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RESEARCH ARTICLE

The Effect of Novel Inflammatory Biomarkers on Determining Early Mortality After Cardiac Surgery in Patients with Chronic Renal Failure

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ABSTRACT

Objective: Various hemogram parameters have been used for predicting mortality in intensive care. In this study, the effect of new inflammatory biomarkers such as mean platelet volume, platelet/lymphocyte ratio, and neutrophil/lymphocyte ratio on early mortality was researched in patients with chronic renal failure, who had a cardiac surgery operation.

Materials and Methods: All the patients with preoperative chronic renal failure who underwent on-pump or off-pump cardiac surgery in our clinic between September 2016-September 2019 were examined. Patients' demographic data, preoperative hemoglobin, platelet/lymphocyte, neutrophil/lymphocyte, and mean platelet volume and postoperative hemoglobin, platelet/lymphocyte, neutrophil/lymphocyte and MPV were reviewed. Whether there is a difference in on-pump and off-pump surgeries on the matter and their 30-day surgical mortality were assessed in intensive care follow-ups.

Results: Of the patients included in the study within the preoperative period, 74 (60%) had DM and 94 (76.4%) were hypertensive. The mean duration of the patients' hospitalization was found as 13.88±2.4 days. Thirty-day surgical mortality: 30 (24.4%); preoperative and postoperative, platelet/lymphocyte, neutrophil/lymphocyte of the patients did not appear significant. It was found that MPV in the on-pump group was significantly higher in both preoperative and postoperative values than in the off-pump group. Preoperative PLR and NLR values were significantly lower ($p<0.05$) in the off-pump group.

Conclusion: MPV is an important marker in determining the postoperative mortality in patients with chronic renal failure who had cardiac surgery.

Keywords: Cardiac surgery, chronic renal failure, inflammatory biomarkers, mortality

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INTRODUCTION

The number of patients with dialysis-dependent chronic renal failure (DDCRF) has increased due to the aging patient population and the availability of better options to manage these kinds of patients.[1] DDCRF is one of the most important causes of mortality and morbidity in cardiovascular patients.[2] The incidence of cardiac diseases is higher in this patient group compared to the normal population.[3] Hemogram is a cheap and quick test providing comprehensive information frequently used in end-stage renal failure. Even though the effects of high-risk patients on health costs have declined over time, they are still of economic importance. A hemoglobin value provides economical and quick information about inflammation.[4] Recently, various hemogram parameters have been used for predicting mortality in intensive care. It has been discovered that the neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte (PLR) ratios are potentially useful inflammation markers in patients undergoing cardiovascular surgery.[5] One recent measure of cardiovascular risk is the rise in mean platelet volume (MPV). One

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important parameter that indicates platelet activation and function is MPV. An important part of the pathophysiology of atherothrombosis is played by active platelets. Studies have shown that components produced by platelets as well as platelet content play an active role in the generation of inflammation during the pathogenesis of atherothrombosis. [5,6] These parameters are important in respect of the easy determination of the high-risk patients, early treatment of the patients, and the prediction of the prognosis of the disease. Our study aims to interpret the correlation between MPV and in-hospital mortality in CABG patients.

MATERIALS and METHODS

In this retrospective study, all the patients who received postoperative hemodialysis between September 1, 2016, and September 1, 2019, were included in the study.

After obtaining the approval of the İstanbul Mehmet Akif Ersoy Thoracic Cardiovascular Surgery Training and Research Hospital Clinical Research Ethics Committee (Date: 10.09.2019, number: 2019-58), the data of the patients hospitalized in the chronic intensive care unit was reviewed from the hospital hospitalization file and electronic registry system. All the patients with chronic renal failure who received postoperative hemodialysis were included in the study. Patients below 18 years of age, patients with unstable hemodynamics who could not receive dialysis treatment and were undergoing continuous renal replacement therapy, and those who had an active infection and primary immunodeficiency were excluded from the study. The study was conducted in accordance with the Declaration of Helsinki.

In our hospital, peripheral venous blood samples were routinely taken from the patients before the operation. The samples were placed in sterile tubes containing a standard amount of anticoagulant. For determining the results of the complete blood count (CBC) parameters, the automatic blood samples were analyzed via SysmexXN: XN Series analyzers one hour after obtaining the samples.

