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# Evaluation of relationship between disease severity, mean platelet volume, and platelet distribution width in stable chronic obstructive pulmonary disease

## Stabil kronik obstrüktif akciğer hastalığında ortalama trombosit hacmi ve trombosit dağılım genişliğinin hastalık şiddeti ile ilişkisinin değerlendirilmesi

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Abstract

Aim: This study was conducted to evaluate the relationship between disease severity, mean platelet volume and platelet distribution width in stable chronic obstructive pulmonary disease.

Methods: The study included 120 consecutive patients with stable chronic obstructive pulmonary disease and 30 consecutive age-matched healthy subjects (control group). Patients were classified as A (mild), B (mild to moderate), C (moderate to severe) and D (severe) defined by the GOLD committee and grouped as A/B (n= 60) and C/D (n=60).

Results: Platelet levels were not different among the groups. Mean platelet volume was lower in all patients than control group (p=0.001). Level of platelet distribution width was higher in all patients than control group (p=0.018). Mean platelet volume in C/D groups were significantly lower than A/B group (p=0.011) and control group (p=0.001). Mean platelet volume in A/B group were also significantly lower than control group (p=0.001). Erythrocyte sedimentation rates were higher in A/B and C/D groups than control group (p=0.007 and p=0.001, respectively). C-reactive protein levels in control group were significantly lower than C/D group (p=0.001). No statistically significant correlations were observed between mean platelet volume and forced expiratory volume in one second and forced expiratory volume in one second/forced vital capacity or between mean platelet volume and other inflammatory parameters in A/B or C/D groups. Significant positive correlations were found between erythrocyte sedimentation rate and C-reactive protein (r=0.375; p=0.003), and between mean platelet volume and platelet large cell ratio (r=0.749; p=0.001) in C and D groups.

Conclusion: It was concluded that mean platelet volume could be used as a negative acute phase reactant in evaluation of disease severity of chronic obstructive pulmonary disease as C-reactive protein.

Keywords: Chronic obstructive pulmonary disease, mean platelet volume, platelet distribution width, forced expiratory volume, forced vital capacity.

Öz

Amaç: Bu çalışmada kronik obstrüktif akciğer hastalığında ortalama trombosit hacmi ve trombosit dağılım genişliği ile hastalık şiddeti arasındaki ilişkinin değerlendirilmesi amaçlandı.

Yöntemler: Çalışmaya 120 ardışık kronik obstrüktif akciğer hastası ve yaşları eşleştirilmiş 30 ardışık sağlıklı kişi (kontrol grubu) alındı. GOLD komitesi tarafından tanımlanan kronik obstrüktif akciğer hastalığı şiddetini belirlemek için hastalar A (hafif), B (hafif-orta), C (orta-şiddetli) ve D (şiddetli) olarak sınıflandı ve A/B (n=60) ve C/D (n=60) olarak gruplandı.

Bulgular: Gruplar arasında trombosit düzeylerinin istatistiksel olarak anlamlı olmadığı bulundu. Ortalama trombosit hacmi tüm hastalarda kontrollere göre daha düşüktü (p=0,001). Tüm hastalarda trombosit dağılım genişliği düzeyleri kontrol grubundan daha yüksekti (p=0,018). Ortalama trombosit hacmi C/D grubunda, A/B grubu (p=0,011) ve kontrol grubundan (p=0,001) anlamlı olarak düşük bulundu. Ortalama trombosit hacmi, A/B grubunda kontrol grubundan anlamlı derecede düşük bulundu (p=0,001). Eritrosit sedimantasyon hızı A/B ve C/D gruplarında kontrol grubundan daha yüksek iken (sırasıyla, p=0,007 ve p=0,001). C-reaktif protein düzeyleri kontrol grubunda C/D grubundan anlamlı derecede düşük bulundu (p=0,001). A/B veya C/D gruplarında ortalama trombosit hacmi ile bir saniyedeki zorlu ekspiratuar hacim, bir saniyedeki zorlu ekspiratuar hacim/zorlu vital kapasite oranı ve diğer inflamatuar parametreler arasında istatistiksel olarak anlamlı bir ilişki görülmedi. C/D grubunda eritrosit sedimantasyon hızı, C-reaktif protein düzeyleri (r=0.375; p=0,003) ile ve ortalama trombosit hacmi de büyük hücreli platelet oranı ile (r=0,749; p=0,001) pozitif korelasyon gösterdi.

