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Original Article / *Özgün Makale*

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

İzole koroner arter baypas greftleme sonrası postkardiyotomi nötrofil/lenfosit oranı ve trombosit sayısı arasındaki ilişkinin erken dönem majör advers olaylar üzerine etkisi

Mustafa Abanoz[1], Mesut Engin[2]

Institution where the research was done:
University of Health Sciences, Şanlıurfa Mehmet Akif Inan Training and Research Hospital, Şanlıurfa, Turkey

Author Affiliations:
[1]Department of Cardiovascular Surgery, University of Health Sciences, Şanlıurfa Mehmet Akif Inan Training and Research Hospital, Şanlıurfa, Turkey
[2]Department of Cardiovascular Surgery, University of Health Sciences, Bursa Yüksek Ihtisas Training and Research Hospital, Bursa, Turkey

ABSTRACT

Background: In this study, we aimed to investigate the role of post-cardiotomy neutrophil, lymphocyte, and platelet counts in predicting major adverse events after coronary artery bypass grafting.

Methods: A total of 373 patients (257 males, 116 females; median age 63, range 33 to 85 years) who underwent isolated coronary artery bypass grafting under cardiopulmonary bypass between January 2015 and January 2020 were retrospectively analyzed. The patients who did not develop any postoperative major adverse event were included in Group 1, while those who did constituted Group 2. Preoperative neutrophil-to-lymphocyte ratio, postcardiotomy neutrophil-to-lymphocyte ratio, postoperative Day 1 neutrophil-to-lymphocyte ratio, and neutrophil-to-lymphocyte x platelet ratio were calculated.

Results: Preoperative neutrophil counts, C-reactive protein values, neutrophil-to-lymphocyte ratio, total perfusion time, and length of intensive care unit and hospital stay were significantly higher in Group 2 (p=0.019, p=0.028, p<0.001, p=0.027, p<0.001, and p<0.001, respectively). Post-cardiotomy neutrophil, neutrophil-to-lymphocyte ratio, and neutrophil-to-lymphocyte x platelet ratio, along with the postoperative first day white blood cell count, neutrophil, C-reactive protein, neutrophil-to-lymphocyte ratio, and neutrophil-to-lymphocyte x platelet ratio were significantly higher in Group 2 (p=0.004, p<0.001, p<0.001, p=0.019, p=0.003, p=0.001, p<0.001, and p=0.041, respectively). The post-cardiotomy platelet and lymphocyte counts and postoperative first day lymphocyte counts were significantly lower in Group 2 (p<0.001, p=0.007, and p=0.009, respectively).

Conclusion: Post-cardiotomy neutrophil-to-lymphocyte ratio and neutrophil-to-lymphocyte x platelet ratio can be easily accessible, inexpensive complete blood count parameters and may be more valuable in predicting major adverse events in patients undergoing coronary artery bypass grafting.

Keywords: Coronary artery bypass grafting, extracorporeal circulation, inflammation, leukocytes, neutrophil/lymphocyte ratio, platelet count.

ÖZ

Amaç: Bu çalışmada, koroner arter baypas greftleme sonrasında majör advers olayları öngörmede postkardiyotomi nötrofil, lenfosit ve trombosit sayısının rolü araştırıldı.

Çalışma planı: Ocak 2015 - Ocak 2020 tarihleri arasında kardiyopulmoner baypas ile izole koroner arter baypas greftleme yapılan toplam 373 hasta (257 erkek, 116 kadın; ort. yaş: 63 yıl; dağılım, 33-85 yıl) retrospektif olarak incelendi. Ameliyat sonrası majör advers olay gelişmeyen hastalar Grup 1'e alınırken, gelişen hastalar Grup 2'ye dahil edildi. Ameliyat öncesi nötrofil/lenfosit oranı, postkardiyotomi nötrofil/lenfosit oranı, ameliyat sonrası birinci gün nötrofil/lenfosit oranı ve nötrofil/lenfosit x trombosit oranı hesaplandı.

