## 71. Pulmonary circulation: clinical databases and registries

**366**

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

Rui Baptista[1], José Meireles[2], Ana Agapito[3], Graça Castro[1], António Marinho da Silva[1], Teresa Shiang[4], Ana Oliveira[4], Daniela Ferreira[4], Fabienne Gonçalves[2], Susana Robalo-Martins[5], António Nunes Diogo[5], Abilio Reis[2]. *[1]Cardiology, Hospitais da Universidade de Coimbra, Coimbra, Portugal; [2]Internal Medicine, Hospital Santo António, Porto, Portugal; [3]Cardiology, Hospital Santa Marta, Lisboa, Portugal; [4]Pneumology, Hospital Santos Silva, Vila Nova de Gaia, Portugal; [5]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 (7.7±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 93.5%.
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.

**367**

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

Fernando León[1], Gregorio Pérez-Peñate[1], J. Navarro[1], Gabriel Juliá[1], Antonio García[2], Carlos Cabrera[1], Pedro Cabrera[1], Nazario Ojeda[3], Juan Pulido[4], Iñigo Rúa Figueroa[5]. *[1]Pneumology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain; [2]Cardiology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain; [3]Anestesiology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain; [4]Vascular Radiology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain; [5]Rheumatology, Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria, Spain*

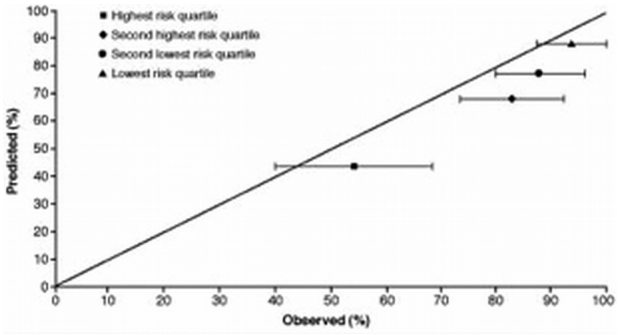
**Background:** Pulmonary arterial hypertension has been reported between 0.5 and 14% in systemic lupus erythematosus (SLE).
**Objectives:** To assess PH prevalence, etiology and risk factors in a SLE cohort.
**Methods:** Prospective cross-sectional study of 158 SLE patients. Doppler echocardiographic (DE), diffusing capacity for CO ($D_LCO$), NtproBNP and dyspnea (Borg scale) were performed in all patients. An echocardiographic exercise test (EE) was conducted in selected patients. When sPAP $\geq$ 45 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 (mPP) $\geq$25 mmHg was accepted as PH. When rest mPP was less than 25 mmHg, an exercise test was conducted. Patients with resting PH (sPAP $\geq$ 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 $\geq$ 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 $\geq$ 2) vs. those without PH (p<0.001). PH patients showed a significant decrease in $D_LCO$ 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 $D_LCO$ not seems to be cost-effective and should be restricted to SLE patients with unexplained dyspnea.

**368**

**External validation of the French predictive model to estimate PAH survival: A REVEAL analysis**

Michael McGoon[1], Raymond Benza[2], Adaani Frost[3], David Badesch[4], C. Gregory Elliott[5,6], Olivier Sitbon[7], Gerald Simonneau[7], Dave Miller[8], Erwan Muros Le Rouzic[9], Marc Humbert[7]. *[1]Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, United States; [2]Division of Cardiology, Allegheny General Hospital, Pittsburgh, PA, United States; [3]Department of Medicine, Baylor College of Medicine, Houston, TX, United States; [4]Division of Pulmonary Sciences and Critical Care Medicine, and Cardiology, University of Colorado Denver, Aurora, CO, United States; [5]Department of Medicine, Intermountain Medical Center, Murray, UT, United States; [6]Department of Medicine, University of Utah, Salt Lake City, UT, United States; [7]Service de Pneumologie, Université Paris-Sud, Inserm U999, AP-HP, Le Kremlin Bicêtre, France; [8]Statistical Analysis, ICON Late Phase & Outcomes Research, San Francisco, CA, United States; [9]Epidemiology, Actelion Pharmaceuticals Ltd, Allschwil, Switzerland*

