Original Article

Impact of increased inflammation biomarkers on periprocedural myocardial infarction in patients undergoing elective percutaneous coronary intervention: a cohort study

Liding Zhao[1,2#], Ya Li[1,2#], Tian Xu[1,2#], Yi Luan[1,2], Qingbo Lv[1,2], Yao Wang[1,2], Xue Lv[1,2], Guosheng Fu[1,2], Wenbin Zhang[1,2]^

[1]Department of Cardiovascular Diseases, Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University, Hangzhou, China; [2]Key Laboratory of Cardiovascular Intervention and Regenerative Medicine of Zhejiang Province, Hangzhou, China

Contributions: (I) Conception and design: W Zhang, L Zhao; (II) Administrative support: W Zhang, G Fu; (III) Provision of study materials or patients: Y Li, Y Luan, T Xu; (IV) Collection and assembly of data: L Zhao, Q Lv, T Xu; (V) Data analysis and interpretation: L Zhao, Y Wang, X Lv, T Xu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Wenbin Zhang, MD, PhD. Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University, No. 3 East of Qingchun Road, Hangzhou 310000, China. Email: 3313011@zju.edu.cn.

Background: The fact that each inflammatory indicator has a forecasting capacity on the occurrence of periprocedural myocardial infarction (PMI) has a controversial existence. The purpose of this study was to explore the role of inflammation biological indicators on PMI in a group of patients undergoing selective percutaneous coronary intervention (PCI).

Methods: The study was carried out both in a retrospective and prospective manner in 7,413 and 1,189 subjects, respectively. In the retrospective cohort study, the association between inflammation biomarkers and PMI was assessed by univariate and multivariate logistic regression. WBC, CRP, and NLR were distributed using k-means clustering into a virtual variable "Inflammatory Trend", and multivariate logistic regression and subgroup analysis were performed. In the prospective cohort study, the endpoints were PMI, cardiovascular death or cardiac arrest. The chi-square test was performed to calculate the relative risk (RR).

Results: In the retrospective cohort study, except WBC, CRP, NLR and virtual variable "Inflammatory trend" were independent risk factors for PMI. The subgroup analysis revealed that CRP can serve as the most stable predictor. In the prospective cohort study, WBC (RR =1.134, P=0.416) has no effect on the incidence of PMI. However, an elevation in the incidence of PMI was observed with an increase of NLR (RR =1.354, P=0.041) and CRP (RR =1.412, P=0.025).

Conclusions: In patients with elective PCI for single-vessel lesions, high CRP increases the risk for PMI. The increase of NLR was an independent risk factor for PMI, especially for patients with hypertension and under the age of 70. WBC has no influence on the occurrence of PMI.

Keywords: White blood cell (WBC); periprocedural myocardial infarction (PMI); neutrophil to lymphocyte ratio; C-reactive protein; percutaneous coronary intervention (PCI)

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^ ORCID: 0000-0003-4746-9570.

Introduction

Percutaneous coronary intervention (PCI), is considered as one of the main strategies to solve the coronary atherosclerotic heart disease problems (1). Technological developments, effective antithrombotic therapies, and advanced instrumentations have greatly improved the prognosis (2) but also increased the overall complexity of the process.

The occurrence of periprocedural myocardial infarction (PMI) may be related to the long-term increase in all-cause mortality (3). Depending upon the diagnostic criteria and the local practice it varies between 5–40% (4,5). CRP has been shown, in patients under PCI with drug-eluting stent implantation, to be associated with the unsatisfactory occurrence of cardiac events after surgery (6-8). However, four out of the six studies suggested a positive correlation between CRP and PMI while the other two suggested no relationship (8-11). Furthermore, white blood cell (WBC) count and neutrophil to lymphocyte ratio (NLR) have been shown to have a connection with the extent and prognosis of coronary artery diseases (CAD) (9,10,12-14) as well as the incidence of PMI (15) while another study suggested that WBC is not a risk factor of PMI (16) As for NLR, some studies have reported that its increase is connected to the elevated risk of PMI in patients undergoing non-urgent PCI, especially for values ≥3 (15), but Bressi *et al.* demonstrated that there was no relationship between preprocedural NLR values and the PMI incidence (17). There are several clinic indicators that reflect the inflammatory state of the patient and fact that each biomarker can predict the incidence of PMI is controversial and needs further assessment.

This study aimed to evaluate the predictive value of NLR, WBC, and CRP on PMI through retrospective as well as prospective cohort studies.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jtd-20-1605).

Methods

This study is a single-center cohort study conducted at Sir Run Run Shaw Hospital, including retrospective and prospective parts. The retrospective study was approved by the Ethics Committee of Sir Run Run Shaw Hospital (NO.20200224-33), and the prospective study was registered at the Chinese Clinical Trial Registry(chiCTR-RPC-17014094), and informed consent was obtained from all patients. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Population and procedures

Patients undergoing elective single coronary artery PCI at Sir Run Run Shaw Hospital between December 2009 to December 2017 were included in the retrospective cohort study. Additional details about the study subjects are listed in *Figure 1*. The prospective study group included a total of 3726 consecutive patients who underwent an elective single coronary artery PCI between January 2018 to April 2019 and finally 1,189 patients were enrolled in this study. Patient inclusion criteria were (I) patients with elective single-branch coronary PCI; (II) normal baseline myocardial enzyme level and cTnI measured at 8, 16, 24 and 48 hours after PCI; (III) availability of preprocedural NLR, CRP, and WBC. Exclusion criteria for the patients were (I) revascularization of more than one main coronary artery during single PCI procedure; (II) no stent implantation; (III) patients with severe heart failure, defined by EF <45% or NT-pro BNP >2,000 pg/mL; (IV) patients with chronic total occlusion or undergoing treatment with cutting balloon angioplasty or percutaneous transluminal coronary rotational ablation; (V) patients recovering from acute myocardial infarction (MI); (VI) patient with one of the periprocedural complications such as thrombosis, coronary artery perforation or dissection; (VII) CRP >10.0 mg/L.

PCI was performed as per the current general guidelines. Before elective single coronary artery PCI, all patients received aspirin plus ticagrelor or clopidogrel at a loading dose of 300, 180, and 300 mg, respectively. Periprocedural anticoagulation and antiplatelet therapy were performed as per the standard regimen before PCI. The types of stents, implantation techniques, and the use of intravascular ultrasound (IVUS), optical coherence tomography (OCT) and fractional flow reserve (FFR) were determined by the operators.

For all the patients, NLR, CRP, and WBC were measured within 24 hours before PCI. The levels of myonecrotic markers (cTnI) were measured before and at 8, 16, 24- and 48-hour' time points after PCI. Complete blood counts were measured using a MEK-6458 automated analyzer (Nihon Kohden). CRP levels were measured with a fully automated enzyme-linked immunoassay using an Aeroset 2.0 analyzer (Abbott Diagnostics, Santa Clara, CA, USA). cTnI was measured using the ultrasensitive Singulex

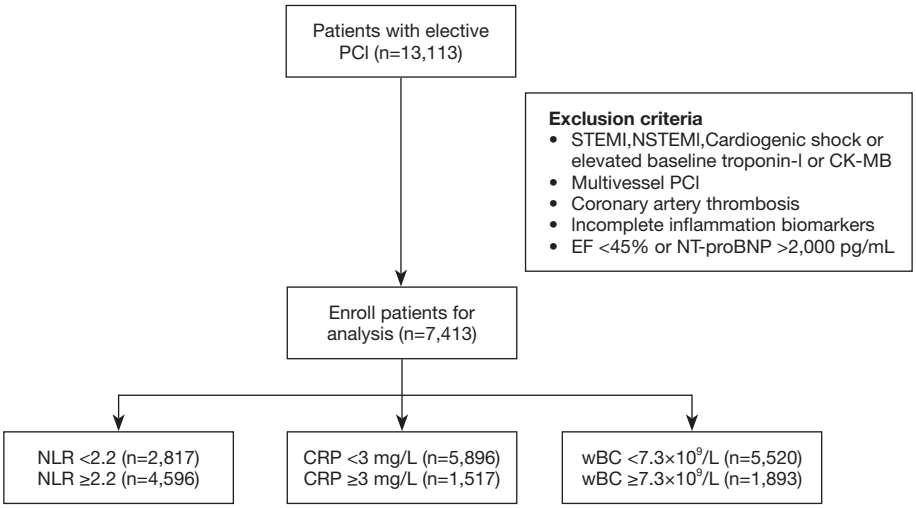

Figure 1 Flow chart for patient inclusion in retrospective cohort study. PCI, percutaneous coronary intervention; STEMI, ST segment Elevation Myocardial Infarction; NSTEMI, non-ST segment Elevation Myocardial Infarction; CK-MB, creatine phosphokinase MB; EF, ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; CRP, C-reactive protein; WBC, white blood cell; NLR, neutrophil to lymphocyte ratio.

