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Comparative Analysis of Neutrophil-to-lymphocyte Ratio, Systemic Immune-Inflammation Index, and Prognostic Nutritional Index in Acute Myocardial Infarction Patients Treated with Percutaneous Coronary Intervention

Perkütan Koroner Girişim ile Tedavi Edilen Akut Miyokart Enfarktüsü Hastalarında Nötrofil-lenfosit Oranı, Sistemik-immun İnflamasyon İndeksi ve Prognostik Nutrisyonel İndeksin Karşılaştırmalı Analizi

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

ABSTRACT

Objective: Acute myocardial infarction constitutes one of the leading reasons for cardiac mortality. Therefore, early identification of high-risk patients provides better prognostic accuracy. This study aimed to investigate the prognostic significance of novel inflammatory biomarkers such as neutrophil-to-lymphocyte ratio, systemic immune-inflammation index, and prognostic nutritional index in acute myocardial infarction patients treated with percutaneous coronary intervention and to compare their predictive abilities with each other.

Methods: A total of 828 acute myocardial infarction patients treated with percutaneous coronary intervention were retrospectively analyzed. The inflammatory indices, such as neutrophil-to-lymphocyte ratio, systemic immune-inflammation index, and prognostic nutritional index, were calculated by admission blood tests. The study population was divided into 2 groups according to the occurrence of major adverse cardiac events, which were defined as all-cause mortality, non-fatal myocardial infarction, and cerebrovascular events.

Results: Multivariate Cox regression analysis determined prognostic nutritional index as an independent predictor of major adverse cardiac event and all-cause mortality (hazard ratio: 1.05, 95% CI: 1.02-1.07, $P < .001$ for major adverse cardiac event and hazard ratio: 1.05, 95% CI: 1.02-1.09, $P = .002$ for all-cause mortality). Receiver operating characteristic curves revealed that the predictive value of prognostic nutritional index with both regard to major adverse cardiac event and all-cause mortality was better than the systemic immune-inflammation index and neutrophil-to-lymphocyte ratio (by DeLong method, area under curve$_{PNI}$ vs. area under curve$_{SII}$ z test = 2.66, $P = .008$; area under curve$_{PNI}$ vs. area under curve$_{NLR}$ z test = 2.8, $P = .006$; area under curve$_{PNI}$ vs. area under curve$_{SII}$ z test = 2.58, $P = .009$; area under curve$_{PNI}$ vs. area under curve$_{NLR}$ z test = 3.28, $P = .001$; respectively).

Conclusions: Prognostic nutritional index was demonstrated as an independent predictor of major adverse cardiac events and all-cause mortality and a more powerful prognostic index than other novel inflammatory biomarkers in acute myocardial infarction patients treated with percutaneous coronary intervention.

Key words: Acute myocardial infarction, neutrophil-to-lymphocyte ratio, prognostic nutritional index, systemic immune-inflammation index

ÖZET

Amaç: Akut miyokart enfarktüsü (AME), kardiyak mortalitenin önde gelen nedenlerinden biridir. Bu nedenle yüksek riskli hastaların erken teşhisi daha iyi prognostik bilgi sağlar. Perkütan koroner girişim (PKG) ile tedavi edilen AME hastalarında nötrofil-lenfosit oranı (NLR), sistemik immün-enflamasyon indeksi (SII) ve prognostik beslenme indeksi (PNI) gibi yeni enflamatuvar biyobelirteçlerin prognostik önemini araştırmayı ve bu biyobelirteçlerin öngörü yeteneklerini birbirleriyle karşılaştırmayı amaçladık.

Yöntemler: PKG ile tedavi edilen toplam 828 AME hastası geriye dönük olarak analiz edildi. NLR, SII ve PNI gibi enflamatuvar indeksler, başvuru kan testleri ile hesaplandı. Çalışma

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popülasyonu, tüm nedenlere bağlı mortalite, ölümcül olmayan ME ve serebrovasküler olaylar olarak tanımlanan majör advers kardiyak olayların (MACE) oluşumuna göre iki gruba ayrıldı.

