



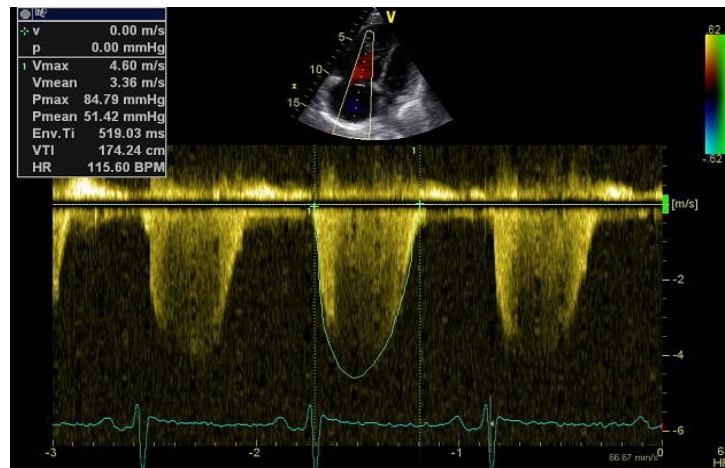
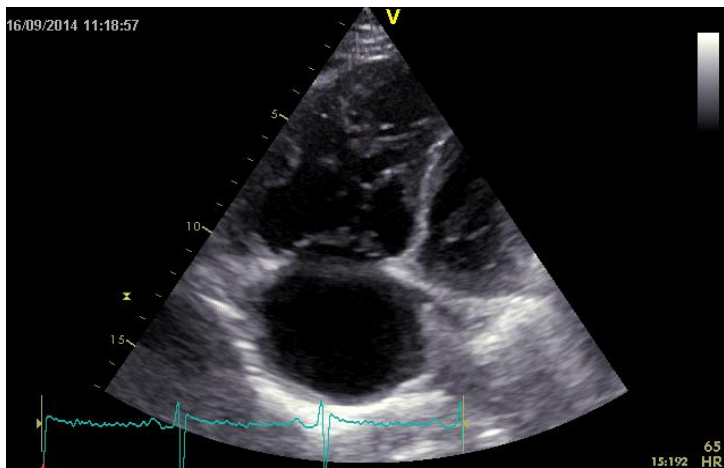
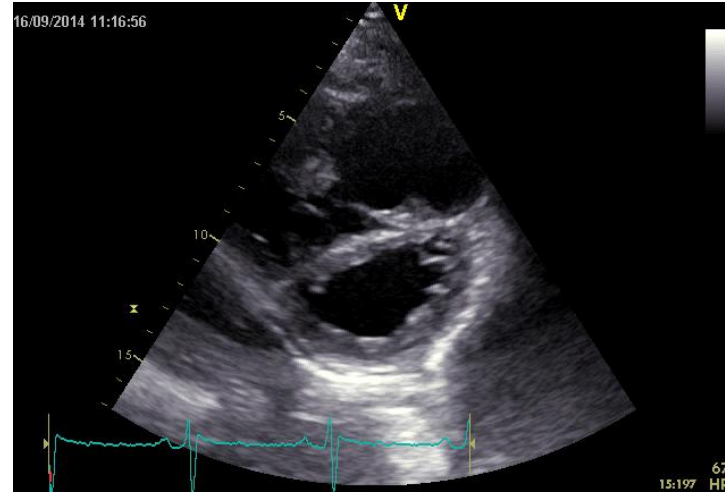
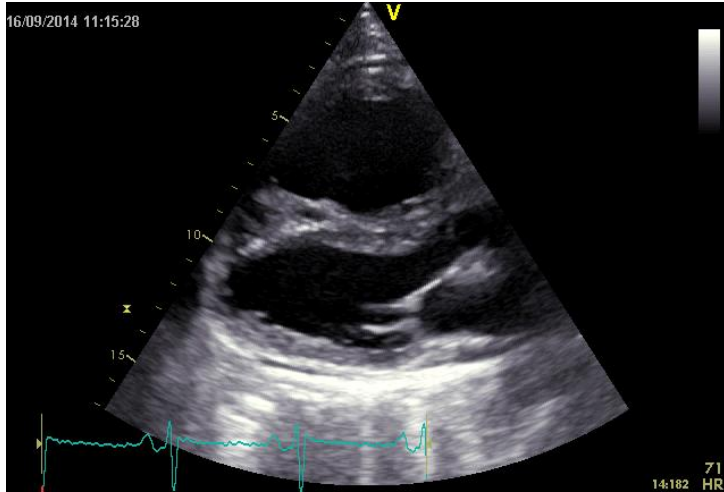
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Plicní hypertenze – *definice*

Martin Hutyra



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).

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

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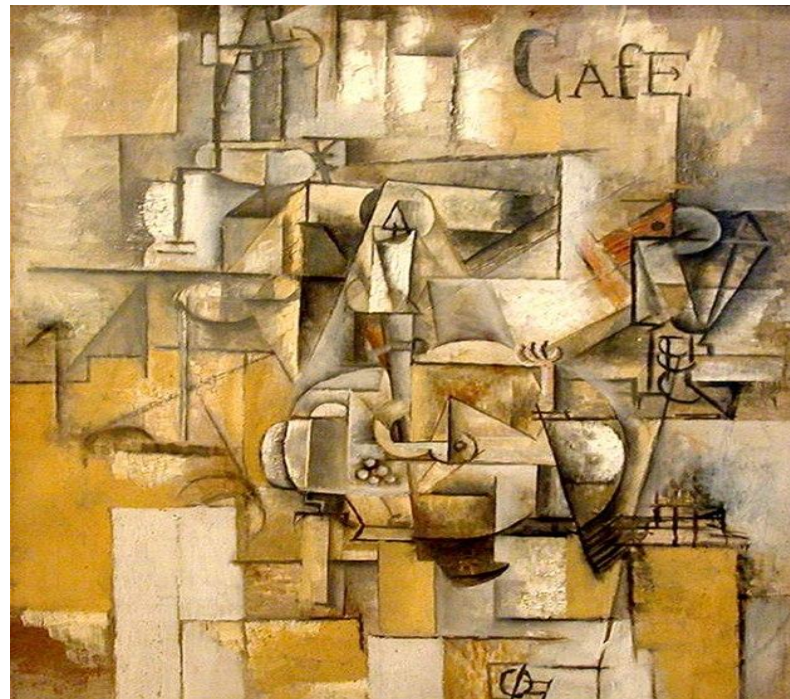
2022 ESC-ERS Guidelines for the diagnosis and management of acute coronary syndromes