Bulgular: Grup 2'de ameliyat öncesi nötrofil sayıları, C reaktif protein değerleri, nötrofil/lenfosit oranı, toplam perfüzyon süresi ve yoğun bakım ünitesinde ve hastanede kalış süresi anlamlı olarak daha yüksekti (sırasıyla, p=0.019, p=0.028, p<0.001, p=0.027, p<0.001 ve p<0.001). Postkardiyotomi nötrofil, nötrofil/lenfosit oranı ve nötrofil/lenfosit x trombosit oranı ile ameliyat sonrası birinci gün beyaz kan hücre sayısı, nötrofil, C-reaktif protein, nötrofil/lenfosit oranı ve nötrofil/lenfosit x trombosit oranı Grup 2'de anlamlı olarak yüksek idi (sırasıyla, p=0.004, p<0.001, p<0.001, p=0.019, p=0.003, p=0.001, p<0.001 ve p=0.041). Grup 2'de postkardiyotomi trombosit ve lenfosit sayısı ve ameliyat sonrası ilk gün lenfosit sayıları ise anlamlı olarak daha düşüktü (sırasıyla, p<0.001, p=0.007 ve p=0.009).

Sonuç: Postkardiyotomi nötrofil/lenfosit oranı ve nötrofil/lenfosit x trombosit oranı kolaylıkla ulaşılabilir ve ucuz hemogram parametrelerinden olup, koroner arter baypas greftleme yapılan hastalarda majör advers olayları öngörmede daha değerli olabilir.

Anahtar sözcükler: Koroner arter baypas greftleme, ekstrakorporeal dolaşım, enflamasyon, lökositler, nötrofil/lenfosit oranı, trombosit sayısı.

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Correspondence: Mesut Engin, MD. SBÜ Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi Kalp ve Damar Cerrahisi Kliniği, 16310 Yıldırım, Bursa, Türkiye.
Tel: +90 507 - 206 66 22 e-mail: mesut_kvc_cor@hotmail.com

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Coronary artery bypass grafting (CABG) surgery is one of the most valuable treatment methods for coronary artery disease. In recent years, with the developments in cardiopulmonary bypass (CPB) technology, these operations can be performed with very low mortality and morbidity rates. However, following these operations, major adverse events (MAEs) such as postoperative rhythm problems, renal failure, cerebrovascular events, and mortality may occur.[1] It is particularly important to anticipate these potential problems and take necessary measures.

Inflammation plays a key role in the pathogenesis and progression of cardiovascular diseases. Therefore, many inflammatory parameters have been the subject of research in terms of showing the progression of CABG operations. One of the most important of these parameters and the subject of many studies is the neutrophil-to-lymphocyte ratio (NLR). Systemic inflammatory response is stimulated during heart surgery with a pump. As a result of this response, the NLR is positively affected, which may induce undesired results in the postoperative period.[2,3] Platelets are important mediators of inflammatory and ischemic damage in vital organs. It has been shown that low platelet count after CABG is associated with early mortality and poor prognosis.[4-6] In addition, the elevation of NLR and decreased platelet count within the first 12 h after major abdominal surgery have been shown to be the predictors for poor postoperative results.[7]

In this study, we aimed to investigate the role of post-cardiotomy NLR and platelet counts in predicting MAEs after CABG under CPB.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at University of Health Sciences, Şanlıurfa Mehmet Akif Inan Training and Research Hospital between January 2015 and January 2020. Patients who underwent isolated CABG under CPB were screened. Demographic data, preoperative blood parameters, and operative data were obtained from the hospital registry. Postoperative variables were accessed from the patients' intensive care unit (ICU) daily observation cards and patient files. Reoperations, emergency operations, patients who had acute coronary syndromes within the past month, combined surgeries, those with systemic inflammatory diseases, those under steroid therapy, those with chronic autoimmune diseases, those with preoperative creatinine values of ≥1.5 mg/dL, left ventricular ejection fraction ≤30%, patients who received intraoperative intra-aortic balloon support, and those with chronic liver and hematological diseases were excluded from the study. Finally, a total of 373 patients (257 males, 116 females; median age 63, range 33 to 85 years) who met the inclusion criteria were included in the study. The European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) values were calculated preoperatively for all patients. The primary outcome measure of the study was the development of an in-hospital major adverse event (MAE). The patients who did not develop postoperative MAEs were included in Group 1 (n=315) and those who did constituted Group 2 (n=58). A written informed consent was obtained from each patient. The study protocol was approved by the Harran University Faculty of Medicine Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Preoperative variables

