CHRONICKÁ TROMBOEMBOLICKÁ PLICNÍ HYPERTENZE

PAVEL JANSA

KLASIFIKACE, DEFINICE

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

1. Pulmonary arterial hypertension

- 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 disease

- 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 and/or hypoxia

- 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 hypertension and other pulmonary artery obstructions

- 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)

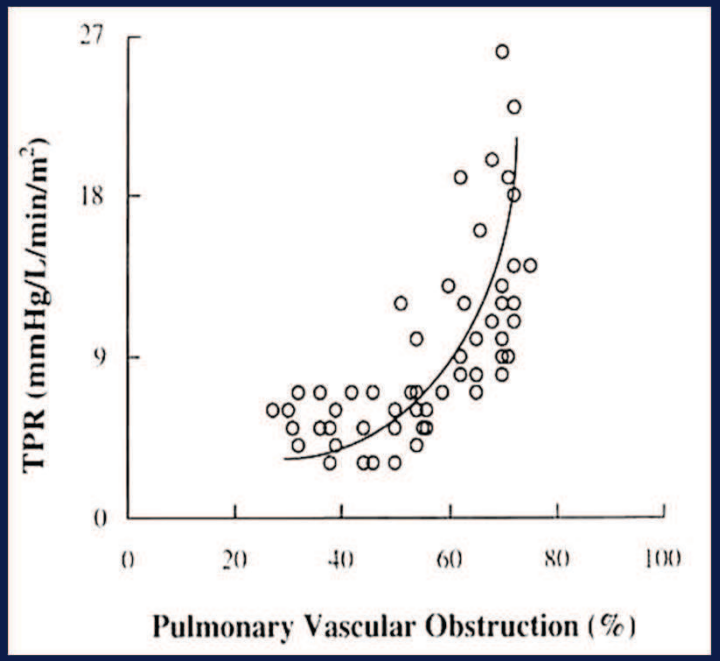
5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

- 5.1 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

Eur Respir J 2015, 46(4):903-75

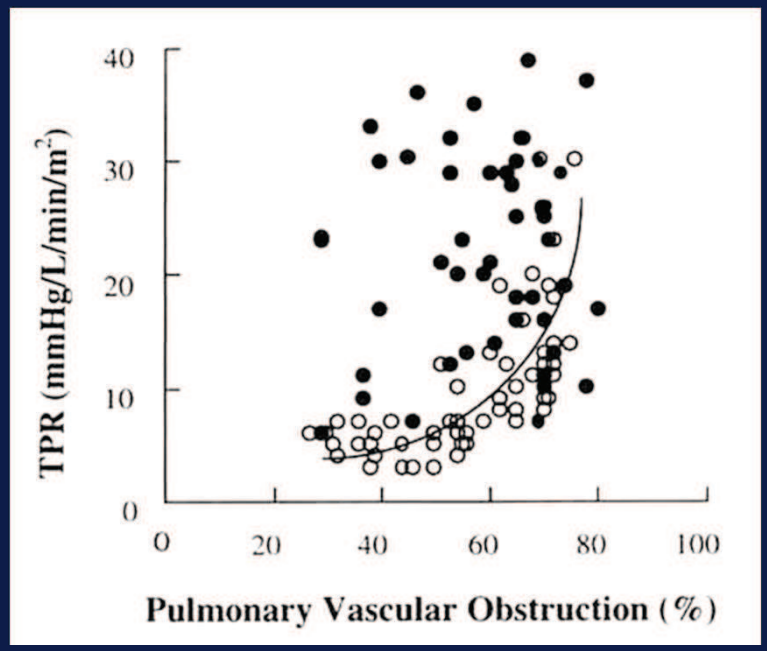
VZTAH TPR A OBSTRUKCE

AKUTNÍ PE (n=31)



Obstrukce

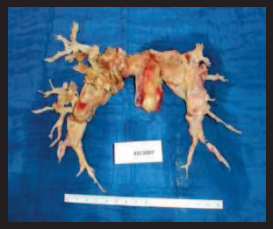
CTEPH (n=45)