Miró



ÚVOD



PULMONARY HYPERTENSION

Prevalence



1%

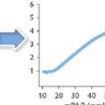
Global population



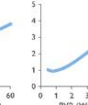
Pulmonary congestion in post-capillary PH

Pulmonary vascular disease / obstruction in pre-capillary PH

Mortality Hazard Ratio



Mortality Hazard Ratio



Right heart failure



CLINICAL CLASSIFICATION

Pulmonary arterial hypertension (PAH)



- Idiopathic/heritable
- Associated conditions

PH associated with left heart disease



- lpcPH
- CpcPH

PH associated with lung disease



- Non-severe PH
- Severe PH

PH associated with pulmonary artery obstructions



- CTEPH
- Other pulmonary obstructions

PH with unclear and/or multifactorial mechanisms



- Haematological disorders
- Systemic disorders

PREVALENCE

Rare



Very common



Common



Rare



Rare



THERAPEUTIC STRATEGIES

Medical therapy

- PAH drugs
- CCB in responders

Lung transplantation

lpcPH:

- Treatment of LHD²

CpcPH:

- Treatment of LHD²
- Potentially: PAH drugs (trials)

PH-lung disease:

- Optimized care of underlying lung disease

Severe PH:

- Potentially: PAH drugs (trials)

Surgical therapy:

- PEA

Interventional:

- BPA

Medical therapy:

- PH drugs

Optimized treatment of underlying disease

- Potentially: PAH drugs (trials)



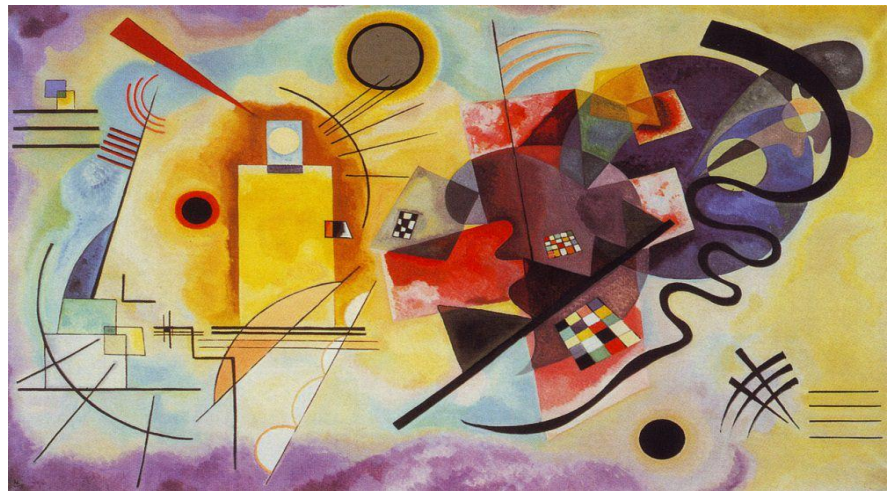
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DEFINICE A KLASIFIKACE



EXECUTIVE BOARD



EB28/13 ✓
16 May 1961

ORIGINAL: ENGLISH

Twenty-eighth Session

Provisional agenda item 3.5

REPORT ON EXPERT COMMITTEE MEETINGS

Report by the Director-General

1. Introduction

In compliance with paragraph 10.6 of the regulations for expert advisory panels and committees,¹ the Director-General is here reporting on the action to be taken with reference to meetings of Expert Committees.

2. Reports

The reports of expert committee meetings which have been prepared in both working languages, since the twenty-seventh session of the Executive Board and are now available for annexation to this report are the following:

Expert Committee on Antibiotics (Standardization of Methods for Conducting Microbic Sensitivity Tests)

Expert Committee on Chronic Cor Pulmonale

Expert Committee on Professional and Technical Education of Medical and Auxiliary Personnel (Recommended Requirements for Schools of Public Health)

Expert Committee on Public Health Administration (Planning of Public Health Services)

Expert Committee on Specifications for Pharmaceutical Preparations - Sub-Committee on Non-Proprietary Names

Expert Committee on Specifications for Pharmaceutical Preparations

In 1961, a report of the WHO Expert Committee on Chronic Cor Pulmonale mentioned clearly that the mean pulmonary arterial pressure (mPAP) **does not normally exceed 15 mmHg** when the subject is at rest in a lying position, and that the value was **little affected by age and never exceeded 20 mmHg.**

CLINICAL PROGRESS

Chronic Cor Pulmonale
Report of an Expert Committee*

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Foreword

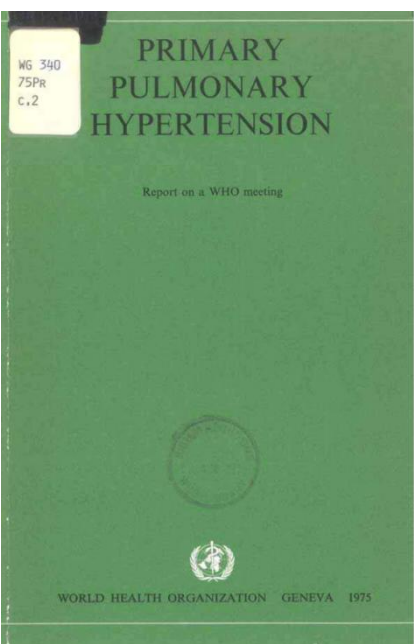
IN THE early months of 1960, the Director-General of the World Health Organization appointed an Expert Committee to inquire into and write a report on the subject of cor pulmonale.

In order to facilitate the preliminary study, as well as the actual deliberations of the Committee, two consultants were appointed, to prepare a survey of the subject: Professor H. Denolin, Chargé de cours à l'Université de Bruxelles; and Dr. C. M. Fletcher, Senior Lecturer in Medicine, Postgraduate Medical School, London. This, a sixty-page report, was

put together by Drs. Denolin and Fletcher during July, 1960, and made available to Committee members shortly thereafter.