Bulgular: PNI, çok değişkenli Cox regresyon analizine göre MACE ve tüm nedenlere bağlı mortalitenin bağımsız bir öngördürücüsü olarak belirlendi (Hazard oranı [HR] 1,05, %95 güven aralığı [GA] 1,02-1,07, MACE için $P < ,001$; HR 1,05, %95 GA 1,02-1,09, $P = ,002$ tüm nedenlere bağlı mortalite için). ROC eğrileri, hem MACE hem de tüm nedenlere bağlı mortalite açısından PNI'nin prediktif değerinin SII ve NLR'den daha iyi olduğunu ortaya koydu. (DeLong yöntemiyle, AUC [eğri altındaki alan] PNI ile AUCSII *z* testi=2,66, $P = ,008$; AUCPNI ile AUCNLR *z* testi = 2,8, $P = ,006$; AUCPNI ile AUCSII *z* testi = 2,58, $P = ,009$; AUCPNI ve AUCNLR *z* testi=3,28, $P = ,001$; sırasıyla).

Sonuç: PNI, PKG ile tedavi edilen AME hastalarında MACE ve tüm nedenlere bağlı mortalitenin bağımsız bir öngördürücüsü ve diğer yeni enflamatuvar biyobelirteçlerden daha güçlü bir prognostik indeks olarak gösterildi.

Anahtar Kelimeler: Akut miyokart enfarktüsü, nötrofil/lenfosit oranı, prognostik beslenme indeksi, sistemik immün-enflamasyon indeksi

Inflammation plays a crucial role in the initiation and progression process of atherosclerosis. Besides local inflammation of the myocardium, patients suffering from acute myocardial infarction (AMI) present excessive systemic inflammatory response.[1] Despite advances in percutaneous coronary intervention (PCI) techniques and medical therapy strategies, mortality still remains an important issue for patients with AMI.[2] Thus, early risk stratification in AMI patients is of clinical importance.

Systemic inflammation markers have been suggested as predictors of major adverse cardiovascular events (MACE) in patients with AMI.[3,4] In this context, it seems reasonable to use systemic inflammatory biomarkers for risk stratification of patients with AMI since they are easily calculable and readily available. Several studies have demonstrated the prognostic significance of the neutrophil-to-lymphocyte ratio (NLR), a well-accepted risk index, in patients with acute coronary syndromes.[5,6] Besides, the systemic immune inflammation index (SII), which is a new inflammatory marker that integrates neutrophils, platelets, and lymphocytes, has been examined and adopted in various malignancies.[7,8] It was found to be an independent risk factor for the severity of stable coronary artery disease (CAD) and an indicator to predict in-hospital and long-term clinical results for elderly AMI patients.[9-11] Also, recent studies reported that higher SII values were related to no-reflow phenomenon and short- and long-term mortality in patients with AMI.[12,13]

Moreover, another novel inflammatory marker, prognostic nutritional index (PNI), was examined in different malignancies, stable CAD, and many other cardiovascular diseases.[14-16] However, the utility of PNI for estimating MACE in patients with AMI remains controversial.

Therefore, we aimed to investigate the prognostic values of these novel inflammatory biomarkers on MACE in patients with AMI who underwent PCI and to compare their predictive abilities with each other.

ABBREVIATIONS

AMI	Acute myocardial infarction
AUC	Area under the curve
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CI	Confidence interval
CI-AKI	Contrast-induced acute kidney injury
CRP	C-reactive protein
DM	Diabetes mellitus
ECG	Electrocardiogram
EF	Ejection fraction
GRACE	The Global Registry of Acute Coronary Events
HL	Hyperlipidemia
HTN	Hypertension
MACE	Major adverse cardiovascular events
NLR	Neutrophil-to-lymphocyte ratio
PCI	Percutaneous coronary intervention
PNI	Prognostic nutritional index
ROC	Receiver operating characteristic
RS	Risk score
SII	Systemic immune inflammation index
STEMI	ST elevation myocardial infarction

Methods

A total of 880 AMI patients who underwent PCI between January 2018 and December 2019 were retrospectively analyzed in our single-center study. The fourth universal definition of MI was used to define the diagnostic criteria for AMI.[17] Exclusion criteria were defined as treatment with thrombolytic drugs within the previous 24 hours, need for urgent coronary artery bypass graft (CABG) surgery, contraindications for dual antiplatelet therapy, patients with atrial fibrillation or on oral anticoagulant therapy, end-stage renal and/or liver disease, active infection, malignancy, being on immunosuppressive drug therapy, severe frailty, and priorly diagnosed systemic inflammatory disease. Of the enrolled patients, a total of 25 patients were excluded due to having at least one of these exclusion criteria. Also, 18 patients who had missing laboratory data and an additional 9 patients who refused to participate in the study were excluded. This resulted in 828 patients meeting the criteria for final analysis. This study complied with the edicts of the 1975 Declaration of Helsinki and was approved by the local ethics committee of Sisli Hamidiye Etfal Education and Research Hospital (No: 3319, 8 June 2021).

