

## Investigation of Systemic Immune Inflammatory Index and Prognostic Nutritional Index in Prediction of Major Adverse Cardiovascular and Cerebral Events Occurring After Coronary Artery Bypass Operations

Koroner Arter Bypass Operasyonları Sonrasında Ortaya Çıkan Major Advers Kardiyovasküler Ve Serebral Olayları Öngörmeye Sistemik İmmün İnflamatuar İndeks Ve Prognostik Nutrisyonel İndeksin Yerlerinin Araştırılması

Mustafa Abanoz<sup>1</sup>, Mesut Engin<sup>2\*</sup>

1.University of Health Sciences, Mehmet Akif İnan Training and Research Hospital, Department of Cardiovascular Surgery, Şanlıurfa, Turkey

2.University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Cardiovascular Surgery, Bursa, Turkey

### ABSTRACT

**Aim:** The most valuable treatment method for coronary artery disease is coronary artery bypass graft (CABG) surgery. Major cardiovascular and cerebral events (MACCE) are important challenges, and it is particularly important to reveal possible risk factors in this regard. In this study, we aimed to investigate the predictive areas of the prognostic nutritional index (PNI) and the systemic immune inflammation index (SII) on early postoperatively developing MACCE, in patients who underwent isolated CABG operation.

**Methods:** The patients between the ages of 20 and 85 years who underwent consecutive isolated CABG operation in our clinic between May 15th, 2016, and May 15th, 2020, were included in the study retrospectively. In the postoperative period (within a month), those who did not develop MACCE were recorded as Group 1, and those who developed MACCE as Group 2.

**Results:** A total of 297 consecutive patients were included in the study. Group 1 had 263 patients with a median age of 63 (32-80), Group 2 had 34 patients with a median age of 70 (36-85) (P=0.008). There was no difference between the groups in terms of gender, history of cerebrovascular events, smoking, body mass index, hyperlipidemia, ejection fraction, and chronic obstructive pulmonary disease rates. As a result of multivariate analysis, advanced age (OR: 1.230 CI 95%: 1.050-1.319 P=0.024), NLR (OR: 1.974 CI 95%: 1.614-3.120, P=0.009), SII (OR: 3.880, CI 95%: 2.690-6.150, P<0.001) and PNI (OR: 2.424, CI 95%: 1.880-3.880, P=0.002) values were determined as independent predictors for predicting early postoperative MACCE.

**Conclusions:** With this study we revealed that SII and PNI values, which are among the inflammatory parameters and which can be obtained cheaply and easily, may be good predictors for MACCE emerging after CABG operations.

**Keywords:** Coronary artery bypass grafting, Inflammation, Nutritional index, Postoperative complication

### ÖZ

**Amaç:** Koroner arter hastalığı için en değerli tedavi yöntemi koroner arter baypas greft (KABG) ameliyatıdır. Başlıca kardiyovasküler ve serebral olaylar (MACCE) önemli sorunlardır ve bu konuda olası risk faktörlerini ortaya çıkarmak çok önemlidir. Bu çalışmada, izole KABG operasyonu geçiren hastalarda erken postoperatif gelişen MACCE üzerine prognostik nutrisyonel indeks (PNI) ve sistemik immün inflamasyon indeksi (SII)'in prediktif yerlerini araştırmayı amaçladık.

**Yöntemler:** Kliniğimizde 15.05.2016-15.05.2020 tarihleri arasında ardışık izole KABG operasyonu geçiren 20-85 yaşları arasındaki hastalar retrospektif olarak çalışmaya dahil edildi. Postoperatif dönemde (bir ay içinde) MACCE gelişmeyenler Grup 1, MACCE gelişenler Grup 2 olarak kaydedildi.

**Bulgular:** Çalışmaya toplam 297 ardışık hasta dahil edildi. Grup 1'de medyan yaşı 63 (32-80) olan 263 hasta, Grup 2'de medyan yaşı 70 (36-85) olan 34 hasta vardı (P = 0.008). Gruplar arasında cinsiyet, serebrovasküler olay öyküsü, sigara kullanımı, vücut kitle indeksi, hiperlipidemi, ejeksiyon fraksiyonu ve kronik obstrüktif akciğer hastalığı oranları açısından fark yoktu. Çok değişkenli analizin sonucunda ileri yaş (OR: 1.230 CI 95%: 1.050-1.319 P=0.024), NLR (OR: 1.974 CI 95%: 1.614-3.120, P=0.009), SII (OR: 3.880, CI 95%: 2.690-6.150, P<0.001) and PNI (OR: 2.424, CI 95%: 1.880-3.880, P=0.002) değerleri erken postoperatif MACCE'yi öngörmeye bağımsız prediktörler olarak tespit edildi.