Recently, various hemogram parameters have been used to predict mortality in the intensive care unit. Among these parameters, the mean platelet volume (MPV), neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) have been used. With these parameters, we compared preoperative and postoperative values to easily identify the high-risk patients, initiate their treatment at an early stage, and predict the prognosis of the disease.

The patients were divided into two groups. The patients were divided according to the use of cardiopulmonary bypass during cardiac surgery, and they were compared among themselves. In addition, preoperative and postoperative values were analyzed to determine whether blood parameters could be evident in early predicting 30-day mortality.

The preoperative parameters assessed in patients: demographic data (age, sex), preoperative hemoglobin values, glucose, blood urea nitrogen (BUN), creatinine, platelet/lymphocyte ratio, neutrophil/lymphocyte ratio, MPV and the types of cardiac surgery. Postoperative data that we evaluate are the glucose levels, BUN, creatinine, platelet/lymphocyte ratio, neutrophil/lymphocyte ratio, MPV values of the first day after surgery, hospitalization in the intensive care unit and the deaths occurring in the first 30 days were recorded. Dialysis-dependent patients received hemodialysis three times a week in the preoperative period in compliance with the surgical procedure and dialysis protocol routine in our hospital. Routine cardiac surgery procedures were applied to all the patients. Following the surgery, dialysis was initiated in dialysis-dependent patients in the intensive care unit after hemodynamic stabilization. Hemodialysis was carried out routinely one day before and one day after the surgery. Continuous veno-venous hemodialysis was performed in all the patients, at an early stage in the presence of hyperkalemia or hypervolemia, if necessary, 24 hours after the operation.

Antecubital vein vascular access was used, and midazolam (0.05–0.1 mg/kg) was prescribed prior to invasive radial artery cannulation using an arterial cannula (BD Temse, Belgium). Fentanyl (2 mg/kg), etomidate (0.2 mg/kg), or propofol (1 mg/kg) were used to produce anesthesia. Atracurium (0.5 mg/kg) was administered to aid in the intubation process. Central venous catheterization was carried out from the right internal jugular vein. Throughout the procedure, several vital signs were recorded, including the electrocardiogram, pulse oximetry, end tidal CO_2 ($ETCO_2$), nasopharyngeal temperature, central venous pressure, invasive blood pressure, urine volume, and arterial blood gases.

Following the median sternotomy, left internal mammarian artery (LIMA) and saphenous vein grafts (SVG) were prepared in all the bypass patients. Myocardial protection was ensured by the moderate systemic hypothermia with body temperatures of the on-pump patients at 32–34°C and antegrade blood cardioplegia. Hematocrit was kept around 21–25% during circulation. Blood cardioplegia was employed for myocardial protection. The flow rate was provided as 2.2–2.4 l/m^2. In the postoperative period, intensive care protocol was applied. Patient survival was defined as survival 30 days after cardiac surgery.

Table 1. Demographic data of patients

	Min-max	Median	Mean±SD	n	%
Age	18.00–81.00	62.50	61.72±10.78		
Sex					
Female				51	36.96
Male				87	63.04
Valve					
(–)				84	60.87
(+)				54	39.13
Valve operation					
MVR				41	29.71
AVR				10	7.25
TVA				33	23.91
AAA					
(–)				114	82.61
(+)				24	17.39
CABG					
(–)				38	27.54
(+)				100	72.46
Revision					
(–)				102	73.91
(+)				36	26.09
Complication					
(–)				64	46.38
(+)				74	53.62
30 day mortality					
(–)				104	75.36
(+)				34	24.64

SD: Standard deviation; MVR: Mitral valve replacement; AVR: Aortic valve replacement, TVA: Tricuspid valve annuloplasty; AAA: Abdominal aortic aneurysm; CABG: Coronary artery bypass grafting

Statistical Analysis

The descriptive statistics included were mean, standard deviation, median, lowest, maximum value frequency, and percentage. The Kolmogorov-Smirnov test was used to examine the variable distribution. The quantitative data were compared using the Independent Samples t-test and the Mann-Whitney U test; the qualitative data were compared using the Chi-Squared test. The effect level was tested by logistic regression. SPSS 26.0 (IBM, Armonk, NY, USA) was used for statistical analyses.

