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Preoperative Platelet to Lymphocyte Ratio Is Associated with Early Morbidity and Mortality after Coronary Artery Bypass Grafting

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ABSTRACT

Objective: To investigate the association of platelet to lymphocyte ratio to mortality and morbidity after coronary artery bypass grafting operation.

Methods: We evaluated records of 916 patients who underwent coronary artery bypass grafting operation between January 2009 and May 2014 retrospectively. Patients were grouped as Group 1 (n = 604) if the platelet to lymphocyte ratio was above 142 and Group 2 (n = 312) if platelet to lymphocyte ratio was below 142.

Results: The number of patients who developed a neurologic event during the hospital stay and in the first postoperative month was 7 (1.2%) in Group 1 and 12 (3.8%) in Group 2 for which the difference was statistically significant ($P = .007$). Early term mortality occurred in 3 patients (0.5%) in Group 1 and in 10 patients (3.2%) in Group 2 for which the difference was statistically highly significant ($P = .001$). In univariate and multivariate regression analysis, the preoperative platelet to lymphocyte ratio was determined as an independent risk factor for occurrence of atrial fibrillation in the early postoperative period, reoperation for sternum dehiscence, occurrence of a neurologic event, prolonged stay in the hospital and mortality.

Conclusion: In this study, elevated levels of platelet to lymphocyte ratio were associated with mortality and morbidity after coronary artery bypass grafting operation.

INTRODUCTION

Atherosclerosis is closely linked to inflammation and the role of inflammation in various cardiovascular diseases has been investigated in clinical trials [Libby 2009]. Leukocytes have an important role in the inflammatory process and white blood cells and subgroups have been used to predict prognosis in patients with or without coronary artery disease [Bhat 2013; Min 2014; Horne 2005]. Postoperative elevated levels of C reactive protein (CRP) have been shown to be associated with adverse cardiovascular and cerebrovascular events after off-pump coronary artery bypass grafting (CABG) operations [Bhat 2013]. Newall et al have observed that preoperative levels of leukocytes were associated with mortality after CABG operations [Newall 2006]. Especially neutrophils, platelets, and lymphocytes play an important role in development of atherosclerotic plaques, plaque rupture, and coronary thrombosis [Davi 2007]. In a study, it has been observed that decreased levels of lymphocytes preoperatively were associated with mortality and morbidity after cardiac surgery with a high sensitivity and specificity [Aghdaii 2014].

Neutrophil to lymphocyte ratio (NLR) has recently been shown to be associated with various cardiovascular diseases. Elevated NLR has been shown to be associated with poor prognosis in patients undergoing CABG operations [Bhat 2013]. Elevated levels and activation of platelets in circulation are associated with cardiovascular complications. Recently, platelet to lymphocyte ratio (PLR), which is closely associated with inflammation, has been investigated in various diseases. PLR has also been investigated in cardiovascular diseases, which are closely associated with inflammation [Gary 2013a]. PLR is both associated with inflammation, platelet aggregation, and also associated with atherosclerotic burden [Yüksel 2014]. PLR is accepted as a sensitive marker of inflammation, which is associated with prognosis in breast cancer, ovarian, cancer and colorectal cancer [Proctor 2011]. Recent studies have also revealed the prognostic role of PLR in cardiovascular diseases. In this study, we aimed to investigate the relationship of PLR to morbidity and mortality after CABG operation.

MATERIALS AND METHODS

In this study, the medical records of 1144 patients who underwent isolated CABG due to coronary artery disease by the same surgical team in the Cardiovascular Surgery Clinic of Kocaeli Acibadem Hospital between January 2009 and May 2014 were investigated retrospectively. 916 patients (80.1%) who underwent isolated CABG with cardiopulmonary bypass (CPB) were enrolled in the study, whereas 228 patients (19.9%) were excluded. The number of female patients was 183 (20%) and the average age was 60.8 ± 8.3 years (median: 61 years; range: 32 to 75 years). Patients were grouped into two groups based on the results of previous trials [Oylumlu 2015]. Two groups were determined: Group 1 (n = 604) and Group 2 (n = 312), which consisted of patients with a preoperative PLR value lower than 142 and higher than 142 respectively.

