

Online supplement table S1: Baseline demographics in patients with subtypes of IPAH_{mild-LD} compared with IPAH_{no-LD}

	IPAH _{no-LD}	IPAH _{mild-LD} emphysema	IPAH _{mild-LD} fibrosis	IPAH _{mild-LD} Mixed
Number	303	125	39	26
Female (%)	73	52	39	39
Age	53 ±17 ^{¶, *, #}	70 ±9 ^z	71 ±10 ^z	69 ±11 ^z
WHO FC I/II/III/IV (%)	0/21/60/19	0/9/60/31	0/13/49/38	0/4/50/46
BMI (kg/m²)	29 ±6	28 ±6	29 ±5	28 ±5
mRAP (mmHg)	11 ±6	11 ±5	11 ±5	10 ±5
mPAP (mmHg)	55 ±13 ^{¶, *, #}	51 ±9 ^z	48 ±10 ^z	51 ±8 ^z
PAWP (mmHg)	10 ±3 [¶]	11 ±3 ^z	10 ±4	10 ±3
PVR (WU)	11.9 ±5.8	10.9 ±4.4	11.1 ±4.5	11.8 ±5.2
SvO₂ (%)	62 ±9 [#]	60 ±8	60 ±10	57 ±9 ^z
Cardiac Output (L/min)	4.3 ±1.6	4.1 ±1.5	3.8 ±1.2	3.7 ±1.1
Cardiac Index (L/min/m²)	2.3 ±0.8	2.2 ±0.7	2.1 ±0.6	2.0 ±0.6
FEV1 %	89 ±15	88 ±16	88 ±17	91 ±20
FVC %	100 ±17 [¶]	105 ±17 ^{z, *}	97±19 [¶]	100 ±19
FEV1/FVC	75 ±9 ^{¶, *, #}	66 ±8 ^{z, *}	72 ±7 ^{z, ¶}	71 ±10 ^z
D_{Lco} %pred	56 ±20 ^{¶, *, #}	31 ±14 ^{z, #}	31±13 ^{z, #}	25 ±7 ^{¶, *, z}
ISWD (m)	210 (80, 360) ^{¶, *, #}	90 (40, 190) ^z	60 (20, 140) ^z	90 (30, 120) ^z

Data are presented as mean ±SD or median (Q1, Q3). ^z p<0.05 in comparison to IPAH_{no-LD}, [¶] p<0.05 in comparison to mild LD emphysema, ^{*} p<0.05 in comparison to mild LD fibrosis, [#] p<0.05 in comparison to mild LD mixed

Abbreviations: IPAH = idiopathic pulmonary arterial hypertension, IPAH_{no-LD} = IPAH with no lung disease, IPAH_{mild-LD} = IPAH with mild lung disease, WHO FC = World Health Organisation functional class, BMI = body mass index, mRAP = mean right atrial pressure, mPAP = mean pulmonary arterial pressure, PAWP = pulmonary arterial wedge pressure, PVR = pulmonary vascular resistance, SvO₂ = mixed venous oxygen saturations, D_{Lco} %pred= diffusing capacity for carbon monoxide percent-predicted, ISWD = incremental shuttle walking test distance.

Online supplement table S2: Demographics for subgroups of IPAH

	IPAH_{no-LD}	IPAH_{mild-LD}	IPAH_{D_{LCO}<45}	IPAH_{D_{LCO}≥45}
Number	303	190	79	174
Female (%)	73	47	66	77
Age	53 ±17	70 ±10	65 ±12	48 ±16
WHO FC I/II/III/IV (%)	0/21/60/19	0/9/56/35	0/12/57/31	0/24/65/11
mRAP (mmHg)	11 ±6	11 ±5	11 ±7	11 ±6
mPAP (mmHg)	55 ±13	50 ±9	51 ±10	56 ±14
PAWP (mmHg)	10 ±3	11 ±3	10 ±3	10 ±3
PVR (WU)	11.9 ±5.8	11.1 ±4.5	11.4 ±5.3	12.3 ±6.1
SvO₂ (%)	62 ±9	59 ±9	60 ±9	63 ±9
Cardiac Output (L/min)	4.3 ±1.6	4.0 ±1.4	4.2 ±1.6	4.2 ±1.4
Cardiac Index (L/min/m²)	2.3 ±0.8	2.2 ±0.7	2.3 ±0.9	2.3 ±0.8
FEV1 %	89 ±15	89 ±17	88 ±19	91 ±13
FVC %	100 ±17	103 ±18	100 ±20	100 ±15
FEV1/FVC	75 ±9	68 ±8	71 ±10	76 ±7
D_{LCO} %pred	56 ±20	30 ±13	32 ±7	67 ±13
ISWD (m)	210 (80, 360)	80 (40, 180)	80 (30, 210)	260 (130, 430)
emPHasis-10 score	32 (20,40)	32 (26, 41)	38 (33, 44)	28 (20, 35)
One-year mortality (%)	4.9	21.5	14.2	1.2

