PLICNÍ HYPERTENZE ASOCIOVANÁ S ONEMOCNĚNÍM PLIC

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European Reference Network for rare or low prevalence complex diseases

Network Respiratory Diseases (ERN-LUNG)

Member General University Hospital in Prague — Czechia

KONFLIKT ZÁJMŮ

Honoráře, granty, členství v poradních sborech:

Actelion Pharmaceuticals Ltd, Janssen, AOP Orphan,
Bayer Healthcare, MSD, Arena Pharmaceuticals, Gossamer Bio,
Altavant Sciences GmbH

ESC European Society of Cardiology

European Heart Journal (2022) **00**, 1–114
https://doi.org/10.1093/eurheartj/ehac237

ESC/ERS GUIDELINES

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS).

Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG).

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‡ Representing the Association for European Paediatric and Congenital Cardiology (AEPC)

ESC Clinical Practice Guidelines (CPG) Committee: listed in the Appendix.

ESC subspecialty communities having participated in the development of this document:

Associations: Association of Cardiovascular Nursing & Allied Professions (ACNAP), European Association of Cardiovascular Imaging (EACVI), and Heart Failure Association (HFA).

Councils: Council on Cardiovascular Genomics.

Working Groups: Adult Congenital Heart Disease, Pulmonary Circulation and Right Ventricular Function, Thrombosis.

Patient Forum

Tables of Recommendations

Humbert M et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, *EHJ* 2022, *ERJ* 2022

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

1. Pulmonary arterial hypertension — 1 %

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 Human immunodeficiency virus (HIV) infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease (Table 6)
  - 1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

- 1'.1 Idiopathic
- 1'.2 Heritable
  - 1'.2.1 EIF2AK4 mutation
  - 1'.2.2 Other mutations
- 1'.3 Drugs, toxins and radiation induced
- 1'.4 Associated with:
  - 1'.4.1 Connective tissue disease
  - 1'.4.2 HIV infection

1''. Persistent pulmonary hypertension of the newborn

2. Pulmonary hypertension due to left heart dise — 70 %

- 2.1 Left ventricular systolic dysfunction
- 2.2 Left ventricular diastolic dysfunction
- 2.3 Valvular disease
- 2.4 Congenital / acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
- 2.5 Congenital /acquired pulmonary veins stenosis

3. Pulmonary hypertension due to lung diseases a hypoxia — 20 %

- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental lung diseases (Web Table III)

4. Chronic thromboembolic pulmonary hypertensi and other pulmonary artery obstructions — 4 %

- 4.1 Chronic thromboembolic pulmonary hypertension
- 4.2 Other pulmonary artery obstructions
  - 4.2.1 Angiosarcoma
  - 4.2.2 Other intravascular tumors
  - 4.2.3 Arteritis
  - 4.2.4 Congenital pulmonary arteries stenoses
  - 4.2.5 Parasites (hydatidosis)

5. Pulmonary hypertension with unclear and/or multifactorial mechanisms — 5 %

- 5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
- 5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: pulmonary tumoral thrombotic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

Galie N et al. *Eur Respir J* 2015, 46(4):903-75

KLINICKÁ KLASIFIKACE PLICNÍ HYPERTENZE (2022)

GROUP 1 Pulmonary arterial hypertension (PAH) — 1 %
- 1.1 Idiopathic
  - 1.1.1 Non-responders at vasoreactivity testing
  - 1.1.2 Acute responders at vasoreactivity testing
- 1.2 Heritable[a]
- 1.3 Associated with drugs and toxins[a]
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 HIV infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease
  - 1.4.5 Schistosomiasis
- 1.5 PAH with features of venous/capillary (PVOD/PCH) involvement
- 1.6 Persistent PH of the newborn

GROUP 2 PH associated with left heart disease — 70 %
- 2.1 Heart failure:
  - 2.1.1 with preserved ejection fraction
  - 2.1.2 with reduced or mildly reduced ejection fraction[b]
- 2.2 Valvular heart disease
- 2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH

GROUP 3 PH associated with lung diseases and/or hypoxia — 20 %
- 3.1 Obstructive lung disease or emphysema
- 3.2 Restrictive lung disease
- 3.3 Lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoventilation syndromes
- 3.5 Hypoxia without lung disease (e.g. high altitude)
- 3.6 Developmental lung disorders

GROUP 4 PH associated with pulmonary artery obstructions — 4 %
- 4.1 Chronic thrombo-embolic PH
- 4.2 Other pulmonary artery obstructions[c]

GROUP 5 PH with unclear and/or multifactorial mechanisms — 5 %
- 5.1 Haematological disorders[d]
- 5.2 Systemic disorders[e]
- 5.3 Metabolic disorders[f]
- 5.4 Chronic renal failure with or without haemodialysis
- 5.5 Pulmonary tumour thrombotic microangiopathy
- 5.6 Fibrosing mediastinitis

Humbert M et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension
EHJ 2022, *ERJ* 2022

2015

Definition	Characteristics[a]
PH	PAPm ≥25 mmHg
Pre-capillary PH	PAPm ≥25 mmHg PAWP ≤15 mmHg
Post-capillary PH	PAPm ≥25 mmHg PAWP >15 mmHg
Isolated post-capillary PH (Ipc-PH)	DPG <7 mmHg and/or PVR ≤3 WU[c]
Combined post-capillary and pre-capillary PH (Cpc-PH)	DPG ≥7 mmHg and/or PVR >3 WU[c]

2022

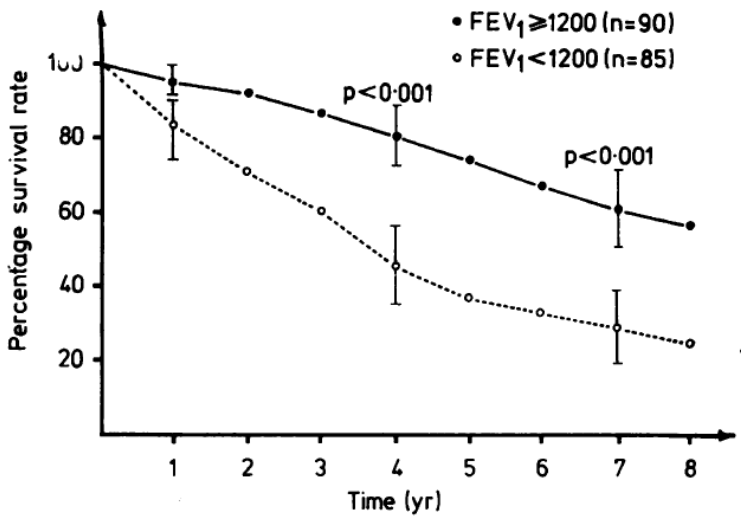
Definition	Haemodynamic characteristics
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR >2 WU
Isolated post-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR ≤2 WU
Combined post- and pre-capillary PH	mPAP >20 mmHg PAWP >15 mmHg PVR >2 WU
Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L/min

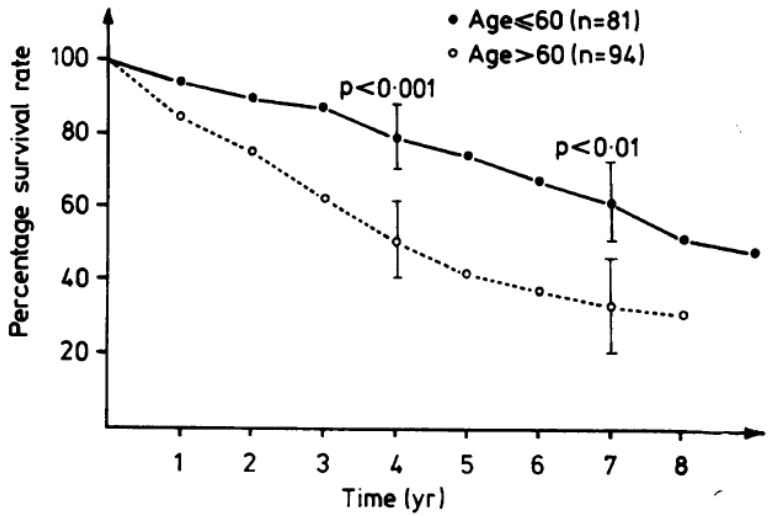
Cor et Vasa 58 (2016)
EHJ 2022, *ERJ* 2022

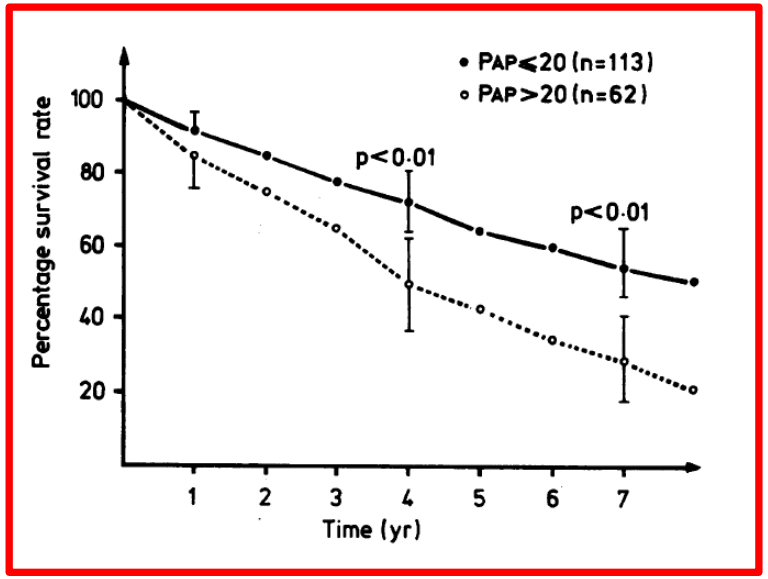
Prognostic value of pulmonary artery pressure in chronic obstructive pulmonary disease

E WEITZENBLUM, C HIRTH, A DUCOLONE, R MIRHOM,
J RASAHOLINJANAHARY, M EHRHART

N=175, RHC 1968-1972, FEV1 40.2 ±11.1 %, PAMP 19.8 ± 7.6 mmHg, CI 3.24 ± 0.93 L/min/m^2
Rekatetrizace: N=64 (po 5.5 letech)