**Sonuçlar:** Bu çalışma ile, ucuz ve kolay elde edilebilen inflammatuar parametreler arasında yer alan SII ve PNI değerlerinin, KABG operasyonlarından sonra ortaya çıkan MACCE için iyi prediktörler olabileceğini ortaya koyduk.

**Anahtar Kelimeler:** Koroner arter baypas greft, İnflamasyon, Nutrisyonel indeks, Postoperatif komplikasyon

Received: 27.04.2021 Accepted: 02.08.2021 Published (Online):31.12.2021

\*Corresponding Author: Mesut Engin, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Cardiovascular Surgery, Mimar Sinan Town. Emniyet Street. Yıldırım / Bursa, Turkey, +90224 295 50 00, mesut\_kvc\_cor@hotmail.com

ORCID: 0000-0003-2418-5823

**To cited:** Abanoz M, Engin M. Investigation of Systemic Immune Inflammatory Index and Prognostic Nutritional Index in Prediction of Major Adverse Cardiovascular and Cerebral Events Occurring After Coronary Artery Bypass Operations. Acta Med. Alanya 2021;5(3):263-269 doi:10.30565/medalanya.929006

## INTRODUCTION

Coronary artery disease (CAD) is one of the important causes of mortality and morbidity today. The most effective treatment method for this disease is coronary artery bypass graft (CABG) surgery. These operations are mostly performed with cardiopulmonary bypass (CPB) [1,2]. Sudden death, postoperative myocardial infarction, cerebrovascular event and decompensated heart failure states that occur after these procedures are known as major postoperative cardiovascular and cerebral events (MACCE). The neutrophil-lymphocyte ratio (NLR), one of the simply obtainable inflammatory parameters with proven efficacy, has been shown as a predictor for MACCE emerging after coronary bypass operations [3]. In addition, it has been shown that other easily obtainable blood parameters such as the platelet lymphocyte ratio (PLR), may also be predictors of mortality and adverse outcomes in cardiovascular surgery [4]. The systemic immune inflammation index (SII), PLR and NLR, values obtained from these blood parameters which have been the subject of many studies, have been used as a prognostic inflammatory marker in various fields of medicine [5-7]. In a recent study, it has been revealed a predictive factor for adverse events after off-pump CABG operations [8].

The prognostic nutritional index (PNI), which can be obtained from routine blood parameters, is a factor that shows the nutritional status and has prognostic significance. PNI value is calculated with a formula that includes albumin value and lymphocyte counts [9]. One particular study showed that PNI value might be associated with morbid results after CABG surgeries [10].

In this current study, the aim was to investigate the predictive places of PNI and SII values on early postoperatively developing MACCE, in patients who underwent isolated CABG operation with CPB.

## PATIENTS AND METHODS

The patients between the ages of 20 and 85 years who underwent consecutive isolated CABG operations with cardiopulmonary bypass in our clinic between May 15th, 2016 and May 15th, 2020 were included in the study retrospectively.

The study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practices and approval of the local ethics committee was duly obtained (HRU/20.14.04 Date: August 17th, 2020). The patients who underwent urgent coronary bypass, the patients scheduled for additional cardiac surgery such as valve and aneurysm, reoperations, those with permanent stroke, those with systemic inflammatory diseases, those with chronic autoimmune disease, the patients with chronic renal failure (Preop creatinine value >2mg/dL), the ones whose left ventricular ejection fraction was 30 and below and those with hematological diseases, were all excluded from the study. As a result of the exclusion criteria, 297 consecutive patients were included in the study. Demographic characteristics of the patients (age, gender, history of systemic diseases such as diabetes mellitus and hypertension, etc.), ejection fractions, preoperative blood parameters (hemogram [White blood cell (WBC)], neutrophil, lymphocyte, NLR, PLR, SII), biochemistry (Creatinine), urea, albumin, C-reactive protein (CRP) were recorded. Pump durations, stay durations during hospitalization and intensive care unit, drainage amounts, used blood product amounts were recorded operatively and postoperatively. In the postoperative period (within a month), those who did not develop MACCE were recorded as Group 1, and those who developed MACCE as Group 2.

