Predictive efficacy of neutrophil-to-lymphocyte ratio for long-term prognosis in new onset acute coronary syndrome: a retrospective cohort study

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Abstract

Background: Inflammation is involved in the pathogenesis and progression of coronary artery diseases (CADs), including acute coronary syndrome. The neutrophil-to-lymphocyte ratio (NLR) has been identified as a novel marker of the pro-inflammatory state. We aimed to evaluate the predictive efficacy of the NLR for the prognosis of patients with new-onset ACS.

Methods: We retrospectively included consecutive patients with new-onset ACS treated with emergency coronary angiography. NLR was measured at baseline and analyzed by tertiles. The severity of coronary lesions was evaluated by the Gensini score. Correlations of NLR with the severity of CAD and the incidence of major adverse cardiovascular diseases (MACEs) during follow-up were determined.

Results: Overall, 737 patients were included. The NLR was positively correlated with the severity of coronary lesions as assessed by Gensini score (P < 0.05). During the follow-up period (mean, 43.49 ± 23.97 months), 65 MACEs occurred. No significant association was detected between baseline NLR and the risk of MACEs during follow-up by either Kaplan–Meier or Cox regression analysis. Multivariable logistic regression analysis showed that a higher NLR was independently associated with coronary lesion severity as measured by the Gensini score (1st tertile vs. 3rd tertile hazard ratio [HR]: 0.527, P < 0.001, and 2nd tertile vs. 3rd tertile HR: 0.474, P = 0.025).

Conclusions: The NLR may be associated with coronary disease severity at baseline but is not associated with adverse outcomes in patients with new-onset ACS.

Ethics Approval Number: 2019XE0208

Keywords: Acute coronary syndrome, Gensini score, Neutrophil and lymphocyte ratio, Major adverse cardiovascular events

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Background

The current understanding of the pathogenesis of atherosclerosis is focused on the "inflammatory hypothesis of atherothrombosis" theory [1, 2]. Inflammatory cells and inflammatory signaling pathways play complex roles in the process of atherosclerosis, including initiating repair after vascular injury and mediating plaque instability and rupture, finally leading to acute coronary events [3–6].
Patients with acute coronary syndrome (ACS), particularly those with new-onset ACS, often have an unstable clinical status and a poor prognosis, and optimization of risk stratification is clinically important in this patient group [7, 8].

Pathological studies have confirmed an increase in white blood cell mobilization in necrotic areas of the myocardium [9]. Moreover, white blood cell count, a clinical marker of universal inflammation, was shown to be independently associated with the risk of mortality and incidence of major adverse cardiovascular events (MACEs) in ACS patients [10, 11]. However, white blood cell count is unstable and tends to be affected by comorbidities such as infection. Interestingly, it has also been indicated that decreased lymphocyte numbers may be associated with acute coronary events [12]. Recent studies showed that the neutrophil-to-lymphocyte ratio (NLR), which incorporates two major subgroups of white blood cells, may confer prognostic efficacy in many diseases, including inflammatory diseases, cardiovascular diseases, and malignancies [13, 14]. It has been suggested that an elevated NLR is associated with increased long-term mortality in patients with acute myocardial infarction (AMI) complicated by left main-and/or three-vessel disease [15]. Moreover, the role of the NLR for the management of patients with coronary artery disease (CAD) has also been evaluated, and the results showed that the NLR is correlated with CAD severity [16–18]. However, these studies were of limited scale and patients with a previous diagnosis of CAD were not excluded. Overall, clinical and experimental data support an important role for inflammation in CAD [1, 2].

Whether the NLR remains a significant prognostic factor after control for the severity of coronary lesions in new-onset ACS remains to be determined. Therefore, in this study, we retrospectively enrolled patients with new-onset ACS to comprehensively evaluate the potential prognostic role of the NLR in these patients.

Methods
Patients and study design
Consecutive patients with a first diagnosis of ACS who were admitted to the Xinjiang Uygur Autonomous Region Traditional Chinese Medicine Hospital affiliated to the Xinjiang Medical University from January 2011 to January 2019 were included. ACS was diagnosed in accordance with previously established guidelines [19]. Patients with the following clinical conditions that may affect the NLR were excluded: hepatic or renal dysfunction, malignant tumors, acute infection, connective tissue disease, physical and chemical damage, previously proven systemic inflammatory disease, and recent surgery. Moreover, patients with a previous diagnosis of CAD were also excluded. The protocol of the study was approved by the ethics committee of our local institution before enrollment of the patients. Informed patient consent was not needed due to the retrospective design of the study.