The membership of the Expert Committee was as follows: Dr. J. Dankmeijer, Professor of Anatomy, Embryology and Physical Anthropology, University of Leiden, the Netherlands; Dr. F. Herles, Professor of Medicine II Internal Clinic, Charles University, Prague, Czechoslovakia; Dr. M. Ibrahim, formerly Professor of Cardiology, Faculty of Medicine, Cairo University, Cairo, Province of Egypt, United Arab Republic; Dr. D. D. Reid, Professor of Epidemiology, Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine, London, England; Dr. D. W. Richards, Lambert Professor of Medicine, College of Physicians and Surgeons, Columbia University, New

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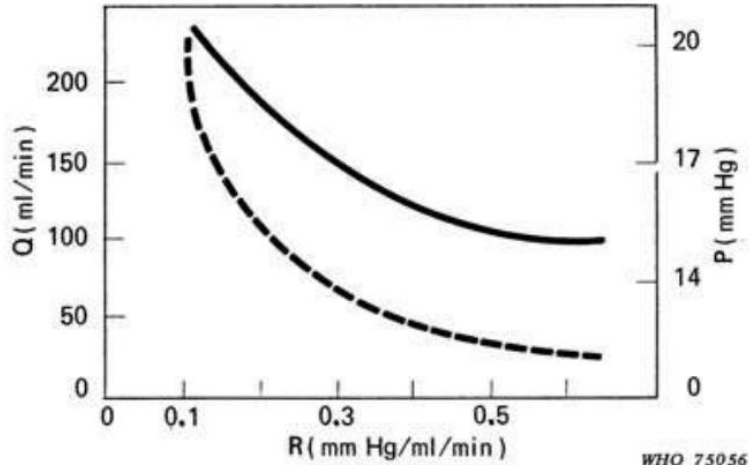
PRIMARY PULMONARY HYPERTENSION

Report on a WHO meeting
Geneva, 15-17 October 1973

Edited by
SHUICHI HATANO
and
TOMA STRASSER
*Cardiovascular Director,
World Health Organization,
Geneva, Switzerland*



WORLD HEALTH ORGANIZATION
GENEVA
1975



WHO 75056

Passive changes in pulmonary vascular resistance (R) at different arterial pressures (P) and at different pulmonary blood flows (Q). Pulmonary venous pressure remains constant throughout. As flow and pressure decrease, resistance increases. The continuous line represents the relationship between P and R, and the interrupted line represents the relationship between Q and R. (Based on a figure in reference no. 4)

Since the 1st World Symposium on Pulmonary Hypertension organised by the WHO in Geneva in 1973, PH has been defined as mPAP ≥ 25 mmHg measured by right heart catheterisation in the supine position at rest. The Geneva WHO meeting was devoted to primary PH, some years after an outbreak related to the intake of the anorexic drug aminorex. In the report of the meeting, it was recognised that this upper limit of normal mPAP of 25 mmHg was somewhat empirical and arbitrarily defined.

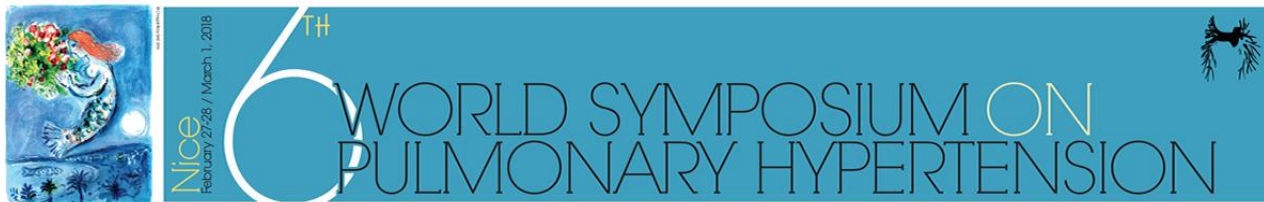
FISHMAN, A. P. Dynamics of the pulmonary circulation. In: Hamilton, W. F. & Dow, P., ed. Handbook of physiology, section 2: circulation, Washington, D. C., American Physiological Society, 1963, vol. 2, pp. 1667-1743



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Hemodynamická definice plicní hypertenze



**Definice
PH**

**MPAP
≥20/25 mmHg**

**Definice
PAH**

**MPAP
≥20/25 mmHg**

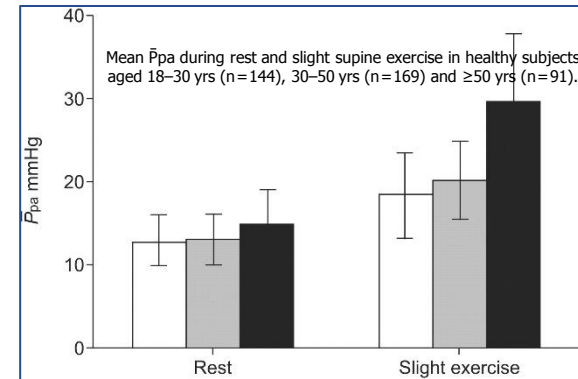
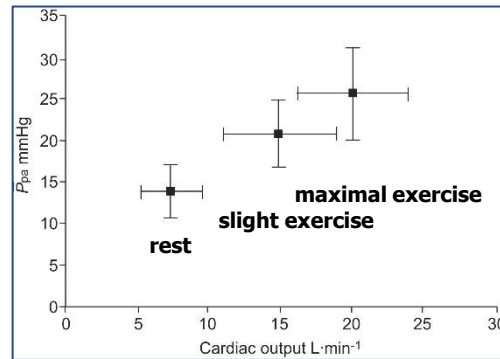
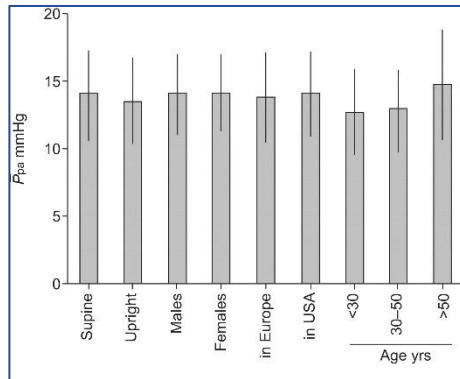
**PAWP
≤15 mmHg**

PVR >3 WU

PAP: pulmonary arterial pressure; PAWP: pulmonary artery wedge pressure; PVR: pulmonary vascular resistance

Co je horní hranice normálního tlaku v plicnici?

RHC studies in healthy individuals to determine **normal values of mPAP** at rest and exercise. Data from 1187 normal subjects from 47 studies were analysed. mPAP at rest was 14.0 ± 3.3 mmHg; this value was independent of sex and ethnicity, and was only slightly influenced by age and posture.



