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Pulmonary hypertension in interstitial lung disease: Prevalence, prognosis and 6 min walk test

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Summary
Background: Pulmonary hypertension (PH) is an important complication to interstitial lung disease (ILD). The aim of the present study was to investigate the prevalence and impact of PH on prognosis and exercise capacity in ILD patients.
Methods: 212 ILD patients were screened for PH by echocardiography. Criteria for PH were either a tricuspid pressure regurgitation gradient >40 mmHg, a tricuspid annular plane systolic excursion <1.8 cm or right ventricular dilatation. If possible, PH was confirmed by right heart catheterisation. Pulmonary function tests and 6 min walk tests (6MWT) were performed.
Results: 29 patients (14%) had PH, 16 (8%) had mild and 13 (6%) had severe PH (mean pulmonary artery pressure ≥ 35 mmHg). Compared to patients without PH, lung function parameters were lower in PH patients, a larger proportion had idiopathic pulmonary fibrosis (IPF) (41 vs 21%, $p = 0.006$), and the hazard ratio for death was 8.5 (95% CI: 4–17). After correction for lung function parameters and the presence of IPF, 6MWT was significantly lower in patients with PH compared to non-PH patients (difference ± SEM: 58 ± 22 m, $p = 0.01$).
Conclusions: PH occurred in 14% of a cohort of patients with ILD and was associated to IPF and lower lung function parameters. Mortality was markedly higher in PH patients, and the presence of PH reduced 6MWT independently of lung function and the presence of IPF. The present results emphasize the need for intensified treatment of patients with ILD and PH.

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Introduction

Pulmonary hypertension (PH), defined by a mean pulmonary artery pressure (MPAP) >25 mmHg, is an important complication to interstitial lung disease (ILD). The gold standard for diagnosis of PH is right heart catheterisation (RHC). Echocardiography remains the best non-invasive screening modality for PH,[1] although it is subjected to inaccuracies.[2,3]

So far, studies investigating the occurrence of PH in ILD have focused on lung transplant candidates with idiopathic pulmonary fibrosis (IPF),[4,5] patients with sarcoidosis,[6,7] or scleroderma-related ILD.[8,9] The results have shown a great variation with regard to prevalence, while PH has been shown to worsen the prognosis in both patients with IPF[4] and scleroderma-related ILD.[10] However, at tertiary referral centres, physicians are faced with a broad and heterogeneous group of patients with ILD, of which several subtypes are rare.[11] At present, very few data describe the occurrence and impact on prognosis of PH in such populations. Furthermore, it is unclear whether PH per se reduces exercise capacity in ILD, or if it simply reflects more advanced lung disease.

The aim of the present study was to estimate the prevalence, the prognostic effect and the impact of PH on exercise capacity measured by the 6 min walk test (6MWT) in ILD patients at a tertiary referral centre in Denmark.

Methods

The study was approved by The Danish Research Ethics Committee, Region Central Jutland (Issue nr: M-20080219) and conducted in accordance with the Helsinki Declaration.

Study subjects

Consecutive patients were recruited during 16 months at a tertiary referral centre for evaluation and treatment of ILD in Denmark. Potential participants included all prevalent and incident cases during the study period with any subtype of ILD, including patients with sarcoidosis stage II–IV. All patients had an echocardiography performed as part of their initial evaluation.

Inclusion criteria were: age >18 years, written consent and a diagnosis of ILD according to ATS/ERS guidelines[12] based on an overall assessment of high-resolution computer tomography (HR-CT) scan, lung function tests, bronchoscopy and biopsy, if available.

Time of inclusion was the date, when echocardiography was performed.

Diagnoses

Patients were divided into eight diagnostic groups (IPF, Non specific interstitial pneumonia, desquamative interstitial pneumonia, hypersensitivity pneumonitis, ILD associated to rheumatologic disorders, sarcoidosis stage II–IV, end-stage fibrosis (manifest end-stage fibrotic changes and indeterminable underlying ILD) and other (including patients with unclassified ILD)).

