellitus. Wang *et al.* (42) found that the TyG index could replace the coronary artery calcification score to predict the severity and prognosis of multivessel lesions in patients with ACS. The conclusions of our study are similar to those of the studies mentioned above; however, there are slight discrepancies owing to the variability in the included risk factors and subgroups.

In terms of the inflammatory index, our nomogram

Table 5 Univariate and multivariate logistic regression analysis of MACCE-related risk factors in the complex lesion group

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Male	1.213 (0.493–2.986)	0.68	–	–
Age	0.972 (0.935–1.010)	0.15	–	–
BMI	0.918 (0.8–1.054)	0.23	–	–
Hypertension	0.622 (0.272–1.419)	0.26	–	–
Diabetes mellitus	1.275 (0.587–2.769)	0.54	–	–
Smoking	1.559 (0.716–3.395)	0.26	–	–
HDL-C	0.674 (0.135–3.371)	0.63	–	–
LDL-C	0.855 (0.505–1.445)	0.56	–	–
TyG index	2.730 (1.535–4.854)	0.001	0.569 (0.176–1.840)	0.35
RLP-C	2.990 (1.729–5.171)	<0.001	3.480 (1.295–9.349)	0.01
sLDL-C	12.378 (4.923–31.125)	<0.001	12.418 (3.513–43.890)	<0.001
Lp(a)	1.018 (1.008–1.027)	<0.001	1.017 (1.004–1.031)	0.01
NLR	1.660 (1.393–1.979)	<0.001	1.600 (1.308–1.957)	<0.001
Hcy	0.977 (0.920–1.039)	0.46	–	–
HbA1c	0.993 (0.773–1.276)	0.96	–	–
CAR	2.316 (0.177–30.318)	0.52	–	–
eGFR	0.998 (0.982–1.013)	0.78	–	–
BNP	1.002 (1.000–1.004)	0.01	1.001 (0.999–1.003)	0.46
LVEF	0.966 (0.918–1.016)	0.18	–	–
SYNTAX score	1.072 (1.021–1.124)	0.005	1.065 (0.986–1.150)	0.11

MACCE, major adverse cardiocerebrovascular event; OR, odds ratio; CI, confidence interval; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride-glucose; RLP-C, remnant lipoprotein cholesterol; sLDL-C, small dense low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); NLR, neutrophil:lymphocyte ratio; Hcy, homocysteine; HbA1c, glycosylated hemoglobin A1c; CAR, high-sensitivity C-reactive protein:albumin ratio; eGFR, epidermal growth factor receptor; BNP, B-type natriuretic peptide; LVEF, left ventricular ejection fraction; SYNTAX, Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

Table 6 Multivariate logistic regression analysis of the new prediction model

Variables	Multivariate analysis	
	OR (95% CI)	P value
RLP-C	2.927 (1.498–5.721)	0.002
sLDL-C	11.228 (3.587–35.145)	<0.001
Lp(a)	1.016 (1.004–1.028)	0.009
NLR	1.640 (1.349–1.993)	<0.001

OR, odds ratio; CI, confidence interval; RLP-C, remnant lipoprotein cholesterol; sLDL-C, small dense low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); NLR, neutrophil:lymphocyte ratio.

identified NLR was an independent risk factor for poor prognosis in patients with UA and complex lesions. Similarly, Soylu *et al.* (43) found a positive correlation between NLR and GRACE and SYNTAX scores in the prognosis and lesion complexity of patients with NSTE-ACS. The study by Yuan *et al.* also showed that the combination of NLR and lipid metabolism indicators demonstrated higher specificity in assessing the severity of coronary artery disease in patients with ACS (44). NLR is a relatively novel inflammatory index that can better reflect the inflammatory and oxidative stress status and is often elevated in patients with coronary artery disease. Long-