Considering this mPAP of 14 mmHg, two standard deviations would suggest mPAP >20 mmHg as above the upper limit of normal (i.e. above the 97.5th percentile). This definition is, therefore, no longer arbitrary, but based on a scientific approach.

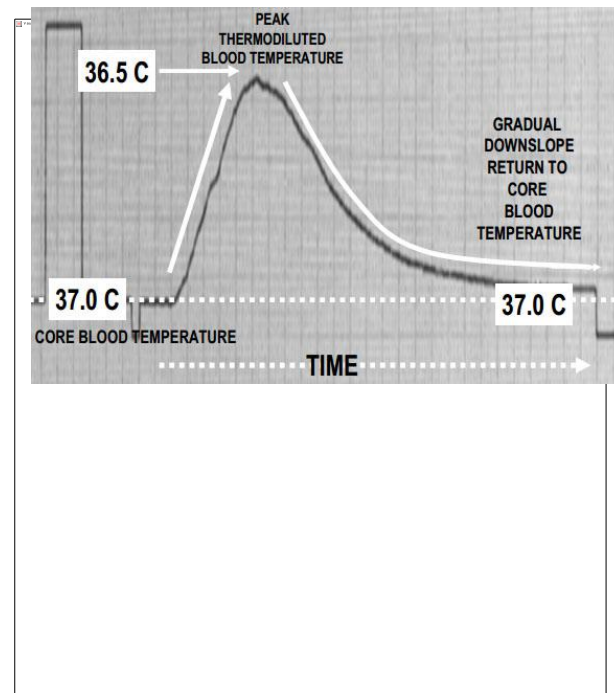
K diagnostice prekapilární PH svědčící o přítomnosti plicní vaskulární nemoci by měla být zahrnuta hodnota PVR...

Including pulmonary vascular resistance ($PVR = (mPAP - PAWP) / CO$) in the definition of pre-capillary PH is essential, allowing discrimination of elevation of PAP due to PVD from those due to elevation of PAWP or due to high CO.

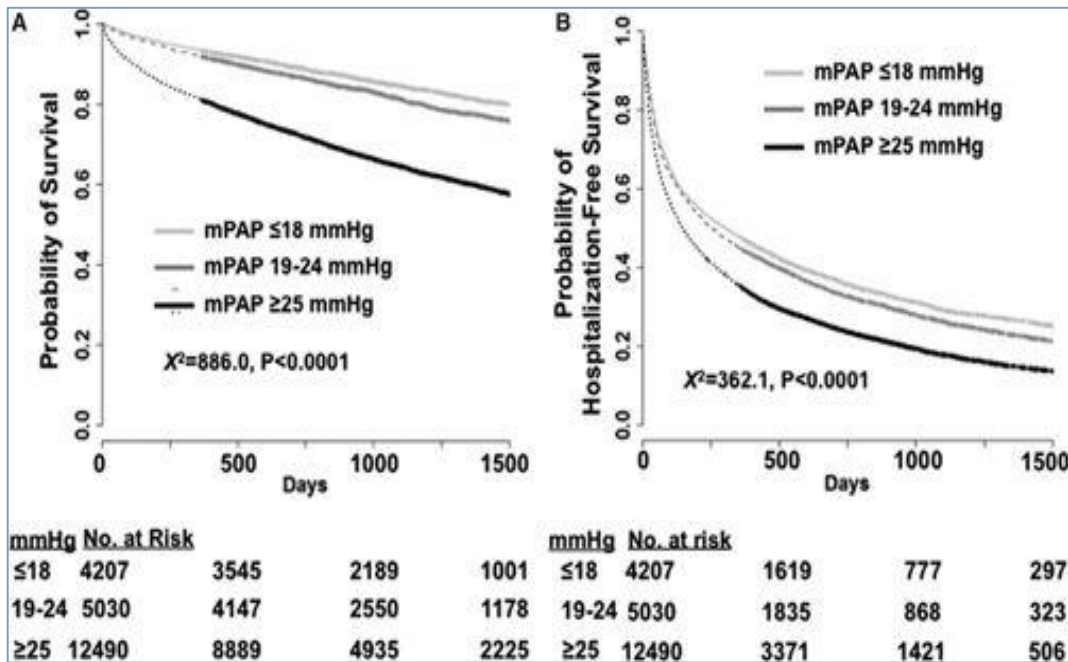
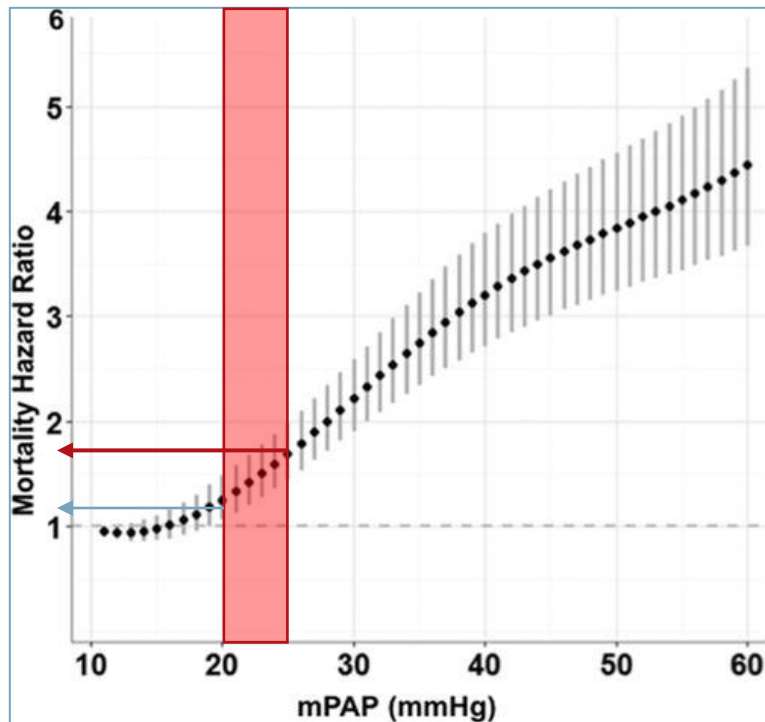
Since the **3rd WSPH held in 2003**, pre-capillary PH of group 1 (PAH) has been defined by the presence of *mPAP* ≥ 25 mmHg with a normal PAWP ≤ 15 mmHg and elevated PVR ≥ 3 Wood Units (WU).