37 patients had a clinical working diagnosis of "unclassified ILD" at the time of inclusion. 21 of these were reclassified into one of the other diagnostic groups after re-evaluation of clinical course, HR-CT scans and biopsies. It was not possible to reclassify 16 patients, who were put in the category "other" types of ILD.

Use of medication and presence of concomitant cardiovascular disease were assessed by interviews and patients' records.

Echocardiography

The tricuspid regurgitation jet was measured by Doppler echocardiography in multiple projections, and the tricuspid pressure regurgitation gradient (TR) was calculated from the modified Bernoulli equation: $4v^2$ (v = peak velocity of tricuspid regurgitation, m/s). Dimensions of the ventricles were evaluated from standard projections. The tricuspid annular plane systolic excursion (TAPSE) was assessed in the four chamber apical window with the M-mode cursor through the lateral tricuspid annulus ring. Respiratory compression of the caval vein was evaluated, and left ventricular systolic function was assessed by shortening fraction and wall motion index.

Criteria for a positive screen for PH on echocardiography were: TR >40 mmHg, right ventricular dilatation or decreased TAPSE (<1.8 cm).[13] If the acoustic windows were too poor to measure at least one of these parameters, patients were excluded from the analysis.

RHC

Patients screened positive for PH on echocardiography were asked to undergo RHC performed with a Swan–Ganz catheter.[14] For patients on oxygen therapy, this treatment was continued during RHC. Otherwise, oxygen was not used. If patients were formerly diagnosed with PH by RHC, and signs of PH on echocardiography were still obvious at inclusion, results from the former RHC were used.

Patient groups

The non-PH group comprised patients screened negative for PH by echocardiography, and patients who were screened positive by echocardiography but had an MPAP <25 mmHg at RHC. Patients with $25 \leq$ MPAP < 35 mmHg or a $40 <$ TR ≤ 60 mmHg in the absence of RHC constituted the mild PH group, and severe PH encompassed patients with MPAP ≥35 mmHg or TR >60 mmHg in the absence of RHC. The PH group included patients with mild or severe PH.

Mortality

Survival status was assessed using the electronic system at Aarhus University Hospital in which deaths are registered on a week-to-week basis.

Lung function

Lung function tests included spirometry, body plethysmography and determination of diffusion capacity for

carbon monoxide (DL_{CO}) (Zan 500 Body, nSpire Health Inc, Louisville, Colorado, USA; PFT pro Body, Jaeger, Hoeckberg, Germany; Spirometer model 6800, Vitalograph, Ennis, Ireland) in accordance with the American Thoracic Society guidelines.[15] Predicted values were calculated as recommended by the European Respiratory Society.[16]

6MWT

6MWT was performed following guidelines from ATS.[17] The tests were conducted on a 30 m track using prescribed supplemental oxygen. Borg dyspnoea score was recorded before and immediately after the 6MWT.

Data analysis

Data were analysed in Stata/IC 10 (StataCorp, College Station, Texas, USA). Survival was analysed with time since inclusion as time scale. Follow-up was censored eight months after inclusion of the last patient. Mortality was estimated by Kaplan–Meier curves and differences in hazard for death (HR) between non-PH and PH patients by Cox-proportional hazard model. A multivariate cox-hazard analysis adjusting for age, lung function parameters and IPF was made. Proportionality was validated by log–log plots. Parametric data were analysed using Student's *t*-test, non-parametric data by rank sum test, proportions by proportion test, and independent effect of PH on 6MWT was assessed by multiple linear regression. Logistic regression was used to calculate odds ratios (OR) for PH.

A *p*-value below 0.05 was regarded as statistically significant. Results from normally distributed data are expressed as means ± SEM, non-parametric data as medians with inter quartile ranges, OR and HR are expressed with 95% confidence intervals (CI).

Results

Patients

268 patients were asked, and 212 accepted to participate. A comparison was made between the participants and the 56 patients who declined to participate. The 56 non-participants did not differ from the participants with respect to age, sex, time from referral, 6MWT (Table 1), diagnoses (Table S1 in data supplement) or mortality (HR for death after correction for age was 1.5 (0.6–4.0), $p = 0.4$ in participants vs non-participants). However, non-participants had higher lung function parameters and were less likely to receive immunosuppressive treatment and oxygen (Table 1). Diagnostic categories of participants are shown in Table 2. Details of rheumatologic disease related ILD are shown in Tables S2 and S3 in the data supplement.