Blood sampling and definitions of CAD risk factors
Venous blood samples were taken when patients initially presented to the emergency department or prior to angiography, and the samples were sent immediately for laboratory analysis. Hypertension was defined if the patient was taking any antihypertensive medications or had blood pressure measurements over 140/90 mmHg on at least two separate occasions [20]. Diabetes was diagnosed based on medical history or measurements of fasting and/or postprandial glucose according to previous guidelines [21]. The estimated glomerular filtration rate (eGFR) was calculated with the Modification of Diet in Renal Diseases equation [22].

Coronary angiography and Gensini score
All patients underwent coronary angiography within 12 h of admission. Two independent investigators assessed the degrees of stenosis of the coronary lesions. Consensus with a third investigator was indicated if disagreement occurred. The Gensini score (GS), which incorporates both the extent of luminal narrowing and the geographic importance of the lesion, was calculated to reflect the severity of coronary lesions [23]. We used the GS instead of the SYNTAX system to reflect the severity of coronary lesions, because the calculation method of SYNTAX integral is more complicated. This limits its use in clinical practice and makes it difficult to apply to emergency patients, such as those with new-onset ACS. Moreover, research has shown that the SYNTAX score cannot be utilized to define future risk as the Gensini score can in patients with non-obstructive CAD [24].

Outcomes
Patients were followed by telephone interview or clinic visit. The primary outcome was all-cause mortality. The secondary outcome was a composite of MACEs, including cardiac mortality, non-fatal myocardial infarction and stroke, stent thrombosis, and revascularization (unplanned repeat PCI).

Statistical analysis
Continuous variables were expressed as mean and standard deviation (SD) or median and interquartile range (IQR), whereas categorical variables were presented as percentages. Patients were grouped according to the terciles of the NLR or GS. One-way analysis of variance (ANOVA) was used to evaluate the difference in normally
distributed numeric variables among the groups, while for the non-normally distributed variables, Mann–Whitney U test or Kruskal–Wallis variance analysis was used. For the categorical variables, a chi-square ($\chi^2$) test was employed. Linear regression analysis was performed to identify the factors associated with the GS. Prognostic factors for the occurrence of mortality and MACEs were analyzed with Kaplan–Meier survival method. Univariate analysis was first performed, and then significant variables were included in the multivariate Cox analysis. A $P$ value $<$ 0.05 indicated a statistically significant difference. All analyses were performed using SPSS 22.0 (SPSS Inc, Chicago, IL, USA).

Results

Characteristics of patients according to NLR
A flow chart outlining patient enrollment is shown in Fig. 1. A total of 737 patients with new on-set ACS were included. The baseline characteristics of the included patients according to the tertiles of NLR are shown in Table 1. The results showed that patients with a higher NLR were more likely to have dyslipidemia and ST-elevation myocardial infarction (STEMI; both $P$ < 0.05).

Incidence of mortality and MACEs according to the NLR
The incidences of clinical outcomes during follow-up (mean, 43.49 ± 23.97 months) for the included patients with new-onset ACS according to the NLR are shown in Table 2. No significant differences in the incidences of all-cause mortality, overall and components of MACEs, or bleeding events were detected among the three groups (all $P \geq 0.05$).

Characteristics of patients according to GS
The baseline characteristics of patients according to the tertiles of GS (1st tertile GS < 49; n = 250, 2nd tertile GS: 49 ~ 85; n = 246, and 3rd tertile GS > 85; n = 241) are shown in Table 3. The percentage of male patients, age, prevalence of diabetes mellitus, and history of smoking differed significantly among the groups according to GS tertile (all $P < 0.05$). However, we found no relationship between other indicators and coronary severity (all $P > 0.05$).