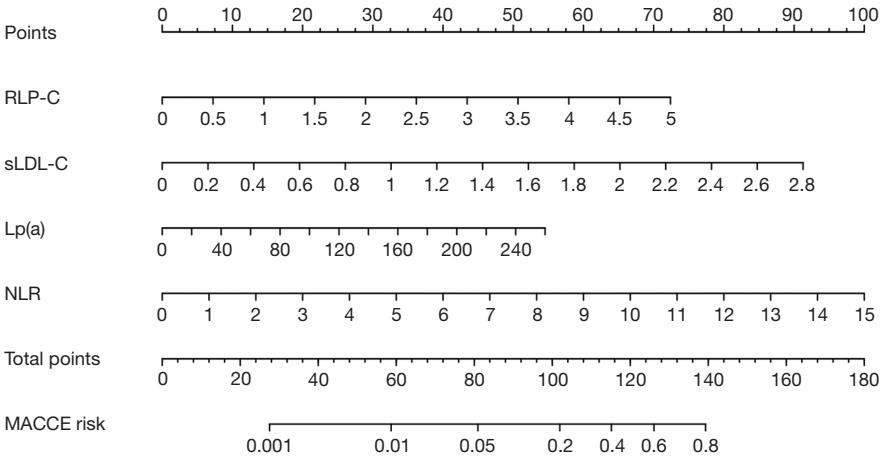

Figure 4 A nomogram predicting MACCEs in the complex lesion group. In the nomogram, each risk factor is located on the corresponding variable axis, and the score for each risk factor corresponds to the "Points" axis. Calculating the sum of the respective risk factor scores corresponds to the "Points" axis, from which each patient's total score can be determined. According to the "Total points" axis, the risk corresponding to each patient's total score for the target event is 0.001–0.8 (risk axis). RLP-C, remnant lipoproteins cholesterol; sLDL-C, small dense low- density lipoprotein cholesterol; Lp(a), lipoprotein (a); NLR, neutrophil:lymphocyte ratio; MACCE, major adverse cardiocerebrovascular event.

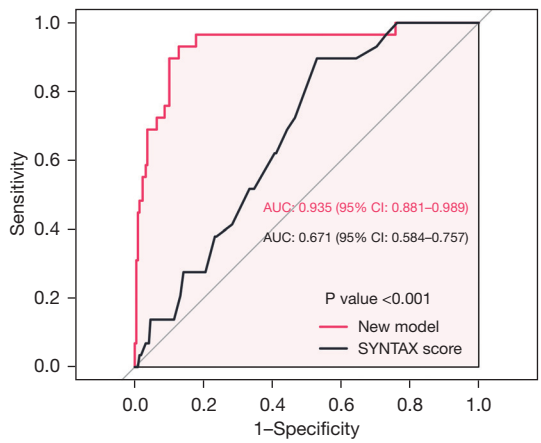

Figure 5 Comparison of ROC curves between our proposed prediction model and the traditional SYNTAX score in predicting the prognosis of patients in complex lesion group. AUC, area under the curve; CI, confidence interval; SYNTAX, Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery; ROC, receiver operating characteristic.

term chronic inflammation and oxidative stress can lead to an increase in NE count, damage to LYN proliferation, and an increase in NLR, all of which are related to MACCEs in patients with UA and complex lesions.

The new prediction model established by the nomogram had a larger AUC than did the SYNTAX score, indicating a better predictive ability for the prognosis of complex lesions of UA. We then applied patients' blood lipid, glucose, and inflammatory indices instead of repeat CAG to predict the outcomes and MACCE occurrence in patients with UA and complex lesions, and these may be early indicators for physicians to enact early prevention. It is possible that the occurrence and prognosis of coronary artery disease are influenced by multiple target factors, including coronary anatomical factors, blood glucose levels, lipid metabolism disorders, and long-term chronic inflammation. The SYNTAX score is an anatomical score that focuses more on evaluating the complexity of patient lesions to guide PCI treatment, whereas the predictive model established in our study focuses more on clinical management during postoperative follow-up. Thus, this novel predictive model has a better ability to predict MACCEs in patients with UA and complex lesions. The predictive ability of this new model is superior to the SYNTAX score, which corroborates the findings of Li *et al.* (45), who also reported the combination of indicators was superior in predicting the lesion complexity of coronary artery disease.

