Original Article

Usefulness of the Neutrophil-to-Lymphocyte Ratio in Predicting the Severity of Coronary Artery Disease: A Gensini Score Assessment

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***Aim*: The usefulness of the white blood cell (WBC) count and neutrophil-to-lymphocyte ratio (NLR) in predicting the severity of stable coronary artery disease (CAD) has not been sufficiently evaluated, particularly based on strict coronary assessments. The aim of the present study was to investigate the WBC count and NLR in predicting the severity of angiographically proven CAD.**

***Methods*: A total of 2,976 CAD patients and 571 non-CAD patients were consecutively enrolled, and the CAD patients were classified into the three groups according to the tertile of the Gensini score (GS, low GS < 18, n = 989; intermediate GS 18-41, n = 995 and high GS > 41, n = 992). The efficacy of the WBC count and NLR in predicting the risk and severity of CAD as well as the correlations between these markers and the GS were analyzed. A receiver operating characteristic (ROC) curve analysis was also performed.**

***Results*: The NLR was found to be an independent predictor of both the presence of CAD (OR = 1.18, 95%CI: 1.09-1.27, p = 0.009) and a high GS (OR = 1.10, 95%CI: 1.01-1.16, p = 0.032). In addition, there were mild positive correlations between the GS and the NLR, WBC and proportions of neutrophils and monocytes. In the ROC curves analysis, the NLR was found to have the largest area under the curve (AUC = 0.63, 95%CI: 0.59-0.67, p = 0.000), with an optimal cut-off value of 2.04 (sensitivity: 62.1%, specificity: 54.8%) for predicting a high GS.**

***Conclusions*: The NLR is a valuable independent predictor of the severity of CAD assessed according to the GS. In particular, an NLR of > 2.04 indicates a higher risk of CAD and greater severity of CAD lesions.**

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Key words: Neutrophil-to-lymphocyte ratio, White blood cell count, Coronary artery disease, Gensini score

Introduction

Coronary artery disease (CAD) is recognized to be a worldwide health threat; therefore, understanding its predictors would greatly aid in disease control and treatment. Importantly, the relationships between various inflammatory markers and CAD have been definitively established[1-3]. Among these markers, the levels of white blood cell (WBC) subtypes, confirmed inflammatory markers that play a crucial role in the pathogenesis of atherogenesis and atherothrombosis[4], have received significant attention. It has been reported that the WBC count and levels of WBC subtypes not only play an important role in the develop-

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ment of CAD, but can also be used to predict the clinical outcomes of patients with CAD[5-7]. Interestingly, the ratio of the absolute number of neutrophils to that of lymphocytes (neutrophil-to-lymphocyte ratio: NLR), a particular WBC parameter, has newly emerged as an inflammatory marker for identifying individuals at risk of CAD[8-13]. However, only recently have studies of the relationship between the NLR and the severity of CAD begun to be conducted.

In addition, previous studies on the relationships between stable CAD and the NLR, WBC count and levels of WBC subtypes are insufficient and limited by a small sample size. Furthermore, the severity of CAD was assessed according to the number of diseased vessels in these studies[14, 15], and receiver operating characteristic (ROC) curves analyses of the NLR and WBC count for predicting CAD severity are few. Moreover, no data are currently available regarding these associations in large Chinese populations. Therefore, our study investigated the value of the NLR, WBC count and levels of WBC subtypes in predicting the risk and severity of CAD in a large Chinese cohort from a single center.

Methods

Study Population

The study protocol complied with the Declaration of Helsinki and was approved by the hospital ethics review board (Fu Wai Hospital & National Center for Cardiovascular Diseases, Beijing, China). Written informed consent was obtained from all participants.

A total of 3,974 consecutive patients undergoing coronary angiography at the Division of Dyslipidemia at Fu Wai Hospital between April 2011 and December 2013 were included in the analysis. Among these patients, 312 had undergone percutaneous coronary intervention (Pre-PCI), 15 had undergone coronary artery bypass grafting (pre-CABG), 44 had a history of myocardial infarction (MI) without treatment with revascularization, 42 had an abnormal baseline cardiac troponin I (cTnI) level, three had clinical evidence of cancer and 11 had chronic inflammatory or active infectious diseases; all of these individuals were excluded. Finally, a total of 3,547 subjects were enrolled in this study, including 2,976 patients with angiographically proven CAD (CAD group) and 571 patients with normal coronary angiography findings (Control group). The subjects' demographic data (age, gender and BMI) and risk factors for CAD, such as smoking habits, diabetes mellitus (DM), hypertension, dyslipidemia and a family history of CAD, were also collected.

Hypertension was diagnosed based on repeated blood pressure measurements of ≥ 140/90 mmHg (at least two times in different environments) or the use of antihypertensive drugs. DM was diagnosed based on a fasting serum glucose level of ≥ 6.99 mmol/L on multiple occasions and/or the use of insulin or oral hypoglycemic agents. Dyslipidemia was diagnosed according to a fasting total cholesterol level of (TC) ≥ 200 mg/dL or triglyceride (TG) level of ≥ 150 mg/dL.

