# Neutrophil to Lymphocyte Ratio in Acute ST-Segment Elevation Myocardial Infarction

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**Abstract:** *Background:* Spontaneous early patency of infarct-related artery (IRA) on arrival for primary percutaneous coronary intervention is associated with better short- and long-term prognosis in patients with ST-segment elevation myocardial infarction (STEMI). We aimed to investigate whether the hemographic parameters on admission are associated with spontaneous IRA patency. *Methods:* This was a retrospective study of 1,625 patients with acute STEMI who underwent primary percutaneous coronary intervention <12 hours after the onset of symptoms. *Results:* Angiography showed patent IRA (prethrombolysis in myocardial infarction [TIMI] grade 3 flow) in 160 (9.8%) patients. Neutrophil count on admission ($7.8 \pm 2.4 \times 10^3/\mu L$ versus $9.7 \pm 3.8 \times 10^3/\mu L$; $P < 0.001$) was significantly lower and lymphocyte count ($2.4 \pm 1.0 \times 10^3/\mu L$ versus $1.9 \pm 1.1 \times 10^3/\mu L$; $P < 0.001$) on admission was significantly higher in the patent IRA group. Neutrophil to lymphocyte ratio (NLR) was significantly lower in the patent IRA group ($4.1 \pm 3.2$ versus $6.9 \pm 5.5$; $P < 0.001$). Admission leukocyte counts ($13 \pm 4.0 \times 10^3/\mu L$ versus $12 \pm 3.4 \times 10^3/\mu L$; $P < 0.001$) and NLR ($7.2 \pm 5.8$ versus $5.5 \pm 4.4$; $P < 0.001$) of the patients with TIMI thrombus score ≥4 were significantly higher than patients with TIMI thrombus score <4. In the multivariate analysis, NLR ≥4.5 (3.17 [95% confidence interval: 2.04–4.92]; $P < 0.001$) was found to be independently predicting an occluded IRA on initial angiography with a sensitivity of 62.7% and a specificity of 70%. *Conclusions:* NLR on admission is significantly related to angiographic thrombus burden and spontaneous early IRA patency in patients with acute STEMI.

**Key Indexing Terms:** Myocardial infarction; Infarct-related artery patency; Neutrophil to lymphocyte ratio; Thrombus burden; Reperfusion. **[Am J Med Sci 2014;348(1):37–42.]**

Plaque rupture and subsequent coronary thrombosis are the main mechanisms initiating acute coronary syndromes.[1] Because atherothrombosis is a dynamic process, the presentation of the patient depends on the degree of thrombotic occlusion in the infarct-related artery (IRA). The presence of preprocedural thrombolysis in myocardial infarction (TIMI) grade 3 flow in the IRA was previously defined as spontaneous reperfusion or IRA patency.[2] Patent IRA was found to be associated with better epicardial flow, higher left ventricular ejection fraction (LVEF), lower in-hospital and long-term mortality rates.[2–4] However, clinical studies investigating the determinants of spontaneous early IRA patency are limited.

As a marker of severity of inflammation, elevated leukocyte count has been shown to be associated with worse clinical outcomes in patients with acute coronary syndromes[5,6] and acute ST-segment elevation myocardial infarction (STEMI).[7–9] The balance between the leukocyte subtypes modulates the inflammatory response. Not only high neutrophil counts[10] but also lymphocytopenia was found to be associated with worse clinical outcomes in patients with acute STEMI.[11,12] Thus, neutrophil to lymphocyte ratio (NLR) has recently emerged as a better indicator of inflammatory state in clinical studies.[13] In patients with angiographically proven coronary artery disease, the predictive value of NLR for mortality was found better, compared with that of leukocyte count and its subtypes.[14] Likewise, NLR on admission was found to be predicting early and late clinical outcomes in patients with STEMI undergoing primary percutaneous coronary intervention (p-PCI).[15,16]

Severity of inflammation and the balance between thrombogenic activity and endogenous lytic activity determine the degree of occlusion in IRA.[17] Thus, we hypothesized that the prognostic value of leukocyte subtypes in STEMI may at least partially be linked to its possible relation to intracoronary thrombus burden and early IRA patency. We aimed to investigate whether hemographic parameters on admission are related to spontaneous early IRA patency.