Patients with any of the following were excluded from the study: peripheral arterial disease; advanced age (>75 years);

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valvular heart disease; decompensated congestive heart failure; congenital cardiac disease; left ventricular systolic function disorder (left ventricular ejection fraction ≤30%); cerebrovascular disease in the last 30 days; renal impairment (serum creatinine >2 mg/dL); chronic obstructive pulmonary disease; malignancy; endocrinologic disorders (hypothyroidism, hyperthyroidism); systemic inflammatory diseases; hematological proliferative disease; low hemoglobin levels (≤10 g/dL); those who were severely overweight (body mass index >30 kg/m^2); who had acute infections; preoperative atrial and ventricular arrhythmia; emergency operations; reoperated on due to hemodynamic instability or bleeding; those who required intraaortic balloon pump; who had an acute myocardial infarction and percutaneous coronary intervention in the last 30 days prior to operation; a diagnosis of active or chronic autoimmune disease; those who had steroid treatment or chemotherapy; or who underwent beating heart or redo CABG.

The demographic and clinical data of the patients were obtained by using the software system of the hospital for records and archives to investigate the patient files, epicrisis, operation notes, and laboratory results. Arterial hypertension was considered in patients with measurements of blood pressure above 140 mmHg systolic and 90 mmHg diastolic at least three times or active use of antihypertensive medication. Diabetes mellitus was defined as fasting plasma glucose levels above 126 mg/dL in at least two different measurements, or active use of anti-diabetic drugs. Smoking was defined as current smoking or ex-smokers who had quit smoking in the last 6 months. Hyperlipidemia was accepted as total cholesterol >220 mg/dL and low-density lipoprotein (LDL)-cholesterol >130 mg/dL or use of antihyperlipidemic drugs.

Approximately 5 to 7 mL venous blood samples were placed into a sterile tube with EDTA. Hematologic parameters were calculated by an automated blood count device (Abbott CELL-DYN 3700; Abbott Laboratory, Abbott Park, IL, USA) following a waiting time of one hour. PLR was calculated by dividing the number of thrombocytes to the number of lymphocytes. NLR was calculated by dividing the number of thrombocytes to the number of neutrophils.

The relationship between PLR and occurrence of atrial fibrillation (AF), neurologic events, reoperation due to sternum detachment and sternal infection, length of hospital stay, and mortality in the postoperative period were sought. Postoperative stroke was accepted as a new focal neurologic deficit for a period longer than 24 hours for which the new ischemic brain damage was shown with computerized tomography or magnetic resonance imaging. The diagnosis of postoperative AF was made by standard 12 derivation electrocardiography (ECG). Morbidity and mortality during the stay in the hospital following operation or the first 30 postoperative days were accepted as postoperative early term morbidity and mortality. Prolonged stay in the hospital was defined as staying in the hospital for 7 days and over.

All of the patients were transferred to the intensive care unit intubated. They were extubated following onset of spontaneous breathing and normalization of orientation and cooperation if the hemodynamic and respiratory functions were appropriate. The patients were followed up by continuous ECG monitorization along the whole time of stay in the intensive care unit and the first 48 hours of stay in the inpatient room. If there was no contraindication, 50 mg/day of metoprolol was started orally for all patients following the first postoperative day. The patients were followed up by rhythm ECG once a day, and pulse and arterial blood pressure measurements in maximum intervals of four hours in the inpatient room.

This study complied with the Declaration of Helsinki and was carried out following approval of the Ethics Committee for Clinical Trials of Medical Faculty of Kocaeli University.

Table 1. Patient Demographic and Clinical Data

Characteristics	PLR < 142 (n = 604) Group 1	PLR ≥ 142 (n = 312) Group 2	*P*
Age, mean ± SD, years	59.9 ± 8.3	60.6 ± 8.3	.18**
Male (%)	491 (67.0)	113 (61.7)	.18*
Female (%)	242 (33.0)	70 (38.3)	0.18*
Hypertension (%)	374 (61.9)	178 (57.1)	0.15*
Diabetes mellitus (%)	201 (33.3)	93 (29.8)	.29*
Smoking (%)	249 (41.2)	118 (38.4)	.32*
Hyperlipidemia (%)	332 (55.0)	169 (54.2)	.82*
Ejection fraction (median)	56 (range: 30-72)	56 (range: 34-72)	.48**

*Pearson chi-squared test or Fisher exact test; **Mann-Whitney U test.

Operative Technique

All of the patients were operated with median sternotomy under general anesthesia and cardiopulmonary bypass (CPB) with aortic and venous cannulations following systemic heparin administration (300 IU/kg). Activated clotting time (ACT) was maintained over 480 seconds during the operations. Standard CPB circuit and surgical management were used. Antegrade hypothermic and hyperkalemic blood cardioplegia was applied to all patients. Surgery was performed under moderate systemic hypothermia (28-30ºC). Cardiopulmonary bypass flow was maintained at 2.2-2.5 L/min/m^2, mean perfusion pressure was maintained between 50 and 80 mmHg, and hematocrit level was maintained between 20 to 25 percent during CPB. For the coronary bypass operations, the left internal mammary artery (LIMA) was preferred for the arterial graft for left anterior descending artery (LAD) revascularization, whereas saphenous venous grafts were used for the other vessels. Distal anastomoses were done during aortic cross clamp period and proximal were done on beating heart onto the ascending aorta using a lateral clamp.