Hypertension was defined as the use of at least one antihypertensive drug and/or arterial blood pressure above 140/90 mmHg; hyperlipidemia as the use of antilipidemic therapy and/or blood low density lipoprotein levels above 150 mg/dL; diabetes mellitus as the antidiabetic medication use, fasting blood glucose level above 126 mg/dL or above 200 mg/dL during routine examinations; preoperative renal failure as creatinine values above 1.5 mg/dL or receiving renal replacement therapy; preoperative carotid artery disease as a preoperative Doppler ultrasonographic evidence with at least one-sided lesion causing stenosis of at least 50%; preoperative chronic obstructive pulmonary disease as a post-bronchodilator forced expiratory volume in 1 sec/forced vital capacity of <70%; and preoperative cerebrovascular accident as having a history of neurological deficit for at least 24 h.

Definition of MAEs

In-hospital mortality was defined as the mortality occurring in the hospital during the postoperative period; postoperative myocardial infarction as having increased biomarker values (creatine kinase-MB or cardiac troponin levels) by at least five-fold, Q waves occurring in at least two electrocardiography leads, or development of ST segment changes or new left bundle branch block; renal failure as postoperative creatinine levels increasing to at least twice the preoperative value or need for renal replacement therapy; cerebrovascular accident as central neurological deficit for at least 24 h after the operation; infection as mediastinal infection involving bone and muscle structures requiring reoperation, pneumonia or septicemia requiring antibiotherapy; serious postoperative rhythm problems as atrial fibrillation and ventricular tachycardia/fibrillation requiring aggressive medical treatment and/or cardioversion, leading to hemodynamic instability and general condition impairment during the postoperative period; bleeding as postoperative drainage disrupting the hemodynamic stability and requiring reoperation; and prolonged ventilation as the need for ventilation for more than 24 h after the operation. The patients who fulfilled at least one of these definitions were included in Group 2.

Laboratory tests

Hematological parameters were examined using an automatic analyzer. Preoperative NLR (pre-NLR), post-cardiotomy NLR (PC-NLR, complete blood count assessment performed within the first hour of postoperative transfer into the ICU), and postoperative Day 1 NLR (po1-NLR) were calculated. The neutrophil-to-lymphocyte x platelet ratio (NLPR) calculation was performed using the following formula:[8]

$$\text{NLPR}=\frac{\text{Neutrophil count}(10^3/\mu\text{L})\text{x}100}{\text{Lymphocyte count}(10^3/\mu\text{L})\text{x Platelet count}(10^3/\mu\text{L}}$$

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to check normality distribution. The Student's t-test was performed to analyze normally distributed data, while the Mann-Whitney U test was used to analyze non-normally distributed data. The categorical variables were compared using the chi-square test. A multivariate logistic regression analysis was carried out to analyze the predictors of poor postoperative results, for which two models were created. The PC-NLR and platelet counts were evaluated separately in Model 1, while they were evaluated as post-cardiotomy NLPR (PC-NLPR) in Model 2. The receiver operating characteristic (ROC) curve analysis was performed to identify the predictive value of pre-NLR and PC-NLPR for poor postoperative results and the areas under the curve (AUC) were calculated. A *p* value of <0.05 was considered statistically significant.

RESULTS

Baseline demographic and clinical features of the patients are presented in Table 1. Group 1 consisted of 315 patients with a median age of 61 (range, 33 to 81) years, while Group 2 had 58 patients with a median age of 66 (range, 39 to 85) years (p=0.018). The groups were similar in terms of sex, hypertension, smoking, body mass index, hyperlipidemia, ejection fraction, and current medical treatments (such as statin use and beta-blocker therapy). Diabetes mellitus, previous coronary intervention rates, and EuroSCORE II values were significantly higher in Group 2 (p=0.015, p=0.032, and p<0.001, respectively).

The preoperative laboratory parameters and operative data of the patients are presented in Table 2. There were no significant differences between the groups in terms of white blood cell (WBC), hematocrit (Hct), platelet counts, urea, creatinine, NLPR, and cross-clamp times. However, the neutrophil counts, C-reactive protein (CRP) values, NLR, total perfusion time, and length of ICU and hospital stay were significantly higher in Group 2 (p=0.019, p=0.028, p<0.001, p=0.027, p<0.001, and p<0.001, respectively).