Demographic, laboratory, and clinical information were gathered from the hospital's medical database. Demographic, laboratory, and clinical data included age, gender, presence of hypertension (HTN), diabetes mellitus (DM), hyperlipidemia (HL), smoking status, prior MI, CABG surgery, PCI, and stroke. Venous blood samples were obtained during hospital admission and included complete blood count and detailed biochemical parameters. The study population was divided into 2 groups according to the occurrence of MACE.

The NLR was calculated by dividing the neutrophil count by the lymphocyte count. The SII was calculated as total

peripheral platelet count × NLR.[7] Prognostic nutritional index was calculated using the following formula: 10 × serum albumin (g/ dL) + 0.005 × total lymphocyte count (per mm^3).[14] The Global Registry of Acute Coronary Events (GRACE) risk score (RS) was calculated based on the initial clinical history, electrocardiogram, and laboratory values obtained at admission. The estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.

All PCI procedures were performed by expert interventional cardiologists under local anesthesia via femoral approach. Prior to the intervention, all patients received 300 mg of aspirin and a loading dose of 600 mg clopidogrel or 180 mg ticagrelor or 60 mg prasugrel. Procedures were carried out using 6 or 7 French guiding catheters. Unfractionated heparin (100 IU/kg or reduced to 60 IU/kg if a glycoprotein IIb-IIIa inhibitor was concurrently being used) was administered to provide prolonged activating clotting time up to 250-300 seconds. Nonionic, low osmolality contrast media was used in all patients. Unless there were no contraindications, dual antiplatelet therapy was continued for 12 months after the procedure.

Major adverse cardiac events were defined as all-cause mortality, non-fatal MI, and cerebrovascular events. Data regarding adverse clinical endpoints were obtained from follow-up calls or the hospital's medical database. The median follow-up time of the study group was determined as 12 months (minimum 1 month, maximum 46 months). Mean follow-up duration in MACE (+) group was 7.1 ± 0.7 months (minimum 1 month, maximum 42 months, median 4 months), and mean follow-up duration in MACE (–) group was 13.8 ± 0.4 months (minimum 1 month, maximum 46 months, median 12 months).

Statistical Analysis

Continuous variables were reported as mean ± standard deviation; while categorical variables were presented as percentages. The Kolmogorov–Smirnov test was performed to test the normality of distributions. The Student's *t*-test or Mann–Whitney *U* test for continuous variables and the chi-square test for categorical variables were used for comparison between the study groups based on MACE. Cox regression analysis was performed to identify independent predictors of MACE and all-cause mortality. The predictive accuracy and performance of the NLR, SII, PNI, and GRACE RS were calculated with receiver operating characteristic (ROC) curves for both MACE and all-cause mortality. These ROC curves were compared using the De-Long method. The cut-off value of PNI for both all-cause mortality and MACE was defined according to ROC analysis. Kaplan–Meier method was used for event-free survival curves. The difference in survival curves between groups was evaluated using the log-rank test. Values of $P < .05$ were considered statistically significant. Statistical Package for the Social Sciences 22 software (IBM Corp.; Armonk, NY, USA) was used to carry out all statistical analysis.

Results

The study included 828 patients who underwent PCI due to AMI. The demographic, clinical, and angiographic features and laboratory parameters of the study group are presented in Tables 1 and 2. All-cause mortality occurred in 69 patients, cerebrovascular accidents in 4 patients, and non-fatal MI in 75 patients.