Laboratory Tests

All baseline laboratory data were acquired from venous blood samples obtained after a 12-hour overnight fast prior to coronary angiography. The levels of WBC, neutrophils, lymphocytes and monocytes were determined using an automated blood cell counter, the Coulter LH780 Hematology Analyzer (Beckman Coulter Ireland Inc. Mervue, Galway, Ireland), and the levels of high-sensitivity C-reactive protein (hs-CRP) were assessed using immunoturbidimetry (Beckmann Assay 360, Bera, California, USA), as previously reported[16, 17]. The NLR was calculated as the ratio of neutrophils to lymphocytes, the levels of which were obtained from the same blood samples. The normal range of hs-CRP in our hospital laboratory is 0-3 mg/L.

Angiographic Examinations

Selective coronary angiography was performed in all enrolled subjects using the standard Judkin's technique, and the results were analyzed by at least two interventional physicians who performed a quantitative coronary angiography (QCA) analysis. CAD was defined as the presence of obstructive stenosis of more than 50% of the vessel lumen diameter in any of the main coronary arteries, including the left main coronary artery (LM), left anterior descending artery (LAD), left circumflex coronary artery (LCX) and right coronary artery (RCA), or main branches of the vascular system.

The severity of CAD was assessed based on the Gensini score (GS), which was determined according to the severity of stenosis as follows: 1 point for < 25% stenosis, 2 points for 26% to 50% stenosis, 4 points for 51% to 75% stenosis, 8 points for 76% to 90% stenosis and 32 points for total occlusion. The score was then multiplied by a factor representing the importance of the lesion's position in the coronary artery system. For example, 5 for the left main coronary artery, 2.5 for the proximal left anterior descending or proximal left circumflex artery, 1.5 for the mid-region, and 1 for the distal left anterior descending or mid-distal region of the left circumflex artery[18, 19].

Table 1. Baseline characteristics of the study population

Variables	CAD group (n=2976)	Control group (n=571)	p-value
Clinical characteristics			
Age, (years)	58.35 ± 9.90	54.90 ± 1.22	0.000
Male, n (%)	2170 (72.9)	234 (56.7)	0.000
Smoking, n (%)	1621 (54.5)	174 (42.1)	0.000
Family history of CAD, n (%)	489 (16.4)	51 (12.3)	0.040
BMI, (kg/m^2)	25.78 ± 3.18	25.27 ± 3.40	0.003
DM, n (%)	819 (27.5)	65 (15.7)	0.000
Hypertension, n (%)	1869 (62.8)	207 (50.1)	0.000
Dyslipidemia, n (%)	2261 (76.0)	251 (60.8)	0.000
Laboratory data			
WBC, (10^9/L)	6.33 ± 1.65	6.20 ± 1.68	0.095
Neutrophil, (10^9/L)	3.82 ± 1.28	3.64 ± 1.30	0.002
Lymphocyte, (10^9/L)	1.87 ± 0.60	1.94 ± 0.62	0.019
Monocyte, (10^9/L)	0.44 ± 0.16	0.44 ± 0.16	0.982
NLR	1.99 (1.55-2.59)	1.83 (1.39-2.44)	0.001
hs-CRP, (mg/L)	1.54 (0.81-3.34)	1.52 (0.78-3.01)	0.046

CAD: coronary artery disease; BMI: body mass index; DM: diabetes mellitus; WBC: white blood cell; NLR: neutrophil-to-lymphocyte ratio; hs-CRP: high-sensitivity C-reactive protein. The NLR and hs-CRP are presented as the median with 25th and 75th percentiles.

The enrolled patients were classified into the three groups based on the tertile of the GS (low GS $<$18 points, n=989; intermediate GS 18-41 points, n=995; high GS $>$41 points, n=992).

Statistical Analysis

All analyses were performed using the SPSS version 19.0 software package (Chicago, Illinois, USA). The Kolmogorov-Smirnov test was used to determine the distribution pattern. Continuous variables are presented as the mean ± SD or median with the 25th and 75th percentiles, as appropriate, and were compared using the t-test [with the results presented as the mean and standard deviation (SD)] or Mann Whitney test [median with the interquartile range (IQR)]. Categorical variables are summarized as frequencies with percentages and were compared using the chi-square test. Variables with a p-value of $<$0.05 in the univariate logistic regression analyses were included in the multivariate logistic regression analysis. The predictive value of the differential counts of WBCs and their subtypes for a high GS was evaluated according to binary logistic regression models using the forward stepwise selection process. The correlations between variables were examined using Spearman and Pearson correlation coefficients, when appropriate. Receiver operating characteristics (ROC) curves were constructed, and the most discriminating cut-off values were determined to assess the predictive value of the NLR, WBC count and levels of WBC subtypes for a high GS. A p-value of less than 0.05 was considered to be statistically significant.

