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Original Article

Predictive value of initial Lp-PLA2, NT-proBNP, and peripheral blood-related ratios for heart failure after early onset infarction in patients with acute myocardial infarction

Xinfeng Li[1], Ting Zhang[2], Wen Xing[3]

[1]*Department of Medical Laboratory, Xianyang Central Hospital, No. 78 Renmin East Road, Weicheng District, Xianyang 712000, Shaanxi, China;* [2]*Operation Room, Xianyang Central Hospital, No. 78 Renmin East Road, Weicheng District, Xianyang 712000, Shaanxi, China;* [3]*Department of Internal Medicine, Northwest University Hospital, No. 229 Taibai North Road, Beilin District, Xi'an 710069, Shaanxi, China*

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Abstract: Objective: To analyze the predictive value of lipoprotein-associated phospholipase A2 (Lp-PLA2), N-terminal prohormone of brain natriuretic peptide (NT-proBNP), and peripheral blood-related ratios at the initial diagnosis for heart failure (HF) after early-onset infarction in patients with acute myocardial infarction (AMI). Methods: This retrospective analysis included 151 patients first diagnosed with AMI at Xianyang Central Hospital from February 2020 to February 2023. Patients were classified into two groups: those who developed HF during hospitalization (HF group, n=45) and those who did not (non-HF group, NHF, n=106). Differences in Lp-PLA2, NT-proBNP, and peripheral blood ratios at initial diagnosis were compared between the groups. Binary logistic regression was used to identify independent risk factors for HF, and a nomogram model was developed based on these factors. Results: HR (P=0.032), C-reactive protein (CRP) (P<0.001), alanine aminotransferase (ALT) (P=0.015), coronary artery lesion score (CALDS) (P<0.001), D-dimer (D-D) (P=0.021), neutrophil-to-lymphocyte ratio (NLR) (P<0.001), Lp-PLA2 (P<0.001), and NT-proBNP (P<0.001) were significantly higher in the HF group than in the NHF group. Left ventricular end-systolic diameter (LVESD) (P<0.001) and left ventricular end-diastolic diameter (LVEDD) (P<0.001) were significantly lower in the HF group. Multifactorial logistic regression identified HR (P=0.034), CRP (P=0.028), CALDS (P=0.007), NLR (P=0.001), Lp-PLA2 (P=0.001), and NT-proBNP (P=0.002) as independent predictors of HF. The AUCs for NLR, Lp-PLA2, and NT-proBNP were 0.806, 0.849, and 0.780, respectively. The nomogram model achieved an AUC of 0.964, significantly outperforming individual indicators per Delong's test, highlighting its superior predictive efficacy. Conclusion: HR, CRP, CALDS, NLR, Lp-PLA2, and NT-proBNP were identified as independent predictors of HR post-AMI myocardial infarction. The constructed nomogram model provides an effective tool for early clinical identification of high-risk patients, potentially improving prognosis and guiding therapeutic strategies.

Keywords: Lp-PLA2, NT-proBNP, peripheral blood-related ratio, acute myocardial infarction, heart failure, predictive value

Introduction

Acute myocardial infarction (AMI) occurs due to coronary atheromatous plaque erosion or rupture, leading to thrombosis that partially or completely obstructs the coronary arteries. This blockage disrupts blood flow to areas of the heart, resulting in cardiac myocyte necrosis [1, 2]. Clinically, AMI often presents with severe and persistent retrosternal or precordial pain not fully alleviated by rest or nitroglycerin, accompanied by changes in ambulatory electrocardiogram (ECG) readings and increased cardiac enzyme levels [3]. By 2030, the number of myocardial infarction patients is expected to rise to 23 million worldwide [4].

Advancements in the management of cardiovascular diseases, such as the establishment of chest pain centers, emergency thrombolysis, and the widespread adoption of percutaneous coronary intervention (PCI), have significantly

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decreased acute-phase mortality in AMI patients [5]. However, concerns about long-term prognosis persist, particularly due to ventricular remodeling and heart failure (HF) within the first 48 hours post-symptom onset [6]. Ventricular remodeling, a self-repair mechanism in response to infarction and healing, often changes cardiac structure and function, potentially leading to HF [7]. Studies indicate that the incidence of asymptomatic left ventricular diastolic dysfunction post-AMI can be as high as 60%, and despite PCI, the hospitalization incidence of HF remains around 28% [8, 9]. Early prediction and intervention to reduce HF mortality pose significant challenges in AMI management [10]. The development of HF after AMI is influenced by the extent of myocardial damage and involves complex mechanisms such as remodeling, neurohormonal activation, increased expression of inflammatory factors, and oxidative stress [11]. Diagnosis of post-infarction HF involves history-taking, physical examination, chest radiography, cardiac ultrasound, and MRI. However, the late onset and nonspecificity of HF symptoms complicate the timely assessment of cardiac function, and are poorly correlated with cardiac insufficiency [12]. While echocardiography and MRI provide detailed evaluations of intracardiac pressures, ventricular ejection fraction, and diastolic dysfunction, patients with abnormal ventricular systolic function may still remain asymptomatic [13].

In recent years, biomarkers have been extensively studied for their roles in prediction, risk stratification, monitoring, and guiding therapy for HF following AMI. Key markers such as lipoprotein-associated phospholipase A2 (Lp-PLA2) and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) play pivotal roles in cardiovascular diseases [14]. Lp-PLA2 is an enzyme implicated in atherosclerosis development through the hydrolysis of oxidized phospholipids in low-density lipoprotein (LDL) particles, producing pro-inflammatory products. Elevated levels of Lp-PLA2 suggest increased inflammatory response and greater instability of atherosclerotic plaques, contributing to HF [15]. Monitoring Lp-PLA2 levels assists in assessing inflammatory burden and identifying high-risk patients.

NT-proBNP is released by cardiac myocytes in response to increased wall tension and myocardial stress. It serves as a crucial biomarker for diagnosing HF and predicting its prognosis, reflecting the degree of myocardial damage and ventricular dysfunction. High NT-proBNP levels in AMI patients denote a higher risk of developing HF, offering insights into the severity of cardiac dysfunction [16]. The combination of Lp-PLA2 and NT-proBNP provides a comprehensive assessment of HF risk in AMI patients. Lp-PLA2 indicates the level of inflammatory processes, while NT-proBNP measures hemodynamic stress. Together, these biomarkers enhance predictive accuracy, facilitating early intervention and improved patient outcomes. Integrating these markers into clinical practice can significantly influence the management and prognosis of AMI patients.

Despite considerable advances in treating HF post-AMI, the occurrence of HF remains a critical factor in worsening patient prognosis. Current predictive tools, while capable of identifying high-risk patients, exhibit limitations in their ability to precisely predict HF after AMI at an early stage. These limitations often relate to the accuracy of early diagnosis and intervention, particularly in utilizing variable patient data to predict HF risk effectively. Therefore, this study aims to develop a comprehensive assessment model based on multiple biomarkers and clinical parameters. By constructing and validating a nomogram model, this study seeks to provide a new clinical tool for the early identification and accurate prediction of HF risk after AMI.

