ORIGINAL ARTICLE

Eastern Journal of Medicine
East J Med 25(1): 97-102, 2020
DOI: 10.5505/2020.24572

Platelet Distribution With is A Usable Parameter in Chronic Obstructive Pulmonary Disease Severity

Buket Mermit Çilingir*, Aysel Sünnetçioğlu

Van Yüzüncü Yıl University School of Medicine Department of Chest Deseases, Van, Turkey

Abstract

Chronic obstructive pulmonary disease (COPD) is a common chronic inflammatory disease with a high mortality and morbidity rate. The aim of our study was to investigate the relationship of hematological parameters including the MPV, PDW and RDW with the severity of COPD.

We retrospectively enrolled patients with the diagnosis of COPD who were admitted to our Pulmonary Diseases Department. A total of 201 patients with COPD, diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, were included in the study. Patients were divided into 4 groups according to the severity of COPD: group A (mild), group B (mild to moderate), group C (moderate to severe), and group D (severe). 159 healthy subjects without any risk factors or chronic diseases who were admitted to our outpatient clinics were included as control.

There was statistically significant difference in PDW values between patients with COPD and controls (p =0. 001). There was no statistically significant difference in MPV values and RDW rates between patients with COPD and controls (p = 0.591, p = 0.677 respectively). Patients in the severe COPD group were older, more often were male, had higher hematocrit values. There were no statistically significant differences in MPV, PDW, and RDW values in the severity of COPD (p=0.639, p=0.082, p=0.662 respectively).

PDW could be used an indicator of hypoxemia, underlying inflammation, and oxidative stress. It could be considered as a new marker in the determination of inflammation in COPD patients with rapid, inexpensive, easily measurable properties with routine CBC analysis. Morover, measurement of changes in PDW value during follow-up can be used to assess the inflammatory response.

Key Words: Chronic obstructive pulmonary disease, Mean platelet volume, Platelet Distribution Width, Red Blood Cell Distribution Width

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the important causes of morbidity and mortality in the world (1). COPD is a component of systemic inflammatory syndrome. It is characterized by the airflow limitation resulting from inflammation and remodeling of the airways (2). It can increase the severity of comorbidities such as ischemic vascular diseases, heart failure, osteoporosis, metabolic syndrome, and depression (3).

According to several studies, platelets and their indices may be used as inflammatory markers for cardiovascular, inflammatory, and thromboembolic diseases. Mean platelet volume (MPV) is an indicator of the platelet function. It shows platelet stimulation and production rate (4,5). Increased MPV is associated with the presence and prognosis of vascular disease, including peripheral, cerebrovascular, and coronary artery disease (6). Also previous studies showed correlations between MPV and disease activity in inflammatory bowel diseases, rheumatoid arthritis, ankylosing spondylitis and diabetes mellitus (7, 8, 9).

However, MPV in COPD is little known. A number of previous studies have shown that high MPV and PDW are associated with increased inflammatory state in the body, as well as with the severity and acute exacerbation of COPD (10,11). Some studies have demonstrated elevated MPV values in COPD patients (12,13). Biljak et al. have reported increased platelet count with reduced MPV in patients with COPD (14). Cui et al. have found that high MPV is a predictor of impaired cardiac and pulmonary function in elderly participants with COPD(15).

The red blood cell distribution width (RDW) is a numerical measure of the size variability of circulating erythrocytes. Recent studies have reported that RDW increases as the severity of COPD progresses and suggested that RDW might be used as a biomarker in the disease severity (16). Also, elevated RDW levels were found to be associated with increased mortality risk in patients with COPD (17).

*Corresponding Author: Buket Mermit Çilingir, Yüzüncü Yıl Üniversitesi School of Medicine Chest Diseases, Van, E-mail: buketmermitcilingir@gmail.com, Phone: (432) 215 04 74
Received: 25.09.2019, **Accepted:** 02.12.2019

Accompanied by these findings the aim of our study was to investigate the relationship of platelet parameters including the MPV, PDW and RDW with the severity of COPD in relatively large population, living in eastern of Turkey.

Materials and Methods

We retrospectively enrolled patients with the diagnosis of COPD who were admitted to our outpatient and emergency clinics at the Pulmonary Diseases Department. A total of 201 patients with COPD, diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, were included in the study (18). COPD was diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, based on past smoking history, clinical evaluation, and pulmonary function tests, showing irreversible airflow obstruction. The disease severity staging was conducted according to the 2017 GOLD guidelines. Patients were divided into 4 groups according to the severity of COPD: group A (mild), group B (mild to moderate), group C (moderate to severe), and group D (severe).

