Pulmonary Hypertension in Interstitial Lung Disease

Richard Wells

Objectives

- Prevalence of pulmonary hypertension (PH) in interstitial lung disease (ILD)
- Pathogenesis of PH in ILD
- Predictive factors and clinical implications of PH in ILD
- Treatment and role of advanced therapies in PH associated with ILD

Interstitial Lung Disease

- Comprises a heterogeneous group of disease with restrictive physiology and impaired gas exchange

- Pulmonary hypertension (PH)in this setting is designated group 3 based on Dana Point 2008 PH classification

Interstitial Lung Disease

- PH in ILD causes dyspnea, fatigue and exercise limitation
- Significant symptom overlap with ILD symptoms
- PH may be missed in ILD until signs of right heart failure develop

Definition of PH in ILD

- Presence of PH in an ILD patient without an alternative cause
- PH is defined as a mean PAP (mPAP) of ≥25mmHg at rest
- PH is considered severe when mPAP ≥25mmHg with cardiac index <2L/min/m^2 or if mPAP≥35mmHg

Prevalence of PH in ILD

- Actual prevalence is uncertain

- Depends on the type of ILD, the differences in patient populations, modality used to detect PH

Behr J and Ryu JH. Pulmonary hypertension in interstitial lung disease. European Respiratory Journal 2008; 31(6): 1357-1367

Caminati A, Cassandro R and Harari A. Pulmonary Hypertension in chronic interstitial lung disease. European Respiratory Review 2013; 22: 292-301

Prevalence of PH in ILD

- Idiopathic pulmonary fibrosis
  - Nathan et al in 2008 retrospective cohort of 44 patients with RHC data on initial transplant evaluation
  - 38.6% had PH at baseline
  - During follow up the majority of non-PH patients developed PH → incidence of 77.8%
  - Overall prevalence of 86.4% at the time of transplant

Nathan et al. Serial development of pulmonary hypertension in patients with idiopathic pulmonary fibrosis. Respiration 2008; 76(3): 288-94.

Prevalence of PH in ILD

- Idiopathic pulmonary fibrosis
  - In 79 IPF patients studied retrospectively 31.6% met criteria for PH
  - >2000 IPF patients on the UNOS registry, the prevalence of PH was around 25%

Lettieri CJ et al. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. Chest 2006; 129: 746-752

Prevalence of PH in ILD

- Sarcoidosis
  - Prospective study in 246 sarcoidosis patients the frequency was 5.7% based on PASP>40mmHg by doppler ultrasound

Handa T et al. Incidence of pulmonary hypertension and its clinical relevance in patients with sarcoidosis. Chest 2006; 129: 1246-1252

Prevalence of PH in ILD

- Connective tissue disease (CTD) with ILD
  - 5-38% of patients with systemic sclerosis
  - 4.3-43% of patients with SLE
  - 21 % patients with rheumatoid arthritis

- PH in CTD can also be due to:
  - group 1 pulmonary arteriopathy
  - group 2 cardiac disease

Lettieri CJ et al. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. Chest 2006; 129: 746-752

Pathogenesis of PH in ILD

- Normally
  - Pulmonary hypertension develops under conditions of global hypoxia that cause widespread pulmonary vasoconstriction
  - Additionally there are ablative changes to the pulmonary vasculature secondary to fibrosis that contribute PH
  - PH here is an adaptive/secondary phenomenon

Pathogenesis of PH in ILD

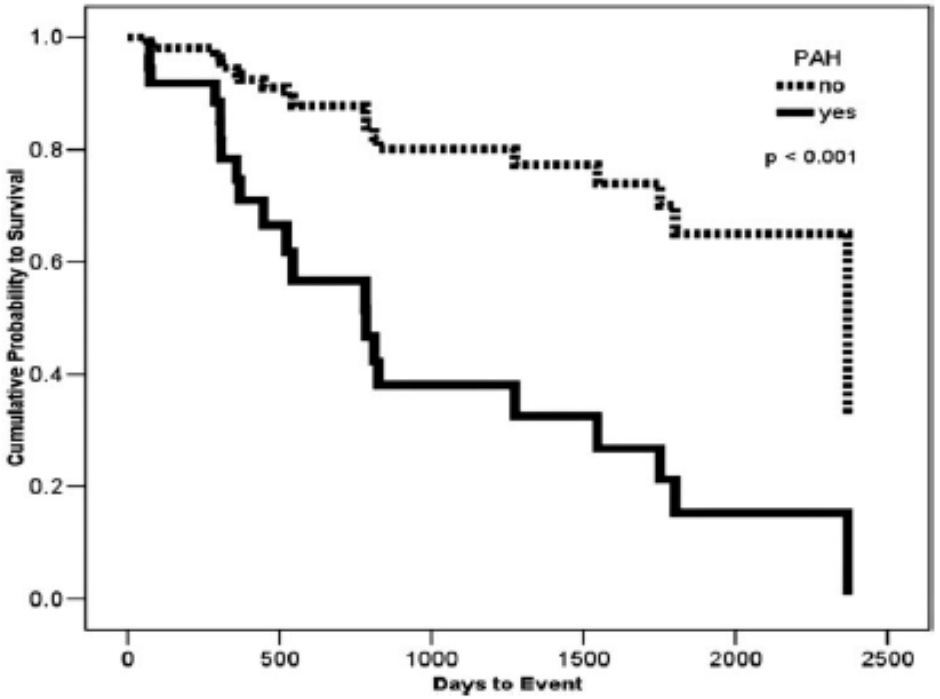
- "Disproportionate PH in ILD"
- Not just hypoxemia and fibrosis
- Derangement in the balance of angiogenesis and pro-fibrotic mediators drives PH
- Disproportionate PH suggests a role for pulmonary vasodilators