Erenna System (at Singulex, Inc., Berkeley, CA, USA). Different parameters such as a peri-procedural myocardial enzyme, patient demographics, clinical manifestations, angiographic and procedural characteristics were collected from hospital information system.

Sample size

The sample size calculation was based on previous studies that investigated the correlation between inflammation biomarkers and PMI, and prognosis after PCI. Significant correlations were observed in the retrospective studies that included no more than 4,500 patients (15,18,19) and in the prospective studies that included no more than 100 patients (20). We therefore aimed at including at least 5,000 patients in retrospective research and 150 patients in prospective research during this study.

Definition of PMI, and other definitions

There have been several investigations for defining an appropriate criterion for PMI (21,22) and these guidelines are being continuously updated (23-26). In this study, PMI was defined as an elevated concentration of cTnI >5× URL along with a normal baseline range 48 hours after the procedure (23). Define WBC ≥7.3×10^9/L, CRP ≥3.0 mg/L, NLR ≥2.2 as exposures. The blood pressure of patients with hypertension was kept below 140/90 mmHg and HbA1c of patients with diabetes mellitus was kept at <6.5%. Estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 was considered as renal insufficiency. The term 'smoking' was used for subjects with current smoking habits or subjects who quitted less than one month ago. The diameters of the intravascular stents were grouped if they were ≥2.5 mm. The term elderly is used to define subjects of age above 70 years.

Bias

This study made some efforts to eliminate potential sources of bias. First, it strictly enrolled consecutive patients according to the inclusion and exclusion criteria; Second, laboratory technicians and data analysts were blinded to the original source of samples and patient information; Third, factors that may affect PMI were included in the multivariate analysis.

Statistical analysis

The statistical analysis was performed using the SPSS 22.0 statistical package. Non-parametric Mann-Whitney U test was used to test the variables. The normal distribution of laboratory assessments was confirmed by Kolmogorov-Smirnov test. The missing values of continuous variables

were replaced by the mean and the missing values of ordinal categorical variables were replaced by the median. In retrospective cohort study, inflammatory biomarkers including NLR, CRP, and WBC were allocated with normal transformation by Blom method and renamed as NNLR, NCRP, and NWBC. k-means clustering using NNLR, NCRP and NWBC were performed using SPSS software to create a virtual variable "Inflammatory Trend". Based upon the results of k-means clustering patients were divided into two groups, cluster I (final gathering center, NNLR –0.4873, NWBC –0.5752, NCRP –0.4918) (n=3,800) and cluster II (final gathering center, NNLR 0.5081, NWBC 0.5999, NCRP 0.5186) (n=3,613). Univariate analysis and multivariate regression analysis of each factor were performed by logistic binary regression analysis. In the prospective cohort study, the difference in the incidence of PMI among each group and the relative risk value were calculated by the chi-square test. Factors associated with PMI were identified by univariate logistic regression. Through the univariate analysis, variables with P value <0.05 were screened out for the test of multiple analyses. Multivariate logistic and linear regressions were performed to identify the relationship between the increase of inflammation biomarkers and PMI. Multivariate logistic regression and chi-square test were also performed in subgroup analysis. P values <0.05 (two-tailed) were considered statistically significant.

Sensitivity analysis

This study investigated the predictability of inflammatory factors on PMI before and after the processing of missing values. For another definition of PMI (cTnI > 3×URL along with a normal baseline range 48 hours after the procedure), this study also explored its relationship with inflammatory factors.

Results

Baseline characteristics

In the retrospective cohort study, 13,113 patients received stent implantation at the Sir Run Run Shaw Hospital between December 2009 and December 2017. Among these 5720 patients were omitted from this group because of the previously defined exclusion criterion. Additional details are provided in *Figure 1*. In all, 7,413 patients receiving elective coronary stent implantation for single-vessel lesions were enrolled. The number of participants with missing CRP, NLR, and WBC data were, 177, 142, and 103, respectively. The mean age of these patients was 66.54±10.21 years, 71.0% were men, 69.0% had hypertension and 25.6% had diabetes mellitus. In the prospective cohort study, 3726 consecutive patients received stent implantation. A total of 2,537 patients were excluded as per the exclusion criteria and finally a total of 1,189 patients were included. The number of participants with missing CRP, NLR, and WBC data were, 52, 36, and 25, respectively. The subject population in prospective study had a mean age of 65.98±9.90 years. Among this, 66.3% were men, 67.8% had hypertension and 27.5% had diabetes mellitus. The levels of myonecrotic markers (cTnI) were measured before and at 8-, 16-, 24- and 48-hours' after PCI. The main demographic, procedural characteristics and angiographic features are listed in *Tables 1,2*. The baseline characteristics of groups divided by WBC, NLR and CRP are shown in *Tables S1-S3*.

PMI ratios and logistic regression analysis in the retrospective cohort study

Comparison with the standard values of WBC < or ≥7.3×10^9/L, CRP < or ≥3.0 mg/L, NLR < or ≥2.2 revealed a higher incidence of PMI in patients with elevated WBC (12.5% *vs.* 14.6%, P value =0.016), CRP (12.3% *vs.* 16.0%, P value <0.001), and NLR (11.1% *vs.* 14.2%, P value <0.001, *Figure 2A*).

The univariate analysis suggested that age, gender, current smoking, hypertension, renal insufficiency, B2C type stent, balloon pre-dilation, balloon post-dilation, total stent length (every 10 mm), CRP, NLR, WBC had predictive value in the incidence of PMI (*Table 3*).

After correction of the confounding factors screened from the univariate analysis, the multivariable logistic regression analysis revealed that age, gender, renal insufficiency, balloon post-dilation, total stent length (every 10 mm), CRP, NLR can serve as independent predictors of PMI. Elevated inflammation biomarker levels except WBC concentration have a connection with an increased incidence risk of PMI (*Table 3*).

In subgroup analysis, predictive values of CRP on PMI was consistent across the patients with age <70 years (OR 1.069, 95 % CI, 1.017–1.124, P value =0.009), no hypertension (OR 1.077, 95 % CI, 1.005–1.154, P value =0.036), male (OR 1.062, 95 % CI, 1.018–1.107, P value =0.005), no renal insufficiency (OR 1.045, 95 % CI, 1.005–1.088, P value =0.027), smoking (OR 1.083, 95%

Table 1 Baseline characteristics of the sample

Characteristics	The retrospective cohort study (n=7,413)	The prospective cohort study (n=1,189)
Age (Years)	66.54±10.21	65.98±9.90
Man, N (%)	5,260 (71.0)	788 (66.3)
BMI	24.57±3.13	25.56±21.76
Current smoking, N (%)	1,634 (22.0)	215 (18.1)
Diabetes, N (%)	1,896 (25.6)	327 (27.5)
Hypertension, N (%)	5,112 (69.0)	806 (67.8)
Previous MI, N (%)	616 (8.3)	336 (28.3)
Previous PCI, N (%)	2,190 (29.5)	0 (0.0)
Previous CABG, N (%)	46 (0.6)	0 (0.0)
Laboratory examination		
NLR	2.80±1.44	2.78±1.29
WBC ($\times10^9$/L)	6.33±1.70	6.24±1.73
PLT ($\times10^9$/L)	172.03±52.85	191.50±59.48
CRP (mg/L)	1.97±1.93	1.98±2.02
LDL-C (mmol/L)	2.03±0.84	2.08±0.90
Renal insufficiency, N (%)	882 (11.9)	140 (11.8)
Baseline medication, N (%)		
ACEI	1,939 (26.2)	122 (10.3)
ARB	2,475 (33.4)	482 (40.5)
Statin	7,281 (98.2)	1,167 (98.1)
Beta blocker	3,771 (50.9)	597 (50.2)
CCB	2,482 (33.5)	463 (38.9)
Aspirin	7,275 (98.1)	1,169 (98.3)
Clopidogrel	7,151 (96.5)	1,072 (90.2)
Ticagrelor	329 (4.4)	204 (17.2)
Bivalirudin	115 (1.6)	128 (10.8)

Values are expressed as mean ± SD or n (%) unless otherwise indicated. NLR, neutrophil to lymphocyte ratio; WBC, white blood cell; PLT, platelet; CRP, C-creative protein; BMI, Body Mass Index; LDL-C, low-density lipoprotein cholesterol; CABG, Coronary Artery Bypass Grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; ACEI, Angiotensin-Converting Enzyme Inhibitors; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.