Sonuç: Bu çalışma kronik obstrüktif akciğer hastalığında klasik pozitif akut faz reaktanı C-reaktif proteinin yanı sıra düşük ortalama trombosit hacmi'nin hastalık şiddetinin değerlendirilmesinde negatif akut faz reaktanı olarak kullanılabileceğini düşündürmektedir.

Anahtar sözcükler: Kronik obstrüktif akciğer hastalığı, ortalama trombosit volümü, trombosit dağılım genişliği, bir saniyedeki zorlu ekspiratuar hacim, zorlu vital kapasite.

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## Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by the limitation of fully reversible airflow. COPD is a very common disease with high mortality. The development of COPD is contributed by genetic and environmental factors, together with progressive and systemic inflammation [1].

Currently, it is known that COPD patients also have systemic effects that are not only localized to the lungs [2, 3]. Patients with COPD and other chronic airway diseases may also have pulmonary hypertension, pulmonary embolism, and thrombocyte dysfunction at the same time; some COPD studies have indicated platelet function disorders and activation in the coagulation system [4, 5]. Mean platelet volume (MPV) is one of the markers of platelet activation that was reported to be associated with inflammation in recent studies [6, 7]. Intensive production of proinflammatory cytokines and acute phase reactants has been reported to affect MPV levels as a megakaryopoiesis inhibitor [8]. It has been reported to be high in some studies in COPD, but low in others [9].

MPV is known to be an early marker of platelet activation. Activated platelets are very important in inflammation, atherogenesis, and atherothrombosis. COPD is associated with cardiovascular disease-related mortality [10]. Platelets, together with their indices of MPV, platelet distribution width (PDW) can be used as markers of inflammation in cardiovascular, inflammatory, and thromboembolic diseases [11, 12]. PDW shows the standard deviation of the logarithmic transformation of platelets. In one study, PDW levels in COPD and pulmonary embolism were found to be elevated, but not associated with disease severity [13].

Despite this widespread and mortal illness, number of cheap and easily accessible parameters currently used in COPD is limited. In this study, we aimed to evaluate the relationship between disease severity and routine parameters such as MPV, PDW in whole blood tests in stable COPD patients.

## Material and methods

The study was approved by the Ethics Committee (24.08.2017, 2017/14) and written informed consent was obtained from each subject. All participants were informed about the study and signed the consent form. This was a retrospective case-control study conducted in the Acibadem University School of Medicine, Acibadem Atakent Hospital, Department of Chest Diseases. A total of 120 consecutive COPD patients and 30 consecutive age-matched control subjects between June 2016 and October 2017 were enrolled in the study.

All the controls with normal pulmonary function tests were recruited from outpatient clinic of our hospital. All the subjects underwent physical examination. Subjects with chronic disease such as diabetes mellitus, hypertension, coronary artery disease, heart failure, irritable bowel disease were not included in the study.

The COPD patients were diagnosed based on the 2016 Global Initiative for Chronic Obstructive Lung Disease (GOLD), and they were classified into four groups (GOLD I/II/III/IV) according to the revised GOLD guidelines based on post-bronchodilator forced expiratory volume in one second (FEV1). According to this classification system (classification of severity of airflow), patients with FEV1 to forced vital capacity (FEV1/FVC) <0.70 were grouped as GOLD I (Mild, FEV1≥80% predicted), GOLD II (Moderate, 50% ≤ FEV1 < 80% predicted), GOLD III (Severe, 30% ≤ FEV1<50% predicted), and GOLD IV (Very severe, FEV1 < 30% predicted) [14]. Patients were divided into four groups [A (mild) / B (mild to moderate), n=60); C (moderate to severe) / D (severe), n=60)] according to the evaluation to determine COPD severity as defined by the GOLD committee. A combined assessment system of COPD severity was used for the classification of patients.