Nathan SD and King CS. Treatment of pulmonary hypertension in idiopathic pulmonary fibrosis: shortfall in efficacy or trial design? Drug Design, Development and Therapy 2014; 8: 875-885

Pulmonary Hypertension in Interstitial Lung Disease

- Most data about PH in ILD comes from IPF studies
- Unclear how much IPF data can be applied to other ILDs
- Additionally clinical studies of PH in IPF typically involve lung transplant patients who are typically younger, have few comorbidities and more severe ILD

Mortality in IPF with PH



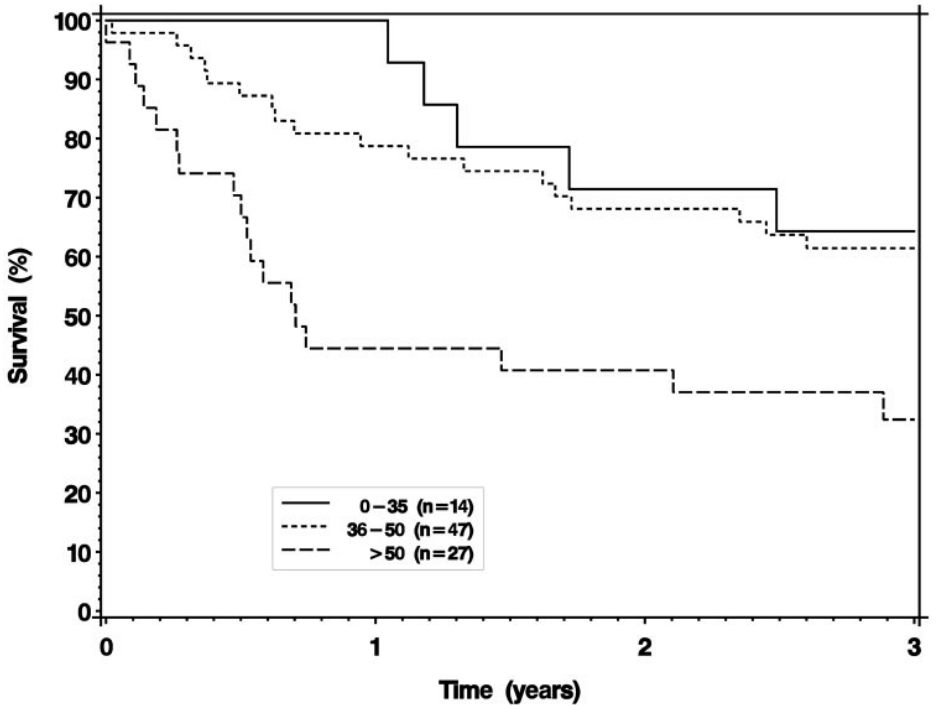


FIGURE 2. PAH as a predictor of survival in patients with IPF.

- PH is a significant predictor of mortality in IPF
- 1 year mortality of 28% with PH versus 5.5% without PH

Lettieri CJ et al. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. Chest 2006; 129: 746-752

Nadrous HF et al. Pylmonary hypertension in patients with idiopathic pulmonary fibrosis. Chest 2005; 128(4):2393-2399

PH in IPF

- Are there any clinical indices that are less invasive to obtain that may aid diagnosis, inform decisions and determine prognosis in IPF associated PH?

Echocardiography

Echocardiography in PH associated with IPF

- Echocardiography is a useful diagnostic tool for studying pulmonary hypertension

