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Echocardiographic evolution of pulmonary artery pressure after acute pulmonary embolism. Results from IPER registry

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ABSTRACT

Aims: The aim of the study is to describe the course of the echocardiographically measured pulmonary artery systolic pressure (PAsP) in a series of patients included in the Italian Pulmonary Embolism Registry (IPER).
Methods: Patients with confirmed PE received an echo-Doppler evaluation within 24 hours from hospital admission and after one year. Pulmonary hypertension (PH) was considered "likely" , "possible" or "unlikely" with a right ventricular-right atrial (RV-RA) pressure gradient > 45 mm Hg, between 32 and 45 mm Hg and ≤ 31 mm Hg and no additional echocardiographic variables suggestive of PH, respectively.
Results: We studied 286 patients (169 females and 117 males, mean age 67 ± 15; mean follow-up 387 ± 45 days): 240 had a baseline tricuspid regurgitation (TR) and a RV-RA gradient of variable degree. PH was considered likely, unlikely and possible in 97, 93 and 50 patients respectively. At FU echocardiography, 6 patients (2.1%) had a likely PH and all of them were part of the group of 97 patients with a baseline likely PH; 24 patients (8.4%) had a possible PH, and 67% of them had an initial likely PH. No patients with a baseline unlikely PH or without TR developed a follow-up PH (both likely or possible). The probability to show a likely PH at FU echocardiography for patients with a baseline RV-RA gradient > 45 mm Hg was 6.2%, while the probability not to have a likely PH for patients with a baseline RV-RA gradient ≤ 45 mm Hg was 100%.
Conclusion: In our study population of patients with acute PE, we observed that those presenting with a baseline echocardiographic RV-RA pressure gradient ≤ 45 mm Hg were completely free from a likely PH after 1-year.

Introduction

The reported prevalence of chronic thromboembolic pulmonary hypertension (CTEPH) after an episode of acute pulmonary embolism (PE) is quite variable [1–3], depending on several factors: 1) severity of initial PE ;2) presence or absence of symptoms suggestive of pulmonary hypertension (PH); 3) methods of investigation: invasive vs non-invasive; 4) criteria to diagnose PH or right ventricular dysfunction (RVD) at echocardiography; 5) presence or absence of a baseline echocardiographic evaluation and 6) duration of follow-up (FU). In spite of the low accuracy of echo-Doppler to correctly measure the degree of PH [4,5], echocardiography remains to date the most utilized and often the only method to investigate, both in the acute phase and over time, the course of pulmonary artery systolic pressure (PAsP). Several studies considered the echocardiographic follow-up at least 6 months after an episode of acute PE [6–14]. Some of them [13,14] correlated the value of echocardiographycally derived PAsP in the acute phase with the persistence of PH 12 or 16 months later. The purpose of the present study is to describe the course of PAsP in a series of patients included in the Italian Pulmonary Embolism Registry [15] and submitted to echocardiography at hospital admission and about one year later.

Methods

Study design

Patients with confirmed PE enrolled in the IPER were considered eligible for the inclusion in this analysis if they received a valuable

Abbreviations: PE, pulmonary embolism; PH, pulmonary hypertension; CTEPH, chronic thromboembolic pulmonary hypertension; RVD, right ventricular dysfunction; RV, right ventricle; RA, right atrium; FU, follow-up; PAsP, pulmonary artery systolic pressure; IPER, Italian pulmonary embolism registry; SD, standard deviation; TL, thrombolysis.

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echocardiography within 24 hours from hospital admission and after about one year. All patients gave informed consent before inclusion in the Registry. Data on clinical features, imaging studies and laboratory tests were collected at presentation, during the hospital stay and at discharge, as previously described [15]. Results of imaging and laboratory strategies were reported according to local standards. Follow-up visits and examinations were suggested at 3-6-12-24-36-48 months after the index episode. Early clinical assessment and risk stratification to identify high-risk and non high-risk patients were performed according to the European Society of Cardiology recommendations [16]. High-risk patients were defined as those who were hemodynamically unstable (persistent arterial blood pressure ≤ 90 mm Hg or a pressure drop of ≥40 mm Hg for >15 minutes if not caused by new-onset arrhythmia, ipovolaemia or sepsis) at presentation. All those patients who were hemodynamically stable at presentation were classified as non-high-risk patients. RVD at echocardiography was diagnosed in the presence of at least one of the following: 1) right to left ventricle end-diastolic diameter ratio > 1 in apical 4-chamber view; 2) right to left ventricle end-diastolic diameter ratio > 0.6 in parasternal long-axis or subcostal 4-chamber views. RVD was not considered of acute onset in the presence of right ventricle wall thickness > 7 mm or documentation of right ventricle overload at previous examinations [13]. For estimating the likelihood of PH at rest, we adopted the arbitrary criteria proposed by the European Society of Cardiology in 2009 [17], based on tricuspid regurgitation (TR) peak velocity. Doppler PAsP was calculated according to the simplified Bernoulli equation, and assuming a right atrial pressure of 5 mm Hg. PH was considered "likely" in the presence of an estimated RV-RA pressure gradient > 45 mm Hg (PAsP > 50 mm Hg) with or without additional echocardiographic signs of RVD (class recommendation/evidence level = 1/B); PH was considered "possible" in the presence of a RV-RA between 32 and 45 mm Hg (PAsP 37-50 mm Hg) with or without additional echocardiographic signs of RVD (class recommendation / evidence level = 2a/C) and, lastly, PH was considered "unlikely" with a RV-RA gradient ≤ 31 mm Hg (PAsP ≤ 36 mm Hg) and no additional echocardiographic variables suggestive of PH (class recommendation / evidence level = 1/B). Patients without an assessable RV-RA gradient at follow-up, due to the absence of TR, but with an assessable RV-RA gradient at baseline were considered as having a normal follow-up RV-RA gradient, provided that no sign of RVD was evident.