This cut-off value of **PVR ≥ 3 WU** is also quite arbitrary since some recent data suggest that **PVR > 2 WU** could be also considered abnormal.

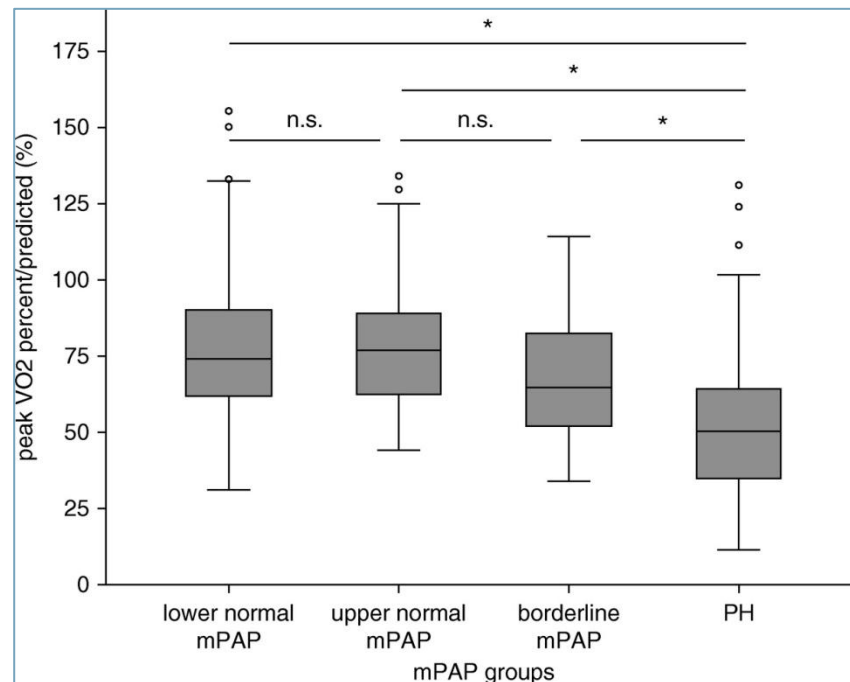
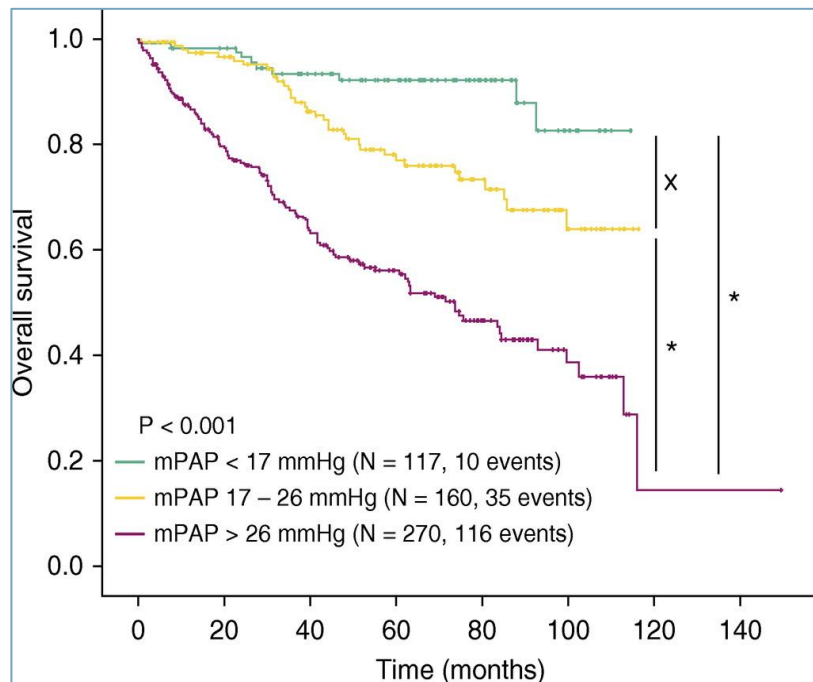
The use of a cut-off value of PVR ≥ 3 WU is conservative, suggesting the presence of a manifest pre-capillary PH. This value of PVR ≥ 3 WU is considered clinically relevant in different clinical situations, suggesting the presence of a significant PVD.



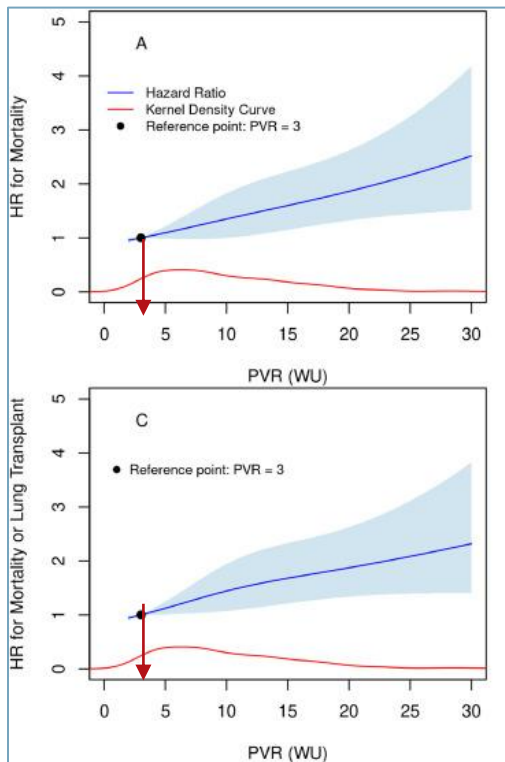
Má hraniční mPAP vliv na prognózu?



Jakou prognostickou informací mPAP přináší?



Má hodnota PVR 2-3 vliv na prognózu?



