Pulmonary hypertension in Portugal: First data from a nationwide registry

Rui Baptista, José Meireles, Ana Agapito, Graça Castro, António Marinho da Silva, Teresa Shiang, Ana Oliveira, Daniela Ferreira, Fabienne Gonçalves, Susana Robalo-Martins, António Nunes Duindo, Abilio Reis, Cardiology, Hospital da Universidade de Coimbra, Coimbra, Portugal; Internal Medicine, Hospital Santo António, Porto, Portugal; Cardiology, Hospital Santa Marta, Lisboa, Portugal; Pneumology, Hospital Santos Silva, Vila Nova de Gaia, Portugal; Cardiology, Hospital de Santa Maria, Lisboa, Portugal

Pulmonary arterial hypertension (PAH) is a rare disease that must be managed in specialized centers integrated in a national network. Availability of epidemiological national data is critical for planning and regulation of healthcare in this field.

We conducted a prospective, observational and multicenter registry in 5 portuguese centers. Adults with PAH and chronic thromboembolic PH (CTEPH) confirmed by right heart cath (RHC) were included. 79 patients were enrolled; 46 (58.2%) classified as PAH and 33 (41.8%) as CTEPH. PAH patients had a mean age of 43.4±16.4 years and the f/m ratio 1.9:1. Idiopathic PAH was present in 17 (37%) patients, followed by connective tissue disease (n=12, 26%), congenital heart disease (n=10, 22%), portopulmonary (n=5, 11%), heritable (n=1, 2%) and other etiologies (n=1, 2%). At baseline most patients were WHO class III or IV (71%). Baseline RHC: elevated RAP (7.2±5.9 mmHg), mPAP (50.6±17.9 mmHg) and mean PVR (11.4±6.5 Wood U), with a low CI (2.7±1.1 L.min-1.m-2). At baseline patients were medicated with conventional therapies; at follow-up, most were on single (50%), double (28%) or triple (9%) combination of specific therapy. 1-year survival was 93%. CTEPH patients were older (60.0±12.5 years) and had higher RAP (11.0±5.2 mmHg, p=0.015), but 1-year survival (93.9%) was similar to PAH patients. Five CTEPH patients underwent pulmonary endarterectomy. We estimated an annual incidence of 1.5 and 1.1 per million in PAH and CTEPH, respectively.

Our report describes nationwide data on the diagnosis, management and clinical course of groups 1 and 4 PH patients. Clinical presentation, hemodynamics and survival are comparable with those reported on other national registries.

1. Pulmonary circulation: clinical databases and registries

366 Pulmonary hypertension in Portugal: First data from a nationwide registry

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367 Pulmonary hypertension in patients with lupus: Prevalence, etiology and risk factors

Fernando León, Gregorio Pérez-Péñate, J. Navarro, Gabriel Juiá, Antonas García, Carlos Cabrera, Pedro Cabrera, Nazario Ojeda, Juan Pulido, Iturgo Rúa Figueroa, Pneumology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain; Cardiology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain; Anesthesiology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain; Vascular Surgery, Radiology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain; Rheumatology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain

Background: Pulmonary arterial hypertension has been reported between 0.5 and 1.4% in systemic lupus erythematosus (SLE). Objectives: To assess PH prevalence, etiology and risk factors in a SLE cohort. Methods: Prospective cross-sectional study of 158 SLE patients. Doppler echocardiographic (DE), diffusing capacity for CO (DLCO), NtproBNP and dyspnea (Borg scale) were performed in all patients. An echocardiographic exercise test (EE) was conducted in selected patients. When sPAP ≥ 20 mmHg (DE) or a positive EE (>20 mmHg increase in PAPs) a right heart catheterization (RHC) at rest or during exercise was performed. A rest mean pulmonary pressure (mPAP) ≥25 mmHg was accepted as PH. When rest mPAP was less than 25 mmHg, an exercise test was conducted. Patients with resting PH (sPAP ≥ 35 and ≤ 45 mmHg) and obvious cardiac disease were excluded from RHC.

Results: Mean age: 45±12.9 years, 94.3% females. Twenty one patients (13.4%) had dyspnea (Borg scale ≥ 2). Eleven patients (6.9%) showed any degree of PH. Eight patients (out of 11) had PH of left cardiac origin. One patient had thromboembolic disease. Two patients had precapillary PH related with SLE. All 11 patients with PH had dyspnea (Borg scale ≥ 2) vs. those without PH (p<0.001). PH patients showed a significant decrease in Dl CO and higher NtproBNP. There were no differences in SLE clinical characteristics between SLE patients and those without PH.