Exclusion criteria for all the patients were respiratory disorders other than COPD, pulmonary embolism, and left ventricular systolic or diastolic dysfunction, comorbidities such as cancer, diabetes, chronic renal insufficiency, hyperthyroidism, hypothyroidism, hepatic dysfunction, lower respiratory tract infection, or COPD attack in the last 6 week, and presence of metabolic syndrome. Detailed medical history was obtained from all participants, and physical examination was performed.

Spirometry tests were done in accordance with the criteria recommended by the European Respiratory Society using computer-assisted spirometry (Vmax22D, Sensor Medics, California, USA). Pulmonary function parameters FEV1, FVC, and FEV1/FVC ratio were measured, and the absolute values and the percentage of expected values of these parameters were analyzed.

Blood samples were obtained before drug use in the morning. Samples were collected in EDTA-containing tubes and anticoagulant-free tubes after an overnight fast. After immediate centrifugation at 3000 g for 10 minutes, at 4 °C, plasma and serum samples were separated in Eppendorf tubes and frozen immediately at -80 °C until analysis.

Complete blood count parameters [White blood cell (WBC) (× 103/μL), hemoglobin (Hb) (g/dL), hematocrit (Htc) (%), platelet (PLT) (×103/μL), MPV (fL), PDW (fL), platelet-large cell ratio (P-LCR) (%), plateletcrit (PCT) (%)] were obtained with automatic hematology analyzer (Siemens-Sysmex, Germany). Serum C-reactive protein (CRP) (mg/L) levels were measured by nephelometry (Siemens-Dimention, Germany). Erythrocyte sedimentation rate (ESR) (mm/h) was measured according to the Westergren method with an established normal range of 0–20 mm/h.

Statistical analysis

SPSS (Statistical Package for Social Sciences) for Windows 20.0 package program was used for statistical evaluations. The relationship between the categorical variables of the groups was examined by chi-square test. Descriptive statistics were obtained, and data were tested for normality using the Kolmogorov-Smirnov test for Gaussian distribution. For comparison of parameters with normal distribution, parametric tests and comparison of parameters with abnormal distribution, non- parametric tests were used. For this purpose, One-Way ANOVA, unpaired student- t, Kruskal-Wallis and Mann-Whitney U tests were used. Relationships between variables were assessed with Pearson's or Spearman's correlation coefficient. The minimal significance (α) and statistical power (1 − β) were set at 0.05 and 0.80 respectively. A p value equal to or lower than 0.05 was considered as statistically significant.

## Results

The baseline characteristics of the study groups are presented in Table 1. FEV1 (%) and FEV1/FVC were lower in patients than control group. WBC (×103/μL), ESR (mm/h) and CRP (mg/L) levels in patient groups were significantly higher than control group (p=0.001 for each). Hb (g/dL) and Htc (%) levels were lower in patient groups than control group (p=0.001 for each). MPV (fL) levels in patient groups were significantly lower than control group (p=0.001). PDW (fL) levels were higher in all patients than control group (p=0.018).

Clinical and laboratory findings in the patients according to the GOLD stage are given in Table 2. Both A/B

group and C/D group have lower FEV1 (%) and FEV1/FVC levels than control group (p=0.001 for each comparison). FEV1 (%) and FEV1/FVC were lower in C and D groups than A and B groups. WBC (× 103/μL) levels in control group and A/B group p=0.002 and p=0.026, respectively) were significantly lower than C/D group. Hb (g/dL) and Htc (%) levels were lower in patient groups than control group (p=0.001 for each). MPV (fL) levels were lower in all patients than control group (p=0.001). However, PDW (fL) levels were higher in all patients than control group (p=0.007). MPV (fL) levels in C/D group were significantly lower than A/B group (p=0.011) and control group (p=0.001). MPV (fL) levels in A/B group were also significantly lower than control group (p=0.001). Furthermore, PDW (fL) levels in control group were significantly lower than A/B and C/D groups (p=0.015 and p=0.007, respectively). While ESR (mm/h) levels were higher in A/B and C/D groups than control group (p=0.007 and p=0.001, respectively); in A/B group, they were lower than C/D group (p=0.049). CRP (mg/L) levels in control group were significantly lower than C/D group (p=0.001).