RESULTS

Of 123 patients, 78 were men and 45 were women, the mean age was 61.7±10.3 years, in the on-pump group 47 were female and 78 were male, in the off-pump group 4 of them were female and 9 were male, and their distribution was determined as 43–83. Of the patients included in the study 74 (60%) had DM and 94 (76.4%) were hypertension patients. The mean duration of the patients' hospitalization was found as 13.88±2.4 days. Thirty-day surgical mortality was 30 (24.4%). All the patients with mortality were undergone on-pump cardiac surgery.

Table 2. Comparison of preoperative and postoperative blood values of patients

	Min-max	Median	Mean±SD
BUN			
Preop	9.0–99.0	33.5	37.6±18.4 [m]
Postop	8.5–90.0	36.5	38.6±14.9 [m]
Glucose			
Preop	60.0–412.0	129.0	146.7±63.6 [m]
Postop	65.0–416.0	171.0	175.3±57.5 [m]
Creatine			
Preop	0.6–13.0	2.5	3.4±2.6 [m]
Postop	1.0–10.5	2.5	3.6±2.3 [m]
Hgb			
Preop	5.9–22.1	10.5	10.6±2.4 [m]
Postop	5.6–12.9	8.9	8.9±1.1 [m]
MPV			
Preop	8.7–15.3	10.8	10.9±1.0 [m]
Postop	9.0–40.1	11.1	11.4±2.7 [m]
PLR			
Preop	7.3–582.4	130.3	156.6±100.1 [m]
Postop	4.4–900.0	222.2	252.7±179.6 [m]
NLR			
Preop	0.4–44.9	3.0	4.7±5.5 [m]
Postop	1.5–316.6	16.0	23.4±39.5 [m]

[m]: Mann–whitney u test. SD: Standard deviation; BUN: Blood urea nitrogen; Hgb: Hemoglobin; MPV: Mean platelet volume; PLR: Platelet lymphocyte ratio; NLR: Neutrophil lymphocyte ratio

Demographic data of the patients were summarized in Table 1, comparison of preoperative and postoperative blood values of patients were shown in Table 2.

In the 30-day mortality group, preoperative and postoperative Hgb, PLR and NLR values did not differ significantly from the 30-day non-mortality group ($p>0.05$). In the 30-day mortality group, preoperative and postoperative MPV values were significantly higher than those of the 30-day non-mortality group ($p<0.05$) (Table 3).

When MPV values were compared in the on-pump and off-pump groups, it was found to be highly significant in

Table 3. Blood values effects on 30-day mortality

	30 day mortality (–)		30 day mortailty (+)		p
	Mean±SD	Median	Mean±SD	Median	
BUN					
Preop	39.3±19.2	34.5	32.5±14.8	30.5	0.081 [m]
Postop	39.9±14.7	38.5	34.7±14.8	33.0	**0.041** [m]
Glucose					
Preop	147.0±63.7	131.0	145.8±64.4	127.0	0.908 [m]
Postop	173.1±59.8	169.5	179.1±57.7	180.0	0.601 [m]
Creatine					
Preop	3.6±2.5	2.7	2.6±2.5	1.5	**0.014** [m]
Postop	3.9±2.4	2.8	2.8±1.9	2.1	**0.005** [m]
Hgb					
Preop	10.6±2.4	10.5	10.7±2.4	10.6	0.886 [m]
Postop	8.9±1.1	8.8	8.9±1.1	8.9	0.466 [m]
MPV					
Preop	10.8±1.0	10.7	11.2±1.1	11.1	**0.043** [m]
Postop	11.4±3.0	10.9	11.5±1.0	11.6	**0.035** [m]
PLR					
Preop	157.0±98.6	128.8	155.4±106.1	142,0	0.838 [m]
Postop	264.6±183.4	233.8	216.2±164.5	163.8	0.097 [m]
NLR					
Preop	4.5±4.7	2.8	5.6±7.4	3.8	0.108 [m]
Postop	25.1±44.9	16.2	18.2±12.6	15.4	0.818 [m]

[m]: Mann-whitney u test. SD: Standard deviation; BUN: Blood urea nitrogen; Hgb: Hemoglobin; MPV: Mean platelet volume; PLR: Platelet lymphocyte ratio; NLR: Neutrophil lymphocyte ratio

finding early mortality at the preoperative (p<0.009) and postoperative values (p<0.007) in the on-pump group.