Table 1. The Clinical and Demographic Features of the Study Population

	MACE (+) (n = 148)	MACE (–) (n = 680)	*P*
Age (years)	63.9 ± 13.2	58.7 ± 11.1	<.001
Male (gender)	112 (75.7%)	533(78.4%)	.47
Body mass index (kg/m^2)	26.3 ± 5.3	26.5 ± 5.9	.88
Diabetes mellitus	67 (45.3%)	222 (32.6%)	.004
Hypertension	77 (52%)	304 (44.7%)	.11
Hyperlipidemia	81 (54.7%)	337 (49.6%)	.25
Smoking	56 (41.2%)	286 (42%)	.95
Previous MI	34 (23%)	133 (19.6%)	.35
Previous PCI	33 (22.3%)	146 (21.5 %)	.83
Previous CABG	12 (8.1%)	38 (5.6%)	.24
Previous stroke	10 (6.5 %)	0 (0%)	<.001
Ejection fraction (%)	41.9 ± 11.1	50.1 ± 8.7	<.001
Length of hospital stay, days	9.8 ± 11.9	6.4 ± 4.6	<.001
Systolic blood pressure (mmHg)	128 ± 30.8	132.1 ± 24.2	.09
Diastolic blood pressure (mmHg)	77.7 ± 16.6	81.5 ± 27.6	.12
Heart rate (beats per minute)	84.3 ± 20.2	79.1 ± 39.5	.03
GRACE risk score	167.6 ± 41.6	143.2 ± 29.7	<.001
SII	964.7 (533.7-1867.1)	724.5 (469.3-1309.1)	.001
PNI	46.2 ± 7.2	50.2 ± 8.5	<.001
NLR	4.02 (2.23-7.07)	3(1.97-5.5)	.002
STEMI (n, %)	102 (68.9%)	365 (57.3%)	<.001
NSTEMI (n, %)	46 (31.1%)	315 (42.7%)	
Killip class ≥2	31 (20.9%)	25 (3.7%)	<.001
In-hospital medication			
Statin	138 (92.9%)	625 (92.1%)	.87
B-blocker	123 (82.9%)	551 (81.1%)	.84
ACE-I/ARB	118 (79.7%)	557 (81.9%)	.78

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CABG, coronary artery bypass grafting; GRACE, Global Registry of Acute Coronary Event; MACE, major adverse cardiovascular events; MI, myocardial infarction; NLR, neutrophil-to-lymphocyte ratio; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; PNI, prognostic nutritional index; SII, systemic immune-inflammation index; STEMI, ST-segment elevation myocardial infarction.

Major adverse cardiac events (+) group was older with more frequent history of DM. History of HTN, HL, male gender, previous MI, prior CABG surgery, and/or PCI were similar between the groups. Serum levels of troponin I, creatine kinase-MB, glucose, neutrophil, creatinine level on admission and the

Table 2. Biochemical and Angiographic Characteristics of the Study Population

	MACE (+) (n=148)	MACE (−) (n=680)	*P*
Serum glucose level on admission (mg/dL)	168.1 ± 84.3	135.5 ± 58.7	<.001
HbA1c (%)	7.2 ± 2.1	6.8 ± 1.8	.05
Creatinine level on admission (mg/dL)	1.23 ± 1.1	0.96 ± 0.5	<.001
Maximum creatinine level (mg/dL)	1.71 ± 1.6	1.06 ± 0.6	<.001
eGFR (mL/min/1.73 m^2)	71.1 ± 24.7	84.7 ± 24.3	<.001
Total cholesterol (mg/dL)	183 ± 38.6	190.1 ± 48.2	.09
LDL (mg/dL)	119.5 ± 34.8	129.3 ± 46.8	.02
HDL (mg/dL)	40.1 ± 12.3	38.8 ± 11.1	.24
Triglyceride (mg/dL)	162.1 ± 126.8	135.5 ± 58.8	.81
Hemoglobin (g/dL)	13.2 ± 2.2	13.6 ± 1.8	.04
White blood cell count (/mm^3)	11716 ± 5036	11075 ± 3693	.08
Lymphocyte count (/mm^3)	2062 ± 1044	2409 ± 1238	.002
Neutrophil count (/mm^3)	8785 ± 4879	7725 ± 3544	.002
Platelet count (/mm^3)	259 910 ± 90 814	255 000 ± 74 465	.48
CK-MB (ng/mL)	152.7 ± 95	106.7 ± 35	.002
Albumin (mg/dL)	3.58 ± 0.51	3.81 ± 0.55	<.001
Contrast media volume (mL)	264.7 ± 125.5	238.6 ± 106.4	.01
Tirofiban use	64 (43.5%)	244 (35.9%)	.08
Number of diseased vessels			
1-vessel disease	57 (39 %)	336 (49.8%)	.03
2-vessel disease	48 (32.9%)	196 (29.1%)	
3-vessel disease	41 (28.1%)	142 (21.1%)	
Infarct related artery			
LAD	76 (51.3%)	267(39%)	.08
CX	20 (13.9%)	120 (17%)	
RCA	47 (32.2%)	284 (41.7%)	
LMCA	5 (3.3%)	9 (1.3%)	