In all subjects, FEV1 (%) positively correlated with FEV1/FVC (r=0.850, p=0.001), Hb (g/dL) (r=0.396, p=0.001) Htc (%) (r=0.291, p=0.001), MPV (fL) (r=0.323, p=0.001) and p-LCR (%) (r=0.181, p=0.027); and very weakly negatively correlated with ESR (mm/h) (r=-0.297, p=0.000) and CRP (mg/L) (r=-0.270, p=0.001). FEV1/FEVC positively correlated with Hb (g/dL) (r=0.390, p=0.001), Htc (%) (r=0.272, p=0.001), MPV (fL) (r=0.371, p=0.001) and p-LCR (%) (r=0.213, p=0.009); also negatively correlated with ESR (mm/h) (r=-0.281, p=0.001) and CRP (mg/L) (r=-0.223, p=0.013). Also, WBC (× 103/μL) levels in all subjects were found as very weakly negatively correlated with FEV1 (%) (r=-0.246, p=0.002) and FEV1/FVC (r=-0.276, p=0.001). Correlation data for all subjects are given in Table 3.

Significant weak correlation was found between ESR (mm/h) and CRP (mg/L) (r=0.474, p=0.000) in A and B groups. Furthermore, in this group, ESR (mm/h) was very weakly negatively correlated with Hb (g/dL) (r=-0.294, p=0.023), Htc (%) (r=-0.311, p=0.016), and WBC (× 103/μL) levels (r=-0.355, p=0.005). MPV (fL) was also found as strongly positively correlated with p-LCR (%) (r=0.988, p=0.001), and very weakly positively correlated with WBC (× 103/μL) levels (r=0.302, p=0.019) (Table 4). While ESR (mm/h) level was negatively correlated with Hb (g/dL) (r=-0.276; p=0.033), it was positively correlated with CRP (mg/L) (r=0.375; p=0.003) in C and D groups. Also in this group, strongly positive correlations were found between MPV (fL) and p-LCR (%) (r=0.749, p=0.001); Hb (g/dL) and Htc (%) (r=0.916, p=0.000); and moderately positive correlation was present between FEV1 (%) and FEV1/FVC (r=0.628, p=0.001) (Table 5).

Table 1. Demographic, clinical and laboratory findings of the groups.

| Variable | Control group (n=30) | All patients (n=120) | p |
|---|---|---|---|
| Age (year) | 54.6±3.2 | 54.2±5.3 | 0.693 |
| F/M | 13/17 | 37/83 | 0.196 |
| FEV1 (%) | 102.0±8.9 | 56.7±24.2 | 0.001 |
| FEV1/FVC | 83.4±4.5 | 58.4±11.6 | 0.001 |
| WBC (× $10^3$/μL) | 7.2±1.6 | 8.7±3.0 | 0.001 |
| Hb (g/dL) | 15.2±1.4 | 13.2±2.1 | 0.001 |
| Htc (%) | 45.7±4.2 | 41.0±5.6 | 0.001 |
| PLT (×$10^3$/μL) | 254.1±64.12 | 255.7±87.0 | 0.923 |
| MPV (fL) | 10.3±0.8 | 9.4±0.8 | 0.001 |
| PDW(fL) | 12.7±2.4 | 11.5±1.7 | 0.018 |
| P-LCR (%) | 25.6±6.1 | 22.7±5.8 | 0.021 |
| PCT (%) | 0.25±0.1 | 0.25±0.1 | 0.619 |
| ESR (mm/h) | 10.7±8.2 | 21.6±13.6 | 0.001 |
| CRP (mg/L) | 0.32±0.2 | 0.62±0.6 | 0.001 |

FEV1: Forced expiratory volume in the first second, FVC: Forced vital capacity, WBC: White blood cell, Hb: Hemoglobin, Htc: Hematocrit, PLT: Platelet, MPV: Mean platelet volume, PDW: Platelet distribution width, P-LCR: Platelet large cell ratio, PCT: Plateletcrit, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein.

