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Original Article

The relationship of platelet lymphocyte ratio with prognosis in patients with chronic obstructive pulmonary disease

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ABSTRACT

Background: The aim of this study is to analyze prognostic biomarkers, and determine the biomarkers which are more sensitive in the patients that were presented with acute chronic obstructive pulmonary disease (COPD) exacerbation to the emergency department.

Materials and Methods: The data of 243 patients presented with acute COPD exacerbation and 122 COPD patients with stable status as control group were analyzed retrospectively. The patients, whose arterial blood gas (ABG) studied, with Acute COPD exacerbation were identified as Group I. The patients whose venous blood gas (VBG) studied were identified as Group II and stable COPD patients whose ABG studied were identified as Control Group. The prognostic biomarker values were compared in the patients of Group I, Group II and Control Group

Results: The mean age of the patients was 68.61 ± 11.02 and the mean age of the control group was 68.25 ± 11.07. It was found that platelet lymphocyte ratio (PLR) values were very high in both Group I and Group II compared to the control Group ($P < 0.001$). There was a significant difference related with mean erythrocyte distribution width (RDW) in Group I, mean erythrocyte volume (MCV)' in group II, MPV and platelet count (PLT) in both Group I and Group II ($P < 0.001$).

Conclusions: Especially in acute COPD exacerbation, PLR may be a useful inflammatory biomarker to reflect the severity and activity of inflammation in COPD patients.

Keywords: chronic obstructive pulmonary disease, biomarker, platelet-lymphocyte ratio, emergency department

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Introduction

COPD affects more than 5% of adult population and causes approximately 2,75 million deaths each year [1]. Also it is the third leading cause of death worldwide [2-4]. COPD is a progressive disease affecting lung parenchyma and peripheral airways, systemically effective with chronic inflammation and widespread with progressive airflow limitation and its attacks can be treated [2-6]. Abnormal inflammatory response and phenotype properties of lungs against harmful gases or particles reinforce the view that systemic inflammation occurs [7]. Recently researchers have found a relationship between systemic inflammation and platelets. It has been shown that platelets play an important role in the pathogenesis of inflammation, thrombosis and atherogenesis by interacting with endothelium, leukocytes or liberating mediators [8,9]. It has been studied with many types of biomarkers, particularly related to platelets, which can be used to detect the prognosis of COPD. PLT, mean platelet volume (MPV), platelet distribution width (PDW), PLR, MCV, RDW [10]. In literature, these biomarkers have been studied separately in patients with acute COPD exacerbation. However, we could not find any studies that examined these biomarkers in COPD patients at the same time and compared the results of which were more sensitive.

The aim of this study is to compare the biomarker values of the patients presented with acute COPD exacerbation in emergency service to the biomarker values of stable COPD patients, to determine the biomarker which is more sensitive for COPD and to investigate the difference status according to gender.

Materials and Methods

This study was carried out in Van Yuzuncu Yıl University, Faculty of Medicine Emergency Department between October 2016 and April 2017. It is a retrospective study. The data were taken from the hospital information system. Criteria for inclusion in the study; patients diagnosed with COPD older than 18 years. Exclusion criteria; patients with heart failure, kidney failure, cancer history, primary valve heart disease, connective tissue diseases, inflammatory bowel disease, liver diseases and hematological system diseases were not included in the study. The files of 861 patients who applied to the emergency department with the complaint of dyspnea due to acute COPD exacerbation were analyzed. According to exclusion criteria, 243 patients were included in the study. The patient group with arterial blood gas (ABG) (n = 100) was taken as group II, the patient with venous blood gas (VBG) (n = 143). 122 patients with COPD registered in the hospital system and whose condition was stable were included in the study as a control group (n = 122). Prognostic biomarkers; PLT, PLR, MPV, MCV, RDW were determined. Biomarker values of Group I, Group II and control Group were compared. Correlation values were investigated. Analysis was made according to gender. This study was approved by the institutional ethics committee of Van Yuzuncu Yıl University (B.30.2.YYU.0.01.00.00/43).

Statistical Analysis

Descriptive statistics for the studied parameters were presented as mean, standard deviation, minimum and maximum values. One-way ANOVA was performed for the comparison of group means. Following One-Way Variance Analysis, Duncan multiple comparison test was also used to determine different groups. For determination linear relationships among the parameters, Pearson correlation analysis was carried out in each group. The significance level was set at $P < 0.05$. All statistical analyses were performed with the SPSS software package (version 21; SPSS Inc., Chicago, IL, USA).

Results

The mean age of 243 patients with acute COPD exacerbation was 68.61 ± 11.02, it was 117 (48.15%) males and 126 (%51.85) females. The mean age of 122 patients in Control Group was 68.25 ± 11.07, 61 (50%) males and 61 (50%) females. The biomarker values of patients in Group I and Group II were compared with those of the Control Group. Compared to the Control Group, a relatively high difference was detected about PLR in both Group I and Group II patients with acute COPD exacerbation ($P < 0.001$). A significant difference for RDW in Group I, MCV in Group II, MPV and PLT in both Group I and Group II was investigated ($P < 0.001$) (Table 1).