Materials and methods

Case acquisition

This retrospective analysis included patients first diagnosed with AMI at Xianyang Central Hospital from February 2020 to February 2023. Inclusion criteria: 1. Diagnosis of AMI confirmed by symptoms of acute chest pain and elevated or normal cardiac enzyme levels, with one or more of the following: significant ST-segment elevation, depression, or Q-wave abnormalities on electrocardiogram; significant stenosis or obstruction of coronary arteries identified by emergency coronary angiography; 2. Completion of PCI; 3. Availability of complete baseline data; 4. Comprehensive laboratory and imaging data. Exclusion criteria: 1. History of HF or previous myocardial infarction; 2. Other cardiac

conditions such as cardiomyopathy or heart valve disease; 3. Respiratory disorders like asthma or chronic obstructive pulmonary disease, interstitial or hepatic fibrosis, sepsis; 4. Severe liver or kidney insufficiency, acute or chronic infections, autoimmune and hematological disorders, and malignancies. The study received ethical approval from the Medical Ethics Committee of Xianyang Central Hospital, (approval number: 20234548).

HF definition

The definition of HF was based on the 2018 Chinese Guidelines for the Diagnosis and Treatment of HF [17]: Diagnosis is confirmed by clear symptoms and/or signs of HF, such as dyspnea, physical activity limitation, and fluid retention; left ventricular ejection fraction (LVEF) under 40%; and a New York Heart Association (NYHA) cardiac function classification of II or higher.

NYHA definition

The NYHA Cardiac Function Classification is a crucial metric for assessing cardiac function in patients with heart disease. It categorizes cardiac function into four grades based on the patient's symptoms and activity tolerance. This classification is instrumental in assessing the severity of HF and guiding clinical treatment. The specific divisions of the NYHA classification are as follows:

NYHA Class I: Patients experience no limitations in daily physical activity. Ordinary physical activity does not cause fatigue, palpitations, dyspnea, or angina.

NYHA Class II: Patients have mild limitations in daily physical activity. They are asymptomatic at rest, but ordinary activities cause fatigue, palpitations, dyspnea, or angina.

NYHA Class III: Patients have significant limitations in daily physical activity. They are asymptomatic at rest, but less than ordinary activities cause fatigue, palpitations, dyspnea, or angina.

NYHA Class IV: Patients experience symptoms during any physical activity and at rest; symptoms of HF are present, with discomfort exacerbated by any physical activity [2].

The rationale for selecting NYHA class ≥II as a study criterion was to ensure that the study population indeed exhibited HF, with symptoms that were consistent and pronounced. Patients in NYHA class I typically show no overt symptoms and are not easily diagnosed with HF, whereas patients in NYHA class II or higher exhibit significant symptoms, allowing for a more accurate assessment of the impact of HF on quality of life and disease progression.

Research target

Based on the inclusion criteria, we initially identified 208 cases. After applying the exclusion criteria, a total of 57 cases were excluded, leaving 151 cases for the study. According to the HF definition, patients were divided into two groups: HF group (n=45) and non-HF (NHF) group (n=106).

Access to information

Patient data were retrieved from the electronic medical records, encompassing age, gender, hypertension, diabetes, smoking history, alcohol use, ST-segment elevation, history of thrombolysis, and vital metrics such as HR, C-Reactive Protein (CRP), Total Cholesterol (TC), Triglycerides (TG), Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Coronary Artery Lesion Degree Score (CALDS), D-Dimer (D-D), left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD), neutrophil-to-lymphocyte ratio (NLR), Lp-PLA2, and NT-proBNP. All assays were conducted within 24 hours of the patient's initial AMI presentation.

Outcome measures

The study involved comparing patients' baseline data, laboratory, and imaging indices. Logistic regression was utilized to identify independent predictors for HF. The effectiveness of these predictors was analyzed using the Receiver Operating Characteristic (ROC) curve to determine their area under the curve (AUC). The ROC curve's cutoff values were employed to categorize predictors, visualized through Nomogram diagrams. The Nomogram model's efficacy was evaluated using the Delong test to compare its AUC with those of individual predictors, supplemented by ROC, calibration curve, and decision curve analysis (DCA) (**Figure 1**).

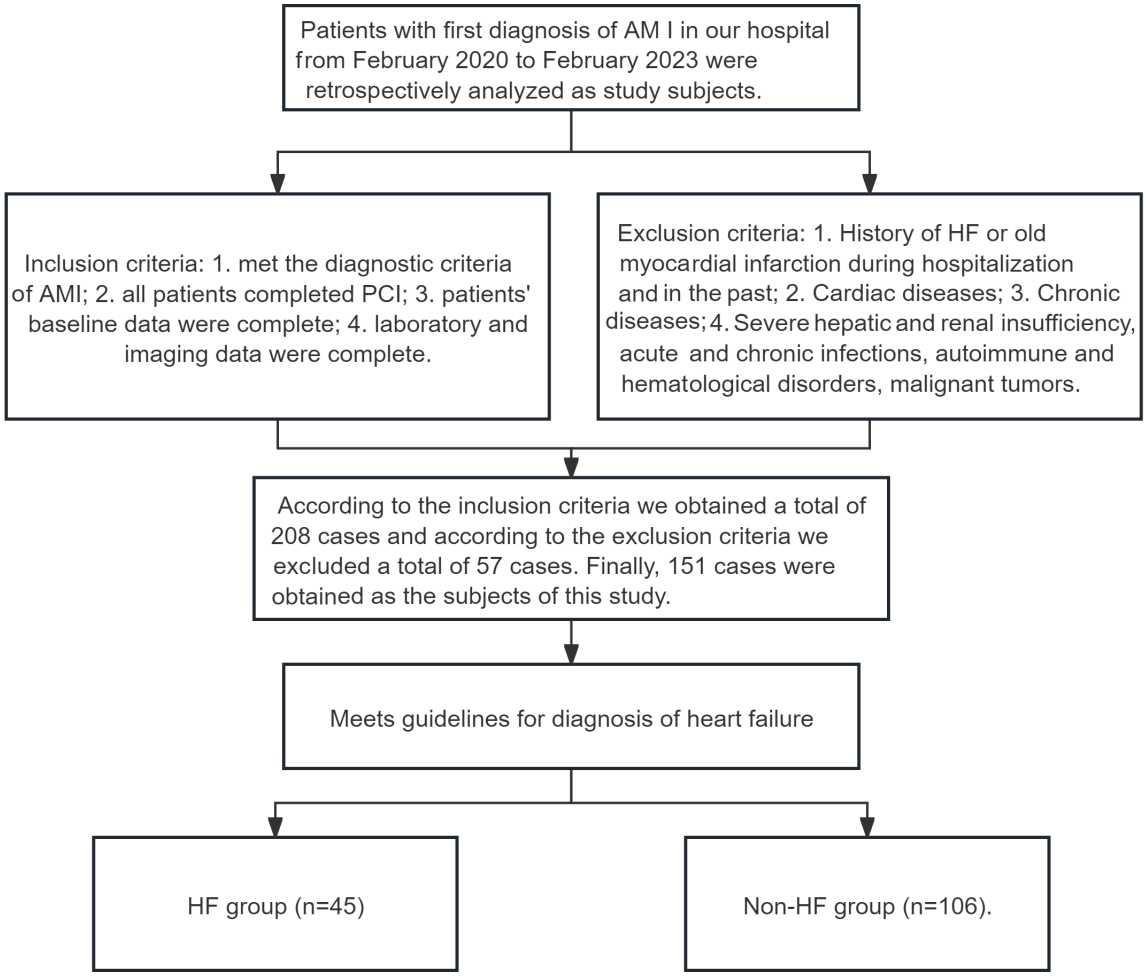

Figure 1. Case acquisition and grouping. HF, Heart Failure; AMI, acute myocardial infarction.