Postoperative blood parameters of the patients are presented in Table 3. Two groups were similar in terms of WBC and Hct values in the post-cardiotomy period. The post-cardiotomy neutrophil, PC-NLR, and PC-NLPR values, along with the postoperative first day WBC, neutrophil, CRP, PO1-NLR, and PO1-NLPR values were significantly higher (p=0.004, p<0.001, p<0.001, p=0.019, p=0.003, p=0.001, p<0.001, and p=0.041, respectively) while post-cardiotomy platelet and lymphocyte counts and postoperative first day lymphocyte counts were significantly lower in Group 2 (p<0.001, p=0.007, and p=0.009, respectively).

Following CABG operations under CPB, logistic regression analysis was performed to evaluate the predictors of MAEs (Table 4). According to the multivariate analysis, the independent predictors of postoperative MAEs included being above the age of 65 years (odds ratio [OR]: 0.670, 95% confidence interval [CI]: 0.576-0.894 p=0.045), EuroSCORE II (OR: 1.497, 95% CI: 1.090-2.165, p=0.005) preoperative CRP (OR: 1.061, 95% CI: 1.015-1.110, p=0.009), postoperative first day CRP (OR: 1.010 95% CI: 1.001-1.020, p=0.030), pre-NLR (OR: 1.130, 95% CI: 1.050-1.216, p=0.001), PC-NLR (OR: 1.520, 95% CI: 1.202-1.921, p<0.001), post-cardiotomy platelet counts (OR: 0.976, 95% CI: 0.678-0.998, p=0.014), and PO1-NLR (OR: 1.127, 95% CI: 1.010-1.257, p=0.033) for Model 1, and EuroSCORE II (OR: 1.230, 95% CI: 1.007-2.112, p=0.012), preoperative CRP (OR: 1.028, 95% CI: 1.009-1.410, p=0.006), postoperative first day CRP (OR: 1.016, 95% CI: 1.006-1.127, p=0.002), pre-NLR (OR: 1.247, 95% CI: 1.076-2.125, p<0.012), and PC-NLPR (OR: 1.968, 95% CI: 1.216-3.419, p<0.001) in Model 2.

Table 1. Baseline demographic characteristics and operative data of patients

	Group 1 (n=315)					Group 2 (n=58)					
Variables	n	%	Mean±SD	Median	IQR	n	%	Mean±SD	Median	IQR	*p*
Age (year)				61	33-81				66	39-85	0.024‡
Sex											
Male	216	68.5				41	70.6				0.748*
Hypertension	210	66.6				40	68.9				0.517*
Diabetes mellitus	63	20				20	34.4				0.015*
Previous PCI	74	23.4				22	37.9				0.032*
Current smoker	76	24.1				15	25.8				0.859*
COPD	37	11.7				13	22.4				0.098*
Previous CVA	26	8.2				9	15.5				0.216*
EuroSCORE II				19	0.5-5.2				2.7	0.5-9.4	<0.001‡
BMI (kg/m^2)				28.4	22.7-38.5				29	23-39	0.240*
Hyperlipidemia	90	28.5				17	29.3				0.896*
Ejection fraction			50.5±7.8					51±9.1			0.142†
ASA use	101	32				23	39.6				0.251*
ACEI/ARB use	115	36.5				23	39.6				0.648*
Statin use	101	32				19	32.7				0.918*
Beta blocker use	127	40.3				25	43.1				0.569*

SD: Standard deviation; IQR: Interquartile range; PCI: Percutaneous coronary intervention; COPD: Chronic obstructive pulmonary disease; CVA: Cerebrovascular accident; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II; BMI: Body mass index; ASA: Acetylsalicylic acid; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; * Chi-square test; † Student's t-test; ‡ Mann-Whitney U test.