### Calculation of Parameters

Preoperative blood parameters of all patients were obtained from blood samples taken from their peripheral venous structures during their admission to our clinic. The sample was collected in tubes containing ethylenediaminetetraacetic acid and was used for automatic blood count with the usual hospital procedures. An automated hematological analyzer was used for measuring hematological parameters (Coulter LH 780 Analyzer, CA, USA). Index values were obtained by using the following formulas from the data in these parameters.

$$\text{PNI} = \text{Albumin (g/L)} + \text{Lymphocyte (10}^3/\mu\text{L)} \times 5$$

$$\text{SII} = \text{Platelet count (10}^3/\mu\text{L)} \times \text{Neutrophil (10}^3/\mu\text{L)} / \text{Lymphocyte (10}^3/\mu\text{L)}$$

## Identification of Major Adverse and Cerebrovascular Events

Postoperative mortality, death occurred within 1 month due to all causes, Postoperative myocardial infarction development, defined as having increased biomarker values (creatinine kinase-MB or cardiac troponin levels) by at least five-fold and Q waves occurring in at least two ECG derivations or occurring of ST segment changes or new left bundle branch block, the need for revascularization, the need for surgery or endovascular revascularization again after the operation, Re-intervention, requiring re-hospitalization due to any cardiovascular cause within one postoperative month, Stroke development, post-operative central neurological deficit that lasts at least 24 hours and Decompensated heart failure, the postoperative need of positive inotropic support (>24 hours) or intraaortic balloon pump, were all defined as postoperative MACCE. Patients who developed at least one of these conditions were recorded as Group 2.

## Statistical Analysis

In our study, the SPSS 21.0 (IBM Statistical Package for the Social Sciences Statistic Inc. version 21.0, Chicago, IL, USA) program was used to analyze the data. Means and standard deviations were calculated for mediational, continuous and ordinal data, using descriptive analysis methods. The “Kolmogorov-Smirnov test and Shapiro-Wilk test” were used for normality distribution analysis. While Student's t test was used for the data presenting normal distribution, the Mann-Whitney U test was used for data that did not conform to normal distribution. This data were shown as mean  $\pm$ sd or as mean (interquartile range). Categorical variables were shown as frequency and percentage, and the “Chi Square test” was used for analysis. Univariate and multivariate binary logistic regression analysis was used to analyze postoperative MACCE predictors. P value's being less than 0.05 was considered statistically significant. In predicting postoperative MACCE, receiver operating characteristics (ROC) curve analysis was performed for NLR, PNI and SII values and the areas under the curve (AUC) were calculated.

## RESULTS

A total of 297 patients were included in the study. Group 1 had 263 patients with a median age of 63 (32-80), Group 2 had 34 patients with a median age of 70 (36-85) (P=0.008). There was no difference between the groups in terms of gender, history of cerebrovascular events, smoking, body mass index, hyperlipidemia, ejection fraction and chronic obstructive pulmonary disease (COPD) rates. Former percutaneous coronary intervention, hypertension (HT), diabetes mellitus (DM) rates and EuroSCORE II values were found to be significantly higher in Group 2 (P=0.041, P=0.034, P=0.011, P<0.001, respectively) (Table 1).

Table 1. Demographic datas and preoperative features of the patients

Variables	Group 1 (N= 263)	Group 2 (N= 34)	P value
Age(years) (mean $\pm$ sd)	63 (32- 80)	70 (36- 85)	0.008‡
Male gender, n(%)	184 (69.9%)	25 (73.5%)	0.745*
Hypertension, n (%)	169 (64.2%)	27 (79.4%)	0.034*
Diabetes mellitus, n (%)	46 (17.5%)	12 (35.3%)	0.011*
Previous PCI, n(%)	65 (24.7%)	13 (38.2%)	0.041*
Current smoker, n (%)	88 (33.4%)	10 (29.4%)	0.678*
COPD, n (%)	28 (10.6%)	7 (20.5%)	0.194*
Previous CVA	12 (4.5%)	4 (11.7%)	0.356*
EuroSCORE II	2.1 (0.5- 6.4)	3 (0.5- 8.9)	<0.001‡
BMI (kg/m <sup>2</sup> )	29.3(23.5- 38.7)	30.2 (24- 39.6)	0.427*
Hyperlipidemia, n(%)	98 (37.2%)	14 (41.1%)	0.598*
Ejection fraction (%)	50 (38- 67)	45(33- 66)	0.072‡

\* Chi-square test, †Student's t test (Data is expressed as mean $\pm$ sd), ‡Mann Whitney U test (Data is expressed as median (interquartile range)) BMI: Body mass index, CVA: Cerebrovascular accident COPD: Chronic obstructive pulmonary disease, EuroSCORE II: European System for Cardiac Operative Risk Evaluation II PCI: Percutaneous coronary intervention

Preoperative laboratory values of the patients are provided in Table 2. Both groups were similar in terms of white blood cell (WBC), hematocrit (Htc), neutrophil, platelet (PLT), urea, creatinine, albumin, PLR, C-reactive protein (CRP) and thyroid function test values. In group 2, while NLR and SII values were significantly higher, PNI and lymphocyte values were significantly lower (P <0.001, for all).