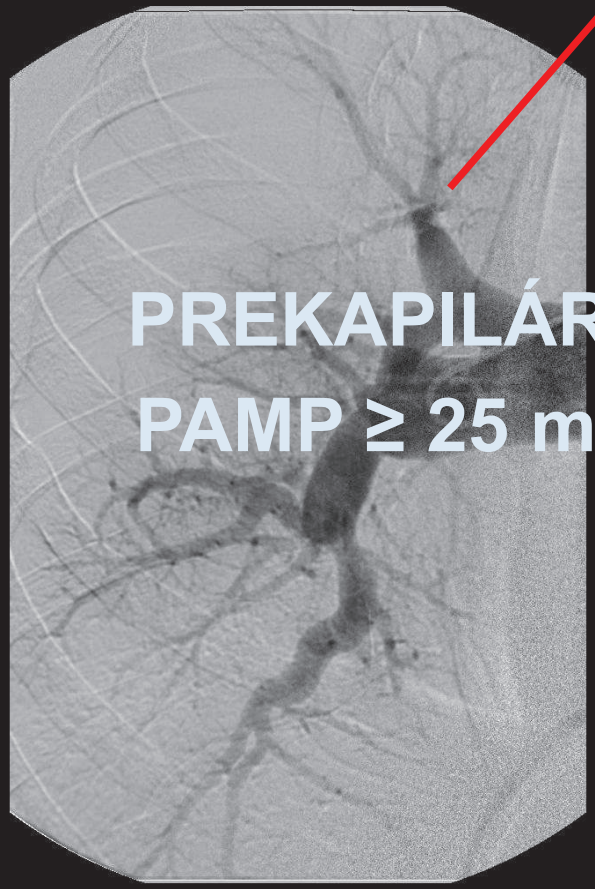


Obstrukce a cévní remodelace

Azarian R et al. ***J Nucl Med*** 1997

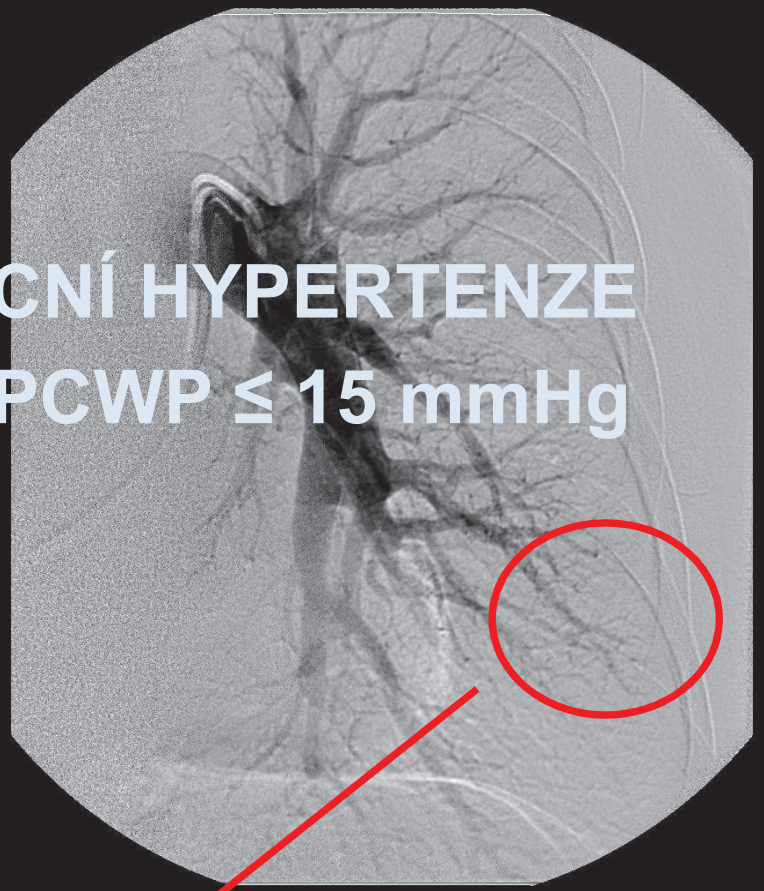
ELASTICKÁ PLICNICE

