VIA MEDICA

ORIGINAL RESEARCH

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Thrombocytopenia as a marker of outcome in patients with acute exacerbation of chronic obstructive pulmonary disease

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Abstract

Introduction: Thrombocytopenia (TP) is associated with poor outcome in patients who are critically ill with pneumonia, burns, and H1N1 influenza. To our knowledge, no similar study in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) has been conducted to date. The aim of this study was to determine the impact of platelet count on the outcome of patients with AECOPD.

Material and methods: Patients admitted to our teaching hospital for AECOPD were divided into two cohorts, those with and without TP. The outcome of all patients was followed.

Results: Of the 200 patients with AECOPD, 55 (27.5%) had TP. Of these, 14 (25.5%) died in the hospital, whereas of the 145 non-TP patents, 11 (7.5%) died (p-value = 0.001). There was a significantly higher transfer rate to the ICU and mechanical ventilation in TP patients. The mean platelet count was significantly lower in patients who died than those who were discharged (161,672 vs. 203,005 cell/μL; p-value = 0.017). There was negative correlation between duration of hospitalization and platelet count.

Conclusion: TP was associated with poor outcome in AECOPD. TP could be considered as a marker for the assessment of inflammation and prognosis in AECOPD patients based on its cost-effective features.

Key words: platelet count, thrombocytopenia, outcome, acute exacerbation of COPD, mortality

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Introduction

The chronic obstructive pulmonary disease (COPD) is an important cause of morbidity and mortality worldwide and a new prediction is that COPD will be the fourth leading cause of death in 2030 [1]. COPD is currently considered as a systemic disorder that is associated with an increased risk of diabetes mellitus, hypertension, and cardiovascular disease [an independent risk factor] [2, 3]. The suggested mechanisms for these associations include hypoxia, oxidative stress, and systemic inflammation in COPD [4, 5].

COPD is characterized by episodic increases in respiratory symptoms known as acute exacerbations of COPD (AECOPD). AECOPDs are associated with an increase in local and systemic inflammation, which may lead to an acute cardiovascular event [6].

Identification of patients that may show a poor prognosis with any disease including AECOPD is important because it could lead to more appropriate therapeutic interventions. Some biomarkers are used to predict AECOPD patient outcome, however, these may require additional tests and thus additional expenses, and might not be available at every center or at any time. Complete blood count (CBC) is an inexpensive, common laboratory test. In addition to their role in hemostasis, platelets regulate an inflammatory re-

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Table 1. Comparison of poor outcome parameters between thrombocytopenic and non-thrombocytopenic patients

	TP	Non-TP	Total	P value	Risk ratio
Died in hospital n (%)	14 (25.0)	11 (7.6)	25 (12.5)	0.001	4.16 (1.75–9.86)
Mechanical ventilation n (%)	17 (30.9)	21 (14.5)	38 (19)	0.008	2.64 (1.26–5.12)
Need ICU n (%)	19 (34.5)	20 (13.8)	39 (19.5)	0.001	1.51 (1.10–2.07)

TP — thrombocytopenia patients, Non-TP — non-thrombocytopenic patients

sponse. In the CBC test, thrombocytosis is used as a marker of acute phase reaction. However, thrombocytopenia (TP) has recently been recognized as a prognostic marker in a variety of acute and critical diseases, including H1N1 influenza [7], community acquired pneumonia [8], acute kidney injury [9, 10], burns [11, 12], as well as in both pediatric and adult critically ill patients [13, 14]. TP may reflect some pathophysiologic disturbances, including disseminated intravascular coagulation, sepsis, macrophage activation, vitamin deficiencies, drug-induced toxicity, and unidentified factors [14]. AECOPD is also associated with an accelerated decline of lung function, impaired health status, reduced physical activity, and increased mortality. To our knowledge, the effect of TP on AECOPD mortality has not been investigated till date. The advantage of using platelets as a predictor of AECOPD patient outcome is that it is readily available in routine complete blood count (CBC), and does not entail additional expenses for its testing. The aim of this study was therefore to determine the correlation between TP and hospital mortality due to AECOPD.

