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ORIGINAL RESEARCH

NLRP3 Inflammasome May Be a Biomarker for Risk Stratification in Patients with Acute Coronary Syndrome

De-Gang Mo[1], Lin Wang[2], Qian-Feng Han[1], Kang Yu[3], Jia-Hui Liu[1], Heng-Chen Yao[1]

[1]Department of Cardiology, Liaocheng People's Hospital Affiliated to Shandong First Medical University, Liaocheng, People's Republic of China; [2]Cardiologic Color Doppler Room, Liaocheng People's Hospital Affiliated to Shandong First Medical University, Liaocheng, People's Republic of China; [3]Department of Laboratory Medicine, Liaocheng People's Hospital Affiliated to Shandong First Medical University, Liaocheng, People's Republic of China

Correspondence : Heng-Chen Yao, Department of Cardiology, Liaocheng People's Hospital Affiliated to Shandong First Medical University, Liaocheng, 252000, People's Republic of China, Email yaohc66@126.com

Purpose: Acute coronary syndrome (ACS) has a high incidence and mortality rate worldwide, which has a considerable negative impact on the global economy. This study aimed to identify a group of ACS patients at a high risk of recurrent adverse cardiac events using the plasma NLRP3 inflammasome.

Patients and methods: ACS patients admitted to Liaocheng People's Hospital between June 2021 and March 2022 were enrolled in this study. Patients were divided into low (levels < 3.84 ng/mL) and high (levels ≥ 3.84 ng/mL) groups based on the median NLRP3 inflammasome levels. The patients were divided into three groups according to the Thrombolysis in Myocardial Infarction Risk Score for Secondary Prevention (TRS-2P): low (scores ≤ 2 points), intermediate (scores = 3 points), and high (score ≥ 4 points) risk. We investigated the relationship between NLRP3 inflammasome and laboratory indicators. Additionally, we examined whether the NLRP3 inflammasome was an independent predictor of high TRS-2P and explored the applicability of the plasma NLRP3 inflammasome for predicting high TRS-2P.

Results: Logistic regression analysis revealed that NLRP3 inflammasome was an independent predictor of high TRS-2P (odds ratio [OR]:2.013; 95% confidence interval [CI]: 1.174–3.452). The area under the receiver operating characteristic curve value of the NLRP3 inflammasome was 0.674 (95% CI: 0.611–0.737; P < 0.001).

Conclusion: NLRP3 inflammasome levels are an independent predictive factor for high TRS-2P levels, which indicates that the NLRP3 inflammasome may help predict the prognosis of ACS patients.

Keywords: NLRP3 inflammasome, biomarker, risk stratification, acute coronary syndrome, thrombolysis in myocardial infarction risk score for secondary prevention, TRS-2P

Introduction

Acute coronary syndrome (ACS) is a group of ischemic diseases, including unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).[1] In 2015, approximately 422.7 million cases of coronary artery disease were reported, with 17.92 million deaths causing a great burden on the global economy.[2] Percutaneous coronary intervention (PCI) can significantly prevent further necrosis of the myocardium and improve the quality of life of patients.[3] Therefore, it is widely used in ACS patients. Using intravascular imaging techniques for PCI guidance reduces the risk of cardiovascular death and adverse events compared those associated with coronary angiography.[4] However, the long-term prognosis of ACS patients remains an unsolved problem.[5] Numerous prognostic indicators of ACS, including lymphocyte-to-monocyte ratio, neutrophil-to-lymphocyte ratio (NLR), triglyceride-glucose index,[6–8] and others, have been reported. However, these biological indicators[6–8] are easily affected by various factors and do not have an exact cutoff value. Therefore, novel biomarkers for predicting the prognosis of ACS patients are required.