The exclusion criteria were; previous hospitalization, use of emergency services, blood transfusions, use of any antiinflammatory medications in the preceding 2 months (systemic steroids, immunosuppressive drugs, etc), history of cancer, connective tissue diseases, inflammatory bowel disorders, or hematological disorders.

Demographic characteristics and medical histories, including comorbid diseases, were recorded. All patients were active smokers. Peripheral venous blood samples were drawn from the antecubital veins of patients after an overnight fasting. The blood samples were put into lithium heparin

containing tubes to avoid pseudothrombocytopenia. Total and differential leukocyte counts, platelet counts, and other platelet indices were measured by an automated hematology analyzer (Abbott Cell - Dyn 3700; Abbott Laboratory, Abbott Park, Illinois, United States). Absolute cell counts were used in the analyses.

159 healthy subjects without any risk factors or chronic diseases who were admitted to our outpatient clinics were included as control. Blood samples for CBC were also taken from control group.

All participants underwent pulmonary function tests, which were performed by the same technician. The best test result of the 3 consecutive measurements was recorded. Forced expiratory volume in 1 second, forced vital capacity (FVC), and percentage of FVC expelled in the first second of forced expiration were measured according to the American Thoracic Society guidelines (19). This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration. The study protocol was approved by the local ethics committee.

Statistics: Descriptive statistics for continuous variables are expressed as Mean, Standard Deviation, Minimum and Maximum value. Categorical variables are expressed as Number and Percentage. One-Way Variance Analysis (ANOVA) was used to compare the group means for continuous variables. Duncan test was used to determine different groups. Pearson correlation coefficients were calculated separately in the groups to determine the relationship between variables. A *P*-value less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed using the Statistical Package for the Social Sciences for Windows v20.0 (SPSS Inc. , Chicago, IL, USA).

Results

A total of 201 patients with COPD and 159 control subjects were included in the study. Demographics, functional parameters, and laboratory results of COPD patients and controls are presented in Table 1.

The mean MPV values of COPD patients were 8.3 ±1.2 fl and 8.4±2.6 fl in control subjects. There was no statistically significant difference in MPV values between patients with COPD and controls (p = 0.591). The mean PDW values of COPD patients were 16.9 ±1.2 fl and 18.3±5.7 fl in control subjects. There was statistically significant difference in PDW values between patients with COPD and controls (p = 0.001). There was no statistically significant difference in platelet values between patients with COPD and controls (p = 0.197).The mean RDW rates of COPD patients were 15.3±2.6 and 15.2±1.9 in control subjects. There was no statistically significant difference in RDW rates between patients with COPD and controls (p = 0.677).

Clinical and laboratory characteristics of patients with chronic obstructive pulmonary disease according to disease severity are presented in Table 2.

The distribution of the COPD groups was as follows: group A, n = 10; group B, n = 53; group C, n = 36; and group D, n = 60. There were statistically significant differences in FEV1 (lt), FVC (lt), and FEV1/FVC(%) values in the severity of COPD (p= 0.001, p= 0.001, p= 0.001 respectively). Patients in the severe COPD group were older, more often were

Table 1. Demographics, functional parameters, and laboratory results of patients during the stable period and controls

Parameters	COPD patients (n = 201)	Control group (n = 159)
age, y (mean $\pm sd$)	64.8 ±11	42.3±14.5
sex, male/female	121/80	81/78
Smoking(never, former, current)	65/63/174	75/50/34
Hb, g/l (mean $\pm sd$)	14.9±4.6	14.7±1.8
Hematocrit (mean $\pm sd$)	49.3±5.8	46.4±5.7
WBC count, /μl (mean $\pm sd$)	10±4.9	11.8±3.5
MPV, fl (mean $\pm sd$)	8.3±1.2	8.4±2.6
platelets, $\times 10^3$/μl (mean $\pm sd$)	247.33±83.2	258±69.7
PDW, fl (mean $\pm sd$)	16.9±1.2	18.3±5.7
RDW, % (mean $\pm sd$)	15.3±2.6	15.2±1.9
WBC count, /μl (mean $\pm sd$)	10±4.9	11.8±3.5

Abbreviations: BMI – body mass index, COPD – chronic obstructive pulmonary disease, CRP – C- reactive protein, FEV1 – forced expiratory volume in 1 second, FVC – forced vital capacity, Hb – hemoglobin, IC – inspiratory capacity, MPV – mean platelet volume, WBC – white blood cell, sd: standard deviation

male, had higher hematocrit values. There were no statistically significant differences in MPV, PDW, and RDW values in the severity of COPD (p=0.639, p=0.082, p=0. 662 respectively).