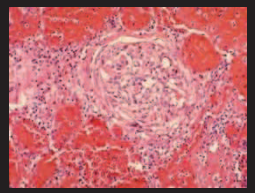




PREKAPILÁRNÍ PLICNÍ HYPERTENZE

PAMP ≥ 25 mmHg, PCWP ≤ 15 mmHg





MUSKULARIZOVANÁ PLICNICE

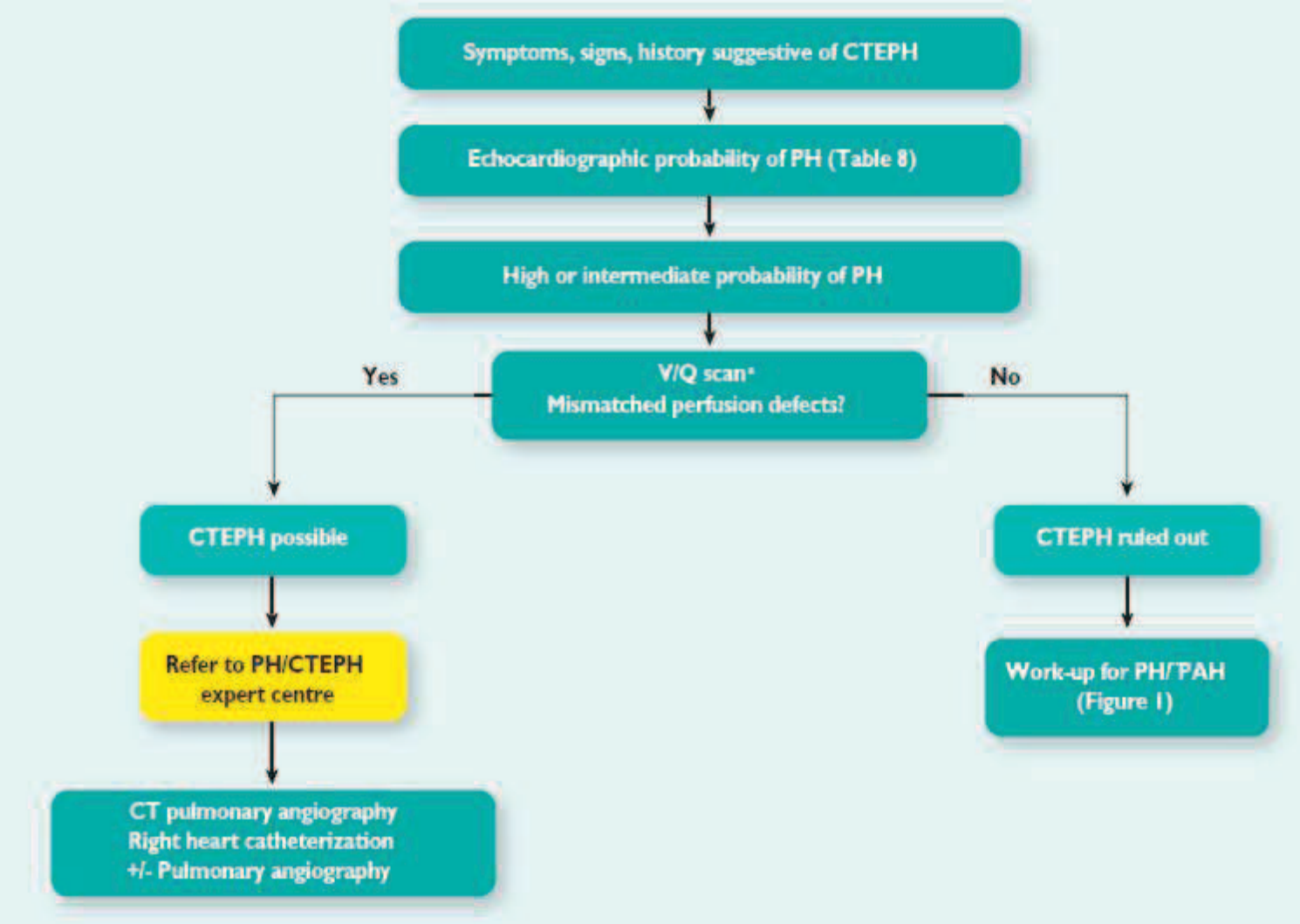