Statistical Analysis

Statistical analysis was performed using the SPSS software version 12.0 (SPSS, Chicago, IL, USA). Among the data measured, the ones showing normal distribution were

Table 2. Preoperative Blood Results and Hematological Parameters

Preoperative Blood Results and Hematological Parameters	PLR < 142 (n = 604) Group 1	PLR ≥ 142 (n = 312) Group 2	P
	Median (min-max)	Median (min-max)	
Hemoglobin (mg/dL)	13.6 (10.4-16.7)	13.7 (10.4-16.5)	.26**
Hematocrit (%)	41.1 (30.3-49.8)	41.2 (30.5-48.9)	.11**
Fasting blood glucose (mg/dL)	95 (70-304	92 (67-307)	.09**
Thrombocyte count (×10³/μL)	274.5 (153-420)	271 (150-420)	.30**
Lymphocyte count (×10³/μL)	2.1 (1.1-3.5)	1.8 (0.9-2.9)	.0001**
Neutrophil count (×10³/μL)	6.8 (3.4-11.9)	7.7 (2.9-11.9)	.0001**
Neutrophil-to-lymphocyte ratio	3.4 (1.3-5.5)	4.3 (2.0-6.5)	.0001**
C-reactive protein (mg/L)	0.48 (0.16-4.90)	0.61 (0.16-4.12)	.0001**
HbA1c levels (%)	5.5 (4.2-11.4)	5.8 (4.5-11.2)	.61**
Low density lipoprotein levels (mg/dL)	132 (87-161)	132 (77-171	.0001

*Pearson chi-squared test or Fisher exact test; **Mann-Whitney U test.

Table 3. Intraoperative and Postoperative Data

Characteristics	PLR < 142 (n = 604) Group 1	PLR ≥ 141 (n = 312) Group 2	P
	Median (min-max)	Median (min-max)	
Aortic cross clamp time (minutes)	51 (19-81)	51 (23-91)	.67**
Cardiopulmonary bypass time (minutes)	85 (42-119)	84 (45-126)	.81**
Amount of drainage (mL)	300 (150-1100)	300 (150-1250)	.06**
Intubation time (hours)	6 (3-22)	6 (3-19)	.27**
Stay in the intensive care unit (hours)	21(17-305)	21 (17-300)	.12**
Use of blood products)	217(35.9%)	118(37.8%)	.57*

*Pearson chi-squared test or Fisher exact test; **Mann-Whitney *U* test.

mentioned as mean ± standard deviation, the ones not showing normal distribution were mentioned as median (minimum-maximum). The data obtained by counting were shown as percentages (%). Among the data measured, the normality of distribution was evaluated by histogram or Kolmogorov-Smirnov test, and the homogeneity of distribution was evaluated by Levene test for equality of variance. Among the data measured, the difference between the groups was evaluated by Student *t* test in normal and homogenous distribution, and by Mann-Whitney *U* test in distribution that was not normal and homogenous. Spearman correlation test was used to detect the relation between all data. Among the data obtained by counting, the differences between the groups were evaluated by parametric or non-parametric Pearson chi-squared test or Fisher exact test according to the distribution being parametric or not. Receiver-operating characteristic (ROC) curve analysis was used to determine the optimum cutoff levels of the preoperative PLR to predict mortality and morbidity. Forward stepwise multivariate logistic regression models were created to identify the independent predictors of postoperative AF. Variables with a *P* value less than .10 in univariate analyses were included in the multivariate model. In case of a *P* value less than .05 among the groups, the difference was accepted as significant.

RESULTS

The demographic characteristics and clinical data of the patients are summarized in Table 1. There were no differences between the two groups in terms of demographic or clinical data.

The preoperative blood analysis and hematological parameters of the patients are summarized in Table 2. Lymphocyte counts (P = .0001), neutrophil counts (P = .0001), NLR (P = .0001), CRP levels (P = .0001), and LDL levels (P = .0001) were significantly different between the groups.