Correlation values of the biomarkers compared to the Control Group; RDW was found to be negatively correlated with MCV, MPV was negatively correlated with MCV and

Table 1. Descriptive statistics and comparison results of the groups for the parameters.

		N	Mean	Std. Dev.	Min.	Max.	P
Age (years)	Group II	143	68.01	10.708	27	94	0.571
	Group I	100	69.48	11.470	38	94	
	Control	122	68.25	11.214	39	98	
	Total	365	68.49	11.077	27	98	
MCV (fl)	Group II	143	85.613 ab	7.479	65.7	103.9	0.022
	Group I	100	87.249 a	7.433	62.9	103.2	
	Control	122	84.459 b	7.429	61.6	101.5	
	Total	365	85.675	7.508	61.6	103.9	
RDW (%)	Group II	143	18.083 a	3.982	13.2	31.4	0.001
	Group I	100	16.775 b	3.300	12.6	29.5	
	Control	122	16.348 b	3.270	12.5	29.7	
	Total	365	17.145	3.647	12.5	31.4	
PLT (103/ μL)	Group II	143	229.26 b	80.377	27	465	0.002
	Group I	100	215.97 b	93.666	29	581	
	Control	122	255.31 a	78.631	63	505	
	Total	365	234.33	84.923	27	581	
MPV (fl)	Group II	143	8.925 a	1.201	6.5	14.3	0.001
	Group I	100	9.083 a	1.356	6.9	14.6	
	Control	122	8.479 b	1.103	6.6	13.9	
	Total	365	8.819	1.237	6.5	14.6	
LY1 (103/ μL)	Group II	143	1.512 b	1.348	0.2	9.7	0.001
	Group I	99	1.408 b	1.097	0.2	7.5	
	Control	122	21.520 a	10.047	1.9	51.4	
	Total	364	8.190	11.158	0.2	51.4	
PLR	Group II	143	240.139 a	183.386	3.65	1135.00	0.001
	Group I	99	233.505 a	178.546	15.87	793.33	
	Control	122	17.675 b	22.177	1.65	186.84	
	Total	364	163.773	180.895	1.65	1135.00	

a, b: Different lower cases represent statistically significant differences among the groups for each parameter ($P < 0.01$).
Abbrev.; MCV: mean corpuscular volume; RDW: red cell distribution; PLT: platelets; MPV: mean platelet volume; LY1: lymphocytes; PLR: platelet-to-lymphocyte ratio.

Table 2. Pearson correlation coefficients for the parameters in group I.

	Age	MCV	RDW	PLT	MPV	LY1	PLR
Age (year)	1						
MCV (fl)	0.126	1					
RDW (%)	-0.278**	-0.438**	1				
PLT (103/ μL)	-0.118	-0.075	-0.185	1			
MPV (fl)	0.095	-0.180	0.289**	-0.428**	1		
LY1 (103/ μL)	-0.054	-0.109	-0.112	0.142	-0.124	1	
PLR Ratio	0.011	-0.007	0.066	0.206*	-0.086	-0.600**	1

**: $P < 0.05$; **: $P < 0.01$.*
Abbrev.: MCV: mean corpuscular volume; RDW: red cell distribution; PLT: platelets; MPV: mean platelet volume; LY1: lymphocytes; PLR: platelet-to-lymphocyte ratio.

Table 3. Pearson correlation coefficients for the parameters in group II

	Age	MCVfl	RDW	PLT103μL	MPVfl	LY1103μ	PLR
Age (year)	1						
MCV (fl)	0.126	1					
RDW (%)	-0.119	-0.676**	1				
PLT(103/ μL)	-0.054	-0.100	-0.088	1			
MPV (fl)	0.013	-0.192*	0.256**	-0.394**	1		
LY1 (103/ μL)	0.092	0.105	-0.010	0.152	-0.026	1	
PLR Ratio	0.022	-0.254*	0.104	0.057	-0.099	-0.545**	1

**: P < 0.05; **: P < 0.01.*
Abbrev.: MCV: mean corpuscular volume; RDW: red cell distribution; PLT: platelets; MPV: mean platelet volume; LY1: lymphocytes; PLR: platelet-to-lymphocyte ratio.

PLT, and positively correlated with RDW (Tables 2,3). Correlation values in Group are as follows; RDW showed a significant negative correlation with age and MCV, and a significant positive correlation with MPV and PaCO2 in Group I. In Group II, RDW showed a significant correlation with MCV, a significant correlation with MPV and PaCO2 (Table 4).

We investigated whether there is a significant difference in biomarkers between groups according to gender. A significant difference was found between men and women in MCV (P = 0.03) and MPV (P = 0.04).

Table 4. Pearson correlation coefficients for the parameters in control group.