Statistical analysis

Data analysis was conducted using SPSS 26.0. Measurement data were tested for normality and handled accordingly; normally distributed data were presented as mean ± standard deviation and analyzed using the independent sample t-test and one-way ANOVA. Non-normally distributed data were expressed as median (interquartile range) and analyzed using nonparametric tests. Categorical data were presented as counts and analyzed with the chi-square test. Binary logistic regression identified characteristic factors independently predicting HF. The optimal cutoff values were determined using Youden's index, and their sensitivity and specificity were calculated. The diagnostic efficacy of each predictor was evaluated by its AUC. Nomograms were constructed using the "rms" package in R (4.3.2), and graphs were plotted using GraphPad Prism 9.5.1. Statistical significance was noted at $P<0.05$.

Results

Comparison of baseline information

Analysis of baseline data between the HF group and the NHF group showed no statistically significant differences in age, gender, hypertension, diabetes mellitus, smoking history, alcohol use history, ST-segment elevation, or history of thrombolysis (all $P>0.05$, **Table 1**).

Laboratory and ultrasound-related indicators

Comparative analysis of laboratory and ultrasound indices between the groups revealed significant differences. HR ($P=0.032$), CRP ($P<0.001$), ALT ($P=0.015$), coronary artery

Table 1. Comparison of clinical data of patients

Considerations	HF (n=45)	NHF (n=106)	Chi-square value	*P*-value
Age				
≥65 years	28	56	1.129	0.288
<65 years	17	50		
Gender				
Male	36	79	0.521	0.47
Female	9	27		
High blood pressure				
Yes	21	42	0.645	0.422
No	24	64		
Diabetes				
Yes	5	16	0.419	0.518
No	40	90		
Smoking history				
Yes	31	61	1.707	0.191
No	14	45		
History of alcohol abuse				
Yes	11	19	0.843	0.358
No	34	87		
ST segment elevation				
Yes	27	73	1.111	0.292
No	18	33		
Thrombolytic history				
Yes	21	42	0.645	0.422
No	24	64		

lesion score (P<0.001), D-D (P=0.021), NLR (P<0.001), Lp-PLA2 (P<0.001), and NT-proBNP (P<0.001) in the HF group were significantly higher than those in the NHF group. Furthermore, LVESD and LVEDD (both P<0.001) were significantly lower in the HF group compared to the NHF group (**Table 2**; **Figure 2**).

Logistics regression screening of patients for predictors of HF

Data previously identified as significant were analyzed using logistic regression. Both univariate and multivariate analyses confirmed that HR (P=0.034), CRP (P=0.028), CALDS (P=0.007), NLR (P=0.001), Lp-PLA2 (P=0.001), and NT-proBNP (P=0.002) were independent predictors of HF (**Figure 3**).

Assessment of the predictive efficacy of independent predictors

ROC curves were plotted for each of the six independent predictors. The AUCs for HR, CRP, and CALDS were all above 0.7. NLR, Lp-PLA2, and NT-proBNP showed AUCs of 0.806, 0.849, and 0.780, respectively, indicating substantial predictive validity for HF (**Figure 4**; **Table 3**).

Nomogram model construction for HF patients

To enhance the interpretability of the data, a visual predictive model was constructed using the cut-off values of the 6 predictors. This Nomogram model integrated all 6 factors, with NT-proBNP being particularly strongly correlated with HF (**Figure 5A**). The ROC curve analysis of the Nomogram model showed an AUC of 0.964, indicating high predictive accuracy (**Figure 5B**). DCA and calibration curves demonstrated that the Nomogram model provided clinical benefits in the 1%-96% range, with a peak benefit rate of 70.19%. The model's fitting to the ideal curve was excellent, indicating robust predictive performance (**Figure 5C**, **5D**).

Delong test to assess predictive efficacy of predictive models versus individual indicators

At the study's conclusion, the Delong test was used to compare the predictive differences between the Nomogram model and the individual indicators. The results indicated that the AUC of the Nomogram model was significantly higher than that of the individual indicators alone, confirming that the Nomogram model's predictive efficacy is more clinically valuable (**Table 4**).

Discussion

AMI is a leading cause of death globally, with HF being a prevalent and costly complication [18]. Clinically, HF is often evaluated through history-taking, physical examination, serum BNP testing, and cardiac ultrasound [19]. However, HF symptoms are not specific and are often severe by the time they manifest. Moreover, cardiac ultrasound, while helpful, may detect structural

Table 2. Comparison of Laboratory and Ultrasound Related Indicators

Variable	Method	HF (n=45)	NHF (n=106)	Statistic	*P* value
HR (times/minute)	t-test	84.51±20.91	77.20±12.01	2.197	0.032
CRP (mg/L)	t-test	6.35±2.25	4.80±1.95	4.027	<0.001
TC (mmol/L)	t-test	4.49±1.66	4.84±1.59	-1.205	0.232
TG (mmol/L)	t-test	1.59±0.59	1.68±0.80	-0.754	0.453
AST (U/L)	t-test	130.47±55.19	135.60±55.53	-0.521	0.604
ALT (U/L)	t-test	53.50±17.00	46.27±14.24	2.505	0.015
Coronary artery lesion severity score	Mann-Whitney U	61.00 [44.00, 89.00]	42.50 [25.25, 60.00]	3.741	<0.001
D-D (ng/ml)	Mann-Whitney U	1033.23 [446.06, 1653.15]	634.01 [436.66, 999.42]	2.522	0.012
LVESD (mm)	t-test	30.45±4.60	34.47±5.65	-4.575	<0.001
LVEDD (mm)	t-test	45.85±5.17	48.69±5.28	-3.061	0.003
NLR	t-test	7.44±1.29	6.03±1.09	6.880	<0.001
Lp-PLA2/(μg/L)	Mann-Whitney U	278.15 [257.46, 290.08]	236.47 [219.71, 249.81]	6.770	<0.001
NT-proBNP/(ng/L)	t-test	923.75±122.75	795.34±105.47	6.663	<0.001

Note: HR, Heart Rate; CRP, C-Reactive Protein; TC, Total Cholesterol; TG, Triglycerides; AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; CALDS, Coronary Artery Lesion Degree Score; D-D, D-Dimer; LVESD, Left Ventricular End-Systolic Diameter; LVEDD, Left Ventricular End-Diastolic Diameter; NLR, Neutrophil-to-Lymphocyte Ratio; Lp-PLA2, Lipoprotein-Phospholipase A2; NT-proBNP, N-Terminal Prohormone of Brain Natriuretic Peptide; HF, Heart Failure; NHF, non-heart failure.