## METHODS

### Study Population

We retrospectively reviewed 1,625 patients with acute STEMIs who were treated with p-PCI. The inclusion criteria were as follows: (1) presentation within the 1st 12 hours of the onset of chest pain, (2) ST elevation of at least 1 mm in 2 or more contiguous leads (2 mm for leads V1–V3), or new onset left bundle branch block and (3) being treated with stent implantation. Patent IRA was defined as the presence of preprocedural TIMI grade 3 flow. A written informed consent for the procedure was obtained from all study patients, and the study protocol was approved by the hospital's ethical committee.

### Study Protocol

All patients received chewable aspirin 300 mg and a loading dose of clopidogrel 300 to 600 mg on admission and intravenous standard heparin 70 U/kg before the procedure. All p-PCI procedures were performed by experienced interventional cardiologists through a femoral approach using a 7Fr guiding catheter. During the period of hospitalization, all patients were given acetylsalicylic acid (150 mg/d) and clopidogrel (75 mg/d). Postprocedural transthoracic echocardiography (Vivid 3 or Vivid 5; GE Vingmed Ultrasound AS, Horten, Norway) was performed during in-hospital period. The LVEF was calculated using the biplane Simpson's method.

All coronary hemodynamic data that had been recorded and stored off-line were analyzed by 2 independent investigators. Preprocedural TIMI flow grade, IRA, severity of the lesions and number of diseased vessels were noted. Angiographic thrombus burden was graded using TIMI thrombus classification, and TIMI

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*Submitted May 21, 2013; accepted in revised form August 6, 2013.*

*The authors have no financial or other conflicts of interest to disclose.*

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thrombus score >4 was defined as high-grade angiographic thrombus. Postprocedural final TIMI flow grade and myocardial blush grade were also assessed, as described previously.[18]

Clinical and demographic properties of the patients were recorded from hospital files and computer records. Blood samples for hemographic and biochemical parameters, including serum C-reactive protein (IMMAGE Nephelometer; Beckman Coulter, Inc, Fullerton, CA) were obtained on admission.

### Statistical Analysis

Continuous variables are expressed as mean ± standard deviation. Categorical variables are expressed as percentages. Group means for continuous variables were compared using independent-samples *t* test. Categorical variables were compared using $\chi^2$ test. Pearson's or Spearman's correlation tests were used for the correlation analysis. Multivariate logistic regression analysis was applied to identify the independent predictors of IRA patency. All variables showing significance values <0.05 on univariate analysis (pain-to-door time, Killip class ≥2, leukocyte count, NLR, CRP, baseline troponin I and low-density lipoprotein cholesterol) were included in the multivariate analysis. NLR was included in the model both as a continous variable and a categorical variable dichotomized according to the optimal cut-off value of 4.5 determined by receiver operating characteristics (ROC) curve analysis. Two-tailed *P* values <0.05 were considered to indicate statistical significance. SPSS version 11.5 (SPSS, Inc, Chicago, IL) was used in all statistical analysis.

## RESULTS

### Study Patients

The study population consists of 1,625 patients with acute STEMIs (82% men; mean age, 56 ± 12 years). In the baseline angiography, 160 (9.8%) patients had patent IRA (pre-TIMI grade 3 flow). The patients were subgrouped according to the spontaneous early IRA patency. There was no significant difference between patent IRA and occluded IRA groups with respect to age, gender, infarct localization and the frequency of diabetes and hypertension. Although the patients in the patent IRA group were transferred to the hospital earlier (140 ± 111 versus 175 ± 122 minutes; $P = 0.001$), door to balloon times were statistically similar (31 ± 7.3 versus 32 ± 7.2 minutes; $P = 0.25$). In the occluded IRA group, Killip class ≥2 (9.4% versus 16%; $P = 0.024$) and cardiogenic shock on admission were significantly more frequent (1.3% versus 5.3%; $P = 0.019$). There was no significant difference between the 2 groups with respect to previous medication, periprocedural tirofiban use and clopidogrel loading doses (Table 1).