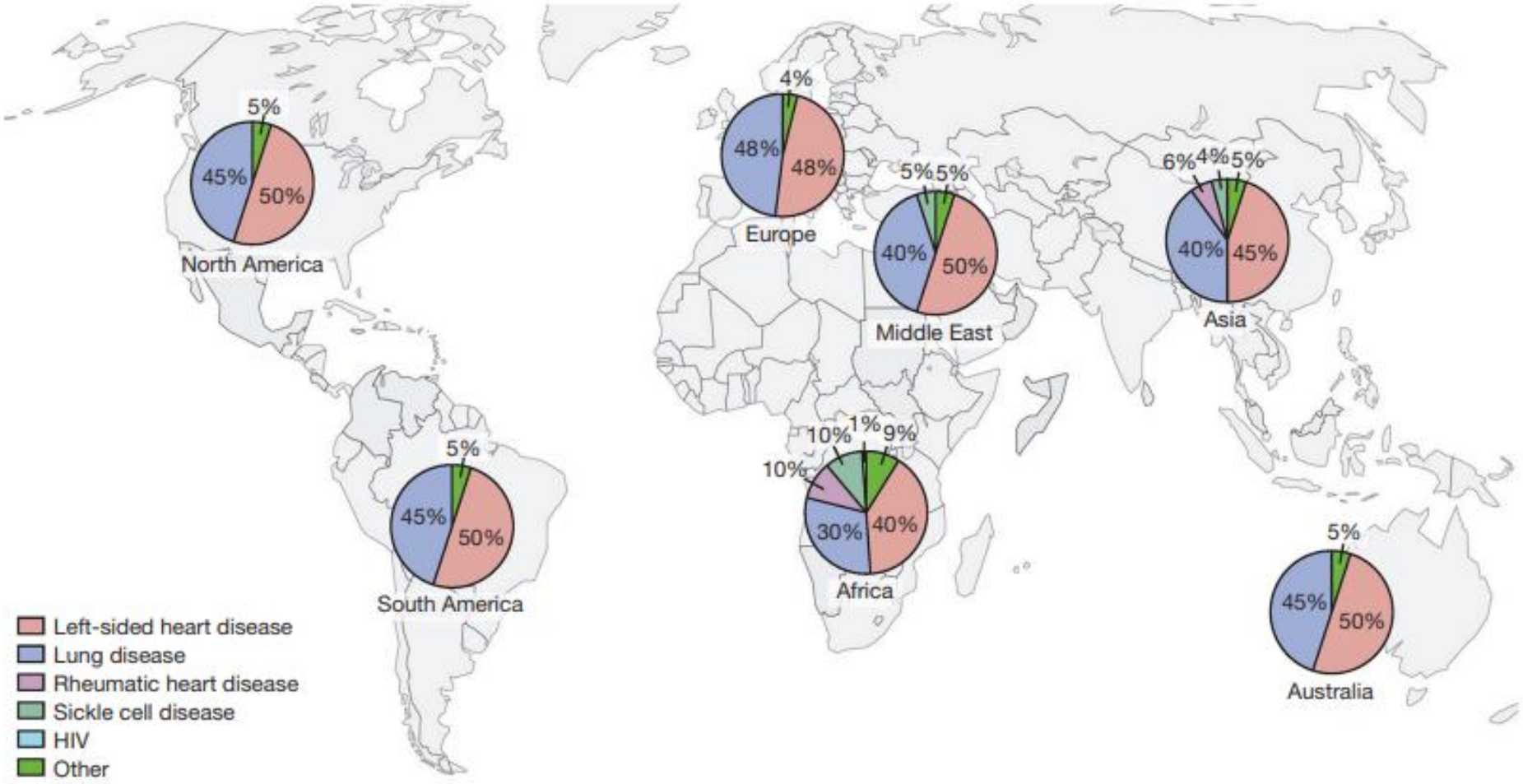






Thorax 1981 ;36:752-758

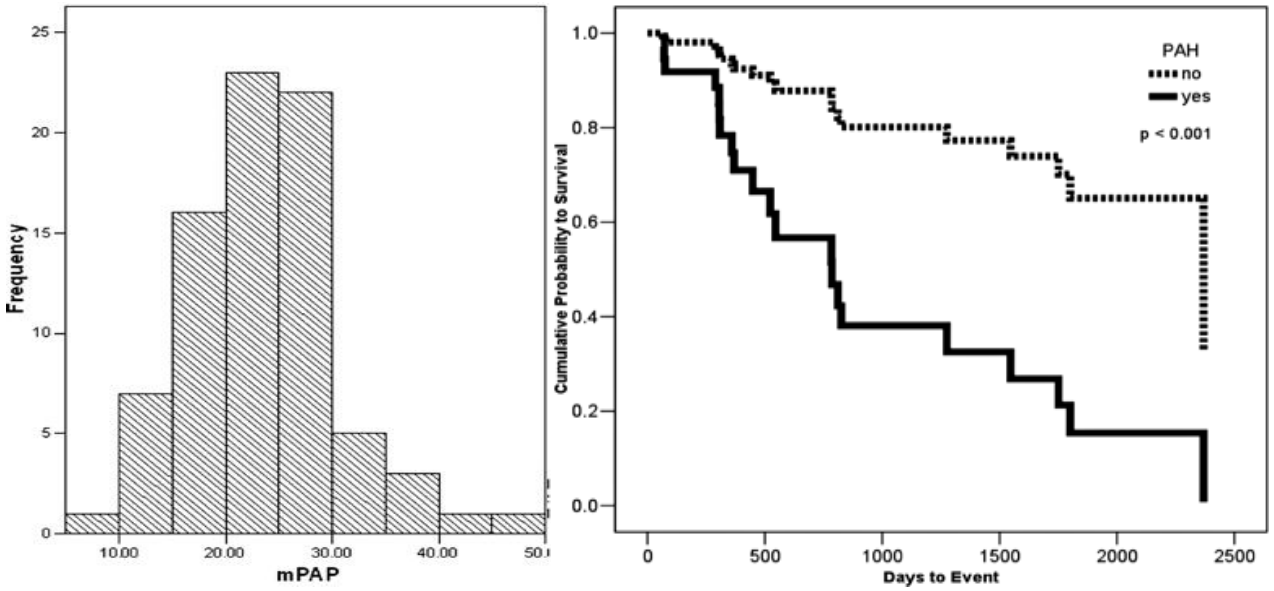
CELOSVĚTOVÁ PREVALENCE PLICNÍ HYPERTENZE



Dzudie A et al. *Cardiovasc Diagn Ther* 2020;10(2):316-324

Prevalence and Outcomes of Pulmonary Arterial Hypertension in Advanced Idiopathic Pulmonary Fibrosis*

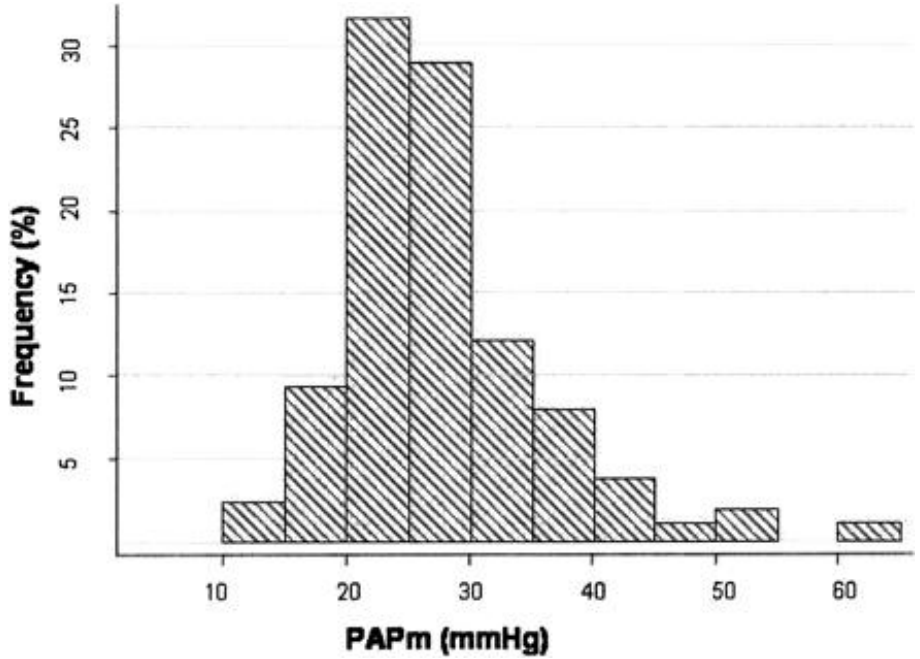
Christopher J. Lettieri, MD; Steven D. Nathan, MD, FCCP; Scott D. Barnett, PhD; Shahzad Ahmad, MD; and Andrew F. Shorr, MD, MPH, FCCP



n=79
plicní hypertenze 31.6 % (PAMP 29.5 mmHg)

Pulmonary Hemodynamics in Advanced COPD Candidates for Lung Volume Reduction Surgery or Lung Transplantation*

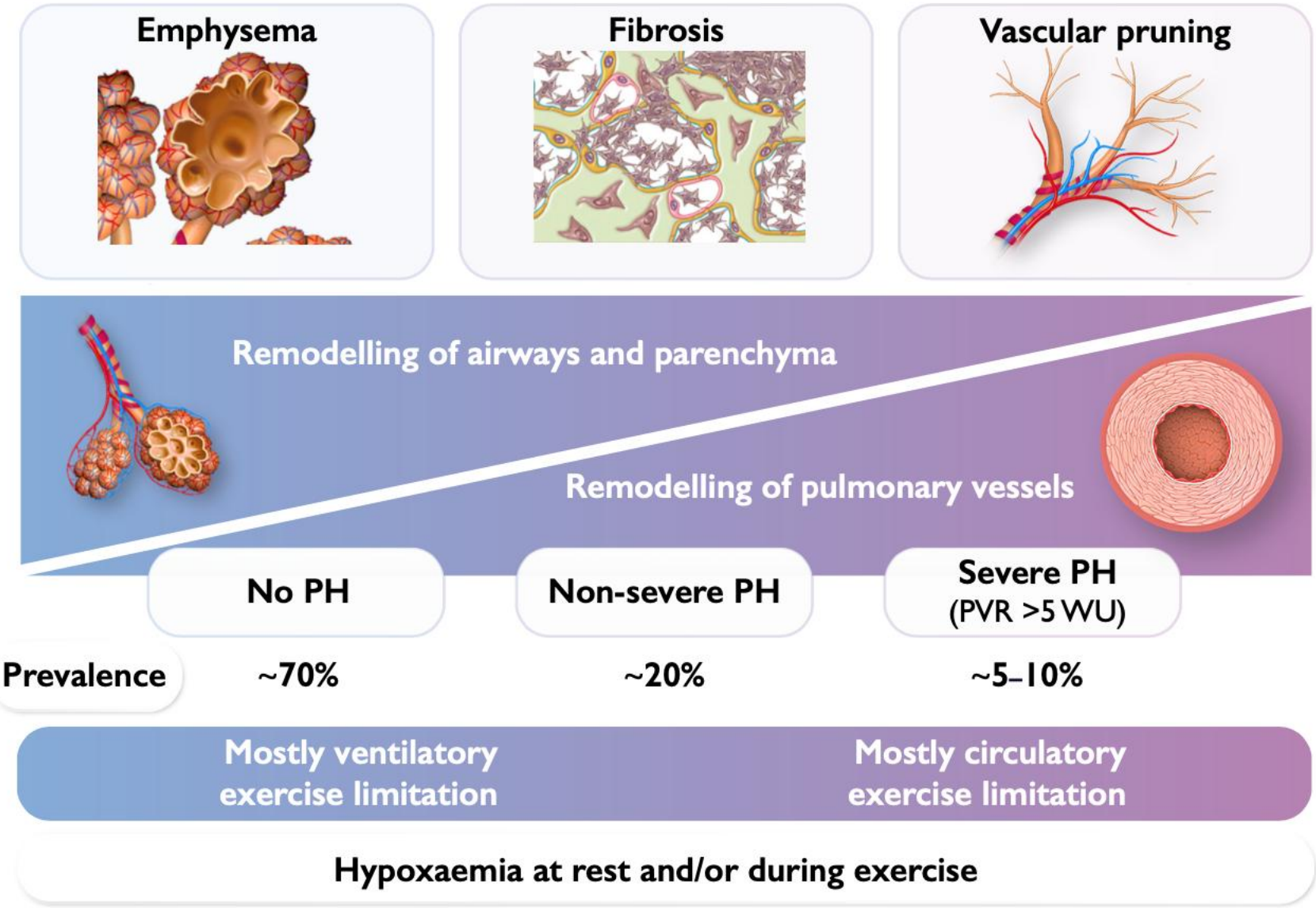
Gabriel Thabut, MD; Gaëlle Dauriat, MD; Jean Baptiste Stern, MD; Damien Logeart, MD; Antoine Lévy, MD; Rolana Marrash-Chahla, MD; and Hervé Mal, MD



n=247
PAMP (mmHg): 50 % > 25, 12 % > 35, 5 % > 40 mmHg

Chest 2006, 129: 746-752, *Chest* 2005, 127: 1531-36

PLICNÍ HYPERTENZE ASOCIOVANÁ S PLICNÍMI ONEMOCNĚNÍMI

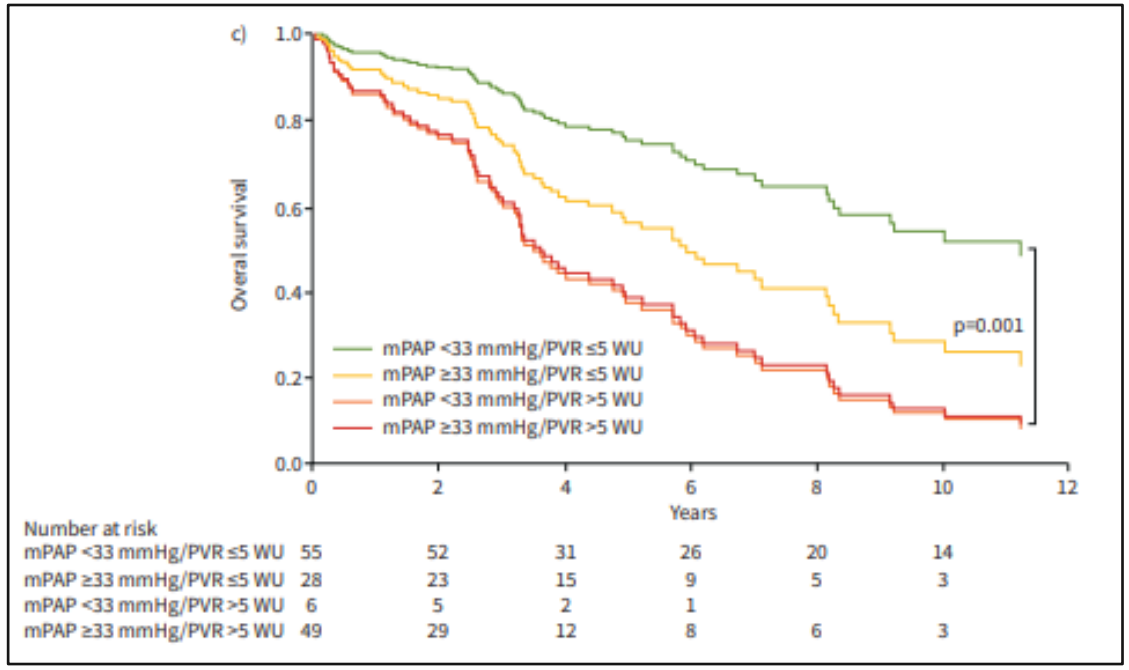


Těžká PH
PVR > 5 WU

- Bez vztahu k plicním objemům
- Hypoxémie
- Nízká DLco

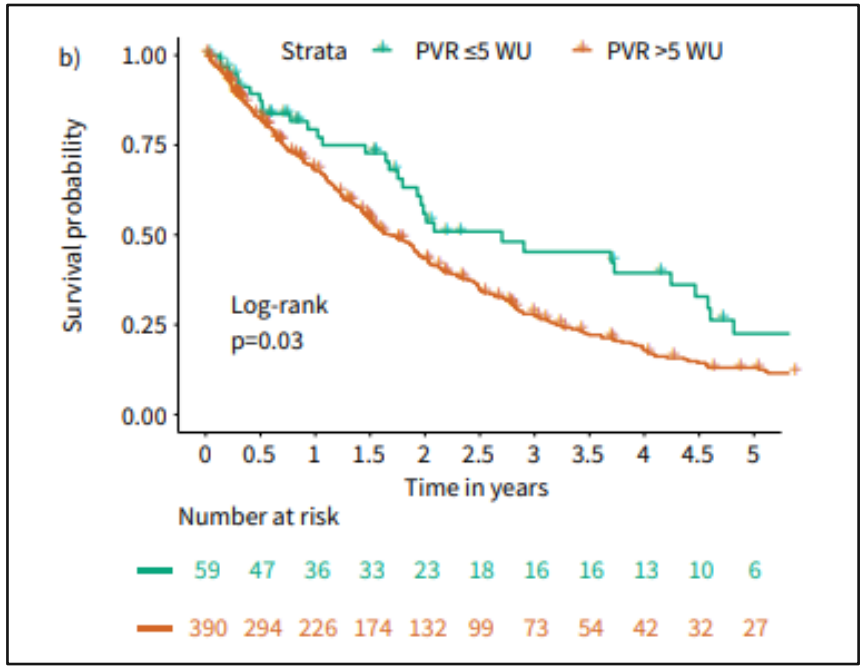
Humbert M et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, *EHJ* 2022, *ERJ* 2022