Results

Baseline Characteristics

The baseline clinical characteristics and laboratory data of the CAD and control groups are summarized in **Table 1**. As shown in **Table 1**, age and BMI were significantly higher in the CAD group than in the control group. In addition, the percentage of men, smokers and a history of CAD, DM, hypertension or dyslipidemia were significantly higher in the CAD group than in the control group.

Moreover, the NLR, hs-CRP level and neutrophil and lymphocyte counts were significantly different between the patients with CAD and those in the control group (p=0.002, 0.001, 0.046 and 0.019, respectively). In addition, the NLR values were significantly higher in the CAD patients than in the control subjects [1.99 (1.55-2.59) vs. 1.83 (1.39-2.44)], as were the plasma CRP levels [1.54 (0.81-3.34) vs. 1.52 (0.78-3.01), p=0.046].

The cohort in the current study consisted of 2,976 CAD patients, with a mean GS of 37.71 ± 33.45 [28 (12-52), range: 2 to 232 points]. The baseline demo-

Table 2. Baseline characteristics based on the tertile of the Gensini score

Variables	Low GS (< 18, *n* = 989)	Intermediate GS (18-41, *n* = 995)	High GS (> 41, *n* = 992)	*p*-value
Clinical characteristics				
Age, (years)	57.82 ± 9.70	58.10 ± 9.56	59.16 ± 10.36	0.006
Male, n (%)	689 (69.7)	729 (73.3)	785 (79.1)	0.000
Smoking, n (%)	529 (53.5)	543 (54.6)	576 (58.1)	0.072
Family history of CAD, n (%)	157 (15.9)	170 (17.1)	197 (19.9)	0.015
BMI, (kg/m^2)	25.64 ± 3.15	25.77 ± 3.23	25.94 ± 3.16	0.118
DM, n (%)	215 (21.7)	262 (26.3)	351 (35.4)	0.000
Hypertension, n (%)	612 (61.9)	630 (63.3)	658 (66.3)	0.048
Dyslipidemia, n (%)	765 (77.4)	762 (76.6)	773 (77.9)	0.791
Prior treatment				
Aspirin	901 (91.1)	873 (87.8)	908 (91.5)	0.137
Statin	644 (65.1)	716 (72.0)	666 (67.1)	0.016
Beta-blocker	528 (53.3)	542 (54.5)	535 (53.9)	0.951
ACE-I/ARB	269 (27.2)	256 (25.7)	248 (25.0)	0.765

GS: Gensini score; BMI: body mass index; DM: diabetes mellitus; ACE-I: angiotensin-converting enzyme inhibitor; ARB: angiotensin-receptor blocker; *p*-value: *p*-value for trend

graphic, clinical and laboratory data for the enrolled subjects classified according to the tertile of the GS (low-GS group: 33.2%; intermediate-GS group: 33.4%; high-GS group: 33.3%) are summarized in **Table 2** and **Fig. 1**. There were significant differences in age, gender and the frequencies of statin treatment, DM, hypertension and a family history of CAD among the groups (**Table 2**). More importantly, the NLR, WBC count and neutrophil and monocyte levels were significantly different among the groups classified according to the GS, as demonstrated in a trend analysis and on a comparison test (**Fig. 1**).

Univariate and Multivariate Analyses

According to the multivariate logistic regression analysis (**Table 3**), only the NLR and hs-CRP level were found to be independent predictive markers for CAD (OR = 1.18, 95% CI: 1.09-1.27, $p = 0.009$, and OR = 1.05, 95% CI: 1.02-1.08, $p = 0.000$, respectively). More importantly, as shown in **Table 4**, the results of the multivariate logistic regression analysis of variables predicting a high GS suggested that only the NLR and hs-CRP level were independent predictors of the severity of CAD, after adjusting for gender, age, BMI, current smoking, hypertension, dyslipidemia and a family history of CAD (OR = 1.10, 95% CI: 1.01-1.16, $p = 0.032$, and OR = 1.06, 95% CI: 1.03-1.08, $p = 0.000$, respectively). Moreover, age, gender and DM were identified to be independent predictors of a high GS (**Table 4**).

Correlations between the WBC Count and Subtype Levels and the GS

We used Spearman and Pearson correlation analyses to examine the correlations between the NLR, WBC count and levels of WBC subtypes and the GS in the patients with CAD. As shown in **Fig. 2**, there were mild positive but significant correlations between the WBC count, neutrophil count, monocyte count and NLR and the GS, whereas no correlations were observed between the lymphocyte count and the GS in the present study.