The perioperative characteristics of the patients are given in Table 2. There was no difference between the groups in terms of perfusion times, chest tube drainage amounts, the amount of

used blood products and the number of distal anastomosis. Inotropic support need rates, durations of intensive care and total hospitalization were significantly higher in Group 2 (P=0.014, P <0.001, P <0.001, respectively).

Table 2. Preoperative laboratory variables and perioperative features of the patients of the patients

Variables	Group 1 (n=263)	Group 2 (n=34)	P value ‡
White blood Cell (103/ $\mu$ L)	8.4 (4.7- 14.8)	8.7 (5.1- 15.1)	0.216
Hematocrit (%)	42 (33- 52)	39 (32- 50)	0.198
Platelet (103/ $\mu$ L)	251.6 (136- 476.5)	260.6 (140- 490.7)	0.118
Neutrophil (103/ $\mu$ L)	4.4 (1.9- 9.9)	4.8 (2.6- 10.2)	0.069
Lymphocyte(103/ $\mu$ L)	2 (0.9- 4.2)	1.7 (0.7- 3.3)	<0.001
Creatinine, mg/dL	1 (0.5- 1.9)	0.96 (0.7- 2)	0.229
Urea, mg/dL	16 (14- 34)	18 (12- 40)	0.416
Albumin (g/L)	39.6 (35- 55)	37.5 (33- 52)	0.109
Free T3 (pg/mL)	2.7 (2.2- 4.9)	2.9 (2.3- 5.2)	0.365
Free T4 (ng/dL)	0.9 (0.6- 1.1)	0.8 (0.7-1.3)	0.497
TSH ( $\mu$ IU/L)	1.4 (0.9- 4.4)	1.5 (0.8- 4.6)	0.414
C Reactive protein (mg/dL)	9.4(0.4- 60.3)	9.8 (0.7- 69)	0.112
NLR	2.4 (1- 6.9)	3.2 (1.3- 10)	<0.001
PLR	151.4 (118.6- 234.7)	156.9 (122.5- 244.6)	0.065
SII	730 (540-2594)	1240 (630- 3276)	<0.001
PNI	50 (36-70)	44 (37- 61)	<0.001
Total perfusion time	100 (55- 175)	106 (57- 180)	0.114
Cross-clamp time	72 (33- 88)	75 (35- 90)	0.317
Total chest tube drainage (ml)	500 (350- 1600)	600 (400- 1700)	0.156
Inotropic support, n(%)	27 (10.2)	9 (26.4)	0.014
Packed blood products (units)	5 (5- 10)	6 (4- 11)	0.127
Number of distal anastomoses, n	3 (1- 5)	3 (1- 5)	0.714
Total ICU stay (days)	2 (2- 5)	4 (2-18)	<0.001
Total hospital stay (days)	7 (6- 13)	11 (12- 23)	<0.001

‡Mann Whitney U test, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet lymphocyte ratio, SII: Systemic immune inflammation index, PNI: Prognostic nutritional index, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid stimulating hormone

Logistic regression analysis was performed to predict MACCE predictors early occurring after CABG operations done accompanied by cardiopulmonary bypass (Table 3). In univariate analysis advanced age (OR [odds ratio]: 1.394,

95% CI [confidence interval]: 1.090-1.856, P=0.010), hypertension (OR: 0.774, 95% CI: 0.557-0.992, P=0.038), DM (OR: 0.796, 95% CI: 0.589-0.892, P=0.013), EuroSCORE II (OR: 5.228, 95% CI: 3.794-6.445, P <0.001), need for inotropic support (OR: 1.210, 95% CI: 1.114-1.645, P=0.017), low lymphocyte count (OR: 1.478, 95% CI: 1.116-1.898, P< 0.001), NLR (OR: 2.267, 95% CI: 1.912-3.869, P <0.001), high SII (OR: 4.114, 95% CI: 2.794-6.434, P< 0.001), low PNI (OR: 2.914, 95% CI: 1.894-3.365, P <0.001) values were found to be significantly correlated with the development of MACCE. As a result of multivariate analysis, advanced age (OR: 1.230 CI 95%: 1.050-1.319 P=0.024), NLR (OR: 1.974 CI 95%: 1.614-3.120, P=0.009), SII (OR: 3.880, CI 95%: 2.690-6.150, P<0.001) and PNI (OR: 2.424, CI 95%: 1.880-3.880, P=0.002) values were determined as independent predictors for predicting early postoperative MACCE.

In ROC curve analysis, the cut-off value for preoperative NLR was 2.9 (AUC: 0.710, 95% CI: 0.623-0.797 P <0.001, 73.5% sensitivity and 65.6% specificity), cut-off value for SII was 912.4 (AUC: 0.864, 95% CI: 0.789-0.940 P <0.001, 82.6% sensitivity and 73.4% specificity) and cut-off value for PNI was 46.4 (AUC: 0.730, 95% CI: 0.645-0.815, P <0.001, 75.4% sensitivity and 68.6% specificity) (Figure 1 and Figure 2).