**Background:** The French Pulmonary Hypertension Network (FPHN) and Registry to EValuate **E**arly **A**nd **L**ong-term Pulmonary Arterial Hypertension (PAH) Disease Management (REVEAL) recently developed models to predict survival in PAH patients (pts).
**Aims and objectives:** The FPHN equation was tested in a REVEAL cohort to assess its generalizability in a different PAH population.
**Methods:** The REVEAL validation cohort had 436 recently diagnosed (<1 year before enrollment), treatment-naïve, ≥18-year-old patients (pts) with idiopathic, familial, or anorexigen-induced PAH, divided into subgroups with non-missing (n=292) and missing (n=144) data for all FPHN equation parameters.
**Results:** The FPHN and REVEAL cohorts had similar characteristics. FPHN follow-up (f/u) was ≥3 years; REVEAL validation cohort and subgroup with non-missing data had a mean f/u from diagnosis of 29.2 and 30.1 months, respectively. FPHN model parameters applied to REVEAL showed a good correlation of estimated hazard ratios between the two studies and robust C index of 0.72 (95% CI, 0.64–0.80). Risk stratification based on the FPHN equation showed good discrimination in REVEAL between high and low-risk pts. Survival in REVEAL correlated with FPHN equation predictions and was slightly better than predicted (figure).




| | Predicted | Observed (estimate ± SE) |
|---|---|---|
| Lowest risk quartile (N = 73) | 87.7% | 93.3 ± 3.2% |
| Second lowest risk quartile (N = 73) | 77.1% | 87.7 ± 4.1% |
| Second highest risk quartile (N = 73) | 68.0% | 82.5 ± 4.8% |
| Highest risk quartile (N = 73) | 43.4% | 53.9 ± 7.2% |

**Conclusion:** The FPHN equation accurately stratified a matched US population according to risk, suggesting its prognostic generalizability in PAH pts.

**369**

**External validation of the REVEAL risk score calculator for PAH survival: A French pulmonary hypertension network analysis**

Olivier Sitbon[1], Marc Humbert[1], Gérald Simonneau[1], Jean-Christophe Lemarie[2], Dave Miller[3], Erwan Muros Le Rouzic[4], Virginie Gressin[5], David Badesch[6], Raymond Benza[7], C. Gregory Elliott[8], Adaani Frost[9], Michael McGoon[10]. *[1]Service de Pneumologie, Hôpital Universitaire de Bicêtre, Université Paris-Sud, Le Kremlin Bicêtre, France; [2]Effi-Stat, Effi-Stat, Paris, France; [3]Statistical Analysis, ICON Late Phase & Outcomes Research, San Francisco, CA, United States; [4]Global Medical Science & Communication, Actelion Pharmaceuticals Ltd., Allschwil, Switzerland; [5]Medical Affairs, Actelion Pharmaceuticals France, Paris, France; [6]Division of Pulmonary Sciences and Critical Care Medicine, and Cardiology of Colorado, Aurora, CO, United States; [7]Division of Cardiology, Allegheny General Hospital, Pittsburgh, PA, United States; [8]Department of Medicine, Intermountain Medical Center, Murray, UT, United States; [9]Department of Medicine, Baylor College of Medicine, Houston, TX, United States; [10]Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, United States*

**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 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%, 86.4%, 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.

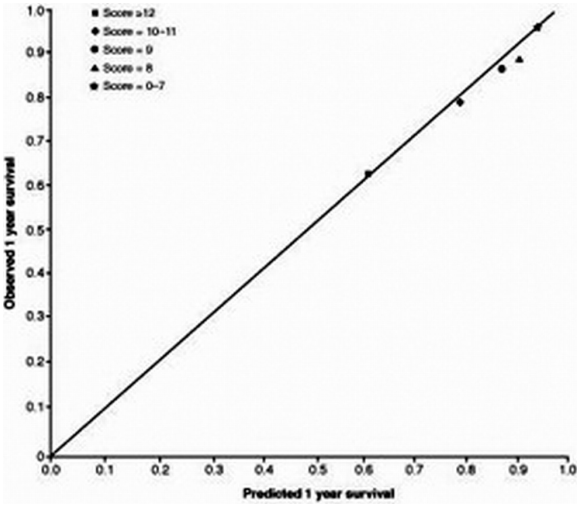



Figure 1. Predicted versus observed 1-year survival in FPHN.