CI, 1.007–1.166, P value =0.033, *Figure 2B*). For NLR, the predictive values in each subgroups, such as patients with age <70 years (OR 1.088, 95% CI, 1.014–1.167, P value =0.019), hypertension (OR 1.055, 95% CI, 1.001–1.113, P value =0.047), no renal insufficiency (OR 1.059, 95% CI, 1.002–1.118, P value =0.041, *Figure 2C*). Data for each group is shown in *Figure 2*.

K-means clustering

In term of patients' demographics, the inflammation biomarkers such as NLR, CRP, WBC and platelet count of cluster II (NLR 3.49, WBC 7.30×10^9/L, CRP 2.81 mg/L) were significantly higher than cluster I (NLR 2.14, WBC 5.41×10^9/L, CRP 1.17 mg/L, P value <0.001). The proportion of male patients in cluster II with smoking,

Table 2 Baseline characteristics of distribution of lesion vessels in patients

	The retrospective cohort study (n=7,413)	The prospective cohort study (n=1,189)
LM, N (%)	432 (5.8)	67 (5.6)
LAD, N (%)	3,969 (53.5)	642 (54.0)
LCX, N (%)	1,220 (16.5)	191 (16.1)
RCA, N (%)	2,133 (28.8)	342 (28.8)
AHA/ACC type B2/C, N (%)	2,180 (29.4)	747 (62.8)
Coronary calcification, N (%)	816 (11.0)	121 (10.8)
CTO, N (%)	0 (0.0)	0 (0.0)
FFR/IVUS/OCT, N (%)	679 (9.2)	233 (19.6)
Stents number ≥2, N (%)	2,666 (36.0)	187 (15.7)
Total stent length (mm)	33.66±21.28	39.14±21.84
Stent diameter ≥2.5 mm, N (%)	6,630 (89.4)	1,102 (92.7)
Ballon pre-dilation, N (%)	6,350 (85.7)	1,081 (90.9)
Ballon post-dilation, N (%)	6,767 (91.3)	1,168 (98.2)

Values are expressed as mean ± SD or n (%) unless otherwise indicated. LM, left main; LAD, left anterior descending branch; LCX, left circumflex artery; RCA, right coronary artery; AHA/ACC, American College of Cardiology/American Heart Association; CTO, chronic total occlusion; FFR, fractional flow reserve; IVUS, intravascular ultrasound; OCT, optical coherent tomography.

hypertension, diabetes, and renal insufficiency was higher. Patients in cluster II were older, had higher BMI, higher low-density lipoprotein and higher platelet count, *Table S4*.

Higher rate of PMI was found in patients of cluster II (11.3% *vs.* 14.8%, P value <0.001, *Figure 2A*). After correction of confounding factors screened from univariate analysis, the virtual variable inflammatory trend had a predictive value for PMI (OR 1.202, 95% CI, 1.042–1.387, P value =0.012, *Table S5*). In the subgroup analysis, the virtual variable inflammatory trend served as an independent predictor of PMI in female patients (OR 1.315, 95% CI, 1.026–1.685, P value =0.031), hypertension (OR 1.217, 95% CI, 1.030–1.438, P value =0.021), no current smoking (OR 1.234, 95 % CI, 1.051–1.499, P value =0.010), no renal insufficiency (OR 1.192, 95 % CI, 1.020–1.392, P value =0.027, *Figure S1*).

PMI ratios and Chi-square test in the prospective cohort study

The prospective cohort study employed the same cut-off points for inflammatory markers as the retrospective study. There are higher incidence of PMI in patients with elevated CRP (13.9% *vs.* 19.7%, P value =0.025) and NLR (12.4% *vs.* 16.8%, P value =0.041), but in patients with elevated WBC (14.7% *vs.* 16.6%, P value =0.416), this study did not observe significant differences (*Figure 3A*).

The RR of patients with elevated CRP was 1.412 (95% CI, 1.049–1.190, P value =0.025, *Figure 3B*). The RR of patients with WBC concentration >7.30×10^9/L was 1.134 (95% CI, 0.839–1.531, P value =0.416, *Figure 3C*). The relative risk (RR) of patients with elevated NLR was 1.354 (95% CI, 1.009–1.818, P value =0.041, *Figure 3D*).

In the subgroup analysis of NLR, the RR value was statistically significant in subjects of age <70 years (RR 1.503, 95% CI, 1.005–2.247, P value =0.044), hypertension (RR 1.612, 95 % CI, 1.121–2.318, P value =0.008, *Figure 3D*). The relationship between CRP and PMI was consistent across above mentioned subgroups of patients such as population of hypertension (RR 1.411, 95 % CI, 1.005–1.981, P value =0.0496), female (RR 1.875, 95 % CI, 1.205–2.916, P value =0.006), no current smoking (RR 1.442, 95% CI, 1.048–1.984, P value =0.027), no renal insufficiency (RR 1.431, 95 % CI, 1.018–2.012, P value =0.042), *Figure 3B*.

Overall, in the retrospective cohort study, CRP and NLR were found as independent risk factors for PMI. We also found that WBC cannot be considered as a risk factor. The subgroup analysis revealed that CRP was the most