ROC Curve Analysis

Fig. 3 shows the findings of the ROC curves analysis of the NLR, WBC count and levels of the WBC subtypes for predicting a high GS. The NLR was found to have the highest AUC at 0.63 (95% CI: 0.59-0.67, $p = 0.000$) among all of the markers, even the hs-CRP level. As shown in **Fig. 3**, the AUC values of the other markers were all less than 0.60. In addition, an NLR of 2.04 was identified to be an effective cut-off point for detecting a high GS (> 41 points), with a sensitivity of 62.1% and a specificity of 54.8%. When we divided all subjects enrolled in this study into the two groups based on the NLR cut-off value of 2.04 determined in the ROC analysis (**Table 5** and **Fig. 4**), the serum hs-CRP levels and GS values were significantly increased in the high-NLR group compared to that observed in the low-NLR group [1.35 (0.71-2.51) vs. 1.88 (0.91-4.06), $p = 0.000$ and 26 (12-48) vs. 30 (14-56), $p = 0.000$, respectively]. More-

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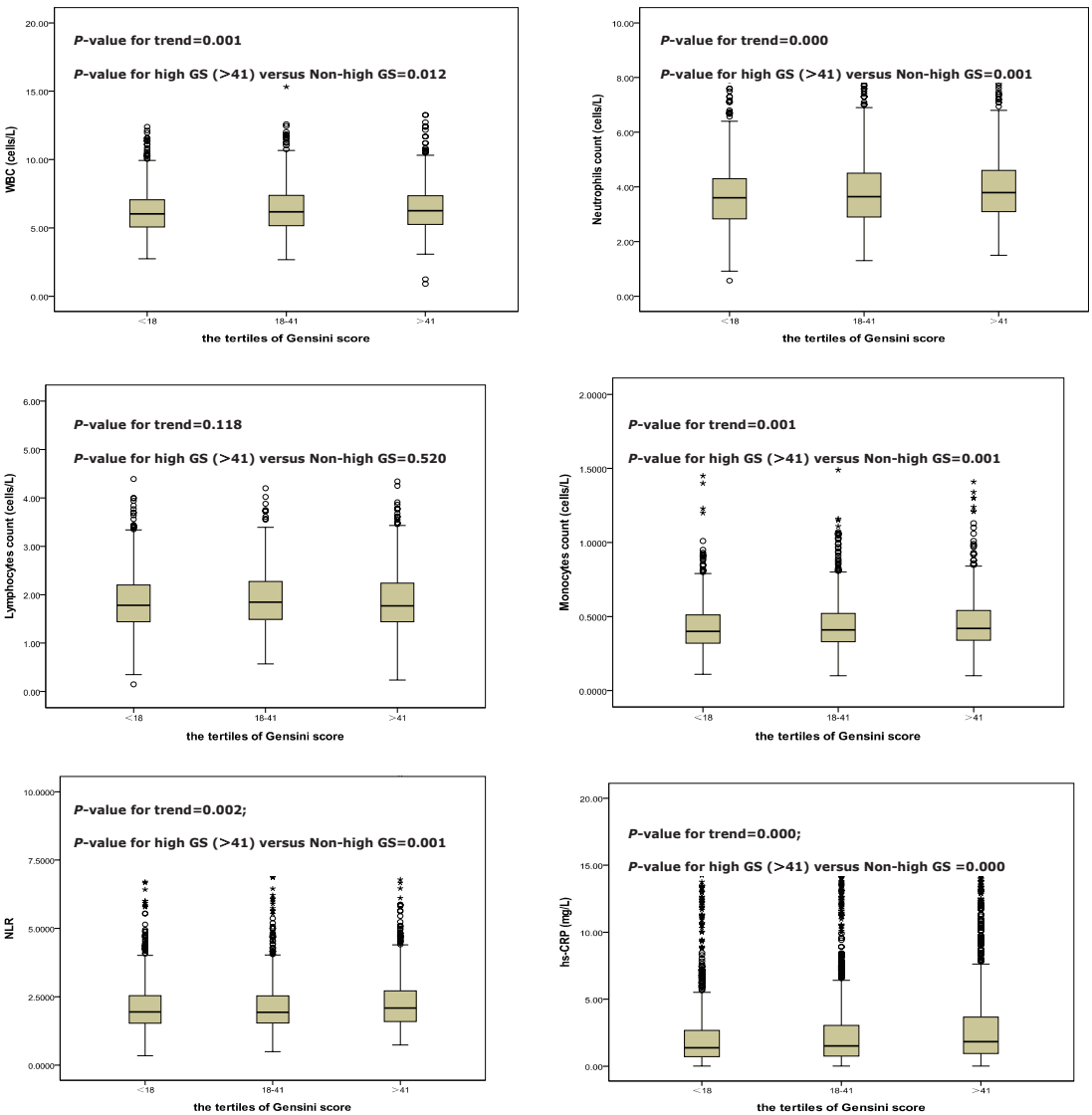

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Variables	Low GS (<18, *n*=989)	Intermediate GS (18-41, *n*=995)	High GS (>41, *n*=992)	*p*-value[a]	*p*-value[b]
WBC (10^9/L)	6.18±1.55	6.38±1.68	6.44±1.71	0.001	0.012
Neutrophil (10^9/L)	3.69±1.21	3.84±1.30	3.94±1.33	0.000	0.001
Lymphocyte (10^9/L)	1.85±0.58	1.91±0.59	1.86±0.64	0.118	0.520
Monocyte (10^9/L)	0.43±0.15	0.44±0.16	0.46±0.17	0.001	0.001
NLR	1.89 (1.48-2.50)	1.94 (1.54-2.66)	2.10 (1.60-2.78)	0.002	0.001
hs-CRP (mg/L)	1.37 (0.71-2.67)	1.52 (0.75-3.07)	1.83 (0.95-3.67)	0.000	0.000

Fig. 1. Laboratory parameters (NLR, hs-CRP level and WBC, neutrophil, lymphocyte and monocyte counts) according to the Gensini score (A, B).