Conclusions: Our data confirm the low prevalence of precapillary PH in SLE. We found a preponderance of cardiac etiology. A PH screening program based on DE, NtproBNP and Dl CO not seems to be cost-effective and should be restricted to SLE patients with unexplained dyspnea.
A REVEAL risk score calculator was accurate and well calibrated in the FPHN, suggesting its prognostic generalizability in a different PAH population and in everyday clinical practice.

### Baseline characteristics of idiopathic PAH patients with severely reduced diffusion capacity

**Patients**: 80 patients with idiopathic PAH.

**Aims**: To evaluate the prognostic performance of an FPHN risk score calculator and external validation in a different PAH population.

**Methods**: The FPHN equation was tested in a REVEAL cohort to assess its generalizability in a different PAH population.

**Results**: The FPHN equation showed good discrimination, with a C-index of 0.72 (95% CI, 0.56-0.80). Risk stratification based on the FPHN equation showed good discrimination in REVEAL between high and low-risk groups. Survival in REVEAL correlated with FPHN equation predictions and was slightly better than predicted (Figure).

**Conclusion**: The FPHN risk score calculator was accurate and well calibrated in the FPHN, suggesting its prognostic generalizability in a different PAH population and in everyday clinical practice.

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**Table 1: Baseline characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>DLCO (%) of predicted (n=96)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (years)</td>
<td>64 (25-84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex</td>
<td>26 (45)</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26 (20-36)</td>
<td>0.435</td>
</tr>
<tr>
<td>Smoking</td>
<td>41 (76)</td>
<td>0.901</td>
</tr>
<tr>
<td>Pack-years</td>
<td>25 (9-62)</td>
<td>0.577</td>
</tr>
</tbody>
</table>

**Comorbidities**

- **Coronary disease (%)**: 15 (20) (p < 0.001)

**Lung function**

- **FEV1 (%) of predicted**: 82 ± 17 (p = 0.005)
- **FVC (%) of predicted**: 94 ± 20 (p = 0.000)
- **FEV1/FVC (%)**: 65 ± 11 (p = 0.006)
- **TLCo (%) of predicted**: 94 ± 15 (p = 0.302)

**Laboratory tests**

- **HB (mmol/L)**: 9.5 (7.0-12.2) (p = 0.057)
- **NT-proBNP (ng/L)**: 160 (33-5,844,655) (p = 0.241)

**Hemodynamics**

- **mPAP (mmHg)**: 50 (27-90) (p = 0.346)
- **PVR (dynes s/cm²)**: 835 (395-2,067) (p = 0.217)
- **mPAP (mmHg)**: 7 (1-24) (p = 0.356)
- **SvO2 (%)**: 64 (41-76) (p = 0.284)

**Introduction**

The French Pulmonary Hypertension Network (FPHN) and the Registry to Evaluate Early And Long-term Pulmonary Arterial Hypertension (PAH) Disease Management (REVEAL) have recently developed predictive models for survival in patients with PAH.

**Aims and objectives**

The REVEAL risk score calculator was assessed in a FPHN cohort to evaluate its generalizability in a different PAH population.

**Methods**: French validation cohort was built to approximate the inclusion/exclusion criteria originally defined by REVEAL. For each patient, the risk score was evaluated using the most recent assessment of risk at any clinic visit from November 2006 or later.

**Results**: The French validation cohort had 1738 patients (pts) with group 1 PAH, mean ± standard deviation 6-min walk distance of 356 ± 130 m and 53% pts in functional class III. Observed 1-yr survival for patients with risk scores of 1-7, 8, 9, 10-11, or 12+ were 96.4%, 88.6%, 84.6%, 78.7%, and 62.1%, respectively (Figure) falling close to the predicted risk for each of these 5 pre-specified risk strata. The c-index for the risk calculator was 0.729.

**Conclusion**: The REVEAL risk score calculator was accurate and well calibrated in the FPHN, suggesting its prognostic generalizability in a different PAH population and in everyday clinical practice.
371 'Idiopathic' pulmonary arterial hypertension with preserved lung function but co-existing parenchymal abnormalities: Response to treatment and survival

Vivek Iyer

Hepatopulmonary syndrome: Long-term survival in the Mayo Clinic

Vivek Iyer

Methods: Patients with idiopathic or familial PAH were included. Patients were grouped based on the finding of a bimodal distribution in DLCO-values.

Results: A total of 170 patients were included. DLCO groups were DLCO <45% (N=58) and ≥45% of predicted (N=112). Group characteristics are shown in table 1.

Conclusions: Compared with IPAH patients with moderate low or normal DLCO, IPAH patients with a severely reduced DLCO were characterized at baseline by a higher age, increased number of males, more often a history of smoking and coronary disease, and a lower exercise performance. No differences however were found in hemodynamic parameters.

