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Research Article

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DOES THE MEAN PLATELET VOLUME (MPV) HAVE ANY IMPORTANCE IN THE EVALUATION OF CARDIOVASCULAR DISEASE IN COPD PATIENTS?

ORTALAMA TROMBOSİT HACMİ (MPV) KOAH'LI HASTALARDA KARDİYOVASKÜLER HASTALIKLARIN DEĞERLENDİRİLMESİNDE ÖNEMLİ MİDİR?

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Öz

Amaç: Ortalama trombosit hacmi (MPV) trombosit aktivasyonunun bir indeksidir. Bu çalışmada, göğüs hastalıkları bölümüne başvuran KOAH ve kardiyovasküler hastalık olan hastalar ile MPV arasındaki ilişkiyi değerlendirmeyi amaçladık.

Materyal ve Metot: Sigara içen 535 (%71,80) ve sigara içmeyen, 210 (%28,20) hasta MPV ve diğer parametrelerle karşılaştırıldı.

Bulgular: Sigara içenlerde beyaz kan hücrelerinin (Wbc), hemoglobin (Hgb) ve Hematokrit (Htc) düzeyleri sigara içmeyenlere göre istatistiksel olarak anlamlı derecede yüksekti (p<0,001). Sigara içenlerde MPV düzeyleri, sigara içmeyenlere göre istatistiksel olarak yüksekti [MPV seviyeleri, 10,10 (8-14,20), 9,60 (6,40-11,80), sırasıyla p<0,001]. Sigara içenlerde 106 KOAH hastası vardı. KOAH hastaları ve KOAH'lı olmayan ve sigara içmeyen hastalar arasında trombosit ve MPV düzeyindeki farklılıklar istatistiksel olarak anlamlıydı [10,20 (8,30-14), 9,60 (6,40-11,80), sırasıyla p=0,001]. Ayrıca, kardiyovasküler komorbiditeleri (CVC) olan KOAH hastalarının MPV seviyeleri, CVC'siz hastalardan daha yüksekti.

Sonuç: Bu çalışmada sigara içenlerde ve KOAH hastalarında sigara içmeyenlere göre daha yüksek MPV ve daha yüksek trombosit değerleri gösterilmiştir. Sonuç olarak yüksek MPV düzeylerinin KOAH'lı hastalarda tromboza eğilimi artırabileceği düşünülmüştür. Bununla birlikte, KOAH'ın MPV ve CVC ile ilişkisi hakkında daha fazla araştırma yapılması gerekmektedir.

Anahtar Kelimeler: Sigara, KOAH, MPV, tromboz,

Abstract

Objectives: : Mean platelet volume (MPV) is an index of platelet activation. In this study, we aimed to evaluate the relationship between in patients with COPD and cardiovasculary disease who present to chest diseases department and MPV.

Materials and Methods: Smoker 535 (71.80%) and non-smoker, 210 (28.20%) subjects were compared for MPV and other parameters. Accordingly, patients with and without COPD were compared in terms of MPV and other parameters.

Results: The levels of white blood cells (Wbc), hemoglobin (Hgb) and hematocrit (Htc) in smokers were statistically significantly higher than non-smokers (p<0.001). The level of MPV in smokers was statistically higher than non-smokers [the levels of MPV were, 10.10 (8-14.20), 9.60 (6.40-11.80),respectively p<0.001]. There were 106 cases of COPD among smokers. The differences in levels of platelets and MPV between patients with COPD and nonsmoker patients without COPD were [10.20 (8.30-14), 9.60 (6.40-11.80), respectively p=0.001] statistically significant. Also, MPV levels of COPD patients with cardiovascular comorbidities (CVC) were higher than that of the patients without CVC.

Conclusion: In this study, higher MPV and higher platelet values have been shown in smokers and COPD patients compared with non- smokers. As a result, consider that high MPV levels may increase the tendency to thrombosis, with COPD. However, further larger studies are warranted about the relationship of COPD with MPV and CVC.

Keywords: Cigarette, COPD, MPV, thrombosis.