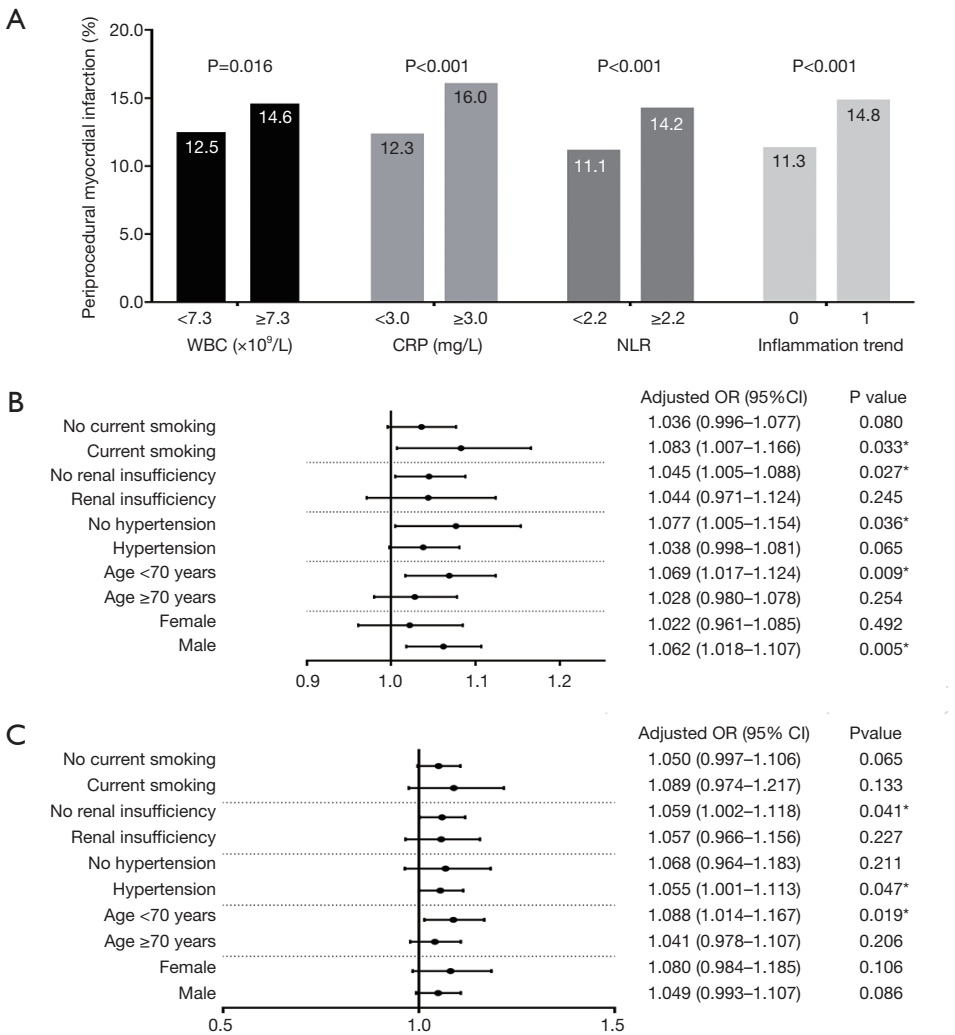

Figure 2 PMI ratios and logistic regression analysis in retrospective cohort study. (A) Difference in the incidence of PMI between groups divided according to WBC, NLR, CRP and Inflammatory trend (n=7,413). (B) The relationship between CRP and PMI was analysed by multivariable logistic regression analysis in predefined subgroups. (C) The relationship between NLR and PMI was analysed by multivariable logistic regression analysis in predefined subgroups. *, P<0.05. PMI, periprocedural myocardial infarction; CRP, C-reactive protein; WBC, white blood cell; NLR, neutrophil to lymphocyte ratio.

stable predictor. The virtual variable inflammatory trend had predictive values for PMI particularly in the female population, or patients with hypertension, no current smoking, and no renal insufficiency. It was observed that, in a prospective cohort study, the increase of CRP and NLR can elevate the incidence of PMI, while WBC has no effect.

Sensitivity analysis

In the analysis, prior to the replacement of the missing value, the retrospective study showed that CRP (OR 1.045, 95 % CI, 1.009–1.083, P value =0.013), and NLR (OR 1.054, 95% CI, 1.005–1.105, P value =0.031) were risk factors for PMI, while WBC (OR 1.015, 95 % CI, 0.972–1.060, P value =0.498) was not; In the prospective studies, the PMI incidence was higher in patients with elevated CRP (13.9% *vs.* 19.7%, P value =0.025) and NLR (12.4% *vs.* 16.8%, P value =0.041), while WBC had no effect on the incidence of PMI. 2. For another definition of PMI (cTnI > 3×URL along with a normal baseline range 48 hours after the

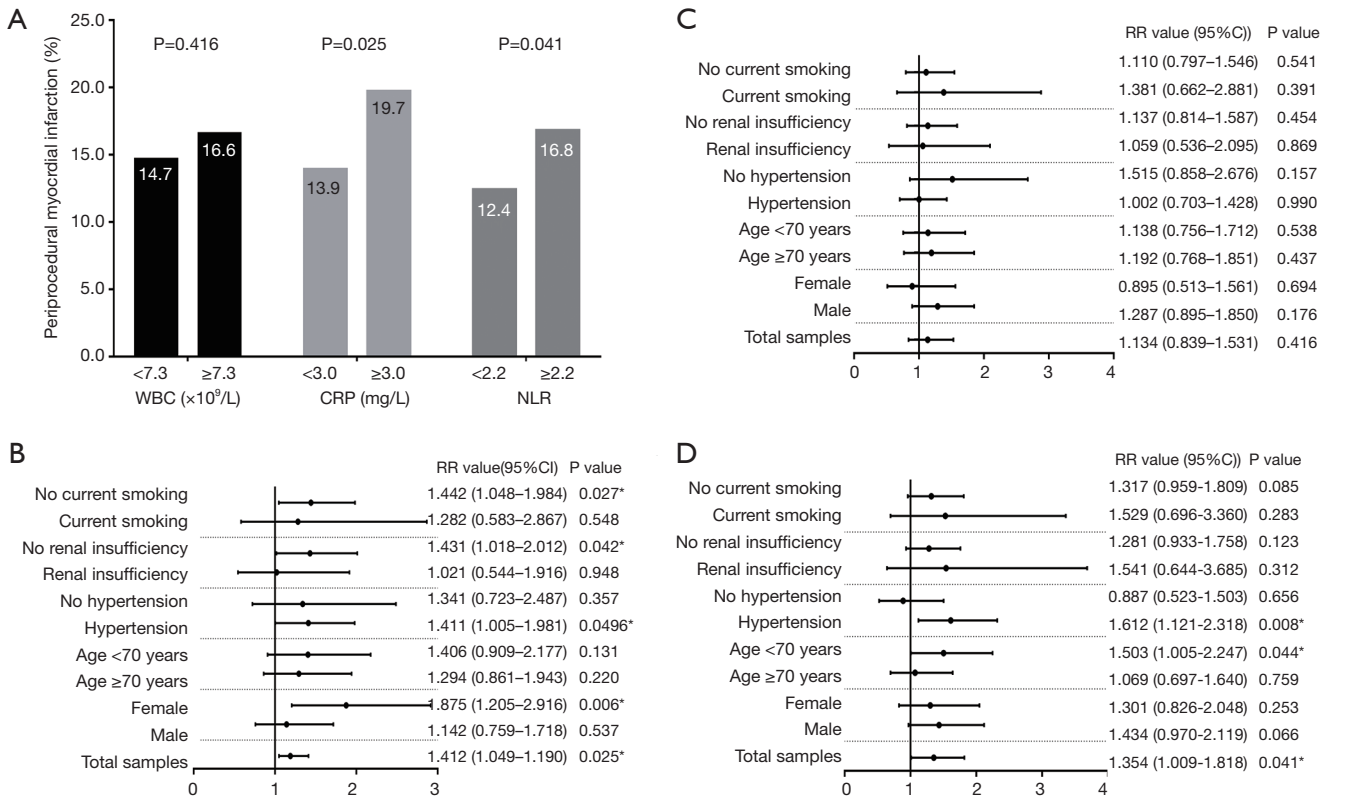

Figure 3 PMI ratios and Chi-square test in prospective cohort study. (A) Difference in the incidence of PMI between groups divided according to WBC, NLR and CRP (n=1,189). (B) The relationship between CRP and PMI was analysed by Chi-square test in the sample and predefined subgroups. (C) The relationship between WBC and PMI was analysed by Chi-square test in the sample and predefined subgroups. (D) The relationship between NLR and PMI was analysed by Chi-square test in the sample and predefined subgroups. *, P<0.05. PMI, periprocedural myocardial infarction; CRP, C-reactive protein; WBC, white blood cell; NLR, neutrophil to lymphocyte ratio; RR, relative risk.

procedure), the retrospective study showed that CRP (OR 1.043, 95% CI, 1.012–1.074, P value =0.006), and NLR (OR 1.058, 95% CI, 1.016–1.103, P value =0.007) were risk factors for PMI, while WBC (OR 0.989, 95% CI, 0.954–1.026, P value =0.560) was not; In the prospective studies, the PMI incidence was higher in patients with elevated CRP (21.0% *vs.* 26.1%, P value =0.042) and NLR (18.5% *vs.* 24.1%, P value =0.022), and WBC (21.7% *vs.* 23.1%, P value =0.416) had no effect on the incidence of PMI.