Table 2. Preoperative laboratory data and perioperative data of patients

	Group 1 (n=315)		Group 2 (n=58)		
Variables	Median	IQR	Median	IQR	*p*‡
White blood cell (10^3/µL)	8.1	4.3-15	8.3	4.9-14.9	0.329
Hematocrit (%)	40.9	32.4-51.5	41	33-49.5	0.314
Platelet (10^3/µL)	241.6	130-488.3	254	136-456.2	0.367
Neutrophil (10^3/µL)	4.6	1.7-10.6	4.9	2.8-11.2	0.019
Lymphocyte (10^3/µL)	2	0.7-4.1	1.8	0.8-3.4	0.003
Creatinine (mg/dL)	1.1	0.5-1.49	0.94	0.6-1.49	0.317
Urea (mg/dL)	12	10-22	12	10-24	0.263
C-reactive protein (mg/dL)	8.3	0.2-57.4	10.8	0.9-73	0.028
NLR	2.5	0.9-7.3	3.2	1.2-9.9	<0.001
NLPR	1	0.2-4.6	1	0.3-4.7	0.330
Total perfusion time (min)	105	45-163	110	50-165	0.027
Cross-clamp time (min)	75	28-90	79	30-96	0.646
Number of distal anastomoses	3	1-5	3	1-5	0.829
Total ICU stay (days)	2	2-4	4	2-21	<0.001
Total hospital stay (days)	7	6-10	11	10-28	<0.001

IQR: Interquartile range; NLR: Neutrophil-to-lymphocyte ratio; NLPR: Neutrophil-to-lymphocyte x platelet ratio; ‡ Mann-Whitney U test.

Table 3. Postoperative laboratory data of patients

		Group 1 (n=315)		Group 2 (n=58)		
Variables		Median	IQR	Median	IQR	*p*
White blood cell ($10^3/\mu L$)	Post-cardiotomy	11	4.4-26.1	11.7	5.3-26.6	0.081
	First day	11.7	4-22.5	12.1	8.3-22.3	0.019
Hematocrit (%)	Post-cardiotomy	24	22.5-32	24	21-30.4	0.127
	First day	27	24-35.6	26.5	23.7-37	0.320
Platelet ($10^3/\mu L$)	Post-cardiotomy	143.2	73.4-326	129.5	70.9-230	<0.001
	First day	178	96.9-398.7	165.4	112.4-378.6	0.109
Neutrophil ($10^3/\mu L$)	Post-cardiotomy	9.5	3.7-18.8	11	4.4-19.4	0.004
	First day	9	3.2-14	9.9	5.8-16.6	0.003
Lymphocyte ($10^3/\mu L$)	Post-cardiotomy	1	0.1-4	0.8	0.3-2.4	0.007
	First day	1.2	0.3-2.9	1.1	0.3-2.4	0.009
C-reactive protein (mg/dL)	Post-cardiotomy	-	-	-	-	-
	First day	86	6.5-213	103.5	53.7-235	0.001
NLR	Post-cardiotomy	10	4-23.5	12.4	4.8-38.9	<0.001
	First day	6.8	2.5-18.3	8.7	4.1-15	<0.001
NLPR	Post-cardiotomy	7.1	2-21.3	12	2.1-41.4	<0.001
	First day	3.7	1-19.6	4.4	1.2-21.1	0.041

IQR: Interquartile range; NLR: Neutrophil-to-lymphocyte ratio; NLPR: Neutrophil-to-lymphocyte x platelet ratio; ‡ Mann-Whitney U test.

Table 4. Logistic regression analysis results

	Univariate analysis			Multivariate analysis		
Variables	*p*	Exp(B) Odds ratio	95% CI Lower upper	*p*	Exp(B) Odds ratio	95% CI Lower upper
Age >65	0.008	0.440	0.241-0.805	0.045* 0.098†	0.670* 0.978†	0.576-0.894* 0.864-1.090†
Previous PCI	0.022	0.502	0.278-0.907	0.128* 0.905†	1.005* 1.164†	0.867-1.100* 0.095-14.212†
Diabetes mellitus	0.016	0.475	0.259-0.872	0.229* 0.456†	0.894* 1.110†	0.756-1.009* 0.990-1.326†
Ejection fraction (%)	0.148	1.010	0.786-1.110	-	-	-
Body mass index	0.216	0.976	0.877-1.090	-	-	-
EuroSCORE II	<0.001	2.015	1.478-3.794	0.005* 0.012†	1.497* 1.230†	1.090-2.165* 1.007-2.112†
Preoperative C-reactive protein	0.001	1.062	1.025-1.100	0.009* 0.006†	1.061* 1.028†	1.015-1.110* 1.009-1.410†
Postoperative day 1 C-reactive protein	<0.001	1.017	1.009-1.025	0.030* 0.002†	1.010* 1.016†	1.001-1.020* 1.006-1.127†
Total perfusion time	0.023	1.015	1.002-1.028	0.150* 0.173†	1.011* 1.011†	0.996-1.026* 0.995-1.027†
Preoperative NLR	<0.001	1.184	1.108-1.265	0.001* <0.001†	1.130* 1.247†	1.050-1.216* 1.076-2.125†
Post-cardiotomy NLR	<0.001	1.615	1.312-1.988	<0.001* -	1.520* -	1.202-1.921* -
Post-cardiotomy platelet count	<0.001	0.984	0.976-0.992	0.014* -	0.976* -	0.678-0.998* -
Post-cardiotomy NLPR	<0.001	2.264	1.176-3.378	- <0.001†	- 1.968†	- 1.216-3.419†
Postoperative day 1 NLR	0.001	1.161	1.062-1.268	0.033* 0.218†	1.127* 1.075†	1.010-1.257* 0.958-1.207†