- Not a perfect test

Echocardiography in PH associated with IPF

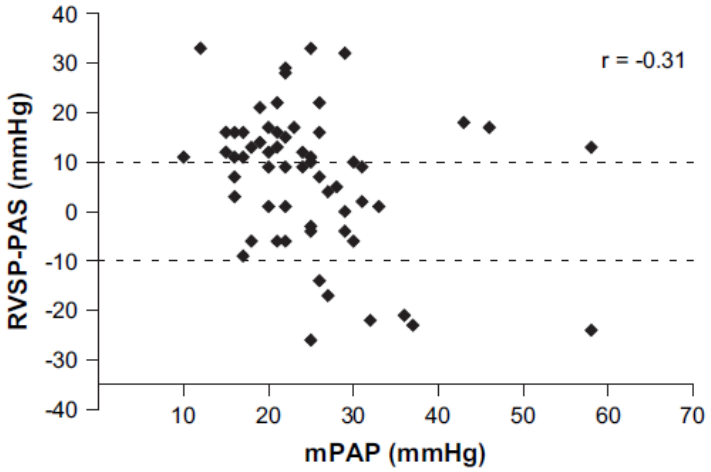
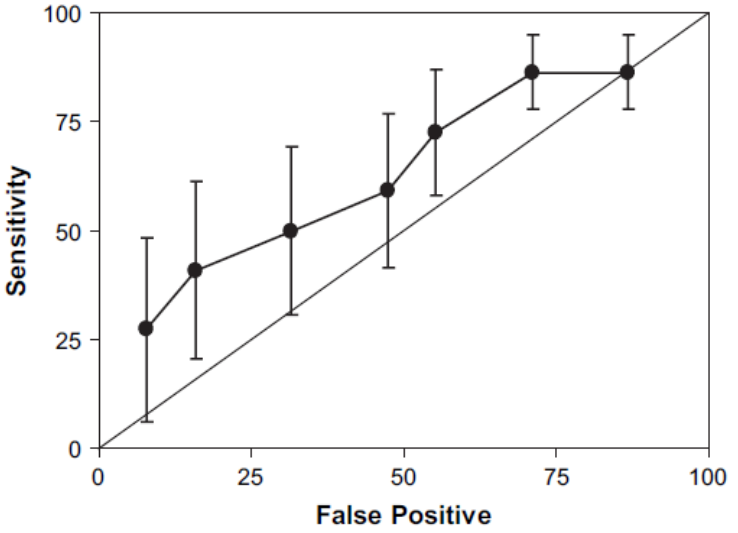


Figure 2 Accuracy of the $RVSP_{echo}$ compared to the $PASP_{cath}$ pressure as measured by right-heart catheterization in relation to the mean PAP.



$RVSP_{echo}$ (mmHg)	Diagnostic and 95% CI Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
$RVSP_{echo}$ > 30	86.4 (69.8-95.0)	13.2 (3.3-30.9)	34.4	64.8
$RVSP_{echo}$ > 35	86.4 (69.8-95.0)	28.9 (14.1-47.8)	39.0	80.1
$RVSP_{echo}$ > 40	72.7 (51.6-87.1)	44.7 (26.7-63.0)	40.9	75.7
$RVSP_{echo}$ > 45	59.1 (38.7-76.8)	52.6 (33.5-69.8)	39.6	70.9
$RVSP_{echo}$ > 50	50.0 (30.7-69.3)	68.4 (48.3-82.9)	45.5	72.0
$RVSP_{echo}$ > 55	40.9 (23.2-61.3)	84.2 (60.4-91.6)	57.7	73.0
$RVSP_{echo}$ > 60	27.3 (12.9-48.4)	92.1 (73.9-98.9)	64.5	70.6

Figure 3 Diagnostic accuracy of incremental thresholds of the $RVSP_{echo}$ for the detection of PH in IPF depicted as a receiver operator characteristic curve.

Nathan SD et al. Right ventricular systolic pressure by echocardiography as a predictor of pulmonary hypertension in idiopathic pulmonary fibrosis. Respiratory Medicine 2008; 102: 1305-1310

Echocardiography in PH associated with IPF

- RVSP overestimated $PASP_{cath}$ in 48.3% and underestimated in $PASP_{cath}$ in 11.8% of cases

- Positive predictive value of RVSP can be improved when combined with PFT and 6MWT data

Nathan SD et al. Right ventricular systolic pressure by echocardiography as a predictor of pulmonary hypertension in idiopathic pulmonary fibrosis. Respiratory Medicine 2008; 102: 1305-1310

Echocardiography in PH associated with IPF

- Cohort of 374 lung transplant candidates
- Comparing echo to RHC
- Echo overestimated PASP by more than 10mmHg in 52% of cases

Arcasoy et al. Echocardiographic assessment of pulmonary hypertension in patients with advanced lung disease. Am J of Resp and Crit Care Medicine 2003; 167(5): 735-740

Echocardiography in PH associated with IPF

- Other echo measures are useful to identify PH-related abnormalities
  - RA enlargement
  - RV enlargement
  - Right ventricular dysfunction

Echocardiography in PH associated with IPF

- Rivera-Lebron et al in 2013
- Retrospective cohort of 135 IPF patients receiving RHC and TTE each within 24 hours of each other
- 29% had PH (mean mPAP 31+/- 6mmHg)

Rivera-Lebron B et al. Echocardiographic and hemodynamic predictors of mortality in idiopathic pulmonary fibrosis. Chest 2013; 144(2): 564-570

Echocardiography in PH associated with IPF

Table 3—*Cox Proportional Hazards Models for RV Echocardiographic Predictors of Mortality*