The intraoperative and postoperative data of the patients are shown in Table 3. There were no statistically significant differences between the two groups in terms of intraoperative and postoperative patient data. The average number of coronary grafts was 3.24 ± 0.96 (median: 3; range: 1-6) in Group 1, and 3.40 ± 0.93 (median: 3; range: 1-7) in Group 2, which was statistically significantly different between the groups (P = .04). Postoperative inotropic support was required in 41 patients (6.8%) in Group 1 and in 25 patients (8.0%) in Group 2, which was not statistically different between the groups (P = .50).

Neurologic events of any type (transient ischemic attack, speech disorder, hemiplegia, or hemiparesia) in the hospital and in the first postoperative month occurred in 7 patients (1.2%) in Group 1 and in 12 patients (3.8%) in Group 2, for which the difference between the groups was statistically significant (P = .007). Likewise, mortality in the hospital and in the first postoperative month occurred in 3 patients (0.5%) in Group 1 and in 10 patients (3.2%) in Group 2, for which the difference between the groups was statistically highly significant (P = .001).

Among 916 patients, postoperative AF occurred in

Table 4. Univariate and Multivariate Regression Analysis of Risk Factors for Sternum Revision and Total Duration of Hospital Stay

	Sternum Revision				Total Duration Of Hospital Stay			
Variables	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Male sex	0.99 (0.33-3.02)	.99	-	-	0.62 (0.39-1.00)	.049	0.70 (0.40-1.20)	.20
Age	0.99 (0.94-1.04)	.70	-	-	1.02 (0.99-1.05)	.12	-	-
Ejection fraction	0.95 (0.91-1.00)	.07	-	-	1.00 (0.98-1.02)	.96	-	-
Diabetes mellitus	0.70 (0.25-1.95)	.49	-	-	0.83 (0.52-1.32)	.43	-	-
Hypertension	1.55 (0.59-4.08)	.37	-	-	0.75 (0.49-1.15)	.19	-	-
Hyperlipidemia	0.67 (0.28-1.64)	.38	-	-	1.17 (0.77-1.79)	.47	-	-
Smoking	0.16 (0.04-0.70)	.02	0.18 (0.04-0.78)	.02	0.81 (0.53-1.26)	.35	-	-
Fasting blood glucose	0.99 (0.98-1.00)	.42	-	-	0.99 (0.98-1.00)	.31	-	-
Preoperative LDL	1.01 (0.98-1.03)	.67	-	-	1.01 (0.99-1.03)	.12	-	-
Preoperative platelet	0.99 (0.98-1.00)	.04	0.94 (0.89-0.99)	.03	1.00 (0.99-1.01)	.78	-	-
Preoperative lymphocyte	0.26 (0.09-0.72)	.01	4.50 (2.39-6.61)	.03	0.67 (0.43-1.03)	.07	-	-
PLR	1.05 (1.02-1.08)	.005	1.12 (1.01-1.25)	.03	1.04 (1.02-1.05)	.0001	1.03 (1.01-1.05)	.008
Preoperative neutrophil	1.12 (0.84-1.50)	.43	-	-	1.14 (0.99-1.30)	.07	-	-
NLR	3.38 (1.93-5.91)	.0001	2.95 (1.32-6.63)	.009	1.68 (1.30-2.18)	.0001	1.26 (9.91-1.74)	.17
Preoperative CRP	1.42 (0.64-3.15)	.40	-	-	1.46 (0.96-2.21)	.08	-	-
Preoperative hematocrit	0.97 (0.87-1.08)	.59	-	-	1.00 (0.95-1.06)	.93	-	-
Preoperative hemoglobin	0.96 (0.70-1.30)	.77	-	-	0.98 (0.85-1.14)	.80	-	-
Aortic cross clamp time	0.99 (0.95-1.03)	.52	-	-	1.02 (1.00-1.04)	.02	1.01 (0.97-1.05)	.69
CPB time	0.99 (0.96-1.02)	.45	-	-	1.02 (1.00-1.03)	.03	1.01 (0.97-1.04)	0.75
Intubation time	0.98 (0.77-1.25)	.89	-	-	1.49 (1.33-1.67)	.0001	1.44 (1.28-1.62)	.0001
Use of blood products	0.93 (0.37-2.36)	.88	-	-	0.91 (0.59-1.42)	.68	-	-
Use of inotropic support	1.56 (0.35-6.89)	.56	-	-	1.97 (1.02-3.84)	.04	1.08 (0.49-2.35)	.85
Amount of drainage	1.00 (0.99-1.01)	.81	-	-	1.00 (0.99-1.01)	.02	1.00 (0.99-1.01)	.71

PLR indicates platelet to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; CPB, cardiopulmonary bypass; LDL, low-density lipoprotein; CRP, C-reactive protein.