![Flowchart of patient enrollment](image-url)
|                          | 1st tertile ≤ 3.37 (n = 245) | 2nd tertile 3.38-6.93 (n = 245) | 3rd tertile ≥ 6.94 (n = 247) | t/Z/χ² | P       |
|--------------------------|-------------------------------|---------------------------------|------------------------------|--------|---------|
| Sex (male/female)        | 200/45                        | 203/42                          | 213/34                       | 2.039  | 0.361   |
| Age (years)              | 58.20 ± 12.46                 | 57.20 ± 12.45                   | 58.64 ± 12.04                | 0.877  | 0.417   |
| Hypertension             | 113 (46.1)                    | 115 (46.9)                      | 103 (41.7)                   | 1.582  | 0.453   |
| Diabetes mellitus        | 76 (31.0)                     | 64 (26.1)                       | 53 (21.5)                    | 5.820  | 0.054   |
| DM treatment             |                               |                                 |                              |        |         |
| Diet only                | 4 (6.6)                       | 2 (3.6)                         | 2 (4.9)                      | 3.808  | 0.433   |
| Oral hypoglycemic drugs  | 23 (37.7)                     | 30 (54.5)                       | 21 (51.2)                    |        |         |
| Insulin                  | 34 (55.7)                     | 23 (41.8)                       | 18 (43.9)                    |        |         |
| Smoking                  |                               |                                 |                              | 9.319  | 0.054   |
| Never smoker             | 110 (44.9)                    | 132 (53.9)                      | 115 (46.6)                   |        |         |
| Former smoker            | 19 (7.8)                      | 7 (2.9)                         | 11 (4.5)                     |        |         |
| Current smoker           | 116 (47.3)                    | 106 (43.3)                      | 121 (49.0)                   |        |         |
| Alcohol drinking         |                               |                                 |                              | 2.390  | 0.433   |
| Never drinking           | 151 (61.9)                    | 149 (61.3)                      | 146 (59.3)                   |        |         |
| Former drinking          | 35 (14.3)                     | 35 (14.4)                       | 46 (18.7)                    |        |         |
| Current drinking         | 58 (23.8)                     | 59 (24.3)                       | 54 (22.0)                    |        |         |
| Family history of CAD    | 99 (40.4)                     | 101 (41.2)                      | 97 (39.3)                    | 0.197  | 0.906   |
| SBP (mmHg)               | 122.02 ± 20.97                | 122.91 ± 19.32                  | 122.21 ± 19.17               | 0.137  | 0.872   |
| DBP (mmHg)               | 75.96 ± 13.59                 | 76.75 ± 12.90                   | 77.23 ± 13.84                | 0.567  | 0.567   |
| Heart rate (bpm)         | 82.78 ± 15.31                 | 80.54 ± 14.71                   | 82.50 ± 15.03                | 1.618  | 0.199   |
| BMII (kg/m²)             | 25.11 ± 5.28                  | 25.04 ± 5.15                    | 24.63 ± 5.94                 | 0.475  | 0.622   |
| HDL-C (mmol/l)           | 0.95 ± 0.26                   | 1.00 ± 0.26                     | 1.01 ± 0.26                  | 2.575  | 0.077   |
| LDL-C (mmol/l)           | 2.93 ± 0.91                   | 2.96 ± 0.84                     | 2.97 ± 0.85                  | 0.095  | 0.910   |
| TC (mmol/l)              | 4.61 ± 1.22                   | 4.66 ± 1.26                     | 4.59 ± 1.08                  | 0.181  | 0.834   |
| TG (mmol/l)              | 1.76 ± 1.13                   | 2.04 ± 1.06^a                   | 2.26 ± 1.12^ab               | 11.988 | < 0.001 |
| ApoA1 (g/L)              | 1.21 ± 0.29                   | 1.28 ± 0.53                     | 1.22 ± 0.27                  | 1.604  | 0.202   |
| ApoB (g/L)               | 0.92 ± 0.49                   | 0.90 ± 0.27                     | 0.91 ± 0.26                  | 0.160  | 0.852   |
| Lp (a) (g/L)             | 244.88 ± 258.72               | 236.56 ± 227                    | 239.63 ± 214.2               | 0.059  | 0.942   |
| Creatinine (mmol/L)      | 79.27 ± 36.5                  | 81.75 ± 56.31                   | 79.25 ± 35.77                | 0.259  | 0.772   |
| BUN (mmol/L)             | 5.42 ± 2.76                   | 5.69 ± 2.26                     | 5.68 ± 2.81                  | 0.833  | 0.435   |
| Uric acid (mmol/L)       | 334.27 ± 90.96                | 326.4 ± 88.92                   | 325.73 ± 99.45               | 0.629  | 0.534   |
| WBC                      | 9.03 ± 3.31                   | 11.05 ± 3.35^a                  | 12.32 ± 3.41^ab              | 61.212 | < 0.001 |
| Monocyte count           | 0.63 ± 0.24                   | 0.66 ± 0.34                     | 0.46 ± 0.32^ab               | 30.768 | < 0.001 |
| PLR                      | 89.94 ± 35.62                 | 145.34 ± 110.94^a               | 265.13 ± 175.65^ab           | 132.705| < 0.001 |
| RBC                      | 4.77 ± 0.72                   | 4.85 ± 0.58                     | 4.65 ± 0.82^b                | 4.852  | 0.008   |
| HGB                      | 145.04 ± 22.16                | 144.99 ± 26.14                  | 142.53 ± 28.78               | 0.759  | 0.468   |
| PLT                      | 224.49 ± 71.94                | 229.48 ± 144.24                 | 236.26 ± 162.19              | 0.492  | 0.612   |
| MPV                      | 10.16 ± 1.43                  | 10.26 ± 1.24                    | 10.14 ± 1.66                 | 0.499  | 0.608   |
| PDW                      | 13.36 ± 3.83                  | 13.43 ± 3.71                    | 13.31 ± 3.22                 | 0.065  | 0.937   |
| PCT                      | 0.24 ± 0.08                   | 0.23 ± 0.09                     | 0.25 ± 0.12                  | 1.632  | 0.196   |
| Clinical diagnosis       |                               |                                 |                              |        |         |
| UA                       | 52 (21.2)                     | 29 (11.8)                       | 19 (7.7)                     | 20.160 | < 0.001 |
| NSTEMI                   | 26 (10.7)                     | 30 (12.2)                       | 31 (12.6)                    |        |         |
| STEMI                    | 167 (68.2)                    | 186 (75.9)                      | 197 (79.8)                   |        |         |
| Coronary artery lesion   |                               |                                 |                              |        |         |
| UPLMT                    | 22 (9.2)                      | 25 (10.6)                       | 21 (8.7)                     | 0.526  | 0.769   |
| LAD                      | 217 (88.9)                    | 211 (86.5)                      | 216 (87.8)                   | 0.687  | 0.709   |
| LCX                      | 155 (64.3)                    | 147 (61.0)                      | 155 (63.0)                   | 0.577  | 0.749   |
| RCA                      | 179 (74.0)                    | 178 (73.3)                      | 186 (75.3)                   | 0.278  | 0.870   |
Factors associated with coronary lesion severity as detected by Gensini Score