CI: Confidence interval; PCI: Percutaneous coronary intervention; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II; NLR: Neutrophil-to-lymphocyte ratio; NLPR: Neutrophil-to-lymphocyte x platelet ratio; * Multivariate analysis Model 1, † Multivariate analysis Model 2.

Table 5. Receiver operating characteristic curve analysis

	Univariate analysis			Multivariate analysis		
Variables	Cut-off	AUC	95% CI Lower upper	Sensitivity	Specificity	*p*
Preoperative NLR	2.4	0.653	0.573- 0.733	77.6%	48.3%	<0.001
Post-cardiotomy NLR	13.3	0.667	0.586- 0.748	60.8%	80.6%	<0.001
Post-cardiotomy NLPR	11.2	0.762	0.658- 0.836	66.9%	88.9%	<0.001
Postoperative day 1 NLR	6.8	0.657	0.590- 0.724	79.3%	50.2%	<0.001

AUC: Area under curve; CI: Confidence interval; NLR: Neutrophil-to-lymphocyte ratio; NLPR: Neutrophil-to-lymphocyte x platelet ratio.

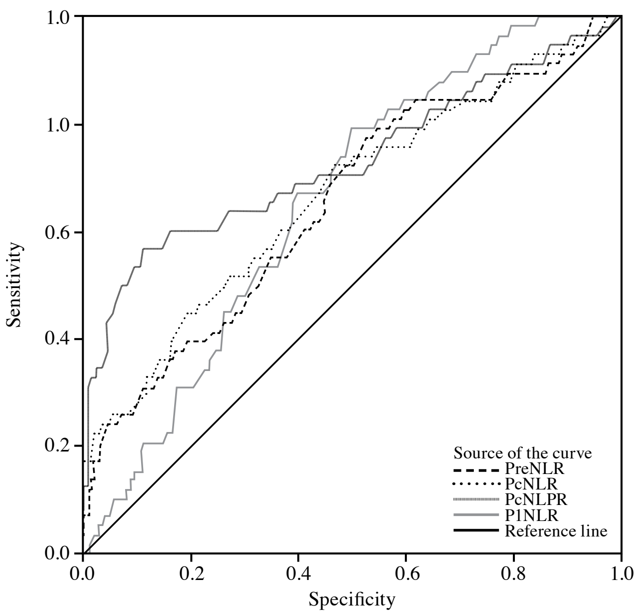

Figure 1. Receiver operating characteristic curve analysis.

The ROC analysis revealed that the cut-off values for pre-NLR, PC-NLR, PC-NLPR, and PO1-NLR were 3.24 (77.6% sensitivity, 48.3% specificity), 13.3 (60.8% sensitivity, 80.6% specificity), 11.2 (66.9% sensitivity, 88.9% specificity), and 6.8 (79.3% sensitivity, 50.2% specificity), respectively (Table 5, Figure 1).