Introduction

It is expected that Chronic obstructive pulmonary disease (COPD) will be the third cause of mortality in the world in 2020.[1-2] The blood leukocytes, C-reactive protein (CRP) and the other cytokines are increased to relate to the inflammation in COPD[3-5] since COPD is a chronic, systemic and inflammatory disease.[1] An increase of acute-phase reactants and cytokines leads to both airway limitation and systemic inflammation. Comorbidities and obstruction is created by increase of inflammation in COPD.

Mean platelet volume (MPV) is one of the platelet activation indicator and is determined by routine hemogram test that is easily applicable. It has been shown as a marker of endothelial dysfunction and disease activator in the recent studies in the different diseases.[6-10] Activated platelets are important in atherogenesis, thrombosis and inflammation.[11] MPV which is related to the activated platelet levels could be an indicator about cardiovascular comorbidities and inflammation in COPD.[11]

In this study, we aimed to assess the importance of MPV in evaluation of cardiovascular comorbidities and prognosis in the follow up COPD.

Materials and Methods

In pulmonology department of Ankara Atatürk Research and Training Hospital, between 2012-2014, smoker 535 (71.80%) cases and non-smoker healthy 210 (28.20%) subjects totally 745 outpatients were enrolled in this study. Ages, genders, civil and educational status of all patients and all the comorbidities were recorded. Consumption of cigarettes was recorded as packs/year in smokers. Fagerström test as nicotine dependence questionnaire was performed to smokers for evaluation of the degree of smoking addiction. The carbon monoxide levels in the breath of smokers were measured with bed front picoSmokerlyser portable carbon monoxide meter. The pulmonary functions of all participants were analyzed with a brand spirometer according to the standards of American Thoracic Society. The pulmonary function test (PFT) was explained to each participant in detail and the best of three reproducible tests was accepted. The measured (actual) and percentage of predicted (predicted%) values of forced expiratory volume in 1 sec (FEV_1), forced vital capacity (FVC), FEV_1 as a percentage of FVC (FEV_1/FVC), forced expiratory flow in 25% and 75% of forced vital capacity ($FEF_{25-75\%}$) parameters of each participant were considered. The predicted % values were calculated automatically according to age, sex and height. According to the results of PFT, patients were classified as with and without chronic obstructive pulmonary disease (COPD). The presence of post-bronchodilator FEV_1/FVC<70% confirms the COPD diagnosis. The patients with COPD were classified as GOLD 1, 2, 3, 4 according to the FEV_1 % predicted. FEV_1 ≥80% predicted classified as GOLD 1, 50%≤ FEV1<80% predicted classified as GOLD 2, 30%≤ FEV1<50% predicted classified as GOLD 3 and FEV_1 <30% predicted classified as

GOLD 4.[1] Cardiovascular comorbidities (Congestive Heart Failure, Atrial Fibrillation, Coronary Artery Disease, Hypertension) were recorded in patients with COPD.

Serum levels of white blood cells (Wbc), hemoglobin (Hgb), hematocrit (Htc), platelet (Plt), mean platelet volume (MPV), cholesterol (Chol), high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (Tg) were measured and compared between smokers and non-smokers. Accordingly, patients with and without COPD were compared in terms MPV and other parameters. And also MPV and other parameters were compared according to the stage of COPD. Also, ethics consent was obtained from hospital ethics committee (Ethics no: 17.12.2014-247).

The findings of the study were assessed for statistical analysis using SPSS (Statistical Package for Social Sciences) 20.00 program. Descriptive statistics were computed for each of the variables analyzed. Results are presented as mean ± standard deviation (sd). In order to compare the different groups stratified by age and sex, the independent samples t-test and Chi-squared test were used. Kruskal-Wallis test was used for the comparison of the average of the independent samples of more than two groups for nonparametric data. *p*-value <0.05 was considered as significant.

Results

The mean age of all patients was 45± 13.00 (16- 85) and 48.10% (358) of the patients were female, while 51.90% (387) were men. There were 535 (71.80%) smokers and 210 (28.20%) non-smokers. The mean age of smokers was 43.40± 11.50 (16- 73) and 38.50% (206) of them were female, 61.50% (329) were men. The mean age of non-smokers was 48.40± 15.80 (16- 85) and 72.40% (152) of them were female, 27.60% (58) were men. There was no significant difference between smokers and non-smokers about the distribution of age and gender. Mean consumption of cigarettes as packs/year was determined as 25 (1-240) packs/year in smokers. According to the results of Fagerström test, scores of tobacco dependence was detected as 3 (0-9). The levels of white blood cells (Wbc), hemoglobin (Hgb) and hematocrit (Htc) in smokers were statistically higher than non-smokers. The level of MPV in smokers was statistically significantly higher than non-smokers (Figure 1). The levels of cholesterol (chol), HDL and Tg in smokers were statistically significantly different than non-smokers. These results are shown in Table 1.