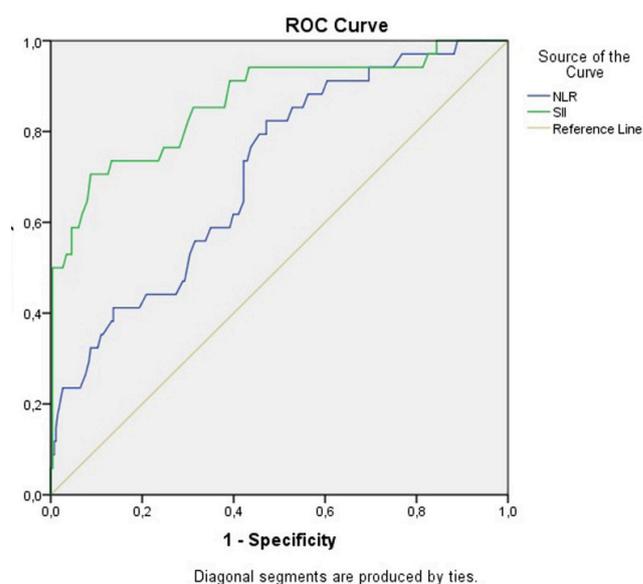


Figure 1: ROC (Receiver operation characteristic) curve and AUC (Area under the curve) for NLR and SII for predicting MACCE. (NLR: cut off: 2.9, AUC: 0.710, 95%CI:0.623- 0.797 P< 0.001, 73.5% sensitivity and 65.6% specificity)(SII: cut-off: 912.4, AUC: 0.864, 95%CI:0.789-0.940 P < 0.001, 82.6% sensitivity and 73.4% specificity)

Table 3. Binary logistic regression analysis to identify factors affecting development of major adverse cardiac and cerebrovascular events

Variables	Univariate analysis			Multivariate analysis		
	P	Exp(B) Odds Ratio	95% C.I. Lower Upper	P	Exp(B) Odds Ratio	95% C.I. Lower Upper
Age	0.010	1.394	1.090- 1.856	0.024	1.230	1.050- 1.319
Hypertension	0.038	0.774	0.557- 0.992	0.198	0.712	0.664- 1.110
Diabetes Mellitus	0.013	0.796	0.589- 0.892	0.170	0.610	0.512- 1.210
EuroSCORE II	<0.001	5.228	3.794- 6.445	--	--	--
Total perfusion time	0.158	1.312	0.945- 1.756	--	--	--
Inotropic support	0.017	1.210	1.114- 1.645	0.218	0.850	0.790- 1.312
Blood product use (units)	0.134	1.080	0.879- 1.114	--	--	--
Lymphocyte(103/μL)	<0.001	1.478	1.116- 1.898	--	--	--
NLR	<0.001	2.267	1.912- 3.869	0.009	1.974	1.614- 3.120
PLR	0.070	1.009	0.792- 1.234	--	--	--
SII	<0.001	4.114	2.794- 6.434	<0.001	3.880	2.690- 6.150
PNI	<0.001	2.914	1.894- 3.365	0.002	2.424	1.880- 3.880

All numerical data included as continuous variable. The goodness of fit of the multivariate model was confirmed by a P-value of 0.734 in the Hosmer-Lemeshow test. EuroSCORE II: European System for Cardiac Operative Risk Evaluation II, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet lymphocyte ratio, SII: Systemic immune inflammation index, PNI: Prognostic nutritional index

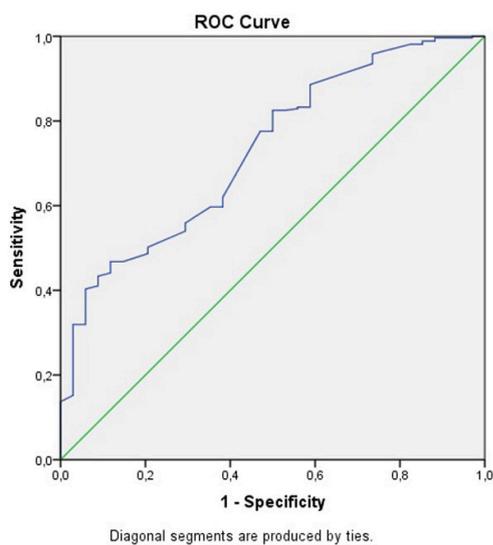


Figure 2: ROC (Receiver operation characteristic) curve and AUC (Area under the curve) for PNI for predicting MACCE (Cut off: 46.4, AUC: 0.730, 95%CI:0.645- 0.815, P< 0.001, 75.4% sensitivity and 68.6% specificity)