The results of multivariable logistic regression analysis showed that a higher NLR was independently associated with coronary lesion severity as measured by the GS (1st tertile vs. 3rd tertile hazard ratio [HR]: 0.527, \( P < 0.001 \), and 2nd tertile vs. 3rd tertile HR: 0.474, \( P = 0.025 \)). The other factors independently related to GS included advanced age (HR: 1.033, \( P < 0.001 \)), male gender (HR: 1.835, \( P < 0.001 \)), and the absence of diabetes (HR: 0.507, \( P < 0.001 \); Table 4).

Predictors of clinical outcomes

Overall, 65 patients experienced MACEs during follow-up, including 23 (35.38%) cases of cardiac mortality, 6 (9.23%) cases of nonfatal MI, 2 (3.08%) cases of ST, 33 (50.77%) cases of revascularization, and three (4.62%) cases of nonfatal stroke. The NLR was not correlated with MACEs either as a continuous variable or according to tertiles (both \( P > 0.05 \)). Kaplan–Meier analysis also showed that age, systolic blood pressure, and higher GS were potential independent predictors of poor outcomes. Taken together, our results do not support incorporation of baseline NLR as a prognostic factor for new-onset ACS patients.

Discussion

The results of this retrospective cohort study showed that, although a higher NLR at baseline was independently associated with the severity of coronary lesions in new-onset ACS patients as evidenced by GS, the NLR was not a predictor of adverse clinical outcome during follow-up. We found that advanced age, elevated systolic BP, and higher GS were potential independent predictors of poor outcomes. Taken together, our results do not support incorporation of baseline NLR as a prognostic factor for new-onset ACS patients.

The key pathophysiologic processes for ACS include the rupture of a vulnerable plaque and subsequent formation of thrombosis [25, 26], and the role of inflammation in these processes has not only been confirmed by pathological studies, but also shown in some optical
Table 3  Baseline characteristics of the included patients according to the GS tertiles