Table 2. Clinical and laboratory findings of the groups according to the GOLD stage.

| Variable | Control group (n=30) | A/B group (n=60) | C/D group (n=60) | p | | |
|---|---|---|---|---|---|---|
| | | | | Control vs A/B | Control vs C/D | A/B vs C/D |
| Age (year) | 54.6±3.2 | 54.2 ±6.8 | 54.2 ±3.2 | 0.777 | 0.609 | 0.959 |
| F/M | 13/17 | 22/38 | 15/45 | 0.546 | 0.078 | 0.169 |
| FEV1 (%) | 102.0±8.9 | 77.5 ±13.9 | 36.0 ±10.3 | 0.001 | 0.001 | 0.001 |
| FEV1/FVC | 83.4±4.5 | 66.2 ±6.1 | 5765±10.3 | 0.001 | 0.001 | 0.001 |
| WBC (×$10^3$/μL) | 7.2±1.6 | 8.1 ±2.5 | 9.3±3.3 | 0.105 | 0.002 | 0.026 |
| Hb (g/dL) | 15.2±1.4 | 13.7 ±2.1 | 12.7 ±2.0 | 0.001 | 0.001 | 0.012 |
| Htc (%) | 45.7±4.2 | 41.6 ±5.2 | 40.3 ±6.0 | 0.001 | 0.001 | 0.215 |
| PLT (×$10^3$/μL) | 254.1±64.2 | 252.8 ±68.6 | 258.6±102.7 | 0.935 | 0.827 | 0.720 |
| MPV (fL) | 10.3±0.8 | 9.7 ±0.8 | 9.3±0.7 | 0.001 | 0.001 | 0.011 |
| PDW(fL) | 11.4 ±1.9 | 11.7 ±1.5 | 12.7±2.4 | 0.015 | 0.007 | 0.405 |
| P-LCR (%) | 25.6±6.1 | 23.3 ±5.3 | 22.1 ±6.3 | 0.066 | 0.012 | 0.247 |
| PCT (%) | 0.25±0.1 | 0.24 ±0.1 | 0.25±0.1 | 0.587 | 0.482 | 0.318 |
| ESR (mm/h) | 10.7±8.2 | 18.5 ±12.3 | 24.7±14.9 | 0.007 | 0.001 | 0.049 |
| CRP (mg/L) | 0.32±0.2 | 0.52 ±0.5 | 0.78 ±0.6 | 0.062 | 0.001 | 0.080 |

FEV1: Forced expiratory volume in the first second. FVC: Forced vital capacity. WBC: White blood cell. Hb: Hemoglobin. Htc: Hematocrit. PLT: Platelet. MPV: Mean platelet volume. PDW: Platelet distribution width. P-LCR: Platelet large cell ratio. PCT: Plateletcrit. ESR: Erythrocyte sedimentation rate. CRP: C-reactive protein.

## Discussion

COPD is an important public health problem in our country as in other countries. Many studies have shown that there is an obvious increase in inflammation in airways during exacerbations among COPD patients who are generally categorized as mild, moderate and severe [14, 15]. Recently, MPV has been used as a simple and promising marker in several inflammatory circumstances. While MPV levels were lower in all patients than controls, PDW levels were higher in all patients than controls. MPV levels in C/D group were significantly lower than A/B group and control group. MPV levels in A/B group were also significantly lower than control group. The decreased MPV could be used as a negative acute phase reactant in the evaluation of disease severity in COPD as well as the classic positive acute phase reactant CRP.

Inflammatory parameters as WBC, ESR and CRP levels in patient groups were significantly higher than control group in the current study. WBC levels were significantly negatively correlated with ESR in A and B groups, and with FEV1 and FEV1/FVC in all subjects. ESR levels were positively correlated with CRP in C and D groups. Milacić et al. [16] showed that the higher the CRP level, the higher was the class of disease severity according to GOLD and the CRP value to correlate with the severity of the COPD clinical presentation. However, the leukocyte count did not show any significant correlation with the severity of COPD. No statistically significant correlations were found between the level of CRP, the leukocyte count, and comorbidities. Simonovska et al. [17] found statistically significant differences in the mean value of CRP in patients with different level of bronchial obstruction. For many years, an easily measurable and noninvasive parameter which might reflect systemic inflammation has been researched. CRP has been the most selective biomarker among the 36 plasma biomarkers for confirming COPD exacerbation and predicting COPD severity as our study [19]. WBC, ESR, and CRP are still the most frequently used infection markers in daily clinical practice [18].