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In recent years, an increasing number of studies have shown that inflammation plays an important role in acute myocardial infarction (AMI), and it has a great impact on the prognosis.[9,10] NACHT, LRR, and PYD domain-containing protein 3 (NLRP3) inflammasome, composed of NLRP3, apoptosis speck-like protein (ASC), and pro-caspase 1, plays an important role in the inflammatory stage.[11,12] Moreover, studies have shown that the size of myocardial infarction can be reduced, and cardiac function can be preserved by inhibiting the NLRP3 inflammasome in animal models.[13–15] In clinical research, the NLRP3 inflammasome is related to the severity and prognosis of ACS patients.[16,17] The studies by Afrasyab et al and Peng et al were conducted at the peripheral blood monocyte and platelet levels, respectively. While our study was performed at the plasma level. In addition, we explored the relationship between the NLRP3 inflammasome and thrombolysis in the myocardial infarction risk score for secondary prevention (TRS-2P).

TRS-2P has been used to predict recurrent cardiovascular events in ACS patients.[18,19] We aimed to use the TRS-2P to evaluate the NLRP3 inflammasome as a potential biomarker to better identify patients with a high risk of recurrent adverse cardiac events.

Methods

Participants and Design

ACS patients who underwent coronary angiography at the Liaocheng People's Hospital between June 2021 and March 2022 were enrolled. The diagnosis of myocardial infarction was defined according to the fourth universal definition of myocardial infarction,[20] and UA pectoris, according to the 2021 AHA/ACC guidelines for evaluating and diagnosing chest pain.[21] Patients with infections, cancer, immune system diseases, acute stroke, liver dysfunction, renal insufficiency, and previous cardiac insufficiency were excluded from this study because these diseases may affect the NLRP3 expression in plasma, resulting in experimental bias. A study flowchart is shown in Figure 1. This study was approved by the Medical Ethics Committee of Liaocheng People's Hospital (approval number: 2021096). All procedures were performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients.

Data Collection and Laboratory Testing

The demographic characteristics of the patients included age, sex, smoking status, hypertension, type 2 diabetes mellitus (T2DM), and previous medication history, including aspirin, clopidogrel, and statins. Hematological indices were white

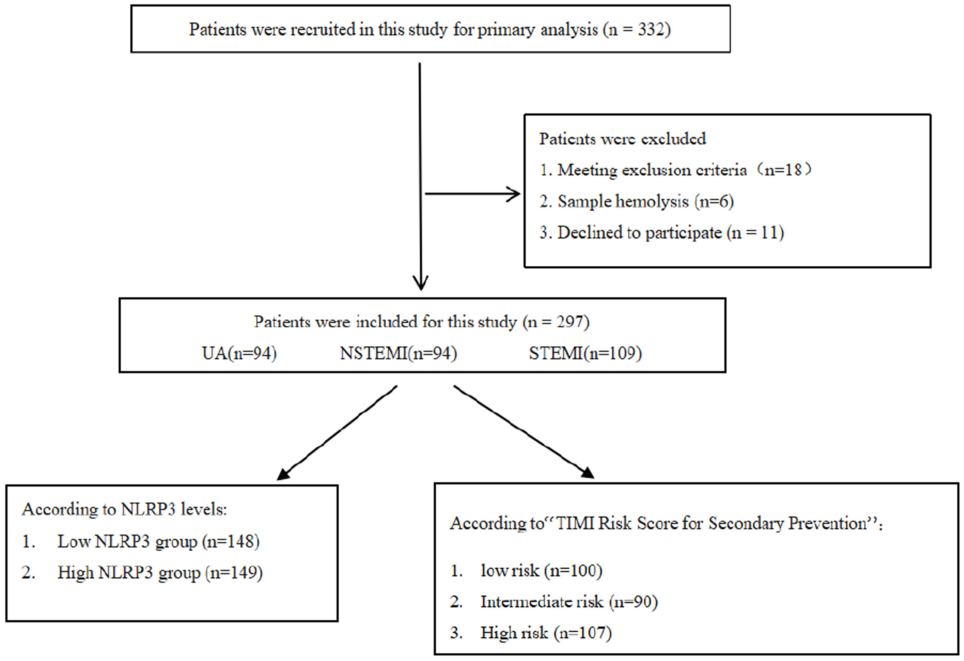

Figure 1 Flowchart of the study patients.

blood cell (WBC), C-reactive protein (CRP), D-dimer, troponin I (cTnI), type B natriuretic peptide (BNP), low-density lipoprotein cholesterol, and creatinine (Cr). The echocardiographic indices included the left ventricle end-diastolic dimension and left ventricle ejection fraction (LVEF). All data were obtained from the case system of the Liaocheng People's Hospital.

