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The prevalence and predicting factors of pulmonary thromboembolism in patients with exacerbated chronic obstructive pulmonary disease

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Abstract

Introduction: The risk of pulmonary thromboembolism (PTE) in patients with exacerbated chronic obstructive pulmonary disease (e-COPD) is higher than in non-COPD states. The study aimed to evaluate the prevalence and the parameters that are critical for finding the incidence of PTE in patients with e-COPD.

Material and methods: This cross-sectional study was performed on 68 consecutive patients with the e-COPD, referred to the Pulmonary Disease Department at the Shariati Hospital in Tehran between 2013 and 2014. In addition to collecting data on the history of disease and physical examination, arterial blood sampling, spirometry, electrocardiography and echocardiography were performed for all patients. All subjects underwent computed tomography pulmonary angiography (CT-PA) as a method of choice for diagnosing PTE.

Results: Out of 68 cases, five (7.4%) had CT angiography findings suggesting PTE. These patients were all male and had a higher mean age (79 vs. 65 years), lower mean systolic blood pressure (88.36 vs. 118.33 mmHg), and a higher mean heart rate (133.12 vs 90.33 beats/min), compared to e-COPD patients without PTE. Arterial blood gas analysis in individuals with PTE demonstrated a lower HCO_3 (2.33 vs. 9.44 mEq/l) and PCO_2 (44.35 vs. 51.43 mm Hg) levels. The mean left ventricular ejection fraction (LVEF) was lower in patients with PTE (34.14 $\pm$ 4.49% vs. 46.94 $\pm$ 8.27%).

Conclusion: The prevalence of PTE in our series of patients with e-COPD was 7.4%. According to the study results, male gender, advanced age, hypotension, tachycardia, and respiratory alkalosis are factors indicating possible PTE among subjects with e-COPD.

Key words: pulmonary thromboembolism (PTE), exacerbated COPD (e-COPD), computed tomography pulmonary angiography (CT-PA), systolic blood pressure (SBP), left ventricular ejection fraction (LVEF)

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Introduction

Diagnosis and management of exacerbated chronic obstructive pulmonary disease (e-COPD) are challenging in both ambulatory and inpatient clinical settings [1]. In addition, e-COPD can accompany and mask the features of a number of cardiopulmonary conditions, including PTE, which makes the situation even more complicated [2].

In fact, because of their frequent concomitant occurrence, there are no proven clinical criteria to help delineate PTE from COPD [3]. This is attributable to the overlapping clinical features and the non-specificity of the signs and symptoms of both conditions [4]. Both of the disorders can have an insidious onset. Unlike e-COPD, which is recognized clinically, imaging studies are required to confirm the diagnosis of PTE [5].

Given the high mortality rates among patients with untreated PTE reaching 25% in some individuals, it is crucial to consider PTE when managing patients with e-COPD [6].

The risk of PTE in COPD patients is twice that of non-COPD states [7, 8]. PTE is expected to develop in almost one-fifth of subjects with COPD and the simultaneous occurrence of these conditions can lead to a significant increase in morbidity and mortality rates [9, 10]. Optimal management of these patients requires timely diagnosis, and this, in turn, necessitates a high index of clinical suspicion.

This study was designed to highlight clinical and paraclinical parameters that can predict a high risk of concomitant PTE in patients with e-COPD.

Material and methods

Study design and population

This is a cross-sectional study, performed at the Department of Pulmonary Diseases, Shariati Hospital affiliated to Tehran University of Medical Sciences in 2013 and 2014. Sixty-eight consecutive patients with e-COPD were enrolled.

Inclusion criteria

Patients who were diagnosed with COPD basing on their signs and symptoms, medical and family history and results of pulmonary function tests (spirometry). The consensus over the definition of e-COPD, achieved by a working group in 2000, was used to identify the study subjects: a sustained worsening of a patient's condition, from a stable state and beyond normal daily-variations, which is acute in the onset and necessitates a change in the regular medication in a patient with underlying COPD [11, 12].

Exclusion criteria

Individuals with a history of warfarin use, active cancer, surgery within the last two months, or not allowed to use contrast media, were excluded.

