IJC Heart & Vessels 4 (2014) 161–169

Contents lists available at ScienceDirect

IJC Heart & Vessels

journal homepage: http://www.journals.elsevier.com/ijc-heart-and-vessels

Increase of pulmonary artery wedge pressure above 15 mm Hg in patients with pre-capillary pulmonary hypertension

Julien Wain-Hobson [a,*], Rémi Sabatier [a], Mamadou Koné [b], Damien Legallois [a], Thérèse Lognoné [a], Ziad Dahdouh [a], Farzin Beygui [a], Gilles Grollier [a], Paul Milliez [a], Emmanuel Bergot [c], Vincent Roule [a]

[a] CHU de Caen, Department of Cardiology, Caen F-14000, France
[b] CHU de Caen, Department of Biostatistics and Clinical Research, Caen F-14000, France
[c] CHU de Caen, Department of Pneumology, Caen F-14000, France

ARTICLE INFO

Article history:
Received 21 April 2014
Accepted 23 April 2014
Available online 2 May 2014

Keywords:
Pulmonary hypertension
Heart failure
Pulmonary artery wedge pressure
Left ventricular diastolic dysfunction

ABSTRACT

Aims: Daily practice shows that patients with pre-capillary pulmonary hypertension (PH) may develop a secondary elevation of their pulmonary artery wedge pressure (PAWP) above the 15 mm Hg limit. This phenomenon has not been precisely described yet. We aimed at identifying factors present at initial diagnosis that could predict this secondary elevation of PAWP, its possible causes and impact on survival.
Methods and results: We included 90 patients followed between 2004 and 2011 in our center. At the end of follow-up (3.0 ± 1.6 years), patients were divided into two groups according to the successive PAWP measurements (always ≤ 15 mm Hg or >15 mm Hg on at least one right heart catheterization (RHC)). Demographical, biological, echographic and hemodynamical data at first RHC were compared. Possible causes for PAWP >15 mm Hg were searched. A Kaplan–Meier method was used to assess differences in survival. One third of our cohort developed an elevation of PAWP above 15 mm Hg and patients with idiopathic pulmonary arterial hypertension were at smaller risk (OR 0.20 [0.05–0.82]; p = 0.026). We did not identify any other baseline predictive factors. We highlighted several possible causes and factors that may unmask an underlying left ventricular diastolic dysfunction. Survival was not different between both groups (p = 0.42).
Conclusion: Secondary elevation of PAWP in pre-capillary PH was frequent but less observed in idiopathic PH. We detailed many possible causes that can be sought, many of which may be related to an underlying left ventricular diastolic dysfunction.

1. Introduction

Pulmonary Hypertension (PH) is a life threatening disease characterized by a progressive increase of pulmonary blood pressure and a pulmonary vascular remodeling [1] that often leads to right ventricular failure and death. Pre-capillary PH is defined by a mean pulmonary arterial pressure (mPAP) ≥25 mm Hg and a pulmonary artery wedge pressure (PAWP) ≤15 mm Hg. It is classically opposed to post-capillary PH due to left heart disease.

Nevertheless, daily practice shows that, regardless of the initial etiology of pre-capillary PH, some patients develop a secondary elevation of their pulmonary artery wedge pressure during follow-up. In a recent study from the REVEAL registry, a PAWP >15 mm Hg was measured in 30% of PAH patients on successive right heart catheterizations (RHC), regardless of initial PAWP [2]. For the time being, the characteristics and the evolution of pre-capillary PH patients with a secondary increase of PAWP has not been described yet. Through this observational study, we aimed at defining demographic, biological and hemodynamic markers present at initial diagnosis of pre-capillary PH that could predict this secondary elevation of PAWP and at analyzing its possible causes. Furthermore, we evaluated whether this evolution of the disease towards a mixed form of PH had an impact on all-cause mortality.

Abbreviations: 6MWT, six minute walking test; BMI, body mass index; BNP, brain natriuretic protein; CAD, coronary artery disease; CI, cardiac index; CO, cardiac output; dPAP, diastolic pulmonary arterial pressure; DPG, diastolic pressure gradient; ECG, electrocardiogram; ELISA, enzyme linked immune sorbent assay; LBBB, left bundle branch block; LVDD, left ventricular diastolic dysfunction; LVEDP, left ventricular end diastolic pressure; LVEF, left ventricular ejection fraction; MDRD, modification of the diet in renal disease formula; mPAP, mean pulmonary arterial pressure; PAH, pulmonary arterial hypertension; PAWP, pulmonary artery wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RBBB, right bundle branch block; RHC, right heart catheterization; RVEDP, right ventricular end diastolic pressure; sPAP, systolic pulmonary arterial pressure; SVT, supra ventricular tachycardia; TPG, transpulmonary gradient; TTE, transthoracic cardiac echography; WHO, World Health Organization functional class of dyspnea; WU, wood units.