DISCUSSION

Routine blood parameters have been extensively studied in predicting MAEs after CABG operations. Although more sophisticated markers have been developed in recent years, routine blood parameters are easy to obtain and inexpensive, which has led clinicians to further research the subject. The NLR is the most researched marker in the diagnosis and prognosis of cardiovascular diseases. In this study, we showed that PC-NLR was more predictive of undesired results after CABG in low-risk patients, compared to pre-NLR and PO1-NLR (OR: 1.520, p<0.001 for PC-NLR, OR: 1.130 p=0.001 for pre-NLR, OR: 1.127, p=0.033 for PO1-NLR). In the multivariate logistic regression analysis, Model 2 revealed that the PC-NLPR rate obtained by adding the platelet count to the NLR was more predictive than the NLR alone (OR: 1.968, p<0.001). In the ROC curve analysis, we found that the PC-NLPR had the highest specificity in predicting postoperative MAEs (cut-off: 11.2, 66.9% sensitivity, and 88.9% specificity).

Mortality is the most catastrophic result that can occur after CABG. Renal failure, cerebrovascular accident, serious infection, serious postoperative rhythm problems, and bleeding can lead to mortality, as well as prolonged hospital stay and increased number of working days lost. All these postoperative conditions can be defined as MAEs, and each of these events is associated with inflammation. In a study, the increased NLR was found to be associated with postoperative MAEs such as mortality, renal failure, infection, and prolonged ventilation after open heart surgery.[9] In another study, increased NLR and low platelet values posed an increased risk of renal failure and increased all-cause mortality during the postoperative period.[8] In contrary to these studies, we found that the relationship between PC-NLR value and platelet count obtained in the early postoperative period might be a good predictor for MAEs.

The NLR, which can be easily obtained from complete blood count parameters, has been extensively investigated in the field of cardiovascular surgery as in other fields of medicine.[10,11] The cellular immune system is stimulated with lymphocyte activation, due to which neutrophilia occurs. Therefore, the NLR increases with the increase in the neutrophil ratio and decrease in the lymphocyte count, which has prognostic significance in various diseases.[12] There are basically two reasons why the prognostic value of NLR is important. The first is that this value is less affected by possible physiological conditions, such as dehydration and exercise, compared to other inflammatory parameters. Another reason is that it is obtained by obtaining the ratio of neutrophils and lymphocytes, which are the parameters of the immune complement system. While the increase of neutrophils reveals non-specific inflammation, low lymphocyte counts indicate poor general health status and physiological stress.[13]

In their study, Gibson et al.[14] investigated the effect of pre-NLR value on mortality after CABG. In this study, 1,938 prospectively included patients were followed for a mean of 3.6 years. As a result of univariate and multivariate analyses, the increased pre-NLR was found as an independent predictor of cardiovascular mortality (hazard ratio: 1.08 per unit, p=0.008). In another study, the effect of pre- and postoperative second day NLR values on the results after cardiac surgery was investigated, and the increased perioperative NLR values were found to be significantly associated with morbidity and mortality following the operation.[15] In the retrospective cohort study of Silberman et al.[9] including 3,027 cardiac surgeries, the effect of pre-NLR on undesired results was investigated, and increased NLR values were found to be associated with morbid results such as prolonged ventilation, mortality, and low cardiac output syndrome. In both our multivariate analyses, we determined that the pre-NLR was an independent predictor of postoperative in-hospital morbidity and mortality.

The main purpose of our study was to investigate the possible effect of the CPB system on NLR in the early period and MAEs. In CABG operations with pumps, the blood comes into contact with the outer surfaces and, thus, inflammatory changes occur. The kallikrein is activated, which eventually activates neutrophils, leading to chemotactic stimulation and organ damage. Activated cytokines and free oxygen radicals released from the neutrophil granules contribute to this damage.[16] T and B cells, which are the components of the adaptive immune system, can be also activated during cardiac surgery and in the early period.[17] The postoperative results may be affected due to all aforementioned reasons.[18]

Although there are numerous studies in the literature investigating the NLR obtained on Day 1, 2, and 7 after open heart surgeries, the PC-NLR research has been very limited.[19] This may be due the fact that prospective studies remain restricted and routine hemogram assessment is not performed upon entry to the ICU in most clinics. Kim et al.[20] retrospectively investigated the effects of pre-NLR, PC-NLR, and NLR calculated on the first postoperative day on mortality and renal failure in 590 patients who underwent cardiac surgery to identify whether PC-NLR and NLR obtained on the first day after the operation were associated with early-stage renal failure. In addition, when used as a continuous variable, the PC-NLR value was determined as an independent predictor of one-year mortality due to all causes (OR: 1.02, p=0.006). Above 10, this variable was found to be quite highly predictive of one-year mortality (OR: 8.40, 95% CI: 2.50-28.17, p<0.001). In our study, we found that, compared to other variables, the PC-NLR was more predictive of postoperative MAEs in both multivariate analyses.