Table 1. Baseline characteristics, 6MWD and survival of IPAH

<table>
<thead>
<tr>
<th></th>
<th>With parenchymal abnormalities</th>
<th>Without parenchymal abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=48)</td>
<td>(n=307)</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>68</td>
<td>50</td>
</tr>
<tr>
<td>% female</td>
<td>42%</td>
<td>70%</td>
</tr>
<tr>
<td>6MWD, m</td>
<td>209</td>
<td>292</td>
</tr>
<tr>
<td>6MWD at 3 months, m</td>
<td>52</td>
<td>40</td>
</tr>
<tr>
<td>mPAP, mmHg</td>
<td>49</td>
<td>54</td>
</tr>
<tr>
<td>Cardiac index, L/min/m²</td>
<td>2.1</td>
<td>2.1</td>
</tr>
<tr>
<td>PVRL, WU</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>1 year survival</td>
<td>74%</td>
<td>93%</td>
</tr>
<tr>
<td>3 year survival</td>
<td>45%</td>
<td>73%</td>
</tr>
</tbody>
</table>

Conclusion: Despite similar baseline haemodynamics and response to treatment, survival of ‘IPAH with coexisting parenchymal abnormalities appears worse compared with IPAH without parenchymal abnormalities. Age and age related co-morbidities may account for the difference in long term outcome between the 2 groups.

Methods: Survival was assessed using Kaplan-Meier methodology for 106 HPS patients from 1986 through 2010.

Results: 49 HPS patients underwent LT post-LT survival (1, 3, 5 and 10 year) did not differ between groups based on PaO₂ at the time of HPS diagnosis. Improvements in overall survivals at 1, 3 and 5 years post-LT in those HPS patients transplanted after 2002 (MELD exception era, n=28) (92, 87 and 87%, respectively) as compared to those transplanted prior to that time (pre MELD era, n=21) (71, 67 and 67%, respectively) did not reach statistical significance (P=0.09) (figure 1). Model for Endstage Liver Disease (MELD) exception to facilitate LT was granted to 18 patients since 2002 with post-LT survival of 15/18 patients (83%) and no wait-list mortality.

Methods and results: Every consecutive patient undergoing right heart catheterization with proven PH was included in the Giessen registry from 1994 to 2011. Differences in survival between the etiologic groups were highly significant (p<0.001), with 1-, 3-, and 5-year survival rates of 88.2%, 72.2%, 59.4%, respectively in pulmonary-arterial hypertension (PAH), 67.0% (PVH), 63.7% (LD-PH), 61.9% (CTEPH) as compared to 79.5%, 52.7%, and 38.1%, respectively in lung disease associated PH (PH-LD, N=546).

Conclusion: Long-term outcome after LT in HPS is favorable. The survival patterns from the time of LT were not influenced by pre-LT PaO₂. Limited experience with HPS-MELD exception suggests a positive impact on survival with no wait-list mortality.

373 Survival in patients with different groups of pulmonary hypertension

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Background: Several markers have been suggested to be associated with severity and/or prognosis of disease in patients with pulmonary hypertension (PH). Reports on survival and its determinants in patients with pulmonary hypertension mostly focus on the subgroup of pulmonary arterial hypertension (PAH). Data on other subgroups is rare.

Methods and results: Every consecutive patient undergoing right heart catheterization with proven PH was included in the Giessen registry from 1994 to 2011. Differences in survival between the etiologic groups were highly significant (p<0.001), with 1-, 3-, and 5-year survival rates of 88.2%, 72.2%, 59.4%, respectively in pulmonary-arterial hypertension (PAH), 67.0% (PVH), 63.7% (LD-PH), 61.9% (CTEPH) as compared to 79.5%, 52.7%, and 38.1%, respectively in lung disease associated PH (PH-LD, N=546).

Chronic thromboembolic pulmonary hypertension (CTEPH, N=459) had the best survival rates with 80.9%, 77.4%, and 66.7%, pulmonary venous hypertension (N=307) was intermediate. Age also differed between the groups: mean age at diagnosis was 51.3 (PAH), 67.0 (PVH), 63.7 (LD-PH), 61.9 (CTEPH) years, respectively. In multivariate analysis, age, gender, NYHA functional class, uric acid, urea, brain natriuretic peptide, heart rate, sodium, six-minute walk test distance, cardiac output, and systolic blood pressure at baseline were significantly associated with survival.

Conclusions: In this report we present data on long term survival and its determinants from patients with all subtypes of pulmonary hypertension. We aim to assess the utility and validity of a new prognostic score for different forms of PH based on comprehensive databases from the PH centers Giessen and Imperial College in London.