Elevated pulmonary vascular resistance predicts mortality in COPD patients



N=139, věk 68, 55 % mužů
PAMP 35 (27–43) mmHg, PVR 4.3 (2.9–7.3) WU, FEV1 56±20%

Pulmonary vascular resistance predicts mortality in patients with pulmonary hypertension associated with interstitial lung disease: results from the COMPERA registry

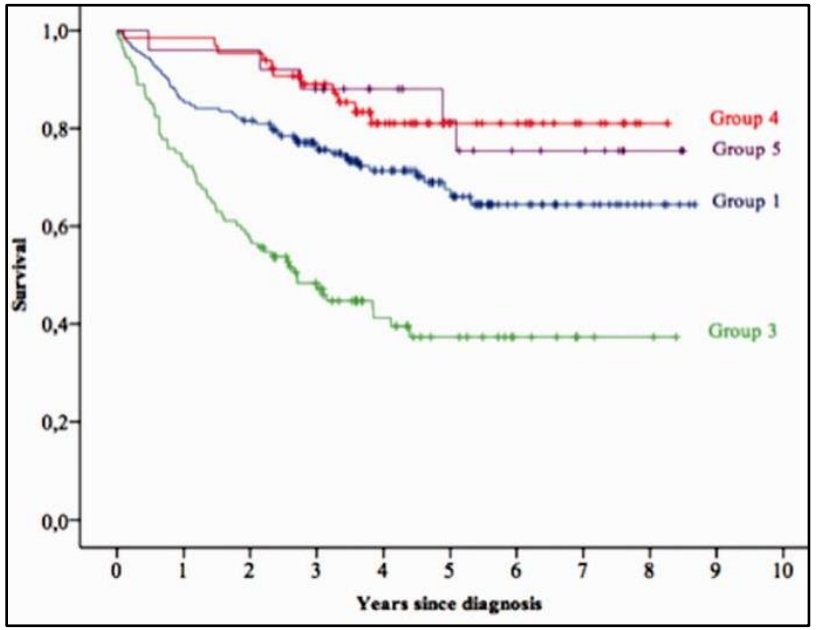


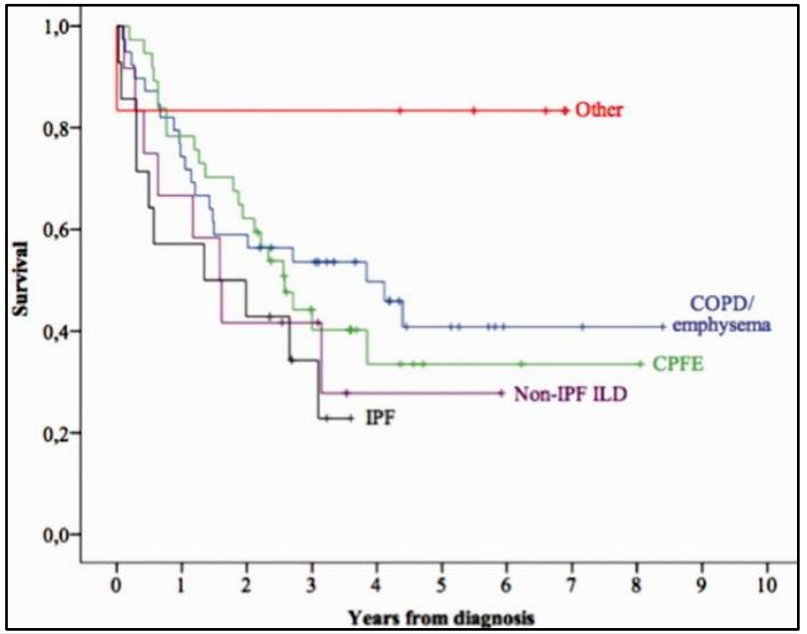
N=449, věk 73, 65 % mužů
PAMP 39 (33, 46) mmHg, PVR 7.6 (6.0, 10.6) WU,
TLC 72 (60, 86) %, FEV1 69 (55, 81) %

Zeder K et al. *Eur Respir J* 2021; 58: 2100944,
Olsson KM et al. . *Eur Respir J* 2021; 58: 2101483

Pulmonary hypertension in chronic lung diseases: comparison to other pulmonary hypertension groups

N=363, 2006-2014
Skupina 1 164 (45.2%), **skupina 3** 109 (30%), **skupina 4** 65 (17.9%), **skupina 5** 25 (6.9%)

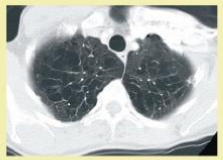




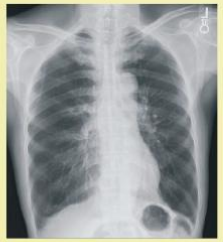
	Overall	Group 1	Group 3	Group 4	Group 5	P*
Pericardial effusion (n (%))	57 (15.7)	26 (15.8)	18 (16.5)	8 (12.3)	5 (20)	0.82
mPAP† (mmHg)	40 (25–83)	38 (25–83)	41 (26–72)	42 (26–68)	35 (26–63)	0.01
PCWP† (mmHg)	9 (1–15)	9 (1–15)	10 (2–15)	8 (1–15)	11 (3–15)	0.13
PVR† (WU)	9.1 (3.3–45.5)	8.5 (3.3–28.5)	9.7 (3.9–23.1)	10.3 (4.5–45.5)	7.4 (3.9–17.9)	0.001
CI† (L/min/m^2)	2.4 (0.8–5.6)	2.6 (1.1–5.2)	2.4 (1.1–4)	2.2 (0.8–3.7)	3 (1.7–5.6)	0.001
RAP† (mmHg)	6 (0–27)	6 (0–27)	6 (1–21)	5 (0–21)	6 (0–16)	0.54
SvO2† (%)	64 (25–94)	66 (33–93)	61 (40–93)	61 (25–94)	65 (34–89)	<0.001

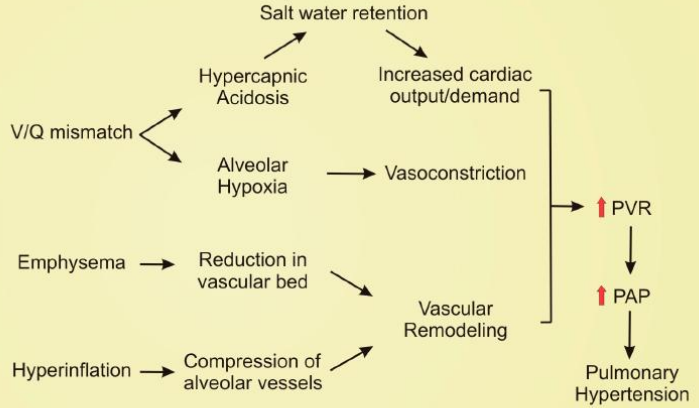
Chebib N. et. al. *Pulmonary Circulation* 2018; 8(2) 1–10