According to the results of pulmonary function test, there were 106 cases of COPD in smokers. The levels of platelets and MPV in patients with COPD were higher than that of the patients without COPD, however this difference was not statistically significant. These results are shown in Table 2.

Table 1. Demographic characteristics and comparison of other parameters in smokers and non-smokers.

	SMOKERS	NON-SMOKERS	P-value
	n (%) 535 (71.80%)	**n (%) 210 (28.20%)**	
Age	43.40 (16-75)	48.40 (16-85)	**<0.001**
Female/Male	206/329 38.50/61.50	152/58 72.40/27.60	**<0.001**
White Blood Cell*	8000 (3400-19600)	6750 (3600-19500)	**<0.001**
Hemoglobin	14.90 (7.30-18.30)	13.60 (9.10-17.80)	**<0.001**
Hematocrit	44.40 (21.20-70.00)	40.30 (30.60-50.80)	**<0.001**
Platelet	230 (49-439)	255 (116-505)	**<0.001**
Cholesterol	190 (72-418)	195 (93-331)	**0.05**
HDL*	40 (13-81)	49 (25-100)	**<0.001**
LDL*	114 (27-234)	115 (20-235)	0.32
TG*	137 (27-980)	113 (34-84)	**<0.001**
MPV*	8.90 (6.10-9.10)	10.20 (6.40-14.10)	**<0.001**

Abbreviation: HDL: High-Density Lipoprotein **LDL:** Low-Density Lipoprotein **TG:** Triglyceride, **MPV:** Mean Platelet Volume.

Table 2. Comparison of parameters in patients with and without COPD among smokers.

	PATIENTS WITH COPD	PATIENTS WITHOUT COPD	P value
	n (%) 106 (20%)	**n (%) 429 (80%)**	
FEV1	70.50 (37-76)	95 (40-137)	**<0.001**
FEV_1/FVC	65 (51-72)	83 (77-121)	**<0.001**
White Blood Cell*	8862 (4000-17700)	7900 (4000-19600)	**<0.001**
Hemoglobin	14.90 (11.40-18.30)	15 (7.30-18.30)	<0.60
Hematocrit	44.20 (35.80-58.80)	44.3 (31.70-54)	<0.72
Platelet	236 (129-438)	225 (49-439)	<0.06
Cholesterol	188 (72-418)	192 (111-307)	0.15
HDL*	40 (13-134)	38 (25-74)	<0.10
LDL*	112 (27-234)	118 (53-412)	0.06
TG*	136 (30-930)	142 (63-463)	<0.27
MPV*	10.20 (8.30-14)	10.10 (8.00-14)	<0.31

Abbreviation: HDL: High Density Lipoprotein **LDL:** Low Density Lipoprotein **TG:** Triglyceride, **MPV:** Mean Platelet Volume.

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Table 3. Comparison of parameters according to the stage of COPD patients.

	STAGE 1	STAGE 2	STAGE 3	STAGE 4	P value
n (%)	**14 (13.20%)**	**61 (57.50%)**	**13 (12.30%)**	**18 (17%)**	
WBC*	9150 (5800-12900)	8000 (4000-17700)	8600 (5600-15000)	8650 (5800-17500)	0.43
Hgb	15.00 (12,00-16,70)	14.70 (11,40-18,30)	16.00 (12.80-16.60)	14.10 (11.10-16.00)	<0.001*
Htc	45.90 (38.00-49.00)	43.80 (35.80-58.80)	47.40 (42.60-52)	42.00 (35.60-47.60)	**<0.001****
Plt	266 (183-338)	229 (154-438)	229 (149-331)	245 (171-304)	**0.20**
Chol*	185 (130-287)	189 (111-307)	185 (113-243)	196 (134-243)	0.85
HDL*	38 (28-62)	37 (25-66)	38 (30-50)	38 (26-74)	0.81
LDL*	125 (83-412)	116 (64-197)	120 (70-154)	131 (76-176)	0.77
TG*	136 (88-310)	149 (36-370)	106 (50-463)	129 (80-305)	0.29
MPV*	9.80 (8.80-13.20)	10,30 (8.30-14.00)	9.50 (9,00-12.30)	10.5 (8.60-13.70)	0.13