Certain limitations to this study should be acknowledged. First, we employed a retrospective single-center design,

and further large-scale, multicenter, randomized clinical trials with longer follow-up periods are needed. Second, although we identified novel lipid indices, such as Lp(a) and sLDL-C, as risk factors, there is currently no widely used treatment for effectively suppressing these risk factors and their progression. Although the novel small interfering RNA lipid-lowering drug, inclisiran, can control LDL-C levels while reducing Lp(a), it has not yet been widely used in clinical practice. Third, the lack of an external validation sample for the nomogram. Fourth, the lack of precise information regarding the time interval between the onset of UA symptoms and the performance of diagnostic tests represents a limitation of the study. Finally, the multiple metabolic indicators and stent implantation data examined in this study were not included in the genome-wide association study and UK Biobank study data sources; therefore, Mendelian randomization analyses could not be conducted.

Conclusions

In this study, blood lipid and glucose levels and inflammatory indices were found to be associated with the occurrence of complex lesions in UA. Compared with the SYNTAX score, the new model constructed using high RLP-C level, high sLDL-C level, high Lp(a) level, and high NLR level had a stronger ability to predict MACCEs in patients with UA and complex lesions during follow-up. We developed a multitarget and multisystem metabolic-related risk factor model for predicting the occurrence and prognosis of complex lesions in UA. Our findings may offer novel insights into the early identification of patients with UA and complex lesions and improve the prevention and treatment targets for cardiologists in the long-term clinical management of patients with UA after PCI.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2024-2122/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2024-2122/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2024-2122/prf

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2024-2122/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Ethics Committee of Beijing Chaoyang Hospital, Capital Medical University (No. 2024-345) and conformed to the principles of the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from all patients.

References

1. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J 2023;44:3720-826.
2. Chan MY, Shah BR, Gao F, et al. Recalibration of the Global Registry of Acute Coronary Events risk score in a multiethnic Asian population. Am Heart J 2011;162:291-9.
3. Sianos G, Morel MA, Kappetein AP, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention 2005;1:219-27.
4. Ogasawara K, Mashiba S, Wada Y, et al. A serum amyloid A and LDL complex as a new prognostic marker in stable coronary artery disease. Atherosclerosis 2004;174:349-56.
5. Fagundes A Jr, Morrow DA, Oyama K, et al. Biomarker Prediction of Complex Coronary Revascularization Procedures in the FOURIER Trial. J Am Coll Cardiol 2022;80:887-97.