INCIDENCE CTEPH

Česká republika, ~ 10 mil. obyvatel

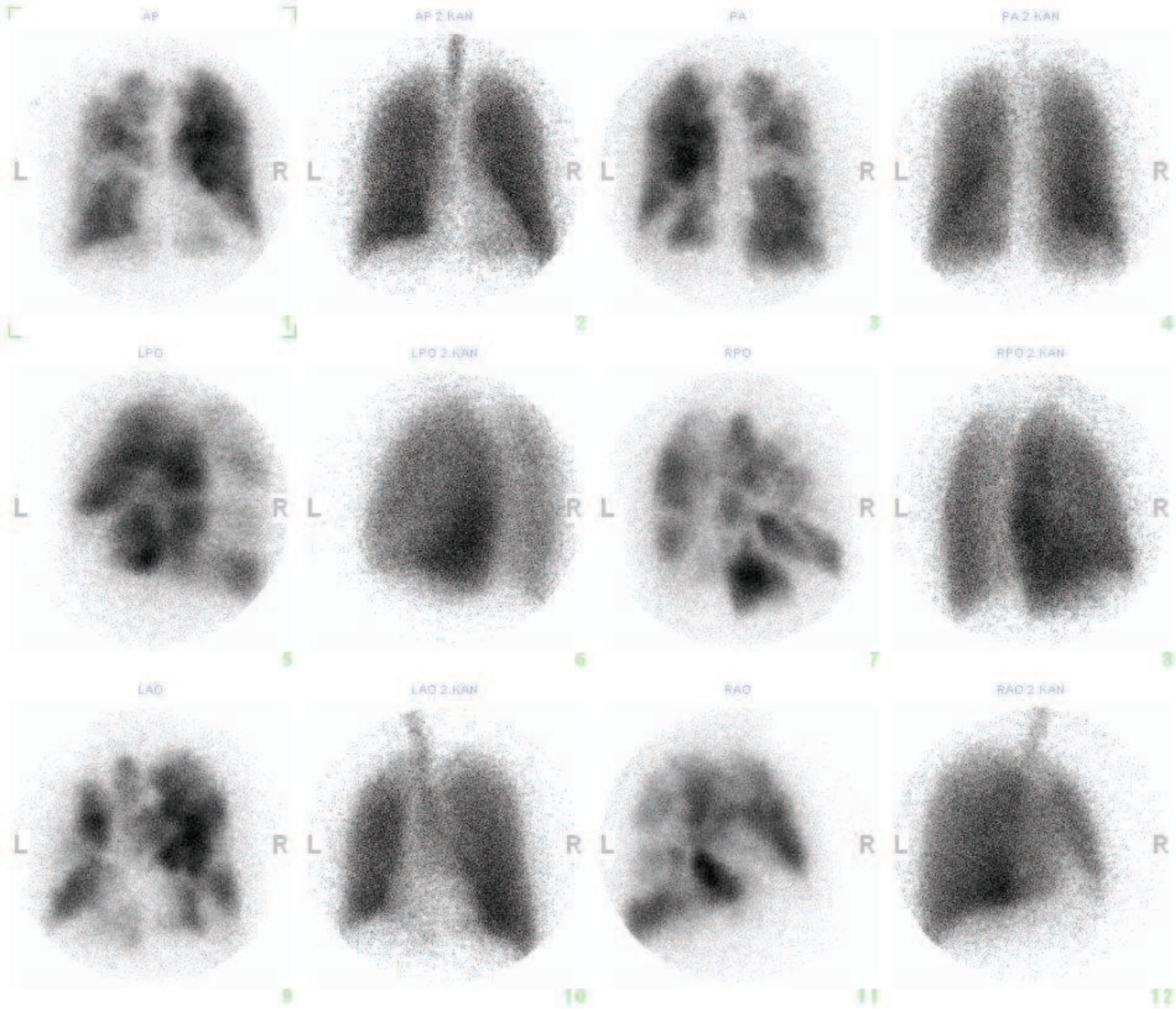
Akutní PE	15.000 případů/rok
CTEPH odhad	150-200/rok
CTEPH dg	~ 50 případů/rok