An enzyme-linked immunosorbent assay (ELISA) was used to determine NLRP3 inflammasome levels. Blood samples were collected in tubes containing ethylenediaminetetraacetic . After collecting the blood samples, they were immediately centrifuged at 1000 rpm for 15 min and stored at −80 °C. When all the samples were collected, they were thawed for ELISA. The plasma NLRP3 inflammasome level was determined strictly following the manufacturer's instructions (Ml560903-2; Mlbio, China).

TRS-2P

The original version conferred 1 point for each of nine cardiovascular risk factors: heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke, prior coronary artery bypass graft surgery, peripheral vascular disease, estimated glomerular filtration rate < 60 $mL \cdot min^{1} \cdot 1.73\ m^{2}$, and current smoking. To stratify risk in ACS patients, the score was adapted to include prior MI as a risk factor to obtain a maximum 10-point score.[22] The patients were divided into three groups: low (scores ≤ 2 points), intermediate (scores = 3 points), and high (scores ≥ 4 points) risk.

Statistical Analysis

SPSS software (version 26.0; SPSS NY., USA) was used for the statistical analysis. The Shapiro–Wilk test was used to test whether the data were normally distributed. Non-normal distribution data were expressed as median (interquartile range), which were compared using the Mann–Whitney *U*-test in two groups. Non-normal distribution data among the three groups were tested using the Kruskal–Wallis H-test. Categorical variables were expressed as frequencies (percentages) and compared using the chi-square test. Pearson's or Spearman correlation was used to compare the correlation between the NLRP3 inflammasome and other indices. Logistic regression analysis was performed to determine whether NLRP3 inflammasome was an independent predictor of high TRS-2P levels. In the univariate analysis, variables with an unadjusted P-value < 0.05 stepped in the multifactor logistic regression model. To evaluate the fit of the multifactor logistic regression model, Omnibus and Hosmer-Lemeshow tests were performed. The receiver operating characteristic (ROC) curve was used to further explore the applicability of the plasma NLRP3 inflammasome in predicting high TRS-2P. Each test was two-sided, and P-values < 0.05 were considered statistically significant.

Results

Patient Characteristics

This study included 297 patients (94 with UA, 94 with NSTEMI, and 109 with STEMI). The baseline patient characteristics are presented in Table 1. The three groups were significantly different in sex, smoking status, hypertension, previous medication history, NLRP3 inflammasome, WBC, and CRP, D-dimer, cTnI, BNP levels, and LVEF (P < 0.05).

In the subgroup analysis, all patients were divided into two groups according to NLRP3 inflammasome levels: the low (NLRP3 levels < 3.84 ng/mL) and high (NLRP3 level ≥3.84 ng/mL) groups. In the high NLRP3 inflammasome group, patients were older, with high WBC, CRP, D-dimer, cTnI, BNP, and Cr levels, and low LVEF levels (Table 2). Furthermore, we divided the patients into three subgroups according to TRS-2P (Table 3). As the risk increased, the percentage of patients who were smokers, had hypertension and had T2DM increased. Age, NLRP3 inflammasome levels, WBC count and D-dimer, cTnI, and BNP levels increased with increasing scores. However, the LVEF decreased in the high-risk group.

Correlation Analysis Between NLRP3 Inflammasome and Other Indicators

NLRP3 inflammasome levels were positively correlated with age (r =0.165, P =0.004), WBC (r = 0.192, P = 0.001), CRP (r = 0.220, P < 0.001), D-dimer (r = 0.219, P < 0.001), cTnI (r = 0.200, P = 0.001), BNP (r = 0.324, P < 0.001), and Cr (r = 0.135, P =0.020) and inversely correlated with LVEF (r = −0.245, P < 0.001) (Table 4).