|                        | 1st tertile ≤ 45 (n = 250) | 2nd tertile 49–85 (n = 246) | 3rd tertile ≥ 85 (n = 241) | t/Z/χ² | P     |
|------------------------|-----------------------------|-----------------------------|-----------------------------|--------|-------|
| Sex (male/female)      | 171/79                      | 191/55                      | 200/41                      | 14.814 | 0.001 |
| Age (years)            | 55.37±12.26                 | 58.23±11.84ª                | 60.53±12.34ª                | 11.111 | <0.001|
| Hypertension           | 106 (42.4)                  | 111 (45.1)                  | 114 (47.3)                  | 1.199  | 0.549 |
| Diabes mellitus        | 45 (18.0)                    | 66 (26.8)                   | 82 (34.0)ª                  | 16.381 | <0.001|
| Diabetes mellitus      | 0.846                       | 0.932                       |                             | 0.032  | 0.932 |
| Smoking                |                             |                             |                             | 9.963  | 0.041 |
| Never smoker           | 134 (53.6)                  | 119 (48.4)                  | 104 (43.2)                  |        |       |
| Former smoker          | 16 (6.4)                    | 13 (5.3)                    | 8 (3.3)                     |        |       |
| Current smoker         | 100 (40.0)                  | 114 (46.3)                  | 129 (53.5)                  |        |       |
| Alcohol drinking       |                             |                             |                             | 1.053  | 0.092 |
| Never drinking         | 147 (58.8)                  | 153 (63.2)                  | 146 (60.6)                  |        |       |
| Former drinking        | 41 (16.4)                   | 36 (14.9)                   | 39 (16.2)                   |        |       |
| Current drinking       | 62 (24.8)                   | 53 (21.9)                   | 56 (23.2)                   |        |       |
| Family history of CAD  | 95 (38.0)                   | 100 (40.7)                  | 102 (42.3)                  | 0.972  | 0.615 |
| SBP (mmHg)             | 123.72±20.64                | 122.37±18.87                | 121±19.85                   | 1.157  | 0.315 |
| DBP (mmHg)             | 76.86±13.88                 | 77.45±13.12                 | 75.62±13.3                 | 1.174  | 0.310 |
| Heart rate             | 80.42±14.05                 | 81.78±14.26                 | 83.68±16.58                | 2.930  | 0.054 |
| BMI (kg/m²)            | 24.78±5.95                  | 24.9±5.05                   | 25.11±5.36                 | 0.203  | 0.817 |
| HDL-C (mmol/l)         | 0.96±0.23                   | 0.99±0.26                   | 1.01±0.28                  | 2.152  | 0.117 |
| LDL-C (mmol/l)         | 2.88±0.85                   | 2.94±0.74                   | 3.04±1                     | 1.434  | 0.239 |
| TC (mmol/l)            | 4.63±1.23                   | 4.57±1.98                   | 4.68±1.34                  | 0.374  | 0.688 |
| TG (mmol/l)            | 2.14±2.15                   | 2.15±2.13                   | 1.98±1.45                  | 0.426  | 0.653 |
| ApoA1 (g/L)            | 1.2±0.26                    | 1.23±0.3                    | 1.29±0.53                  | 2.710  | 0.067 |
| ApoB (g/L)             | 0.9±0.27                    | 0.88±0.23                   | 0.96±0.52                  | 2.433  | 0.089 |
| Lp(a) (g/L)            | 234.48±232.84               | 263.47±280.29               | 222±172.39                 | 1.505  | 0.223 |
| Cr (mmol/L)            | 80.9±35.25                  | 80.52±42.9                  | 78.84±52.29                | 0.150  | 0.860 |
| BUN (mmol/l)           | 5.71±2.91                   | 5.59±2.87                   | 5.5±1.95                   | 0.394  | 0.674 |
| Uric acid (μmol/L)     | 326.22±92.64                | 335.89±94.27                | 324.19±92.59               | 1.009  | 0.337 |
| WBC                    | 10.88±3.74                  | 10.87±3.71                  | 10.64±3.29                 | 0.339  | 0.712 |
| Neutrophil count       | 8.13±3.63                   | 8.37±3.58                   | 8.11±3.15                  | 0.419  | 0.658 |
| Lymphocyte count       | 1.95±1.27                   | 1.76±0.96                   | 1.81±1.07                  | 1.954  | 0.142 |
| NLR                    | 5.24±3.90                   | 6.41±5.24                   | 7.46±5.51                  | 12.506 | <0.001|
| NLR tertiles           |                             |                             |                             | 19.287 | 0.001 |
| 1st tertile            | 104 (41.6)                  | 77 (31.3)                   | 64 (26.6)                   |        |       |
| 2nd tertile            | 84 (33.6)                   | 84 (34.1)                   | 77 (32.0)                   |        |       |
| 3rd tertile            | 62 (24.8)                   | 85 (34.6)                   | 100 (41.5)                  |        |       |
| Monocyte count         | 0.59±0.32                   | 0.58±0.32                   | 0.57±0.31                  | 0.258  | 0.773 |
| PLR                    | 158.09±122.37               | 176.51±159.31               | 166.74±142.57              | 1.042  | 0.353 |
| RBC                    | 4.75±0.70                   | 4.74±0.73                   | 4.79±0.72                  | 0.399  | 0.672 |
| HGB                    | 145.15±24.97                | 142.77±27.85                | 144.62±24.6                | 0.579  | 0.561 |
| PLT                    | 223.74±69.67                | 242.01±203.23               | 224.52±77.66               | 1.508  | 0.222 |
| MPV                    | 10.20±1.29                  | 10.16±1.75                  | 10.2±1.28                  | 0.065  | 0.937 |
| PDW                    | 13.66±3.35                  | 13.44±3.78                  | 12.98±3.63                 | 2.298  | 0.101 |
| PCT                    | 0.24±0.08                   | 0.24±0.11                   | 0.24±0.10                  | 0.239  | 0.788 |
| Clinical diagnosis     |                             |                             |                             | 1.672  | 0.796 |
| UA                     | 38 (15.2)                   | 32 (13.0)                   | 30 (12.4)                   |        |       |
coherence tomography-based studies [6, 27]. Therefore, it has been proposed that the NLR, a novel but easily obtained marker of inflammation, may be a prognostic factor for ACS patients. Indeed, some previous studies suggested a prognostic role for the NLR in CAD patients. In a recent study with 636 STEMI patients, the NLR was significantly associated with in-hospital mortality [28]. Moreover, a post-hoc analysis showed that the NLR is associated with increased long-term mortality in patients with acute myocardial infarction (AMI) complicated by left main- and/or three-vessel disease [15]. However, in our retrospective cohort study, we did not find a significant association between a high NLR and poor prognosis in these patients, despite the relatively longer follow-up duration in our study compared with previous studies. The mechanisms have yet to be fully determined. Previous studies showed that the NLR changes dramatically, with the maximal level seen during the occurrence of inflammatory-related events [29]. Because neutrophils have a short life span and faster turnover, it is better to observe neutrophils in a dynamic manner rather than in a single measurement. Moreover, our study had a longer follow-up duration than previous ones, which may indicate that the potential prognostic role of the NLR in ACS is only acute. The relationships of NLR with ACS, overall mortality, and cancer survival have generally been thought to be driven by chronic inflammation [1, 2]. However, patients with a previous diagnosis of CAD were excluded in our study, and whether the NLR is associated with new-onset ACS has not been well established and remains incompletely understood. To the best of our knowledge, the potential link between NLR and new onset ACS has not been reported.