**DISCUSSION**

Coronary bypass surgery is the most effective method for atherosclerotic heart disease, and it can be performed successfully in many clinics today. EuroSCORE II has been largely accepted and is widely used to predict mortality in cardiac surgery. However, several concerns were raised, the score showing poor calibration in some patient groups in whom it underestimated the risk [11]. Also in a study, a simple inflammatuar marker was

revealed as a risk factor for the development of MACCE, independent of EuroSCORE [3]. In this sense, in recent years, inflammatory parameters have been widely researched in predicting the prognosis of cardiovascular diseases [3- 5]. In this current study, NLR, SII and PNI values were determined as independent predictors for MACCE, which can be seen in the postoperative period, as well as known risk factors such as age.

Inflammation plays an important role in the pathogenesis and progression of cardiovascular diseases as well as in many diseases. Although many parameters can be used in clinical practice, neutrophils, lymphocytes, thrombocytes and calculations made related to these parameters have been the subject of many clinical studies [12, 13]. Thrombocytes are important inflammatory parameters that mediate the release of cytokines and chemokines, which have important effects on vascular wall inflammation and shear stress formation. In the case of severe chronic inflammation, megakaryocyte proliferation is triggered, and thrombocytosis occurs [14]. Neutrophils, on the other hand, attach to the damaged areas in the vascular bed and cause the relevant chemokines to come to the region, thus atherosclerosis progresses [15]. However, the cellular immune system is mainly responsible for the inflammatory response that occurs after cardiac surgery. This cellular immune system

is activated by lymphocytes, thus increasing neutrophil numbers [16].

In light of this information, NLR and PLR values, which have been the subject of many clinical studies, appear as important prognostic markers. In a study conducted in the field of congenital heart surgery, it has been shown that the preoperative NLR value can be a predictor for low cardiac output syndrome that may occur in the postoperative period [17]. In another cohort study, the predictive role of NLR rate for mortal and morbid outcomes in coronary intensive care units was investigated. At the end of this study, it was shown that the high NLR value could be a predictor for 30-day mortality in these patients as well as renal and respiratory problems in intensive care unit [18].

In the study in which 751 patients were included, who underwent CABG operations, conducted by Gürbüz et al., the patients were followed for an average of 7.8 years and the effect of NLR value on MACCE development was investigated. In this study, the NLR cut-off value for MACCE prediction was found to be 4.32, and the NLR elevation was revealed as a risk factor for the development of MACCE independent of EuroSCORE [3]. In a study conducted by Saskın et al., the effect of preoperatively calculated PLR value on postoperative outcomes in patients who underwent CABG was investigated. In this study, preoperative high PLR values were found to be associated with early atrial fibrillation, prolonged intensive care durations, neurological events and mortality [19]. In another study conducted in this direction, high PLR value was determined as an independent predictor for postoperative atrial fibrillation [20]. In a recent study done by Navani et al., no relationship was determined between PLR value and early atrial fibrillation, stroke, prolonged ventilation, postoperative myocardial infarction and mortality in patients who underwent CABG [21]. In our study, although the preoperative NLR value for MACCE was an independent predictor, PLR value was not correlated with MACCE.

Recently, the SII value obtained from thrombocyte, neutrophil and lymphocyte values has been used as a prognostic marker in other fields of medicine. This parameter was first defined by Hu et al in 2014. In that study, it was shown that it is related

to bad prognosis in patients with hepatocellular cancer and that it can be used in determining treatment strategies [22].

In a study conducted in the cardiovascular field, coronary artery patients, who had 5602 percutaneous coronary interventions, were included. In this study, the predictive role of SII in predicting major adverse cardiac events after PCI was investigated. High SII values were found to be associated with cardiac death, fatal stroke and nonfatal stroke. At the end of the study, the authors emphasized that the SII value in CAD patients undergoing PCI is more predictive than known risk factors [23]. In a recent study conducted by Dey et al., the role of SII value in predicting postoperative bad outcomes in patients, who underwent off-pump CABG operation was investigated. At the conclusion of the study, the authors determined the SII value as an independent predictor for predicting postoperative poor outcomes. In addition, high inotropic support was found to be associated with poor postoperative outcomes [8]. In our study, SII value was determined as an independent predictor for postoperative MACCE. Also, a correlation between increased use of inotropic agents and MACCE were found.