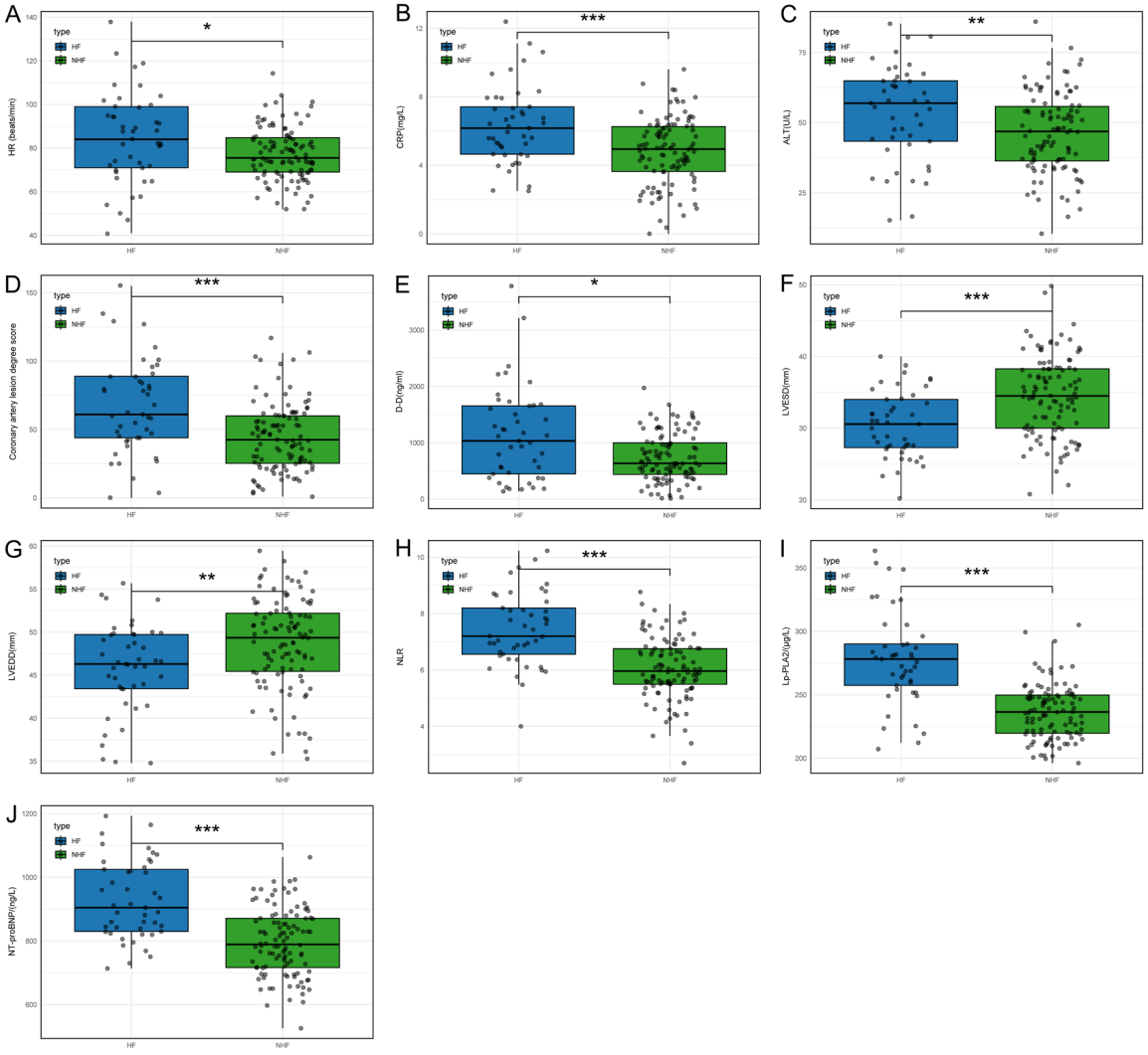

Figure 2. Demonstration of metrics that differ between HF and NHF labs and ultrasound in the two groups. A. Comparison of HR measures. B. Comparison of CRP measures. C. Comparison of ALT measures. D. Comparison of coro-

nary artery lesion degree score measures. E. Comparison of D-D measures. F. Comparison of LVESD measures. G. Comparison of LVEDD measures. H. Comparison of NLR measures. I. Comparison of Lp-PLA2 measures. J. Comparison of NT-proBNP measures. Note: HR, Heart Rate; CRP, C-Reactive Protein; ALT, Alanine Aminotransferase; CALDS, Coronary Artery Lesion Degree Score; D-D, D-Dimer; LVESD, Left Ventricular End-Systolic Diameter; LVEDD, Left Ventricular End-Diastolic Diameter; NLR, Neutrophil-to-Lymphocyte Ratio; Lp-PLA2, Lipoprotein-Phospholipase A2; NT-proBNP, N-Terminal Prohormone of Brain Natriuretic Peptide; HF, Heart Failure; NHF, non-heart failure. *P<0.05, **P<0.01, ***P<0.001.

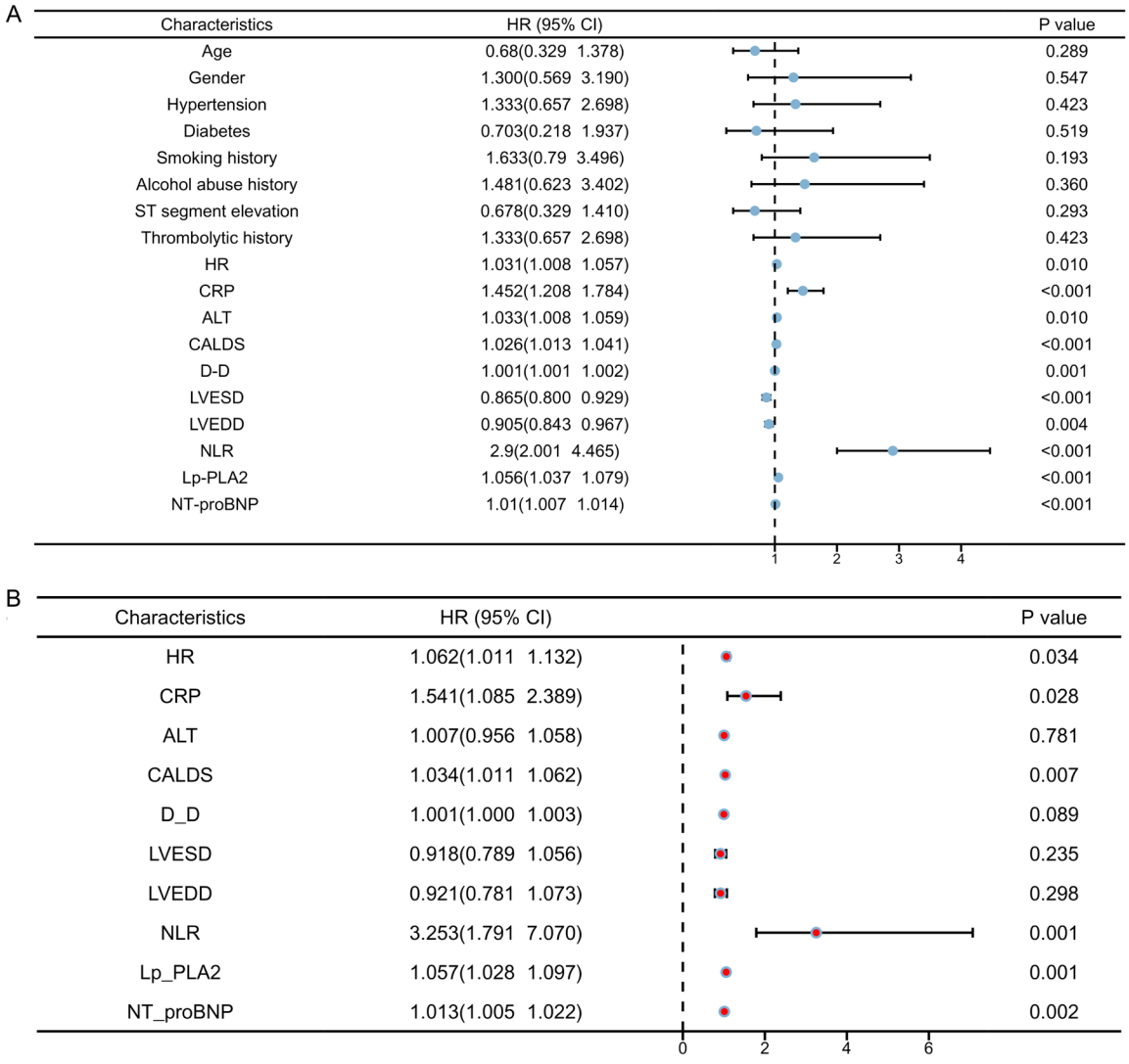

Figure 3. Logistic regression screening for predictors of HF occurrence. A. One-way logistic regression screening for predictors of HF occurrence. B. Multifactorial logistic regression screening for independent predictors of HF occurrence. Note: HR, Heart Rate; CRP, C-Reactive Protein; ALT, Alanine Aminotransferase; CALDS, Coronary Artery Lesion Degree Score; D-D, D-Dimer; LVESD, Left Ventricular End-Systolic Diameter; LVEDD, Left Ventricular End-Diastolic Diameter; NLR, Neutrophil-to-Lymphocyte Ratio; Lp-PLA2, Lipoprotein-Phospholipase A2; NT-proBNP, N-Terminal Prohormone of Brain Natriuretic Peptide; HF, Heart Failure.

abnormalities without overt symptoms, making its reliability somewhat subjective. Additionally, cardiac ultrasound procedures are costly, time-consuming, and not always readily available at the bedside in many hospitals, which hampers early HF assessment [20].