Another explanation is that the potential prognostic role of the NLR in ACS is confounded by factors related to the severity of coronary lesions, such as the GS. Therefore, the prognostic efficacy of the NLR is limited in a model that incorporates factors reflecting the severity of coronary lesions. Our results indicated that the NLR is significantly correlated with coronary lesion severity as evidenced by the GS. The results of our present study confirm the previous concept that inflammation correlates with the degree of coronary stenosis in CAD patients. Pathophysiologically, myocardial ischemia can induce an immediate rise in the plasma NLR, the magnitude of which is proportional

Table 3 (continued)

| Variables | 1st tertile ≤ 45 (n = 250) | 2nd tertile 49–85 (n = 246) | 3rd tertile ≥ 85 (n = 241) | t/Z/χ² | P |
|-----------|----------------|--------------------|----------------|-------|---|
| NSTEMI    | 32 (12.8)     | 26 (10.6)          | 29 (12.0)      |       |   |
| STEMI     | 180 (72.0)    | 188 (76.4)         | 182 (75.5)     |       |   |
| Aspirin   | 18 (7.2)      | 23 (9.3)           | 33 (13.7)      | 5.923 | 0.052 |
| Statins   | 17 (6.8)      | 19 (7.7)           | 31 (12.9)ab    | 6.029 | 0.043 |
| β-Blockers| 15 (6.0)      | 12 (4.9)           | 17 (7.1)       | 1.027 | 0.598 |
| ACEI/ARB  | 7 (2.8)       | 8 (3.3)            | 12 (5.0)       | 1.828 | 0.401 |
| CCB       | 32 (12.8)     | 34 (13.8)          | 36 (14.9)      | 0.470 | 0.790 |