DIAGNOSTIKA

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



Eur Respir J 2015, 46(4):903-75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Ventilation–Perfusion Scintigraphy Is More Sensitive than Multidetector CTPA in Detecting Chronic Thromboembolic Pulmonary Disease as a Treatable Cause of Pulmonary Hypertension

Nina Tunariu[1], Simon J.R. Gibbs[2,3], Zarni Win[4], Wendy Gin-Sing[2], Alison Graham[1], Philip Gishen[1], and Adil AL-Nahhas[3,4]

[1]Department of Radiology, Hammersmith Hospital, London, United Kingdom; [2]Department of Cardiology, Hammersmith Hospital, London, United Kingdom; [3]Imperial College, London, United Kingdom; and [4]Department of Nuclear Medicine, Hammersmith Hospital, London, United Kingdom

J Nucl Med 2007; 48:680–684

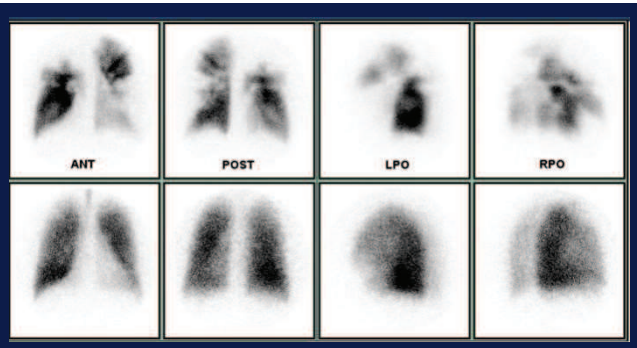
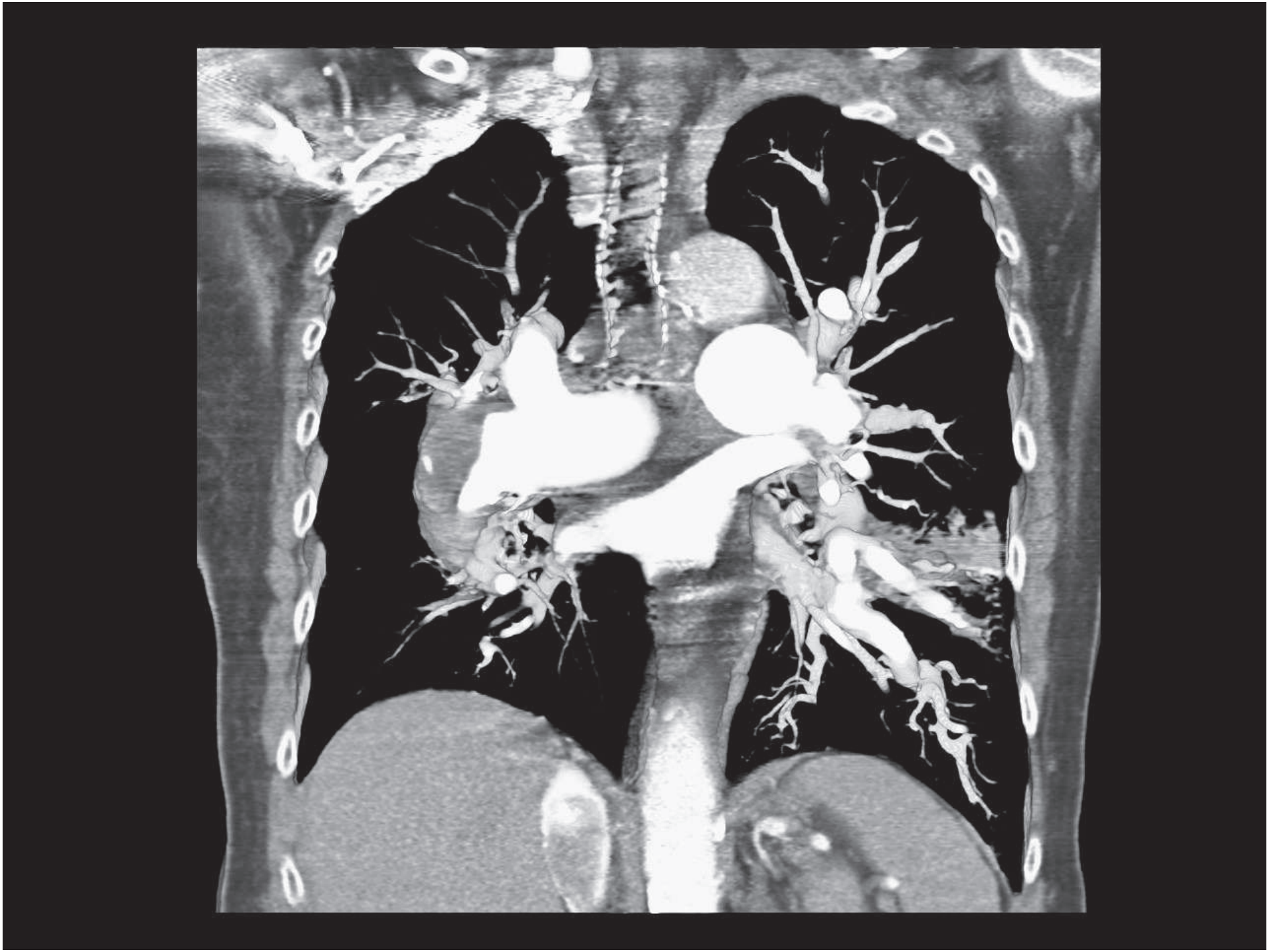
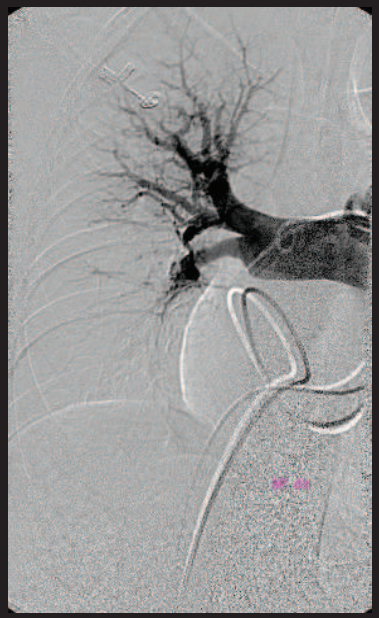
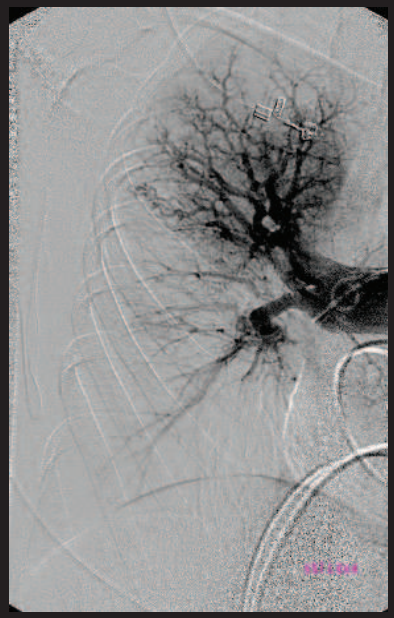


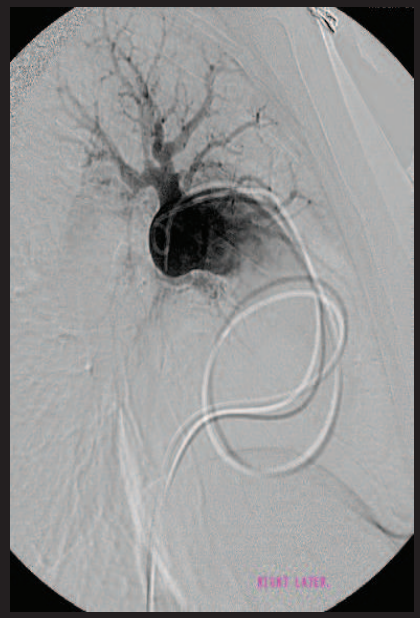
TABLE 1
Summary of V/Q Scans and CTPA Results