Discussion

Over the past few years, clinical researchers across the world have shown great interest in the prevention of perioperative complications. Magnetic resonance imaging (MRI) have demonstrated that most patients have myocardial injury during the perioperative period of PCI (27). Therefore, it is important to identify predictors of PMI during PCI. Inflammation is a recognized risk factor for CAD (28). It is considered as a leading mechanism for the course of development of atherosclerosis. Inflammatory biomarkers such as CRP and NLR are closely related to PMI incidence and enhanced risk stratification (15,18,20). However, their utility as a biomarker is still controversial. Some studies have reported that the increase in NLR is connected to the elevated risk of PMI in patients undergoing non-urgent PCI especially for values ≥3 (15). A study by Bressi *et al.* have demonstrated that there was no relationship between preprocedural NLR values and the incidence of PMI during the elective percutaneous coronary intervention (17). Also, the findings of the studies focused on exploring a relationship between cardiac troponin and CRP are

Table 3 Logistics regression of inflammation biomarkers

Variable	Simple regression				Multiple regression			
	OR	95 % CI		P	OR	95 % CI		P
WBC	1.046	1.006	1.087	0.025	1.013	0.971	1.057	0.548
CRP	1.079	1.045	1.114	<0.001	1.046	1.011	1.083	0.010*
NLR	1.106	1.062	1.153	<0.001	1.056	1.007	1.107	0.024*
Age	1.025	1.018	1.032	<0.001	1.020	1.012	1.028	<0.001*
Man	0.740	0.641	0.854	<0.001	0.732	0.624	0.859	<0.001*
BMI	0.979	0.957	1.000	0.054				
Current smoking	0.881	0.683	0.962	0.016	0.970	0.803	1.173	0.755
Diabetes	1.157	0.995	1.346	0.059				
Hypertension	1.448	1.240	1.629	<0.001	1.156	0.981	1.363	0.083
LDL-C >1.8 mmol/L	0.885	0.773	1.014	0.078				
Renal insufficiency	1.766	1.472	2.118	<0.001	1.266	1.034	1.551	0.023*
CCB	1.097	0.952	1.264	0.199				
AHA/ACC Type B2/C	1.346	1.166	1.552	<0.001	1.143	0.982	1.330	0.084
Balloon pre-dilation	1.334	1.082	1.645	0.007	1.147	0.992	1.427	0.220
Balloon post-dilation	1.784	1.332	2.388	<0.001	1.425	1.052	1.929	0.022*
Total stent length (Every 10 mm)	1.325	1.288	1.363	<0.001	1.312	1.274	1.351	<0.001*
Stent size >2.5 mm	1.067	0.852	1.335	0.141				

Values are expressed as mean ± SD or n (%) unless otherwise indicated. *, P<0.05. OR odds ratio. Dichotomized values with statistical significance are described in the table. WBC, white blood cell; CRP, C-creative protein; NLR, neutrophil to lymphocyte ratio; BMI, Body Mass Index; LDL-C, low-density lipoprotein cholesterol; AHA/ACC, American College of Cardiology/American Heart Association.

contradictory. Four out of the six studies suggest a positive correlation between CRP and PMI while the other two suggest no relationship (8,10,11,14). Preoperative WBC is independently associated with higher perioperative cardiac enzyme release and mortality after PCI (19). Another study suggests that WBC is not independently associated with PMI (16). The current study is aimed at exploring the connection between the increase of inflammatory biomarkers and the incidence of PMI in patients with elective PCI both in retrospective and prospective manner.

The present study provided evidence that elevated inflammation biomarkers, NLR and CRP, were independent factors on PMI especially after adjusting factors related to the lesions and procedural characteristics. WBC and CRP are well-known inflammation markers and key factors in the process of hemostasis and thrombosis. An elevated level of total WBC count, in a previous study on patients with acute MI, was considered to have a connection with increased poor prognosis and mortality (29). Also, pre-procedural CRP or WBC levels were found to be associated with PMI (18,19,30). In this study, WBC level seems to have no effect on the occurrence of PMI, which is consistent with the findings (16) of Verdoia *et al*., suggesting that low-level increase of myocardial enzymes might have a correlation with WBC but not the high level. Recently NLR is being considered as a new type of inflammation sensitive marker. Few studies have reported that it could serve as an indicator for predicting clinical prognosis of patients who suffer from stable CAD (9,13). In patients undergoing elective PCI Elevated NLR level increases the risk of PMI in patients undergoing elective coronary intervention (15). The theory that three scenarios promote thrombosis, proposed by Virchow, believes that inflammation plays a crucial role in thrombus formation (31,32). In the human circulatory system, the presence of inflammatory reactions can increase levels of clotting factors such as fibrinogen. Platelets play

a momentous role in the process causing instability to the atherosclerotic plaques after enhanced responsiveness, which is mediated by reactive oxygen species, cytokines and other mediators (33) is strictly linked with the enhanced pro-thrombotic status (28). Both retrospective and prospective cohort studies suggest that the predictive value of CRP is better than NLR. However, after combining the results of mutual verification between the two studies, when comparing CRP with NLR, no obvious pros and cons in the stability of predicting PMI were found.

It is worth mentioning that renal insufficiency and total stent length were also found as risk factors for PMI in this study. Renal insufficiency, as previously reported, has characteristics disturbances due to high perfusion and reduced coronary blood flow due to microvascular abnormalities (34). In addition to the sudden decrease in partially activated prothrombin and thrombin time caused by hemodialysis, it also increases the risk of massive thromboembolism and hypercoagulation (35). The findings related to the influence of total stent length in this study corroborate with previous reports (36). The fact that whether this association includes confounding factors of plaque lesions, or directly reflects the larger vascular damage due to long stent length requires further exploration. For balloon post-dilation, although the exact mechanism or its association with PMI is unclear, plasma b-type natriuretic peptide levels were significantly elevated post-dilation. In addition, increased levels of troponin I and high sensitive CRP post-dilation suggests the possibility of more MI and inflammation (37). Further research is required on these aspects as well.

The present study differs from earlier reports in different ways. First, for a single-center study, the sample size is considerable. Also, complementary information can be obtained from both prospective and retrospective findings. As the subjects with multi-vessel PCI were excluded the influence of pathological features and interventional operations for other vessels were minimized leading to accurate conclusions. We also did not include PMI subjects due to mechanical damage such as aortic dissection and branch occlusion, this can further help to precisely identify the effect of the inflammation biomarkers on PMI. Subgroup analysis was conducted to further explore specific populations.

Using only one or two biomarkers to reflect inflammation is highly susceptible to interference by other factors therefore, we have integrated different inflammatory indicators into a unified system to reflect overall inflammatory status through k-means clustering. Interestingly there was a relationship between the virtual variable inflammatory trend and the incidence of PMI, indicating that it is feasible to use a unified model to combine inflammation-related indicators in order to predict the incidence of PMI accurately.

This study includes retrospective and prospective research, and the two parts of the study are consistent with category boundaries of variables. Besides, the endpoint event indicators of this study were collected in the hospital within 48 hours after PCI, the follow-up rates were very high, negating attrition bias. The inclusion and exclusion criteria of this study were strictly enforced, thereby increasing the chance of reflecting the status of single CAD patients. These factors strengthen the study's external validity.

First, as a single-center study, residual confounding or selection bias cannot be completely ruled out. Second, as mentioned the disturbances due to mechanical damages such as aortic dissection and branch occlusion were ignored in order to precisely measure the influence of inflammatory markers. Even though chest pain was recorded in many cases the electrocardiogram changes could not be collected as the paper ECG ink disappeared over a long period of time. This further makes the PMI defined in this study not completely consistent with the fourth definition of myocardial infarction which includes additional non-cardiac markers. Third, plaque characteristics could also influence the occurrence of PMI. In this study, we can only define the characteristics of the lesion by angiography results due to the unavailability of FFR/IVUS/OCT in most patients.

Conclusions

In patients with elective PCI for single-vessel lesions, a higher CRP increases the risk of PMI, particularly in patients of no current smoking or renal insufficiency. The increase of NLR was an independent risk factor for PMI, especially for patients under the age of 70 and hypertension. WBC level seems to have no impact on the occurrence of PMI.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The retrospective study was approved by the Ethics Committee of Sir Run Run Shaw Hospital of Zhejiang University (NO.20200224-33), The prospective study was registered at the Chinese Clinical Trial Registry(chiCTR-RPC-17014094), and informed consent was obtained from all patients. This study did not include subjects under 18 years of age or those with limited capacity for civil conduct.