103 patients (17.1%) in Group 1 and 127 patients (40.7%) in Group 2, which showed a statistically highly significant difference between the groups (*P* = .0001). The number of patients reoperated due to sternum detachment and sternal infection, which are two causes of postoperative morbidity, were 7 (1.2%) in Group 1 and 13 (4.2%) in Group 2; this showed a statistically highly significant difference between the groups (*P* = .003).

The average length of stay in the hospital was 5.3 ± 1.1 (median: 5; range: 5-18) days in Group 1 and 6.4 ± 1.5 (median: 6; range: 5-18) days in Group 2. When compared regarding the length of stay in the hospital, there was a statistically highly significant difference between the groups (*P* = .0001).

The results of univariate and multivariate regression analysis of factors taking effect on length of stay of the patients in the hospital are shown in Table 4. With univariate regression analysis, male sex (*P* = .049), preoperative PLR (*P* = .0001), preoperative NLR (*P* = .0001), aortic cross clamp time (*P* = .02), CPB time (*P* = .03), length of duration of intubation (*P* = .0001), postoperative use of inotropic drugs (*P* = .04), and amount of drainage (*P* = .02) were found associated to length of stay in the hospital. In multivariate analysis of variables associated with prolonged stay in the hospital, preoperative PLR (OR: 1.03, 95% CI: 1.01-1.05, *P* = .008), duration of intubation (OR: 1.44, 95% CI: 1.29-1.62, *P* = .0001) were detected as independent risk factors.

The results of univariate and multivariate regression analysis of factors taking effect on reoperations due to sternum infection and detachment are shown in Table 4. With univariate analysis, smoking (*P* = .02), preoperative platelet count (*P* = .04), preoperative lymphocyte count (*P* = .01), NLR (*P* = .0001) and PLR (*P* = .005) were found associated with reoperations for sternum revision in the early postoperative period. In multivariate regression analysis of these variables, smoking (OR: 0.18, 95% CI: 0.04-0.78,

Table 5. Univariate and Multivariate Regression Analysis of Risk Factors for Postoperative AF and Neurological Events

	Neurologic Events				Postoperative Atrial Fibrillation			
Variables	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
Male sex	0.69 (0.25-1.95)	.49	-	-	0.90 (0.62-1.30)	.56	-	-
Age	1.02 (0.96-1.08)	.56	-	-	1.00 (0.98-1.01)	.66	-	-
Ejection fraction	0.97 (0.92-1.02)	.23	-	-	0.99 (0.98-1.00)	.82	-	-
Diabetes mellitus	0.56 (0.18-1.70)	.30	-	-	0.85 (0.62-1.18)	.34	-	-
Hypertension	1.87 (0.67-5.23)	.23	-	-	0.83 (0.62-1.13)	.24	-	-
Hyperlipidemia	1.14 (0.46-2.87)	.78	-	-	0.89 (0.66-1.21)	.46	-	-
Smoking	0.87 (0.34-2.23)	.77	-	-	0.97 (0.72-1.32)	.86	-	-
Fasting blood glucose	0.99 (0.98-1.01)	.28	-	-	1.00 (0.99-1.01)	.13		
Preoperative LDL	1.02 (0.99-1.05)	.17	-	-	1.00 (0.99-1.01)	.78		
Preoperative platelet	1.00 (0.99-1.01)	.94	-	-	1.00 (0.99-1.01)	.24	-	-
Preoperative lymphocyte	0.50 (0.19-1.33)	.17	-	-	0.80 (0.59-1.08)	.15	-	-
PLR	1.06 (1.02-1.10)	.001	1.06 (1.01-1.06)	.006	1.05 (1.04-1.06)	.0001	1.03 (1.02-1.04)	.0001
Preoperative neutrophil	1.07 (0.80-1.44)	.64	-	-	1.28 (1.15-1.41)	.0001	1.19 (1.07-1.33)	.001
NLR	1.52 (0.88-2.63)	.14	-	-	1.81 (1.49-2.19)	.0001	1.17 (0.92-1.50)	.20
Preoperative CRP	2.58 (1.51-4.40)	.001	2.37 (1.34-4.17)	.003	2.78 (1.89-4.11)	.0001	1.89 (1.28-2.79)	.001
Preoperative hematocrit	1.02 (0.91-1.14)	.75	-	-	0.96 (0.92-1.00)	.049	0.95 (0.92-0.99)	.01
Preoperative hemoglobin	1.19 (0.85-1.66)	.31	-	-	0.91 (0.82-1.01)	.07	-	-
Aortic cross clamp time	0.98 (0.95-1.02)	.37	-	-	1.00 (0.99-1.01)	.85	-	-
CPB time	0.99 (0.97-1.02)	.62	-	-	1.00 (0.99-1.01)	.60	-	-
Intubation time	1.02 (0.80-1.28)	.94	-	-	1.01 (0.94-1.09)	.75	-	-
Use of blood products	0.61 (0.22-1.72)	.35	-	-	1.19 (0.87-1.61)	.28	-	-
Use of inotropic support	3.59 (1.16-11.15)	.03	4.23 (1.31-13.7)	.07	1.04 (0.59-1.84)	.90	-	-
Amount of drainage	0.99 (0.98-1.01)	.62	-	-	1.00 (0.99-1.01)	.20	-	-