The parameters related to the platelet size reflect platelet activity and are termed the platelet indices. The routinely available indices which describe platelet morphology and function are PLT, the platelet-to-lymphocyte ratio (PLR), MPV, and PDW [20]. But, in the current study, PLT of control subjects and patient groups revealed no significant difference, while MPV levels in patient groups were significantly lower than control group. PDW levels were higher in all patients than control group.

MPV levels in C/D group were significantly lower than A/B group and control group. MPV levels in A/B group were also

Table 3. Correlations for biochemical parameters in all subjects.

| | FEV1 (%) | FEV1 / FVC | WBC ($\times10^3/\mu L$) | Hb (g/dL) | Htc (%) | MPV (fL) | P-LCR (%) | CRP (mg/L) |
|---|---|---|---|---|---|---|---|---|
| FEV1 (%) | - | r=0.850 p=0.001 | r=-0.246 p=0.002 | r=0.396 p=0.001 | r=0.291 p=0.001 | r=0.323 p=0.001 | r=0.181 p=0.027 | r= -0.270 p=0.001 |
| FEV1/FVC | r=0.850 p=0.001 | - | r=-0.276 p=0.001 | r=0.390 p=0.001 | r=0.272 p=0.001 | r=0.371 p=0.001 | r=0.213 p=0.009 | r=-0.203 p=0.013 |
| WBC ($\times10^3/\mu L$) | r=-0.246 p=0.002 | r=-0.276 p=0.001 | - | r=-0.044 p=0.591 | r=0.002 p=0.977 | r=-0.005 p=0.951 | r=0.084 p=0.306 | r=0.190 p=0.020 |
| Hb (g/dL) | r=0.396 p=0.001 | r=0.390 p=0.001 | r=-0.044 p=0.591 | - | r=0.925 p=0.001 | r=0.203 p=0.013 | r=0.110 p=0.179 | r=-0.329 p=0.001 |
| Htc (%) | r=0.291 p=0.001 | r=0.272 p=0.001 | r=0.002 p=0.977 | r=0.925 p=0.001 | - | r=0.165 p=0.043 | r=0.150 p=0.067 | r=-0.235 p=0.004 |
| MPV (fL) | r=0.323 p=0.001 | r=0.371 p=0.001 | r=-0.005 p=0.951 | r=0.203 p=0.013 | r=0.165 p=0.043 | - | r=0.800 p=0.001 | r=-0.308 p=0.001 |
| P-LCR (%) | r=0.181 p=0.027 | r=0.213 p=0.009 | r=0.084 p=0.306 | r=0.110 p=0.179 | r=0.150 p=0.067 | r=0.800 p=0.001 | - | r=-0.172 p=0.035 |
| ESR (mm/ h) | r=-0.297 p=0.001 | r=-0.281 p=0.001 | r=-0.012 p=0.885 | r=-0.383 p=0.001 | r=-0.345 p=0.001 | r=-0.226 p=0.005 | r=-0.120 p=0.144 | r=0.446 p=0.001 |

FEV1: Forced expiratory volume in the first second. FVC: Forced vital capacity. WBC: White blood cell. Hb: Hemoglobin. Htc: Hematocrit. PLT: Platelet. MPV: Mean platelet volume. P-LCR: Platelet large cell ratio. ESR: Erythrocyte sedimentation rate. CRP: C-reactive protein.

Table 4. Correlations for biochemical parameters in A and B groups.

