

# Using simple blood count for the diagnosis of pulmonary embolism in chronic obstructive pulmonary disease exacerbations: are we there yet?

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Pulmonary embolism (PE) often occurs in patients with COPD,<sup>1,2</sup> especially in those who are elderly, suffer from polycythemia,<sup>3,4</sup> and/or have reduced physical activity.<sup>5</sup> The risk of a patient with COPD to develop PE increases further during acute exacerbation of COPD (AECOPD) and may reach up to approximately 25% in patients hospitalized for AECOPD.<sup>6</sup> Systemic inflammation<sup>3,4</sup> and increased blood levels of procoagulant factors, such as fibrinogen and factor XIII,<sup>7</sup> seem to contribute to an increased risk of PE during AECOPD. Furthermore, the causes of AECOPD such as infections result in increased risk of venous thromboembolism (VTE).<sup>2</sup>

The diagnosis of PE in patients with AECOPD is a clinical challenge, since it is difficult to differentiate other causes of COPD exacerbation from PE due to common presenting signs and symptoms. The presentation of common symptoms of AECOPD, such as dyspnea and tachypnea, might result in the diagnosis of PE being overlooked. Thus, during the course of AECOPD, it is difficult to distinguish between patients with and without PE on the basis of any of the following: symptoms, physical signs, abnormalities on chest X-ray, and differences in alveolar-arterial oxygen pressure gradient.<sup>8</sup> Also partial pressure of carbon dioxide levels are not useful in the diagnosis of PE in a patient with AECOPD, since they may not fall but can even rise due to the inability to increase minute ventilation in response to the increase in dead space caused by acute PE. The diagnosis of PE in a patient with AECOPD is of great importance, since delays in diagnosis and treatment are related to poor outcomes.

D-dimers were used to exclude PE in patients with low or moderate probability of the disease. However, COPD itself may cause false-positive results in the D-dimer test, and contradictory results were described in relation to the D-dimer levels in patients with stable COPD.<sup>7,9</sup> It was

also shown that D-dimer levels may increase in patients with AECOPD irrespective of the presence of VTE,<sup>10</sup> although patients with COPD exacerbation and VTE had higher D-dimer levels than those with COPD without VTE.<sup>10</sup>

Finally, the question as to whether to perform a computed tomography pulmonary angiography (CTPA) in patients with PE must be addressed because of issues of radiation exposure and side effects related to iodine injection, such as allergy and renal impairment, which are factors that may limit the use of CTPA in patients with several more severe chronic illnesses.

In this issue of the *Polish Archives of Internal Medicine (Pol Arch Intern Med)*, Białas et al<sup>11</sup> used monocyte to large platelet ratio (MLPR) for the identification of patients with COPD who were hospitalized for AECOPD and might have had concomitant PE. After carefully excluding patients with comorbidities that are known to influence the number of monocytes and/or large platelet counts, they calculated a cutoff value above which they were able to identify patients with PE with high sensitivity and specificity. MLPR seemed to have greater accuracy for the recognition of these patients compared with the traditional D-dimer test. Although the study is retrospective and includes a relatively small number of patients, it gives a clear message that MLPR can serve as a useful biomarker for the selection of patients who should probably be further evaluated for PE using imaging techniques.

The percentage of patients hospitalized for AECOPD who were found to also have PE was 23.76%, which is similar to previous studies reporting a percentage of approximately 25% in hospitalized patients.<sup>6</sup> It is important to stress that patients who had severe cardiovascular comorbidities on admission were excluded from this analysis, and this slightly limits our understanding of the performance of MLPR in

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a more general population of hospitalized patients with COPD and suspected PE. These patients may be in the greatest need for a rapid point-of-care test for the diagnosis or exclusion of PE as part of their differential diagnosis, and they would represent a potential candidate population for future studies.

A higher clinical suspicion of PE due to increased awareness of the disease by clinicians using diagnostic algorithms, including D-dimer, causes harmful consequences, such as radiation exposure and nephrotoxicity because of contrast material used for CTPA. In a previous study,<sup>12</sup> D-dimer test showed an area under the curve (AUC) of 0.752 (95% confidence interval [CI], 0.672–0.831) for the diagnosis of PE in patients with AECOPD, while a higher cut-off value of 0.95 pg/ml had a sensitivity of 70% and a specificity of 71% for the exclusion of PE. Interestingly, the AUC in the study by Białas et al<sup>11</sup> had a much poorer accuracy in comparison with CTPA with an AUC of 0.565 (95% CI, 0.414–0.713), showing that this biomarker cannot possibly be used in this group of patients. Whether this is related to some specific characteristics of the patients included in the present analysis or to the method used for the measurement of D-dimer levels in the current hospital needs to be considered before minimizing the role of D-dimer levels determined by an enzyme-linked immunosorbent assay in the exclusion of PE.

The analysis by Białas et al<sup>11</sup> has some limitations. Besides the retrospective design with the inherent weaknesses, the authors decided to exclude some patients with comorbidities (eg, cardiovascular) that are clinically relevant for the differential diagnosis of PE in the setting of AECOPD. The limited number of patients for a retrospective study also represents another point for skepticism and, therefore, prior to any clinical application, the MLPR needs to be validated in other cohorts and in prospective trials. Should the diagnostic performance of this novel marker in the present analysis be confirmed in other settings, its clinical importance may be proven significant, especially in settings where CTPA may not be readily available or in patients where the use of CTPA is contraindicated or is expected to be associated with clinical risks.

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