Echocardiography

Values for TR were obtained in 164 and for TAPSE in 183 patients. In four patients, neither TR, TAPSE nor the right ventricle could be assessed sufficiently, and the echocardiogram was therefore regarded as inconclusive. Thirty patients were screened positive for PH. In patients screened negative, there were no significant differences in lung function, 6MWT or TAPSE between patients with and without a measurable TR (results shown in Table S4, supplementary data). Three patients had a TAPSE below 1.8 cm, but no other indices of PH. In one, a TAPSE of 1.7 cm was explained by a former myocardial infarction. In two, TAPSE was 1.6 and 1.4, but both patients had a measurable TR below 30 mmHg, and no dilatation of the right ventricle. These three patients were kept in the non-PH group.

RHC

RHC data from 18 patients screened positive for PH were obtained. Seven of these had an existing diagnosis of PH based on RHC (median time from diagnosis to inclusion was 23 (7–36) months). At inclusion, all seven had obvious signs of PH on echocardiography (TR = 77 ± 5 mmHg, TAPSE = 1.8 ± 0.3 cm, right ventricular dilatation was present in five). Median time between RHC and inclusion was within 1.5 (1–2) months of inclusion in the remaining patients ($n = 11$). In one patient, the diagnosis of PH was discarded (MPAP = 16 mmHg). One patient had a pulmonary capillary wedge pressure (PCWP) above 15 (PCWP = 16 mmHg, MPAP = 44 mmHg, pulmonary vascular resistance = 6.5 wood units). Due to the overall clinical assessment, this patient was kept in the severe PH group. MPAP in patients with severe PH was 43 ± 2 mmHg, and 62% of these had right ventricular dilatation as opposed to 6% in the mild PH group. 12 patients screened positive for PH did not accept to undergo RHC. These had a mean TR of 53 ± 4 mmHg and TAPSE of 2.1 ± 0.14 cm.

Prevalence of PH

Based on echocardiography and RHC, 14% had PH, 8% had mild PH and 6% had severe PH.

Demographics

Compared to patients with no PH, PH patients were older, time from referral was longer, they were more likely to receive treatment with immunosuppressives and oxygen (Table 3) and more likely to have IPF (41 vs 21%, $p = 0.006$). The OR for PH in patients with IPF compared to patients without IPF was 2.9 (1.03–8.2), $p = 0.043$ when Dlco, TLC, FEV_1 and FVC (as % of expected), was corrected for $n = 199$. In patients with mild PH, hypertension and former myocardial infarction were more frequent (Table S5 in data supplement).

Lung function

In PH patients, Dlco, FEV_1 and FVC, were lower than in patients without PH. Only Dlco was decreased in patients with severe PH compared to non-PH patients (Table 4). The median time from inclusion to lung function tests was 0 (0–1) months.

Table 1 Comparison between participants and non-participants.

Demographics		Participants Total $n = 212$	n	Non-participants Total $n = 56$	n	P vs participants
Age	(years)	61 ± 0.9	212	64 ± 1.8	56	0.052
Female	(% of patients)	52	212	63	56	0.2
BMI	(kg/m^2)	27 ± 0.4	212	27 ± 0.7	56	0.7
Time from referral	(months) (Median)	11 (0–46)	212	13 (1.5–34)	55	0.7
Immunosuppressive treatment	(% of patients)	63	212	34*	56	0.03
Oxygen treatment	(% of patients)	16	212	11*	55	0.01
Lung transplant candidates	(% of patients)	4	212	0*	56	0.01
Lung function						
Dlco	(% of expected)	45 ± 1	208	49 ± 2	55	0.1
TLC	(% of expected)	69 ± 1	210	75 ± 2*	53	0.01
FVC	(% of expected)	71 ± 2	212	83 ± 3*	55	<0.0001
FEV_1	(% of expected)	67 ± 1	212	79 ± 3*	55	0.001
Six minute walk test						
Distance	(metres)	424 ± 8	205	407 ± 18	49	0.4

Comparison of demographic data, lung function and 6 min walk test in participants, and patients who declined to participate in the study. Total n indicates number of patients in each group. n indicates the number of patients in whom data were available. * = $p < 0.05$ vs non-participants. Results are expressed as proportions or means ± SEM. Time from referral is expressed as the median with inter quartile ranges.