The age and gender distribution of the patients did not differ significantly (p>0.05). The complication rate did not differ significantly (p>0.05) in the on-pump and off-pump groups. The 30-day mortality rate did not differ significantly (p>0.05). Preoperative and postoperative MPV values did not differ significantly (p>0.05). Preoperative PLR and NLR values were significantly lower (p<0.05) in the off-pump group. Postoperative PLR and NLR values did not differ significantly (p>0.05) (Table 4).

In the univariate model, the significant effectiveness of HGB, PLR and NLR values (p<0.05) was observed in predicting the on-pump and off-pump groups. In the multivariate reduced model, a significant-independent (p<0.05) effectiveness of PLR was observed in predicting the group that entered and did not enter the cardiopulmonary bypass in surgery (Table 5).

DISCUSSION

The demographics, MPV, neutrophil, lymphocyte, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and serum creatine values were evaluated in each case file. The preoperative and postoperative 24th hour values of the hemogram parameters of all the cases were used in the study. Predicting mortality and taking necessary precautions will prevent prolongation of hospitalization. Considering the high costs of patient care and the high economic burden in intensive care units, it is apparent how significant it is to detect and prevent complications in advance.

Coronary artery bypass grafting (CABG) is one of the most common operations in patients with end-stage renal disease (ESRD). However, CABG results are not excellent for the postoperative period. Despite high medical costs, they are inclined to complications such as low quality of life, ischemic heart disease, stroke, infection, and death.[7,8] Current studies focus rather on high mortality in intensive care units, and

Table 4. Comparison of patients with on-pump and off-pump cardiac surgery

	On-pump cardiovascular surgery				Off-pump cardiovascular surgery				p	
	Mean±SD	n	%	Median	Mean±SD	n	%	Median		
Age	61.7±10.2			62.0	62.0±16.0			67.0	0.387	m
Sex										
Female		47	37.6			4	30.8		0.627	x^2
Male		78	62.4			9	69.2			
Complication										
(–)		58	46.4			6	46.2		0.986	x^2
(+)		67	53.6			7	53.8			
Discharged										
(–)		40	32.0			5	38.5		0.636	x^2
(+)		85	68.0			8	61.5			
Death until 30th day										
(–)		94	75.2			10	76.9		0.891	x^2
(+)		31	24.8			3	23.1			
BUN										
Preop	38.4±18.9			34.0	29.8±9.3			29.0	0.183	m
Postop	39.2±15.2			37.0	32.8±9.5			35.0	0.170	m
Glucose										
Preop	145.9±65.8			126.0	154.2±38.5			159.0	0.156	m
Postop	177.4±59.1			172.5	155.2±35.8			151.0	0.122	m
Creatine										
Preop	3.4±2.6			2.5	2.9±1.9			2.0	0.875	m
Postop	3.6±2.3			2.6	3.6±2.3			2.4	0.638	m
Hgb										
Preop	10.8±2.4			10.8	9.1±1.8			8.5	**0.006**	m
Postop	8.9±1.1			8.9	8.6±1.5			8.3	0.158	m
MPV										
Preop	10.9±1.0			10.8	10.5±1.1			10.2	0.124	m
Postop	11.5±2.8			11.1	10.8±0.9			10.5	0.138	m
PLR										
Preop	147.0±90.1			127.5	249.0±142.2			237.5	**0.008**	m
Postop	254.5±174.3			225.5	235.3±232.1			165.4	0.351	m
NLR										
Preop	4.3±5.2			2.9	9.4±6.2			7.8	**0.000**	m
Postop	24.4±41.3			16.1	13.6±10.4			12.5	0.075	m

m: Mann-whitney u test; X^2: Chi-square test. SD: Standard deviation; BUN: Blood urea nitrogen, Hbg: Hemoglobin; MPV: Mean platelet volume; PLR: Platelet lymphocyte ratio; NLR: Neutrophil lymphocyte ratio

the cause-effect studies have significance. In this study, it was found in patients who had chronic renal failure and underwent the CABG operation whether blood parameters, especially MPV, NLR, and PLR, had a predictive effect on mortality. There are various publications available on the relationship between these parameters and cardiovascular diseases.[9,10] The frequency of the prevalently known risk factors related to coronary heart disease increases as patients age