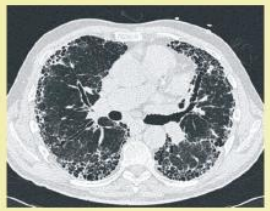
PATOFYZIOLOLGIE PH U PLICNÍCH ONEMOCNĚNÍ



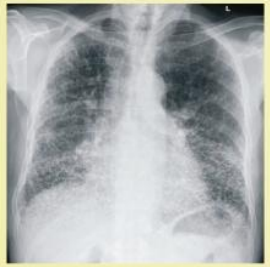
Chronic Obstructive Pulmonary Disease

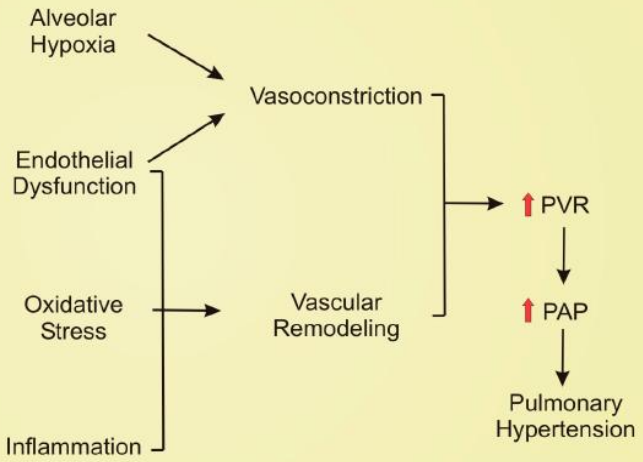


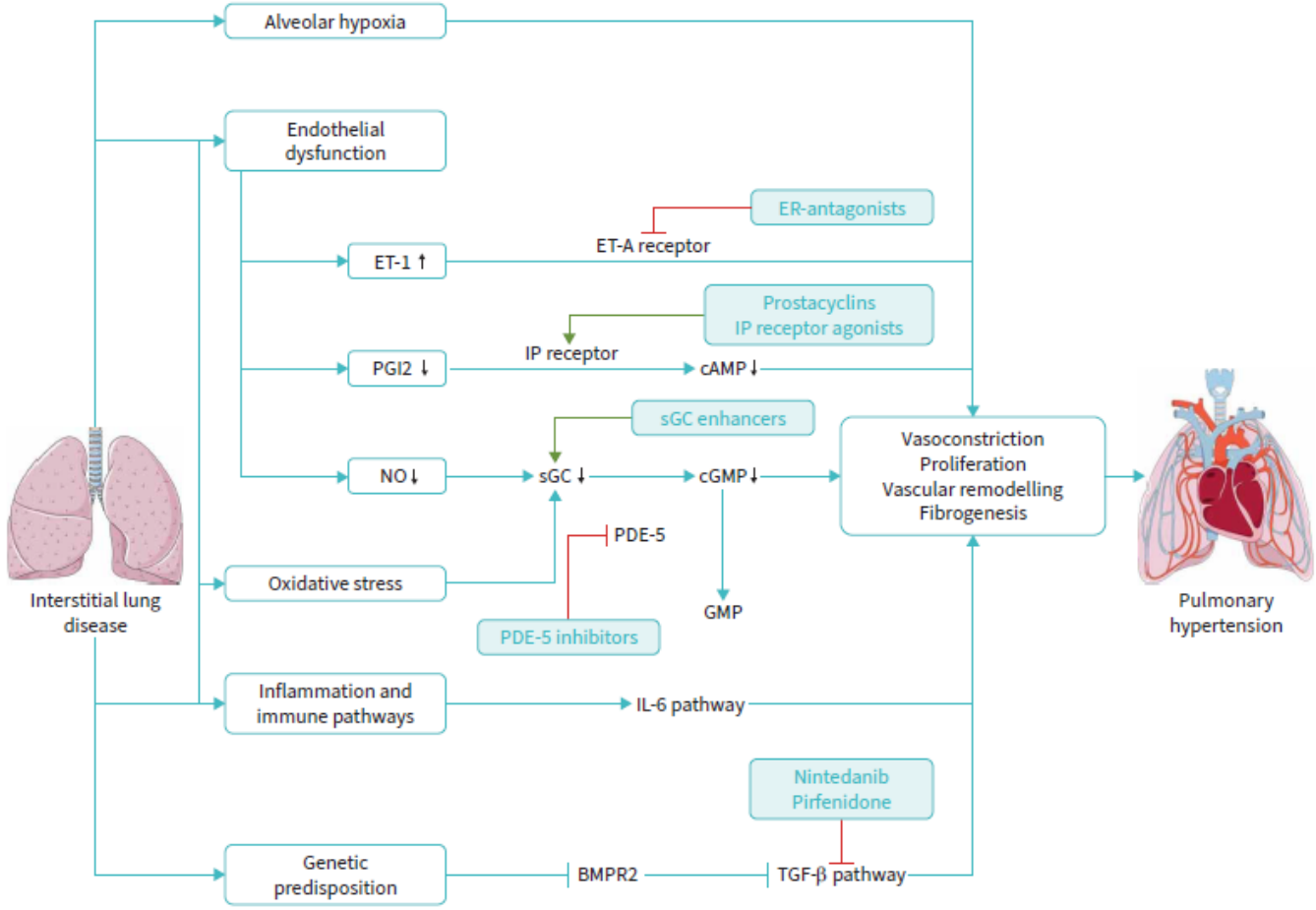




Interstitial Lung Disease





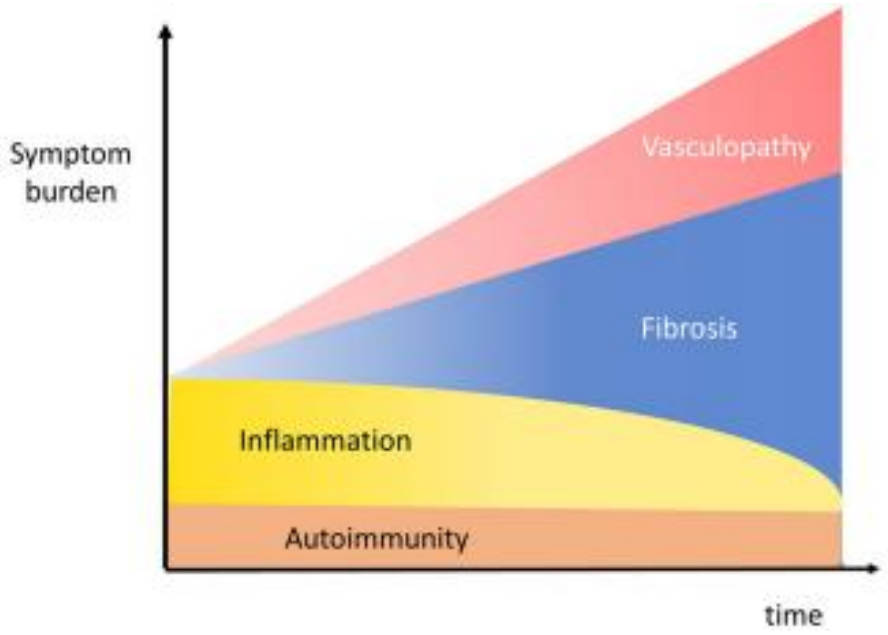


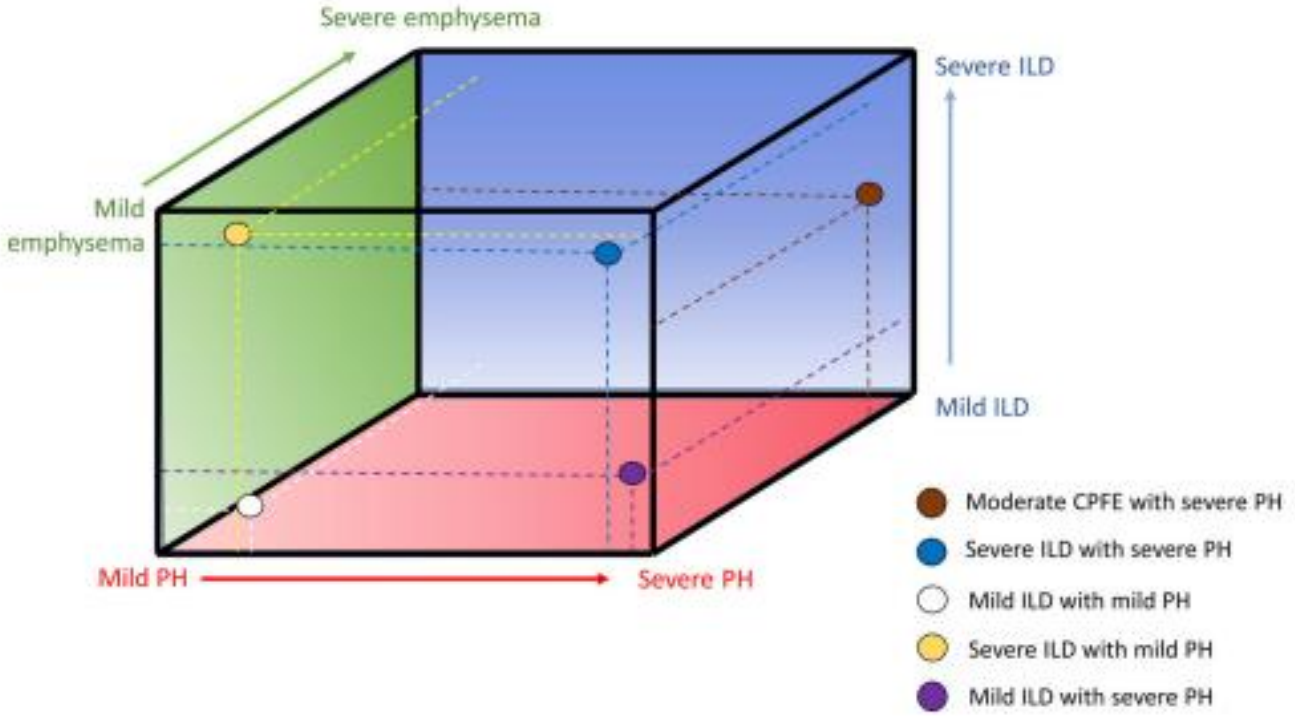
PVR≤5WU

PVR>5WU

Gonzales J et al. *Pharmaceuticals 2023*, 16, 418, Dhont S et al. *ERJ Open Res* 2022; 8: 00272-2022

Pathogenesis, clinical features, and phenotypes of pulmonary hypertension associated with interstitial lung disease: A consensus statement from the Pulmonary Vascular Research Institute's Innovative Drug Development Initiative - Group 3 Pulmonary Hypertension

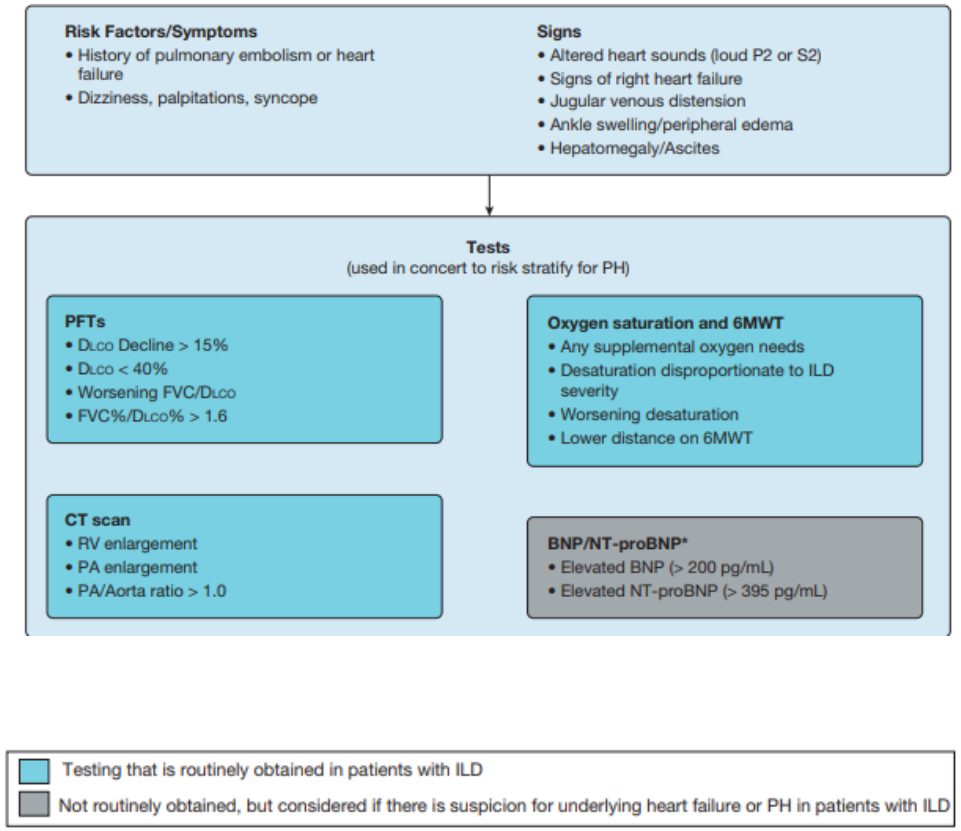




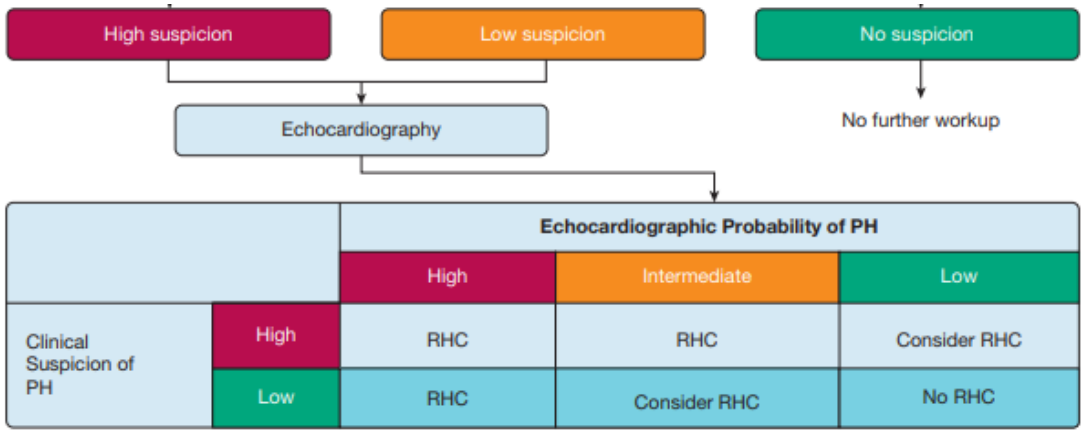
Piccari L et al. *Pulmonary Circulation*. 2023;13:e12213.

DIAGNOSTIKA PH U PLICNÍCH ONEMOCNĚNÍ

suspekce

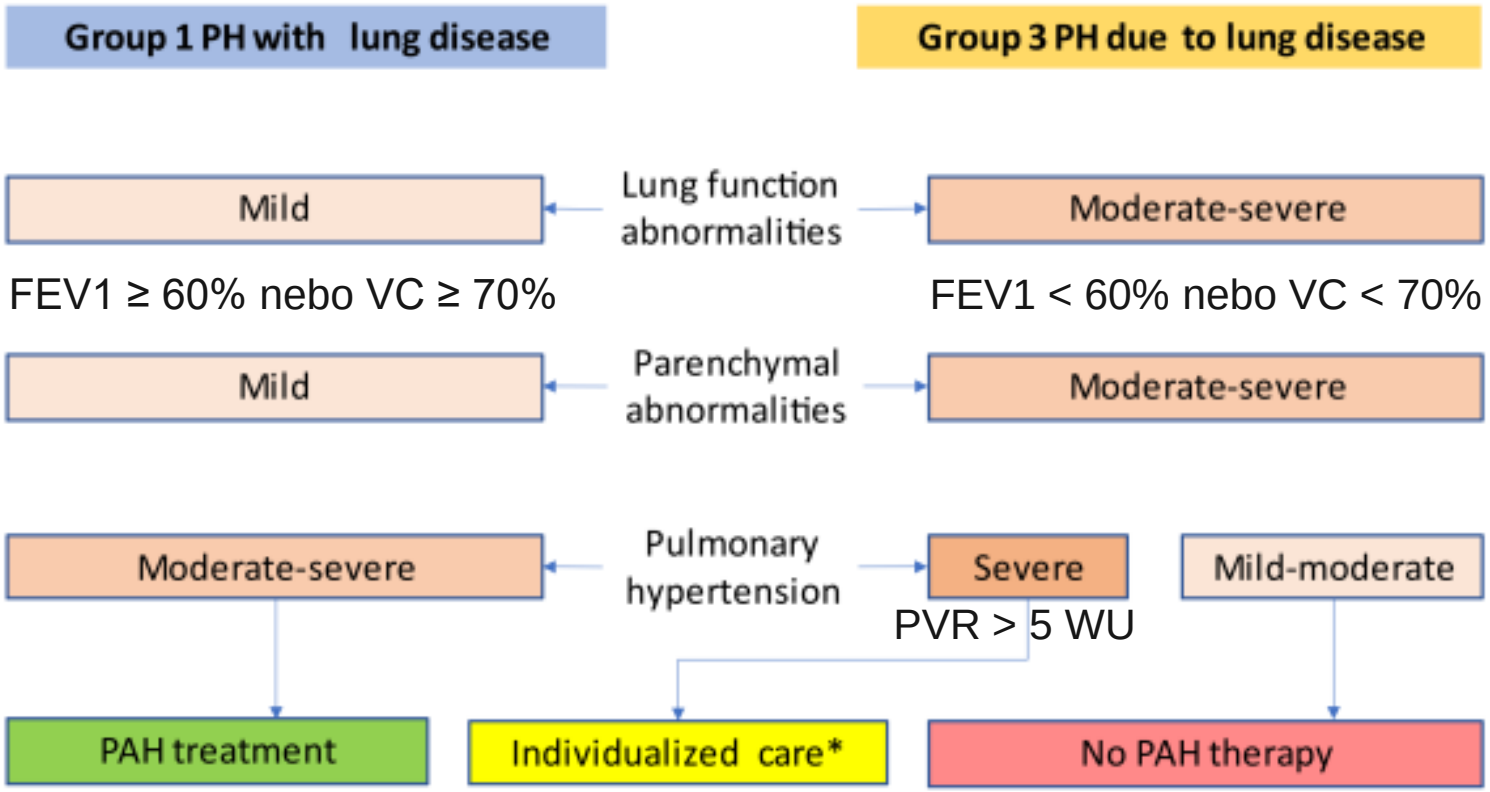


detekce→konfirmace



Rahaghi FF et al. *CHEST* 2022; 162(1):145-155

The Challenge to Decide between Pulmonary Hypertension Due to Chronic Lung Disease and PAH with Chronic Lung Disease



Olschewski H. *Diagnostics* 2021, 11, 311

Léčba: Léčba základního plicního onemocnění , DDOT pokud indikována , CPAP pokud indikován, plicní RHB programy, Zvážení LuTx
U kombinované etiologie PH adekvátní léčba, specifická vazodilatační léčba?

