Functional Characteristics of COPD Patients Admitted for Acute Pulmonary Embolism

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Abstract

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a known risk factor for pulmonary embolism (PE); however, neither the clinical nor the pulmonary function characteristics are well described in COPD patients admitted for PE.

Methods: We conducted a retrospective cohort study of 395 patients admitted for acute PE in a tertiary hospital setting. In COPD patients, clinical characteristics and pulmonary function were compared between the survivor and non-survivor groups during a 3-month follow-up period after PE.

Results: Thirty-three patients (8.3%) had previously documented diagnoses of COPD with moderate to severe airflow obstruction at least 6 months prior to the development of PE. The total number of deaths after three months of follow-up was 9 (27%) in COPD patients and 65 (17%) in patients without COPD (p = 0.03). PE was the leading cause of death in COPD. Only 15% of COPD patients had previous frequent exacerbations. The diffusion lung capacity for carbon monoxide (DLco, % predicted) was the only statistically significant variable that differed between the survivor and non-survivor groups of COPD patients (p = 0.002). The non-survivor group had decreased DLco values, with a DLco equal to or lesser than 60% being the best predictive value of mortality in these patients (AUC=0.88; p < 0.001).

Conclusion: COPD patients admitted for PE presented a higher risk of mortality than non-COPD patients. The COPD patient non-survivor group showed an important reduction of DLco prior to PE development. The degree of airflow obstruction; however, was similar between COPD survivors and non-survivors.

Keywords

COPD, Pulmonary Function, Pulmonary Embolism, Comorbidities

Introduction

Pulmonary embolism (PE) is a common cause of mortality, with an overall incidence rate of 69 cases per 100.000 inhabitants [1]. The clinical presentation and severity of PE are influenced by certain risk factors previously described in literature [2]. During the last decade, there has been increased evidence that chronic obstructive pulmonary disease (COPD) is a risk factor for Venous Thrombo Embolism (VTE) [3,4]. Moreover, COPD patients present more frequently with PE than with deep venous thrombosis (DVT) [6,7], which has been shown to contribute to the poorer prognoses in these patients [5-7]. Furthermore, similarities between the clinical manifestations of acute exacerbation of COPD (AECOPD) and PE have been shown to generate diagnostic challenges [8]. Currently, there is very little information available with regards to the functional respiratory characteristics of COPD patients admitted for PE and/or the clinical variables capable of predicting the clinical course of these patients [7]. The percentage of COPD patients admitted for PE does not exceed 10%, possibly due to the aforementioned diagnostic difficulties in this group [9,10]. According to recent studies though, despite the low percentage of COPD cases admitted for PE, these patients still have a higher risk of mortality [7]. Therefore, more information with regards to essential pulmonary functional characteristics and parameters of these patients would help to better diagnose and therefore rapidly identify therapeutic modalities for improved COPD patient survival.

Consequently, the objectives of this current study were: 1) to analyze the clinical and pulmonary function profile of COPD patients admitted for acute PE and; 2) to Identify predictors of mortality in this group of patients.
We conducted a retrospective cohort study of 395 patients admitted for acute PE between January 2007 and December 2011 in a tertiary hospital setting. Patients were classified using the Wells criteria as having low, moderate or high risk for PE, as described previously [11]. Pe's were documented by either a positive helical computed tomography scan, a high-probability and/or an intermediate-likelihood DVT [11]. PEs were further categorized as low, moderate or high risk for PE, as described previously [12]. The main results demonstrate that while clinically stable, approximately 65% of COPD patients who were both clinically stable and whose diagnoses were made at least 2 months prior to admission for PE in order to avoid over-diagnosis.

COPD was defined on the basis of smoking history and a post bronchodilator FEV1/FVC ratio less than 0.7 [13]. We included COPD patients who were both clinically stable and whose diagnoses were made at least 2 months prior to admission for PE in order to avoid over-diagnosis.