NLR=neutrophil-to-lymphocyte ratio; WBC=white blood cell; hs-CRP=high-sensitivity C-reactive protein. The NLR and hs-CRP are presented as the median with 25th and 75th percentiles. *p*-value[a]=*p*-value for trend; *p*-value[b]=*p*-value for a high GS (>41 points) versus a normal or low GS.

Table 3. Univariate and multivariate logistic regression analyses of traditional risk factors and laboratory parameters to identify independent predictors of CAD

Variables	Univariate		*p*-value	Multivariate		*p*-value
	OR	95% CI		OR	95% CI	
Age, (years)	1.03	1.00-1.05	0.041	0.98	0.97-0.99	0.000
Male, n (%)	1.91	1.59-2.30	0.000	1.97	1.54-2.52	0.000
Family history of CAD, n (%)	1.42	1.10-1.82	0.006	1.48	1.14-1.92	0.004
BMI, (kg/m^2)	0.94	0.91-0.97	0.000	0.95	0.92-0.98	0.001
DM, n (%)	1.47	1.19-1.83	0.000	1.28	1.02-1.61	0.033
Dyslipidemia, n (%)	1.98	1.63-2.39	0.000	1.80	1.47-2.21	0.000
NLR	1.29	1.10-1.42	0.000	1.18	1.09-1.27	0.009
hs-CRP, (mg/L)	1.02	1.00-1.05	0.048	1.05	1.02-1.08	0.000

CAD: coronary artery disease; BMI: body mass index; DM: diabetes mellitus; NLR: neutrophil-to-lymphocyte ratio; hs-CRP: high-sensitivity C-reactive protein; OR: odds ratio; CI: confidence interval

Table 4. Univariate and multivariate logistic regression analyses to identify independent predictors of a high Gensini score (>41 points)

Variables	Univariate		*p*-value	Multivariate		*p*-value
	OR	95% CI		OR	95% CI	
Age, (years)	1.01	1.00-1.02	0.009	1.02	1.01-1.02	0.001
Male, n (%)	1.45	1.21-1.73	0.000	1.56	1.24-1.95	0.000
DM, n (%)	1.72	1.46-2.02	0.000	1.69	1.42-2.01	0.000
NLR	1.11	1.04-1.18	0.001	1.10	1.01-1.16	0.032
hs-CRP, (mg/L)	1.06	1.04-1.08	0.000	1.06	1.03-1.08	0.000

DM: diabetes mellitus; NLR: neutrophil-to-lymphocyte ratio; hs-CRP: high-sensitivity C-reactive protein; OR: odds ratio; CI: confidence interval

over, the frequency of CAD was significantly increased in the high-NLR group (81.4% vs. 86.3%, $p=0.000$), as were age and the proportions of smokers and men.

Discussion

The main findings of our study are as follows: (1) the baseline NLR was found to be an independent predictor of both the presence of CAD and a high GS (>41 points), while traditional risk factors, including age, gender and DM, were identified to be independent predictors of a high GS; (2) the NLR had the highest AUC in the ROC curves analysis among all markers, even the hs-CRP level, and an NLR of 2.04 was identified as the optimal cut-off point for predicting a high GS (>41 points); (3) the hs-CRP level, GS and frequency of CAD were significantly higher among the patients with an NLR of >2.04 than in those with an NLR of ≤2.04. These findings have important clinical implications for the future application of the NLR in predicting the incidence of CAD and the severity of coronary stenosis.

Multiple studies have demonstrated strong and consistent relationships between various inflammatory markers and cardiovascular disease, and the inflammatory process plays a key role in both the initiation and progression of atherosclerosis[20-24]. It has also been demonstrated that the WBC count is an independent predictor of cardiovascular events and all-cause mortality and may be used to identify high-risk individuals without traditional cardiovascular risk factors[14, 15, 25-28]. Regarding stable CAD, parameters of WBCs and their subtypes, including the NLR, have been reported to be associated with the severity of CAD, as determined based on the number of diseased vessel in the early stage. For example, Arbel *et al*. evaluated 3,005 consecutive patients undergoing coronary angiography for various indications and found that the NLR was related to the severity of CAD[14]. Unfortunately, in that study, the CAD severity was assessed according to the number of diseased vessels. In the present study, we found that the counts of WBCs and their subtypes