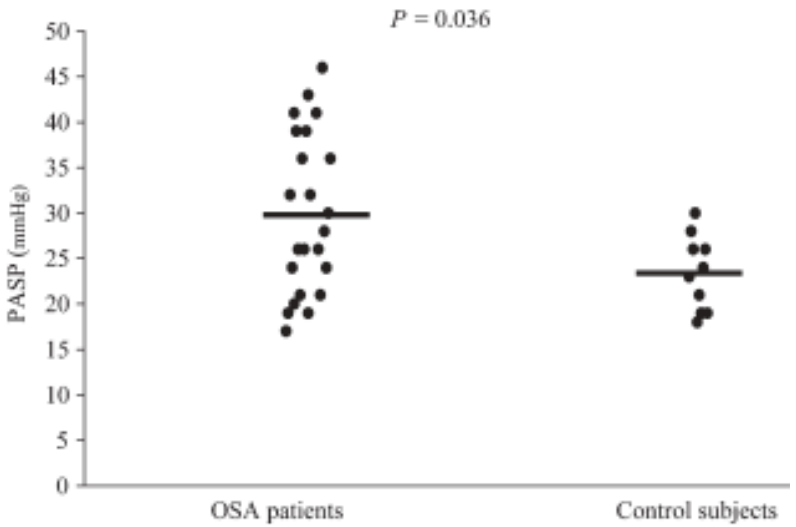
EHJ 2022, *ERJ* 2022

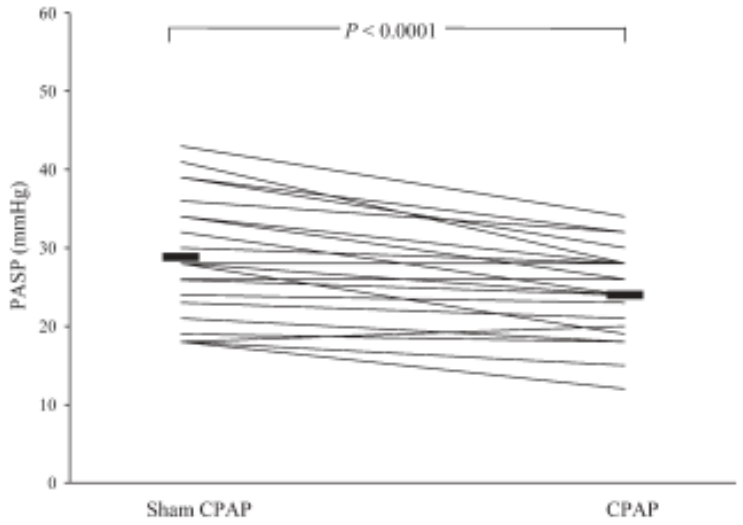
Léčba: Léčba základního plicního onemocnění , DDOT pokud indikována , CPAP pokud indikován, plicní RHB programy, Zvážení LuTx
U kombinované etiologie PH adekvátní léčba, specifická vazodilatační léčba?

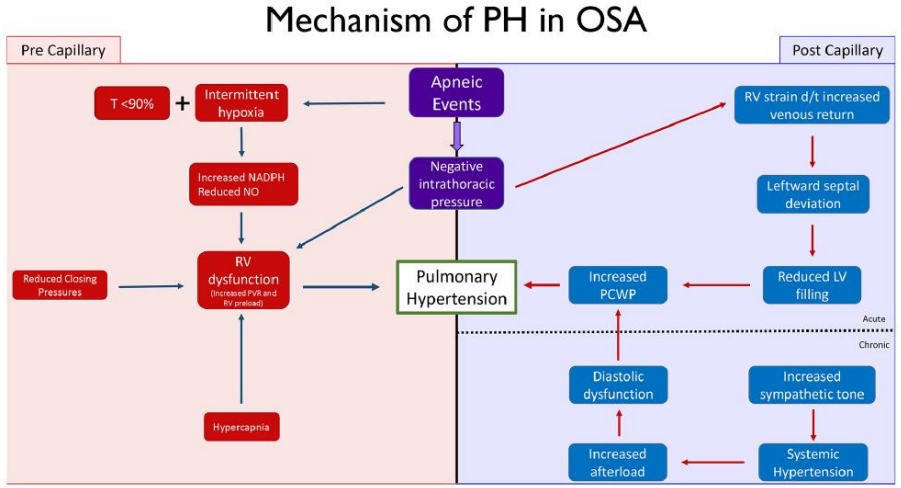
Pulmonary hypertension in obstructive sleep apnoea: effects of continuous positive airway pressure

A randomized, controlled cross-over study

23 pacientů s OSA (AHI 44.1 + 29.3), 10 kontrol
Randomizace: 12 týdnů účinná vs předstíraná léčba přetlakem, neinvazivní odhad tlaků v plicnici
Efekt významnější u pacientů s diastolickou dysfunkcí







European Heart Journal (2006) 27, 1106–1113
Pharmacology & Therapeutics (2021) 227, 107935
EHJ 2022, *ERJ* 2022

PLICNÍ HYPERTENZE ASOCIOVANÁ S PLICNÍMI ONEMOCNĚNÍMI

Léčba: Léčba základního plicního onemocnění , DDOT pokud indikována , CPAP pokud indikován, plicní RHB programy, Zvážení LuTx
U kombinované etiologie PH adekvátní léčba, specifická vazodilatační léčba?

Trial Study	Therapy	Target	Outcome
Chronic Obstructive Pulmonary Disease-Associated Pulmonary Hypertension (COPD-PH)			
Blanco et al., 2010	Sildenafil	NO	Reduced mean PAP
Blanco et al., 2013	Sildenafil and pulmonary rehabilitation	NO	No improvement in cycle endurance time
Goudie et al., 2014	Tadalafil	NO	No improvement in 6MWD
SPHERIC-1 Vitulo et al., 2017	Sildenafil	NO	Reduced PVR
Stolz et al., 2008	Bosentan	ET-1	No improvement in 6MWD
Valerio et al., 2009	Bosentan	ET-1	Reduced mean PAP and PVR, Increased 6MWD, and reduced BODE index

Humbert M et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, *EHJ* 2022, *ERJ* 2022
Gonzales J et al. Pharmacology and Emerging Therapies for Group 3 Pulmonary Hypertension Due to Chronic Lung Disease. *Pharmaceuticals* 2023, 16, 418

PLICNÍ HYPERTENZE ASOCIOVANÁ S PLICNÍMI ONEMOCNĚNÍMI

Léčba: Léčba základního plicního onemocnění , DDOT pokud indikována , CPAP pokud indikován, plicní RHB programy, Zvážení LuTx

U kombinované etiologie PH adekvátní léčba, specifická vazodilatační léčba?

Trial Study	Therapy	Target	Outcome
Pulmonary Fibrosis-Associated Pulmonary Hypertension (PF-PH)			
STEP-IPF Zisman et al., 2010	Sildenafil	NO	No improvement in 6MWD
Behr et al., 2021	Sildenafil and Pirfenidone	NO	No improvement in 6MWD, respiratory hospitalization, or mortality
RISE-IIP Nathan et al., 2019	Riociguat	NO	No improvement in 6MWD; increased adverse events and mortality
iNO-PF Nathan et al., 2020	Pulsed inhaled NO	NO	Increased moderate/vigorous physical activity
ARTEMIS-IPF Raghu et al., 2013	Ambrisentan	ET-1	No improvement in lung function, respiratory hospitalization, or death; Increased harm
BPHIT Corte et al., 2014	Bosentan	ET-1	No decrease to PVR index of 20% or more
INCREASE Waxman et al., 2021	Inhaled Treprostinil	Prostacyclin	Improvement in 6MWD

Humbert M et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, *EHJ* 2022, *ERJ* 2022

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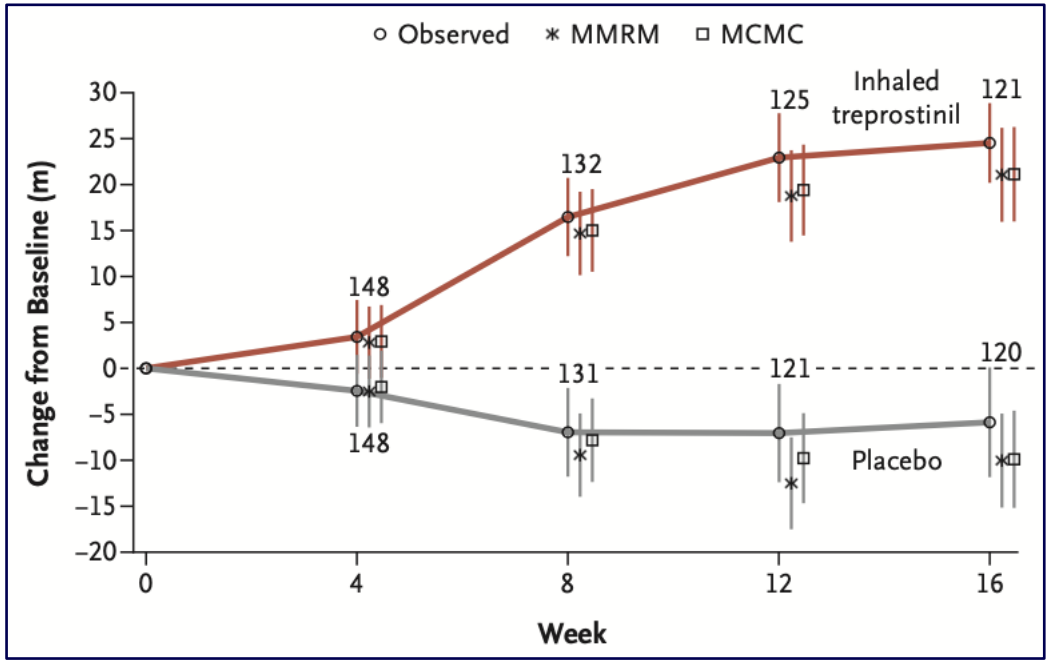
Gonzales J et al. Pharmacology and Emerging Therapies for Group 3 Pulmonary Hypertension Due to Chronic Lung Disease. *Pharmaceuticals* 2023, 16, 418

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inhaled Treprostinil in Pulmonary Hypertension Due to Interstitial Lung Disease

N=326, PH u ILD, inhal. treprostinil 12 vdechů (celkem 72 µg) 4x denně vs placebo
Prekapilární PH, PVR více než 3 WU, FVC méně než 70 %, 68 (21 %) předčasně ukončilo studii



End Point	Inhaled Treprostinil (N=163)	Placebo (N=163)	Treatment Effect (95% CI)	P Value
Primary end point				
Change in peak 6-minute walk distance from baseline to wk 16 — m†	21.08±5.12	−10.04±5.12	31.12±7.25 (16.85 to 45.39)‡	<0.001
Secondary end points§				
Change in plasma concentration of NT-proBNP from baseline to wk 16¶				
Mean (±SD) change — pg/ml	−396.35±1904.90	1453.95±7296.20		
Median — pg/ml	−22.65	20.65		
Range — pg/ml	−11,433.0 to 5373.1	−5483.3 to 87,148.3		
Ratio to baseline	0.85±0.06	1.46±0.11	0.58±0.06 (0.47 to 0.72)‖	<0.001
Occurrence of clinical worsening — no. (%)			0.61 (0.4 to 0.92)**	0.04
Any event	37 (22.7)	54 (33.1)		
Hospitalization for cardiopulmonary indication	18 (11.0)	24 (14.7)		
Decrease in 6-minute walk distance of >15% from baseline	13 (8.0)	26 (16.0)		
Death from any cause	4 (2.5)	4 (2.5)		
Lung transplantation	2 (1.2)	0		
Least-squares mean change in peak 6-minute walk distance from baseline to wk 12 — m†	18.77±4.99	−12.52±5.01	31.29±7.07 (17.37 to 45.21)‡	<0.001
Least-squares mean change in trough 6-minute walk distance from baseline to wk 15 — m	9.3±5.5	−12.7±5.5	21.99±7.7 (6.85 to 37.14)‡	0.005††

Waxman A et al. *N Engl J Med* 2021;384:325-34.

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Waxman A, Restrepo-Jaramillo R, Thenappan T, et al. Inhaled treprostinil in pulmonary hypertension due to interstitial lung disease. N Engl J Med 2021;384:325-34. DOI: 10.1056/NEJMoa2008470

	Inhaled Treprostinil (N=163)	Placebo (N=163)	All Patients (N=326)
6-minute walk distance, meters; mean (range)	254.1 (100-538)	265.1 (30-505)	259.6 (30-538)
Median	256.0	260.0	259.0
Pulmonary vascular resistance, Woods units; mean (range)	6.369 (3.11-18.05)	6.013 (3.06-17.62)	6.191 (3.06-18.05)
Median	5.570	5.060	5.275
NT-proBNP, pg/mL; mean (range)	1857.53 (10.2-21942.0)	1808.86 (23.0-16297.0)	1832.88 (10.2-21942.0)
Median*	550.50	420.80	503.85
Pulmonary arterial pressure, mmHg; mean (range)	37.2 (25-74)	36.0 (25-61)	36.6 (25-74)
Median	35.0	35.0	35.0
Pulmonary capillary wedge pressure, mmHg; mean (range)	10.1 (2-20)	9.6 (0-15)	9.8 (0-20)
Median	10.0	10.0	10.0
Pulmonary function tests			
FEV_1 % Predicted; mean (range)	63.9 (23, 120)	65.0 (22, 145)	
Median	63.0	63.0	
FVC % Predicted; mean (range)	62.5 (24, 130)	63.8 (20, 134)	
Median	60.0	61.0	
TLC % Predicted; mean (range)	62.9 (25, 126)	64.2 (30, 109)	
Median	62.0	62.5	
DLCO % Predicted; mean (range)	30.0 (5, 86)	28.1 (1, 86)	
Median	29.0	26.0	

Waxman A et al. *N Engl J Med* 2021;384:325-34.