Material and methods

Medical records of 200 patients with initial and final diagnoses of AECOP were reviewed. On the bases of platelet count on admission day, the patients were divided into two cohorts, namely, patients with TP and those without. Patient outcome and duration of hospitalization were recorded. Thrombocytopenia was defined as a platelet count of < 150,000/μL. Poor outcome was defined as death during the hospital stay, a need to transfer to the intensive care units (ICU), or intubation with or without mechanical ventilation. The following patients were excluded from the study: a) patients with recorded concomitant hematologic or oncologic disease or any disease affecting platelet counts, b) patients without CBC tests performed on admission day, and c] an initial or final diagnosis other than AECOPD.

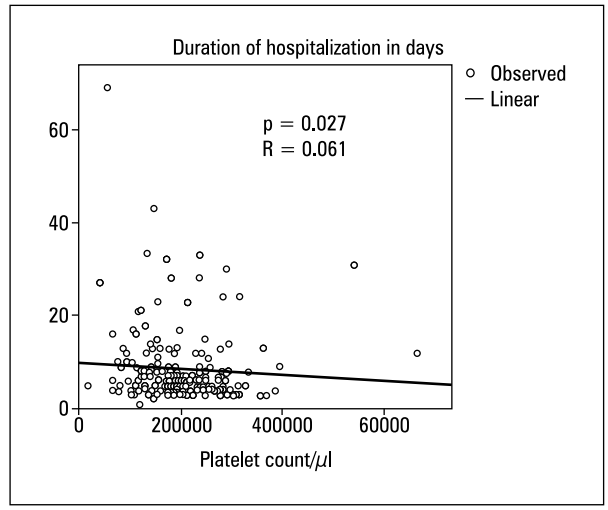

Figure1. Correlation of duration of hospitalization (in days) with platelet count

Chi-square test was used to compare the prevalence of TP between patients who died due to AECOPD and those that survived. Continuous variables were presented as the mean ± SD and were compared using the student's t-test. A p-value < 0.05 was considered statistically significant. These analyses were performed with SPSS 19 IBM version.

Results

We studied 200 patients (122 males, 61%; 78 females, 39%). The study population had a mean age of 68.92 ± 11.47 years. Of the 200 patients with AECOPD, 25 (12.5%) died in the hospital and 55 (27.5%) had TP. A statistically higher percentage of patients with TP died in the hospital, as well as required mechanical ventilation and care at the ICU (Table 1). Platelet count was significantly lower among patients who died in the hospital (mean ± SD = 161,672.00 ± 81,266.268) compared to the patients who survived the disease (mean ± SD = 203,005.71 ± 79,887.600 cell/μL), with a p-value = 0.017. Patients with TP had a longer hospital stay (mean: 10.47 days vs.

7.68 days, p = 0.027). Duration of hospitalization was inversely correlated with platelet count (R = 0.061; Fig. 1).

Discussion

This cohort study clearly showed a significant correlation between TP and higher mortality in patients with AECOPD. It is well known that white blood cells play an important role in host defense against pathogenic organisms [15]; these cells can recruit leukocytes and progenitor cells to sites of inflammation. Platelet granules store and secrete a number of bioactive substances, which, in addition to platelet aggregation and coagulation, cause chemotaxis, neutrophil and monocyte adhesion, and cell survival and proliferation [16]. Platelets are involved in inflammation, atherogenesis, and atherothrombosis. Platelets have immune system-modulating properties and promote the release of chemokines and cytokines. Platelets interact with each other and with monocytes and neutrophils [9].

