ISHLT LUNG TRANSPLANTATION. November 2020
JOURNAL WATCH

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Hoeper MM et al. Idiopathic pulmonary arterial hypertension phenotypes determined by cluster analysis from the COMPERA registry

J Heart Lung Transplant. 2020 September 29; DOI:https://doi.org/10.1016/j.healun.2020.09.011

STUDY HIGHLIGHTS

Background: IPAH is characterized by pre-capillary PH of unknown origin. There is considerable variability in the clinical presentation.

Objective: Cluster analysis of large patient cohort from the COMPERA registry to identify clinical phenotypes of adult patients with IPAH.

Design: Prospective registry analysis (Clinicaltrials.gov identifier NCT01347216). 841 treatment naïve IPAH patients. Hierarchical agglomerative clustering analysis using baseline parameters of age, sex, DLCO, smoking status, and comorbidities/risk factors for left heart disease (obesity, hypertension, coronary heart disease, diabetes mellitus).

Outcomes: survival, treatment response (functional class, change in 6MWD and BNP/NT-proBNP).

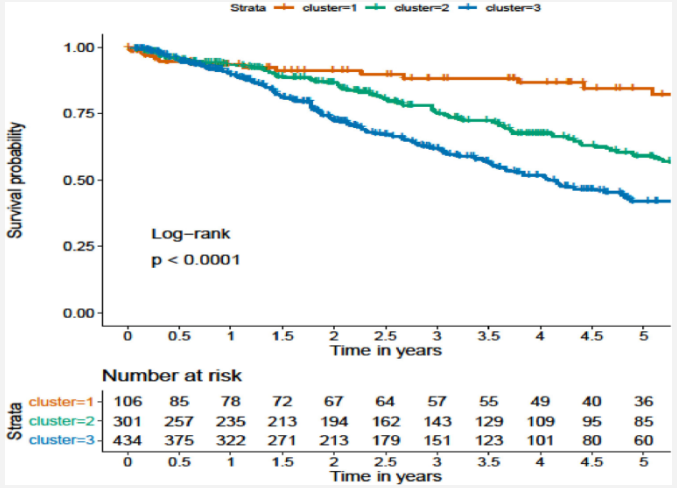
Three clusters were identified:

Cluster 1: 106 (12.6%) patients, median age 45 years, 76% female, 31% with smoking history, no comorbidities, all with DLCO ≥45% pred.

Cluster 2: 301 (35.8%) patients, median age 75 years, 98% female, 0% with smoking history, 94% with at least 1 co-morbidity. 34% with DLCO <45% pred.

Cluster 3: 434 (51.6%) patients, median age 72 years, 72% male, 79% with smoking history (median: 33 pack years), 91% with at least 1 comorbidity. 53% with DLCO <45% pred.

Factors differentiating Cluster 3 from Cluster 2: increased frequency of male sex, smoking history and DLCO <45% (cardiopulmonary phenotype)



Results:

Cluster 1 had a better response to PAH treatment than the other clusters.

5 year survival was 84.6% in Cluster 1, 59.2% in Cluster 2, and 42.2% in Cluster 3 ($p < 0.001$).

Adjusted for age, the survival differences between Clusters 1 and 3 and Clusters 2 and 3 remained significant

Limitations

- Enrollment/selection bias
- Incomplete datasets
- Variables of interest selected in advance, necessitating a degree of assumption.
- The number of variables considered in this cluster analysis was relatively low.

Reviewer comments:

Whilst IPAH phenotypes may differ in clinical presentation, response to therapy, and survival, poor survival in cluster 2 and 3 may also reflect the impact of age and comorbidities, which are well established risk factors for poor survival in PAH.

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DesJardin et al., Age-related differences in hemodynamics and functional status in pulmonary arterial hypertension: Baseline results from the Pulmonary Arterial Hypertension Association Registry.

J Heart Lung Transplant. 2020 Sept;39(9):945-953.

STUDY HIGHLIGHTS

Question: What is the relationship between age and hemodynamic and functional assessment in PAH?