TABLE 1. Baseline and procedural characteristics

| Variables | Patent IRA (n = 160) | Occluded IRA (n = 1465) | *P* |
|---|---|---|---|
| Age (yr) | 56 ± 11 | 56 ± 12 | 0.56 |
| Female, n (%) | 28 (18) | 274 (19) | 0.71 |
| Diabetes mellitus, n (%) | 39 (24) | 334 (23) | 0.65 |
| Hypertension, n (%) | 64 (40) | 582 (39.7) | 0.94 |
| Dyslipidemia, n (%) | 73 (46) | 565 (39) | 0.10 |
| Current smoker, n (%) | 88 (55) | 783 (53) | 0.70 |
| Previous myocardial infarction, n (%) | 6 (3.8) | 85 (5.8) | 0.28 |
| Previous PCI, n (%) | 11 (6.9) | 116 (7.9) | 0.64 |
| Previous CABG, n (%) | 3 (1.9) | 45 (3.1) | 0.39 |
| Anterior wall infarction, n (%) | 82 (51) | 727 (50) | 0.69 |
| Pre-infarction angina, n (%) | 41 (26) | 358 (24) | 0.74 |
| Pain-to-door time (min) | 140 ± 111 | 175 ± 122 | 0.001 |
| Door-to-balloon time (min) | 31 ± 7.3 | 32 ± 7.2 | 0.25 |
| Killip class ≥2, n (%) | 15 (9.4) | 237 (16) | 0.024 |
| Shock on admission, n (%) | 2 (1.3) | 77 (5.3) | 0.019 |
| Prior medication, n (%) | | | |
| Aspirin | 15 (9.4) | 129 (8.8) | 0.81 |
| Clopidogrel | 0 (0.0) | 28 (1.9) | 0.10 |
| β-blocker | 15 (9.4) | 165 (11) | 0.47 |
| ACE-I/ARB | 29 (18) | 305 (21) | 0.42 |
| Statin | 35 (22) | 276 (19) | 0.35 |
| Tirofiban use before procedure, n (%) | 64 (40) | 653 (45) | 0.26 |
| Clopidogrel loading dose, 600 mg, n (%) | 158 (99) | 1440 (98) | 0.66 |
| IRA, n (%) | | | |
| Left anterior descending | 83 (52) | 724 (49) | 0.55 |
| Circumflex | 24 (15) | 189 (13) | 0.45 |
| Right coronary artery | 51 (32) | 517 (35) | 0.39 |
| Left main/diagonal/ saphenous | 2 (1.3) | 27 (1.8) | 1 |
| Three-vessel disease, n (%) | 12 (7.5) | 161 (11) | 0.17 |
| PCI with stent implantation, n (%) | 157 (98) | 1376 (94) | 0.029 |
| Final TIMI 3 flow, n (%) | 157 (98) | 1275 (87) | <0.001 |
| Myocardial blush grade 3, n (%) | 91 (72) | 441 (39) | <0.001 |
| Peak creatine kinase-MB (IU/L) | 125 ± 97 | 241 ± 182 | <0.001 |
| Peak troponin I (ng/mL) | 53 ± 63 | 126 ± 111 | <0.001 |
| Postprocedural LVEF (%) | 52 ± 6.2 | 46 ± 8.2 | <0.001 |

IRA, infarct-related artery; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction.

### Laboratory Parameters on Admission and Infarct-related Artery Patency

Of the hemographic parameters, leukocyte (11 ± 2.9 × $10^3/\mu L$ versus 12 ± 3.9 × $10^3/\mu L$; $P < 0.001$) and neutrophil counts (7.8 ± 2.4 × $10^3/\mu L$ versus 9.7 ± 3.8 × $10^3/\mu L$; $P < 0.001$) on admission were significantly lower and lymphocyte count (2.4 ± 1.0 × $10^3/\mu L$ versus 1.9 ± 1.1 × $10^3/\mu L$; $P < 0.001$) on admission was significantly higher in the patent IRA group. Accordingly, NLR was also significantly lower in the patent IRA group (4.1 ± 3.2 versus 6.9 ± 5.5; $P < 0.001$). Troponin I (3.0 ± 5.5 versus 5.4 ± 9.6 ng/mL; $P = 0.002$) level was significantly lower, and low-density lipoprotein cholesterol level was significantly higher (123 ± 43 versus 114 ± 38 mg/dL; $P = 0.008$) in the patent IRA group. There was no significant difference with respect to other hemographic and biochemical parameters (Table 2).

CRP levels were significantly lower in the patent IRA group (10 ± 7.7 versus 14 ± 13 mg/L; $P = 0.001$). Despite