*There were significant differences between stage 2-3 and stage 3-4 in terms of Hb (p=0.04, p=0.005).
** There were significant differences between stage 2-3 and stage 3-4 in terms of Htc (p=0.003, p=0.002).
Abbreviation: WBC: White Blood Cell, Chol: Cholesterol, **TG:** Triglyceride, **HDL:** High Density Lipoprotein **LDL:** Low Density Lipoprotein **TG:** Triglyceride, **MPV:** Mean Platelet Volume.

Table 4. Comparison of parameters in COPD patients and non-smokers.

	COPD PATIENTS	NON- SMOKERS	P value
n (%)	**106 (14.20%)**	**210 (28.10%)**	
WBC*	6700 (3600-19500)	8300 (4000-17700)	**<0.001**
Hgb	14.90 (11.10-18.30)	13.50 (9.10-17.80)	**<0.001**
Htc	44.20 (35.60-58.80)	40.20 (30.60-50.80)	**<0.001**
Plt	234 (149-438)	259 (116-505)	**<0.001**
Chol*	190 (111-307)	197 (108-331)	0.24
HDL	37 (25-74)	49 (25-100)	**<0.001**
LDL	119 (64-412)	119 (20-235)	0.88
TG*	141 (36-463)	113 (34-841)	**<0.001**
MPV*	10.20 (8.30-14.00)	9.60 (6.40-11.80)	**<0.001**

Abbreviation: WBC: White Blood Cell, Chol: Cholesterol, **TG:** Triglyceride, **HDL:** High Density Lipoprotein **LDL:** Low Density Lipoprotein **TG:** Triglyceride, **MPV:** Mean Platelet Volume.

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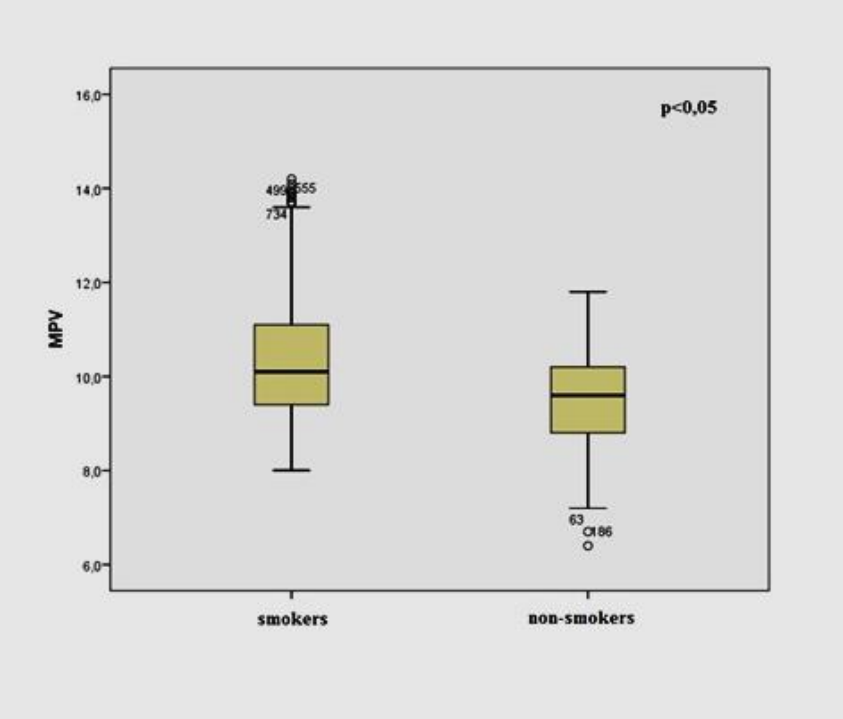

Figure 1. Comparison of serum Mean Platelet Volume levels in COPD patients with smokers and non-smokers.