**Data analysis**

Results

Results are expressed as the mean ± standard deviation (SD) for normally distributed variables. Categorical data are reported as numbers and percentages. Comparisons between subsets of COPD patients (survivor and non-survivor groups) were performed using an unpaired T-test for continuous variables and a chi-square test for categorical variables. Furthermore, as comparisons retained only Diffusion Lung Capacity (DLco) (expressed as percentage of predicted) [14], a Receiver Operating Characteristic (ROC) analysis was performed with mortality as the “gold standard” reference in order to determine the best cut-off point for DLco during the 3 month follow up period. Likewise, the area under the curve (AUC) was calculated for ROC curve non-parametrically [15,16]. The predictive values [17] were also calculated, both positive predictive value (PPV) and negative predictive value (NPV), in order to evaluate the best possible and negative results of the procedure. Afterwards, we explored the diagnostic capacity for prediction of DLco in the interval of 45% and 65% of the predicted value. Respective cut-off points were then selected that included the best sensitivity and specificity [18]. We also evaluated the means and the 95% confidence intervals (95% CI) for sensitivity, specificity, PPV and NPV. Calculations were done with SPSS/PC (version 18.0, SPSS Inc., Chicago, IL, USA). A p-value of < 0.05 was considered significant.

**Methods**

**Study design and measurements**

We conducted a retrospective cohort study of 395 patients admitted for acute PE between January 2007 and December 2011 in a tertiary hospital setting. Patients were classified using the Wells criteria as having low, moderate or high risk for PE, as described previously [11]. Pe's were documented by either a positive helical computed tomography scan, a high-probability and/or an intermediate-probability ventilation-perfusion lung scan, a positive pulmonary angiography, or the visualization of a thrombus positioned in the right ventricle or right atrium on echocardiography [12]. Deep vein thrombosis (DVT) was diagnosed following acute symptoms of DVT and confirmed by compression ultrasonography or contrast venography of the lower extremities. Furthermore, complementary information was collected, such as: demographic data, symptoms at presentation, the type of diagnostic method used, risk factors for DVT and information pertaining to treatment and complications. In particular, major bleeding complications were defined as either bleeding requiring transfusion of two or more units of blood or a fatal bleed. Moreover, immobilized patients were categorized under two different categories: 1) non-surgical patients who had been immobilized for ≥4 days; 2) immobilized surgical patients, who had undergone a surgical procedure within last 2 months preceding PE development.

COPD was defined on the basis of smoking history and a post bronchodilator FEV1/FVC ratio less than 0.7 [13]. We included COPD patients who were both clinically stable and whose diagnoses were made at least 2 months prior to admission for PE in order to avoid over-diagnosis.

**Discussion**

To our knowledge this is the first study reporting clinical and respiratory functional characteristics of COPD patients admitted for PE. The main results demonstrate that while clinically stable,
Chronic pulmonary embolism, primary pulmonary hypertension (pph) and other pulmonary vascular diseases can also result in a decline in \( \text{DLCO} \) \cite{25}. For these reasons, an objective reduction of \( \text{DLCO} \) prior to pe admission may explain the results of this current study.

We consider various factors of our study to provide relevant implications not only for future research but as well as clinical management and stratification of COPD patients with pe. Firstly, the initial clinical evaluations of COPD patients, including the calculations for \( \text{PE} \) risk stratification, are usually based on classical scales \cite{11,26}. However, these scales do not take into consideration the severity of disease (i.e. Airflow limitation, dyspnea, etc.) Of COPD patients prior to pe development. This latter aspect was specifically researched throughout this study. Secondly, this study demonstrates that an adequate risk analysis could be beneficial for the improvement of individualized strategies on prevention, treatment and even follow-up following pe in this particular patient population \cite{27}.

The present study does though carry a series of limitations, among which is the size of the patient sample, its gender bias, as well as its retrospective nature. It should also be mentioned that lack of information concerning the degree of emphysema or presence of pulmonary hypertension could possibly have impacted the result interpretation of this study. However, these limitations were also offset by two important strengths: 1) patients included in this study represented a homogenous group with a confirmed diagnosis COPD, which avoided possible over diagnosis; and 2) all of the pulmonary function studies were performed in the same laboratory, using a common systematic methodology.

In conclusion, the present findings showed that COPD patients admitted for pe have an elevated mortality when compared to non-COPD patients. Moreover, this study demonstrated for the first time, that COPD mortality from pe was associated with a manifested reduction in \( \text{DLCO} \) prior to admission when compared to COPD survivors post-pe.

The present study constitutes a first attempt to increase our understanding of the complexity of \( \text{PE} \) pathogenesis in COPD patients. Future multicentric investigations though are warranted in order to confirm and expand on this study’s findings.

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**References**