Mortality

Median follow-up time from inclusion was 1.1 (0.9–1.6) years. There were 32 deaths, 16 in the PH and 16 in the non-PH group. Survival curves for non-PH and PH patients are depicted in Fig. 1. The HR for death after inclusion was 8.5 (4–17), $p < 0.001$, in the PH group compared to non-PH patients. After adjusting for age, lung function, IPF and time from referral in a multivariate cox-hazard analysis, PH still significantly raised the risk of death (HR = 7.8 (3.1–20), $p < 0.0001$) (bivariate cox-regression analysis of the individual parameters are displayed in Table S7, supplementary data). There were no statistical significant differences in survival between IPF and non-IPF patients in the PH group (HR = 1.5 (0.5–4.0), $p = 0.440$), between patients who had RHC performed compared to those who had not (HR = 2.0 (0.7–6.5), $p = 0.21$), or between PH patients requiring and not requiring oxygen treatment (HR for death: 2.6 (0.7–9.0), $p = 0.145$).

6MWT

Compared to patients without PH, PH patients had shorter 6MWTs (Fig. 2A). PH patients were also more likely to desaturate below 88%[18] (Table 4). Borg dyspnoea score was significantly higher in mild PH compared to the non-PH group (Table 4). Corrected for age, gender, BMI, lung function parameters and the presence of IPF ($n = 199$), the difference in 6MWT between patients without and with PH was 58 ± 22 m, $p = 0.01$. Looking at mild and severe PH separately, 6MWT in mild-PH patients did not differ significantly from non-PH patients (33 ± 27 m, $p = 0.2$), while severe PH reduced 6MWT by 89 ± 31 m ($p = 0.005$)

Table 2 Distribution of diagnoses in patients with no, mild and severe PH.

ILD diagnosis (% of patients)	All patients Total $n = 212$	No PH Total $n = 179$	Mild PH Total $n = 16$	P mild vs no PH	Severe PH Total $n = 13$	P Severe vs No PH	P Severe vs mild PH
IPF	23	21	31	0.3	54*	0.006	0.2
NSIP	15	16	6	0.3	0	0.11	0.4
DIP	6	7	0	0.3	8	0.9	0.3
Hypersens. pneumonitis	7	8	0	0.2	0	0.3	–
Rheumatologic disease	19	19	25	0.6	15	0.7	0.5
Sarcoidosis	10	9	13	0.7	8	0.7	0.7
Endstage	4	3	13*	0.045	8	0.3	0.7
Other	16	17	13	0.6	8	0.4	0.7

Distribution of diagnoses in participants with no, mild and severe PH. Total n indicates number of patients in each group. Data were available in all participants. * = $p < 0.05$ vs no PH analysed by proportion test. Results are expressed as proportions. Other comprises: (eosinophilic pneumonia ($n = 1$) Respiratory bronchiolitis associated-ILD ($n = 2$), cryptogenic organizing pneumonia ($n = 1$), lymphoid interstitial pneumonia ($n = 1$), alveolar proteinosis ($n = 2$), Histiocytosis X ($n = 2$), medically induced ILD ($n = 4$), inorganic dust exposure ($n = 1$), acute interstitial pneumonitis ($n = 1$), granulomatous interstitial lung disease ($n = 3$), unclassified ($n = 16$)). Hypersens. pneumonitis: hypersensitivity pneumonitis. *: Proportion significantly higher than in patients with no PH.

Table 3 Comparison of demographics in participants with and without PH.