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Supplementary

Table S1 Baseline characteristics according to CRP levels

Characteristics	The retrospective cohort study			The prospective cohort study		
	CRP <3 mg/L (n=5,896)	CRP ≥3 mg/L (n=1,517)	P value	CRP <3 mg/L (n=940)	CRP ≥3 mg/L (n=249)	P value
Age (Years)	66.23±10.22	66.77±10.10	<0.001	65.28±9.83	68.63±9.70	<0.001
Man, N (%)	4,223 (71.6)	1,037 (68.4)	0.012	631 (67.1)	157 (63.1)	0.227
BMI	2,4.50±3.11	24.86±3.19	<0.001	25.61±23.91	25.38±10.13	0.146
Current smoking, N (%)	1,271 (21.6)	363 (23.9)	0.047	167 (17.8)	48 (19.3)	0.582
Diabetes, N (%)	1,484 (25.2)	412 (27.2)	0.113	256 (27.2)	71 (28.5)	0.688
Hypertension, N (%)	4,027 (68.3)	1,085 (71.5)	0.016	625 (66.5)	181 (72.7)	0.063
Previous MI, N (%)	509 (8.6)	107 (7.1)	0.047	258 (27.4)	78 (31.3)	0.227
Previous PCI, N (%)	1,820 (30.9)	370 (24.4)	<0.001	0	0	1.000
Previous CABG, N (%)	34 (0.6)	12 (0.8)	0.343	0	0	1.000
Laboratory examination						
NLR	2.74±1.40	3.05±1.56	<0.001	2.69±1.23	3.10±1.47	<0.001
WBC ($\times10^9$/L)	6.22±1.66	6.75±1.78	<0.001	6.15±1.69	6.57±1.86	<0.001
PLT ($\times10^9$/L)	169.86±52.41	180.45±53.71	<0.001	189.71±57.36	198.23±66.58	0.137
CRP (mg/L)	1.15±0.72	5.15±1.86	<0.001	1.10±0.73	5.28±1.91	<0.001
LDL-C (mmol/L)	1.88±0.82	2.18±0.86	<0.001	2.06±0.89	2.18±0.92	0.076
Renal insufficiency, N (%)	613 (10.4)	269 (17.7)	<0.001	82 (8.7)	58 (23.3)	<0.001
Baseline medication, N (%)						
ACEI	1,550 (26.3)	389 (25.6)	0.610	100 (10.6)	22 (8.8)	0.405
ARB	1,952 (33.1)	523 (34.5)	0.313	377 (40.1)	105 (42.2)	0.556
Statin	5,790 (98.2)	1,491 (98.3)	0.826	924 (98.3)	243 (97.6)	0.462
Beta blocker	2,992 (50.7)	779 (51.4)	0.674	477 (50.7)	120 (48.2)	0.474
CCB	1,901 (32.2)	581 (38.3)	<0.001	357 (38.0)	106 (42.6)	0.187
Aspirin	5,789 (98.2)	1,486 (98.0)	0.557	924 (98.3)	245 (98.4)	0.917
Clopidogrel	5,696 (96.6)	1,455 (95.9)	0.191	854 (90.9)	218 (87.6)	0.120
Ticagrelor	253 (4.3)	76 (5.0)	0.225	156 (16.6)	48 (19.3)	0.319
Bivalirudin	91 (1.5)	24 (1.6)	0.913	86 (9.1)	42 (16.9)	<0.001
Distribution of lesion vessels, N (%)						
LM	338 (5.7)	94 (6.2)	0.492	53 (5.6)	14 (5.6)	<0.001
LAD	3,194 (54.2)	775 (51.1)	0.032	499 (53.1)	143 (57.4)	0.992
LCX	981 (16.6)	239 (15.8)	0.408	156 (16.6)	35 (14.1)	0.332
RCA	1,653 (28.0)	480 (31.6)	0.006	276 (29.4)	66 (26.5)	0.376
AHA/ACC type B2/C, N (%)	1,703 (28.9)	477 (31.4)	0.051	590 (62.8)	157 (63.1)	0.934
Coronary calcification, N (%)	610 (10.3)	206 (13.6)	<0.001	96 (10.2)	25 (10.0)	0.936
CTO, N (%)	0 (0.0)	0 (0.0)	1.000	0 (0.0)	0 (0.0)	1.000
FFR/IVUS/OCT, N (%)	545 (9.2)	134 (8.8)	0.621	191 (20.3)	42 (16.9)	0.223
Stents number ≥2, N (%)	2,086 (35.4)	580 (38.2)	0.039	146 (15.5)	41 (16.5)	0.719
Total stent length (mm)	36.35±21.23	37.84±21.44	0.005	38.80±21.52	40.39±23.00	0.037
Stent diameter ≥2.5 mm, N (%)	5,291 (89.7)	1,339 (88.3)	0.096	874 (93.0)	228 (91.6)	0.447
Ballon pre-dilation, N (%)	5,026 (85.2)	1,324 (87.3)	0.044	855 (91.0)	226 (90.8)	0.924
Ballon post-dilation, N (%)	5,365 (91.0)	1,402 (92.4)	0.079	927 (98.6)	241 (96.8)	0.051

Values are expressed as mean ± SD or n (%) unless otherwise indicated. NLR, neutrophil to lymphocyte ratio; WBC, white blood cell; PLT, platelet; CRP, C-creative protein; BMI, Body Mass Index; LDL-C, low-density lipoprotein cholesterol; CABG, Coronary Artery Bypass Grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; ACEI, Angiotensin-Converting Enzyme Inhibitors; ARB, Angiotensin receptor blocker; CCB, Calcium channel blocker; LM, left main; LAD, left anterior descending branch; LCX, left circumflex artery; RCA, right coronary artery; AHA/ACC, American College of Cardiology/American Heart Association; CTO, chronic total occlusion; FFR, Fractional Flow Reserve; IVUS, intravascular ultrasound; OCT, optical coherent tomography.

Table S2 Baseline characteristics according to NLR levels

Characteristics	The retrospective cohort study			The prospective cohort study		
	NLR <2.2 (n=2,817)	NLR ≥2.2 (n=4,596)	P value	NLR <2.2 (n=444)	NLR ≥2.2 (n=745)	P value
Age (Years)	64.98±10.14	67.50±10.14	<0.001	64.39±9.85	66.92±9.81	<0.001
Man, N (%)	1847 (65.6)	3413 (74.3)	<0.001	269 (60.6)	519 (69.7)	0.001
BMI	24.76±3.04	24.46±3.17	<0.001	25.84±21.79	25.40±21.75	0.059
Current smoking, N (%)	651 (23.1)	9,883 (21.4)	0.083	87 (19.6)	128 (17.2)	0.296
Diabetes, N (%)	682 (24.2)	1,214 (26.4)	0.035	117 (26.4)	210 (28.2)	0.493
Hypertension, N (%)	1,845 (65.5)	3,267 (71.1)	<0.001	291 (65.5)	515 (69.1)	0.201
Previous MI, N (%)	213 (7.6)	403 (8.8)	0.068	115 (25.9)	221 (29.7)	0.163
Previous PCI, N (%)	803 (28.5)	1,387 (30.2)	0.125	0	0	1.000
Previous CABG, N (%)	17 (0.6)	29 (0.6)	0.884	0	0	1.000
Laboratory examination						
NLR	1.70±0.34	3.47±1.47	<0.001	1.70±0.33	3.42±1.23	<0.001
WBC ($\times10^9$/L)	5.99±1.57	6.54±1.74	<0.001	5.89±1.61	6.44±1.77	<0.001
PLT ($\times10^9$/L)	174.37±51.79	170.59±53.44	<0.001	191.53±56.37	191.42±61.30	0.652
CRP (mg/L)	1.76±1.72	2.09±2.04	<0.001	1.78±1.88	2.09±2.09	0.010
LDL-C (mmol/L)	2.12±0.86	1.97±0.82	<0.001	2.25±0.96	1.99±0.84	<0.001
Renal insufficiency, N (%)	227 (8.1)	655 (14.3)	<0.001	32 (7.2)	108 (14.5)	<0.001
Baseline medication						
ACEI, N (%)	692 (24.6)	1,247 (27.1)	0.015	41 (9.2)	81 (10.9)	0.368
ARB, N (%)	888 (31.5)	1,587 (34.5)	0.008	175 (39.4)	307 (41.2)	0.542
Statin, N (%)	2,766 (98.2)	4,515 (98.2)	0.879	430 (96.8)	737 (98.9)	0.010
Beta blocker, N (%)	1,437 (51.0)	2,334 (50.8)	0.849	218 (49.1)	379 (50.9)	0.554
CCB, N (%)	896 (31.8)	1,586 (34.5)	0.017	161 (36.3)	302 (40.5)	0.144
Aspirin, N (%)	2,766 (98.2)	4,509 (98.1)	0.799	434 (97.7)	735 (98.7)	0.238
Clopidogrel, N (%)	2,742 (97.3)	4,409 (95.9)	0.001	413 (93.0)	659 (88.5)	0.011
Ticagrelor, N (%)	95 (3.4)	234 (5.1)	<0.001	61 (13.7)	143 (19.2)	0.016
Bivalirudin, N (%)	39 (1.4)	76 (1.7)	0.363	45 (10.1)	83 (11.1)	0.588
Distribution of lesion vessels						
LM, N (%)	158 (5.6)	274 (6.0)	0.529	23 (5.2)	44 (5.9)	0.600
LAD, N (%)	1,576 (55.9)	2,393 (52.1)	0.001	248 (55.9)	394 (52.9)	0.320
LCX, N (%)	432 (15.3)	788 (17.1)	0.041	69 (15.5)	122 (16.4)	0.704
RCA, N (%)	780 (27.7)	1,353 (29.4)	0.106	120 (27.0)	222 (29.8)	0.307
AHA/ACC type B2/C, N (%)	802 (28.5)	1,378 (30.0)	0.165	279 (62.8)	478 (62.8)	0.995
Coronary calcification, N (%)	286 (10.2)	530 (11.5)	0.066	33 (7.4)	88 (11.8)	0.016
CTO, N (%)	0 (0.0)	0 (0.0)	1.000	0	0	1.000
FFR/IVUS/OCT, N (%)	277 (9.8)	402 (8.7)	0.116	89 (20.0)	144 (19.3)	0.764
Stents number ≥2, N (%)	936 (33.2)	1,730 (37.6)	<0.001	68 (15.3)	119 (16.0)	0.763
Total stent length (mm)	35.29±20.54	37.50±21.68	<0.001	37.62±20.165	40.04±22.75	0.206
Stent diameter ≥2.5 mm, N (%)	2,523 (89.6)	4,107 (89.4)	0.782	412 (92.8)	690 (92.6)	0.911
Ballon pre-dilation, N (%)	2,408 (85.5)	3,942 (85.8)	0.730	403 (90.8)	678 (91.0)	0.889
Ballon post-dilation, N (%)	2,586 (91.8)	4,181 (91.0)	0.219	439 (98.9)	729 (97.9)	0.196

