Relation of Neutrophil to Lymphocyte Ratio With Periprocedural Myocardial Damage in Patients Undergoing Elective Percutaneous Coronary Intervention

Edoardo Bressi, MD, Fabio Mangiacapra, MD, PhD*, Elisabetta Ricottini, MD, Ilaria Cavallari, MD, Iginio Colaiori, MD, Giuseppe Di Gioia, MD, Antonio Creta, MD, and Germano Di Sciascio, MD

Neutrophil to lymphocyte ratio (NLR) has been proposed as a marker of cardiovascular risk. The potential relation between NLR and periprocedural myocardial damage after percutaneous coronary intervention (PCI) is unclear. We enrolled 502 consecutive patients with stable coronary artery disease undergoing elective PCI. Blood samples were drawn in all patients at baseline, 6 hours, and 24 hours after PCI for complete blood cell count and cardiac biomarkers (creatine kinase-MB and troponin T [Tn-T]) assessment. NLR was calculated as the ratio between the absolute number of neutrophil over the absolute number of lymphocyte. Periprocedural myocardial infarction (PMI) was defined according to the 2012 universal definition of myocardial infarction. In the overall population, a significant postprocedural increase in NLR was observed (3.255 [2.763 to 3.995] at baseline, 4.430 [3.390 to 6.020] at 6 hours, 4.720 [3.940 to 5.750] at 24 hours, p <0.0001). PMI occurred in 33 patients (6.6%). Baseline NLR was similar in patients with and without PMI (3.250 [2.820 to 3.885] vs 3.260 [2.750 to 4.000], p = 0.898); however, patients who developed PMI showed significantly higher NLR both at 6 hours (5.750 [4.360 to 9.095] vs 4.370 [3.370 to 5.950], p <0.001) and 24 hours (5.180 [4.440 to 8.065] vs 4.670 [3.920 to 5.710], p = 0.003). Among patients who developed PMI, periprocedural NLR increase showed a moderate positive correlation with both creatine kinase-MB (rho = 0.377, p = 0.031) and troponin T increase (rho = 0.506, p = 0.003). In conclusion, preprocedural NLR values do not impact on the occurrence of PMI during elective PCI; however, PCI procedures induce a significant increase in NLR that seems to be proportional to the magnitude of periprocedural myocardial damage. **(Am J Cardiol 2016;118:980–984)**

Neutrophil to lymphocyte ratio (NLR), an inexpensive parameter easily acquirable from complete blood count, has been recently proposed as a marker of cardiovascular risk,[1,2] able to predict clinical outcomes in patients with both stable coronary artery disease (CAD) and acute coronary syndromes,[3,4] including those treated with percutaneous coronary intervention (PCI).[5,6] In this study, we tested the hypothesis of an association between high NLR and periprocedural myocardial necrosis in patients undergoing elective PCI.

Methods

In this observational study, we prospectively enrolled a total of 502 consecutive patients with clinically stable CAD undergoing elective PCI from February 2013 to November 2014. Exclusion criteria were acute coronary syndromes with ST-elevation, severe left ventricular dysfunction (ejection fraction <30%), chronic total occlusion, lesions with extensive calcifications requiring rotational atherectomy, bypass surgery in the previous 3 months, severe pulmonary disease, neoplasm, therapy with corticosteroids within the previous year, chronic inflammatory disease, and active infection at time of intervention. A local ethical committee approved the study, and all patients signed written informed consent for participation and data collection. All patients were on chronic aspirin treatment and received either 600-mg clopidogrel loading dose (at least 6 hours before intervention) or were on therapy with clopidogrel 75 mg/day for at least 5 days. Procedural anticoagulation was achieved by administration of unfractionated heparin (100 U/kg) in all patients. Technicalities of the procedure, including the use of glycoprotein IIb/IIIa inhibitors, were left to the operator's discretion. Procedural success was defined as a reduction in percent diameter stenosis to below 30% and the presence of Thrombolysis In Myocardial Infarction flow grade 3 in the main vessel and all side branches ≥2 mm in diameter. Blood samples were drawn in all patients at pre-PCI (baseline), 6 hours, and 24 hours after intervention for complete blood cell count and cardiac biomarkers assessment. At all time points, NLR was derived for all patients using the whole blood cell count considering for each patient the ratio obtained from the absolute number of neutrophil over the absolute number of lymphocyte. For whole blood cell count, fluorescent flow cytometry and hydrodynamic focusing technologies were used (XT-4000i hematology analyzer Sysmex; Mississauga, Ontario, Canada). Delta NLR was defined as the maximal variation of NLR

Department of Cardiovascular Sciences, Campus Bio-Medico University, Rome, Italy. Manuscript received March 9, 2016; revised manuscript received and accepted July 5, 2016.