Design: Retrospective analysis of PAH patients in the Pulmonary Hypertension Association Registry

Inclusion: 769 PAH patients age ≥18 were included. Patients with CTEPH, persistent PH of the newborn, and PH due to congenital heart disease were excluded.

Outcomes: Hemodynamic profile and functional risk assessment in different age groups

Results: Older patients had more CTD-PAH and less drug induced-PAH. Increased age was associated with reduced 6MWD and lower mPAP. Pulmonary arterial compliance (PAC), cardiac index, RV stroke work index, and % predicted 6MWD were unrelated to age. Relative to their PVR, older patients had lower PAC and worse RV performance.

CENTRAL FIGURES

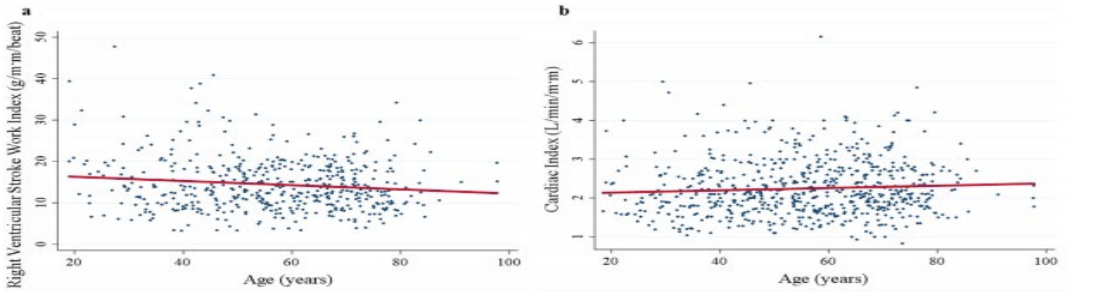

Figure 2 Changes in baseline right ventricular function by age. **(a)** Age and right ventricular stroke work index. **(b)** Age and cardiac index.

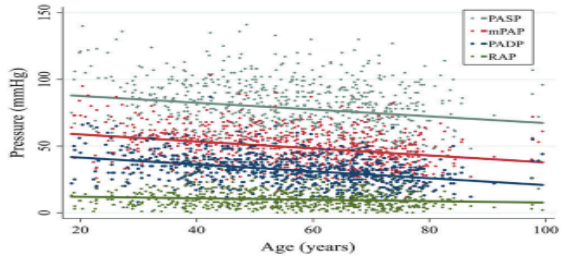

Figure 3 Changes in baseline pulmonary artery and right atrial pressures by age. mPAP, mean pulmonary artery pressure; PADP, pulmonary artery diastolic pressure; PASP, pulmonary artery systolic pressure; RAP, right atrial pressure.

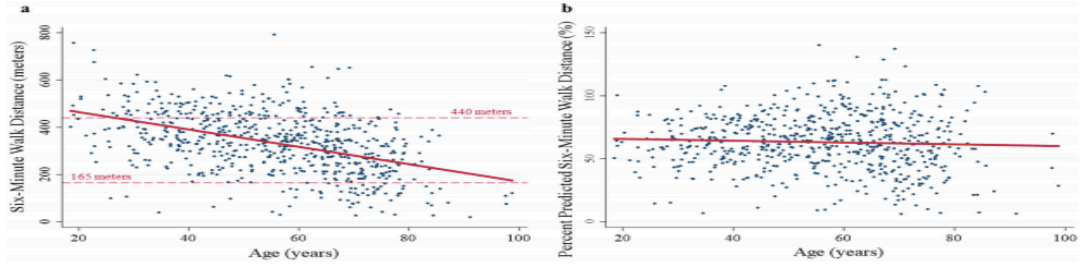

Figure 4 Changes in 6-minute walk distance by age. **(a)** Age and absolute 6-minute walk distance. **(b)** Age and percent predicted 6-minute walk distance.