In this study, we utilized logistic regression to identify laboratory and ultrasound-related markers predictive of HF. We found that HR, CRP, CALDS, NLR, Lp-PLA2, and NT-proBNP are all independent predictors of HF. CALDS quantifies the severity of coronary artery stenosis and

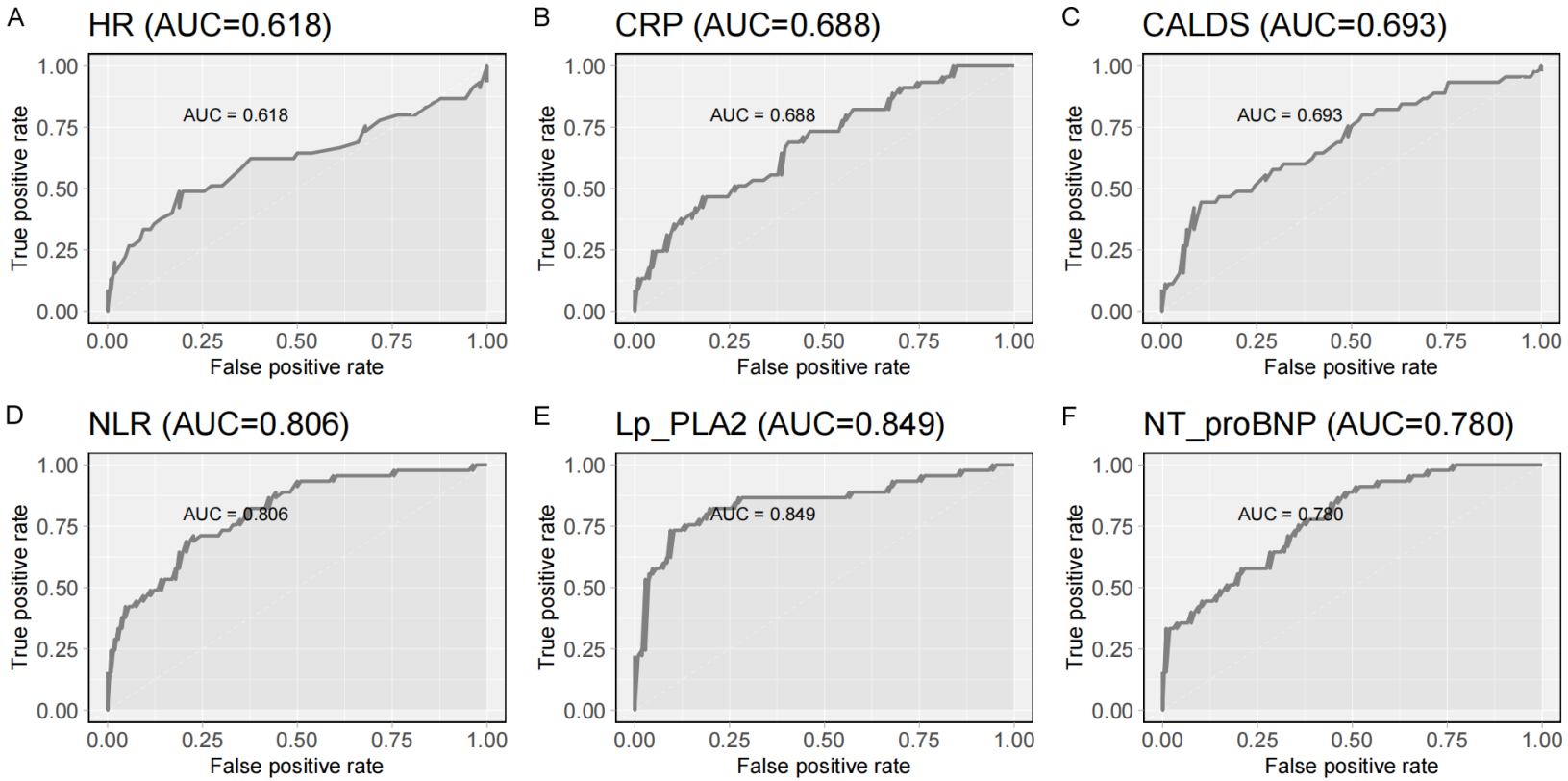

Figure 4. ROC curves of independent predictors in predicting HF. A. ROC curve analysis of HR in predicting the AUC of HF. B. ROC curve analysis of CRP in predicting the AUC of HF. C. ROC curve analysis of CALSD in predicting the AUC of HF. D. ROC curve analysis of NLR in predicting the AUC of HF. E. ROC curve analysis of Lp-PLA2 in predicting the AUC of HF. F. ROC curve analysis of NT-proBNP in predicting the AUC of HF. Note: HR, Heart Rate; CRP, C-Reactive Protein; CALDS, Coronary Artery Lesion Degree Score; NLR, Neutrophil-to-Lymphocyte Ratio; Lp-PLA2, Lipoprotein-Phospholipase A2; NT-proBNP, N-Terminal Prohormone of Brain Natriuretic Peptide; HF, Heart Failure; ROC, Receiver Operating Characteristic curve; AUC, area under curve.

Table 3. ROC curve parameters

Marker	HR	CRP	CALDS	NLR	Lp_PLA2	NT_proBNP
AUC	0.618	0.688	0.693	0.806	0.849	0.78
CI_lower_upper	0.507-0.729	0.595-0.780	0.596-0.789	0.730-0.882	0.771-0.927	0.703-0.858
Specificity	81.13%	82.08%	89.62%	77.36%	90.57%	51.89%
Sensitivity	48.89%	46.67%	44.44%	71.11%	73.33%	88.89%
Youden_index	30.02%	28.74%	34.07%	48.47%	63.90%	40.78%
Cut_off	87.5	6.41	75.5	6.775	259.295	793.71
Accuracy	71.52%	71.52%	76.16%	75.50%	85.43%	62.91%
Precision	48.89%	46.67%	44.44%	71.11%	73.33%	88.89%
F1_Score	50.57%	49.41%	52.63%	63.37%	75.00%	58.82%

Note: HR, Heart Rate; CRP, C-Reactive Protein; CALDS, Coronary Artery Lesion Degree Score; NLR, Neutrophil-to-Lymphocyte Ratio; Lp-PLA2, Lipoprotein-Phospholipase A2; NT-proBNP, N-Terminal Prohormone of Brain Natriuretic Peptide; HF, Heart Failure; ROC, Receiver Operating Characteristic curve.