	Age	MCV	RDW	PLT	MPV	LY1	PaCO2	PLR
Age (year)	1							
RDW (%)	0.016	-0.717**	1					
PLT (103/ μL)	-0.001	-0.064	-0.060	1				
MPV(fl)	0.018	-0.373**	0.240**	-0.232**	1			
LY1(103/ μL)	-0.111	0.161	-0.194*	-0.111	-0.070	1		
PLR Ratio	0.106	-0.079	0.039	0.377**	0.046	-0.566**	-0.138	1

**: P < 0.05; **: P < 0.01.*
Abbrev.: MCV: mean corpuscular volume; RDW: red cell distribution; PLT: platelets; MPV: mean platelet volume; LY1: lymphocytes; PLR: platelet-to-lymphocyte ratio.

Discussion

The key findings in the study on biomarkers and blood gas used to determine severity and prognosis of COPD are; PLR values in Group I and Group II increased significantly compared to the Control Group in Acute COPD exacerbation. According to data in literature; platelets can lead various systemic inflammatory conditions by releasing different cytokines and mediators while playing an active role in the immune system [11]. In this study, increasing of PLR value derives from the increase in platelet number and decrease in lymphocyte number in an inflammatory. It is a useful biomarker to reflect the severity and activity of inflammatory in the COPD patients especially during acute exacerbation. When Kurtipek et al. compared PLR values between the patients with acute COPD exacerbation and the ones with stable COPD, they found that PLR value was significantly high in the patients with acute COPD exacerbation. Actually they found that the number of lymphocyte in peripheric blood was inversely correlated with inflammation in body and therefore PLR was associated with poor outcomes in the COPD patients [12] Kumar et al. found that PLR was associated with 90-day mortality increase of patients with Acute COPD exacerbation in their studies. PLR is prognostically a new scientific contribution in chronic inflammatory disorders

such as COPD [13]. The most important cause of high PLR value is the very low number of lymphocyte in acute COPD exacerbations. In this study, a considerable decrease in the number of lymphocyte was found in the COPD patients during acute exacerbations. Results of the study are consistent with both acute exacerbation and prognostic data in literature.

In the studies according to the GOLD categories of COPD, they show that RDW levels are associated with increased mortality risk. In their studies, Tertemiz et al. showed that high RDW levels were associated with severity of disease and low survival rates in COPD patients [14]. Seyhan et al. think that RDW may be high due to inflammation and oxidative stress and therefore high RDW levels may reflect an inflammatory condition in COPD patients. Thus, RDW level is one of the most important factors showing mortality [15]. Kalemci et al. showed that RDW and PDW values were independently related to the severity of COPD in another study [10]. Ozgul et al. determined that RDW levels in COPD patients were significantly higher than in healthy individuals in their studies [16]. As stated in these results, RDW became more prominent. However, PLR value has been found to be more prominent in our study. When RDW values in Group I and Group II were compared to the ones in the Control Group, it was determined that there was a significant difference in Group II, but not in Group I. RDW values in Group I and Group II were negatively correlated with MCV values and the results in our study were partially consistent with data in literature.

MPV value is one of the platelet function indices showing the platelet production rate and stimulation. In a literature survey by Ulasli et al. investigated that MPV decreased during COPD exacerbation compared to stable period and the Control Group [17]. Decrease in MPV values may show increased systemic inflammation during COPD exacerbation, therefore MPV can be used as a negative acute phase reactant during acute COPD exacerbation. However, Makhouf et al. reported that MPV and PDW values in COPD patients were significantly higher than in Control Group [18]. Steiropoulos et al. reported that MPV and WBC levels in the COPD patients were higher than in smokers having normal respiratory function; hence, there may be vascular risk together with COPD [1]. In this study MPV values were found to be high in acute COPD exacerbations. Measurements of variances in MPV during follow-up can be considered as a rapid and reliable tool in the assessment of inflammatory responses. These results show platelet activation and increased systemic inflammation in COPD patients. In a study by Karadeniz et al. showed a higher platelet number in COPD patients during acute exacerbation [19]. The study by Harrison et al. reported that there was a significant increase in thrombocytosis of the patients with acute COPD exacerbation in one-year. They stated that thrombocytosis caused a significant increase especially in hospital mortality, and it was correlated with the symptoms of type II respiratory failure and severity of exacerbation [20]. Chen et al. investigated that inflammatory biomarkers observed in routine blood tests can widely be used as differential diagnosis and prognostic assessment factors in many cases such as inflammatory diseases, cancer and cardiovascular diseases [21].

The limitation of this study was the low number of patients and its retrospective nature.

In conclusion, since the elevation of PLR in an inflammatory condition reflects the increase in platelet number and the decrease in lymphocyte, it is a useful inflammatory biomarker to reflect the severity and activity of inflammation particularly during acute exacerbation in COPD patients. In this study, PLR is more sensitive than other biomarkers used in the treatments and follow-up of the prognosis of COPD patients. Thus, PLR can be used as a biomarker in the follow-up of acute COPD exacerbation in emergency departments.

Declaration of conflicting interests

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