	Unadjusted Model			Adjusted Model[a]			Censored at Lung Transplantation[b]		
Variable	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
RV:LV	3.8	1.5-9.7	.006	4.5	1.7-11.9	.003	5.6	1.6-19.8	.008
TAPSE < 1.6 cm	2.0	1.0-3.7	.05	1.9	1.0-3.7	.06	1.5	.7-3.5	.31
TAPSE (continuous)	.7	.4-1.2	.22	.8	.5-1.5	.56	.8	.3-2.1	.60
Moderate to severe RA dilation	2.4	1.2-4.7	.009	2.9	1.4-5.9	.004	3.0	1.2-7.8	.02
Moderate to severe RV dilation	2.6	1.4-4.6	.001	2.7	1.4-5.4	.004	3.2	1.4-7.8	.008
Moderate to severe RV dysfunction	4.9	2.5-9.6	< .001	5.5	2.6-11.5	< .001	7.5	2.7-20.8	< .001
RVSP, for 5 mm Hg increase	1.1	1.1-1.2	< .001	1.2	1.1-1.3	< .001	1.2	1.1-1.4	.002
RVOT VTI	.9	.9-1.0	.16	.9	.9-1.0	.17	.8	.7-1.0	.01
RVOT AT	1.0	.9-1.0	.46	1.0	.9-1.0	.64	1.0	.9-1.0	.11
Notching of RVOT	1.4	.8-2.3	.27	1.4	.8-2.4	.25	2.4	1.0-5.4	.05

HR = hazard ratio. See Table 2 legend for expansion of other abbreviations.

[a]Adjusted for age, sex, race/ethnicity, height, weight, FVC and transplant status.

[b]Adjusted for age, sex, race/ethnicity, height, weight, FVC.

Rivera-Lebron B et al. Echocardiographic and hemodynamic predictors of mortality in idiopathic pulmonary fibrosis. Chest 2013; 144(2): 564-570

Pulmonary Function Tests

PFT in PH associated with IPF

Table 3—*Baseline Pulmonary Function Data by SPAP Subgroups**

Characteristics	SPAP ≤ 35 mm Hg (n = 14) No.	SPAP ≤ 35 mm Hg (n = 14) Mean ± SD (Median, Range)	SPAP > 35 to ≤ 50 mm Hg (n = 47) No.	SPAP > 35 to ≤ 50 mm Hg (n = 47) Mean ± SD (Median, Range)	SPAP > 50 mm Hg (n = 27) No.	SPAP > 50 mm Hg (n = 27) Mean ± SD (Median, Range)	p Value†
FVC, % predicted	14	72.3 ± 15.2 (72.0, 52.2–109.6)	36	63.5 ± 15.1 (60.7, 35.1–95.4)	22	68.0 ± 20.2 (68.2, 34.2–113.3)	0.229
D_{LCO}, % predicted	11	53.9 ± 16.5 (53.5, 27.2–79.1)	36	54.3 ± 15.8 (52.6, 32.7–100.5)	20	38.8 ± 12.3 (38.0, 17.8–60.4)	0.002
FEV_1, % predicted	14	77.1 ± 14.9 (77.5, 59.4–115.0)	36	67.0 ± 16.5 (61.4, 35.4–103.6)	22	65.8 ± 17.9 (69.5, 29.1–91.4)	0.151
Oxygen saturation at rest, %	7	93.9 ± 1.8 (94.0, 91.0–96.0)	24	93.3 ± 1.9 (93.0, 90.0–97.0)	17	91.6 ± 3.4 (93.0, 84.0–95.0)	0.211
Oxygen saturation with exercise, %	7	87.4 ± 6.2 (90.0, 74.0–92.0)	24	85.3 ± 5.6 (86.0, 75.0–97.0)	13	84.8 ± 6.8 (86.0, 67.0–92.0)	0.360
PaO_2 at rest, mm Hg	8	74.9 ± 9.1 (75.5, 57.0–85.0)	34	74.2 ± 11.5 (74.0, 47.0–96.0)	15	62.1 ± 14.3 (60.0, 42.0–93.0)	0.013
$PaCO_2$ at rest, mm Hg	8	36.1 ± 3.2 (36.2, 31.0–40.0)	34	36.5 ± 3.3 (36.0, 30.0–46.0)	15	34.3 ± 5.6 (36.0, 20.0–40.0)	0.655
Alveolar-arterial oxygen gradient at rest	8	23.9 ± 12.3 (25.0, 11.0–45.0)	34	24.0 ± 11.6 (23.5, 5.0–56.0)	13	34.4 ± 14.0 (38.0, 7.0–55.0)	0.076

*Percentages may not total 100 due to rounding.
†Kruskal-Wallis test.

- Patients with SPAP>50mmHg had more impaired DLCO and PaO2
- FEV1, FVC and FEV1/FVC ratio had no correlation with SPAP

Nadrous HF et al. Pulmonary hypertension in patients with idiopathic pulmonary fibrosis. Chest 2005; 128(4):2393-2399

PFT in PH associated with IPF

Table 1—*Patient Characteristics Based on the Presence or Absence of PAH

Characteristics	MAP ≤ 25 mm Hg (n = 54)	MAP > 25 mm Hg (n = 25)	p Value
Age, yr	56.2 ± 1.0	54.7 ± 3.8	0.27
Male gender, %	72.2	64.0	0.23
Supplemental oxygen, %	17.6	66.7	< 0.001
FVC, % predicted	52.5 ± 11.9	49.3 ± 11.0	0.13
TLC, % predicted	55.5 ± 10.7	57.8 ± 12.1	0.27
DLCO, % predicted	37.6 ± 11.3	31.1 ± 10.1	0.04
mPAP, mm Hg	19.1 ± 3.7	29.5 ± 3.3	n/a
RAP, mm Hg	4.3 ± 2.8	5.3 ± 3.5	0.14
Cardiac index, L/min/m^2	2.8 ± 0.4	3.2 ± 1.3	0.20
PAWP, mm Hg	8.4 ± 3.5	9.3 ± 3.5	0.22
Ejection fraction, %	61.5 ± 5.9	59.4 ± 5.0	0.12
Mortality rate, %	29.9	60.0	0.001
1-yr mortality rate, %	5.5	28.8	0.002

*Values are given as the mean ± SD, unless otherwise indicated. RAP = right atrial pressure; MAP = mean arterial pressure.