Table 1 The Baseline Characteristics of the Patients

Variable	UA n = 94	NSTEMI n = 94	STEMI n = 109	P-value
Age (year)	66 (15)	65 (17)	64 (18)	0.412
Male, n (%)	53 (55.3)*	68 (72.3)	77 (70.6)	0.037
Smoking, n (%)	28 (29.8)*	44 (46.8)	52 (47.7)	0.017
Hypertension, n (%)	69 (73.4)*	66 (70.2)#	59 (54.1)#	0.008
T2DM, n (%)	29 (30.1)	25 (26.6)	36 (33.0)	0.604
Aspirin, n (%)	38 (40.4)*	34 (36.2)#	21 (19.3)#	0.002
Clopidogrel, n (%)	21(22.3)*	22 (23.4)#	5 (4.6)#	<0.001
Statins, n (%)	34 (36.2)	35 (37.2)#	18 (16.5)#	0.001
NLRP3 (ng/mL)	3.1 (2.6)*	4.0 (6.2)	4.4 (7.4)	<0.001
WBC ($\times 10^9$/L)	6.2 (2.1)*	8.0 (3.2)#	9.8 (3.9)#	<0.001
CRP (mg/L)	1.5 (2.3)*	2.8 (6.0)	3.2 (13.9)	<0.001
D-dimer (ng/mL)	0.3 (0.5)*	0.3 (0.5)	0.4 (0.6)	0.003
cTnI (ng/mL)	0.01 (0.0)*	0.6 (2.0)#	6.2 (15.0)#	<0.001
BNP (pg/mL)	89 (103.5)*	723.5 (2223.8)	858 (2280.0)	<0.001
LDL (mmol/L)	2.5 (1.2)	2.7 (1.2)	2.8 (1.1)	0.243
Cr (mmol/L)	72.5 (22.6)	72.1 (19.5)	69.9 (23.4)	0.292
LVDD (mm)	45 (5)	46 (7)	46 (5)	0.217
LVEF (%)	62 (4)*	57 (18)#	47 (12)#	<0.001

Notes: P-value: the three groups were compared. #p<0.05 on comparison between NSTEMI and STEMI. *p<0.05 on comparison between UA and AMI (STEMI and NSTEMI).

Abbreviations: UA, unstable angina; NSTEMI, non–ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; T2DM, type 2 diabetes mellitus; NLRP3, NACHT, LRR, and PYD domain-containing protein 3; WBC, white blood cell; CRP, C-reactive protein; cTnI, Troponin I; BNP, type B natriuretic peptide; LDL, low-density lipoprotein cholesterol; Cr, creatinine; LVDD, left ventricular end-diastolic dimension; LVEF, left ventricle ejection fraction.

Table 2 Basic Characteristics of Patients by NLRP3 Levels

Variable	NLRP3 Levels < 3.84 ng/mL (n = 148)	NLRP3 Levels≥3.84 ng/mL (n = 149)	P-value
Age (year)	63 (16)	66 (18)	0.012
Male, n (%)	100 (67.6)	97 (65.1)	0.653
Smoking, n (%)	60 (40.5)	64 (43.0)	0.673
Hypertension, n (%)	99 (66.9)	95 (63.8)	0.571
T2DM, n (%)	48 (32.4)	42 (28.2)	0.426
WBC ($\times 10^9$/L)	7.4 (3.3)	8.2 (4.7)	0.009
CRP (mg/L)	1.6 (3.6)	3.1 (10.2)	<0.001
D-dimer (ng/mL)	0.29 (0.38)	0.44 (0.66)	0.001
cTnI (ng/mL)	0.12 (2.79)	0.91 (6.53)	0.001
BNP (pg/mL)	156.5 (748)	623 (2297)	<0.001
LDL (mmol/L)	2.68 (1.25)	2.65 (1.09)	0.243
Cr (mmol/L)	69.8 (21.6)	74.5 (24.8)	0.027
LVDD (mm)	45 (5)	46 (5)	0.281
LVEF (%)	60 (15)	51 (18)	<0.001