Methods

After admission, a complete history — taking and a physical examination were performed. An arterial blood sample was obtained to assess blood gases. Furthermore, an electrocardiogram test was carried out to detect abnormalities in heart rate, blocks, atrial fibrillation, ST-T changes, or the presence of the SlQ3T3 pattern. Echocardiography was also performed to show evidence of pulmonary PTE, including right ventricular hy-

pokinesia or intraventricular septum deviation. Patients also did a pulmonary function test. Finally, within three days of their admission, all subjects underwent computed tomography pulmonary angiography (CTPA) to detect PTE, as this is the method of choice for diagnosing PTE in our center. For patients with a BMI < 30, 130 ml of contrast media, the administered slice thickness was 3 mm, and the voltage was 120 sq. For individuals with a BMI above 30, 150 ml of contrast media, a slice thickness of 2 mm and a voltage of 140 kv were selected. Thromboembolism was defined as intraluminal filling defects or obstruction of the pulmonary vessel lumen.

Statistical analysis

Quantitative variables were presented as the mean ± standard deviation (SD) and were summarized by absolute frequencies and percentages for categorical variables. Categorical variables were compared using chi-square test or Fisher exact test when more than 20% of cells with an expected count of less than 5 were observed. Quantitative variables were also compared with t-test or Mann-Whitney U test. For the statistical analysis, SPSS version 16.0 (SPSS Inc., Chicago, IL) was employed. P values of 0.05 or less were considered statistically significant.

Results

A total of 68 subjects (38 males, 55.9%) with e-COPD entered the study. Patients had a mean age of 67.75 ± 9.26 years (range 50 to 88 years and a median 68 years). Five cases (7.4%) showed positive CT angiography findings for PTE. A comparison of the different clinical and paraclinical characteristics of e-COPD patients with and without PTE is presented in Table 1.

Patients with PTE showed significantly lower systolic blood pressure (SBP), arterial blood CO_2 pressure, arterial blood HC03 concentration and left ventricular ejection fraction (LVEF) compared with those without PTE. Parameters, including the patient's age and mean heart rate were significantly higher in subjects with PTE compared with the other group. Although individuals with PTE had statistically significant higher arterial blood pH, the difference is not clinically significant. The two groups were statistically different in terms of diastolic blood pressure, arterial O_2 saturations before or after receiving nasal oxygen, FEV_1, FVC, pulmonary artery pressure (PAP), or mitral valve regurgitation.

Table 1. Comparison of the patients with and without pulmonary thromboembolism (PTE)

Characteristics	PTE (n = 5)	Non-PTE (n = 63)	p-values
Age, year, mean (range), median	65.7 (64–81) 63	66.9 (63–83) 61	0.35
Male/female, number (%)	3 (60)/2 (40)	30 (47.6)/33 (52.4)	0.103*
Systolic blood pressure, mm Hg, Mean ($\pm$ SD)	88.3 ($\pm$ 1.53)	118.3 ($\pm$ 20.18)	< 0.001
Diastolic blood pressure, mm Hg, Mean ($\pm$ SD)	65.0 ($\pm$ 5.0)	73.90 ($\pm$ 13.11)	0.064
Heart rate, Mean ($\pm$ SD)	132.0 ($\pm$ 7.21)	90.33 ($\pm$ 12.07)	< 0.001
Arterial blood saturation, Mean ($\pm$ SD)	93.33 ($\pm$ 7.64)	85.00 ($\pm$ 10.44)	0.101
Arterial blood gas PH, Mean ($\pm$ SD)	7.46 ($\pm$ 0.03)	7.36 ($\pm$ 0.06)	0.024
CO_2, Mean ($\pm$ SD)	42.33 ($\pm$ 2.52)	51.43 ($\pm$ 11.91)	0.002
HCO_3, Mean ($\pm$ SD)	2.3 ($\pm$ 0.00)	3.25 ($\pm$ 9.44)	< 0.01
Spirometry FVC, Mean ($\pm$ SD)	58.81 ($\pm$ 12.00)	60.59 ($\pm$ 15.93)	0.559
FEV_1, Mean ($\pm$ SD)	4.41 ($\pm$ 12.00)	5.15 ($\pm$ 19.98)	0.779
Cardiovascular LVEF, Mean ($\pm$ SD)	35.00 ($\pm$ 5.00)	46.94 ($\pm$ 8.27)	0.038
PAP, Mean ($\pm$ SD)	36.00 ($\pm$ 1.00)	42.35 ($\pm$ 16.26)	0.505
Heart valve abnormalities MR	0 (0.0%)	12 (19.0%)	0.039
Tricuspid	1 (20%)	12 (19.0%)	0.705

