Prevalence of deep vein thrombosis in patients affected by exacerbation of mild to moderate COPD at stage I-II of GOLD classification

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Abstract

Introduction: Little information exists about the incidence of deep vein thrombosis (DVT) in patients affected by chronic obstructive pulmonary disease (COPD) admitted for acute exacerbation. The aim of this study is to evaluate the prevalence of DVT in COPD patients, using complete venous ultrasonography (US) as a screening tool.

Material and methods: One hundred patients with mild to moderate COPD admitted for exacerbation were consecutively included. All patients underwent clinical evaluation, chest radiography, electrocardiogram, spirometry, blood gases, laboratory testing, and complete venous US to detect DVT.

Results: Overall 6 (6%) DVT were detected. Three (3%) were proximal, 3 (3%) affected the distal veins. Five out of the 6 patients with DVT were symptomatic. All patients with DVT received anticoagulant treatment for 3-6 months.

Conclusions: Our findings suggest that subjects with exacerbation of mild to moderate COPD are at low risk of DVT.

Key words: deep vein thrombosis, COPD, ultrasound.

Introduction

An intermediate risk (about 15%) of venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), has been reported in patients admitted to Internal Medicine Units [1]. Among them, chronic obstructive pulmonary disease (COPD) is undoubtedly represented, but insufficient data are available in this setting. Moreover, studies are based on different methods and diagnostic criteria and inhomogeneous patient characteristics. A study performing radio-labelled fibrinogen scanning showed a rate of VTE in COPD patients with acute exacerbation of about 45% [2]. Ultrasonography (US) scan is the gold standard for the diagnosis of DVT [3]. Studies performing US found rates of VTE between 0 [4] and 10% [5, 6] during exacerbation of COPD. In particular, Fraisse et al. found a risk of VTE of about 28% in patients with respiratory failure in mechanical ventilation without thromboprophylaxis [7]. Accordingly, a meta-analysis by Ambrosetti et al. showed a prevalence of DVT of about 10% in this setting [8].

The aim of our study was to determine the prevalence of DVT in patients affected by COPD in mild to moderate stage of GOLD (Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease NHLBI/WHO global initiative for chronic obstructive lung disease) classification [9] using complete lower limb venous US.

Material and methods

Subjects

We performed a prospective study on the prevalence of DVT in patients admitted to our Pneumology and Rehabilitation Unit for exacerbation of mild to moderate COPD, using complete US scan as a diagnostic tool.

One hundred patients, affected by acute exacerbation of mild to moderate COPD, were consecutively included in the study during the period from December 2005 to May 2006. Informed written consent was obtained from all participants. COPD was diagnosed according to GOLD classification [9]. Exacerbation was defined as the presence of two of three cardinal symptoms (worsening dyspnoea, increase in sputum purulence, increase in sputum volume).

Entry criteria

Only patients with acute exacerbation of mild to moderate COPD were included. Patients with previous diagnosis or clinical history of VTE and on anticoagulant treatment for any reason, or affected by malignancy and severe heart failure [New York Heart Association (NYHA) class III and IV], were excluded. None of them had a relevant reduction in mobility, needed long-term oxygen therapy, oxygen supplementation during exacerbation or mechanical ventilation. None of them received antithrombotic prophylaxis. Comorbidities of COPD patients are detailed in Table I.

Table I. Characteristics of study subjects

Variable	Value
Age (years)	69±8*
Gender (M/F)	61/39
Weight (kg)	76.1±13.4*
Height (cm)	161.9±7.8*
Leukocyte count (×10^9/l)	10.09±0.74*
Haematocrit (%)	43.3±4.1*
Haemoglobin (g/dl)	14.4±1.4*
Fibrinogen (mg/dl)	3.1±1.0*
FEV_1[+] (% of predicted value)	64±8*
FVC[‡] (% of predicted value)	72±26*
FEV_1/FVC	70±10*
PaO_2[§] (mm Hg)	70.8±8.3*
$PaCO_2$[Δ] (mm Hg)	40.5±6.4*
Arterial hypertension	11**
Diabetes mellitus	4**
Atrial fibrillation	4**
Thyroid dysfunction	2**
Venous insufficiency	10**
Peripheral artery disease	1**
Myocardial infarction	4**
Transient ischaemic attack	1**

**Data expressed as mean ± SD*
[+]FEV_1 – forced expiratory volume in one second
[‡]FVC – forced vital capacity
[§]PaO_2 – partial pressure of oxygen in arterial blood
[Δ]$PaCO_2$ – partial pressure of carbon dioxide in arterial blood
***Absolute frequency*