There are no similar studies involving COPD patients to which we could compare our results. Lopez-Delgado et al. [7] reported that in patients with H1N1 influenza, TP at admission was associated with a lower survival rate (55% vs. 92.5%). They suggested that the presence of TP was indicative that the immune system elicited an inadequate response to the H1N1 infection. In another study involving patients with community-acquired pneumonia, those with TP more often presented with severe sepsis, septic shock, ICU admission, and the need for invasive mechanical ventilation [17]. TP was associated with higher mortality in acute kidney injury patients requiring dialysis [18].

Previous reports have demonstrated that a prothrombotic condition exists in COPD, whereas others described an increase in platelet activation in COPD patients. Elevated platelet arginase activity is usually observed in COPD patients and this is due to alterations in nitric oxide metabolism [19]. Ferroni et al. [20] showed that soluble P-selectin, a marker of platelet hyperactivity, was higher in COPD patients. COPD patients show a higher number of platelet-monocyte aggregates, which is indicative of platelet activation; this further increases in AECOPD [21]. Ashitani et al. [22] reported an increase in a marker of platelet activation (beta-thromboglobulin) and markers of coagulation-fibrinolysis-system (fibrinopeptide A, thrombin antithrombin III complex, and tissue plasminogen activator-plasminogen activator inhibitor) in 40 COPD patients compared to the control group. They concluded that this clotting factor is an independent predictor of an acute exacerbation [22]. During AECOPD, an exaggerated shift in the hemostatic balance occurs due to an increase in platelet aggregation, which was caused by acute disturbances in gas exchange and hypoxemia. This enhanced platelet activity directly damages lung vessels and/or induces the release of mediators [23, 24].

A possible explanation for the association between poor prognosis and TP is that TP might be a marker of bacterial infection and sepsis, causing a higher morbidity rate in AECOPD patients with TP. Sepsis is the leading cause of TP in critically ill patients [25].

The important limitation of this study is that the investigation was conducted at a single center. This significantly limits the generalizability of our results. Further studies are necessary, in particular with focusing on investigating the cause of death in AECOPD patients with TP. In addition better understanding of the role of platelets in the outcomes of patients with AECOPD may generate new therapeutic modalities for COPD.

Conclusions

1. TP was associated with poor AECOPD patient outcome.
2. TP could be considered as a marker for the assessment of inflammation and prognosis in AECOPD patients based on its cost-effective features.

Conflict of interest

The authors declare no conflict of interest.

References:

1. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS medicine 2006; 3: e442.
2. Vanfleteren LE, Spruit MA, Groenen M et al. Clusters of comorbidities based on validated objective measurements and systemic inflammation in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2013; 187: 728–735. doi: 10.1164/rccm.201209-1665OC.
3. Curkendall SM, DeLuise C, Jones JK et al. Cardiovascular disease in patients with chronic obstructive pulmonary disease, Saskatchewan Canada cardiovascular disease in COPD patients. Annals of Epidemiology 2006; 16: 63–70.
4. Macnee W, Maclay J, McAllister D. Cardiovascular injury and repair in chronic obstructive pulmonary disease. Proceedings of the American Thoracic Society 2008; 5: 824–833. doi: 10.1513/pats.200807-071TH.
5. Mills NL, Miller JJ, Anand A et al. Increased arterial stiffness in patients with chronic obstructive pulmonary disease: a mechanism for increased cardiovascular risk. Thorax 2008; 63: 306–311.
6. McAllister DA, Maclay JD, Mills NL et al. Diagnosis of myocardial infarction following hospitalisation for exacer-