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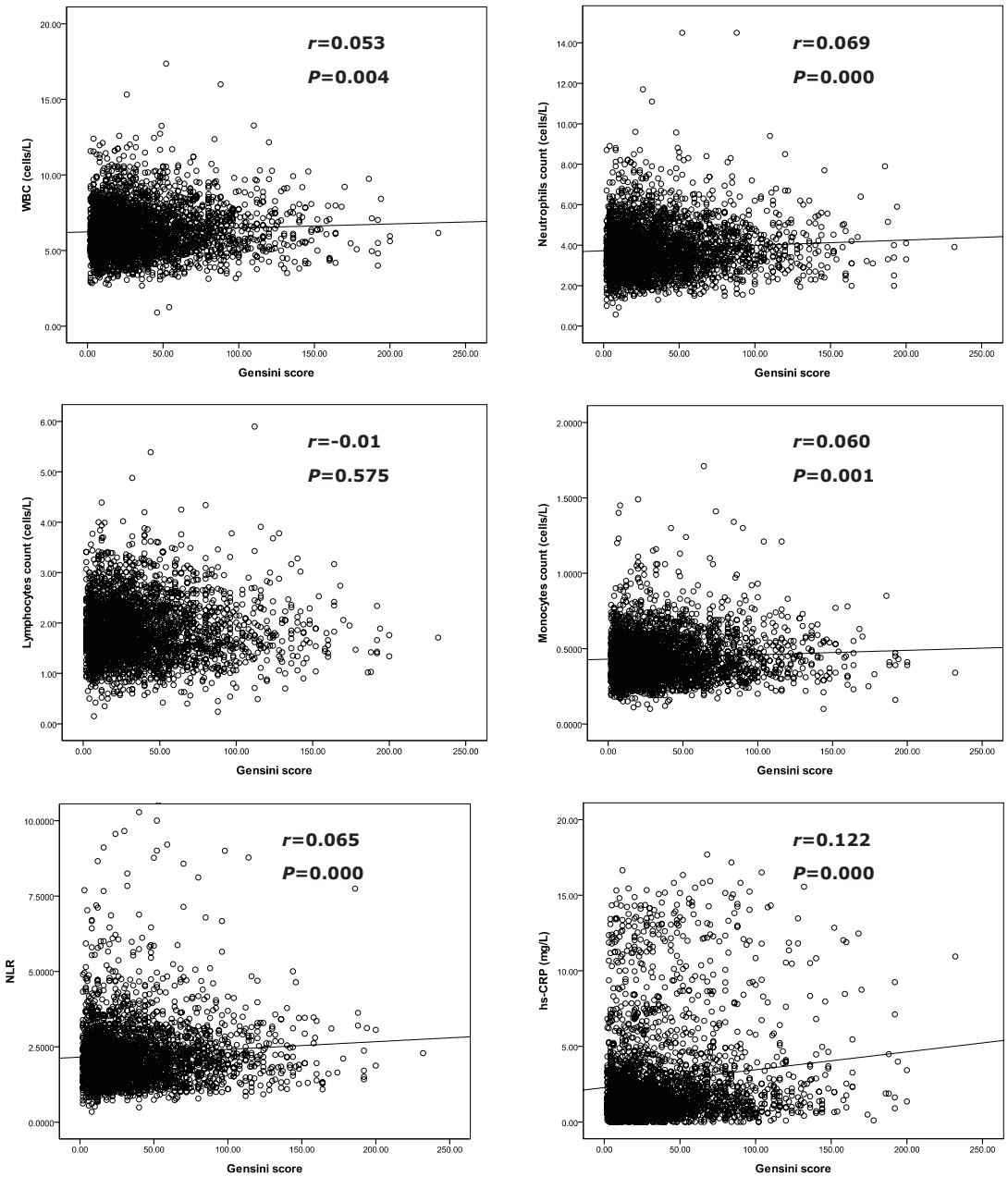

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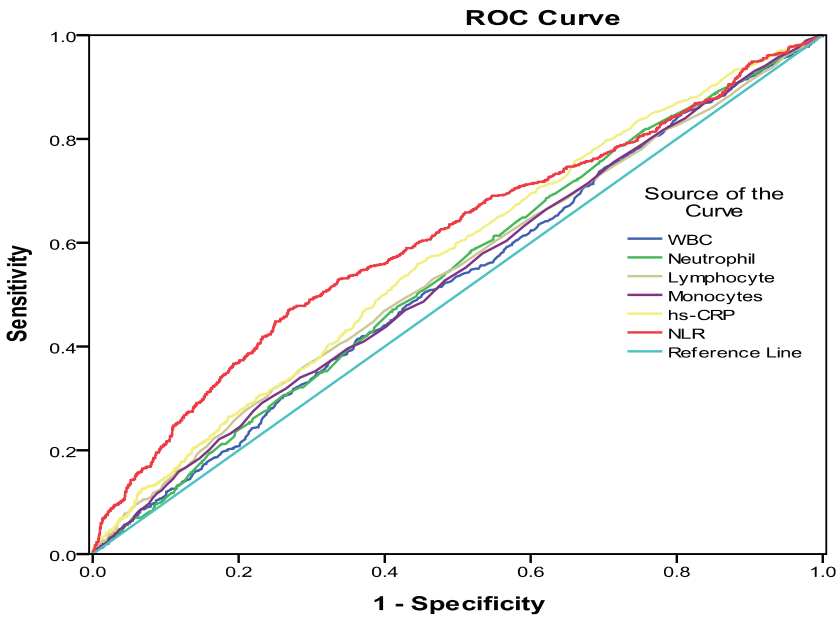
Variables	WBC (10^9/L)	Neutrophil (10^9/L)	Lymphocyte (10^9/L)	Monocyte (10^9/L)	NLR	hs-CRP (mg/L)
r	0.053	0.069	−0.01	0.060	0.065	0.122
p-value	0.004	0.000	0.575	0.001	0.000	0.000