Abbreviations: NLRP3, NACHT, LRR, and PYD domain-containing protein 3; T2DM, type 2 diabetes mellitus; WBC, white blood cell; CRP, C-reactive protein; cTnI, Troponin I; BNP, type B natriuretic peptide; LDL, low-density lipoprotein cholesterol; Cr, creatinine; LVDD, left ventricular end-diastolic dimension; LVEF, left ventricle ejection fraction.

Multivariate Logistic Regression Model for Predicting High TRS-2P

Logistic regression analysis was performed to analyze the value of the NLRP3 inflammasome as a potential biomarker for the prediction of high TRS-2P. The results revealed that NLRP3 inflammasome (odds ratio [OR]: 2.013; 95%

Table 3 Patients Stratified by "TRS-2P"

Variable	Low Risk (n= 100)	Intermediate Risk (n = 90)	High Risk (n = 107)	P-value
Age (year)	61 (14)	62 (16)	69 (17)	<0.001
Male, n (%)	60 (60.00)	64 (71.11)	73 (68.22)	0.236
Smoking, n (%)	24 (24)	46 (51.11)	54 (50.47)	<0.001
Hypertension, n (%)	53 (53)	55 (58.89)	88 (82.24)	<0.001
T2DM, n (%)	17 (17)	26 (28.89)	47 (43.93)	<0.001
NLRP3 (ng/mL)	3.09 (2.57)	3.76 (4.20)	4.63 (5.90)	<0.001
WBC ($\times 10^9$/L)	6.33 (2.32)	8.77 (3.80)	8.89 (3.96)	<0.001
CRP (mg/L)	1.14 (2.34)	3.20 (5.14)	3.16 (11.06)	<0.001
D-dimer (ng/mL)	0.27 (0.36)	0.34 (0.48)	0.46 (0.7)	<0.001
cTnI (ng/mL)	0.01 (0.05)	1.10 (4.71)	1.50 (7.85)	<0.001
BNP (pg/mL)	82 (72)	389 (1161)	1320 (2577)	<0.001
LDL (mmol/L)	2.56 (1.09)	2.92 (1.20)	2.59 (1.22)	0.092
Cr (mmol/L)	70.05 (21.70)	71.20 (20.05)	72.50 (26.60)	0.189
LVDD (mm)	45 (5)	47 (7)	45 (6)	0.025
LVEF (%)	62 (4)	54 (16)	48 (17)	<0.001

Abbreviations: T2DM, type 2 diabetes mellitus; NLRP3, NACHT, LRR, and PYD domain-containing protein 3; WBC, white blood cell; CRP, C-reactive protein; cTnI, Troponin I; BNP, type B natriuretic peptide; LDL, low-density lipoprotein cholesterol; Cr, creatinine; LVDD, left ventricular end-diastolic dimension; LVEF, left ventricle ejection fraction.

Table 4 Correlation Analysis Between NLRP3 and Laboratory Indicators

Variable	R	P-value
Age	0.165	0.004
Male	0.003	0.957
Smoking	0.092	0.114
Hypertension	−0.053	0.365
T2DM	−0.016	0.783
WBC	0.192	0.001
CRP	0.220	<0.001
D-dimer	0.219	<0.001
cTnI	0.200	0.001
BNP	0.324	<0.001
LDL	−0.071	0.227
Cr	0.135	0.020
LVDD	0.076	0.193
LVEF	−0.245	<0.001

Abbreviations: NLRP3, NACHT, LRR, and PYD domain-containing protein 3; T2DM, type 2 diabetes mellitus; WBC, white blood cell; CRP, C-reactive protein; cTnI, Troponin I; BNP, type B natriuretic peptide; LDL, low-density lipoprotein cholesterol; Cr, creatinine; LVDD, left ventricular end-diastolic dimension; LVEF, left ventricle ejection fraction.

confidence interval [CI]: 1.174–3.452) and WBC (OR:1.107; 95% CI:1.020–1.202) were independent predictors of high TRS-2P (Table 5). The omnibus test showed that the overall model is meaningful ($P < 0.001$; Table 6). The Hosmer-Lemeshow test indicated that the model has a good fit. (Chi-square:10.933; $P > 0.05$; Table 6).

