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Prognostic value of neutrophil/lymphocyte ratio in patients with ST-elevated myocardial infarction undergoing primary coronary intervention: A prospective, multicenter study

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ABSTRACT

Objective: The pre-procedural neutrophil to lymphocyte ratio (N/L) is associated with adverse outcomes among patients with coronary artery disease but its prognostic value in ST-segment elevation myocardial infarction (STEMI) has not been fully investigated. This study evaluated the relations between pre-procedural N/L ratio and the in-hospital and long-term outcomes in STEMI patients undergoing primary percutaneous coronary intervention (PCI).

Methods: A total of 682 STEMI patients presented within the first 6 h of symptom onset were enrolled and stratified according to tertiles of N/L ratio based on the blood samples obtained in the emergency room upon admission.

Results: The mean follow-up period was 43.3 months (1–131 months). In-hospital in-stent thrombosis, non-fatal myocardial infarction, and cardiovascular mortality increased as the N/L tertile ratio increased ($p<0.001$, $p<0.001$, $p=0.003$, respectively). Long-term in-stent thrombosis, non-fatal myocardial infarction and cardiovascular mortality also increased as the N/L ratio increased ($p<0.001$, $p<0.001$, $p=0.002$, respectively). On multivariate analysis, N/L ratio remained an independent predictor for both in-hospital (OR 1.189, 95% CI 1.000–1.339; $p<0.001$) and long-term major (OR 1.228, 95% CI 1.136–1.328; $p<0.001$) adverse cardiac events.

Conclusion: The N/L ratio was an independent predictor of both in-hospital and long-term adverse outcomes among STEMI patients undergoing primary PCI. Our findings suggest that this inexpensive, universally available hematological marker may be incorporated into the current established risk assessment model for STEMI.

1. Introduction

Inflammation plays a role in the initiation and progression of the atherosclerotic process [1,2]. Due to a growing recognition of its role, recent studies have focused on inflammatory markers and their associations with outcomes in patients with ST-segment elevation myocardial infarction (STEMI). Recently, our single center study demonstrated that pre-procedural neutrophil/lymphocyte (N/L) ratio is an independent predictor for impaired coronary flow after primary percutaneous coronary intervention (PCI) and in-hospital major adverse cardiac events (MACE) in STEMI patients [3]. Published studies evaluating the prognostic value of N/L ratio for long-term outcomes in STEMI patients are limited by single-center recruitment and considerably small sample size [4,5].

We therefore evaluated the relations between the pre-procedural N/L ratio and the in-hospital and long-term outcomes in STEMI patients undergoing primary PCI in this prospective multicenter study.

2. Methods

2.1. Study population

A total of 1016 consecutive STEMI patients presented within 6 h from symptom onset were prospectively screened. Of which, 334 patients were excluded because of not receiving primary PCI ($n=117$), missing laboratory values ($n=135$) or lacking clinical follow-up data ($n=82$). The final study population consisted of 682 patients. All participants were treated with primary PCI. STEMI was defined as: typical chest pain >30 min with ST elevation of

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Table 1
Baseline characteristics.