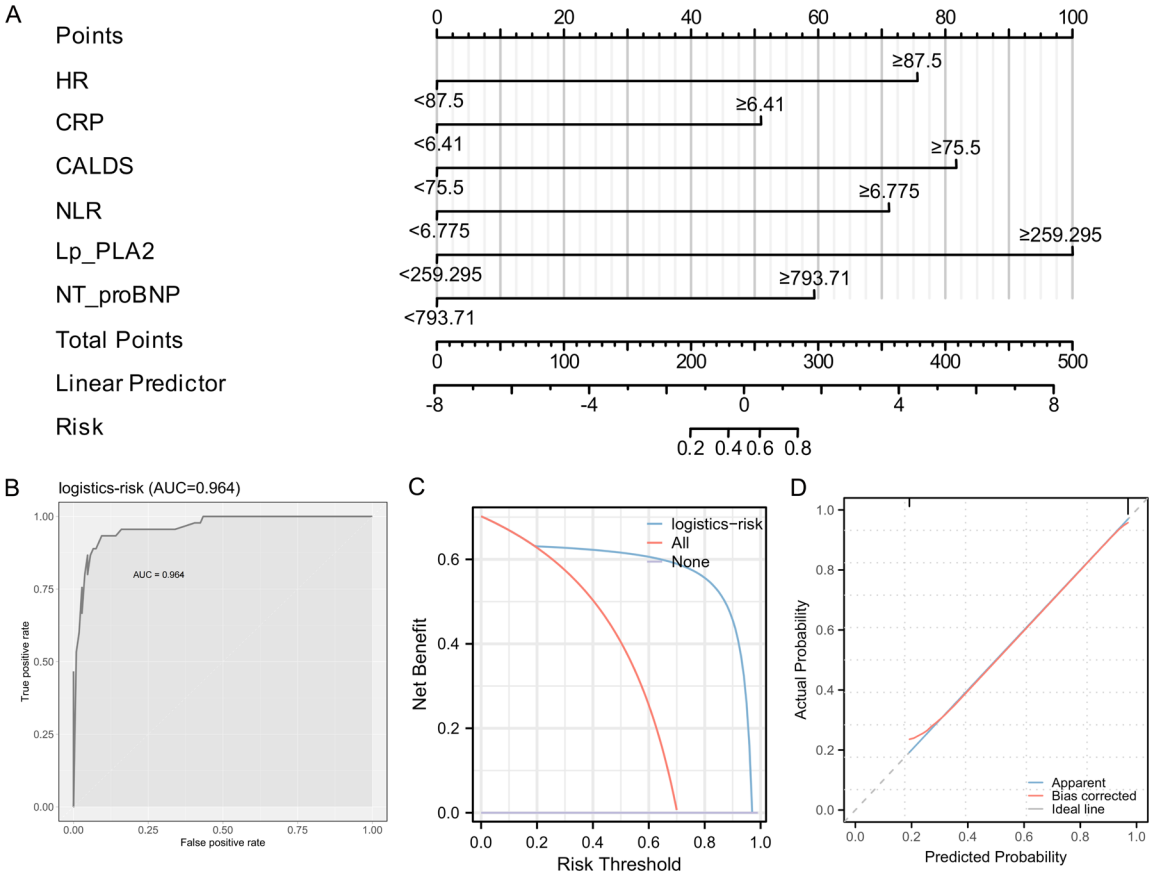

Figure 5. Construction and internal validation of nomogram prediction models. A. Nomogram Prediction Model. B. ROC curve to analyze the effectiveness of Nomogram prediction model in predicting HF. C. Decision curve analysis curve analyzing the benefit rate of Nomogram prediction model in predicting HF. D. Calibration curve analyzing the stability of nomogram prediction model in predicting HF. Note: HR, Heart Rate; CRP, C-Reactive Protein; CALDS, Coronary Artery Lesion Degree Score; NLR, Neutrophil-to-Lymphocyte Ratio; Lp-PLA2, Lipoprotein-Phospholipase A2; NT-proBNP, N-Terminal Prohormone of Brain Natriuretic Peptide; HF, Heart Failure; ROC, Receiver Operating Characteristic curve.

plaque. In coronary artery disease, stenosis or obstruction leads to myocardial ischemia or necrosis, significantly impairing cardiac function [21]. Studies have shown that higher

Table 4. Comparison of ROC curves

Marker1	Marker2	Z_value	*P*_value	AUC difference	95% CI
HR	Logistics-risk	-5.963	<0.001	-0.345	-0.459 - -0.232
CRP	Logistics-risk	-5.798	<0.001	-0.276	-0.370 - -0.183
CALDS	Logistics-risk	-5.362	<0.001	-0.271	-0.370 - -0.172
NLR	Logistics-risk	-4.138	<0.001	-0.158	-0.233 - -0.083
Lp_PLA2	Logistics-risk	-3.02	0.003	-0.115	-0.189 - -0.040
NT_proBNP	Logistics-risk	-4.693	<0.001	-0.184	-0.260 - -0.107

Note: HR, Heart Rate; CRP, C-Reactive Protein; CALDS, Coronary Artery Lesion Degree Score; NLR, Neutrophil-to-Lymphocyte Ratio; Lp-PLA2, Lipoprotein-Phospholipase A2; NT-proBNP, N-Terminal Prohormone of Brain Natriuretic Peptide; HF, Heart Failure; ROC, Receiver Operating Characteristic curve.

CALDS correlates with more severe coronary insufficiency, extensive myocardial damage, and reduced cardiac compensatory capacity, thus increasing the risk of HF [22].

Elevated HR is an early indicator of HF, reflecting an increase in autonomic nervous system activity, particularly sympathetic activity. Post-AMI, compensatory mechanisms strive to maintain cardiac output by increasing HR. However, this increment exacerbates myocardial oxygen demand and subsequently aggravates cardiac dysfunction [23]. Additionally, elevated HR is associated with ventricular remodeling and myocardial fibrosis, both critical in the development of HF. Previous research by Ford et al. [24] recognized increased resting HR as a predictor of HF development. Moreover, Givi et al. [25] noted that tachycardia significantly heightens hospitalization and mortality rates in HF patients, establishing it as a strong predictive factor.

CRP is an acute phase response protein used to assess inflammation levels in the body [26]. Following a myocardial infarction, myocardial ischemia and necrosis trigger a systemic inflammatory response, which rapidly elevates CRP levels. Persistent inflammation can damage cardiomyocytes, leading to ventricular remodeling, myocardial fibrosis, and diminished cardiac function. Elevated CRP levels generally indicate a heightened risk of HF in patients with AMI [27]. Previous studies [28] have identified CRP as a potent predictor of HF across different ejection fraction levels, acting through an independent inflammatory pathway. Burger et al. [26] recognized CRP as an independent risk marker for HF development in patients with pre-existing cardiovascular disease. These findings support ongoing clinical trials that investigate the potential of anti-inflammatory medications to mitigate HF.

Additionally, Redwine [29] in a cross-sectional study involving 270 patients with stage B HF, observed that those with elevated CRP levels exhibited greater cognitive decline both at baseline and follow-up, suggesting that low-grade systemic inflammation might contribute to early cognitive dysfunction in HF patients. These insights underscore the prognostic significance of CRP in heart disease and emphasize the need for further exploration into anti-inflammatory strategies to reduce HF and its associated complications.

NLR, Lp-PLA2, and NT-proBNP are recognized as independent indicators of inflammatory response, lipid metabolism, and cardiac functional load, respectively. Changes in these markers are closely associated with the development of HF following AMI [30, 31]. Post-myocardial infarction, activation of the immune system, disturbances in lipid metabolism, and neurohormonal shifts initiate a series of pathophysiological responses. An elevated NLR indicates heightened inflammation, while a decrease in lymphocytes reflects a compromised immune response [32]. Increased neutrophil counts are linked to extensive myocardial injury and inflammation, whereas reduced lymphocyte counts suggest immune suppression. Elevated NLR, as a composite inflammatory marker, is directly linked to ventricular remodeling and myocardial fibrosis, indicating a dysregulated immune response following myocardial injury [33].