Table 5 Logistic Regression Analysis of Predictors of High Risk in ACS Patients

Variables	OR	95% CI	P-value	Adjusted OR	95% CI	P-value
Male	1.143	0.690–1.893	0.604			
HR	1.030	1.012–1.048	0.001	1.017	0.997–1.037	0.105
NLRP3	2.497	1.530–4.074	< 0.001	2.013	1.174–3.452	0.011
WBC	1.137	1.059–1.222	< 0.001	1.107	1.020–1.202	0.015
CRP	1.020	1.006–1.034	0.005	1.010	0.996–1.024	0.151
D-dimer	1.369	1.065–1.759	0.014	1.108	0.849–1.446	0.451
cTnI	1.034	1.003–1.066	0.030			
LDL	1.114	0.838–1.481	0.458			
uric acid	0.338	0.999–1.003	1.001			

Abbreviations: ACS, acute coronary syndrome; OR, odds ratio; CI, confidence interval; HR, heart rate; WBC, white blood cell; CRP, C-reactive protein; cTnI, Troponin I; LDL, low-density lipoprotein cholesterol.

Table 6 Omnibus and Hosmer-Lemeshow Tests

Test Method	Chi-Square	Degrees of Freedom	P-value
Omnibus test	33.975	5	<0.001
Hosmer-Lemeshow test	10.933	8	0.206

Performance of NLRP3 Inflammasome in the Prediction of High TRS-2P

ROC analysis was conducted to test the performance of the NLRP3 inflammasome in predicting high TRS-2P levels (Figure 2). The area under the curve value of the NLRP3 inflammasome was 0.674 (95% CI: 0.611–0.737; P < 0.001). The cutoff was 3.51 ng/mL, and the sensitivity and specificity were 75.7% and 70.6%, respectively.

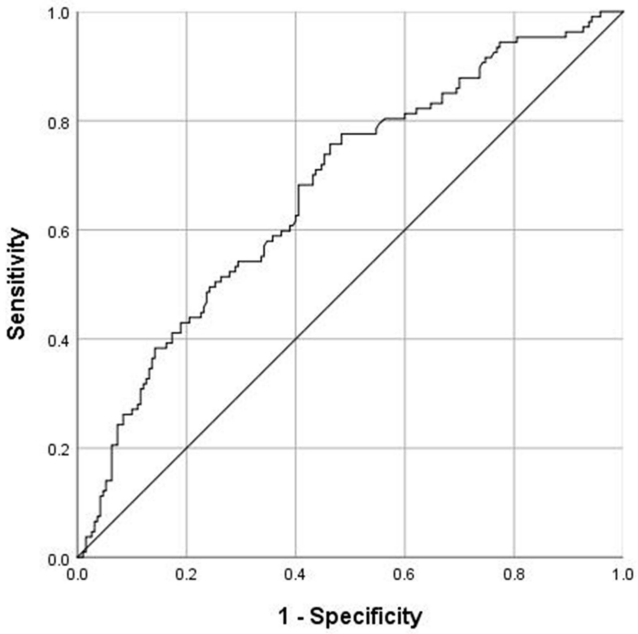

Figure 2 ROC curve of the NLRP3 inflammasome for predicting high TRS-2P. The area under the curve value of NLRP3 inflammasome was 0.674 (95% CI: 0.611–0.737; P< 0.001). The cutoff value was 3.51 ng/mL, and the sensitivity and specificity were 75.7% and 70.6%, respectively.