* Comparison has been made inside each group; FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 second; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; PAP: pulmonary artery pressure

Discussion

Our study was designed to assess the prevalence of PTE among patients with COPD and to determine the clinical and paraclinical parameters that could suggest a higher risk of PTE in patients with e-COPD. According to the study results, gender and advanced age seem to be factors potentially affecting the incidence of PTE. Patients with PTE were male and had a higher mean age in comparison with the group without detectable thromboembolism. Our results contrasted those of Chen *et al.* [12] who found a lower average age among their series of patients with PTE.

Other findings include lower SBP, higher respiratory rate and increased heart rate in PTE subjects, all of which are expected discoveries in this setting. In a survey conducted by Stein *et al.* [13], tachypnea was found in 73%, tachycardia in 30%, and pleuritic chest pain in 66% of patients with PTE. Tachycardia was a more permanent and valid feature of PTE in other studies, and heart rate less than 90 beats/min contradicted the diagnosis [14]. The studies of arterial blood gasses could also help raise suspicion for PTE. Patients with COPD exacerbation usually develop hypercapnia due to ventilation failure, the severity of which correlates with the severity of the exacerbation.

In addition, a rise in HCO_3 is expected in these patients. In contrast, individuals with PTE lose more blood CO_2 due to their tachypnea state, and the levels of HCO_3 drop as well as produce a state of respiratory alkalosis. Therefore, a low or normal pCO_2 level, as well as reduced HCO_3 levels during COPD exacerbation, could be indicative of a simultaneous PTE.

Patients with COPD develop pulmonary hypertension as their earliest cardiovascular complication. Endothelial dysfunction, destruction and altered tonicity of the pulmonary vascular bed as well as changes in blood gas exchange are the respiratory mechanisms. However, the cardiac compensatory mechanisms manage to maintain normal cardiac output in the stable state. Therefore, left-sided heart failure is not a common finding in patients with COPD. A review of the prevalence of left ventricular systolic dysfunction in subjects with COPD showed a prevalence of 10–40% in unselected COPD patients and a prevalence of 23–32% in individuals with an exacerbation of the disease. However, left ventricular systolic dysfunction was not a common finding among selected COPD patients in whom coronary artery disease was excluded (0–16%) [15]. Therefore, while a reduction in LVEF is expected in a number of patients with e-COPD, this reduction should raise suspicion of superimposed PTE, since low

LVEF is not a constant feature in subjects with e-COPD.

In this study, the prevalence of PTE among e-COPD patients was 7.4%, which is considerably lower than that reported in other surveys (Range 3.3–33%) [16–20]. It is possible that a number of persons with both PTE and e-COPD, who had a more critical condition, were primarily diagnosed with PTE, or had expired in the emergency department, therefore did not enter the study. In addition, the failure of CT-PA to diagnose a smaller peripheral embolism might have contributed to the obtained low figure.

Conclusion

The prevalence of PTE in patients with e-COPD is higher than that expected in the general population or non-COPD conditions. Therefore, physicians attending these patients need to keep this correlation in mind for their timely diagnosis and management. However, it is usually not easy to diagnose PTE in the context of e-COPD because of their numerous common clinical features and PTE symptoms and non-specificity. The results of our study suggest that in patients with e-COPD, a number of parameters could raise the possibility of concurrent PTE. According to these results, a drop in systolic blood pressure, tachycardia, the normocapneic state with decreased HCO_3 levels and a significant decrease in LVEF are findings in e-COPD patients which should warn the physician of a possible concomitant PTE.

Conflict of interest

The authors declare no conflict of interest.

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