REVIEWER'S COMMENTS

- In tracing the relationship between pulmonary arterial compliance and age, it is unclear which parameter in pulmonary arterial compliance calculation accounted for lack of variation with age.
- Factors that affect the RV ability to condition to increased afterload need to be considered.
- Relationship between functional measures and age is confounded by factors other than PAH.

Limitations:

- Important data on patients' comorbid conditions and PAH therapy was not presented.

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Yogeswaran A et al. Risk assessment in severe pulmonary hypertension due to interstitial lung disease.

J Heart Lung Transplant. 2020 Oct;39(10):1118-1125.

STUDY HIGHLIGHTS

Question: What is the prognostic value of a truncated version of the European Society of Cardiology/European Respiratory Society (ESC/ERS) pulmonary hypertension (PH) risk stratification scheme in severe PH with interstitial lung disease (ILD)?

Design: Retrospective single center study

Inclusion: All ILD patients who were referred for invasive diagnostic workup of suspected severe PH

Outcomes: Transplant (Tx) free survival, stratified by risk grade

Results: 5-year Tx-free survival of low, intermediate and high-risk patients was 43%, 15%, 4% (*P*=0.01) respectively.

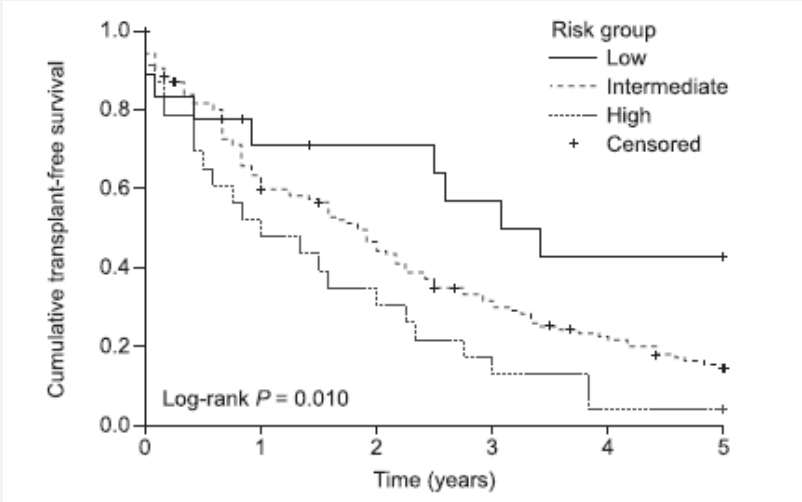
CENTRAL FIGURES

Table 1 Variables and Thresholds Included in the Risk Stratification Scheme Used in This Study (8 of 12 Parameters From the ESC/ERS Scheme[2])

Risk stratification parameter	Low risk (Grade 1)	Intermediate risk (Grade 2)	High risk (Grade 3)
WHO functional class	I, II	III	IV
6MWD, m	>440	165–440	<165
BNP, ng/liter	<50	50–300	>300
RA area, cm^2	<18	18–26	>26
Pericardial effusion	No	No or minimal	Yes
RA pressure, mm Hg	<8	8–14	>14
Cardiac index, liter/min/m^2	≥2.5	2.0–2.4	<2.0
SvO_2, %	>65	60–65	<60

Abbreviations: 6MWD, 6-minute walk distance; BNP, brain natriuretic peptide; ESC/ERS, European Society of Cardiology/European Respiratory Society; RA, right atrial; SvO_2, mixed venous oxygen saturation; WHO, World Health Organization.

Risk stratification scheme is clinically relevant for prediction of Tx-free survival in patients with severe PH due to ILD



REVIEWER'S COMMENTS

- A major strength is the inclusion of all ILD patients (not just IPF, IIP)
- Mean (±SD) mPAP was 42 (±8)
- Tx was an infrequent outcome (only 5%)
- DLCO was not associated with increased mortality in severe PH with ILD, hence outcomes may have been driven primarily by RV function
- Role of PAH specific therapies remains unclear

Limitations:

- Retrospective single center analysis
- Possibility of selection and enrollment bias