6. Xiao Z, Riletu A, Yan X, et al. Association of serum cystatin C level and major adverse cardiovascular events in patients with percutaneous coronary intervention. Cardiovasc Diagn Ther 2024;14:621-9.
7. Gladding PA, Legget M, Fatkin D, et al. Polygenic Risk Scores in Coronary Artery Disease and Atrial Fibrillation. Heart Lung Circ 2020;29:634-40.
8. Sun L, Li H, Lin X. Linking of metabolomic biomarkers with cardiometabolic health in Chinese population. J Diabetes 2019;11:280-91.
9. Qu Y, Huang X, Zhang W, et al. Differentially expressed miR-127, miR-150, and miR-145 in serum extracellular vesicles are novel diagnostic biomarkers of unstable angina. Cardiovasc Diagn Ther 2023;13:866-78.
10. Wang J, Li T, Gu Y, et al. The value of anxiety and depression in predicting physical function and major adverse cardiovascular events in patients with acute coronary syndrome. J Thorac Dis 2024;16:6849-62.
11. Chen Z, Zhang L, Li R, et al. The development and validation of a prognostic prediction modeling study in acute myocardial infarction patients after percutaneous coronary intervention: hemorrhea and major cardiovascular adverse events. J Thorac Dis 2024;16:6216-28.
12. Giustino G, Chieffo A, Palmerini T, et al. Efficacy and Safety of Dual Antiplatelet Therapy After Complex PCI. J Am Coll Cardiol 2016;68:1851-64.
13. Varbo A, Benn M, Tybjærg-Hansen A, et al. Remnant cholesterol as a causal risk factor for ischemic heart disease. J Am Coll Cardiol 2013;61:427-36.
14. Mazidi M, Kengne AP, Katsiki N, et al. Lipid accumulation product and triglycerides/glucose index are useful predictors of insulin resistance. J Diabetes Complications 2018;32:266-70.
15. Verdoia M, Barbieri L, Di Giovine G, et al. Neutrophil to Lymphocyte Ratio and the Extent of Coronary Artery Disease: Results From a Large Cohort Study. Angiology 2016;67:75-82.
16. Karabağ Y, Çağdaş M, Rencuzogullari I, et al. Relationship between C-reactive protein/albumin ratio and coronary artery disease severity in patients with stable angina pectoris. J Clin Lab Anal 2018;32:e22457.
17. Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344-51.
18. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction (2018). Circulation 2018;138:e618-51.
19. Song FH, Zheng YY, Tang JN, et al. A Correlation Between Monocyte to Lymphocyte Ratio and Long-Term Prognosis in Patients With Coronary Artery Disease After PCI. Clin Appl Thromb Hemost 2021;27:1076029621999717.
20. Dai XY, Zheng YY, Tang JN, et al. Alkaline phosphatase-to-albumin ratio as a novel predictor of long-term adverse outcomes in coronary artery disease patients who underwent PCI. Biosci Rep 2021;41:BSR20203904.
21. Kawashima H, Ono M, Hara H, et al. Ten-Year All-Cause Mortality Following Staged Percutaneous Revascularization in Patients With Complex Coronary Artery Disease. Cardiovasc Revasc Med 2022;38:124-6.
22. Agrawal H, Teleb M, Lahsaei S, et al. Routine Angiographic Follow-Up After Coronary Artery Disease Revascularization: Is Seeing Believing? Curr Cardiol Rep 2018;20:17.
23. Wang H, Gong H, Liu Y, et al. Relationship between lncRNA-Ang362 and prognosis of patients with coronary heart disease after percutaneous coronary intervention. Biosci Rep 2020;40:BSR20201524.
24. Sivri S, Sökmen E, Çelik M, et al. Nesfatin-1 Levels Predict Angiographic No-Reflow in Patients with ST-Segment Elevation Myocardial Infarction. Acta Cardiol Sin 2020;36:318-25.
25. Liu Y, Zhang C, Jiang L, et al. Relationship Between High-Sensitivity C-Reactive Protein and Long-Term Outcomes in Elderly Patients With 3-Vessel Disease. Angiology 2022;73:60-7.
26. He WF, Jiang L, Chen YY, et al. The association of baseline N-terminal pro-B-type natriuretic peptide with short and long-term prognosis following percutaneous coronary intervention in non-ST segment elevation acute coronary syndrome with multivessel coronary artery disease: a retrospective cohort study. BMC Cardiovasc Disord 2021;21:202.
27. Kotecha D, Flather MD, Atar D, et al. B-type natriuretic peptide trumps other prognostic markers in patients assessed for coronary disease. BMC Med 2019;17:72.
28. Xu N, Tang XF, Yao Y, et al. Lipoprotein(a) levels are associated with coronary severity but not with outcomes in Chinese patients underwent percutaneous coronary intervention. Nutr Metab Cardiovasc Dis 2020;30:265-73.
29. Chieng D, Pang J, Ellis KL, et al. Elevated lipoprotein(a) and low-density lipoprotein cholesterol as predictors of the severity and complexity of angiographic lesions in patients with premature coronary artery disease. J Clin Lipidol 2018;12:1019-26.
30. Kaiser Y, Daghem M, Tzolos E, et al. Association of