Fig. 2. Correlations between the NLR, hs-CRP level and WBC, neutrophil, lymphocyte and monocyte counts and the Gensini score in the CAD patients (A, B).

N = 2,976. NLR = neutrophil-to-lymphocyte ratio; WBC = white blood cell; hs-CRP = high-sensitivity C-reactive protein; CAD = coronary artery disease



Variables	AUC	95% CI	*p*-value
WBC	0.53	0.50-0.55	0.021
Neutrophil	0.54	0.52-0.56	0.000
Lymphocyte	0.52	0.50-0.54	0.001
Monocyte	0.53	0.50-0.55	0.002
NLR	0.63	0.59-0.67	0.000
hs-CRP	0.57	0.55-0.58	0.000

Fig. 3. Receiver operating characteristics (ROC) curve analysis of the predictive power of the NLR, WBC count and WBC subtype levels for a high GS.

WBC = white blood cell; NLR = neutrophil-to-lymphocyte ratio; hs-CRP = high-sensitivity C-reactive protein

was useful, inexpensive and widely available markers of inflammation for predicting the risk and severity of CAD, consistent with the results of our previous study of diabetic patients with stable CAD[17].

In fact, the NLR is a widely available marker of inflammation. For example, a high NLR has been reported to exhibit a correlation with the severity and both short- and long-term mortality of acute coronary syndrome (ACS), as well as the progression of heart failure, even in patients undergoing successful bare-metal stent implantation[11-13, 22, 28, 29]. It has also been reported that an increased NLR ratio is associated with the incidence of ventricular arrhythmia during PCI[30, 31] and a worse outcome after CABG[11]. Moreover, an elevated NLR, both independently and in combination with other disease markers and risk factors, is a significant predictor of the development, progression and mortality of stable CAD[4, 11, 23, 32, 33]. Horne *et al.* were among the first to observe the significance of assessing the NLR in patients with stable CAD. In their prospective observational study, a total of 3,227 patients with angiographically assessed CAD without a history of acute MI were followed for more than six years[4]. The authors subsequently found that total WBC count was an independent predictor of death/MI in the patients with or at high risk for CAD, although the most effective risk prediction was observed for the NLR, with the hazard ratio increasing by 2.2-fold for quartile (Q) 4 versus Q1. Thereafter, Tsai J.C. and colleagues studied more than 800 high-risk Korean adult patients (with diabetes mellitus and metabolic syndrome) and determined that NLR was associated with both metabolic syndrome and the risk of ischemic cardiovascular disease[33]. Another prospective study analyzed the predictive ability for cardiac events of the differential WBC count versus

Table 5. Characteristics of the groups according to the NLR

Variables	NLR ≤ 2.04 (n = 1909)	NLR > 2.04 (n = 1638)	p-value
Age, (years)	57.56 ± 10.15	58.77 ± 10.28	0.000
Male, n (%)	1264 (66.2)	1275 (77.84)	0.000
Smoking, n (%)	966 (50.6)	938 (57.3)	0.000
Family history of CAD, n (%)	307 (16.1)	247 (15.1)	0.255
BMI, (kg/m^2)	25.74 ± 3.22	25.60 ± 3.21	0.221
DM, n(%)	499 (26.1)	447 (27.3)	0.492
Hypertension, n (%)	1177 (61.7)	1037 (63.3)	0.364
Dyslipidemia, n (%)	1440 (75.4)	1220 (74.5)	0.480
CAD, n (%)	1554 (81.4)	1414 (86.3)	0.000
Gensini score	26 (12-48)	30 (14-56)	0.000
hs-CRP, (mg/L)	1.35 (0.71-2.51)	1.88 (0.91-4.06)	0.000

BMI: body mass index; DM: diabetes mellitus; CAD: coronary artery disease; hs-CRP: high-sensitivity C-reactive protein; NLR: neutrophil-to-lymphocyte ratio. The NLR and hs-CRP are presented as the median with the 25th and 75th percentiles.