Abbreviations are as in Table 1

Table 4 Factors independently correlated with the severity of coronary arterial atherosclerosis as detected by GS: multivariate logistic regression analysis

| Variables | B | SE | Wald | P | HR | 95% CI |
|-----------|----|----|------|---|----|-------|
| Age       | 0.032 | 0.006 | 27.046 | <0.001 | 1.033 | 1.020 1.045 |
| Sex (male vs female) | 0.607 | 0.173 | 12.363 | <0.001 | 1.835 | 1.309 2.575 |
| Diabetes mellitus (No vs Yes) | −0.680 | 0.163 | 17.508 | <0.001 | 0.507 | 0.368 0.696 |
| Smoking | | | | | | |
| Never smoker vs current drinking | −0.178 | 0.152 | 2.501 | 0.079 | 0.837 | 0.216 1.255 |
| Former smoker vs current drinking | −0.237 | 0.171 | 3.390 | 0.059 | 0.790 | 0.310 1.098 |
| Statins | −0.470 | 0.245 | 3.666 | 0.056 | 0.625 | 0.386 1.011 |
| NLR group | | | | | | |
| 1st tertile vs 3rd tertile | −0.640 | 0.174 | 13.526 | <0.001 | 0.527 | 0.375 0.742 |
| 2nd tertile vs 3rd tertile | −0.747 | 0.334 | 4.993 | 0.025 | 0.474 | 0.246 0.912 |

CI, confidence interval; HR, hazard ratio
to the severity of ischemia, although the neutrophil half-life is short [30]. Subsequently, a state of stress and inflammation, as seen in ACS patients, could result in increased levels of inflammatory markers in the blood circulation, accompanied by increased blood cortisol levels. An increase in cortisol has been shown to induce apoptosis, which in turn leads to lymphopenia and even inversion of the CD4+/CD8+ T lymphocyte ratio [31]. Therefore, an elevated NLR represents an exaggerated inflammatory response that may reflect coronary atherosclerosis progression [16–18], and to some extent, may predict the acute prognosis in these patients [15, 32–34]. On the other hand, medications such as statins are well known to have anti-inflammatory actions [35], and the common use of statins during the post-acute phase of ACS may also reduce the prognostic efficacy of the NLR for long-term outcomes in ACS patients. Xinjiang is characterized by the integration of diverse ethnic cultures, but people in Xinjiang generally do not have a deep understanding of cardiovascular disease. Accordingly, a low treatment rate and poor adherence are common problems of hypertension management in this area. Therefore, it appears that although approximately 50% of the patients had hypertension, only 3–15% of patients were receiving treatment with antihypertensive agents. We are working hard to actively promote popularization of the science of cardiovascular diseases in different forms and languages in this region.