		No PH Total $n = 179$	PH Total $n = 29$	p (PH vs No PH)
Age	(years)	60 ± 1	65 ± 2*	0.04
Female	(% of patients)	51	55	0.7
BMI	(kg/m^2)	27 ± 0.4	26 ± 1	0.4
Time from referral	(months) (Median)	10 (0–39)	39 (8–53)*	0.008
Immunosuppressive treatment	(% of patients)	58	86*	0.004
Oxygen treatment	(% of patients)	9	62*	<0.0001
PH specific treatment	(% of patients)	0	21*	<0.0001
Lung transplant candidates	(% of patients)	3	10	0.05

Demographic data for patients included in the study. *: $p < 0.05$ vs no PH. n indicates number of patients in each group. Total n indicates number of patients in each group. Data were available in all cases. Results are expressed as proportions or means ± SEM. Time from referral is expressed as the median with inter quartile ranges.

(Fig. 2B). This was not changed significantly by omitting Dlco from the analysis.

Patients with a 6MWT distance below the 25th percentile (≤345 m) had significantly higher OR for PH than patients with longer 6MWT distance. Correcting for lung function parameters and IPF, the OR for PH in those with a 6MWT distance below 345 m was 4.9 (1.68–14.3), $p = 0.004$, $n = 199$.

The median time from 6MWT to inclusion was 0 (0–3) months.

Discussion

The main findings of this study were that 14% of patients with mixed types of ILD at a tertiary referral centre had PH, and that 8% and 6% of patients had mild and severe PH, respectively. Furthermore, the study underlines the adverse effect of PH on mortality, and shows that PH independently of lung function impairment restricts exercise capacity measured by the 6MWT with a clinically relevant magnitude.[19]

Prevalence

In relation to PH, focus is often on IPF patients, and the present study confirms that IPF may be the most important ILD when it comes to PH; IPF was markedly over-represented in the group with severe PH. Also, in a logistic regression analysis, IPF came out as an independent risk factor for PH. This result should, however, be interpreted with caution due to a limited number of PH patients for each variable in the analysis. An altered production of humoral factors such as increased TGF-β[20] and endothelin-1[21] levels and decreased levels of NO[22] have been shown to be involved in the pathophysiology of both IPF and PAH. This may be a plausible explanation for the association between IPF and PH besides parenchymal architectural distortion.

Table 4 Lung function parameters and 6 min walk test in patients with no, mild and severe PH.

	No PH Total $n = 179$	n	PH Total $n = 29$	n	P vs No PH	Mild PH Total $n = 16$	n	P vs No PH	Severe PH Total $n = 13$	n	P vs No PH	P vs mild PH
Lung function (% of expected)												
Dlco	47 ± 1	177	29 ± 3*	28	<0.0001	36 ± 5*	15	0.01	21 ± 3* †	13	<0.0001	0.02
TLC	70 ± 1	178	65 ± 3	29	0.13	64 ± 4	16	0.2	66 ± 4	13	0.4	0.8
FVC	73 ± 2	179	60 ± 4*	29	0.003	56 ± 5*	16	0.002	66 ± 8	13	0.2	0.3
FEV_1	69 ± 2	179	55 ± 4*	29	0.001	51 ± 5*	16	0.002	60 ± 7	13	0.13	0.3
6 min walk test												
Distance (m)	442 ± 9	174	311 ± 20*	28	<0.0001	343 ± 27*	16	0.001	267 ± 28*	12	<0.0001	0.06
Saturation < 88% (% of Pts)	45	173	86*	28	<0.0001	82*	16	0.006	92*	12	0.002	0.4
Borg dyspnoea score (Median)												
Before	0 (0–1)	169	1 (0–2)*	26	0.007	2 (0–2.5)*	16	0.003	0.25 (0–1)	10	0.50	0.08
After	4 (2–7)	169	5.8 (4–7)*	26	0.01	6 (3.5–7.5)*	16	0.04	5 (4–7)	10	0.12	0.7

Lung function and 6 min walk test in participants without and with PH. *: $p < 0.05$ vs no PH. †: $p < 0.05$ vs mild PH. Total n indicates number of patients in each group. n indicates number of patients from whom data were available. Results are expressed as proportions or means ± SEM. Borg dyspnoea score is expressed as medians with inter quartile range.