The Journal of Heart and Lung Transplantation
The Official Publication of the International Society for Heart and Lung Transplantation

THE LANCET
Respiratory Medicine

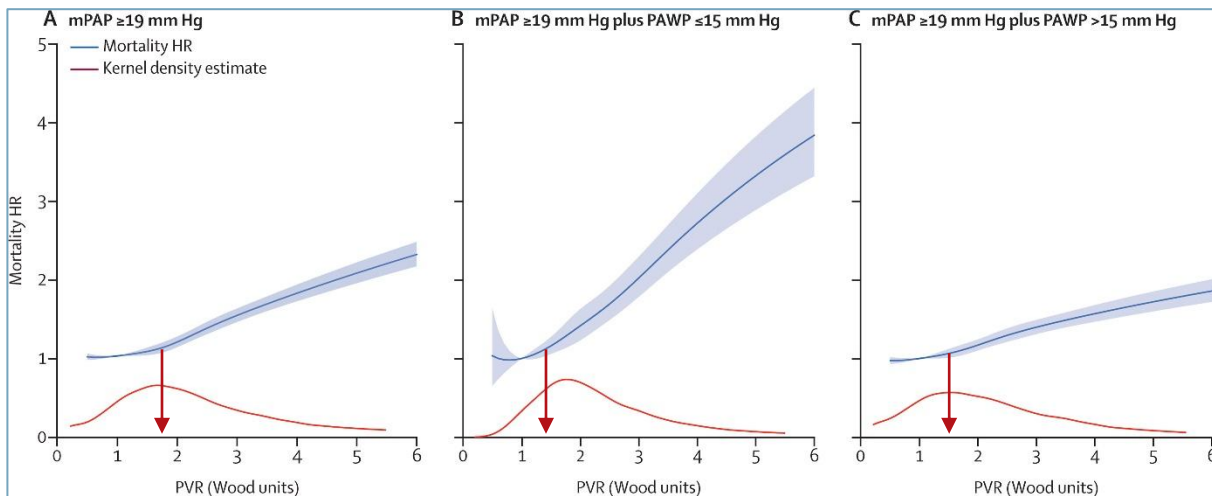
FULL LENGTH ARTICLE | VOLUME 40, ISSUE 7, P614-622, JULY 01, 2021

Is pulmonary vascular resistance index better than pulmonary vascular resistance in predicting outcomes in pulmonary arterial hypertension?

ARTICLES | VOLUME 8, ISSUE 9, P873-884, SEPTEMBER 01, 2020

Pulmonary vascular resistance and clinical outcomes in patients with pulmonary hypertension: a retrospective cohort study

Bradley A Maron, MD, ¹ Evan L Brittain, MD, ¹ Edward Hess, MS, Stephen W Waldo, MD, Prof Anna E Barón, PhD, Shi Huang, PhD, et al. Show all authors · Show footnotes

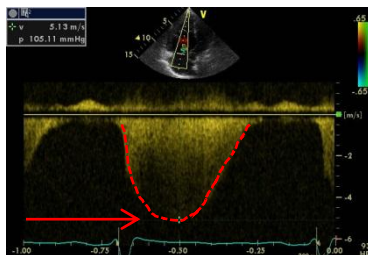
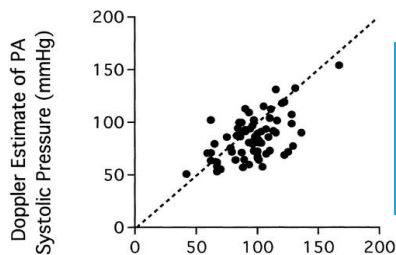


Echokardiografie je nejpoužívanějším screenigovým nástrojem

- Dvourozměrná echokardiografie** hodnotí funkci pravé komory (RV). Dysfunkce RV má širokou škálu etiologií, z nichž PH je nejběžnější.
- Dopplerovská echokardiografie** je užitečná, protože odhaduje rychlost trikuspidálního regurgitativního paprsku (TR jet), což je odhad systolického tlaku v pravé komoře (eRSVP) / systolického tlaku v plicní tepně (ePASP).
- Zátěžová echokardiografie** detekuje plicní hypertenzi vyvolanou zátěží, její použití pro screening PAH u pacientů se SSc zůstává do značné míry výzkumnou.

Několik studií pacientů s SSc se známými rizikovými faktory pro PAH i bez nich uvádí míru zvýšeného odhadovaného PASP v rozmezí od 11-14%. Existují však falešně pozitivní i negativní výsledky, které naznačují, že pro screening není echokardiografie vhodná samotná.

Wigley FM, Lima JA, Mayes M, et al. The prevalence of undiagnosed pulmonary arterial hypertension in subjects with connective tissue disease at the secondary health care level of community-based rheumatologists (the UNCOVER study). Arthritis Rheum 2005; 52:2125.
Hesselstrand R, Ekman R, Eskilsson J, et al. Screening for pulmonary hypertension in systemic sclerosis: the longitudinal development of tricuspid gradient in 227 consecutive patients, 1992-2001. Rheumatology (Oxford) 2005; 44:366.
Gladue H, Steen V, Allanore Y, et al. Combination of echocardiographic and pulmonary function test measures improves sensitivity for diagnosis of systemic sclerosis-associated pulmonary arterial hypertension: analysis of 2 cohorts. J Rheumatol 2013; 40:1706.



Alan L. Hinderliter. Circulation. Effects of Long-term Infusion of Prostacyclin (Epoprostenol) on Echocardiographic Measures of Right Ventricular Structure and Function in Primary Pulmonary Hypertension, Volume: 95, Issue: 6, Pages: 1479-1486, DOI: (10.1161/01.CIR.95.6.1479)

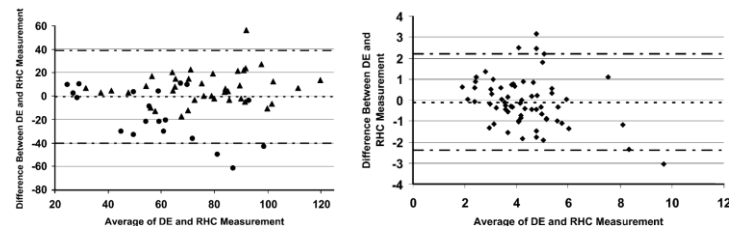
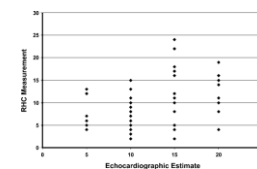
Accuracy of Doppler Echocardiography in the Hemodynamic Assessment of Pulmonary Hypertension