Variable	Neutrophil/lymphocyte ratio			p value
	Tertile 1 (<2.3) (n=227)	Tertile 2 (2.3–4.4) (n=228)	Tertile 3 (>4.4) (n=227)	
Age (year)	60.0±12.5	60.9±12.0	61.7±12.4	0.344
Men	184 (81%)	172 (75%)	179 (79%)	0.340
Hypertension	74 (33%)	90 (40%)	76 (34%)	0.247
Diabetes mellitus	50 (22%)	69 (30%)	64 (28%)	0.119
Smoke	100 (44%)	101 (44%)	94 (41%)	0.789
Previous coronary artery disease	30 (13%)	52 (23%)	43 (19%)	0.029
Body mass index (kg/m^2)	25.4±3.9	25.7±3.3	25.1±3.1	0.201
Peak creatinine kinase-MB (U/l)	47.3±25.0	53.9±35.0	49.2±27.0	0.615
Troponin-I (ng/ml)	5.7±4.3	7.2±5.1	4.6±3.9	0.135
High sensitive C-reactive protein (mg/l)	2.2±1.9	4.9±3.3	7.6±5.9	<0.001
Glomerular filtration rate (ml/min/1.73 m^2)	85.3±25.1	84.1±23.5	85.4±24.1	0.674
LVEF on admission (%)	49.3±11.6	48.8±15.1	47.9±13.0	0.199
Triglyceride (mg/dl)	138.3±80.6	131.3±68.4	128.3±85.8	0.389
Low density lypoprotein (mg/dl)	125.5±55.3	119.3±36.1	121.5±59.3	0.432
High density lypoprotein (mg/dl)	37.1±9.3	38.4±9.8	38.2±10.5	0.299
Total cholesterol (mg/dl)	187.2±46.9	184.2±45.8	180.6±50.8	0.349
Serum glucose (mg/dl)	155.0±69.2	169.3±102.5	174.5±95.2	0.062
Hemoglobin (g/l)	14.3±2.1	14.3±2.7	14.1±1.9	0.536
Platelet (/mm^3)	244.2±69.8	242.8±63.9	259.6±71.6	0.359
White blood cell (10^3/μl)				
Neutrophil (%)	56.0±7.1	68.4±5.8	80.3±5.9	<0.001
Lymphocyte (%)	32.4±6.1	21.7±2.9	12.8±3.2	<0.001
Eosinophil (%)	2.2±1.2	2.3±1.2	2.1±1.3	0.695
Monocyte (%)	8.3±4.6	8.2±3.9	8.4±4.3	0.504
Neutrophil/lymphocyte ratio	1.8±0.4	3.2±0.5	6.8±2.5	<0.001
Glycoprotein IIb/IIIa antagonist	39 (17%)	45 (20%)	49 (22%)	0.493
Pain-to-balloon time (h)	4.0±1.7	4.3±1.6	4.4±1.5	0.006
Hospitalization (day)	7.5±2.3	8.2±2.5	7.8±2.6	0.374
Previous medications				
Angiotensin-converting enzyme inhibitors	133 (59%)	141 (62%)	145 (64%)	0.508
B-blocker	115 (51%)	127 (56%)	131 (58%)	0.303
Statin	112 (49%)	120 (53%)	124 (55%)	0.525
Aspirin	110 (49%)	126 (55%)	132 (58%)	0.106
Diuretics	31 (14%)	32 (14%)	35 (15%)	0.853
infract-related artery				
Left anterior descending	99 (44%)	111 (49%)	109 (48%)	0.500
Right coronary	76 (24%)	68 (30%)	78 (34%)	0.549
Left circumflex	50 (22%)	48 (21%)	40 (18%)	0.471
Number of coronary arteries narrowed				
1	152 (67%)	127 (56%)	118 (52%)	0.003
>1	75 (33%)	101 (44%)	109 (48%)	
Primary percutaneous coronary intervention				
Stent implantation	220 (97%)	215 (94%)	218 (96%)	0.411
Bare metal stent	198 (87%)	201 (88%)	197 (87%)	
Drug eluting stent	22 (10%)	14 (6%)	21 (9%)	
Stent diameter (mm)	3.2±0.4	3.3±0.8	3.2±0.4	0.540
Stent length (mm)	17.4±4.3	17.5±4.3	17.9±4.8	0.414
No-reflow	34 (15%)	70 (31%)	119 (52%)	<0.001

Data are expressed as mean±standard deviation for normally distributed data and percentage (%) for categorical variables.

>1 mm in at least 2 consecutive leads on the electrocardiogram or new onset left bundle brunch block. Based on the N/L ratio upon admission, patients were stratified into tertiles (1st tertile: <2.3, 2nd tertile: 2.3–4.4 and 3rd tertile: >4.4). No-reflow was defined as post-PCI Thrombolysis in Myocardial Infarction (TIMI) Flow Grade 0, 1, or 2 [1,2,6]. Additional exclusion criteria included treatment with fibrinolytics in the previous 24 h, active infection, past history of a systemic inflammatory process, malignancy, end-stage liver disease, and renal failure. Informed consent was obtained from all patients and the local Ethics Committee approved the protocol.

2.2. Coronary angiography and PCI procedure

All primary PCI were performed using the standard femoral approach with a 7-French guiding catheter. After administration of 5000 IU of intravenous heparin (70 U/kg) and a 300 mg loading dose of both aspirin and clopidogrel, direct stenting was performed whenever possible, and in the remaining cases, balloon pre-dilatation was performed. The operator determined the choice of stents (bare metal or drug-eluting stent). In patients who were treated with tirofiban, the agent was administrated after primary PCI in the coronary care unit. The systemic bolus of tirofiban was used at operator's discretion, as was the 12-hour continuous infusion. In addition, an intracoronary injection of 100 μg nitroglycerine was given during the procedure to achieve maximal coronary artery dilation.

2.3. Laboratory analysis and echocardiography

In all patients, antecubital venous blood samples for laboratory analysis were collected at emergency rooms. High-sensitivity C-reactive protein (Hs-CRP) was measured using a BN2 model nephelometer (Dade-Behring) within 5 min of sampling. Common blood counting parameters were measured by a Sysmex K-1000 auto analyzer within 5 min of sampling. Transthoracic echocardiography was performed on each patient immediately after primary PCI in the coronary care unit. All measurements were performed using a commercially available machine (Vivid 7®, GE Vingmed Ultrasound A/S, Horten, Norway) with a 3.5-MHz transducer. Simpson's method was used to assess the left ventricular ejection fraction (LVEF), as recommended by the American Society of Echocardiography [7].

2.4. Follow-up and major adverse cardiac events

Follow-up data were obtained from hospital records or through patient interviews (in person or by telephone), their families, or patient's primary care physicians. MACE were defined as in-stent thrombosis, non-fatal MI, and cardiovascular mortality during the in-hospital or long-term follow-up period. In-stent thrombosis was defined as the presence of angiographically documented total occlusion. Non-fatal MI was defined as the recurrence of chest pain and/or the development of new ECG changes accompanied by a new rise ≥20% of cardiac biomarkers measured during the event. Cardiovascular mortality