Discussion

This study demonstrated that the plasma level of the NLRP3 inflammasome in AMI patients was higher than that in UA patients, and the level of the NLRP3 inflammasome was correlated with age, WBC count, CRP, D-dimer, BNP levels, and LVEF. To our knowledge, this is the first study to identify plasma NLRP3 inflammasome levels as an independent predictive factor of high TRS-2P. These findings suggest that the NLRP3 inflammasome can be used to predict the prognosis of ACS patients.

Previous studies have shown that the NLRP3 inflammasome is elevated in ACS patients.[16,17] However, their study was based on platelet and peripheral monocyte levels. To our knowledge, this is the first study to investigate the plasma NLRP3 inflammasome and link it to TRS-2P. Toldo et al[23] have reviewed the mechanisms of NLRP3 inflammasome activation through the kinase and oxidative stress pathways in AMI. In the analysis of AMI subgroups, the STEMI and NSTEMI groups exhibited no significant differences. No studies have compared the expression of the plasma NLRP3 inflammasome in STEMI and NSTEMI patients.

Couchie et al[24] found that human plasma thioredoxin-80 levels increased with age and promoted the activation of the NLRP3 inflammasome through the Akt2/mechanistic target of the rapamycin-C1/70S6K pathway. A recent study also revealed that serum concentrations of pro-inflammatory cytokines, including IL-1α/β, TNF-α, IL-6, and NLRP3, significantly increased with age.[25] This was consistent with our study, wherein patients in the high NLRP3 group were older. Because this was a retrospective study with a small sample size, the relationship between age and the NLRP3 inflammasome may be stronger if a larger sample size is assessed. Our study shows that the level of NLRP3 inflammasome is higher in AMI than that of UA and positively correlated with WBC and CRP levels, which is consistent with previous studies.[16,17] NLRP3 inflammasome activation in AMI is mediated by a dual-signal model.[26] Various endogenous molecules promote the expression of the NLRP3 gene and lead to the recombination of NLRP3, which mediates apoptosis and inflammatory response.[27] In our study, WBC and CRP were associated with NLRP3 inflammasome. To date, we have shown that the NLRP3 inflammasome can increase the expression of CRP via the caspase-1/IL-6 pathway.[28] Bian et al[29] found CRP increased the expression of NLRP3 via the NF-κB pathway. Therefore, we speculate that NLRP3 and CRP interact with each other. In recent years, an increasing number of clinical studies have shown that D-dimer is related to the prognosis of ACS patients.[30–32] In our study, patients with high TRS-2P had high D-dimer levels, which was consistent with previous studies.[30–32] In addition, NLRP3 inflammasome levels positively correlated with D-dimer levels, suggesting that NLRP3 inflammasome levels may be associated with the prognosis of patients with ACS. Previous studies have shown that uric acid is important in inflammation and is associated with mortality in ACS patients.[33,34] However, our study observed no correlation between uric acid and TRS-2P. This might have been due to the small sample size and sampling errors.

Furthermore, TRS-2P has been used to predict recurrent cardiovascular events in patients with ACS.[18,19] In animal experiments, NLRP3 inflammasome has been associated with cardiac remodeling and function. A study including an experimental mouse model revealed that a specific NLRP3 inhibitor, MCC950, can alleviate fibrosis and improve cardiac function by suppressing early inflammatory responses post-MI.[35] Similarly, Zhao et al also demonstrated that MCC950 could attenuate cardiac remodeling by inhibiting cardiac hypertrophy, fibrosis, and inflammation.[36] As another specific NLRP3 inhibitor, OLT1177 has also been widely studied. In a large non-reperfused anterior MI mouse model, it preserved β-adrenergic responsiveness and prevented left ventricular diastolic dysfunction.[37] Researchers have recently identified many substances related to NLRP3 inflammasome. Nie et al[38] unearthed that inhalation of H_2 can ameliorate myocardial infarction-induced cardiac remodeling and fibrosis in rats with MI. In another study, the LuQi Formula inhibited the activation of the NLRP3/ASC/caspase-1/IL-1β cascade, decreasing inflammatory and delayed ventricular remodeling.[39] In summary, the NLRP3 inflammasome has been confirmed to potentiate the cardiac inflammatory response and cardiac remodeling, which lays a foundation for its use in predicting the prognosis of ACS patients. Per current clinical research, drugs suppress the NLRP3 inflammasome directly or indirectly via IL-1 activity. In a randomized trial involving patients with chronic coronary disease, the risk of cardiovascular events was significantly lower among those who received 0.5 mg of colchicine once daily than among those who received a placebo.[40] A LoDoCo2 biomarker sub-study found that colchicine can reduce the extracellular vesicle NLRP3 protein levels.[41] However, we do not recommend increasing the dose of colchicine during acute inflammatory reaction because its side effects increase with its increasing dose, including