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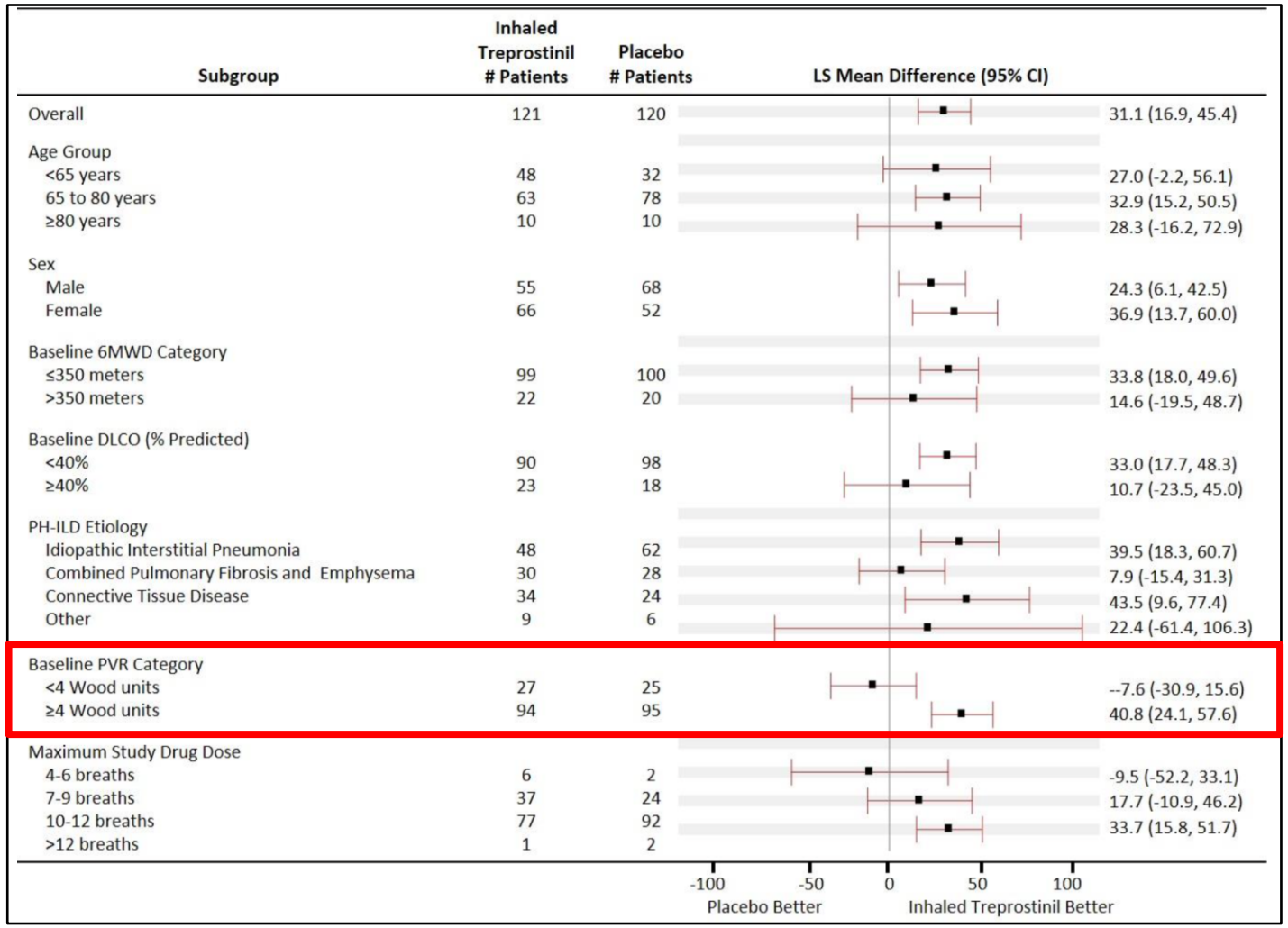
Subgroup	Inhaled Treprostinil # Patients	Placebo # Patients	LS Mean Difference (95% CI)
Overall	121	120	31.1 (16.9, 45.4)
Age Group			
<65 years	48	32	27.0 (-2.2, 56.1)
65 to 80 years	63	78	32.9 (15.2, 50.5)
≥80 years	10	10	28.3 (-16.2, 72.9)
Sex			
Male	55	68	24.3 (6.1, 42.5)
Female	66	52	36.9 (13.7, 60.0)
Baseline 6MWD Category			
≤350 meters	99	100	33.8 (18.0, 49.6)
>350 meters	22	20	14.6 (-19.5, 48.7)
Baseline DLCO (% Predicted)			
<40%	90	98	33.0 (17.7, 48.3)
≥40%	23	18	10.7 (-23.5, 45.0)
PH-ILD Etiology			
Idiopathic Interstitial Pneumonia	48	62	39.5 (18.3, 60.7)
Combined Pulmonary Fibrosis and Emphysema	30	28	7.9 (-15.4, 31.3)
Connective Tissue Disease	34	24	43.5 (9.6, 77.4)
Other	9	6	22.4 (-61.4, 106.3)
Baseline PVR Category			
<4 Wood units	27	25	--7.6 (-30.9, 15.6)
≥4 Wood units	94	95	40.8 (24.1, 57.6)
Maximum Study Drug Dose			
4-6 breaths	6	2	-9.5 (-52.2, 33.1)
7-9 breaths	37	24	17.7 (-10.9, 46.2)
10-12 breaths	77	92	33.7 (15.8, 51.7)
>12 breaths	1	2	

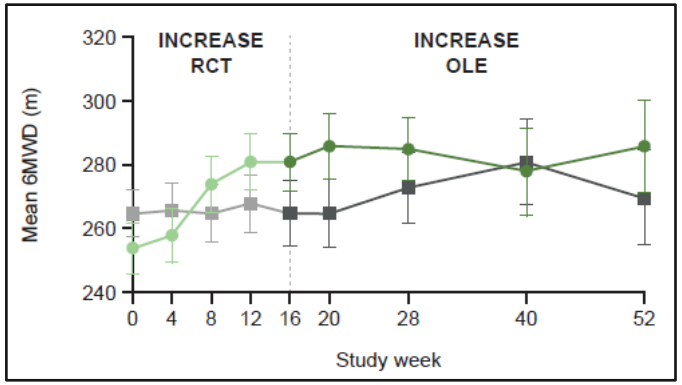


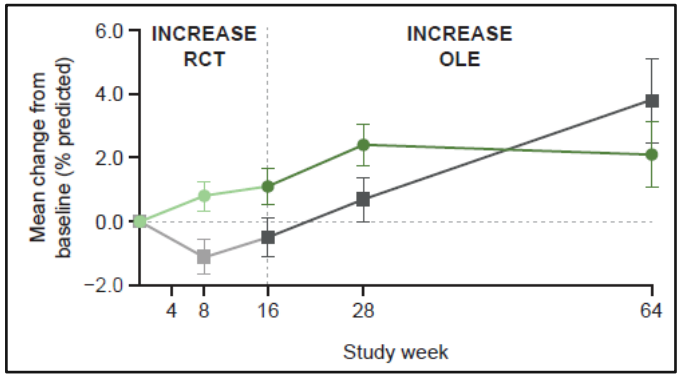
Waxman A et al. *N Engl J Med* 2021;384:325-34.

Long-term inhaled treprostinil for PH-ILD: INCREASE open-label extension study

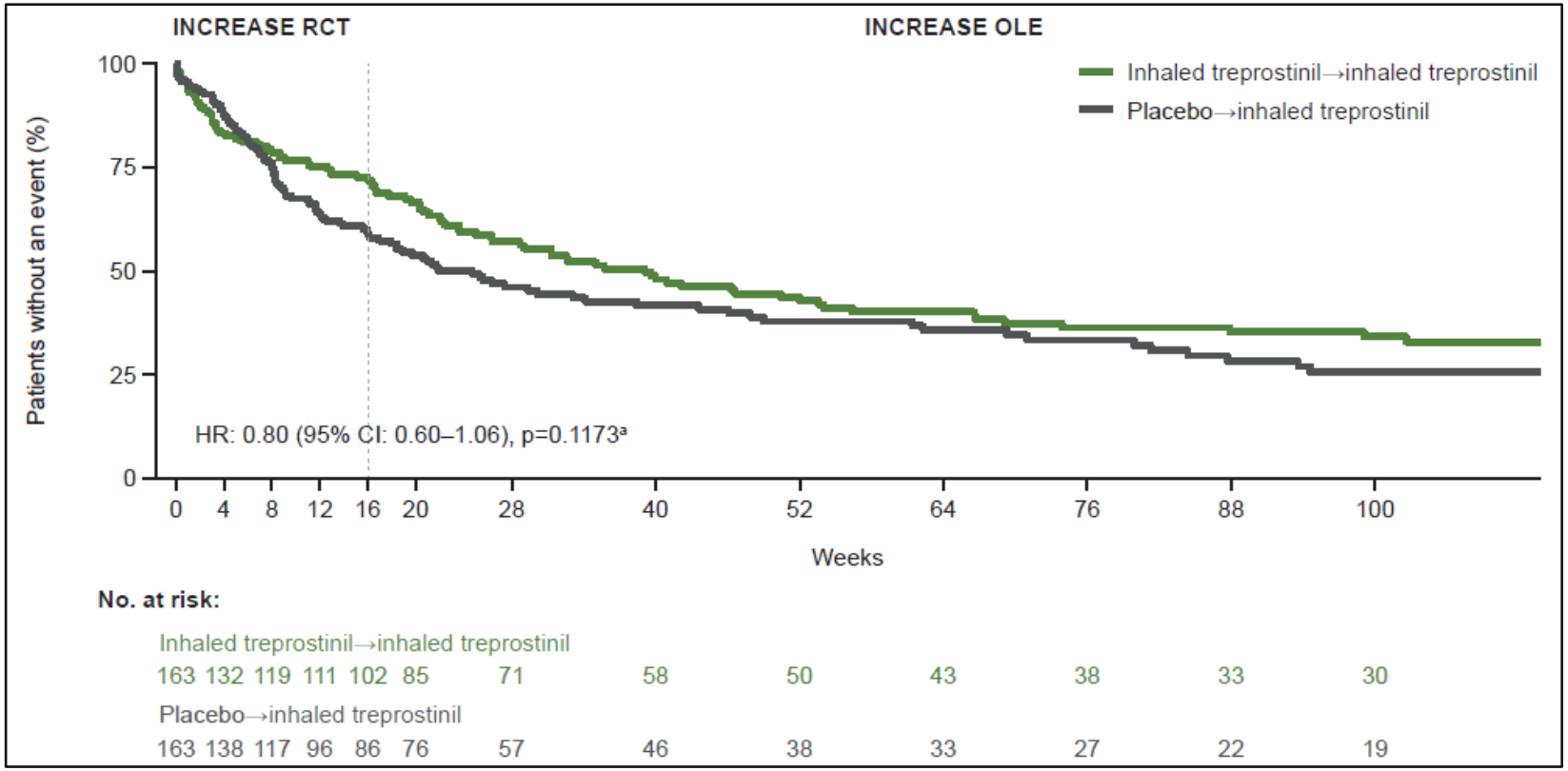
108 týdnů po skončení DB, N=242
Ukončení léčby: 172 (71 %)
úmrtí (n=56), rozhodnutí pacienta (n=41), nežádoucí účinky (n=29), ostatní (n=46)

6MWT (m)





FVC (%)



Čas do exacerbace (týdny)

Waxman A et al. *Eur Respir J* 2023; 2023 Apr 20;2202414

Pulmonary Hypertension in Patients with Chronic Fibrosing Idiopathic Interstitial Pneumonias

Registr COMPERA, IPAH (n = 798), PH-IIP (n = 151), PAPm ≥ 25 mmHg, PAWP ≤15 mmHg
PH-IPP respondér na specifickou léčbu: 6MWD ≥ 20 m nebo zlepšení NYHA třídy

	IPAH (n = 798)	PH-IIP (n = 151)	p value
Female (n, %)	478 (59.9%)	56 (37.1%)	<0.001
Age, years (mean, SD)	64.5±15.8	71.1±10.7	<0.001
BMI, kg/m^2 (mean/SD)	28.0±6.7	26.9±5.0	0.033
6MWD, m (mean, SD)	303±129	251±116	<0.001
WHO Class I (n, %)	3 (0.4%)	0	*
WHO Class II (n, %)	98 (12.5%)	4 (2.7%)	*
WHO Class III (n, %)	568 (72.4%)	106 (71.6%)	*
WHO Class IV (n, %)	115 (14.7%)	38 (25.7%)	*
TLC (% pred)	95.3±17.2	68.8±17.0	<0.001
FVC (% pred)	82.1±21.6	62.9±20.0	<0.001
FEV_1 (% pred)	76.7±21.4	67.7±20.2	0.001
DLCO (% pred)	50.1±20.5	28.5±15.8	<0.001
paO_2 (mmHg)[a]	62.4±13.4	56.3±10.4	<0.001
$paCO_2$ (mmHg)[a]	34.5±7.1	37.4±5.5	0.001
RAP, mmHg	8.6±5.0	5.9±4.8	<0.001
mPAP, mmHg	45±13	37±9	<0.001
PAWP, mmHg	9.6±3.4	8.0±3.8	<0.001
PVR, dyn.s.cm^{-5}	793±433	649±268	0.001
CI, L/min/m^2	2.2±0.7	2.1±0.6	0.438
SvO_2, %	63±9	64±8	0.063
Bilirubin (mg/dl)	0.7 (0.5–1.0)	0.6 (0.5–0.9)	0.011
Creatinine (mg/dl)	1.0 (0.8–1.3)	1.0 (0.8–1.3)	0.755
Uric acid (mg/dl)	7.2 (5.7–9.0)	7.1 (5.7–8.3)	0.224
NT-proBNP (ng/L)	1,627 (577–3,487)	1,029 (373–2901)	0.065
BNP (ng/L)	233 (93–469)	114 (59–256)	0.009

	IPAH (n = 798)	PH-IIP (n = 151)	p value
Baseline			
ERA monotherapy	172 (21.6%)	11 (7.3%)	<0.001
PDE-5 inhibitor monotherapy	461 (57.8%)	133 (88.1%)	<0.001
PCA monotherapy	13 (1.6%)	0	t.n.a.
Other monotherapy	29 (3.6%)	0	t.n.a.
ERA+PDE-5 inhibitor	85 (10.7%)	4 (2.6%)	0.001
Other double combination therapies	29 (3.6%)	3 (2.0%)	0.459
1 year			
ERA monotherapy	72 (13.6%)	4 (4.7%)	0.020
PDE-5 inhibitor monotherapy	228 (43.1%)	75 (87.2%)	<0.001
PCA monotherapy	0	1 (1.2%)	t.n.a.
Other monotherapy	8 (1.5%)	0	t.n.a.
ERA+PDE-5 inhibitor	129 (24.4%)	2 (2.3%)	<0.001
Other double combination therapies	42 (7.9%)	0	0.002
Triple combination therapy	33 (6.2%)	0	t.n.a.
No therapy	17 (3.2%)	4 (4.7%)	t.n.a.