See page 983 for disclosure information.

*Corresponding author: Tel: (+39) 06-225411612; fax: (+39) 06-225411638.

E-mail address: f.mangiacapra@unicampus.it (F. Mangiacapra).

0002-9149/16/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2016.07.015

Table 1
Clinical characteristics

Variable	All patients (n=502)	Periprocedural MI		p value
		Yes (n=33)	No (n=469)	
Mean age (years)	67.0 ± 9.8	67.5 ± 11.7	66.9 ± 9.6	0.724
Men	393 (78%)	29 (88%)	364 (78%)	0.196
Body mass index (kg/m^2)	27.8 ± 4.1	26.8 ± 4.5	27.9 ± 4.0	0.207
Hypertension*	409 (81%)	26 (79%)	382 (82%)	0.681
Dyslipidemia†	357 (71%)	23 (70%)	334 (71%)	0.852
Diabetes Mellitus	208 (41%)	11 (33%)	197 (42%)	0.328
Smoker	100 (20%)	6 (18%)	94 (20%)	0.796
LV ejection fraction (%)	55.4 ± 7.9	56.6 ± 6.0	55.3 ± 8.0	0.382
Prior myocardial infarction	188 (37%)	14 (42%)	174 (37%)	0.541
Prior percutaneous coronary intervention	209 (42%)	11 (33%)	198 (42%)	0.312
Prior coronary bypass	31 (6%)	2 (6%)	29 (6%)	1.000
Chronic kidney disease	90 (18%)	4 (12%)	86 (18%)	0.484
Clinical presentation				0.569
Stable angina pectoris	331 (66%)	20 (61%)	311 (66%)	
NSTE-ACS	171 (34%)	13 (39%)	158 (34%)	
N° of narrowed coronary arteries	1.76 ± 0.79	1.79 ± 0.78	1.75 ± 0.79	0.817

Data are expressed as mean ± SD or as number (percentage).
MI = myocardial infarction; NSTE-ACS = non-ST segment elevation acute coronary syndrome.
* Systolic blood pressure: >140 mm Hg and/or diastolic blood pressure >90 mm Hg or current antihypertensive treatment.
† Total cholesterol >200 mg/dl or statin therapy.

Table 2
Procedural characteristics and laboratory data

Variable	All patients (n=502)	Periprocedural MI		p value
		Yes (n=33)	No (n=469)	
Multivessel PCI	96 (19%)	4 (12%)	92 (20%)	0.611
Lesion Type				0.117
A	91 (15%)	3 (8%)	88 (15%)	
B1	231 (38%)	10 (27%)	221 (39%)	
B2	191 (32%)	18 (49%)	173 (31%)	
C	89 (15%)	6 (16%)	83 (15%)	
Bifurcation Lesion	44 (7%)	7 (19%)	37 (7%)	0.013
No. of stent implanted	1.41 ± 0.91	1.55 ± 0.83	1.40 ± 0.91	0.382
Total stent length (mm)	18.79 ± 8.32	19.82 ± 8.16	18.71 ± 8.34	0.460
Stent diameter (mm)	2.94 ± 1.31	2.94 ± 0.87	2.94 ± 1.35	0.972
Glycoprotein IIb/IIIa inhibitors	38 (6%)	3 (8%)	35 (6%)	0.501
Procedural success	499 (99%)	32 (97%)	494 (99%)	0.176
Neutrophil count				
Pre-PCI (cells/microl)	3962 ± 1392	4090 ± 1265	3952 ± 1401	0.582
6 hours (cells/microl)	5240 ± 2104	6583 ± 2765	5144 ± 2018	<0.001
24 hours (cells/microl)	5391 ± 1759	6591 ± 1977	5305 ± 1713	<0.001
Lymphocyte count				
Pre-PCI (cells/microl)	1143 ± 324	1214 ± 373	1138 ± 320	0.196
6 hours (cells/microl)	1104 ± 346	1054 ± 397	1107 ± 342	0.390
24 hours (cells/microl)	1118 ± 368	1168 ± 438	1115 ± 363	0.425

Data are expressed as mean ± SD or as number (percentage).
MI = myocardial infarction; PCI = percutaneous coronary intervention.

values from baseline to post-PCI. Cardiac biomarkers creatine kinase-MB [CK-MB] and troponin T [Tn-T] levels were obtained using the Access 2 immunochemiluminometric assay (Beckman Coulter, Fullerton, California). Periprocedural myocardial infarction (PMI) was defined according to the 2012 universal definition of myocardial infarction.[7]