CK-MB, creatine kinase MB; CX, circumflex artery; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LAD, left anterior descending coronary artery; LDL, low-density lipoprotein; LMCA, left main coronary artery; MACE, major adverse cardiovascular events; RCA, right coronary artery.

maximum level of creatinine, SII and GRACE RS, number of patients with ST-segment elevation MI, multivessel disease, contrast-induced acute kidney injury (CI-AKI), Killip class > 2, and rehospitalization for cardiovascular diseases were significantly higher in MACE (+) group. Serum levels of hemoglobin, albumin and lymphocytes, ejection fraction (EF), PNI, and smoking rates were lower in MACE (+) group.

The results of the Cox multivariate analysis are shown in Table 3. This analysis was based on the following variables: age, male gender, DM, HTN, previous MI, EF, baseline creatinine level, SII, NLR, and PNI. Among these variables, age, PNI, SII, EF, and baseline creatinine levels were identified as independent predictors of MACE, and age, PNI, EF, and baseline creatinine levels were found to be independent predictors for all-cause mortality.

Receiver operating characteristic analysis comparing the predictive accuracy of NLR, SII, PNI, and GRACE RS for MACE and all-cause mortality are shown in Figures 1 and 2. Based on 95% CI, the areas under the curve (AUC) for NLR, SII, PNI, and GRACE RS were 0.59 (95% CI: 0.53-0.64), 0.58 (95% CI: 0.53-0.63), 0.65 (95% CI: 0.60-0.70), and 0.68 (95% CI: 0.63-0.73), respectively ($P=.001$, $P=.002$, $P < .001$, and $P < .001$, respectively) in predicting MACE. The areas under the curve for NLR, SII, PNI, and GRACE RS were 0.56 (95% CI: 0.49-0.64), 0.58 (95% CI: 0.51-0.65), 0.68 (95% CI: 0.62-0.74), and 0.79 (95% CI: 0.73-0.86), respectively ($P=.07$, $P=.04$, $P < .001$, $P < .001$, respectively) in predicting all-cause mortality. We performed a pair-wise comparison of ROC curves and found that the discrimination ability of PNI with regard to MACE was better than the NLR and SII, similar to that of GRACE RS (by DeLong method, AUC_{PNI} vs. AUC_{SII}, $P=.008$; AUC_{PNI} vs. AUC_{NLR}, $P=.006$; AUC_{PNI} vs. AUC_{GRACE}, $P=.031$). Also, the discrimination ability of PNI with regard to all-cause mortality was better than the NLR and SII and was worse than the GRACE RS (by DeLong method, AUC_{PNI} vs. AUC_{SII} $P=.009$; AUC_{PNI} vs. AUC_{NLR} , $P=.001$; AUC_{PNI} vs. AUC_{GRACE}, $P=.007$).

The cut-off value for PNI regarding MACE and all-cause mortality was calculated by ROC analysis. The ideal PNI cut-off value was <48, with 62% sensitivity and 60% specificity for all-cause mortality and 60% sensitivity and 61% specificity for MACE. The study population was divided into 2 groups according to the PNI cut-off value (PNI < 48). The incidence of MACE was 23.9% (n=88) in the PNI < 48 group and 13% (n=60) in the PNI > 48 group ($P < .001$). The incidence of all-cause mortality was 11.7% (n=43) for the PNI < 48 group and 5.7% (n =26) for the PNI > 48 group ($P=.002$). Kaplan–Meier analysis showed that the PNI < 48 group had a significantly higher incidence of both MACE and all-cause mortality [P (log-rank) $P < .001$ for MACE; $P=.002$ for all-cause mortality] (Figures 3 and 4).

Discussion

The principal finding of our study is that PNI, a newly defined inflammatory biomarker, was identified as an independent predictor of MACE and all-cause mortality in patients with AMI who underwent PCI. In the comparative analysis, the discrimination ability of PNI was better than other novel inflammatory indices. Additionally, our results suggested that these simple biomarkers may be as useful as the traditional clinical GRACE RS in patients with AMI. Since these biomarkers can be calculated easily and quickly, it may be much more reasonable to use them to provide robust risk stratification even in hospital admission.