Abbreviations: IPAH = idiopathic pulmonary arterial hypertension, IPAH_{no-LD} = IPAH with no lung disease, IPAH_{mild-LD} = IPAH with mild lung disease, IPAH_{D_{LCO}<45} = IPAH with D_{LCO} <45%, IPAH_{D_{LCO}≥45} = IPAH with D_{LCO} ≥45%, WHO FC = World Health Organisation functional class, BMI = body mass index, mRAP = mean right atrial pressure, mPAP = mean pulmonary arterial pressure, PAWP = pulmonary arterial wedge pressure, PVR = pulmonary vascular resistance, SvO₂ = mixed venous oxygen saturations, D_{LCO} %pred = diffusing capacity for carbon monoxide percent predicted, ISWD = incremental shuttle walking test distance.

Online supplement table S3: Demographics in patients with follow-up data available

	IPAH _{no-LD}	IPAH _{mild-LD}	IPAH _{DlCO<45}	IPAH _{DlCO≥45}	IPAH _{no-LD} *	IPAH _{mild-LD} *
Number	215	124	47	139	79	32
Female (%)	73 [¶]	47 [¶]	66	77	85 [#]	31 [#]
Age	51 ±17 [¶]	70 ±10 [¶]	65 ±13 [‡]	48 ±16 [‡]	51 ±17 [#]	69 ±9 [#]
WHO FC I/II/III/IV (%)	0/23/60/17	0/10/64/26	0/11/66/23	0/26/63/11	0/16/70/14	0/3/63/34
BMI (kg/m ²)	29 ±6	28 ±6	29 ±6	29 ±6	30 ±7	30 ±6
mRAP (mmHg)	11 ±6	11 ±5	11 ±6	11 ±6	13 ±6	12 ±4
mPAP (mmHg)	56 ±12 [¶]	50 ±9 [¶]	52 ±9 [‡]	56 ±13 [‡]	60 ±13 [#]	55 ±10 [#]
PAWP (mmHg)	10 ±3	11 ±3	10 ±3	10 ±3	10 ±4 [#]	12 ±3 [#]
PVR (WU)	12.0 ±5.7 [¶]	10.7 ±4.4 [¶]	11.6 ±4.8	12.4 ±5.9	14.4 ±5.0 [#]	11.6 ±3.8 [#]
SvO ₂ (%)	62 ±9 [¶]	59 ±9 [¶]	60 ±10 [‡]	63 ±9 [‡]	60 ±9	58 ±6
Cardiac Output (L/min)	4.3 ±1.5	4.0 ±1.4	4.1 ±1.5	4.1 ±1.3	3.8 ±1.2	3.9 ±1.3
Cardiac Index (L/min/m ²)	2.3 ±0.8	2.2 ±0.7	2.2 ±0.7	2.3 ±0.7	2.1 ±0.6	2.0 ±0.6
FEV1 %	90 ±15	88 ±17	88 ±20	91 ±13	88 ±14	91 ±17
FVC %	101 ±17	103 ±17	102 ±22	101 ±15	101 ±18	107 ±16
FEV1/FVC	75 ±8 [¶]	67 ±9 [¶]	70 ±10 [‡]	76 ±7 [‡]	74 ±9 [#]	68 ±10 [#]
Dlco %pred	58 ±19 [¶]	31 ±14 [¶]	32 ±7 [‡]	67 ±13 [‡]	57 ±18 [#]	33 ±14 [#]
ISWD (m)	210 (80, 360) [¶]	90 (40, 180) [¶]	70 (20, 200) [‡]	265 (130, 430) [‡]	210 (90, 340) [#]	130 (50, 210) [#]
Treatment (%)						
None	1	0	0	1	0	0
CCB	6	1	0	9	0	0
Oral mono	13	34	17	11	0	0
Combo oral	48	45	53	47	66	69
Prostanoid +/- oral	32	20	30	32	34	31

* denotes subgroups of patients receiving combination oral therapy within 6 months of diagnosis

Data are presented as mean \pm SD or median (Q1, Q3). [¶] p<0.05 between IPAH_{no-LD} and IPAH_{mild-LD}, [¥] p<0.05 between IPAH_{DlCO<45} and IPAH_{DlCO \geq 45}, [#] p<0.05 between IPAH_{no-LD} and IPAH_{mild-LD} (patients receiving oral combination therapy within 6 months of diagnosis)

Abbreviations: IPAH = idiopathic pulmonary arterial hypertension, IPAH_{no-LD} = IPAH with no lung disease, IPAH_{mild-LD} = IPAH with mild lung disease, IPAH_{DlCO<45} = IPAH with DlCO <45%, IPAH_{DlCO \geq 45} = IPAH with DlCO \geq 45%, WHO FC = World Health Organisation functional class, BMI = body mass index, mRAP = mean right atrial pressure, mPAP = mean pulmonary arterial pressure, PAWP = pulmonary arterial wedge pressure, PVR = pulmonary vascular resistance, SvO₂ = mixed venous oxygen saturations, DlCO %pred = diffusing capacity for carbon monoxide percent predicted, ISWD = incremental shuttle walking test distance.