The enhanced inflammatory response increases the heart pressure load, thereby promoting the progression of HF [34]. The interplay between inflammation and abnormal lipid metabolism further exacerbates atherosclerosis and myocardial injury, elevating the risk of HF. NT-proBNP, a critical biomarker of cardiac pressure load, rises following AMI due to ventricular dilation and increased wall tension [35]. This

biomarker directly correlates with cardiac pressure load, predicting worsening cardiac function and HF severity. Budolfsen et al. [36] have shown that NT-proBNP effectively excludes HF in patients with atrial fibrillation, offering a high negative predictive value. Similarly, Wang et al. [37] found that both NLR and NT-proBNP independently predict HF. Moreover, Lp-PLA2 is recognized as an independent predictor of acute HF prognosis and holds significant clinical value for diagnostic and prognostic assessments. These three indices - NLR, Lp-PLA2, and NT-proBNP - reflect distinct aspects of post-AMI pathophysiology, with inflammatory responses, abnormal lipid metabolism, and increased cardiac load collectively contributing to ventricular remodeling and myocardial fibrosis, significantly heightening HF risk [38].

In this study, the predictive value of HR, CRP, CALDS, NLR, Lp-PLA2, and NT-proBNP as independent predictors was assessed and validated through logistic regression analysis. A Nomogram model incorporating these indicators into a composite scoring system, dichotomized by cut-off values, was used to evaluate patients' HF risk. The model's AUC reached 0.964, indicating outstanding predictive accuracy for identifying patients at high risk of HF post-AMI. The DCA demonstrated that the Nomogram model was beneficial across a 1%-96% threshold range, achieving a maximum benefit rate of 70.19%. The calibration curve confirmed a high concordance between the model's predictions and actual outcomes, indicating robust stability and reproducibility. Liu et al. [39] reported AUCs of 0.763 for brain natriuretic peptide, 0.829 for cystatin C, and 0.893 for the a combined assay in predicting HF post-AMI, with values significantly lower than the Nomogram's AUC in our study, emphasizing the advantages of a comprehensive clinical assessment.

Despite its promising results, this study has limitations, such as the need for a larger sample size, improved external validation, model optimization, and the inclusion of additional biomarkers to enhance the model's versatility and accuracy. Furthermore, the specific roles of each predictor in the pathophysiological mechanisms of HF warrant deeper exploration. Focus areas should include inflammation, specifically how CRP and NLR function within the inflammatory pathways of HF; lipid metabolism, particularly the role of Lp-PLA2 in lipid disorders and its impact on plaque stability; and cardiac stress, exploring how NT-proBNP contributes to myocardial strain. By deepening our understanding of these mechanisms, we can develop more precise interventions to effectively prevent and treat HF, ultimately improving patient outcomes. Future discussions should address these gaps, providing more comprehensive theoretical support and clinical guidance.

In summary, this study identified HR, CRP, CALDS, NLR, Lp-PLA2, and NT-proBNP as independent predictors of HF after AMI using logistic regression and developed a Nomogram model. This model serves as an effective tool for the early identification of high-risk HF patients post-AMI, aiding in improving their prognosis.

Disclosure of conflict of interest

None.

Address correspondence to: Wen Xing, Department of Internal Medicine, Northwest University Hospital, No. 229 Taibai North Road, Beilin District, Xi'an 710069, Shaanxi, China. E-mail: xingwen_323@126.com

References

[1] Barnett R. Acute myocardial infarction. Lancet 2019; 393: 2580.
[2] Lindahl B and Mills NL. A new clinical classification of acute myocardial infarction. Nat Med 2023; 29: 2200-2205.
[3] Xie C, He M and Xiang Y. Nitroglycerin plus clopidogrel for acute myocardial infarction and the effect on cardiac function indices. Pak J Pharm Sci 2023; 36: 973-979.
[4] Shao C, Wang J, Tian J and Tang YD. Coronary artery disease: from mechanism to clinical practice. Adv Exp Med Biol 2020; 1177: 1-36.
[5] Zhao Y, Ding S, Peng W, Zhang Y and Xu Y. A smart chest pain center to improve quality control and reduce doctor's workload of acute myocardial infarction. Crit Pathw Cardiol 2020; 19: 161-165.
[6] Docherty KF, Jackson AM, Macartney M, Campbell RT, Petrie MC, Pfeffer MA, McMurray JJV and Jhund PS. Declining risk of heart failure hospitalization following first acute myocardial infarction in Scotland between 1991-2016. Eur J Heart Fail 2023; 25: 1213-1224.

[7] Arnautu DA, Andor M, Buz BF, Tomescu MC, Vacarescu C, Crisan S, Gaita D, Luca CT and Cozma D. Left ventricular remodeling and heart failure predictors in acute myocardial infarction patients with preserved left ventricular ejection fraction after successful percutaneous intervention in Western Romania. Life (Basel) 2022; 12: 1636.

[8] Weir RA, McMurray JJ and Velazquez EJ. Epidemiology of heart failure and left ventricular systolic dysfunction after acute myocardial infarction: prevalence, clinical characteristics, and prognostic importance. Am J Cardiol 2006; 97: 13F-25F.

[9] Desta L, Jernberg T, Löfman I, Hofman-Bang C, Hagerman I, Spaak J and Persson H. Incidence, temporal trends, and prognostic impact of heart failure complicating acute myocardial infarction. The SWEDEHEART registry (Swedish web-system for enhancement and development of evidence-based care in heart disease evaluated according to recommended therapies): a study of 199,851 patients admitted with index acute myocardial infarctions, 1996 to 2008. JACC Heart Fail 2015; 3: 234-242.

[10] Liang Z, Yang Y, Wang F, Liu J, Liu L, Mo Y and Wang M. Assessing the early prognosis of heart failure after acute myocardial infarction using left ventricular pressure-strain loop: a prospective randomized controlled clinical study. Quant Imaging Med Surg 2024; 14: 1957-1970.

[11] Wellings J, Kostis JB, Sargsyan D, Cabrera J and Kostis WJ; Myocardial Infarction Data Acquisition System (MIDAS 31) Study Group. Risk factors and trends in incidence of heart failure following acute myocardial infarction. Am J Cardiol 2018; 122: 1-5.

[12] Wang WH, Mar GY, Wei KC, Cheng CC and Huang WC. Risk factors and outcomes of heart failure following first-episode of acute myocardial infarction-a case series study of 161,384 cases. Healthcare (Basel) 2021; 9: 1382.

[13] McGivery K, Atkinson P, Lewis D, Taylor L, Harris T, Gadd K, Fraser J and Stoica G. Emergency department ultrasound for the detection of B-lines in the early diagnosis of acute decompensated heart failure: a systematic review and meta-analysis. CJEM 2018; 20: 343-352.

[14] Berezin AA, Lichtenauer M, Boxhammer E, Stöhr E and Berezin AE. Discriminative value of serum irisin in prediction of heart failure with different phenotypes among patients with type 2 diabetes mellitus. Cells 2022; 11: 2794.

[15] Kunutsor SK, Voutilainen A, Kurl S and Laukkanen JA. Serum copper-to-zinc ratio is associated with heart failure and improves risk prediction in middle-aged and older Caucasian men: a prospective study. Nutr Metab Cardiovasc Dis 2022; 32: 1924-1935.