Lipoprotein(a) With Atherosclerotic Plaque Progression. J Am Coll Cardiol 2022;79:223-33.
31. Nurmohamed NS, Gaillard EL, Malkasian S, et al. Lipoprotein(a) and Long-Term Plaque Progression, Low-Density Plaque, and Pericoronary Inflammation. JAMA Cardiol 2024;9:826-34.
32. Sekimoto T, Koba S, Mori H, et al. Small Dense Low-Density Lipoprotein Cholesterol: A Residual Risk for Rapid Progression of Non-Culprit Coronary Lesion in Patients with Acute Coronary Syndrome. J Atheroscler Thromb 2021;28:1161-74.
33. Ishii J, Kashiwabara K, Ozaki Y, et al. Small Dense Low-Density Lipoprotein Cholesterol and Cardiovascular Risk in Statin-Treated Patients with Coronary Artery Disease. J Atheroscler Thromb 2022;29:1458-74.
34. Sharma SB, Garg S. Small dense LDL: risk factor for coronary artery disease (CAD) and its therapeutic modulation. Indian J Biochem Biophys 2012;49:77-85.
35. Kexin W, Yaodong D, Wen G, et al. Association of Increased Remnant Cholesterol and the Risk of Coronary Artery Disease: A Retrospective Study. Front Cardiovasc Med 2021;8:740596.
36. Wang K, Ding Y, Wang R, et al. Remnant Cholesterol and the Risk of Coronary Artery Disease in Patients With Type 2 Diabetes. Angiology 2023;74:745-53.
37. Chevli PA, Islam T, Pokharel Y, et al. Association between remnant lipoprotein cholesterol, high-sensitivity C-reactive protein, and risk of atherosclerotic cardiovascular disease events in the Multi-Ethnic Study of Atherosclerosis (MESA). J Clin Lipidol 2022;16:870-7.
38. Delialis D, Georgiopoulos G, Aivalioti E, et al. Remnant cholesterol and atherosclerotic disease in high cardiovascular risk patients. Beyond LDL cholesterol and hypolipidemic treatment. Hellenic J Cardiol 2022;66:26-31.
39. Wang Y, Wang Y, Sun S, et al. Triglyceride-glucose index level and variability and outcomes in patients with acute coronary syndrome undergoing percutaneous coronary intervention: an observational cohort study. Lipids Health Dis 2022;21:134.
40. Wu Z, Liu L, Wang W, et al. Triglyceride-glucose index in the prediction of adverse cardiovascular events in patients with premature coronary artery disease: a retrospective cohort study. Cardiovasc Diabetol 2022;21:142.
41. Wang X, Xu W, Song Q, et al. Association between the triglyceride-glucose index and severity of coronary artery disease. Cardiovasc Diabetol 2022;21:168.
42. Wang J, Huang X, Fu C, et al. Association between triglyceride glucose index, coronary artery calcification and multivessel coronary disease in Chinese patients with acute coronary syndrome. Cardiovasc Diabetol 2022;21:187.
43. Soylu K, Gedikli Ö, Dagasan G, et al. Neutrophil-to-lymphocyte ratio predicts coronary artery lesion complexity and mortality after non-ST-segment elevation acute coronary syndrome. Rev Port Cardiol 2015;34:465-71.
44. Yuan S, Li L, Pu T, et al. The relationship between NLR, LDL-C/HDL-C, NHR and coronary artery disease. PLoS One 2024;19:e0290805.
45. Li S, Guo YL, Zhao X, et al. Novel and traditional lipid-related biomarkers and their combinations in predicting coronary severity. Sci Rep 2017;7:360.

(English Language Editor: J. Gray)

Cite this article as: Xu Y, Ma G, Xie B, Zhao J, Liu X, Zhang J, Chen M. Correlation of blood lipids, glucose, and inflammatory indices with the occurrence and prognosis of lesion complexity in unstable angina, a retrospective cohort study. J Thorac Dis 2025;17(1):413-428. doi: 10.21037/jtd-2024-2122