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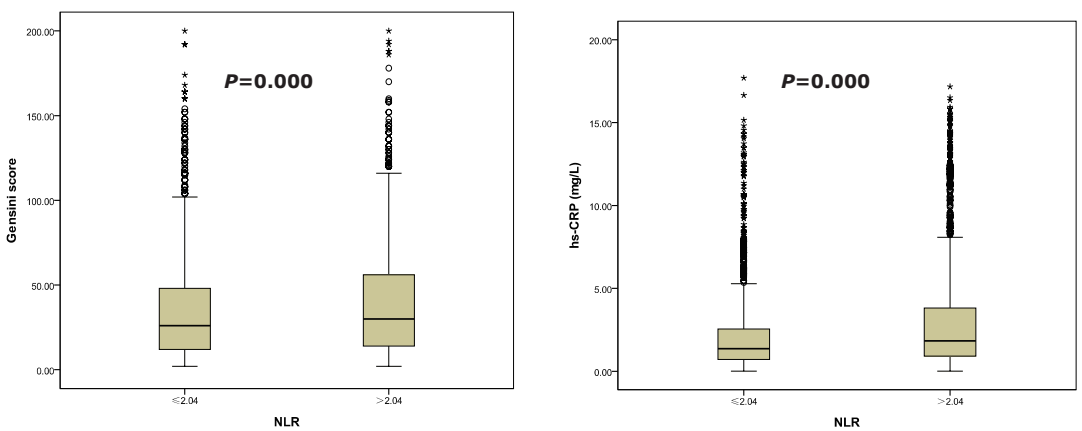

B

Variables	NLR ≤ 2.04 (n = 1909)	NLR > 2.04 (n = 1638)	p-value
Gensini score	26 (12-48)	30 (14-56)	0.000
hs-CRP, (mg/L)	1.35 (0.71-2.51)	1.88 (0.91-4.06)	0.000
CAD, n (%)	1554 (81.4)	1414 (86.3)	0.000

Fig. 4. Gensini scores, hs-CRP levels and frequency of CAD in each group according to the NLR (A, B).

The GS and hs-CRP are presented as the median with 25th and 75th percentiles. p = 0.000 for all. hs-CRP = high-sensitivity C-reactive protein; CAD = coronary artery disease

established risk factors in 422 CAD patients[23]. In that study, a high NLR (5.19 ± 3.81), together with the CRP level, was found to be associated with significantly increased rates of cardiac death and non-fatal MI in patients with stable CAD during a three-year follow-up period. However, in all of these studies, the severity of CAD was assessed based on the number of diseased vessels. In addition, these studies focused pri-

marily on outcomes, and no data regarding the relationship between the NLR and the severity of CAD were provided.

The SYNTAX score and Gensini score are well-known angiographic tools for grading the complexity and/or severity of CAD. However, investigators have only begun to study the relationships between the NLR and the Gensini or SYNTAX score to assess the complexity or severity of CAD within the last several years[15, 34-37]. For example, Tanındı A. *et al.*[34] investigated the relationships between the NLR and the severity and complexity of CAD (as assessed according to the Gensini and SYNTAX scores) as well as myocardial perfusion (based on the myocardial blush grade) in 151 stable angina pectoris (SAP) or ACS patients and concluded that the NLR was significantly correlated with the Gensini and SYNTAX scores in both groups. In addition, Altun B. *et al.* assessed the above relationship in an ACS population using the SYNTAX score. In that study of 287 patients, the NLR was found to be significantly correlated with the SYNTAX score in both the ST elevation myocardial infarction (STEMI) and NSTE-ACS groups[35]. Furthermore, three other studies reported this relationship in SAP populations[15, 36, 37]. Kaya H. *et al.*[36] used the Gensini score, whereas Sönmez O. *et al.*[15] and Kaya A. *et al.*[37] used the SYNTAX score, to assess the severity and complexity of CAD. Rather consistently, the NLR was found to be an independent predictor of a high Gensini or SYNTAX score in these studies. However, all of the above studies are limited by their sample size in elucidating the correlation between the NLR and the severity or complexity of CAD roundly and completely.

The GS is a relatively simple and widely used tool for evaluating the severity of coronary stenosis. For this reason, we choose the GS as a parameter of the severity of CAD in the present study. In this study, the sample size was relatively large and the severity of CAD was assessed according to the GS. Accordingly, our data may be used to confirm and extend the findings of previous studies with regard to the usefulness of the NLR in patients with stable CAD.

Interestingly, in the present study, the ROC curve analysis for predicting a high GS in CAD patients showed that NLR had the highest AUC among all markers, even the hs-CRP level. This finding indicates that the NLR may be a superior marker for identifying severe stenosis among patients with CAD. In addition to traditionally used markers, the NLR is an inexpensive and easy to obtain tool for risk stratification in patients with CAD.

Conclusion

In conclusion, the present data demonstrate that NLR is a valuable independent predictor of the severity of CAD assessed according to the GS; with an NLR of >2.04, thus indicates a higher risk for CAD and more severe CAD lesions.

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Conflicts of Interest

None.

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