Statistical analysis

Data are described as mean ± standard deviation (SD) for continuous variables and absolute and relative frequencies for categorical data. Comparisons between groups were performed with unpaired t-test for continuous data and chi-square test for categorical data, unless otherwise specified. Linear regression was performed by ordinary least square to assess the relationship between baseline and follow-up gradient values. Multiple logistic regression was performed to identify baseline variables associated with the presence of PH at FU. P-values < 0.05 were considered statistically significant. Statistical analysis was conducted using the SAS software package ver. 9.1.3 running on Windows Xp (SAS Institute, Cary, NC, USA).

Results

Out of the 1716 patients enrolled in the registry, 1186 (69.1%) received an echocardiogram within 24 hours from presentation; 76 of them did not survive the acute phase. One thousand-one hundred and ten patients were therefore suitable for echocardiographic follow-up (FU). Eight hundred and twenty one patients (74.2%) were excluded from the present study because a second echocardiogram was not performed after one year and 3 patients were excluded due to documented episodes of recurrent PE. Twenty six of 49 (53%) IPER centers performed an echocardiogram after 1 year. Two hundred and eighty six patients (Fig. 1) form therefore the study population (169 females and 117 males, mean age 67 ± 15; mean follow-up 387 ± 45 days). Thirty four patients were classified as high-risk patients and 252 as non-high-risk patients. At FU visit, 251 (87.8%) patients were receiving a vitamin K antagonist, 10 (3.5%) a low-molecular weight heparin or fondaparinux Excluded patients were similar to the study patients with respect to age, gender, systolic blood pressure and the majority of risk factors, while immobilization > three days was more common and thrombolytic treatment was less common in this group (Table 1). Non-high-risk patients excluded from the study were similar to the non-high-risk patients of the study group as for the baseline RV-RA pressure gradient. According to the presence or absence of TR at baseline echocardiography, two groups of patients were identified: group 1 (N = 240), with TR and RV-RA gradient of variable degree and

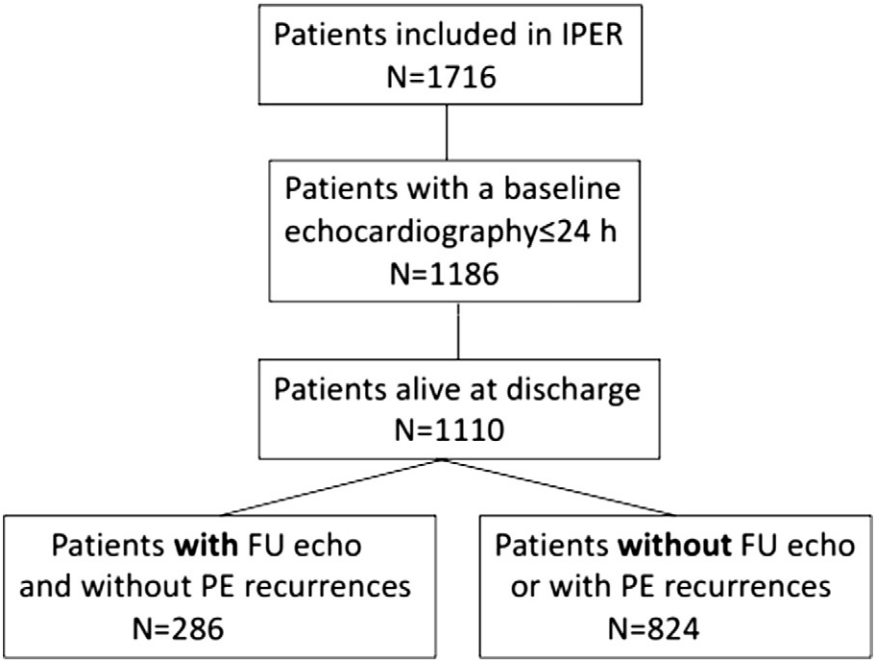

Fig. 1. Flow-chart of the study.