* Corresponding author at: Cardiology department, University hospital of Caen, Avenue cote de nacre 14033 Caen, France. Tel.: +33 2 31 06 30 48; fax: +33 2 31 06 44 18.
E-mail address: julienwh@hotmail.fr (J. Wain-Hobson).

http://dx.doi.org/10.1016/j.ijchv.2014.04.011

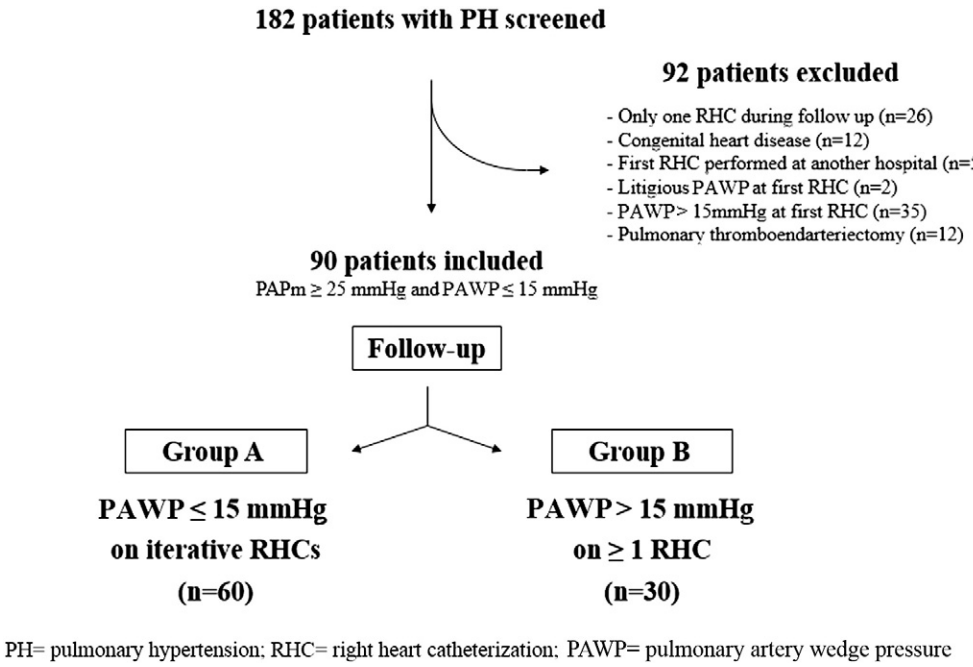

Fig. 1. Flow chart of patient section process.

2. Material and methods

2.1. Design

This is a descriptive, monocentric study with retrospective analysis of a prospective acquired PH regional register.

2.2. Study population

We screened 182 files of patients diagnosed at our Regional Centre for Pulmonary Hypertension between May 2004 and March 2011. All patients were also included prospectively in the French registry for Pulmonary Hypertension [3]. They all gave written informed consent.

We included all patients who had ≥2 RHC during follow-up and an initial RHC showing pre-capillary PH according to current international guidelines [4,5] defined by a mean pulmonary arterial pressure (mPAP) ≥25 mm Hg and a PAWP ≤15 mm Hg at rest. Consequently, patients belonged to groups 1, 3, 4 and 5 of the Dana Point classification [4,5]. All patients had pulmonary vascular resistance (PVR) >3 WU. We excluded patients that had only one RHC during follow-up, adults with congenital heart defects, patients whose first RHC was not performed at our hospital as hemodynamic curves could not be reviewed, those with a first RHC showing a litigious PAWP or a PAWP ≥15 mm Hg at reviewing hemodynamic curves and patients who had undergone pulmonary thromboendarterectomy.

Cardiovascular risk factors and medical history, treatment, electrocardiogram (ECG), six minute walking test (6MWT), biological parameters and hemodynamical parameters were all recorded on the day of the first RHC. Biological testing was made for renal function, brain natriuretic peptide (BNP by ELISA) and troponin (TnI by ELISA). Transthoracic echocardiography (TTE) at initial diagnosis could not always be performed on the same day as RHC, which explains why only left ventricular ejection fraction (LVEF) using Simpson's biplane method, pericardial effusion and echographic signs of ventricular interdependency were taken in account.

2.3. Cardiac catheterization

Patients underwent standard RHC using a Swan–Ganz catheter with brachial or femoral venous access. The zero level was placed at the midthoracic line. The following measurements were obtained: heart rate, systolic pulmonary arterial pressure (sPAP), diastolic pulmonary arterial pressure (dPAP), mPAP, PAWP, right ventricular end-diastolic pressure (RVEDP), right atrial pressure (RAP), cardiac output (CO) determined by thermodilution (mean of three consecutive measurements without >10% variation), cardiac index (CI), and PVR calculated from the standard formula PVR = (mPAP-PAWP)/CO. Transpulmonary gradient (TPG) was defined as mPAP-PAWP and diastolic pressure gradient (DPG) as dPAP-PAWP. Vasoreactivity testing using inhaled nitric oxide was performed on the first RHC. PAWP was measured at end-expiration. Hemodynamic curves obtained from RHC were anonymously reviewed by four specialists (E.B., R.S., V.R. and J.W.H.). Discrepancies in reviewing were resolved by consensus.

2.4. Follow-up

Patients were followed on a regular basis with a clinical examination every 3 months plus an annual daytime hospitalization with 6MWT, ECG, pulmonary function testing, RHC, TTE and biologic samples. RHC was performed after every dose change of PAH specific treatments. Any acute pathological manifestation would lead to hospitalization, necessary complementary examinations and adaptation of treatment. Long term treatment was started and adapted according to the international guidelines [4,5]. Patients who had a PAWP >15 mm Hg during follow-up and had multiple (≥3) cardiovascular risk factors underwent a coronary angiography.

Survival follow-up was performed on June 1st, 2012 by telephone interview with the general practitioner or the patient. All-cause mortality was used for analyses. At this time, we divided patients into two different groups: Group A was composed of patients with a strict pre-capillary PAH (i.e. with a measurement of PAWP ≤15 mm Hg on every RHC performed during follow-up) and Group B included patients who had at least one RHC with a PAWP >15 mm Hg during this period of time.