Anthropometric and laboratory measurements

Each study participant underwent clinical evaluation, chest radiography, electrocardiogram, spirometry, blood gases, and other laboratory testing on the day of admission (Table I). Body weight of all patients was measured on the same scale. The subjects wore lightweight examination gowns and had emptied their bladders immediately before the measurement [10]. Body height was determined to the nearest centimetre with a vertical metal ruler with subjects standing barefoot [10]. Pulmonary function tests were performed according to American Thoracic Society standards [11] using the spirometer V-max 229 Encove (Sensor Medics, Milan, Italy). Forced expiratory volume in 1 s (FEV_1) was expressed as percentage of the predicted normal value [11].

Other laboratory and US diagnosis of DVT

D-dimer levels were measured with the quantitative assay "Automated latex enhanced immunoassay" (HemosIL), with a cut-off of 500 µg/l. Venous US was performed by the same operator on admission within 24 hours and 7 days and 1 month later. G.E. Logiq 7 Echo-Color-Doppler ultrasound equipment (General Electric Medical System, Wisconsin, USA) with linear transducer (7/14 MHz) was used, according to a previously validated technique [12]. Both lower limbs were scanned, including proximal (iliac-femoral and popliteus veins) and distal venous scan (gastrocnemius and soleus muscle veins and tibio-peroneal veins). Compression ultrasonography (CUS) was used. Color Doppler for the flow characteristics and grey grading for endoluminal images were accessory criteria. The scan was considered negative when complete compression of the vessel was found, with normal color Doppler signal and without exogenous endoluminal images. All patients underwent follow-up after 3 months.

Statistical analysis

Calculations were made with the StatView II program (Abacus Concepts, Berkeley, CA). All data are expressed as means ± standard deviation (SD) [13].

Results

Overall 6 out of the 100 patients (6%) were detected to have DVT (3 males, 3 females) using US on day 1. Three (2 males, 1 female) of them (3%) had proximal (femoro-popliteal) DVT, 3 (1 male, 2 females) (3%) had distal DVT. Twenty percent of all patients presented symptoms of DVT. Five (83%) out of the 6 patients with DVT (3 with proximal and 2 with distal DVT) were symptomatic. D-dimer test was >500 µg/l in 4 out of the 6 DVT patients; it was <500 µg/l in less than 20% of all COPD patients.

All patients with DVT received anticoagulant treatment for 3-6 months. At 1 month follow-up no new DVT was detected. No patient presented clinical symptoms of DVT in the following 3 months.

Discussion

VTE is a common and severe complication in hospitalized medical patients. Among the heterogeneous group of subjects included in the Medenox trial, showing an intermediate risk for VTE (about 15%), COPD patients were widely represented [1]. Further analyses distinguished more homogeneous risk categories, such as COPD with respiratory failure or serious concomitant infection [14]. Most of the studies considered patients with complex clinical conditions concomitant to COPD, strongly implied in the pathogenesis of VTE, such as immobility, infections, and acute respiratory failure [7, 14]. These studies are not easily comparable, as they used different methods to detect DVT and often included patients not homogeneous as regards the severity of COPD.

It is known that D-dimer levels have limited clinical value in hospitalized patients, due to comorbidities responsible for false positive results [15]. Accordingly, 80% of our patients had a positive D-dimer assay, whereas only 6% were affected by DVT.

Many trials reported the extreme accuracy of US scan in patients with symptomatic DVT, with very high sensitivity and specificity (97 and 98%, respectively) [3]. More controversial is the diagnostic accuracy in asymptomatic patients and in distal DVT [3]. Nevertheless, proximal and distal venous US scan and its reliability were documented in recent trials in patients with clinically suspected lower extremity DVT [16].

Our study documented a low incidence of both proximal and distal DVT in mild to moderate COPD, as detected by complete venous US scan. It should be outlined that the selection of our patients aimed to exclude the influence of other concomitant clinical conditions at risk of DVT. Unlike other studies, we also included distal DVT, representing about 50% of the total.

In conclusion the present study shows that patients with mild to moderate COPD, without other high-risk conditions, are at low risk of DVT and therefore should be individually considered for antithrombotic prophylaxis. Although there is no evidence that can help in identifying patients at higher risk, our findings, which need further and more complete evaluation, suggest that a complete venous US scan could represent a reliable diagnostic tool for the detection of DVT in symptomatic patients with exacerbation of mild to moderate COPD.

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