PLR indicates platelet to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; CPB, cardiopulmonary bypass; LDL, low-density lipoprotein; CRP, C-reactive protein.

P = .02), preoperative platelet count (OR: 0.94, 95% CI: 0.89-0.99, *P* = .03), preoperative lymphocyte count (OR: 4.50, 95% CI: 2.39-6.61, *P* = .03), preoperative PLR (OR: 1.06, 95% CI: 1.03-1.10, *P* = .001), and preoperative NLR (OR: 2.95, 95% CI: 1.32-6.63, *P* = .009) were detected as independent risk factors for sternum revision in the early postoperative period.

The results of univariate and multivariate regression analysis of patients who developed a neurologic event in the early postoperative period are shown in Table 5. With univariate analysis, preoperative PLR (*P* = .001), preoperative NLR (*P* = .001), and postoperative use of inotropic drugs (*P* = .03) were found associated with occurrence of a neurologic event in the early postoperative period. In multivariate regression analysis of these variables, preoperative PLR (OR: 1.03, 95% CI: 1.01-1.06, *P* = .01), preoperative NLR (OR: 2.37, 95% CI: 1.34-4.17, *P* = .003), and postoperative use of inotropic drugs (OR: 4.23, 95% CI: 1.31-13.7, *P* = .07) were detected as independent risk factors for neurologic events to occur in the early postoperative period.

The results of univariate and multivariate regression analysis of patients who developed AF in the early postoperative period were shown in Table 5. With univariate analysis, preoperative neutrophil count (*P* = .0001), preoperative PLR (*P* = .0001), preoperative NLR (*P* = .0001), preoperative CRP (*P* = .0001), and preoperative hematocrit (*P* = .049) were found associated with occurrence of early postoperative AF. In multivariate regression analysis of these variables, preoperative neutrophil count (OR: 1.19, 95% CI: 1.07-1.33, *P* = .001), preoperative PLR (OR: 1.03, 95% CI: 1.02-1.04, *P* = .0001), preoperative CRP (OR: 1.89, 95% CI: 1.28-2.79, *P* = .001), and preoperative hematocrit (OR: 0.95, 95% CI: 0.92-0.99, *P* = .01) were detected as an independent risk factor for occurrence of AF in the early postoperative period.

The results of univariate and multivariate regression analysis of patients who died in the early postoperative period

Table 6. Univariate and Multivariate Regression Analysis of Risk Factors for Mortality

	Mortality			
Variables	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Male sex	0.56 (0.17-1.83)	.33	-	-
Age	1.00 (0.94-1.07)	.97	-	-
Ejection fraction	1.07 (0.99-1.15)	.08	-	-
Diabetes mellitus	0.94 (0.29-3.08)	.92	-	-
Hypertension	0.41 (0.13-1.25)	.12	-	-
Hyperlipidemia	1.88 (0.58-6.15)	.30	-	-
Smoking	1.29 (0.43-3.86)	.65	-	-
Fasting blood glucose	1.00 (0.99-1.01)	.89	-	-
Preoperative LDL	1.06 (1.02-1.10)	.004	1.03 (1.00-1.06)	.045
Preoperative platelet	1.00 (0.99-1.01)	.99	-	-
Preoperative lymphocyte	0.50 (0.16-1.62)	.25	-	-
PLR	1.09 (1.04-1.14)	.0001	1.06 (1.00-1.12)	.045
Preoperative neutrophil	1.33 (0.94-1.90)	.11	-	-
NLR	2.76 (1.42-5.40)	.003	1.54 (0.66-3.61)	.32
Preoperative CRP	2.12 (1.09-4.12)	.03	1.48 (0.65-3.35)	.35
Preoperative hematocrit	1.02 (0.89-1.17)	.79	-	-
Preoperative hemoglobin	1.43 (0.93-2.20)	.11	-	-
Aortic cross clamp time	0.99 (0.94-1.03)	.54	-	-
CPB time	0.99 (0.96-1.02)	.70	-	-
Intubation time	1.00 (0.75-1.33)	.98	-	-
Use of blood products	1.09 (0.35-3.35)	.89	-	-
Amount of drainage	1.00 (0.99-1.01)	.96	-	-