Prognostic nutritional index is an important parameter obtained from lymphocyte and albumin values and an indicator of malnutrition status. The bad prognostic effect of low lymphocyte in cardiovascular diseases is known. Albumin, on the other hand, is a protein that has anti-inflammatory and antioxidant effects as well as effects on osmotic pressure. Therefore, a low albumin rate is a poor prognostic condition for cardiovascular diseases [24]. In line with this information, low PNI value appears as a poor prognostic marker. The effect of PNI value on postoperative outcomes was investigated in a retrospective study by Lee et al., in which patients, who underwent open heart surgery with CPB, were included. At the end of the multivariate analysis performed in this study, low PNI value, high CPB duration and advanced age were determined as independent predictors for early postoperative complications [25]. Low PNI value was also found as an independent predictor for development of MACCE in our study.

#### **LIMITATIONS OF THE STUDY**

The most important limitation of our study is that it is a single center retrospective study, as a result, the number of patients was also limited. In addition, the inequality of age groups is another limitation. The effects of highly sensitive CRP, procalcitonin and interleukin 6 and similar inflammatory parameters could not be evaluated due to the retrospective design of the study. Although prognostic nutritional index is a simple calculable indicator of malnutrition status, studies with a large number of patients are needed to fully elucidate the mechanism of its effect on bad results.

### CONCLUSION

It is particularly important to anticipate the risks of complications after coronary bypass operations. Therefore, in addition to various risk scoring systems, various inflammatory biomarkers have also been studied. In this current study, it was demonstrated that SII and PNI values, which are among the inflammatory parameters and which can be obtained cheaply and easily, may be good predictors for MACCE emerging after CABG operations.

**Conflict of Interest:** The author declares no conflict of interest related to this article.

**Funding sources:** The author declares that this study has received no financial support

**Ethics Committee Approval:** The study was approved by the ethics committee of Harran University Faculty of Medicine (HRU/20.14.04 Date: 17.08.2020)

**Peer-review:** Externally and internally peer reviewed.

### REFERENCES

1. Pala A, Taner T, Tatli AB, Ozsin KK, Yavuz S. The Effect of Preoperative Hematocrit Level on Early Outcomes After Coronary Artery Bypass Surgery. *Cureus*. 2020;12(4):e7811. doi: 10.7759/cureus.7811.
2. Çoner A, Akıncı S, Akbay E, Budak AB, Saba T, Müderrisoğlu H. Development of De Novo Chronic Total Occlusion in Native Coronary Arteries of Coronary Artery Bypass Grafting Surgery Patients *Acta Med. Alanya*. 2020;4(3):230-5. doi: 10.30565/medalanya.731636.
3. Gurbuz O, Kumtepe G, Ozkan H, Karal IH, Velioglu Y, Ercan A, et al. Predictive Value of Neutrophil-Lymphocyte Ratio for Long-Term Cardiovascular Event Following Coronary Artery Bypass Grafting. *Braz J Cardiovasc Surg*. 2020;35(3):274-84. doi: 10.21470/1678-9741-2018-0362.
4. Raffaele S, Nicola I, Noemi L, Michele P, Michele A, Umberto MB, et al. Neutrophil-to-lymphocyte Ratio and Platelet-to-lymphocyte Ratio as Biomarkers for Cardiovascular Surgery Procedures: A Literature Review. *Rev Recent Clin Trials*. 2021;16(2):173-9 doi: 10.2174/1574887115999201027145406.
5. Agus HZ, Kahraman S, Arslan C, Yildirim C, Erturk M, Kalkan AK, et al. Systemic immune-inflammation index predicts mortality in infective endocarditis. *J Saudi Heart As-*

soc. 2020;32(1):58-64. doi: 10.37616/2212-5043.1010.