Values are expressed as mean ± SD or n (%) unless otherwise indicated. NLR, neutrophil to lymphocyte ratio; WBC, white blood cell; PLT, platelet; CRP, C-creative protein; BMI, Body Mass Index; LDL-C, low-density lipoprotein cholesterol; CABG, Coronary Artery Bypass Grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; ACEI, Angiotensin-Converting Enzyme Inhibitors; ARB, Angiotensin receptor blocker; CCB, Calcium channel blocker; LM, left main; LAD, left anterior descending branch; LCX, left circumflex artery; RCA, right coronary artery; AHA/ACC, American College of Cardiology/American Heart Association; CTO, chronic total occlusion; FFR, Fractional Flow Reserve; IVUS, intravascular ultrasound; OCT, optical coherent tomography.

Table S3 Baseline characteristics according to WBC levels

	The retrospective cohort study			The prospective cohort study		
	WBC <7.3×10^9/L (n=5,520)	WBC ≥7.3×10^9/L (n=1,893)	P value	WBC <7.3×10^9/L (n=894)	WBC ≥ 7.3×10^9/L (n=295)	P value
Age (Years)	66.99±9.95	65.24±10.82	<0.001	66.55±9.45	64.26±10.97	0.003
Man, N (%)	3,843 (69.6)	1,417 (74.9)	<0.001	578 (64.7)	210 (71.2)	0.040
BMI	24.40±3.12	25.08±3.10	<0.001	25.37±24.07	26.15±12.37	<0.001
Current smoking, N (%)	1,119 (20.3)	515 (27.2)	<0.001	148 (16.6)	67 (22.7)	0.017
Diabetes, N (%)	1,358 (24.6)	538 (28.4)	0.001	220 (24.6)	107 (36.3)	<0.001
Hypertension, N (%)	3,797 (68.8)	1,315 (69.5)	0.581	591 (66.1)	215 (72.9)	0.031
Previous MI, N (%)	463 (8.4)	153 (8.1)	0.678	224 (25.1)	112 (38.0)	<0.001
Previous PCI, N (%)	1,654 (30.0)	536 (28.3)	0.175	0	0	1.000
Previous CABG, N (%)	35 (0.6)	11 (0.6)	0.800	0	0	1.000
Laboratory examination						
NLR	2.67±1.31	3.17±1.71	<0.001	2.66±1.16	3,12±1.59	<0.001
WBC (×10^9/L)	5.56±1.01	8.56±1.25	<0.001	5.47±1,01	8.58±1.30	<0.001
PLT (×10^9/L)	163.85±47.47	195.89±60.04	<0.001	185.30±57.81	210.27±60.62	<0.001
CRP (mg/L)	1.80±1.80	2.45±2.19	<0.001	1.84±0.94	2.40±2.19	<0.001
LDL-C (mmol/L)	2.01±0.84	2.09±0.83	<0.001	2.06±0.89	2.15±0.92	0.095
Renal insufficiency	628 (11.4)	254 (13.4)	0.018	101 (11.3)	39 (13.2)	0.374
Baseline medication						<0.001
ACEI	1,435 (26.0)	504 (26.6)	0.592	88 (9.8)	34 (11.5)	0.409
ARB	1,820 (33.0)	655 (34.6)	0.194	348 (38.9)	134 (45.4)	0.049
Statin	5,425 (98.3)	1,856 (98.0)	0.507	876 (98.0)	291 (98.6)	0.468
Beta blocker	2,762 (50.0)	1,009 (53.3)	0.014	422 (47.2)	175 (59.3)	<0.001
CCB	1,781 (32.3)	701 (37.0)	<0.001	325 (36.4)	138 (46.8)	0.001
Aspirin	5,423 (98.2)	1,852 (97.8)	0.256	877 (98.1)	292 (99.0)	0.306
Clopidogrel	5,338 (96.7)	1,813 (95.8)	0.059	805 (90.0)	267 (90.5)	0.817
Ticagrelor	223 (4.0)	106 (5.6)	0.004	146 (16.3)	58 (19.7)	0.189
Bivalirudin	76 (1.4)	39 (2.1)	0.038	95 (10.6)	33 (11.2)	0.788
Distribution of lesion vessels						
LM	329 (6.0)	103 (5.4)	0.406	54 (6.0)	13 (4.4)	0.292
LAD	2,991 (54.2)	978 (51.7)	0.058	488 (54.6)	154 (52.2)	0.477
LCX	897 (16.3)	323 (17.1)	0.411	150 (16.8)	41 (13.9)	0.243
RCA	1,563 (28.3)	570 (30.1)	0.136	246 (27.5)	96 (32.5)	0.098
AHA/ACC type B2/C, N (%)	1,619 (39.3)	561 (29.6)	0.801	554 (62.0)	193 (65.4)	0.287
Coronary calcification, N (%)	612 (11.1)	204 (10.8)	0.710	92 (10.3)	29 (9.8)	0.821
CTO, N (%)	0 (0.0)	0 (0.0)	1.000	0	0	1.000
FFR/IVUS/OCT, N (%)	487 (8.8)	192 (10.1)	0.086	173 (19.4)	60 (20.3)	0.711
Stents number≥ 2, N (%)	1,937 (35.1)	729 (38.5)	0.007	142 (15.9)	45 (15.3)	0.797
Total stent length (mm)	36.00±20.77	38.57±22.59	<0.001	38.61±21.64	40.67±22.39	0.142
Stent diameter≥2.5mm, N (%)	4,934 (89.4)	1,696 (89.6)	0.798	830 (92.8)	272 (92.2)	0.715
Ballon pre-dilation, N (%)	4,704 (85.2)	1,646 (87.0)	0.063	826 (91.3)	265 (89.8)	0.454
Ballon post-dilation, N (%)	5,043 (91.4)	1,724 (91.1)	0.703	880 (98.4)	288 (97.6)	0.362

Values are expressed as mean ± SD or n (%) unless otherwise indicated. NLR, neutrophil to lymphocyte ratio; WBC, white blood cell; PLT, platelet; CRP, C-creative protein; BMI, Body Mass Index; LDL-C, low-density lipoprotein cholesterol; CABG, Coronary Artery Bypass Grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; ACEI, Angiotensin-Converting Enzyme Inhibitors; ARB, Angiotensin receptor blocker; CCB, Calcium channel blocker; LM, left main; LAD, left anterior descending branch; LCX, left circumflex artery; RCA, right coronary artery; AHA/ACC, American College of Cardiology/American Heart Association; CTO, chronic total occlusion; FFR, Fractional Flow Reserve; IVUS, intravascular ultrasound; OCT, optical coherent tomography.