Moreover, there were no significant correlations between WBC count and neutrophil, eosinophil, basophils, monocytes, lymphocyte percentage in the severity of COPD (p=0.573, p=0.162, p=0.329, p=0. 473, p=0.148, p=0. 148 respectively).

Discussion

In our study, we found that PDW values increased in COPD patient compared with healty subjects, but there was no significant difference between MPV and RDW in COPD patient compared with controls. There were no statistically significant differences in MPV, PDW, and RDW values in the severity of COPD. Moreover, there were no significant correlations between WBC count and neutrophil, eosinophil, basophils, monocytes, lymphocyte percentage in the severity of COPD.

COPD considered a complex systemic disease involving several organs and systems like musculoskeletal, cardiovascular, endocrin. Chronic obstructive pulmonary disease has now been recognized as an inflammatory state including systemic oxidative stress, activation of circulating inflammatory cells, and increased levels of inflammatory cytokines (20,21).

In patients with COPD, there is evidence of platelet activation (20, 21, 22). The mechanisms underlying platelet activation are not clear but hypoxia and chronic inflammation has already been identified to induce platelet activation (13,23). MPV is a marker of platelet activation along with platelet distribution width (PDW) (24, 25).

MPV and PDW has been shown to reflect inflammatory burden in different chronic diseases (7,8). Biljak et al. found that patients with COPD had significantly increased platelet count and reduced MPV compared with healthy controls (14). Onder et al. and Bansal et al. found that MPV values were significantly increased in hypoxic patients with COPD compared with nonhypoxic subjects and controls (12,13). Steiropoulos et al reported that MPW was significantly higher in patients with COPD than in controls, but all control groups were smokers (26). Kalemci et al. reported that, patients with more severe COPD had higher MPV values (27). Studies suggests that inflammation in COPD is linked with platelet activation, as expressed by the elevated MPV (23,24).

On the other hand, similar with our study, Ulaşlı et al. reported that there was no statistically significant difference in MPV values between patients with stable COPD and controls (11). Some studies suggested that the MPV decreases in patients with inflammatory disorders including COPD even during acute

Table 2. Clinical and laboratory characteristics of patients with chronic obstructive pulmonary disease according to disease severity

Parameters	Group1	Group 2	Group 3	Group 4	P value
age, y (mean ± sd)	61±14.6[b]	60.2±10.9[b]	65±10 [ab]	70.9±8.4[a]	0.001
sex, male/female	6/4	43/10	21/15	43/17	0.648
smoking (never, former, current)	5/0/5	18/17/18	9/11/16	17/8/35	0.115
Hb, g/l (mean ± sd)	13.6±2.4	16.4±7.8	14.3±2.6	14.6±1.9	0.311
Hematocrit (mean ± sd)	38.8±7.5	44±10.2	44.5±8.8	48.1±1.2	0.150
WBC count, /µl (mean ± sd)	9.7±4.3	11.1±6	9.3±4.7	10.2±4	0.573
MPV, fl (mean ± sd)	8.2±0.5	8.2±1	8.4±1.4	8.2±1.1	0.639
platelets, $\times 10^3$/µl (mean ± sd)	172.70±62.7[b]	280.43±82.2[a]	234.23±81.9[ab]	247.14±84[ab]	0.002
PDW, fl (mean ± sd)	17.6±1.5	16.7±1.2	16.7±1.4	17.3±1.1	0.082
RDW, % (mean ± sd)	14.9±0.6	14.8±1.8	15.7±3	15±2.4	0.662
WBC count, /µl (mean ± sd)	9.7±4.3	11.1±6	9.3±4.7	10.2±4	0.573
FEV1, lt (mean ± sd)	91.5±8.5[a]	62±6.6[b]	40.4±6[c]	24.3±4.3[d]	0.001
FVC, lt (mean ± sd)	83.7±9.7[a]	69.8±7.3[b]	49.7±9.9[c]	32.9±8[d]	0.001
FEV1/FVC (mean ± sd)	106±8.9[a]	70.3±14.4[b]	61.4±15.7[bc]	52.4±19.2[c]	0.001

a,b,c →: Different lower cases in the same row represent statistically significant differences among the groups.
Abbreviations: FEV1, forced expiratory volume in 1 second; FEV1/FVC, percentage of forced vital capacity expelled in the first second of forced expiration; FVC, forced vital capacity; MPV, mean platelet volume; NLR, neutrophil - to - lymphocyte ratio; PCT, plateletcrit; PDW, platelet distribution width; PLR, platelet - to - lymphocyte ratio; RDW, red cell distribution width; WBC, white blood cell; WMR, white blood cell count to mean platelet volume ratio, sd: standard deviation

exacerbations (11, 15, 26). Also Ulaşlı et al reported that mean MPV values in exacerbation were significantly lower than those in the stable period or in the control group, so it may be used as a negative acute phase reactant. In Günay et al, decrease in MPV was evident during acute exacerbation of COPD similar to the study by Ulasli et al (28).