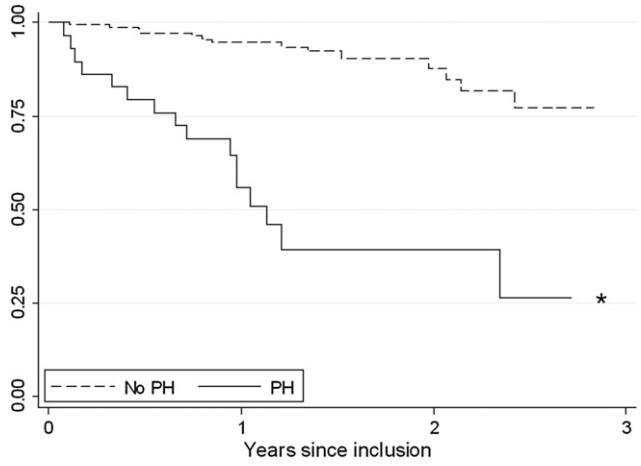

Figure 1 Survival Kaplan—Meier survival curves in patients with and without PH. *: $p < 0.05$ vs no PH.

On the other hand, it is noteworthy that nearly all diagnostic groups were represented in the PH group (Table 2).

In former studies, the prevalence of PH in ILD patients has shown a great variation dependent on the patient population and the design of the study. For example, in consecutive sarcoidosis patients, 5.7% had PH based on echocardiography,[6] while a prevalence of 48% was reported in IPF transplant candidates.[5] A number of studies have investigated lung transplant candidates in whom RHC measurements are done routinely.[4,5,7,23,24] But lung transplant candidates only constitute a small group of patients at referral centres (less than 4% at our institution), and as they have particularly advanced lung disease, the prevalence of PH may be notably higher than in ILD patients in general. Furthermore, a retrospective design has been used in several studies,[4,5,7,9,24—27] where patients were included if data from RHC and/or echocardiography were available. This approach could also tend to overestimate the prevalence of PH, because echocardiography or RHC may have been performed on suspicion of PH. The present study is cross-sectional in design, and we aimed to include patients with ILD, regardless of diagnosis and concomitant cardiovascular disease. We find that the approach used in the present study may reflect the overall prevalence in ILD better, and gives an impression about the proportion of ILD patients who could potentially benefit from specific treatment of PH, if evidence on this subject emerges. However, compared to the 212 participants in the study, the 56 patients who declined to participate had equal Dlco and 6MWT, but higher TLC, FEV_1, and FVCs. Therefore, it cannot be excluded that the prevalence estimated in the present study may also be slightly overestimated.

Prognosis

Prior studies have shown that the presence of PH worsens the prognosis in selected groups of ILD patients with IPF or scleroderma-related ILD,[4,8,28] including a study by Hamada et al.[28] in which the presence of even mildly elevated MPAP had an adverse prognostic effect in IPF patients. In accordance, the present study showed a pronounced effect on the hazard of death after inclusion in patients with PH, even after correction for age, lung function parameters, IPF and time from referral, suggesting that PH is an independent driver of death. However, the number of deaths in the present study was small ($n = 32$), and consequently, the multivariate analysis should be interpreted with care. Nevertheless, the substantial risk of death in approximately 14% of ILD patients at a tertiary referral centre with PH, calls for an increased effort to improve treatment of ILD-related PH, either by addressing the underlying diseases or the pulmonary vasculature more specifically.