Platelets play a significant role in important tasks in the human body, such as hemostasis, tissue regeneration, thromboxane synthesis, and synthesis of adhesion molecules.[21] Cardiac surgery under CPB is known to lead to platelet activation, which can cause complications such as stroke and myocardial infarction in the postoperative period.[22] Its occurrence has been also associated with prolonged intensive care hospitalization, increased mortality, and renal insufficiency in these patients.[23]

Numerous studies have been conducted investigating the effectiveness of increased platelet counts in the diagnosis and prognosis of cardiovascular diseases.[19] However, our study is different in terms of demonstrating the effects of postcardiotomy low platelets on postoperative MAEs. Following cardiac surgery, platelets are effective through possible pathological consequences of bleeding mechanisms rather than thrombosis. As a result of the cellular and humoral system activation that occurs during and after CPB, a complex process involving platelets, vascular endothelium, fibrinogen, and neutrophils occurs, thereby, inducing a pathological process which progresses from bleeding risk to microthrombi.[24] Accordingly, in a study including 4,217 CABG patients by Kertai et al.,[4] decreased postoperative platelet counts were associated with early-stage renal failure and mortality.

In the light of all these data, a new ratio was put forward by Koo et al.[8] in 2018 in predicting potential poor outcomes following cardiac surgery operations. At the beginning of the study, the authors assumed that the NLPR obtained by adding the platelet count to the denominator of NLR could be a more valuable marker in predicting undesired outcomes. In this study, 1,099 adult cardiac surgeries were evaluated, and the NLR and NLPR values were calculated from complete blood count obtained in four different timepoints (preoperative, post-cardiotomy, and postoperative Days 1 and 2). In the multivariate analysis, the highest measured NLPR was found to be an independent predictor of early-stage renal failure and mortality for all five-year causes. In our study, we showed that NLPR was more predictive than NLR alone in predicting early MAEs after CABG. Also, in contrast to this study, we added the values related to the pre-NLR and NLPR to our data tables to achieve more reliable results.

In the current study, for pre-NLR, PC-NLR, PO1-NLR, and PC-NLPR, the ROC curves showed relatively low AUCs. Of note, it is worth to remind that none of these tests are diagnostic, but they are helpful in showing an increased level of inflammation which goes along with MAEs. They are easily accessible, inexpensive complete blood count parameters may be valuable in predicting MAEs. In addition, factors such as diabetes mellitus and age were also found to be higher in Group 2. These variables may be associated with increased MAEs ratios, as well as increased NLR values. Based on our study results, we believe that these blood parameters can be used as a supportive tool in addition to known risk factors.

Nonetheless, there are some limitations to this study. It has a retrospective design which may have led to study biases. In addition, the mean age and the rate of diabetes mellitus were higher in Group 2 than Group 1 which made Group 2 patients more susceptible to postoperative MAEs. Also, blood transfusion was unable to be evaluated in the study; however, the amount of blood transfusion is closely associated with prolonged intubation time and length of ICU and hospital stay, since the increased blood product use results in increased hemolysis, leading to microvascular complications by increasing the free iron content in the blood.[25] Finally, our study is a single center study with a relatively small sample size to make powerful predictions. The main strength of this study, on the other hand, is that the rate of NLPR was, for the first time, found to be associated with MAEs occurring after CABG. We believe that our study would inspire further large-scale, multi-center studies using subgroup analyses for poor postoperative outcomes.

In conclusion, high neutrophil-to-lymphocyte ratios have been accepted as a risk factor for cardiovascular disease. Our study results show that post-cardiotomy neutrophil-to-lymphocyte ratio and neutrophil-to-lymphocyte x platelet ratio, which are easily accessible, inexpensive complete blood count parameters, may be more valuable in predicting postoperative major adverse events. However, further multi-center studies in larger patient series are needed to demonstrate the predictive value of post-cardiotomy neutrophil-to-lymphocyte ratio and neutrophil-to-lymphocyte x platelet ratio.

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