Hoeper MM et al. *PLoS ONE* 10(12): e0141911

Pulmonary Hypertension in Patients with Chronic Fibrosing Idiopathic Interstitial Pneumonias

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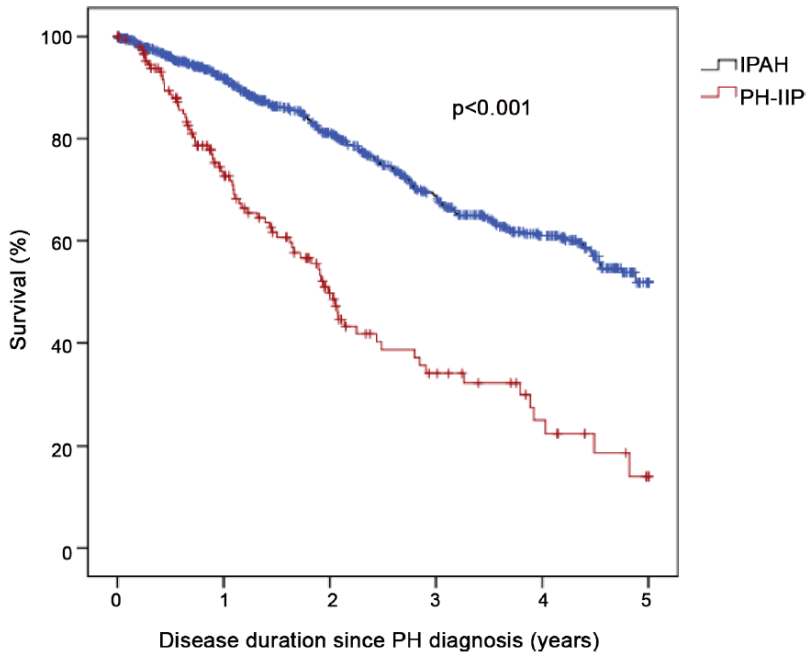
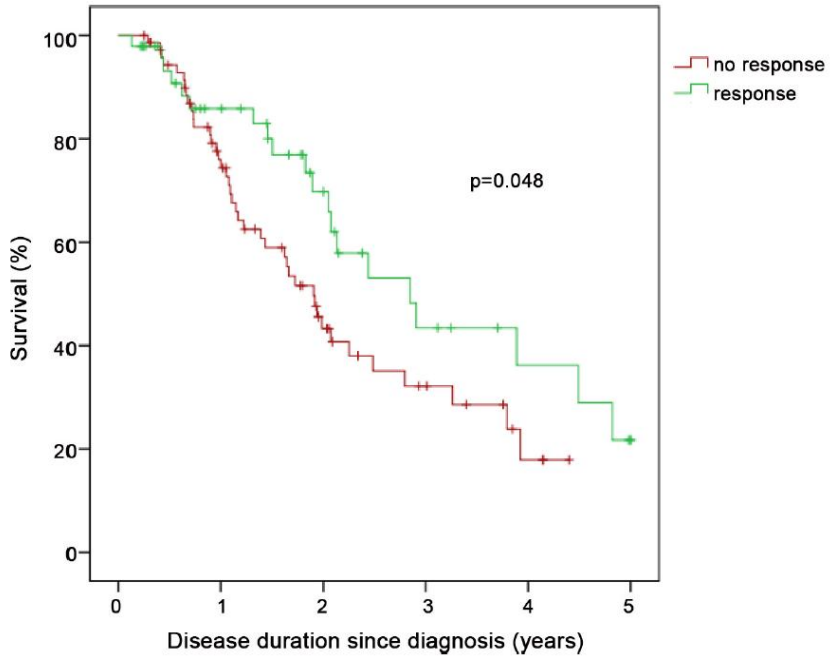


Přežití IPAH vs PH-IPP



Přežití PH-IPP respondéři vs nonrespondéři

Hoeper MM et al. *PLoS ONE* 10(12): e0141911

PLICNÍ HYPERTENZE ASOCIOVANÁ S PLICNÍMI ONEMOCNĚNÍMI

Léčba: Léčba základního plicního onemocnění
DDOT pokud indikována, CPAP pokud indikován, plicní RHB programy, zvážení LuTx
U kombinované etiologie PH adekvátní léčba, specifická vazodilatační léčba?

Inhaled treprostinil may be considered in patients with PH associated with ILD[734]	IIb	B
The use of ambrisentan is not recommended in patients with PH associated with IPF[740]	III	B
The use of riociguat is not recommended in patients with PH associated with IIP[181]	III	B
The use of PAH medication is not recommended in patients with lung disease and non-severe PH[e]	III	C
PDE5is may be considered in patients with severe PH associated with ILD (individual decision-making in PH centres)	IIb	C
The use of PDE5is in patients with ILD and non-severe PH is not recommended	III	C

Humbert M et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, *EHJ* 2022, *ERJ* 2022

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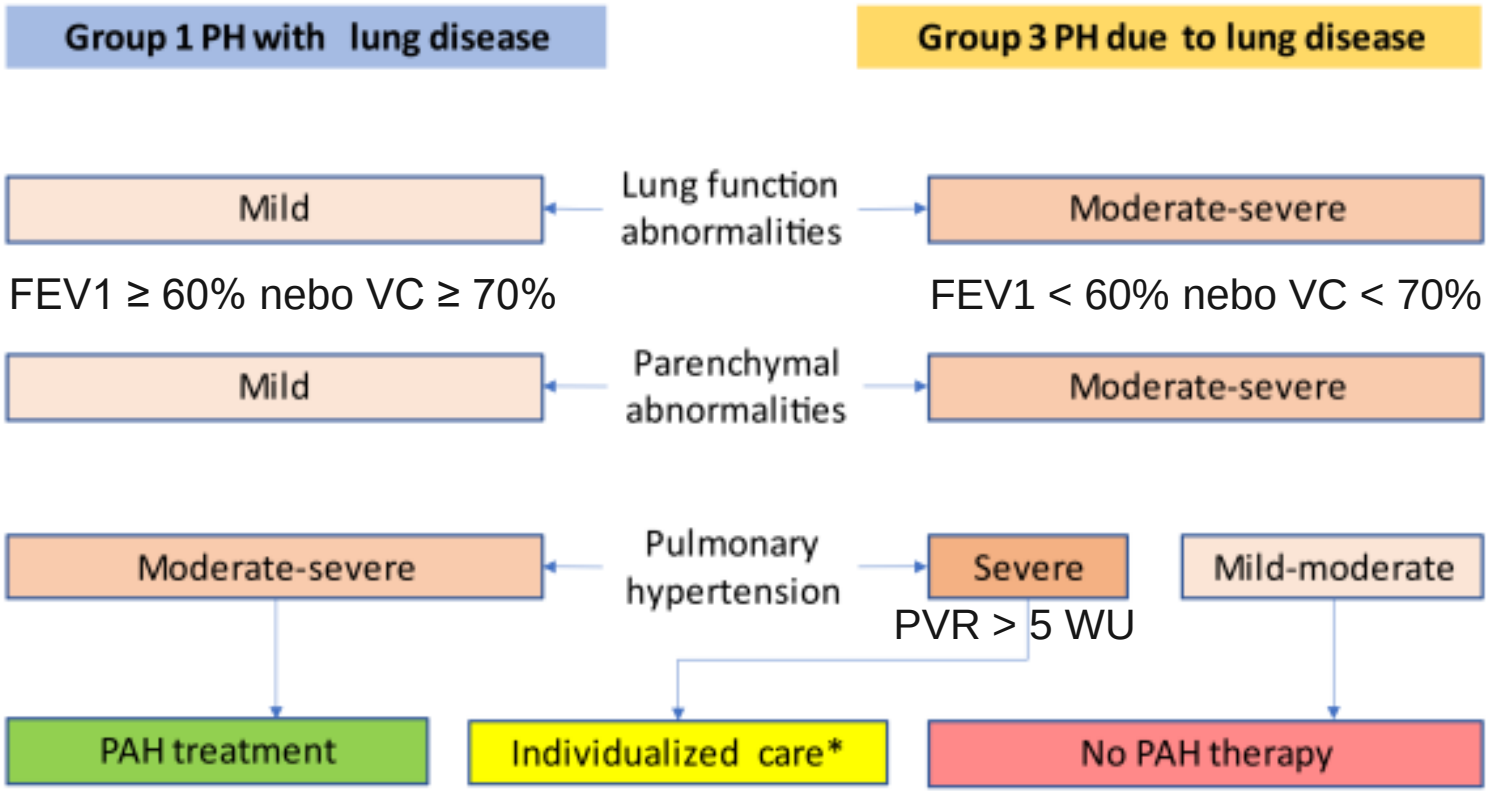
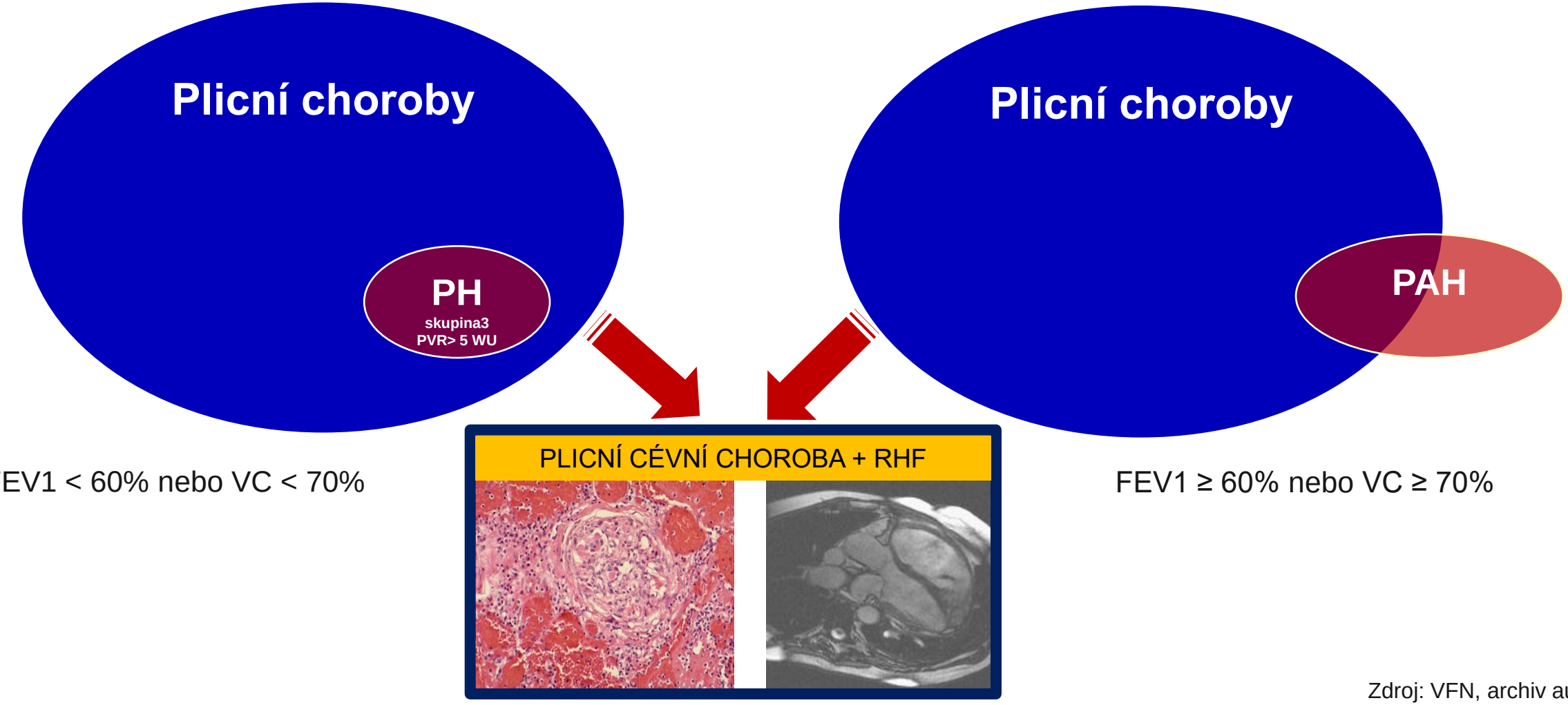
Humbert M et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, *EHJ* 2022, *ERJ* 2022

The Challenge to Decide between Pulmonary Hypertension Due to Chronic Lung Disease and PAH with Chronic Lung Disease