- The presence of RHC diagnosed PH correlated with an impaired DLCO and need for supplemental oxygen

Lettieri CJ et al. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. Chest 2006; 129: 746-752

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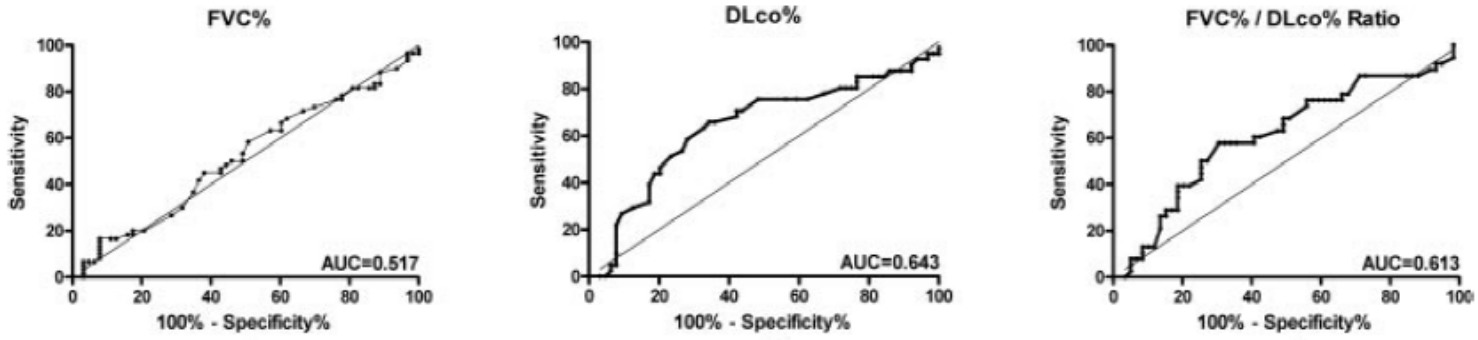
*Values are given as the mean ± SD, unless otherwise indicated. RAP = right atrial pressure; MAP = mean arterial pressure.

- Measures of restrictive lung disease fail to correlate with the presence of PH in IPF

Lettieri CJ et al. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. Chest 2006; 129: 746-752

PFT in PH associated with IPF



FVC range	Sens	Spec
< 70%	79.2	8.6
< 60%	64.6	35.7
< 50%	43.7	54.3
< 40%	16.7	20.0
< 30%	0.0	100.0

DLco range	Sens	Spec
< 50%	85.4	16.4
< 40%	75.7	34.4
< 30%	53.7	72.1
< 20%	19.6	91.8
< 10%	0.0	100.0

FVC% / DLco%	Sens	Spec
> 3.0	12.2	91.8
> 2.0	43.9	73.8
> 1.5	75.6	55.7
> 1.0	92.7	4.9
> 0.5	100.0	0.0

FIGURE 2. ROCs of FVC% (*left*, *A*), DLCO% (*center*, *B*), and FVC%/DLCO% ratio (*right*, *C*). Sens = sensitivity; Spec = specificity; AUC = area under the curve.

- Retrospective study of 118 patients with IPF of whom 48% had RHC-confirmed PH
- Again showed a correlation of DLCO with presence of PH
- FVC/DLCO performed less well than DLCO alone
- FVC was not predictive

Nathan S D et al. Pulmonary hypertension and pulmonary function testing in idiopathic pulmonary fibrosis. Chest 2007: 657-663.

Six Minute Walk Test

PFT in PH associated with IPF

Table 2—*6MWT Measurements Between Those With and Without PAH

Variables	MAP ≤ 25 mm Hg (n = 10)	MAP > 25 mm Hg (n = 24)	p Value
MPAP, mm Hg	18.2 ± 3.6	29.8 ± 5.1	NA
6MWT distance, m	365.9 ± 81.8	143.5 ± 65.5	< 0.001
Spo_2 nadir on 6MWT, %	88.0 ± 3.5	80.1 ± 3.7	< 0.001
Mortality rate, %	37.5	70.0	0.003