Both Biljak et al and Ulasli et al have reported that MPV showed no difference between the stages of COPD severity (11,14). Only Cui et al. found a negative correlation between MPV and percentage predicted FEV1, suggesting higher MPV in more severe obstruction, but they included a very selected population of very old male patients (15).

PDW is the standard deviation of the logarithmic transformation of platelets. It is an index that provides information about the viability of the platelets. Increases in PDW indicate that abnormally large and small platelets are in circulation. PDW was shown to increase in various pulmonary diseases other than COPD such as obstructive sleep apnea syndrome, pulmonary tuberculosis, pulmonary embolism, and pulmonary hypertension (29, 30, 31, 32). Wang et al reported that a significant increase in PDW is related with COPD and pulmonary embolisms (33). Cui et al. also reported that PDW levels are similar in both smoker COPD patients and control subjects. However, they did not observe a relationship between the PDW and disease severity (15). Our results were showing an increased PDW in patients with COPD than in controls. This increase could be related to an elevation in the thrombosis load and increased inflammation. But in contrast, in the other two study, they found no difference in PDW between patients with COPD and controls (26,28).

The RDW is a quantitative measure of anisocytosis. The RDW is typically elevated in conditions of ineffective red cell production and increased red cell destruction (34). An increased RDW reflects a profound deregulation of erythrocyte homeostasis involving both impaired erythropoiesis and abnormal red blood cell survival (35). Seyhan et al observed a relationship between the RDW and increased

mortality of patients with stable COPD (17). Sincer et al. reported that increased RDW may be used to identify right ventricular failure in COPD patients (36). Günay et al. showed that increased RDW level was related in COPD patients. Also, this value was associated with the inflammatory response in COPD patients (31). Kalemci et al reported that, the RDW significantly increased in the severity of COPD. Their results were consistent with previous studies reporting a correlation between RDW and severity of COPD (27).

But in our study there was no statistically significant difference in RDW values between patients with stable COPD and controls and also in disease severity.

The strength of our study group is a large patient series, but limitation is that the COPD group and healty subjects were not age and sex matched. However, as already discussed, this is more representative of everyday clinical practice that patients with COPD were older and more frequently male.

PDW could be used an indicator of hypoxemia, underlying inflammation, and oxidative stress.

It could be considered as a new marker in the determination of inflammation in COPD patients with rapid, inexpensive, easily measurable properties with routine CBC analysis. Moreover, measurement of changes in PDW value during follow-up can be used to assess the inflammatory response.

References

1. Decramer M, Janssens W, Miravitlles M. Chronic obstructive pulmonary disease. Lancet 2012; 379: 134-1351.
2. From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2010. Definition: Chapter 1; 1-7.
3. Salvi S. Tobacco smoking and environmental risk factors for chronic ob−structive pulmonary disease. Clin Chest Med 2014; 35: 17−27.
4. Briggs C. Quality counts: new parameters in blood cell counting. Int J Lab Hematol 2009; 31: 277−297.
5. Mahdavi-Zafarghandi R, Shakiba B, Keramati MR, Tavakkoli M. Plate- let volume indices in patients with varicocele. Clin Exp Reprod Med 2014; 41: 92−95.
6. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des. 2011; 17(1): 47-58.
7. Yazici S, Yazici M, Erer B, et al. The platelet indices in patients with rheumatoid arthritis: mean platelet volume reflects disease activity. Platelets. 2010; 21: 122−125.
8. Kisacik B, Tufan A, Kalyoncu U, et al. Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis. Joint Bone Spine 2008; 75: 291−294.
9. Papanas N, Mavridis G, Karavageli E, Symeonidis G, Maltezos E. Peripheral neuropathy is associated with increased mean platelet volume in type 2 diabetic patients. Platelets 2005; 16(8): 498-499.
10. Makhlouf HA, Sadek SH, Nafady AAH. Platelet function in diabetic and nondiabetic patients with chronic obstructive pulmonary disease: a case control study. Clin Respir J 2018; 12: 48−56.
11. Ulasli SS, Ozyurek BA, Yilmaz EB, Ulubay G. Mean platelet volume as an inflammatory marker in acute exacerbation of chronic obstructive pulmo−nary disease. Pol Arch Med Wewn. 2012; 122: 284−290.
12. Bansal R, Gupta HL, Goel A, Yadav M. Association of increased platelet volume in patients of chronic obstructive pulmonary disease: clinical impli- cations. Journal, Indian Academy of Clinical Medicine 2002; 3: 169−172.
13. Onder I, Topcu S, Dokmetas HS, et al. Platelet aggregation size and volume in chronic obstructive pulmonary disease. Mater Med Pol 1997; 29: 11−13.
14. Biljak VR, Pancirov D, Cepelak I, Popovic´-Grle S, Stjepanovic´ G, Grubis˘ic´ TZ ˇ. Platelet count, mean platelet volume and smoking status in stable chronic obstructive pulmonary disease. Platelets 2011; 22(6): 466-470.
15. Cui H, Liu L, Wei Z, et al. Clinical value of mean platelet volume for impaired cardiopulmonary function in very old male patients with chronic obstructive pulmonary disease. Arch Gerontol Geriatr 2012; 54(2): 109-112.
16. Tertemiz K, Alpaydin AO, Sevinc C, et al. Could "red cell distribution width" predict COPD severity? Rev Port Pneumol 2016; 22: 196−201.
17. Seyhan EC, Özgül MA, Tutar N, et al. Red blood cell distribution and survival in patients with chronic obstructive pulmonary disease. COPD 2013; 10: 416−424.
18. Global Initiative for Chronic Obstructive Lung Disease (GOLD). http://www.goldcopd.org.
19. Association MSotAL. American Thoracic Society Standardization of Spirometry, 1994 Update; 2012.
20. Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. Eur Respir J 2009; 33: 1165−1185.