myelosuppression, neuromuscular toxicity, liver damage, and dermatologic issue.[42] A systematic review and meta-analysis of randomized trials reported that low-dose colchicine could reduce the risk of MACE in patients with coronary disease.[43] In addition to colchicine, other drugs that indirectly inhibit IL-1 by suppressing the NLRP3 pathway, such as anakinra and canakinumab, are also under clinical research. In thetwo clinical studies,[44,45] STEMI patients treated with anakinra (an IL-1 blocker) exhibited reduced CRP levels and reduced incidence of heart failure. NLRP3 inflammasome, as an upstream factor of IL-1 and CRP,[23] may play an important role in the prognosis of STEMI patients. A clinical trial on canakinumab suggested that canakinumab can reduce the occurrence of MACE, accompanied by a decrease in IL-6 and CRP levels.[46] In conclusion, NLRP3 inflammasome has a great impact on the prognosis of ACS patients, which has laid the foundation for distinguishing high-risk patients and administering early intervention. However, the mechanisms by which NLRP3 inflammasome affects prognosis remain unclear. The NLRP3 inflammasome can affect cardiac function, but its activation alone does not affect systolic cardiac dysfunction.[26] Activating NLRP3 causes its downstream IL-1β and IL-18, leading to cardiac dysfunction.[47,48] A recent study indicated that the inhibition of the NLRP3/ IL-1β pathway can alleviate the cardiac inflammatory response, improve cardiac contractility, and attenuate cardiomyopathy in sepsis.[49] Therefore, mechanisms other than the classical mechanism require further study.

In this study, NLRP3 inflammasomes were significantly associated with higher TRS-2P levels, supporting the NLRP3 inflammasome as a potential biomarker for predicting the prognosis of ACS patients. However, further studies are needed to clarify this association.

Our study had several limitations. First, it was a single-center study with a small sample size. Multi-center studies with larger sample sizes may be needed in the future. Second, the plasma NLRP3 inflammasome level was not monitored dynamically. Finally, the study only involved Chinese patients and should be conducted in other ethnic groups. Further research is needed to completely understand the mechanisms by which the NLRP3 inflammasome affects cardiac function and prognosis of patients with ACS.

Conclusions

Plasma NLRP3 inflammasome levels are an independent predictive factor for high TRS-2P, indicating that the NLRP3 inflammasome may be used to predict the prognosis of ACS patients.

Abbreviations

NLRP3, NACHT, LRR, and PYD domain-containing protein 3; ACS, Acute coronary syndrome; UA, unstable angina; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; NLR, neutrophil-to-lymphocyte ratio; ASC, apoptosis speck-like protein; TRS-2P, Thrombolysis in Myocardial Infarction Risk Score for Secondary Prevention; T2DM, type 2 diabetes mellitus; WBC, white blood cell; CRP, C-reactive protein; cTnI, troponin I; BNP, type B natriuretic peptide; Cr, creatinine; LVEF, left ventricle ejection fraction; ELISA, enzyme-linked immunosorbent assay; ROC, receiver operating characteristic; OR, odds ratio; CI, confidence interval.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the Medical Ethics Committee of the Liaocheng People's Hospital. All procedures were performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest associated with this study.

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