6-min walk test

In accordance with other studies,[4,29—32] we found a large difference in 6MWT between patients with and without PH based on the raw data. Borg dyspnoea score was not significantly higher in patients with severe PH indicating that this parameter is not as closely associated to PH as the 6MWT distance. In previous studies, adjustment of the 6MWT for lung function, age, sex and BMI has not been performed.[4,29—34] Even if such factors seem evenly distributed between groups, they may still contribute to or mask the effect of PH. The multivariate analysis performed on our data showed that PH significantly reduced walking distance independently of lung function and the presence of IPF, and also that this effect could be attributed to the patients with severe PH. In patients with severe PH, right

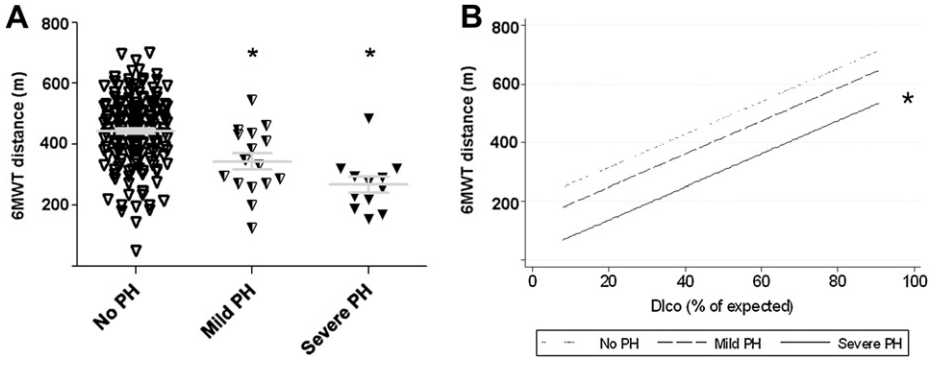

Figure 2 6MWT. A: Dotplot of 6MWT in patients with no, mild and severe PH. Error bars indicate mean ± SEM. B: Model estimated by multiple linear regression showing 6MWT distance for men who did not have IPF with average age (61 years), BMI (27), lung function (TLC = 69, FVC = 71 and FEV_1 = 67) as a function of diffusion capacity and no, mild or severe PH. *$p < 0.05$ vs no PH.

ventricular dilatation, indicating right ventricular failure, occurred frequently, and this is probably an important determinant of exercise tolerance. Other studies have shown that both mild PH and severe PH modifies cardiopulmonary exercise testing,[33,34] but the magnitude of the effect of PH is unclear since univariate analyses were used. The present study is to our knowledge the first to address the independent effect of mild and severe PH on 6MWT.

In short, our results suggest that mild PH may be a marker for severe lung impairment, while severe PH is an independent factor that reduces exercise capacity per se, speaking in favour of further investigations of specific treatment in ILD-related PH.

The results also suggest that a 6MWT distance below 345 m is an independent risk factor for PH.

Study limitations

It is a limitation that not all patients were evaluated for PH by RHC. Echocardiography can produce false positive and negative results,[2] but studies comparing RHC and echocardiography have focused on the echo-estimated systolic pulmonary artery pressure.[2] In the present study reduced TAPSE,[13] right ventricular dilatation and abnormal septal movement were also determined, which may decrease the rate of false negatives. PCWP has been shown to be abnormal in 16% of IPF patients.[27] It cannot be excluded that some of the patients in our study with mild PH that did not undergo RHC could have predominantly pulmonary venous hypertension secondary to diastolic dysfunction of the left ventricle. The higher frequency of hypertension and previous myocardial infarction observed in this group is in accordance with that. Also, it cannot be excluded that some of the patients who did not have RHC undertaken did not have true PH. To diminish selection bias we decided to include patients screened positive for PH, although they refused to undergo RHC. However, it strengthens the study that all patients with severe PH, except one, had RHC undertaken. Furthermore, all participants were evaluated personally by the authors, which is an advantage compared to previous retrospective studies.

Conclusions

The present study showed that the prevalence of PH was 14% in ILD patients at a tertiary referral centre, and that PH patients have a substantially worse prognosis than patients without PH. PH was related to IPF, longer disease duration and impaired lung function parameters. But even corrected for lung function parameters and the presence of IPF, PH limited exercise capacity measured by the 6MWT with a clinically relevant magnitude, indicating that PH is an independent worsening factor in ILD patients. The study thereby underlines the urgent need for new treatment options in ILD patients with PH.

Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.rmed.2012.02.015.

Conflict of interest statement

None.

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