Table S4 Baseline characteristics according to inflammatory trend

	I tertile (n=3,800)	II tertile (n=3,613)	P value
Age (Years)	65.86±9.94	67.25±10.44	<0.001
Man, N (%)	2,585 (68.0)	2,675 (74.0)	<0.001
BMI	24.37±3.14	24.78±3.10	<0.001
Current smoking, N (%)	771 (20.3)	863 (23.9)	<0.001
Diabetes, N (%)	894 (23.5)	1,002 (27.7)	<0.001
Hypertension, N (%)	2,507 (66.0)	2,605 (72.1)	<0.001
Previous MI, N (%)	315 (8.3)	301 (8.3)	0.948
Previous PCI, N (%)	1,188 (31.3)	1,002 (27.7)	0.001
Previous CABG, N (%)	19 (0.5)	27 (0.7)	0.175
Laboratory examination			
NLR	2.14±0.77	3.49±1.65	<0.001
WBC ($\times10^9$/L)	5.41±1.18	7.30±1.62	<0.001
PLT ($\times10^9$/L)	162.99±47.30	181.53±56.59	<0.001
CRP (mg/L)	1.17±1.16	2.81±2.20	<0.001
LDL-C (mmol/L)	2.00±0.83	2.06±0.84	<0.001
Renal insufficiency, N (%)	307 (8.1)	575 (15.9)	<0.001
Baseline medication, N (%)			
ACEI	962 (35.3)	977 (27.0)	0.091
ARB	1,192 (31.4)	1,283 (35.5)	<0.001
Statin	3,744 (98.5)	3,537 (97.9)	0.040
Beta blocker	1,867 (49.1)	1,904 (52.7)	0.002
CCB	1,160 (30.5)	1,322 (36.6)	<0.001
Aspirin	3,737 (98.3)	3,538 (97.9)	0.183
Clopidogrel	3,695 (97.2)	3,456 (95.7)	<0.001
Ticagrelor	124 (3.3)	205 (5.7)	<0.001
Bivalirudin	45 (1.2)	70 (1.9)	0.009
Distribution of lesion vessels, N (%)			
LM	212 (5.6)	220 (6.1)	0.349
LAD	2,103 (55.3)	1,866 (51.6)	0.001
LCX	599 (15.8)	621 (17.2)	0.098
RCA	1,057 (27.8)	1,076 (29.8)	0.062
AHA/ACC type B2/C, N (%)	1,101 (29.0)	1,079 (29.9)	0.400
Coronary calcification, N (%)	388 (10.2)	428 (11.8)	0.025
CTO, N (%)	0 (0.0)	0 (0.0)	1.000
FFR/IVUS/OCT, N (%)	361 (9.5)	318 (8.8)	0.297
Stents number ≥2, N (%)	1,282 (33.7)	1,384 (38.3)	<0.001
Total stent length (mm)	35.15±20.20	38.24±22.25	<0.001
Stent diameter ≥2.5 mm, N (%)	3,422 (90.1)	3,208 (88.8)	0.077
Ballon pre-dilation, N (%)	3,244 (85.4)	3,106 (86.0)	0.462
Ballon post-dilation, N (%)	3469 (91.3)	3,298 (91.3)	0.990

Values are expressed as mean ± SD or n (%) unless otherwise indicated. NLR, neutrophil to lymphocyte ratio; WBC, white blood cell; PLT, platelet; CRP, C-creative protein; BMI, Body Mass Index; LDL-C, low-density lipoprotein cholesterol; CABG, Coronary Artery Bypass Grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; ACEI, Angiotensin-Converting Enzyme Inhibitors; ARB, Angiotensin receptor blocker; CCB, Calcium channel blocker; LM, left main; LAD, left anterior descending branch; LCX, left circumflex artery; RCA, right coronary artery; AHA/ACC, American College of Cardiology/American Heart Association; CTO, chronic total occlusion; FFR, Fractional Flow Reserve; IVUS, intravascular ultrasound; OCT, optical coherent tomography.

Table S5 Logistics regression of the virtual variable inflammatory trend

Variable	Simple regression				Multiple regression			
	OR	95% CI		P	OR	95% CI		P
Inflammatory trend	1.365	1.192	1.564	<0.001	1.202	1.042	1.387	0.012*
Age	1.025	1.018	1.032	<0.001	1.021	1.013	1.029	<0.001*
Man	0.740	0.641	0.854	<0.001	0.739	0.631	0.866	<0.001*
BMI	0.979	0.957	1.000	0.054				
Current smoking	0.881	0.683	0.962	0.016	0.969	0.802	1.171	0.745
Diabetes	1.157	0.995	1.346	0.059				
Hypertension	1.448	1.240	1.629	<0.001	1.161	0.985	1.368	0.075
LDL-C >1.8 mmol/L	0.885	0.773	1.014	0.078				
Renal insufficiency	1.766	1.472	2.118	<0.001	1.294	1.057	1.584	0.013*
CCB	1.097	0.952	1.264	0.199				
AHA/ACC TypeB2/C	1.346	1.166	1.552	<0.001	1.150	0.989	1.338	0.070*
Balloon pre-dilation	1.334	1.082	1.645	0.007	1.161	0.933	1.445	0.181
Balloon post-dilation	1.784	1.332	2.388	<0.001	1.419	1.048	1.919	0.023*
Total stent length (Every 10 mm)	1.325	1.288	1.363	<0.001	1.312	1.275	1.351	<0.001
Stent size >2.5 mm	1.067	0.852	1.335	0.141				

Dichotomized values with statistical significance are described in the table. *, P<0.05. NLR, neutrophil to lymphocyte ratio; WBC, white blood cell; PLT, platelet; CRP, C-creative protein; BMI, Body Mass Index; LDL-C, low-density lipoprotein cholesterol; CABG, Coronary Artery Bypass Grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; ACEI, Angiotensin-Converting Enzyme Inhibitors; ARB, Angiotensin receptor blocker; CCB, Calcium channel blocker; LM, left main; LAD, left anterior descending branch; LCX, left circumflex artery; RCA, right coronary artery; AHA/ACC, American College of Cardiology/American Heart Association; CTO, chronic total occlusion; FFR, Fractional Flow Reserve; IVUS, intravascular ultrasound; OCT, optical coherent tomography.

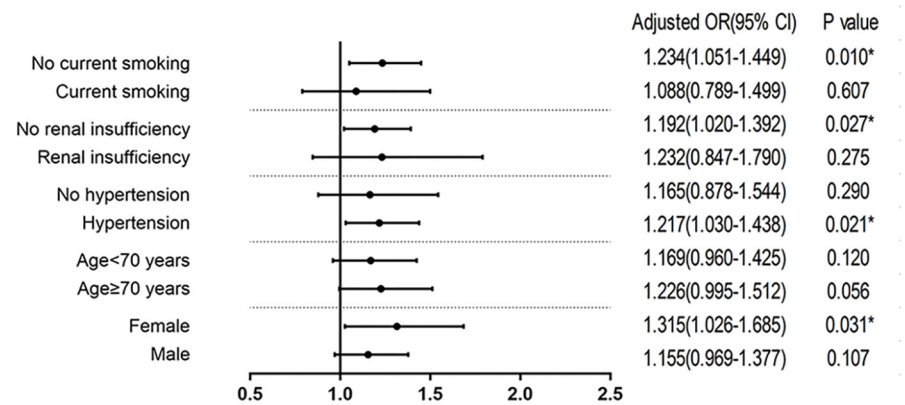

Figure S1 The relationship between inflammatory trend and PMI was analysed by multivariable logistic regression analysis in predefined subgroups. *, P<0.05. PMI, periprocedural myocardial infarction; CRP, C-reactive protein; WBC, white blood cell; NLR, neutrophil to lymphocyte ratio.