Many studies have previously reported that age, Killip class, and EF were significantly associated with mortality in AMI patients.[18,19] Moreover, Abaci et al[20] found that contrast media exposure was associated with increased adverse events independent of

Table 3. Cox Regression Analysis

	MACE				All-Cause Mortality			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95 % CI)	*P*	HR (95% CI)	*P*	HR (95 % CI)	*P*
SII	1.01 (1.00-1.03)	<.001	1.01 (1.00-1.03)	.009	1.01 (1.00-1.02)	.04		
PNI	1.05 (1.04-1.07)	<.001	1.05 (1.02-1.07)	<.001	1.06 (1.04-1.08)	<.001	1.05 (1.02-1.09)	.002
NLR	1.02 (1.01-1.03)	.002			1.02 (1.01-1.04)	.04		
Age	1.04 (1.02-1.05)	<.001	1.02 (1.00-1.03)	.007	1.06 (1.03-1.08)	<.001	1.04 (1.02-1.06)	.001
Male gender	1.16 (0.77-1.43)	.37			1.12 (0.51-1.58)	.73		
Hypertension	1.39 (1.01-1.92)	.04			1.36 (0.85-2.17)	.21		
Diabetes mellitus	1.62 (1.18-2.25)	.003			1.66 (1.03-2.66)	.04		
Previous MI	1.50 (1.02-2.20)	.04			1.95 (1.15-3.29)	.01		
EF	1.07 (1.06-1.09)	<.001	1.06 (1.05-1.08)	<.001	1.12 (1.10-1.14)	<.001	1.11 (1.08-1.13)	<.001
Baseline creatinine	1.21 (1.08-1.36)	.001	1.22(1.06-1.41)	.005	1.22 (1.05-1.43)	.01	1.27 (1.16-1.39)	<.001

EF, ejection fraction; HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction; NLR, neutrophil-to-lymphocyte ratio; PNI, prognostic nutritional index; SII, systemic immune-inflammation index.

the occurrence of CI-AKI in patients who underwent elective coronary angiography. Consistent with the literature, our results showed that age, Killip class, EF, and increased levels of creatinine were strongly related to MACE and all-cause mortality in patients with AMI.

The predictive performance of the NLR, a well-known inflammatory biomarker, was proven for cardiovascular diseases to infectious diseases.[21,22] According to a recent meta-analysis of the 5 randomized clinical trials conducted on 60 087 patients, NLR was demonstrated as a good predictor of all-cause mortality and cardiovascular events.[23] Similarly, our study indicated that higher NLR was associated with increased number of MACE and all-cause mortality in patients with AMI.

With the increasing knowledge on the worse impact of inflammation on clinical outcomes during the course of AMI, clinicians are seeking simple prognostic and inflammatory biomarkers. Our

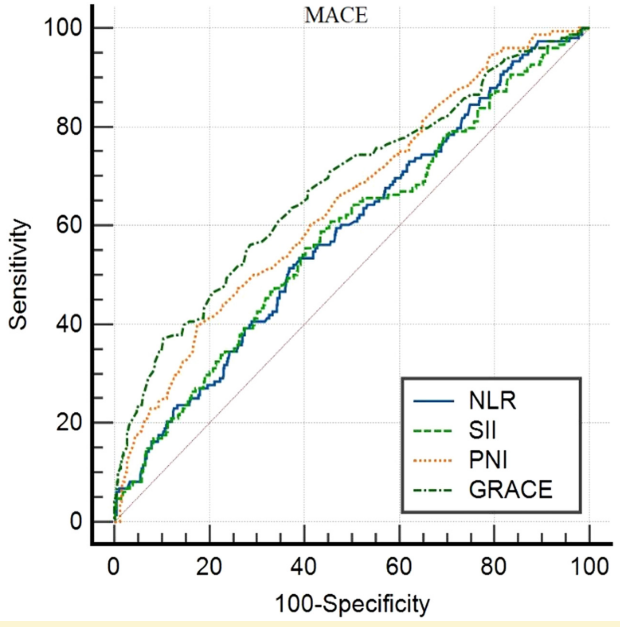

Figure 1. ROC analysis comparing the predictive accuracy of NLR, SII, PNI, and GRACE RS for MACE. GRACE RS, The Global Registry of Acute Coronary Events risk score, MACE, major adverse cardiovascular events; NLR, neutrophil-to-lympho cyte ratio; PNI, prognostic nutritional index; ROC, receiver operating characteristic; SII, systemic immune-inflammation index.