PLR indicates platelet to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; CPB, cardiopulmonary bypass; LDL, low-density lipoprotein; CRP, C-reactive protein.

are shown in Table 6. With univariate analysis, preoperative LDL (*P* = .004), preoperative PLR (*P* = .0001), preoperative NLR (*P* = .003), and preoperative CRP (*P* = .03) were found associated with mortality in the early postoperative period. In multivariate regression analysis of these variables, preoperative PLR (OR: 1.06, 95% CI: 1.00-1.12, *P* = .045), and preoperative LDL (OR: 1.03, 95% CI: 1.00-1.06, *P* = .045) were detected as independent risk factors for mortality in the early postoperative period.

The ROC curves for the PLR were connected with morbidity following CABG (Figure 1). The area under curve (AUC) for the preoperative PLR was 0.953 (95% CI: 0.937-0.968, *P* = .0001). Using a cut-off value of 142.6, the preoperative PLR predicted morbidity with a sensitivity of 92.3% and specificity of 91.9%.

The ROC curves for the PLR were connected with mortality following CABG (Figure 2). The area under curve (AUC) for the preoperative PLR was 0.737 (95% CI: 0.557-0.917, *P* = .003). Using a cut-off value of 148.85, the preoperative PLR predicted mortality with a sensitivity of 76.9% and specificity of 76.5%.

DISCUSSION

In this study, elevated preoperative PLR was associated with in-hospital and early postoperative mortality, neurologic events, atrial fibrillation, sternum revision, and duration of hospital study after isolated CABG operation. To the best of our knowledge this is the first study to evaluate the association of PLR with in hospital and early mortality and morbidity after CABG operation.

Morbidity and complications associated with CABG operation diminish the quality of life of the patient and increases health costs [Pinna Pintor 2003]. There are several risk models to estimate mortality and morbidity associated with CABG and several blood markers were investigated in this regard, but the role of PLR has not been clearly elucidated [De Cocker 2011].

Inflammation has several roles at all stages of atherosclerosis, including initiation, progression, and in the thrombotic complications of this complex disease process [Hansson 2005; Libby 2002]. Several inflammatory biomarkers including white blood cell count, leukocyte subtypes, platelet, CRP, and NLR have been demonstrated to be important prognostic predictors in various cardiovascular diseases [Oylumlu 2015].

Leukocytes and subtypes of leukocytes are the primary cells of inflammation that are associated with adverse cardiac events in cardiovascular diseases [Kaya 2013]. Bagger et al observed that preoperative elevated leukocyte counts were associated with 30-day mortality after CABG operation in 2058 patients [Bagger 2003]. Leukocyte count is a non-specific marker that may increase due to numerous conditions, therefore leukocyte subtypes may be more predictive. Gibson et al observed that elevated leukocyte count was not associated with mortality following CABG operation [Gibson 2010].

Postoperative AF is an important predictor of morbidity after CABG operation. The association between postoperative AF and CRP levels has been shown in several studies. Dernellis et al observed that increased levels of CRP were associated with AF [Dernellis 2006].

Neutrophil lymphocyte ratio is a new inflammatory marker associated with inflammation [Gibson 2010]. Elevated neutrophils and decreased lymphocytes have been shown to be markers of risk for cardiovascular events [Baetta 2010; Benites-Zapata 2015]. Elevated NLR was associated with postoperative atrial fibrillation after CABG [Gibson 2010].

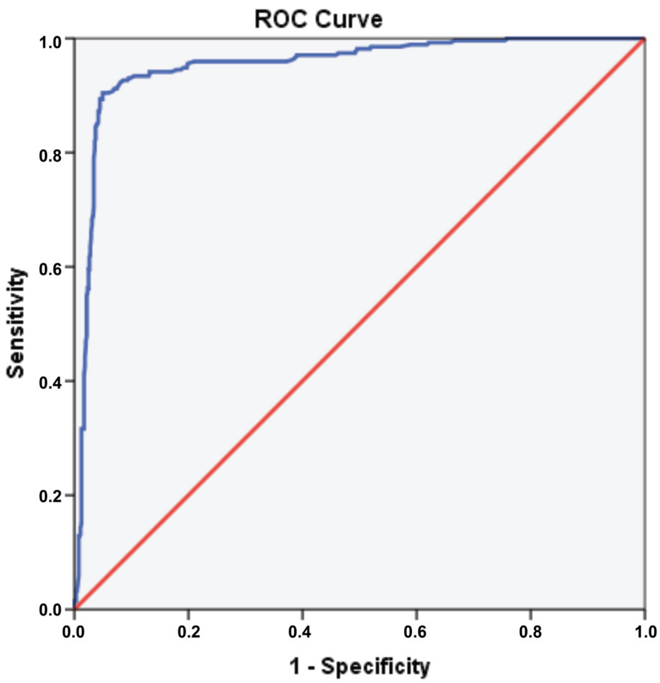

Figure 1. ROC curve analysis for PLR regarding occurrence of postoperative morbidity.