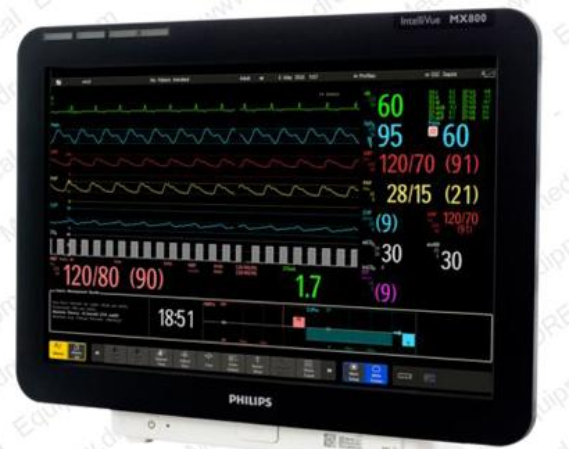
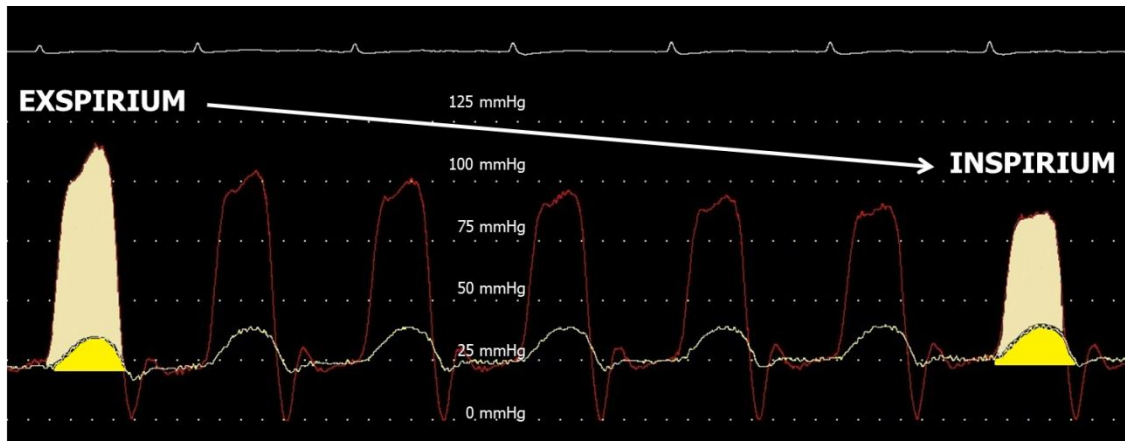
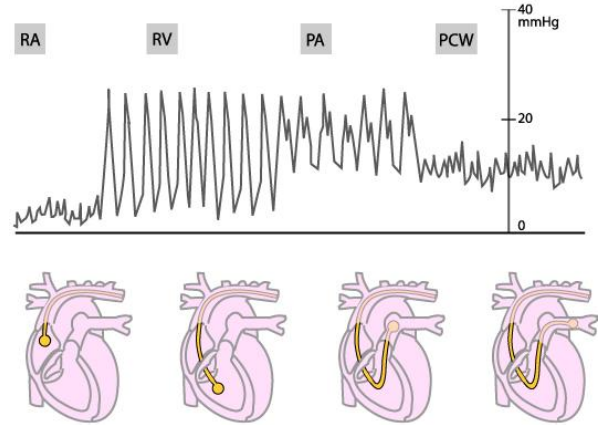
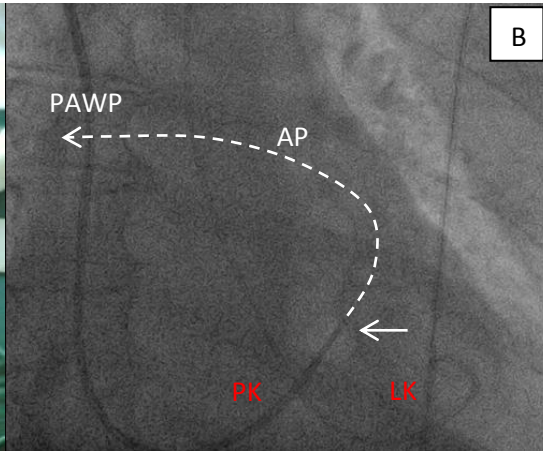
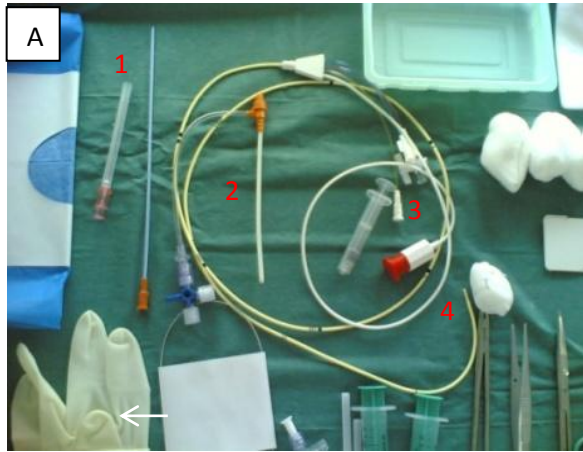
Micah R. Fisher^{1*}, Paul R. Forfia^{2†}, Elzbieta Chamera², Traci Houston-Harris¹, Hunter C. Champion², Reda E. Girgis¹, Mary C. Corretti², and Paul M. Hassoun¹

¹Division of Pulmonary and Critical Care Medicine; ²Division of Cardiology, Department of Medicine, Johns Hopkins University, Baltimore, Maryland

Right-Heart Catheterization	n	Mean	SD
RAP, mm Hg	65	9.4	5.0
PASP, mm Hg	65	68.5	23.9
mPAP, mm Hg	65	41.4	14.6
CO, L/min	65	4.4	1.7

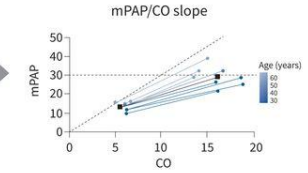
Echocardiogram	n	Mean	SD
RAP, mm Hg	65	12.4	4.7
RVSP, mm Hg	59	70.2	25.1
CO, L/min	64	4.3	1.4





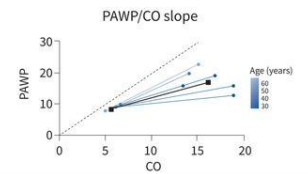
Má vliv zátěžové plicní hypertenze na prognózu?