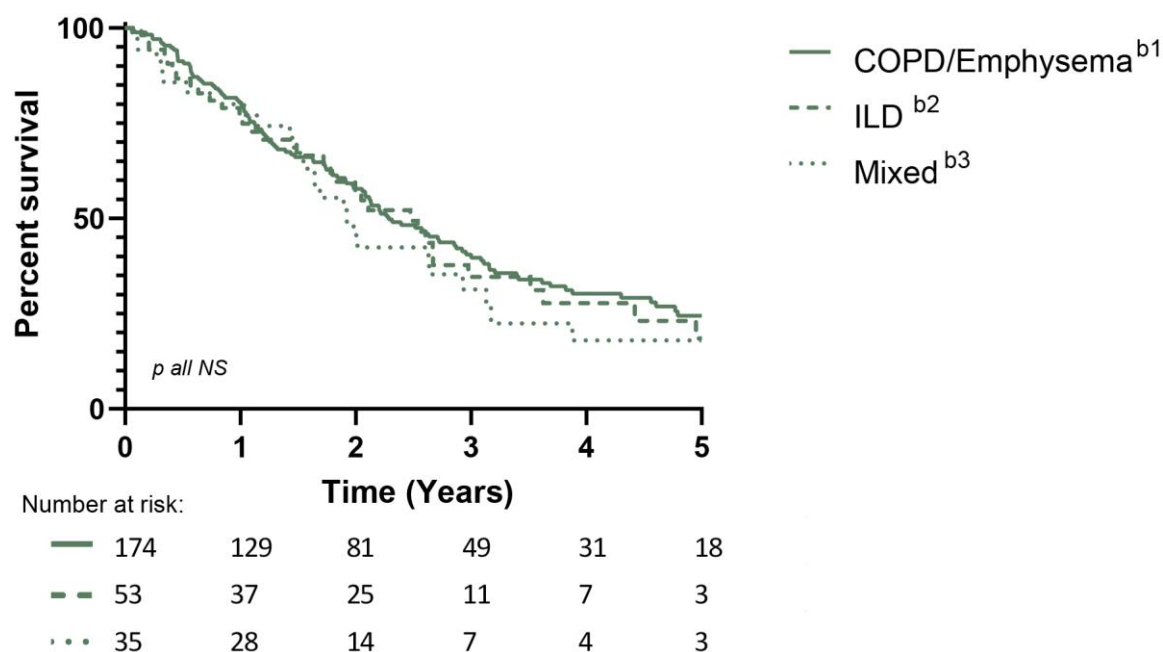


Figure S1. Survival by subtype of lung disease in IPAHmild-LD
 Abbreviations: COPD = chronic obstructive pulmonary disease, ILD = interstitial lung disease, IPAHno-LD = idiopathic pulmonary arterial hypertension with no lung disease.

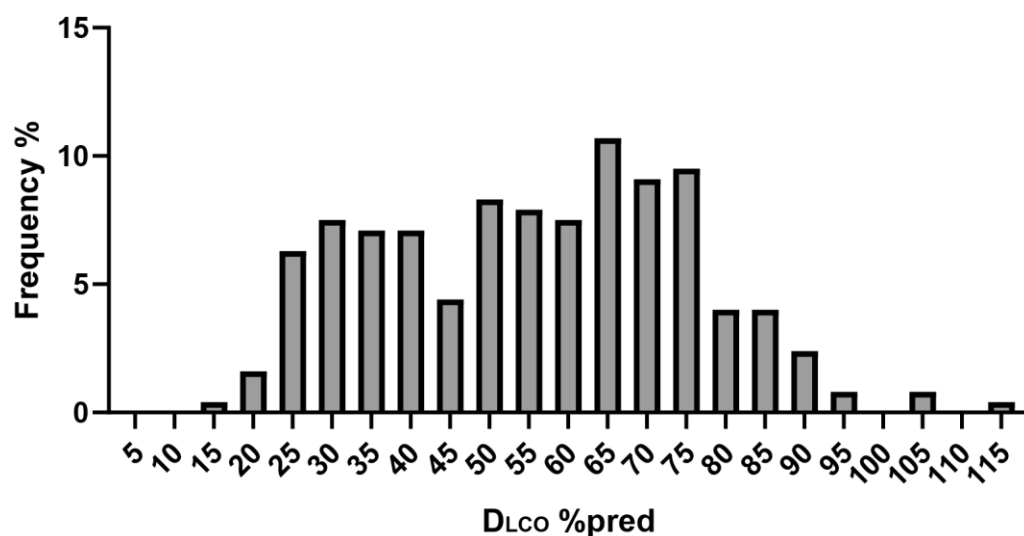


Figure S2: Distribution of DLCO %predicted in patients with IPAHno-LD
 Abbreviations: DLCO %pred = percent-predicted diffusing capacity for carbon monoxide, IPAHno-LD = idiopathic pulmonary arterial hypertension with no lung disease.