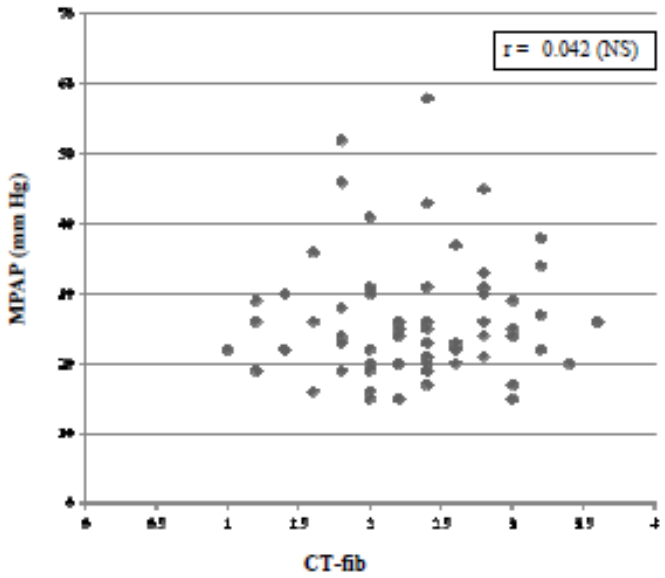
*Values are given as the mean ± SD, unless otherwise indicated. NA = not applicable.

- The presence of PH in IPF correlates with 6 minute walk distance and nadir desaturation

Lettieri CJ et al. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. Chest 2006; 129: 746-752

Radiographic Findings

CT Findings in PH with associated IPF



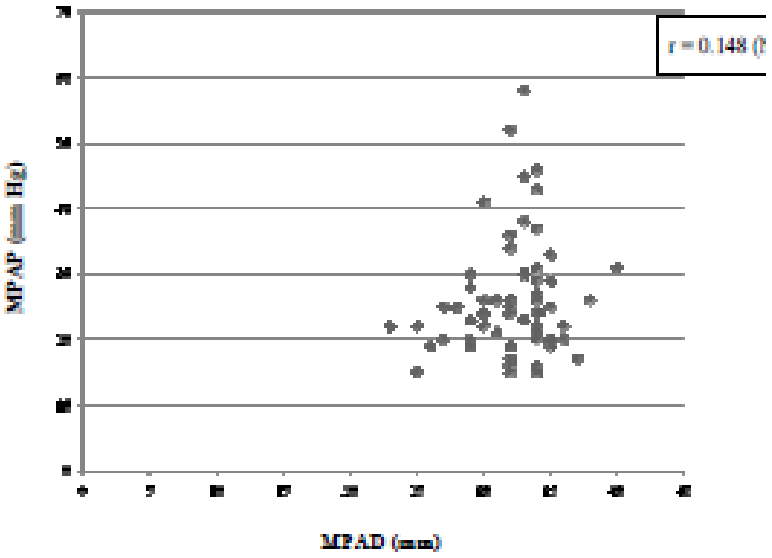


FIGURE 1. Relationship between CT-fib and measured MPAP. NS = not significant.

- No relationship between the presence of PH in IPF
  - Chest CT-determined fibrosis score
  - Ground-glass opacity score
  - Diameter of the main pulmonary artery
  - Ratio of the pulmonary artery to aorta diameter

Zisman D A et al. High-resolution chest CT findings do not predict the presence of pulmonary hypertension in advanced idiopathic pulmonary fibrosis. Chest 2007; 132(3): 773-779

Treatment of PH in ILD

- Therapy for the underlying ILD if possible
- Supplemental O_2 for exercise and resting hypoxemia
- Diuretic therapy

Treatment of PH in ILD

- Listing for lung transplantation
  - Decline in FVC≥10% during 6 months of follow up
  - Decline in DLCO≥15% in 6 months follow up
  - Desaturation to <88% or distance <250m on 6 minute walk test or >50m decline in 6 minute walk distance over 6 month period
  - **Pulmonary hypertension on RHC or 2D echocardiography**
  - Hospitalization because of respiratory decline, pneumothorax or acute exacerbation

Weill D et al. A consensus document for the selection of lung transplant candidates: 2014 – An update from the Pulmonary Transplantation Council of the International Society for Heart and lung Transplantation. Journal of Heart and lung Transplantation 2015; 34(1): 650-656

Treatment of PH in ILD

- Advanced therapies – vasoactive agents
  - ILD patients have not been systematically assessed in studies of pulmonary vasoactive agents
  - Potential for harm from worsened VQ mismatch

Treatment of PH in ILD

ORIGINAL ARTICLE

A Controlled Trial of Sildenafil in Advanced Idiopathic Pulmonary Fibrosis

The Idiopathic Pulmonary Fibrosis Clinical Research Network*

- IPF with DLCO<35% (**no echo or RHC data reported**)
- DB-RCT of 12 weeks of sildenafil (n-89) versus placebo (n-91)
- No effect on 1° outcome of 20% improvement of 6 minute walk distance
- Secondary outcomes including QOL, DLCO and PaO_2 favored treatment arm

The Idiopathic Pulmonary Fibrosis Clinical Research Network. A controlled trial of sildenafil in advanced idiopathic pulmonary fibrosis. NEJM 2010; 363(7): 620-628

Treatment of PH in ILD

Sildenafil Preserves Exercise Capacity in Patients With Idiopathic Pulmonary Fibrosis and Right-sided Ventricular Dysfunction