**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.

**370**

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

Pia Trip[1], Esther Nossent[1], Anco Boonstra[1], Harm Jan Bogaard[1], Frances de Man[1,2], Nico Westerhof[1,2], Katrien Grunberg[3], Anton Vonk-Noordegraaf[1]. *[1]Pulmonary Medicine, VU University Medical Center, Amsterdam, Netherlands; [2]Physiology, VU University Medical Center, Amsterdam, Netherlands; [3]Pathology, VU University Medical Center, Amsterdam, Netherlands*

**Introduction:** Pulmonary arterial hypertension (PAH) is a disease affecting the vasculature of the lung and is known to decrease carbon monoxide diffusion

**Table 1: Baseline characteristics**

| | DLCO <45 % of predicted (N=58) | DLCO ≥ 45 % of predicted (N=112) | p-value |
|---|---|---|---|
| Age at diagnosis (yrs) | 64 (23-84) | 47 (21-79) | <0.001 |
| Sex | 26 (45) | 23 (21) | 0.001 |
| BMI (kg/m²) | 26 (20-36) | 27 (17-45) | 0.435 |
| Smoking | 41 (76) | 50 (48) | 0.001 |
| Pack years | 25 (0-92) | 0 (0-57) | <0.001 |
| **Comorbidities** | | | |
| Coronary disease (%) | 15 (26) | (0) 0 | <0.001 |
| **Lung function** | | | |
| $FEV_1$ (% of predicted) | 82 ± 17 | 90 ± 18 | 0.005 |
| FVC (% of predicted) | 96 ± 20 | 103 ± 20 | 0.050 |
| $FEV_1$/FVC (%) | 68 ± 11 | 73 ± 9 | 0.006 |
| TLC (% of predicted) | 94 ± 15 | 97 ± 15 | 0.302 |
| **Laboratory tests** | | | |
| Hb (mmol/L) | 9.5 (7.0-12.2) | 9.1 (5.0-12.4) | 0.057 |
| NT-proBNP (ng/L) | 1004 (53-8444) | 665 (12-13247) | 0.241 |
| **Hemodynamics** | | | |
| mPAP (mmHg) | 50 (27-90) | 52 (26-91) | 0.336 |
| PCWP (mmHg) | 10 (1-15) | 9 (0-15) | 0.143 |
| CI (L/min²) | 2.3 (1.3-4.3) | 2.5 (1.3-7.3) | 0.190 |
| Heart rate (bpm) | 83 (55-125) | 78 (52-112) | 0.429 |
| TPVR (dynes·s·cm⁻⁵) | 835 (393-2667) | 946 (316-2112) | 0.967 |
| mRAP (mmHg) | 7 (1-24) | 7 (0-30) | 0.815 |
| SaO2 (%) | 92 (81-99) | 95 (61-100) | 0.022 |
| SvO2 (%) | 64 (41-76) | 65 (41-84) | 0.264 |
| **6 MWD** | | | |
| Distance (m) | 276 (20-478) | 418 (151-716) | <0.001 |
| SaO2 exercise (%) | 80 (69-93) | 90 (68-99) | <0.001 |

Values are median (min-max), n (%), or mean ± SD.

capacity (DLCO). Although most patients have a moderately decreased DLCO, a group of patients has severely reduced DLCO. The reason for this low DLCO is unclear. Therefore, the aim of this study is to describe baseline characteristics of idiopathic PAH patients with a low DLCO and compare this group with a group of idiopathic PAH patients with moderate low or normal DLCO.
**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.

**371**
**'Idiopathic' pulmonary arterial hypertension with preserved lung function but co-existing parenchymal abnormalities: Response to treatment and survival**
Yi Ling[1], Martin Johnson[1], David Kiely[2], Robin Condliffe[2], Charlie Elliot[2], J. Simon R Gibbs[3], Luke Howard[3], Joanna Pepke-Zaba[4], Karen Sheares[4], Paul Corris[5], Andrew Fisher[5], James Lordan[5], Sean Gaine[6], J. Gerry Coghlan[7], S. John Wort[8], Michael Gatzoulis[8], Andrew Peacock[1]. *[1]Scottish Pulmonary Vascular Unit, Golden Jubilee National Hospital, Glasgow, United Kingdom; [2]Sheffield Pulmonary Vascular Unit, Royal Hallamshire Hospital, Sheffield, United Kingdom; [3]National Heart and Lung Institute, Imperial College London and Hammersmith Hospital, London, United Kingdom; [4]Pulmonary Vascular Disease Unit, Papworth Hospital, Cambridge, United Kingdom; [5]Northern Pulmonary Vascular Unit, Freeman Hospital, Newcastle, United Kingdom; [6]National Pulmonary Hypertension Unit, Mater Misericordiae University Hospital, Dublin, Ireland; [7]Pulmonary Hypertension Unit, Royal Free Hospital, London, United Kingdom; [8]Royal Brompton Pulmonary Hypertension and Adult Congenital Heart Centre, Brompton Hospital, London, United Kingdom*