Olschewski H. *Diagnostics* 2021, 11, 311

PLICNÍ ONEMOCNĚNÍ A POSTIŽENÍ PLICNÍ CIRKULACE



FEV1 < 60% nebo VC < 70%

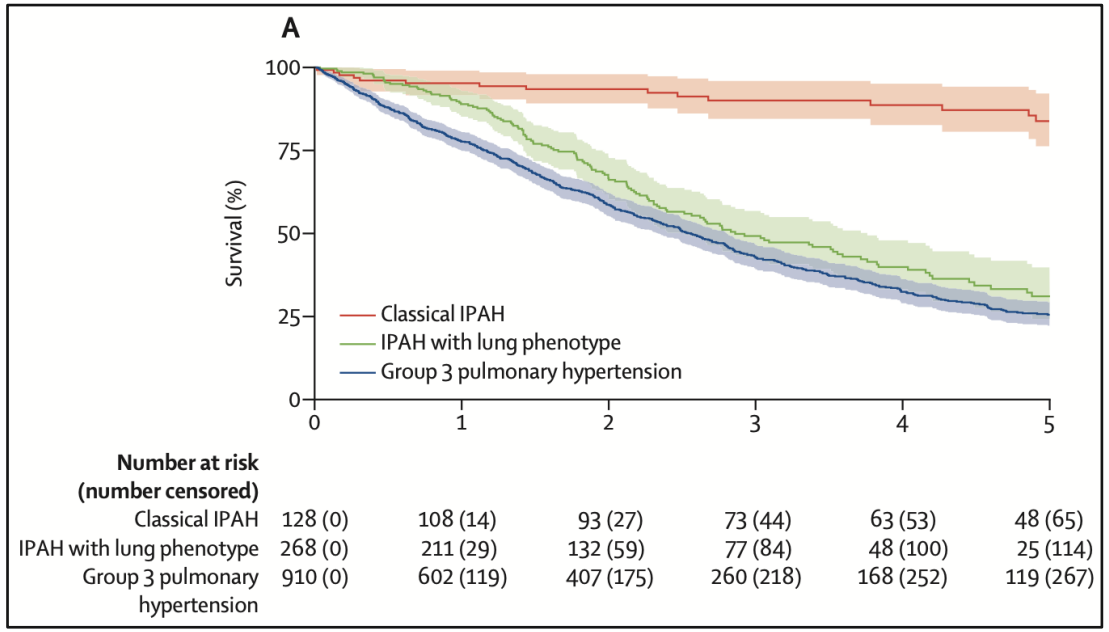
FEV1 ≥ 60% nebo VC ≥ 70%

Zdroj: VFN, archiv autora

Phenotyping of idiopathic pulmonary arterial hypertension: a registry analysis

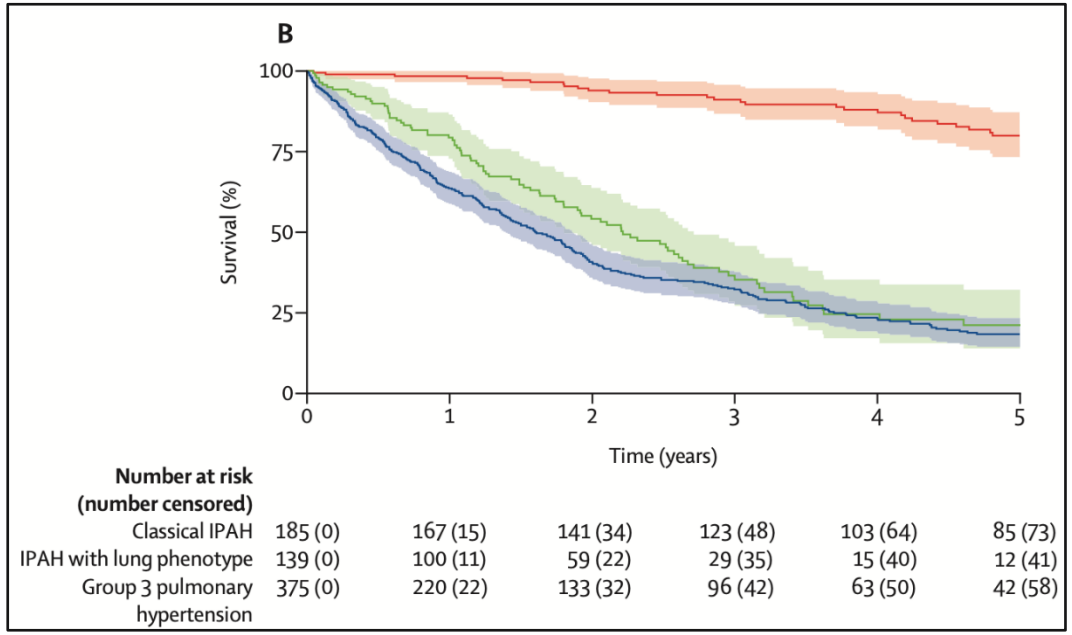
COMPERA (n=1306) and **ASPIRE** (699) registries, patient characteristics, response to therapy, survival

- classical IPAH (DLCO ≥ 45%, absence of cardiopulmonary comorbidities)
- IPAH + lung phenotype (DLCO < 45%, smoking history)
- PH due to lung disease (group 3 pulmonary hypertension)



Number at risk (number censored)						
Classical IPAH	128 (0)	108 (14)	93 (27)	73 (44)	63 (53)	48 (65)
IPAH with lung phenotype	268 (0)	211 (29)	132 (59)	77 (84)	48 (100)	25 (114)
Group 3 pulmonary hypertension	910 (0)	602 (119)	407 (175)	260 (218)	168 (252)	119 (267)

COMPERA registry



Number at risk (number censored)						
Classical IPAH	185 (0)	167 (15)	141 (34)	123 (48)	103 (64)	85 (73)
IPAH with lung phenotype	139 (0)	100 (11)	59 (22)	29 (35)	15 (40)	12 (41)
Group 3 pulmonary hypertension	375 (0)	220 (22)	133 (32)	96 (42)	63 (50)	42 (58)

ASPIRE registry

Hoeper MM et al. *Lancet Respir Med* 2022 Oct;10(10):937-948

KLINICKÁ KLASIFIKACE PLICNÍ HYPERTENZE (2022)

GROUP 1 Pulmonary arterial hypertension (PAH) — 1 %
- 1.1 Idiopathic
  - 1.1.1 Non-responders at vasoreactivity testing
  - 1.1.2 Acute responders at vasoreactivity testing
- 1.2 Heritable[a]
- 1.3 Associated with drugs and toxins[a]
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 HIV infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease
  - 1.4.5 Schistosomiasis
- 1.5 PAH with features of venous/capillary (PVOD/PCH) involvement
- 1.6 Persistent PH of the newborn

GROUP 2 PH associated with left heart disease — 70 %
- 2.1 Heart failure:
  - 2.1.1 with preserved ejection fraction
  - 2.1.2 with reduced or mildly reduced ejection fraction[b]
- 2.2 Valvular heart disease
- 2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH

GROUP 3 PH associated with lung diseases and/or hypoxia — 20 %
- 3.1 Obstructive lung disease or emphysema
- 3.2 Restrictive lung disease
- 3.3 Lung disease with mixed restrictive/obstructive pattern
- 3.4 Hypoventilation syndromes
- 3.5 Hypoxia without lung disease (e.g. high altitude)
- 3.6 Developmental lung disorders

GROUP 4 PH associated with pulmonary artery obstructions — 4 %
- 4.1 Chronic thrombo-embolic PH
- 4.2 Other pulmonary artery obstructions[c]

GROUP 5 PH with unclear and/or multifactorial mechanisms — 5 %
- 5.1 Haematological disorders[d]
- 5.2 Systemic disorders[e]
- 5.3 Metabolic disorders[f]
- 5.4 Chronic renal failure with or without haemodialysis
- 5.5 Pulmonary tumour thrombotic microangiopathy
- 5.6 Fibrosing mediastinitis

Humbert M et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension
EHJ 2022, *ERJ* 2022

PLICNÍ HYPERTENZE V ČR

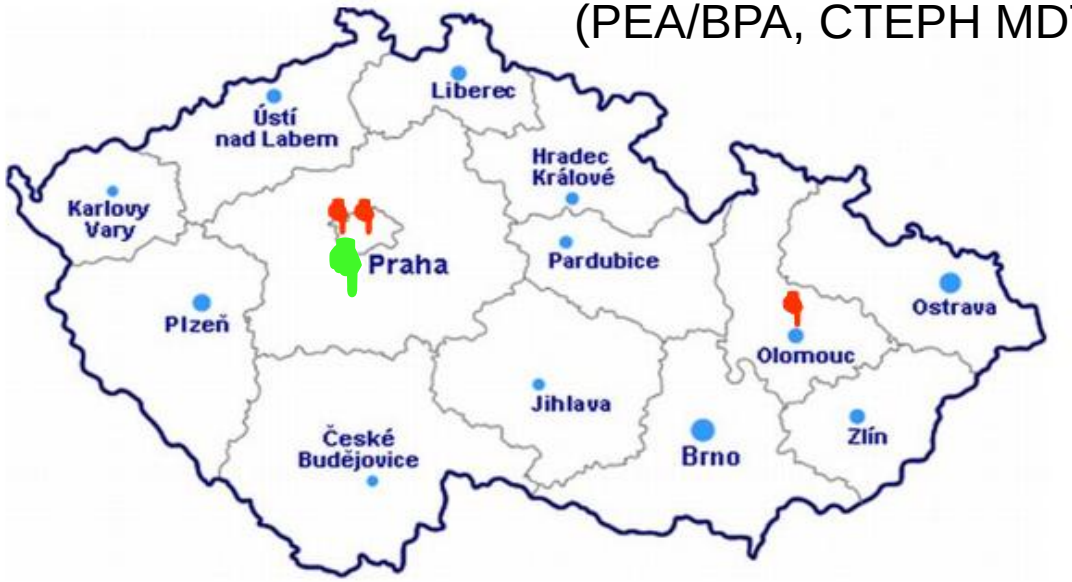
European Reference Network

for rare or low prevalence complex diseases

Network
Respiratory Diseases (ERN-LUNG)

Member
General University Hospital in Prague — Czechia

- 3 expertní centra pro PAH centres
- 1 expertní centrum pro CTEPH (PEA/BPA, CTEPH MDT team)



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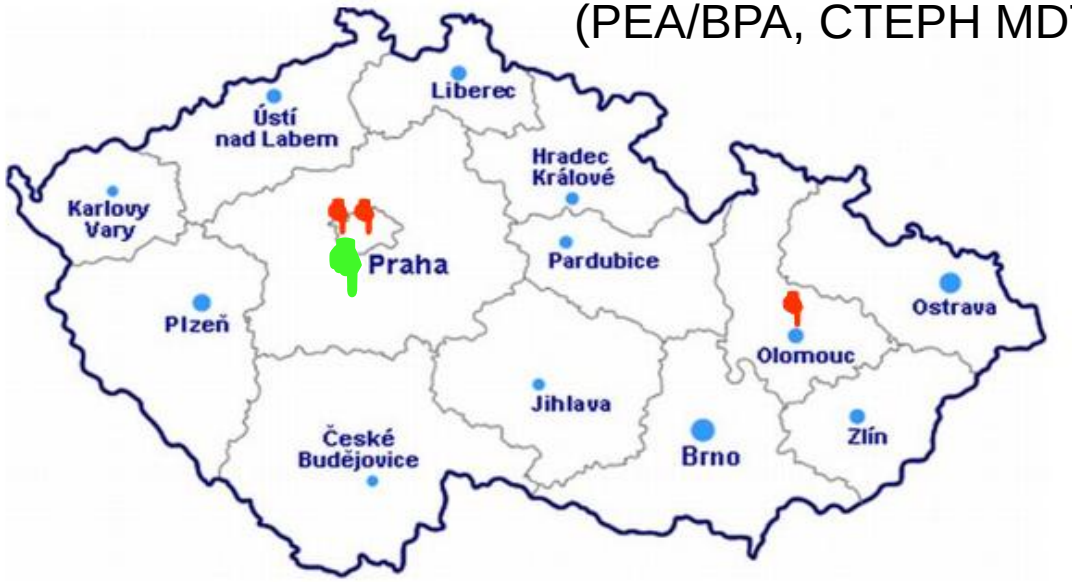
General University Hospital in Prague — Czechia

- 3 expertní centra pro PAH centres
- 1 expertní centrum pro CTEPH (PEA/BPA, CTEPH MDT team)



Diagnostika PH skupiny 3:

Centra pro IPP (ČPFS) ➤ **ECHO** (ČKS) +plicní funkce, V/Q scinti ➤

➤ **MDT (virtuálně)** ➤ **Srdeční katetrizace** ➤ **MDT (virtuálně)** ➤ **Léčba**

SHRNUTÍ

- Plicní hypertenze u plicních chorob je typicky prekapilární, lehká a obtížně léčitelná (PAMP > 20 mmHg, PVR > 2 WU)
- Diferenciální diagnostika je základem adekvátní léčby
  - symptomy, ECHO, plicní funkce, V/Q scinti
  - **kombinace etiologií (OSA, CTEPH, PAH) → adekvátní léčba**
- Těžká PH (PVR > 5 WU) skupiny 3 je indikací k diskusi s centrem pro PH k individuálnímu zvážení specifické léčby
  - **diferenciální diagnostika → adekvátní léčba**

European Reference Network

for rare or low prevalence complex diseases

Network
Respiratory Diseases
(ERN-LUNG)

Member
General University Hospital in Prague — Czechia

www.pph.cz www.cteph.cz

KURZY PLICNÍ HYPERTENZE

- REGISTRACE
- AKREDITACE
- PROGRAM 2022
- POŘADATEL KURZŮ

  Centrum pro plicní hypertenzi
  VFN Praha
- ORGANIZAČNÍ ZAJIŠTĚNÍ

V případě zájmu o tento odborný kurz
nás neváhejte kontaktovat prostřednictvím e-mailu v.strukova@gsymposion.cz,
budeme Vás informovat o nejbližším možném termínu.

24.-25. listopadu 2023

www.pah-cz.cz