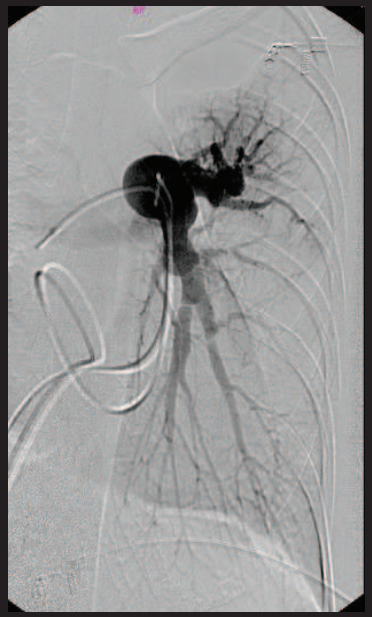
	V/Q			CTPA	
Group	Low probability	Intermediate probability	High probability	Negative	Positive
A (*n* = 78)	2	1	75	38	40
B (*n* = 149)	134	7	8	148	1

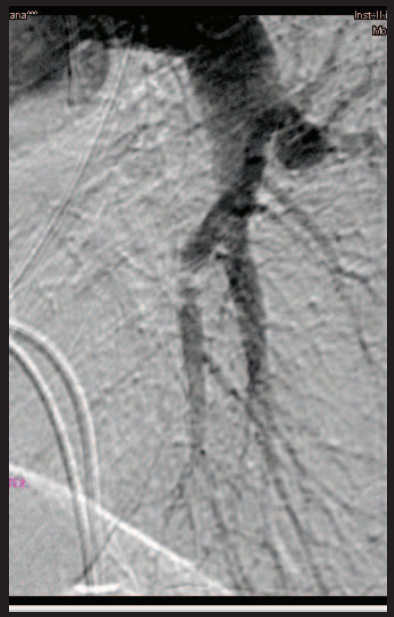


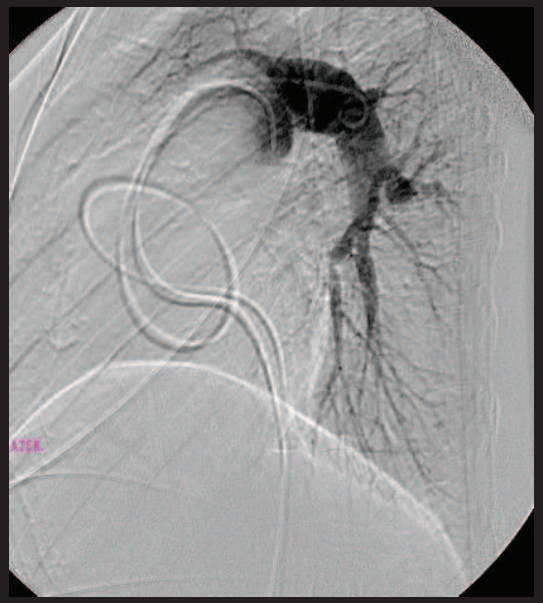