*MeiLan K. Han, MD; David S. Bach, MD; Peter G. Hagan, MD; Eric Yow, MS; Kevin R. Flaherty, MD, FCCP; Galen B. Toews, MD; Kevin J. Anstrom, PhD; and Fernando J. Martinez, MD, FCCP; for the IPFnet Investigators**

- STEP-IPF Subgroup: RV dysfunction on TTE on sildenafil had a favorable effect on 6min walk distance at 12 weeks compared to placebo

Han MK et al. Sildenafil preserves exercise capacity in patients with idiopathic pulmonary fibrosis and right-sided ventricular dysfunction. Chest 2013; 143(6): 1699-1708

Treatment of PH in ILD

- Endothelin receptor antagonists have been studied

- Primarily, the anti-fibrotic effects of ERAs in IPF and not necessarily the effects on PH

Treatment of PH in ILD

BUILD-3: A Randomized, Controlled Trial of Bosentan in Idiopathic Pulmonary Fibrosis

Talmadge E. King, Jr.[1], Kevin K. Brown[2], Ganesh Raghu[3], Roland M. du Bois[4], David A. Lynch[5], Fernando Martinez[6], Dominique Valeyre[7], Isabelle Leconte[8], Adele Morganti[8], Sébastien Roux[8], and Juergen Behr[9]

[1]Department of Medicine, University of California San Francisco, San Francisco, California; [2]Department of Medicine; [5]Division of Radiology, National Jewish Health, Denver, Colorado; [3]Division of Pulmonary and Critical Care Medicine, University of Washington, Seattle, Washington; [4]Imperial College, London, United Kingdom; [6]Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor, Michigan; [7]Department of Pneumology, Avicenne Hospital, University of Paris, Bobigny, France; [8]Clinical Development, Actelion Pharmaceuticals Ltd, Allschwil, Switzerland; and [9]Department of Respiratory and Critical Care Medicine, Ruhr-University, Bochum, Germany

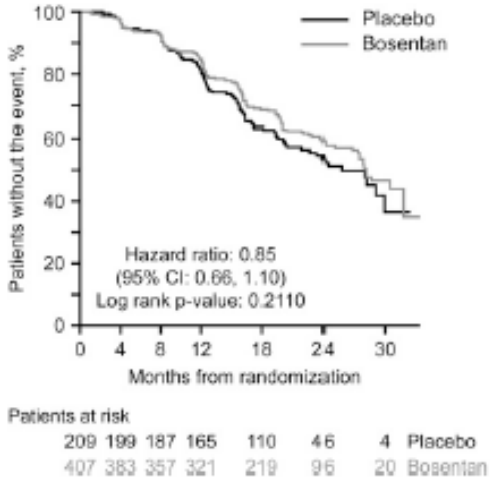


Figure 4. Kaplan–Meier survival estimate for each treatment group. CI = confidence interval.

- DB-RCT
- 616 IPF patients with no reported PH indices
- No effect on time to clinical worsening or all cause mortality

Talmadge et al. BUILD-3: A randomized controlled trial of bosentan in idiopathic pulmonary fibrosis. Am Journal of Respiratory and Critical Care Medicine 2011; 184(1): 92-99.

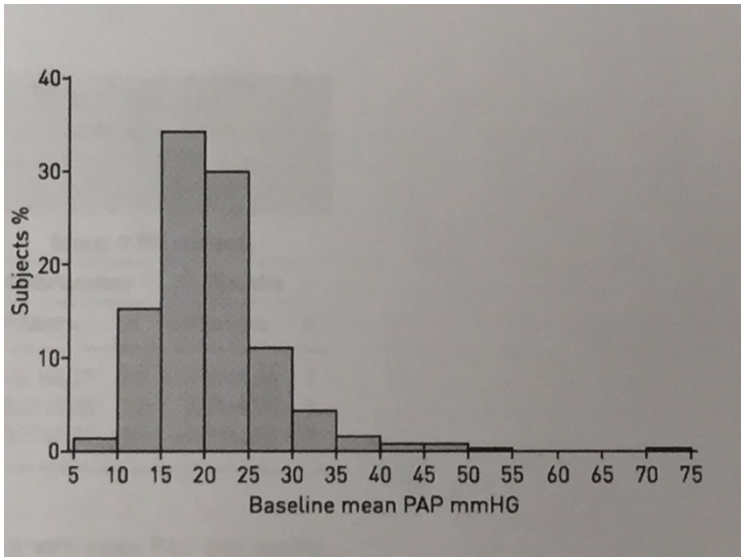
Treatment of PH in ILD

- Artemis-IPF looked at ambrisentan in IPF but stopped early due to a lack of efficacy and evidence of harm
- Artemis-PH geared toward IPF patients with RHC-diagnosed PH
  - Also stopped early
  - Difficulty with recruiting patients with a confident diagnosis of IPF and associated PH
  - Evidence of a lack of efficacy from the PH subgroup (mPAP≥25) of Artemis-IPF
    - Over 48 weeks on ambrisentan no statistically significant differences in hemodynamic parameters on repeat RHC
    - Baseline mean mPAP 29.6 +/-7.53