| | FEV1 (%) | FEV1 / FVC | WBC ($\times10^3/\mu L$) | Hb (g/dL) | Htc (%) | MPV (fL) | P-LCR (%) | CRP (mg/L) |
|---|---|---|---|---|---|---|---|---|
| FEV1 (%) | - | r=0.312 p=0.015 | r=0.149 p=0.257 | r=0.125 p=0.342 | r=0.142 p=0.281 | r=0.030 p=0.822 | r=0.082 p=0.535 | r=0.046 p=0.724 |
| FEV1 / FVC | r=0.312 p=0.015 | - | r=0.112 p=0.394 | r=0.218 p=0.095 | r=0.168 p=0.200 | r=0.135 p=0.302 | r=0.131 p=0.320 | r=0.155 p=0.236 |
| WBC ($\times10^3/\mu L$) | r=0.149 p=0.257 | r=0.112 p=0.394 | - | r=0.040 p=0.762 | r=0.086 p=0.516 | r=0.302 p=0.019 | r=0.309 p=0.016 | r=0.084 p=0.523 |
| Hb (g/dL) | r=0.125 p=0.342 | r=0.218 p=0.095 | r=0.040 p=0.762 | - | r=0.952 p=0.001 | r=-0.032 p=0.807 | r=-0.040 p=0.763 | r=-0.220 p=0.091 |
| Htc (%) | r=0.142 p=0.281 | r=0.168 p=0.200 | r=0.086 p=0.516 | r=0.952 p=0.001 | - | r=-0.044 p=0.741 | r=-0.042 p=0.748 | r=-0.175 p=0.182 |
| MPV (fL) | r=0.030 p=0.822 | r=0.135 p=0.302 | r=0.302 p=0.019 | r=-0.032 p=0.807 | r=-0.044 p=0.741 | - | r=0.988 p=0.001 | r=-0.184 p=0.159 |
| P-LCR (%) | r=0.082 p=0.535 | r=0.131 p=0.320 | r=0.309 p=0.016 | r=-0.040 p=0.763 | r=-0.042 p=0.748 | r=0.988 p=0.001 | - | r=-0.166 p=0.206 |
| ESR (mm/h) | r=-0.038 p=0.776 | r=0.034 p=0.796 | r=-0.355 p=0.005 | r=-0.294 p=0.023 | r=-0.311 p=0.016 | r=-0.146 p=0.265 | r=-0.142 p=0.281 | r=0.474 p=0.001 |

FEV1: Forced expiratory volume in the first second. FVC: Forced vital capacity. WBC: White blood cell. Hb: Hemoglobin. Htc: Hematocrit. PLT: Platelet. MPV: Mean platelet volume. P-LCR: Platelet large cell ratio. ESR: Erythrocyte sedimentation rate. CRP: C-reactive protein.

Table 5. Correlations for biochemical parameters in C and D groups.

| | FEV1 (%) | FEV1 /FVC | WBC ($\times10^3/\mu L$) | Hb (g/dL) | Htc (%) | MPV (fL) | P-LCR (%) | CRP (mg/L) |
|---|---|---|---|---|---|---|---|---|
| FEV1 (%) | - | r=0.628 p=0.001 | r=-0.180 p=0.169 | r=-0.008 p=0.954 | r=-0.099 p=0.451 | r=-0.114 p=0.386 | r=-0.055 p=0.675 | r=0.225 p=0.084 |
| FEV1 /FVC | r=0.628 p=0.001 | - | r=-0.222 p=0.089 | r=-0.130 p=0.324 | r=-0.189 p=0.147 | r=0.095 p=0.471 | r=0.050 p=0.703 | r=0.164 p=0.211 |
| WBC ($\times10^3/\mu L$) | r=-0.180 p=0.169 | r=-0.222 p=0.089 | - | r=0.136 p=0.300 | r=0.134 p=0.309 | r=-0.018 p=0.889 | r=-0.010 p=0.942 | r=0.209 p=0.109 |
| Hb (g/dL) | r=-0.008 p=0.954 | r=-0.130 p=0.324 | r=0.136 p=0.300 | - | r=0.916 p=0.001 | r=0.051 p=0.699 | r=0.063 p=0.635 | r=-0.288 p=0.026 |
| Htc (%) | r=-0.099 p=0.451 | r=-0.189 p=0.147 | r=0.134 p=0.309 | r=0.916 p=0.001 | - | r=0.015 p=0.911 | r=0.152 p=0.248 | r=0.184 p=0.159 |
| MPV (fL) | r=-0.114 p=0.386 | r=0.095 p=0.471 | r=-0.018 p=0.889 | r=0.051 p=0.699 | r=0.015 p=0.911 | - | r=0.749 p=0.001 | r=-0.253 p=0.051 |
| P-LCR (%) | r=-0.055 p=0.675 | r=0.050 p=0.703 | r=-0.010 p=0.942 | r=0.063 p=0.635 | r=0.152 p=0.248 | r=0.749 p=0.001 | - | r=-0.064 p=0.629 |
| ESR (mm/h) | r=0.145 p=0.269 | r=0.041 p=0.753 | r=0.070 p=0.596 | r=-0.276 p=0.033 | r=-0.215 p=0.099 | r=0.035 p=0.789 | r=0.134 p=0.308 | r=0.375 p=0.003 |