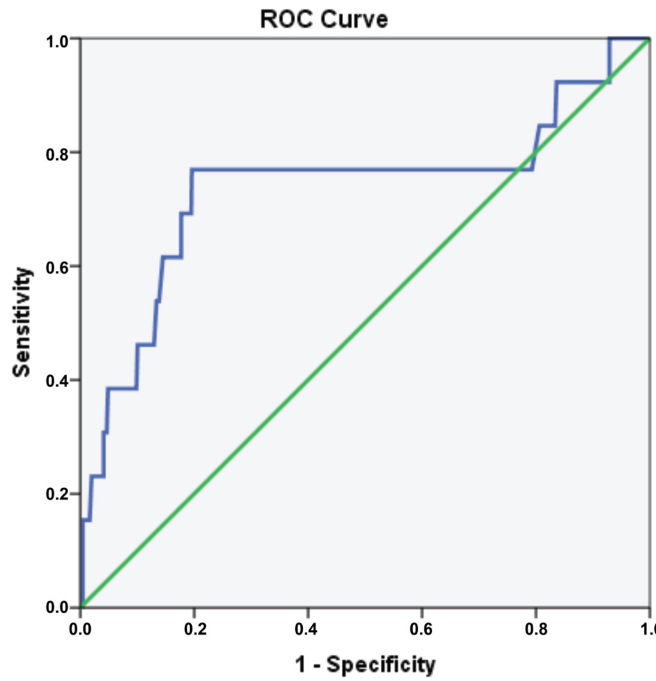

Figure 2. ROC curve analysis for PLR regarding occurrence of postoperative mortality.

It has also been shown that NLR is associated with adverse events following CABG in stable and unstable angina pectoris [Gibson 2007]. Ünal et al observed that preoperative NLR was correlated with mortality after CABG [Ünal 2013]. It has also been shown that elevated NLR was a significant prognostic factor in patients with various malignancies [Kwon 2012].

PLR is a recently defined hematological parameter associated with both aggregation and inflammation pathways, and it can be more valuable than either platelet or lymphocyte counts alone in prediction of coronary artery disease [Azab 2012; Bhatti 2010; Wang 2013].

The ratio of platelets to lymphocytes can be calculated with a simple hemogram analysis of a peripheral blood sample. Zouridakis et al observed that low lymphocyte counts were associated with cardiovascular events in patients with unstable angina pectoris [Zouridakis 2000]. Myocardial ischemia leads to physiologic stress and cortisol release, which leads to decreased lymphocyte counts. On the other hand, elevated platelet counts may be predictive for thrombotic complications [Zouridakis 2000; Ommen 1997; Thomson 1980; Caligiuri 1998].

PLR values were found to be high in various peripheral vascular diseases, coronary artery disease, myocardial infarction, and certain gynecological and hepatobiliary malignancies, and this has been related with a poor prognosis [Azab 2012; Bhatti 2010; Wang 2013; Unal 2013; Gary 2013b].

Azab et al observed higher PLR to be associated with mortality in patients admitted with non-ST segment elevation myocardial infarction [Azab 2012]. Temiz et al observed elevated PLR to be associated with in hospital mortality in patients with ST segment elevation myocardial infarction [Temiz 2014]. In two recent studies it has been observed that PLR is associated with saphenous vein graft disease in stable coronary artery disease [Yayla 2015; Kundi 2015].

Limitations

A few limitations of our study deserve mention. This is a single center retrospective study with a relatively small sample size. Despite the fact that we have found some parameters associated with mortality, we could not draw a causal relationship.

Conclusion

In our study, we observed that elevated PLR was an independent predictor of early mortality, postoperative atrial fibrillation, neurological events, sternum revision, and prolonged hospitalization. PLR, which can easily be obtained from a simple complete blood count, may predict adverse events after CABG. Although we could not establish a causal relationship in this study, the results of this study may have some clinical implications if approved by large-scale prospective studies.

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