Raghu, G et al. Pulmonary hypertension in idiopathic pulmonary fibrosis with mild-to-moderate restriction. European Respiratory Journal 2014; Epub ahead of print

Treatment of PH in ILD

- In IPF, PH is usually mild
- Does not require PAH meds



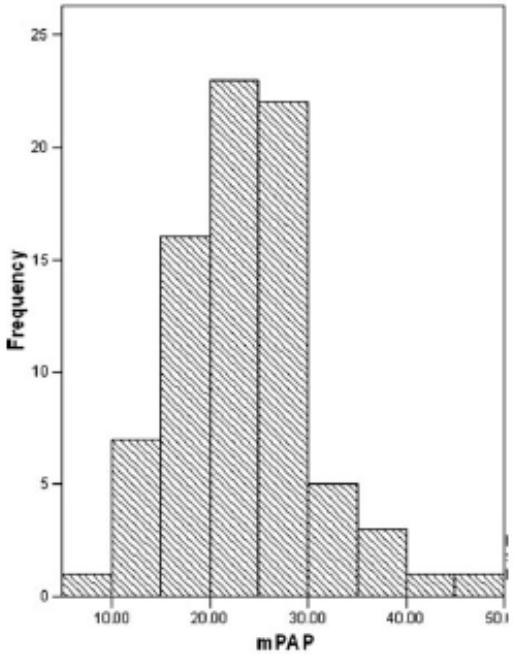


FIGURE 1. mPAP values. Histogram displaying the distribution of mPAPs among the cohort (values expressed in mm Hg). mPAP = mean pulmonary arterial pressure

Lettieri CJ et al. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. Chest 2006; 129: 746-752

Raghu, G et al. Pulmonary hypertension in idiopathic pulmonary fibrosis with mild-to-moderate restriction. European Respiratory Journal 2014; Epub ahead of print

Treatment of PH in ILD

- Severe disproportionate PH is rare, is a different disease that may respond to PAH medications

Adir Y abd Sergio H. Pulmonary hypertension associated with chronic obstructive lung disease and idiopathic fibrosis. Current Opinion in Pulmonary Medicine 2014; 20(5): 414-420

Treatment of PH in ILD

- Disproportionate PH in ILD
  - Is the patient suffering from ILD with resultant disproportionate PH or from PAH with concomitant non-causative ILD?

Treatment of PH in ILD

- Disproportionate PH in ILD

Table 2
Criteria for the presence of severe pulmonary hypertension in patients with chronic lung disease*.

At least 2 of the following criteria must be met:
1. Mean PA pressure (PAPm) >35 mmHg
2. PAPm ≥25 mmHg with limited cardiac output (CI <2.0 l/min/m^2)
3. Pulmonary vascular resistance (PVR) >480 dyn s cm^{-5}

*As a rule, these criteria only apply if other causes of PH (e.g. chronic thromboembolic PH or left ventricular failure) have been excluded.

Hoeper et al. Pulmonary hypertension due to chronic lung disease: updated recommendations of the Cologne Consensus Conference 2011. International Journal of Cardiology 2011; 154S: S45-S53

Treatment of PH in ILD

- Prescribed vasoactive PAH drugs when
  - Invasive assessment and the aforementioned criteria were met
  - Mild to moderate severity in ventilatory limitation (TLC>60%)
  - Rule out left heart disease and CTEPH
- Treat for 3-6 months and re-assess efficacy and justification to continue

Hoeper et al. Pulmonary hypertension due to chronic lung disease: updated recommendations of the Cologne Consensus Conference 2011. International Journal of Cardiology 2011; 154S: S45-S53

Treatment of PH in ILD

5th World Symposium on PH 2013 – Expert Guideline – Management of PH in Chronic Lung Disease

Degree of ventilatory impairment	mPAP <25 at rest	mPAP ≥25 and <35 at rest	mPAP≥35 at rest
IPF FVC≥70%	No PH No PAH treatment	PH classification uncertain No data to support treatment with PAH drugs	Differentiate disproportionate PH from PAH with concomitant non-causative ILD Referral to expert center and undergo a comprehensive evaluation (HRCT, RHC, Complete PFT and CPET) and consideration for PAH meds
IPF FVC≤70%	No PH No PAH treatment	PH classification uncertain No data to support treatment with PAH drugs	Severe IPF Prognosis is very severe – refer to an expert PH and ILD center. Analysis of hemodynamics RHC and CPET and if CO is low or inadequately increasing CO with activity → Reducing PVR Thorough monitoring of gas exchange as patients may experience VQ MM and hypoxemia or normoxia due to higher $ScvO_2$ from improved CO

Seeger W et al. Pulmonary Hypertension in Chronic Lung Diseases. Journal of the American College of Cardiology 2013; 62(25): D109-D116

Summary Points

- PH is common in IPF and mostly mild and does not require PAH meds
- PH based on RHC and echo data predicts increased mortality in IPF/ILD
- DLCO, PaO2, 6MWD, and nadir desat correlate with PH in IPF/ILD
- FVC and CT radiographic indices do not correlate with PH in IPF/ILD
- Disproportionate PH in IPF is a unique diagnosis requiring thorough investigation and consideration for PAH medications in select cases

Thank You