[16] Huang X, Yang S, Chen X, Zhao Q, Pan J, Lai S, Ouyang F, Deng L, Du Y, Chen J, Hu Q, Guo B and Liu J. Development and validation of a clinical predictive model for 1-year prognosis in coronary heart disease patients combine with acute heart failure. Front Cardiovasc Med 2022; 9: 976844.

[17] Heart Failure Group of Chinese Society of Cardiology of Chinese Medical Association; Chinese Heart Failure Association of Chinese Medical Doctor Association; Editorial Board of Chinese Journal of Cardiology. Chinese guidelines for the diagnosis and treatment of heart failure 2018. Zhonghua Xin Xue Guan Bing Za Zhi 2018; 46: 760-789.

[18] Kundi H, Wadhera RK, Strom JB, Valsdottir LR, Shen C, Kazi DS and Yeh RW. Association of frailty with 30-day outcomes for acute myocardial infarction, heart failure, and pneumonia among elderly adults. JAMA Cardiol 2019; 4: 1084-1091.

[19] Yandrapalli S, Malik A, Pemmasani G, Aronow W, Shah F, Lanier G, Cooper H, Jain D, Naidu S, Frishman W and Panza J. Sex differences in heart failure hospitalisation risk following acute myocardial infarction. Heart 2021; 107: 1657-1663.

[20] Xie C, Qi Y and Li D. Value of thoracic echocardiography in the diagnosis of acute heart failure: systematic review and meta-analysis. Altern Ther Health Med 2023; 29: 322-327.

[21] Yang Y, Yang D, Zhao W, He X, Wang X, Wang J, Liu F and Meng Q. Establishment of a nomogram prediction model for coronary artery disease risk in elderly patients with acute myocardial infarction. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2021; 33: 967-972.

[22] Ebrahimi M, Askari VR, Sharifi S, Tabatabaei SM, Rahmani M and Baradaran Rahimi V. Evaluation of long-term outcomes of percutaneous coronary intervention in patients with moderate to severe calcified coronary artery lesions. Health Sci Rep 2023; 6: e1588.

[23] Nwabuo CC, Appiah D, Moreira HT, Vasconcellos HD, Aghaji QN, Ambale-Venkatesh B, Rana JS, Allen NB, Lloyd-Jones DM, Schreiner PJ, Gidding SS and Lima JAC. Temporal changes in resting heart rate, left ventricular dysfunction, heart failure and cardiovascular disease: CARDIA study. Am J Med 2020; 133: 946-953.

[24] Ford I, Robertson M, Komajda M, Böhm M, Borer JS, Tavazzi L and Swedberg K; SHIFT Investigators. Top ten risk factors for morbidity and mortality in patients with chronic systolic heart failure and elevated heart rate: the SHIFT Risk Model. Int J Cardiol 2015; 184: 163-169.

[25] Givi M, Shafie D, Nouri F, Garakyaraghi M, Yadegarfar G and Sarrafzadegan N. Survival rate and predictors of mortality in patients hospitalised with heart failure: a cohort study on the data of Persian registry of cardiovascular disease (PROVE). Postgrad Med J 2018; 94: 318-324.

[26] Burger PM, Koudstaal S, Mosterd A, Fiolet ATL, Teraa M, van der Meer MG, Cramer MJ, Visseren FLJ, Ridker PM and Dorresteijn JAN; UCC-SMART study group. C-reactive protein and risk of incident heart failure in patients with cardiovascular disease. J Am Coll Cardiol 2023; 82: 414-426.

[27] Ribeiro ÉCT, Sangali TD, Clausell NO, Perry IS and Souza GC. C-reactive protein and frailty in heart failure. Am J Cardiol 2022; 166: 65-71.

[28] Park JJ, Yoon M, Cho HW, Cho HJ, Kim KH, Yang DH, Yoo BS, Kang SM, Baek SH, Jeon ES, Kim JJ, Cho MC, Chae SC, Oh BH and Choi DJ. C-reactive protein and statins in heart failure with reduced and preserved ejection fraction. Front Cardiovasc Med 2022; 9: 1064967.

[29] Redwine LS, Hong S, Kohn J, Martinez C, Hurwitz BE, Pung MA, Wilson K, Pruitt C, Greenberg BH and Mills PJ. Systemic inflammation and cognitive decrements in patients with stage B heart failure. Psychosom Med 2022; 84: 133-140.

[30] Li J, Wang X, Jia W, Wang K, Wang W, Diao W, Ou F, Ma J and Yang Y. Association of the systemic immuno-inflammation index, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio with diabetic microvascular complications. Front Endocrinol (Lausanne) 2024; 15: 1367376.

[31] Liang Q, Lei X, Huang X, Fan L and Yu H. Elevated lipoprotein-associated phospholipase A2 is valuable in prediction of coronary slow flow in non-ST-segment elevation myocardial infarction patients. Curr Probl Cardiol 2021; 46: 100596.

[32] Powrózek T, Skwarek-Dziekanowska A, Sobieszek G and Małecka-Massalska T. Correlation between neutrophil-to-lymphocyte ratio, platelets-to-lymphocyte Ratio, C-reactive protein-to-albumin ratio and clinical picture of elderly chronic heart failure patients. J Clin Med 2024; 13: 433.

[33] Ang SP, Chia JE, Jaiswal V, Hanif M and Iglesias J. Prognostic value of neutrophil-to-lymphocyte ratio in patients with acute decompensated heart failure: a meta-analysis. J Clin Med 2024; 13: 1212.

[34] Vakhshoori M, Nemati S, Sabouhi S, Yavari B, Shakarami M, Bondariyan N, Emami SA and Shafie D. Neutrophil to lymphocyte ratio (NLR) prognostic effects on heart failure; a systematic review and meta-analysis. BMC Cardiovasc Disord 2023; 23: 555.

[35] Azzo JD, Dib MJ, Zagkos L, Zhao L, Wang Z, Chang CP, Ebert C, Salman O, Gan S, Zamani P, Cohen JB, van Empel V, Richards AM, Javaheri A, Mann DL, Rietzschel ER, Schafer PH, Seiffert DA, Gill D, Burgess S, Ramirez-Valle F, Gordon DA, Cappola TP and Chirinos JA. Proteomic associations of NT-proBNP (N-terminal Pro-B-Type natriuretic peptide) in heart failure with preserved ejection fraction. Circ Heart Fail 2024; 17: e011146.

[36] Budolfsen C, Schmidt AS, Lauridsen KG, Hoeks CB, Waziri F, Poulsen CB, Riis DN, Rickers H and Løfgren B. NT-proBNP cut-off value for ruling out heart failure in atrial fibrillation patients - a prospective clinical study. Am J Emerg Med 2023; 71: 18-24.

[37] Wang R, Wu J, Ye H, Zhang X and Wang L. Application value of systemic inflammatory indexes in the clinical evaluation of patients with heart failure with preserved ejection fraction (HFpEF). Medicina (Kaunas) 2022; 58: 1473.

[38] Zhang J, Wang L, Zhao Z, Li L and Xia Y. Correlation between levels of serum lipoprotein-associated phospholipase A2 and soluble suppression of tumorigenicity 2 and condition of acute heart failure patients and their predictive value for prognosis. J Healthc Eng 2021; 2021: 1525190.

[39] Liu R and Gao C. Clinical value of combined plasma brain natriuretic peptide and serum cystatin C measurement on the prediction of heart failure in patients after acute myocardial infarction. Braz J Med Biol Res 2023; 56: e12910.