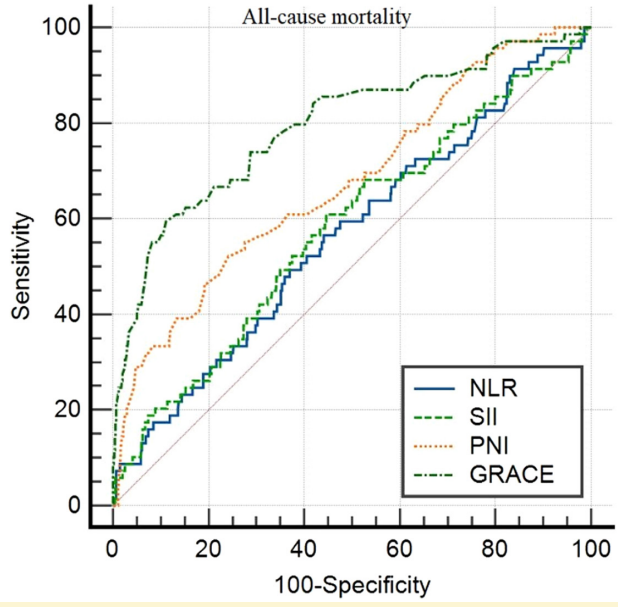

Figure 2. ROC analysis comparing the predictive value of NLR, SII, PNI, and GRACE RS for all-cause mortality. GRACE RS, The Global Registry of Acute Coronary Events risk score; NLR, neutrophil-to-lymphocyte ratio; PNI, prognostic nutritional index; ROC, receiver operating characteristic; SII, systemic immune-inflammation index.

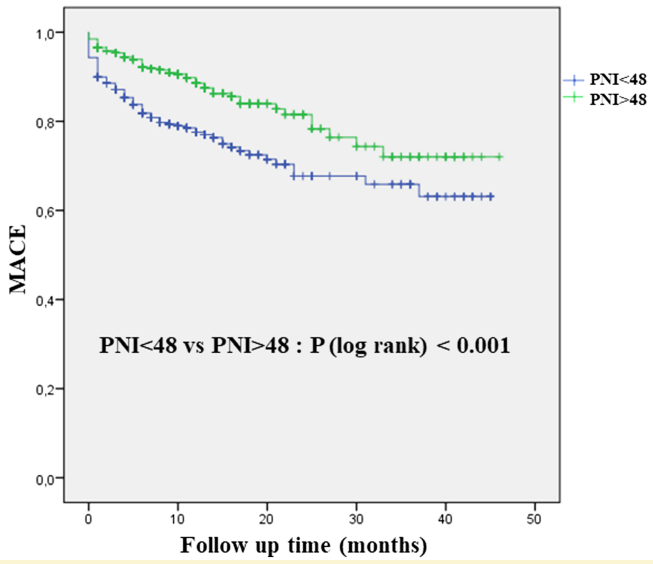

Figure 3. Kaplan–Meier curve for MACE. MACE, major adverse cardiovascular events.

results showed that all the new indexes evaluated in our study were useful for predicting MACE, but the results were superior for PNI. This may be due to the fact that one of its parameters is albumin. Inflammation leads to increased vascular permeability causing decreased serum albumin concentration due to the rapid transfer of albumin out of the vascular compartment.[24] Besides, malnutrition contributes to further decrease in the levels of serum albumin. Prior studies established that decreased levels of serum albumin were associated with poor outcomes and prognosis in patients with acute coronary syndromes.[25] In this regard, albumin may be a better acute phase reactant than hemogram parameters as it reflects the nutritional status besides the inflammatory response. Prognostic nutritional index is calculated based on serum albumin level and total lymphocyte count and provides nutritional, inflammatory, and immunological information. The