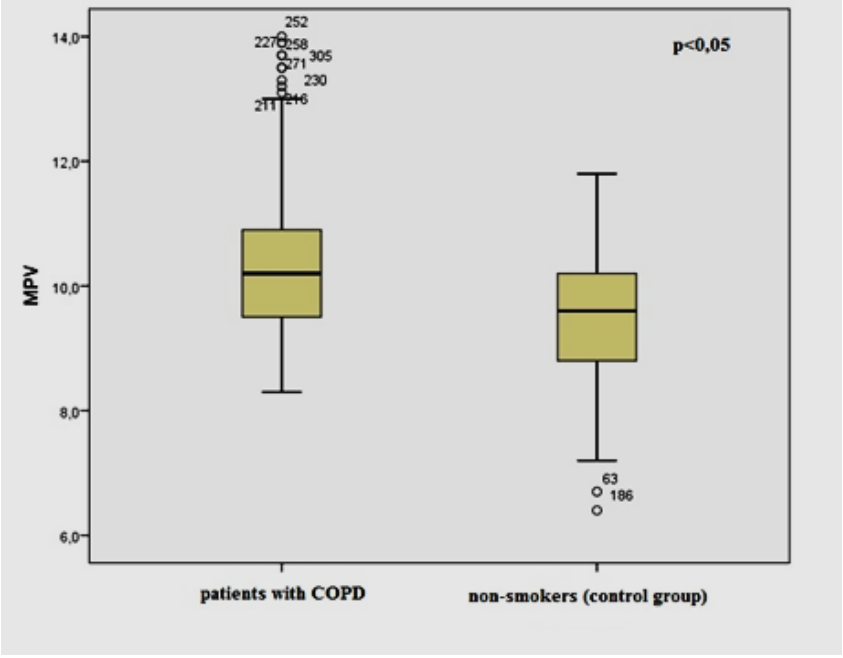

Figure 2. Comparison of serum Mean Platelet Volume levels patients with COPD and non-smokers (control group).

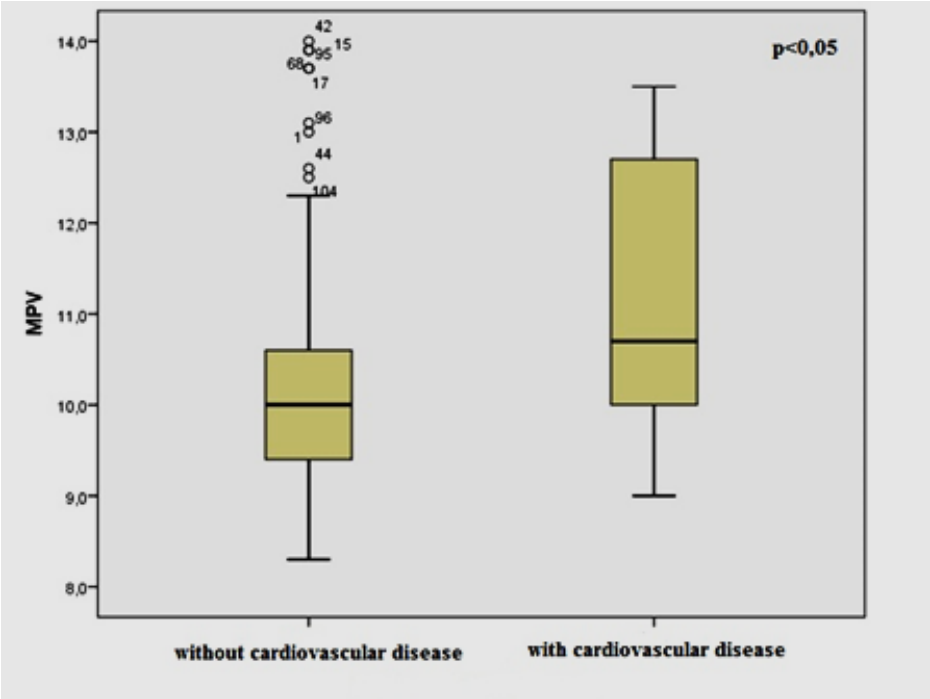

Figure 3. Comparison of serum Mean Platelet Volume levels in COPD patients with cardiovascular disease and without cardiovascular disease.