6. Kim Y, Choi H, Jung SM, Song JJ, Park YB, Lee SW. Systemic immune-inflammation index could estimate the cross-sectional high activity and the poor outcomes in immunosuppressive drug-naïve patients with antineutrophil cytoplasmic antibody-associated vasculitis. *Nephrology (Carlton)* 2019;24(7):711-7. doi: 10.1111/nep.13491.
7. Çakır ÖÖ. The Relationship Between Blood Neutrophil to Lymphocyte Ratio and Tumor Size, Tumor Number, Macrovascular Invasion in Patients with Hepatocellular Carcinoma. *Acta Med. Alanya*. 2019;3(3):207-12. doi: 10.30565/medalanya.551550.
8. Dey S, Kashav R, Kohli JK, Magoon R, Shri I, Walian A, et al. Systemic Immune-Inflammation Index Predicts Poor Outcome After Elective Off-Pump CABG: A Retrospective, Single-Center Study. *J Cardiothorac Vasc Anesth*. 2021;35(8):2397-404. doi: 10.1053/j.jvca.2020.09.092.
9. Engin M, Ozsin KK, Savran M, Guvenc O, Yavuz S, Ozyazicioglu AF. Visceral Adiposity Index and Prognostic Nutritional Index in Predicting Atrial Fibrillation after On-Pump Coronary Artery Bypass Operations: a Prospective Study. *Braz J Cardiovasc Surg*. 2021;36(4):522-9. doi: 10.21470/1678-9741-2020-0044.
10. Teker Acikel ME, Korkut AB. Impact of Controlling Nutritional Status Score (CONUT) and Prognostic Nutritional Index (PIN) on Patients Undergoing Coronary Artery Bypass Graft Surgery. *Heart Surg Forum*. 2019;22(4):E294-7. doi: 10.1532/hsf.2493.
11. Landis C. Why the inflammatory response is important to the cardiac surgical patient. *J Extra Corpor Technol*. 2007;39(4):281-4. PMID: 18293820.
12. Kaya MG. Inflammation and coronary artery disease: as a new biomarker neutrophil/lymphocyte ratio. *Arch Turk Soc Cardiol*. 2013;41(3):191-2. doi: 10.5543/tkda.2013.84484.
13. Abanoz M, Engin M. The effect of the relationship between post-cardiotomy neutrophil/lymphocyte ratio and platelet counts on early major adverse events after isolated coronary artery bypass grafting. *Turk Gogus Kalp Damar Cerrahisi Derg*. 2021;29(1):36-44. doi: 10.5606/tgkdc.dergisi.2021.20873.
14. Langer HF, Gawaz M. Platelet-vessel Wall interactions in atherosclerotic disease. *Thromb Haemost*. 2008;99(3):480-6. doi: 10.1160/TH07-11-0685.
15. Blake GJ, Ridker PM. Inflammatory bio-markers and cardiovascular risk prediction. *J Intern Med*. 2002;252(4):283-94. doi: 10.1046/j.1365-2796.2002.01019.x.
16. Laffey JG, Boylan JF, Cheng DC. The systemic inflammatory response to cardiac surgery: Implications for the anesthesiologist. *Anesthesiology*. 2002;97(1):215–52. doi: 10.1097/0000542-200207000-00030.
17. Iliopoulos I, Alder MN, Cooper DS, Villarreal EG, Loomba R, Sahay RD, et al. Pre-operative neutrophil-lymphocyte ratio predicts low cardiac output in children after cardiac surgery. *Cardiol Young*. 2020;30(4):521-5. doi: 10.1017/S1047951120000487.
18. Sun H, Que J, Peng Y, Ye H, Xiang H, Han Y, et al. The neutrophil-lymphocyte ratio: A promising predictor of mortality in coronary care unit patients - A cohort study. *Int Immunopharmacol*. 2019;74:105692. doi: 10.1016/j.intimp.2019.105692.
19. Şaşkın H, Düzyol Ç, Özcan KS, Aksoy R, Idiz M. Preoperative Platelet to Lymphocyte Ratio Is Associated with Early Morbidity and Mortality after Coronary Artery Bypass Grafting. *Heart Surg Forum*. 2015;18(6):E255-62. doi: 10.1532/hsf.1341.
20. Gungor H, Babu AS, Zencir C, Akpek M, Selvi M, Erkan MH, et al. Association of Preoperative Platelet-to-Lymphocyte Ratio with Atrial Fibrillation after Coronary Artery Bypass Graft Surgery. *Med Princ Pract*. 2017;26(2):164-8. doi: 10.1159/000453614.
21. Navani RV, Baradi A, Colin Huang KL, Jin D, Jiao Y, Nguyen JK, et al. Preoperative Platelet-to-Lymphocyte Ratio Is Not Associated With Postoperative Atrial Fibrillation. *Ann Thorac Surg*. 2020;110(4):1265-70. doi: 10.1016/j.athoracsur.2020.02.008.
22. Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res*. 2014;20(23):6212–22. doi: 10.1158/1078-0432.CCR-14-0442.
23. Yang YL, Wu CH, Hsu PF, Chen SC, Huang SS, Chan WL, et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. *Eur J Clin Invest*. 2020;50(5):e13230. doi: 10.1111/eci.13230.
24. Arques S. Human serum albumin in cardiovascular diseases. *Eur J Intern Med*. 2018;52:8-12. doi: 10.1016/j.ejim.2018.04.014.
25. Lee SI, Ko KP, Choi CH, Park CH, Park KY, Son KH. Does the prognostic nutritional index have a predictive role in the outcomes of adult cardiac surgery? *J Thorac Cardiovasc Surg* 2020;160(1):145-153.e3. doi: 10.1016/j.jtcvs.2019.08.069.

Author / ORCID	Authorship Contribution
Mustafa Abanoz 0000 0003 1821 1706	Concept, design, materials, data collection, analysis, literature review, manuscript writing, supervision and final approval of the article
Mesut Engin 0000 0003 2418 5823	Materials, data collection, analysis, literature review, manuscript writing, supervision and final approval of the article