bation of COPD. Eur Respir J 2012; 39: 1097–1103. doi: 10.1183/09031936.00124811.
7. Lopez-Delgado JC, Rovira A, Esteve F et al. Thrombocytopenia as a mortality risk factor in acute respiratory failure in H1N1 influenza. Swiss medical weekly 2013; 18: w13788. doi: 10.4414/smw.2013.13788.
8. Brogly N, Devos P, Boussekey N, Georges H, Chiche A, Leroy O. Impact of thrombocytopenia on outcome of patients admitted to ICU for severe community-acquired pneumonia. J Infect 2007; 55: 136–140.
9. Chertow GM, Christiansen CL, Cleary PD, Munro C, Lazarus JM. Prognostic stratification in critically ill patients with acute renal failure requiring dialysis. Arch Intern Med 1995; 155: 1505–1511.
10. Samimagham HR, Kheirkhah S, Haghighi A, Najmi Z. Acute kidney injury in intensive care unit: incidence, risk factors and mortality rate. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia 2011; 464–470.
11. Wang Y, Tang HT, Xia ZF et al. Factors affecting survival in adult patients with massive burns. Burns 2010; 36: 57–64. doi: 10.1016/j.burns.2009.04.014.
12. Warner P, Fields AL, Braun LC et al. Thrombocytopenia in the pediatric burn patient. J Burns Care Res 2011; 32: 410–414. doi: 10.1097/BCR.0b013e318217f91b.
13. Agrawal S, Sachdev A, Gupta D, Chugh K. Platelet counts and outcome in the pediatric intensive care unit. Indian J Crit Care Med 2008; 12: 102–108. doi: 10.4103/0972-5229.43678.
14. Moreau D, Timsit JF, Vesin A et al. Platelet count decline: an early prognostic marker in critically ill patients with prolonged ICU stays. Chest 2007; 131: 1735–741.
15. Liu Y, Shaw SK, Ma S, Yang L, Luscinskas FW, Parkos CA. Regulation of leukocyte transmigration: cell surface interactions and signaling events. J Immunol 2004; 172: 7–13.
16. Gawaz M, Langer H, May AE. Platelets in inflammation and atherogenesis. J Clin Invest 2005; 115: 3378–3384.
17. Prina E, Ferrer M, Ranzani OT et al. Thrombocytosis is a marker of poor outcome in community-acquired pneumonia. Chest 2013; 143: 767–775. doi: 10.1378/chest.12-1235.
18. Valente C, Soares M, Rocha E, Cardoso L, Maccariello E. The evaluation of sequential platelet counts has prognostic value for acute kidney injury patients requiring dialysis in the intensive care setting. Clinics 2013; 68: 803–808. doi: 10.6061/clinics/2013(06)13.
19. Guzman-Grenfell A, Nieto-Velazquez N, Torres-Ramos Y et al. Increased platelet and erythrocyte arginase activity in chronic obstructive pulmonary disease associated with tobacco or wood smoke exposure. J Investig Med 2011; 59: 587–592. doi: 10.231/JIM.0b013e31820bf475.
20. Ferroni P, Basili S, Martini F et al. Soluble P-selectin as a marker of platelet hyperactivity in patients with chronic obstructive pulmonary disease. J Investig Med 2000; 48: 21–27.
21. Furman MI, Benoit SE, Barnard MR et al. Increased platelet reactivity and circulating monocyte-platelet aggregates in patients with stable coronary artery disease. J Am Coll Cardiol 1998; 31: 352–358.
22. Ashitani J, Mukae H, Arimura Y, Matsukura S. Elevated plasma procoagulant and fibrinolytic markers in patients with chronic obstructive pulmonary disease. Internal Medicine 2002; 41: 181–185.
23. Wedzicha JA, Cotter FE, Empey DW. Platelet size in patients with chronic airflow obstruction with and without hypoxaemia. Thorax 1988; 43: 61–64.
24. Wedzicha JA, Syndercombe-Court D, Tan KC. Increased platelet aggregate formation in patients with chronic airflow obstruction and hypoxaemia. Thorax 1991; 46: 504–507.
25. Thiolliere F, Serre-Sapin AF, Reignier J et al. Epidemiology and outcome of thrombocytopenic patients in the intensive care unit: results of a prospective multicenter study. Intensive Care Med 2013; 39: 1460–1468. doi: 10.1007/s00134-013-2963-3.