**Background:** $FEV_1$, FVC and/or TLC <60% were used in the French and Scottish registries to exclude patients with pulmonary hypertension (PH) due to lung disease. Similar criteria were used in pivotal PH trials to exclude significant lung disease. However, some patients with preserved pulmonary function who satisfy the standard criteria for idiopathic pulmonary arterial hypertension (IPAH) may nonetheless have evidence of co-existing parenchymal abnormalities on HRCT. It is unclear how response to treatment and survival is affected by the presence of modest lung disease.
**Aim:** To compare the baseline characteristics, change in 6-minute walk distance at 3 months and survival of IPAH with and without co-existing parenchymal abnormalities on HRCT.
**Methods:** All incident cases of IPAH with and without co-existing CT parenchymal abnormalities diagnosed between January 2001 to December 2009 in all eight PH centres in the UK and Ireland were included. All patients have $FEV_1$, FVC and/or TLC≥ 60% predicted.
**Results:**

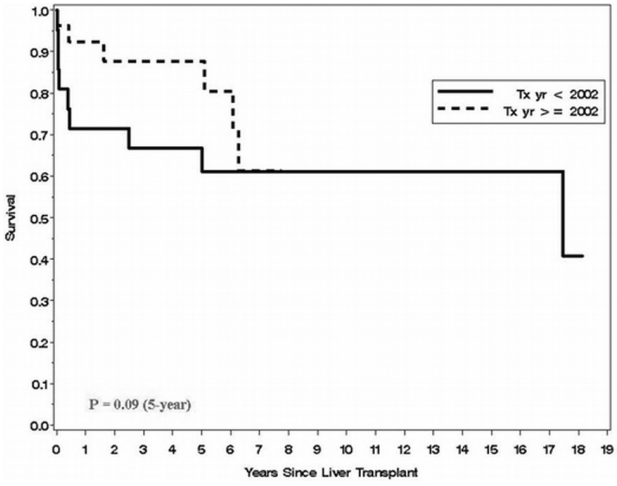
Table 1. Baseline characteristics, Δ6MWD and survival of IPAH

| | With parenchymal abnormalities (n=146) | Without parenchymal abnormalities (n=482) |
|---|---|---|
| Age, yrs | 68 | 50 |
| % female | 42% | 70% |
| 6MWD, m | 209 | 292 |
| Δ6MWD at 3 months, m | 52 | 40 |
| mPAP, mmHg | 49 | 54 |
| Cardiac index, L/min/m$^2$ | 2.1 | 2.1 |
| PVRI, WU·m$^2$ | 21 | 23 |
| 1 year survival | 74% | 93% |
| 3 year survival | 45% | 73% |

**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.

**372**
**Hepatopulmonary syndrome: Long-term survival in the Mayo Clinic experience**
Vivek Iyer, Karen Swanson, Rodrigo Cartin-ceba, Michael Krowka. *Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, United States*

**Introduction:** Hepatopulmonary syndrome (HPS) is an uncommon pulmonary vascular disorder occurring in advanced liver disease, characterized by hypoxemia due to intrapulmonary vascular dilatations. Liver transplantation (LT) improves survival in HPS. We present the largest consecutive series of HPS patients specifically addressing long-term survival relative to the degree of pre-LT hypoxemia.
**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 $Pa0_2$ 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.




**Conclusion:** Long-term outcome after LT in HPS is favorable. The survival patterns from the time of LT were not influenced by pre-LT $PaO_2$. 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**
Henning Tiede[1], Janine Felix[2], Ewout Steyerberg[2], Martin Wilkins[3], Oscar Franco[2], Jacqueline Witteman[2], Werner Seeger[1], Friedrich Grimminger[1], Ardeschir Ghofrani[1]. *[1]University of Giessen Lung Center, University Hospital, Giessen, Germany; [2]Cardiovascular Epidemilogy, Erasmus MC, University Medical Center, Rotterdam, Netherlands; [3]Experimental Medicine, Imperial College, London, United Kingdom*

**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 etiological 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, N=685) 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 89.2%, 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.