$$\frac{mPAP}{CO} = \frac{TPG}{CO} + \frac{PAWP}{CO}$$

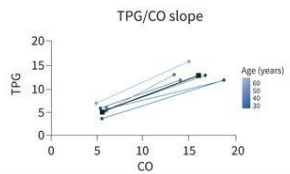


Normal values influenced by body position and age

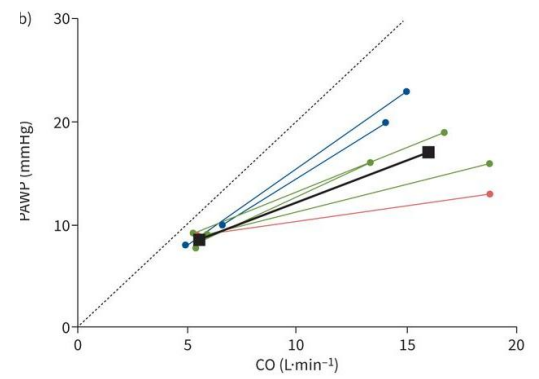
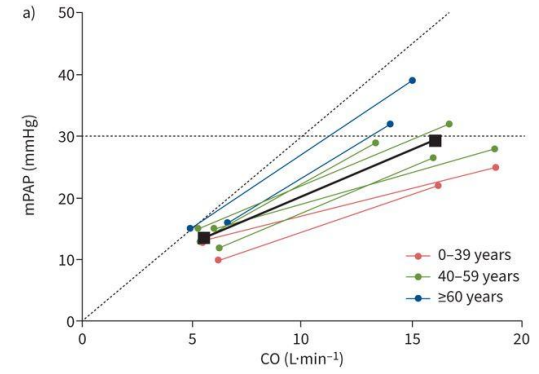
Normal $\leq 1.6-3.3$ WU, dependent on age
 > 3 WU
 Survival $\downarrow^{\#}$
 Heart failure-related hospitalisation $\uparrow^{\#}$



Normal $\leq 0.6-1.8$ WU, dependent on age
 > 2 WU
 Survival $\downarrow^{##}$
 CV events \uparrow^{**}
 Diagnosis: LHD $^{++}$



Normal $\leq \sim 1.2$ WU, independent of age
 Steep TPG/CO slope
 Survival \downarrow^{+}
 CV events $\uparrow^{\$}$
 Diagnosis: PVD f



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

Supplementary data

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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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Definition

PH

Pre-capillary PH

Isolated post-capillary PH

Combined post- and pre-capillary PH

Exercise PH

Haemodynamic characteristics

mPAP >20 mmHg

mPAP >20 mmHg

PAWP ≤15 mmHg

PVR >2 WU

mPAP >20 mmHg

PAWP >15 mmHg

PVR ≤2 WU

mPAP >20 mmHg

PAWP >15 mmHg

PVR >2 WU

mPAP/CO slope between rest and exercise >3 mmHg/L/min

Plicní hypertenze - klasifikace a epidemiologie

Definition	Characteristics ^a	Clinical groups
Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR ≥3 WU	1. PAH 3. PH due to lung diseases 4. CTEPH 5. PH with unclear and/or multifactorial mechanisms
Ipc-PH	mPAP >20 mmHg PAWP >15 mmHg PVR <3 WU	2. PH due to left heart disease 5. PH with unclear and/or multifactorial mechanisms
Cpc-PH	mPAP >20 mmHg PAWP >15 mmHg PVR ≥3 WU	2. PH due to left heart disease 5. PH with unclear and/or multifactorial mechanisms

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Updated Clinical Classification of Pulmonary Hypertension

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Prevalence of PAH in the general population
15–50 cases per million (0.0015–0.0050%)

Prevalence of PAH in at risk populations

CHD: 4–15%
Systemic sclerosis: 8–10%
Portal hypertension: 0.5–10%
HIV: 0.5%
Sickle cell disease: 2%
BMPR2 mutation carriers: 20%

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

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GROUP 1 Pulmonary arterial hypertension (PAH)

- 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

- 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

- 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

- 4.1 Chronic thrombo-embolic PH
- 4.2 Other pulmonary artery obstructions^c

GROUP 5 PH with unclear and/or multifactorial mechanisms

- 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

ZÁVĚRY PRO PRAXI



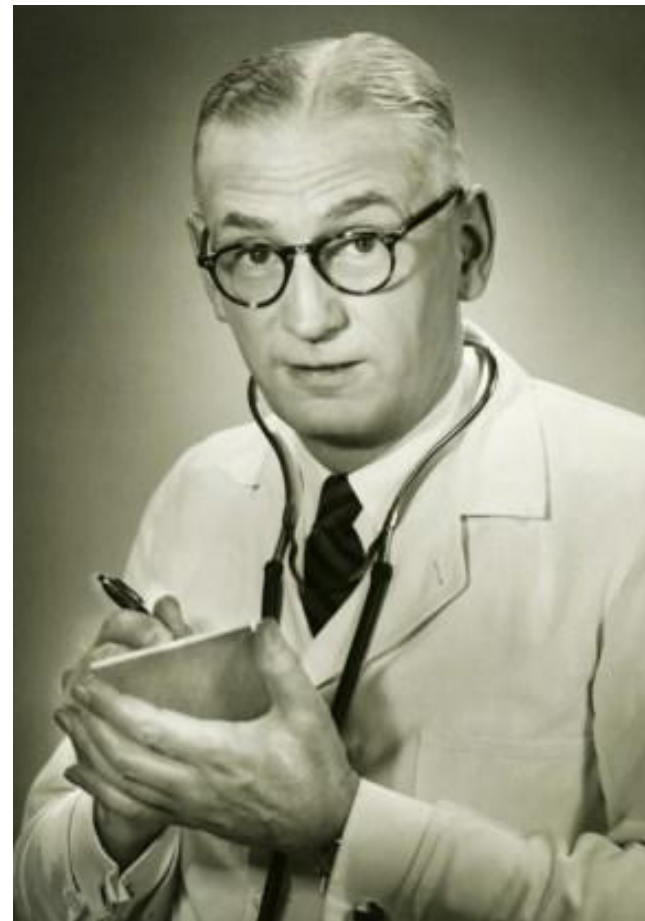
Plicní hypertenze (PH) je definována hemodynamicky zvýšením středního tlaku v plicnici nad 20 mmHg.

Nově definice PH obsahuje termín zátěžové plicní hypertenze

Hodnota PAWP diskriminující mezi prekapilární a postkapilární PH zůstala na hodnotě 15 mmHg

Z definice PH zmizel DPG a TPG, nově tam byla zařazena PVR s cut-off hodnotou 2 WU.

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





DĚKUJEME ZA POZORNOST

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