FEV1: Forced expiratory volume in the first second. FVC: Forced vital capacity. WBC: White blood cell. Hb: Hemoglobin. Htc: Hematocrit. PLT: Platelet. MPV: Mean platelet volume. P-LCR: Platelet large cell ratio. ESR: Erythrocyte sedimentation rate. CRP: C-reactive protein.

significantly lower than control group. MPV has been studied as an inflammatory marker in various diseases [21-23]. Previous studies have reported controversial results regarding evaluation of MPV in COPD [24-33]. The conflicting data might be due to the failure to rule out confounding factors such as body mass index, smoking status, and the use of medications such as statins and angiotensin-converting enzyme inhibitors [34]. In our study, we ruled out respiratory disorders other than COPD, pulmonary

embolism, and left ventricular systolic or diastolic dysfunction, comorbidities such as diabetes, chronic renal insufficiency, hyperthyroidism, hypothyroidism, hepatic dysfunction and various drugs. Kalemci et al. [28] found a significant increase in PDW, MPV, platelets, PLR, and RDW, while mean platelet volume ratio decreased as the COPD severity increases. According to their results, patients with more severe COPD had higher MPV values, unlike our study. Wang et al. [9] found that COPD patients during exacerbation and in stable phase had lower MPV compared to healthy controls. MPV of participants with COPD was higher once patients had recovered from exacerbations. Moreover, reduced MPV was positively related to WBC and CRP levels in exacerbated COPD, not in the stable phase. Ulaslı et al. [26] reported that MPV values were significantly lower in patients during acute exacerbation than in those during the stable period of COPD and in control subjects. They announced that assessment of MPV in COPD exacerbation might indicate systemic inflammation and MPV might be used as a negative acute phase reactant in COPD exacerbation as in our results. There was no correlation between MPV and other inflammatory parameters, FEV1 and FEV1/FVC in stable phase in the current study. COPD may be associated with reduced MPV, independent of clinical manifestations.

PDW is the standard deviation of the logarithmic transformation of platelets. It is an index that provides information about the viability of the platelets to be used in transfusions [28]. Recent studies have reported that there was an increase in PDW, MPV, and PCT values with an increase in the severity of COPD (from A to D) [28]; however, the results were contradictory. Wang et al. [12] reported that a significant increase in PDW was related to COPD with pulmonary embolisms. However, they did not observe a relationship between PDW and disease severity as in our study. PDW levels in control group were significantly lower than A/B and C/D groups in our study. We determined that PDW was independently associated with severe COPD and clinical parameters. By contrast, Steiropoulos et al. [29] noticed no significant differences in MPV and PDW values between patients with different stages of COPD. They found that a significant correlation was noted between MPV and WBC in patients with COPD, and especially in those with severe COPD stage III and very severe COPD stage IV. Analysis of Białas et al. [19] indicated that elevated PDW was associated with reduced survival of patients with COPD and PDW might be used as an inexpensive and repeatable prognostic tool in COPD. Makhlouf et al. [25] reported that PDW, PCT, and CRP were significantly higher in COPD patients, either nondiabetic or diabetic. Koc et al. [35] found that MPV and PDW levels were lower, and WBC was higher in patients with COPD compared to smokers and nonsmoking subjects; however, the platelet count was not significantly different.

This study also has some limitations. First, our sample size is relatively small. Second, dietary habits, physical activity and the exercise level of the subjects were not documented. Third, correlations of systemic blood count parameters with pulmonary function test were relatively weak.

Although the association between MPV, PDW, and COPD was controversial, our results suggested that MPV was decreased and PDW was elevated in patients with COPD. MPV could partly reflect disease severity, not PDW. Platelets play an important role in inflammatory conditions related to COPD. Chronic inflammation is also known to induce platelet activation. Platelet function may be modified by the systemic inflammation associated with COPD. Low MPV count can be used as a negative acute phase reactant in the evaluation of disease severity in COPD as well as the classic positive acute phase reactant, CRP. However, we are of the opinion that the platelet count cannot be used for the evaluation of disease severity in COPD.

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