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ORIGINAL ARTICLE

Predictors of pulmonary hypertension after intermediate-to-high risk pulmonary embolism☆

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KEYWORDS
Chronic thromboembolic pulmonary hypertension;
Pulmonary embolism;
Risk factors;
Body mass index;
Obesity;
Age

Abstract
Background: Pulmonary embolism (PE) is a common cardiovascular emergency that, when combined with chronic thromboembolic pulmonary hypertension (PH), is associated with high mortality and morbidity. We aimed to determine the incidence of and predisposing factors for the development of PH after a PE episode.
Methods: A retrospective study was conducted in 213 patients admitted to an intensive care unit with intermediate-to-high risk PE between 2000 and 2010. Clinical data at admission were collected and the incidence of PH as assessed by echocardiography (estimated pulmonary systolic artery pressure over 40 mmHg) was determined. Multivariate analysis was used to determine predictors of development of PH.
Results: PH was detected in 12.4% of patients after a mean follow-up of three years. Only age (hazard ratio [HR] 1.09, 95% confidence interval [CI] 1.02–1.20 per year; p=0.012) and body mass index (HR 1.19, 95% CI 1.04–1.36) per kg/m^2, p=0.013) emerged as independent predictors of the development of this complication during follow-up.
Conclusions: PH after PE was a relatively common complication in our series. We identified advanced age and increased body mass index as predisposing factors.

PALAVRAS-CHAVE
Hipertensão pulmonar tromboembólica crónica;
Tromboembolia-pulmonar;

Preditores de hipertensão pulmonar após tromboembolia pulmonar de risco intermédio a elevado

Resumo
Introdução: A tromboembolia pulmonar (TEP) é uma emergência cardiovascular comum que, juntamente com a hipertensão pulmonar tromboembólica crónica (HPTEC), se associa a alta

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Fatores de risco;
Índice de massa corporal;
Obesidade;
Idade

mortalidade e morbilidade. Não há ainda consenso quanto à consecutividade destas patologias. Este estudo pretende determinar a incidência e fatores de risco para o desenvolvimento de hipertensão pulmonar (HTP) após uma TEP de risco intermédio a elevado.

Métodos: Estudámos retrospetivamente 213 doentes com TEP de risco intermédio a elevado, entre 2000–2010, e comparamos dados demográficos, clínicos, laboratoriais e imagiológicos entre os doentes que manifestaram HTP durante o seguimento clínico (doentes que, pelo menos três meses após a alta, mantivessem pressões sistólicas na artéria pulmonar acima de 40 mmHg, estimadas por ecocardiografia) com os doentes que mantiveram pressões normais.

Resultados: Identificou-se HTP após a TEP em 12,4% dos doentes. Foram fatores preditores para o desenvolvimento desta complicação a idade (*hazard ratio* [HR] 1,09 [intervalo de confiança {IC} 95% 1,02–1,20] por ano de idade, p=0,012) e o índice de massa corporal (HR 1,19 [IC 95% 1,04-1,36] por kg m^{-2}, p=0,013).

Conclusões: A HTP após uma TEP foi uma complicação relativamente comum na nossa série de doentes com um episódio agudo de TEP de risco intermédio a elevado. Identificamos como fatores preditores do desenvolvimento desta complicação a idade avançada e a obesidade.

Introduction

Pulmonary embolism (PE) is a common cardiovascular emergency that is characterized by occlusion of the pulmonary artery lumen by an embolus, which can lead to potentially fatal but reversible right ventricular failure.[1] Mortality from PE is around 12/10 000 per year,[2–4] reaching 60% for acute episodes.[5]

Clinical presentation at admission is used to stratify patients for short-term risk of death. Those in shock or hypotensive are considered at high risk, those with evidence of right ventricular dysfunction and/or myocardial damage at intermediate risk, and those without shock, hypotension, right ventricular function or markers of myocardial damage at low risk.[6] Anticoagulation should be instituted even before the diagnostic process is complete in cases of high or intermediate probability of PE, while fibrinolysis should be reserved for high-risk patients (class I recommendation) and for certain intermediate-risk patients (class IIb recommendation), in the absence of contraindications.[6] Fibrinolysis has been shown to produce a rapid decrease in perfusion defects and right ventricular dysfunction, but does not reduce mortality in intermediate-risk patients.[7]

While in most patients pulmonary artery occlusion resolves within 6–12 months, development of chronic thromboembolic pulmonary hypertension (CTEPH) can be an extension of the natural history of acute PE.[7] However, there is no consensus on its incidence, reports ranging between 0.6% and 7.0%.[7–11] The association of PE and CTEPH can lead to mortality of 70–90%12 but when correctly diagnosed, most patients can be treated by pulmonary endarterectomy.[13] The pathophysiological continuum between the two entities appears to be influenced not only by incomplete resolution of the acute obstruction, leading to endothelialization of thrombi and thus occlusion or narrowing of pulmonary arteries, but also by histological changes in the pulmonary microvasculature.[14] Various risk factors have been described that favor evolution of acute PE to CTEPH, including age (both younger[10] and older[15]), previous PE,[10] larger perfusion defect,[10] idiopathic presentation,[9,10] pulmonary artery systolic pressure (PASP) at admission $\geq$50 mmHg,[11,16] and initial thrombus size.[13] However, patient selection criteria in these studies were not specific in terms of PE risk stratification at admission.[7–11]

The aim of this study was to determine risk factors for the development of pulmonary hypertension (PH) in a population of patients with acute intermediate-to-high risk PE.

Methods

Data collection

A retrospective analysis was performed of a prospective database of 213 consecutive patients admitted to the coronary care unit of Coimbra University Hospitals with a diagnosis of intermediate-to-high risk PE, between May 13, 2000 and October 15, 2010. The diagnosis was confirmed by computed tomography (CT) angiography or ventilation/perfusion scintigraphy. Clinical data collected at admission enabled retrospective risk stratification based on current guidelines[6]; this was complemented by analysis of patients' medical records. The decision to perform fibrinolysis with alteplase (Actylise®, Boehringer Ingelheim, Germany) was at the discretion of the attending physician, and most patients (n=183) received fibrinolytic therapy. Patients were initially anticoagulated with unfractionated heparin, together with warfarin. Inotropic, vasopressor and ventilatory support were instituted depending on clinical assessment.

The following risk factors for PE were analyzed: advanced age ($\geq$80 years), obesity, lower limb varicose veins, recent immobilization, known thrombophilia, previous venous thromboembolism, pregnancy, use of oral contraceptives, known cancer, heart failure, and recent major trauma or