**Study limitations**

First, as a retrospective observational single-center study with a small sample size, our study may be confounded by recall bias. Our results should be validated in prospective studies. Second, our study included consecutive patients with an initial diagnosis of ACS, and the diagnosis of the patients varied. Third, the NLR was only measured once at admission, and whether changes in the NLR during hospitalization or the NLR at discharge have an impact on the prognosis of these patients remains unknown. Finally, as the study was conducted over 8 years, PCI techniques and medical therapies likely evolved and changed with increasing evidence, which is likely to impact the outcome.
| Variables                          | Univariate |                                  | Multivariate |                                  |
|-----------------------------------|------------|-----------------------------------|--------------|-----------------------------------|
|                                   | HR         | 95% CI                            | P            | HR                               | 95% CI | P            |
| Sex (Male/Female)                 | 1.275      | 0.694–2.342                       | 0.433        | 1.049                            | 1.024–1.075     | <0.001        |
| Age                               | 1.051      | 1.029–1.073                       | <0.001       | 1.049                            | 1.024–1.075     | <0.001        |
| Hypertension                      | 0.918      | 0.562–1.499                       | 0.731        |                                  |          |              |
| Diabetes mellitus                 | 1.175      | 0.676–2.044                       | 0.568        |                                  |          |              |
| Smoking                           |            |                                   |              |                                  |          |              |
| Former smoker vs never smoker     | 1.177      | 0.161–8.616                       | 0.872        |                                  |          |              |
| Current smoker vs never smoker    | 0.842      | 0.516–1.374                       | 0.490        |                                  |          |              |
| Alcohol drinking                  |            |                                   |              |                                  |          |              |
| Former smoker vs never drinking   | 1.061      | 0.526–2.139                       | 0.868        |                                  |          |              |
| Current smoker vs never drinking  | 1.390      | 0.797–2.423                       | 0.246        |                                  |          |              |
| Family history of CAD             | 0.876      | 0.529–1.450                       | 0.605        |                                  |          |              |
| SBP (mmHg)                        | 1.029      | 1.016–1.042                       | <0.001       | 1.029                            | 1.009–1.049     | 0.005        |
| DBP (mmHg)                        | 1.040      | 1.019–1.059                       | <0.001       | 1.007                            | 0.978–1.038     | 0.626        |
| Heart rate                        | 1.008      | 0.992–1.024                       | 0.319        |                                  |          |              |
| BMI                               | 0.965      | 0.928–1.003                       | 0.072        |                                  |          |              |
| HDL-C (mmol/l)                    | 2.371      | 0.909–6.183                       | 0.078        |                                  |          |              |
| LDL-C (mmol/l)                    | 1.238      | 0.913–1.680                       | 0.169        |                                  |          |              |
| TC (mmol/l)                       | 1.132      | 0.905–1.416                       | 0.278        |                                  |          |              |
| TG (mmol/l)                       | 0.956      | 0.813–1.123                       | 0.583        |                                  |          |              |
| ApoA1 (g/L)                       | 1.170      | 0.662–2.067                       | 0.589        |                                  |          |              |
| ApoB (g/L)                        | 1.118      | 0.574–2.181                       | 0.742        |                                  |          |              |
| Lp(a) (g/L)                       | 0.999      | 0.997–1.001                       | 0.150        |                                  |          |              |
| Creatinine (mmol/L)               | 1.001      | 0.994–1.006                       | 0.995        |                                  |          |              |
| BUN (mmol/l)                      | 0.978      | 0.881–1.086                       | 0.675        |                                  |          |              |
| Uric acid (μmol/L)                | 1.001      | 0.997–1.003                       | 0.980        |                                  |          |              |
| NLR group                         |            |                                   |              |                                  |          |              |
| 2nd tertile vs 1st tertile        | 1.155      | 0.643–2.075                       | 0.629        |                                  |          |              |
| 3rd tertile vs 1st tertile        | 0.940      | 0.509–1.734                       | 0.843        |                                  |          |              |
| Monocyte count                    | 0.923      | 0.427–1.996                       | 0.839        |                                  |          |              |
| PLR                               | 1.001      | 0.999–1.002                       | 0.080        |                                  |          |              |
| RBC                               | 1.534      | 1.015–2.318                       | 0.042        | 1.452                            | 0.991–1.038     | 0.056        |
| HGB                               | 1.002      | 0.993–1.012                       | 0.660        |                                  |          |              |
| PLT                               | 1.001      | 0.999–1.002                       | 0.550        |                                  |          |              |
| MPV                              | 1.001      | 0.847–1.180                       | 0.997        |                                  |          |              |
| PDW                               | 0.946      | 0.882–1.016                       | 0.126        |                                  |          |              |
| PCT                               | 1.654      | 0.177–15.465                      | 0.659        |                                  |          |              |
| WBC                               | 0.979      | 0.913–1.049                       | 0.540        |                                  |          |              |
| Clinical diagnosis                |            |                                   |              |                                  |          |              |
| NSTEMI                            | 1.062      | 0.386–2.9222                      | 0.907        |                                  |          |              |
| STEMI                             | 0.862      | 0.3692.012                       | 0.731        |                                  |          |              |
| UPLMT                             | 2.446      | 1.301–4.599                       | 0.006        |                                  |          |              |
| LAD                               | 2.155      | 0.783–5.929                       | 0.137        |                                  |          |              |
| LCX                               | 1.430      | 0.836–2.445                       | 0.191        |                                  |          |              |
| RCA                               | 2.186      | 1.080–4.423                       | 0.030        |                                  |          |              |
| Aspirin                           | 1.085      | 0.495–2.377                       | 0.838        |                                  |          |              |
| Statins                           | 1.230      | 0.562–2.695                       | 0.605        |                                  |          |              |
| β-Blockers                        | 0.756      | 0.237–2.410                       | 0.637        |                                  |          |              |
Table 5 (continued)

| Variables                  | Univariate          | Multivariate         |
|----------------------------|---------------------|----------------------|
|                            | HR  | 95% CI       | P      | HR  | 95% CI       | P      |
|-----------------------------|-----|--------------|-------|-----|--------------|-------|
| ACEI/ARB                    | 0.813 | 0.199–3.323  | 0.773 |     |              |       |
| CCB                        | 0.866 | 0.413–1.815  | 0.703 |     |              |       |
| PCI                         | 0.614 | 0.280–1.345  | 0.223 |     |              |       |
| Gensini group               |     |              |       |     |              |       |
| 2nd tertile vs 1st tertile  | 2.631 | 1.159–5.973  | 0.021 | 1.989 | 0.861–4.596  | 0.107 |
| 3rd tertile vs 1st tertile  | 5.076 | 2.363–10.900 | <0.001| 3.216 | 1.458–7.093  | 0.004 |

Conclusions
The NLR may be associated with coronary lesion severity at baseline but is not associated with adverse outcomes in patients with new-onset ACS.

Competing interests
The authors declare that they have no conflict of interests.

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