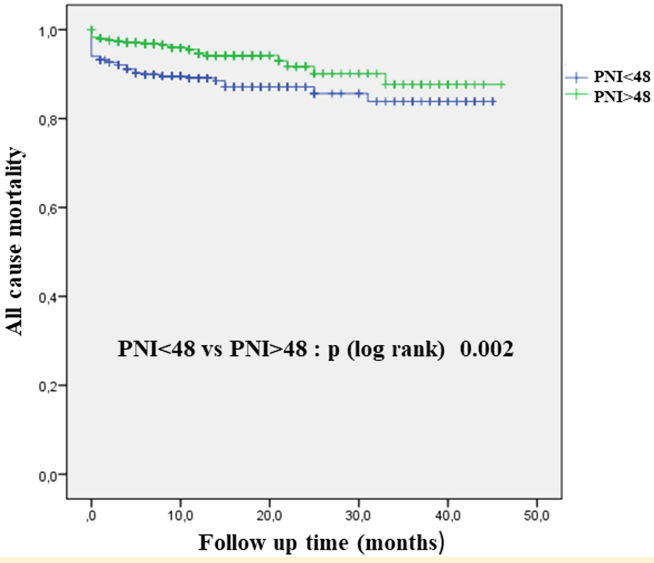

Figure 4. Kaplan–Meier curve for all-cause mortality.

probable mechanism that may explain the relationship between low PNI and adverse clinical outcomes is the reduction in serum albumin, an antioxidant molecule of plasma. Decreased serum albumin leads to an increase in the inflammatory process, platelet aggregation, and blood viscosity; thus causing deterioration of vascular endothelial function.[26] Therefore, the scores involving albumin, like PNI, may have increased predictive value for adverse clinical outcomes.

According to the studies conducted on ST elevation myocardial infarction (STEMI) patients, PNI was found to be an independent predictor of mortality.[27,28] Likewise, our study demonstrated the efficacy of PNI for predicting the prognosis in the entire AMI population. Prior studies suggested that SII was an independent predictor of adverse clinical events in both patients with stable CAD and AMI.[12,13,29,30] Also, our results suggested that higher SII levels were related to increased MACE in AMI patients, as shown in the ROC analysis. However, the predictive ability of SII was not as strong as PNI and it was not demonstrated as an independent predictor of MACE. The higher predictive value of PNI than SII in predicting MACE may be explained by the fact that our study group received at least one of the potent antiaggregant drugs. Platelets, one of the basic parameters of SII, are the target of antiaggregant drugs and form the basis of the treatment in AMI patients.

Global Registry of Acute Coronary Events Risk Score, which includes various clinical, electrocardiogram (ECG), and biochemical parameters, strongly demonstrates in-hospital and long-term mortality in patients with AMI. Although GRACE is the most widely used RS to predict the prognosis of AMI patients in daily clinical practice, requiring much more data and computing systems remain its main limitations. Our findings imply that the predictive ability of PNI for MACE was similar to that of GRACE RS. Although not as powerful as GRACE RS, its predictive value for all-cause mortality was sufficient and effective. Furthermore, PNI can be easily calculated with a simple venous blood sample and can provide information about the clinical course of the patients at the time of hospital admission. As early identification of high-risk patients with AMI is vital to prevent adverse clinical outcomes, PNI may provide easy and rapid identification of high-risk AMI patients at hospital admission compared to GRACE RS.

There were some limitations to be noted in our study. It was a retrospective, single-center, and relatively modest sample-sized study. Therefore, our results may not represent the whole population as levels of these new biomarkers may differ in various ethnical groups. The retrospective design of the study may cause a selection bias. Also, people in developed countries rarely have nutritional deficits, so the PNI value may lose sensitivity in this population. Some parameters, particularly the most important inflammatory markers such as C-reactive protein (CRP) or high sensitive-CRP, were missing due to the retrospective design of our study. Therefore, the predictive value of newly defined hematological biomarkers may be limited without including CRP. Although the discrimination ability of PNI was determined to be better than the other inflammatory indices, future validation of our findings is needed to determine its clinical usefulness of it in patients with AMI who have undergone PCI.

In conclusion, the results of our study demonstrate that PNI is an independent predictor of MACE and all-cause mortality in AMI patients treated with PCI. Moreover, PNI has better discriminative ability than other new inflammatory indexes. Using these novel, easily calculable prognostic inflammatory biomarkers may enable early risk stratification in patients with AMI. Therefore, their widespread use in daily clinical practice may reduce the risk of subsequent adverse events.

Ethics Committee Approval: The study is approved by the local ethics committee of Sisli Hamidiye Etfal Education and Research Hospital (No: 3319, 8 June 2021).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

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