Table 5. Univariate and multivariate logistic regression analyses

	Univariate model			Multivariate model		
	OR	**% 95 CI**	**p**	**OR**	**% 95 CI**	**p**
HGB	1.48	1.07–2.06	**0.018**			
PLR	0.99	0.99–1.00	**0.002**	0.99	0.99–1.00	**0.002**
NLR	0.91	0.84–0.98	**0.014**			

Logistic regression. OR: Odds ratio; CI: Confidence interval; HGB: Hemoglobin; PLR: Platelet lymphocyte ratio; NLR: Neutrophil lymphocyte ratio

and may also fluctuate concerning the sex and lifestyle of the patients. Moreover, some previous studies indicate that MPV values can be used to predict the outcome of the treatment in ischemic stroke patients. Important and common complications such as postoperative atrial fibrillation (AF), early and late morbidity after cardiovascular surgery, cardiovascular events, thromboembolism, cerebrovascular events, and prolonged hospitalization in intensive care units are correlated with increasing healthcare costs and mortality.[11,12] In the meta-analysis study, Chu et al.[13] discovered a significant relationship between the MPV increase and acute myocardial infarction and other cardiovascular diseases. Although a few studies are investigating the relationship between MPV and cardiac arrhythmia, these studies particularly concentrate on AF. The increase in MPV may result from the depletion of small platelets during ischemia.[14,15] Ha et al.[16] similarly reported that MPV values were found higher in AF cases. Hemostatically reactive platelets with more granular and larger platelets that have adhesion receptors causing a decrease in the bleeding time exhibited increased activity.[17] Weymann et al.[15] confirmed that MPV, as a valuable hematological parameter, could strongly predict the proximal and permanent AF occurrence in the complete blood count (CBC) test, therefore, MPV was included in the AF risk classification.[18] For this reason, they defined MPV as a prognostic indicator and a risk factor. In a retrospective analysis of 349 patients with ARF requiring continuous renal replacement therapy (CRRT), Han et al.[19] showed that the mean platelet volume (MPV) ≥10.2 fL is an evident prognostic risk factor for 28-day mortality. In our study on patients who had chronic renal failure and underwent on-pump cardiac surgery, we found a significant decline in the preoperative and postoperative MPV value in the 30-day mortality groups when compared to the 30-day non-mortality group ($p<0.05$) (Table 3). When MPV values were compared in the on-pump and off-pump groups, it was found to be highly significant in finding early mortality at the preoperative ($p<0.009$) and postoperative values ($p<0.007$) in the on-pump group.

NLR may cause renal endothelial damage and poor microcirculation as a result of the inflammatory process brought on by neutrophil infiltration, activated endothelium, lymphocytes, and platelets, even though it is a marker of inflammatory conditions.[20,21] Ünal et al.[6] observed that the preoperative NLR was correlated with the post-CABG mortality. PLR has been employed in the literature to forecast patient prognosis for various ischemia and inflammatory events.[22] Temiz et al.[23] found a correlation between higher PLR and hospital mortality in their patients.

In our study, preoperative and postoperative first day NLR and PLR values were not discovered to be significant in determining the 30-day mortality. Preoperative PLR and NLR values were significantly lower ($p<0.05$) in the off-pump group. Postoperative PLR and NLR values did not differ significantly ($p>0.05$) between on-pump and off-pump groups.

CONCLUSION

In conclusion, they are important markers for determining the postoperative mortality with MPV in patients with chronic renal failure who underwent cardiopulmonary bypass surgery.

Disclosures

Ethics Committee Approval: The study was approved by the İstanbul Mehmet Akif Ersoy Thoracic Cardiovascular Surgery Training and Research Hospital Clinical Research Ethics Committee (No: 2019-58, Date: 10/09/2019).

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