21. Agusti AG. Systemic effects of chronic obstructive pulmonary disease. Proc Am Thorac Soc 2005; 2(4): 367-370.
22. Fimognari FL, Scarlata S, Conte ME, Incalzi RA. Mechanisms of atherothrombosis in chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2008; 3(1): 89-96.
23. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des 2011; 17(1): 47-58.
24. Tsiara S, Elisaf M, Jagroop IA, Mikhailidis DP. Platelets as predictors of vascular risk: is there a practical index of platelet activity? Clin Appl Thromb Hemost 2003; 9(3): 177-190.
25. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia 2010; 14(1): 28-32.
26. Steiropoulos P, Papanas N, Nena E, et al. Mean Platelet Volume and Platelet Distribution Width in Patients With Chronic Obstructive Pulmonary Disease: The Role of Comorbidities. Angiology 2012; 64(7): 535-539.
27. Kalemci S, Akin F, Sarihan A, Sahin C, Zeybek A, Yilmaz N. Relationship between hematological parameters and severity of chronic obstructive pulmonary disease. Pol Arch Intern Med. 2018; 128 (3): 171−177.
28. Günay E, Ulaşlı SS, Akar O, et al. Neutrophil-to-Lymphocyte Ratio in Chronic Obstructive Pulmonary Disease: A Retrospective Study. Inflammation, 2014; 37; No. 2, April
29. Bülbül Y, Aydın ÖE, Örem A. Platelet indices in obstructive sleep ap−nea: the role of mean platelet volume, platelet distribution widht and plateletcrit. Tuberk Toraks 2016; 64: 206.
30. Şahin F, Yazar E, Yıldız P. Prominent features of platelet count, platelet- crit, mean platelet volume and platelet distribution width in pulmonary tu−berculosis. Multidiscip Respir Med 2012; 7: 38.
31. Günay E, Sarinc Ulasli S, et al. Can platelet indices predict obstruc- tion level of pulmonary vascular bed in patients with acute pulmonary em−bolism? Clin Respir J 2014; 8: 33−40.
32. Zheng YG, Yang T, Xiong CM, et al. Platelet distribution width and mean platelet volume in idiopathic pulmonary arterial hypertension. Heart Lung Circ 2015; 24: 56-572.
33. Wang M, Zhang J, Ji Q, et al. Evaluation of platelet distribution width in chronic obstructive pulmonary disease patients with pulmonary embo- lism. Biomarkers 2016; 10: 587−596.
34. Paredi P, Kharitonov SA, Leak D, et al. Exhaled ethane, a marker of lip- id peroxidation, is elevated in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2000; 162: 369−373.
35. Salvagno GL, Sanchis−Gomar F, Picanza A, Lippi G. Red blood cell dis- tribution width: A simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci 2015; 52: 86−105.
36. Sincer I, Zorlu A, Yilmaz MB, et al. Relationship between red cell distribution width and right ventricular dysfunction in patients with chronic obstructive pulmonary disease. Heart and Lung 2012; 41: 238-243.