According to the GOLD classification, there were 14 (13.20%) patients in GOLD stage 1. Sixty-one (57.50%) patients in GOLD stage 2. Thirteen (12.30%) patients in GOLD stage 3. Eighteen (17%) patients in GOLD stage 4. When analyzed according to the stage of patients with COPD, the levels of MPV were not significantly different between groups (p=0,57). Only levels of hemoglobin and hematocrit were significantly different between stages 2- 3 COPD and stage 3-4 COPD (Table 3).

In comparison of COPD patients with non-smokers, significant differences were found between all parameters except cholesterol and LDL levels. The levels of MPV in COPD patients were higher than non-smokers (figure 2). The other levels of parameters are shown in Table 4.

The levels of MPV in COPD patients with cardiovascular disease and without cardiovascular disease were compared, differences were significant between each other groups (p<0.001) (Figure 3).

Discussion

In the present study, we have shown that MPV levels in patients with COPD are higher than that of the patients without COPD. Second endpoint is that MPV levels of COPD patients with cardiovascular comorbidities (CVC) are higher than that of the patients without CVC. Main finding of this study is that increased MPV levels might be a marker of cardiovascular prognosis in COPD in the future. Also, increased MPV levels may be suggested as a poor prognostic factor in the follow up of COPD.

Increased platelet activation is related to the increased platelet volume according to several studies.[12-14] Atherogenesis, inflammation and thrombosis were resulting from increased platelet activation. Hence, hypertension, coronary artery disease, pulmonary hypertension were seen.[15] Also, inflammatory conditions such as obstructive sleep apnea syndrome, sarcoidosis; and lung cancer were reported to be associated with increased levels of MPV in the different studies.[16-] However, increased platelet activation and MPV; were associated with thrombotic diseases such as pulmonary embolism and cerebrovascular diseases.[19-20] There are fewer studies with only small amount of participants about the relation between COPD and MPV.[21-24] It was suggested that MPV levels are increased in the COPD exacerbations compared with the levels in stable phase of COPD in studies.[21] Similar results were reported in smokers.[22] Conversely in the other studies MPV levels are reported to decrease in the exacerbation.[11-23] However, both of them are unclear in terms of underpinning pathogenesis.[21-23] In the current study, we have determined elevated MPV levels both in the COPD patients in stable phase and in the smoker participants compared with the control healthy groups.

The relation between MPV and COPD remains unclear. But, it was known that platelet count, mean platelet volume (MPV) and platelet distrubition width (PDW) are consist of propensity to thrombosis.[9-11] All of them were responded to the atherothrombosis in the vessel. They were influenced from the inflammatory cytokines. Interlokin-6, TNF-α and CRP were the most important cytokines in the pathogenesis of COPD. When these cytokines released to the tissue, endothelial dysfunction is evolved by increased platelet activation in patients with severe degree of COPD. Consequently, submucosal hypertrophy and thrombosis were reported in severe COPD patients. We defined this event as pulmonary hypertension.[24-26]

Increased platelet volume triggers thrombosis in the pulmonary artheriovenous capillary.[26] Moreover, thrombosis by platelet aggregation is facilitated by hypoxemia and/or hypercapnia.[21] Pulmonary hypertension which is the most important factor of the prognosis of COPD was reported in the severe COPD. As a result, MPV levels which is the indicator of thrombosis might be related to pulmonary hypertension and also COPD.

There are some limitations in our study. We didn't consider our patient's factors that affect the MPV levels such as body mass index, CRP and inflammatory cytokines due to the retrospective design of this study. Therefore,

we can not explain the underlying mechanisms. Also, we did not investigate the relationship between increased MPV levels and treatment response of COPD patients. The fact that the data of COPD patients with cardiovascular diseases based on file information was another restrictive factor.

Our study results suggest that increased MPV levels could be related to cardiovascular events in patient with COPD. Smokers had higher MPV levels than non-smokers. In addition, serum MPV levels were found to be higher in patients with COPD than those without cardiovascular disease. As a result, consider that high MPV levels may increase the tendency to thrombosis, with COPD. Thrombosis and inflammation were contribution to cardiovasculary disease. Further expanded studies should be designed on this event of participants with COPD which is covered by multiple prognostic factors.

Conflict of interest

The authors declare no conflict of interest.

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