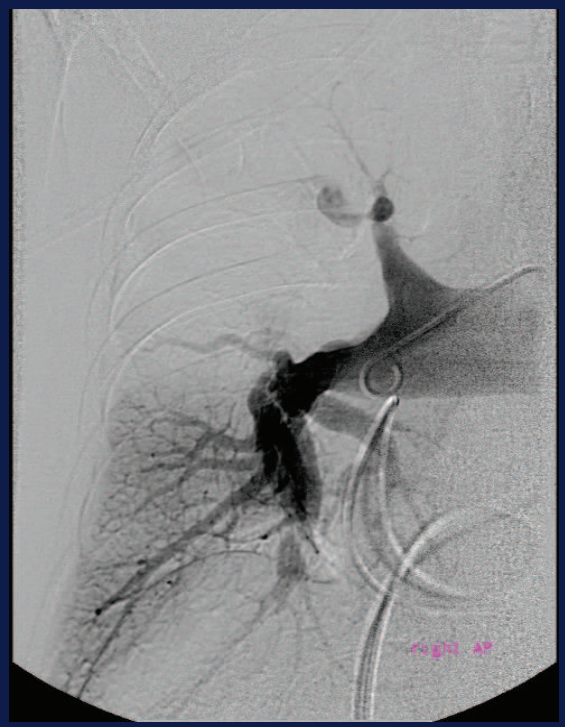


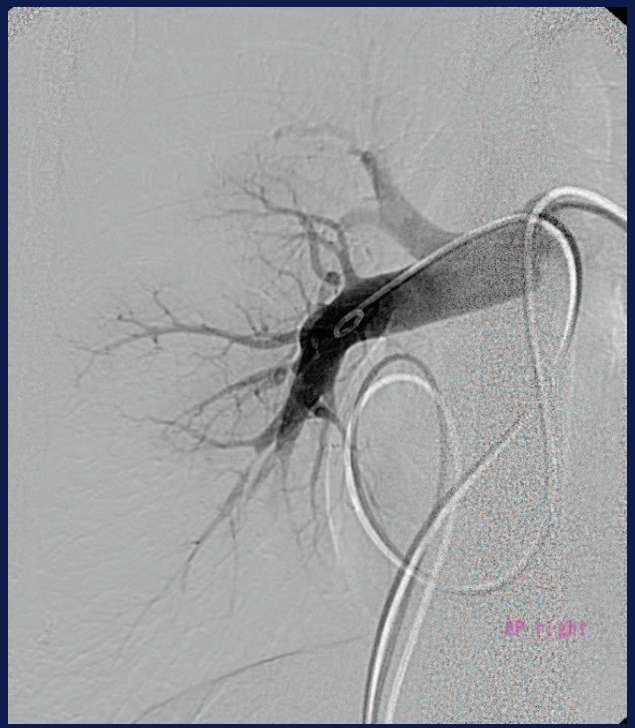


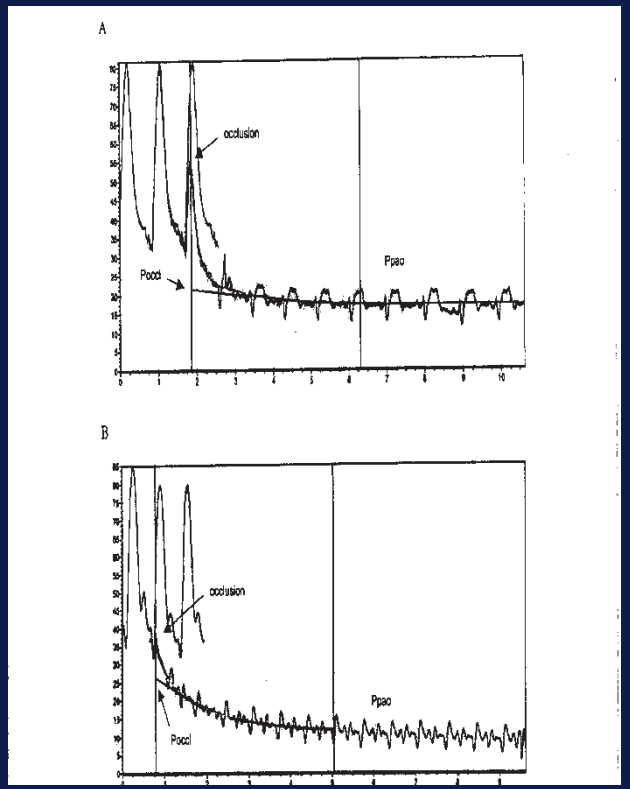
LOKALIZACE OBSTRUKCE U CTEPH

Kim et al.: *Circulation* 2004, 109: 18-22

N=26, Rup (%)= 100x(PAMP-Poccl)/(PAMP-Ppao)

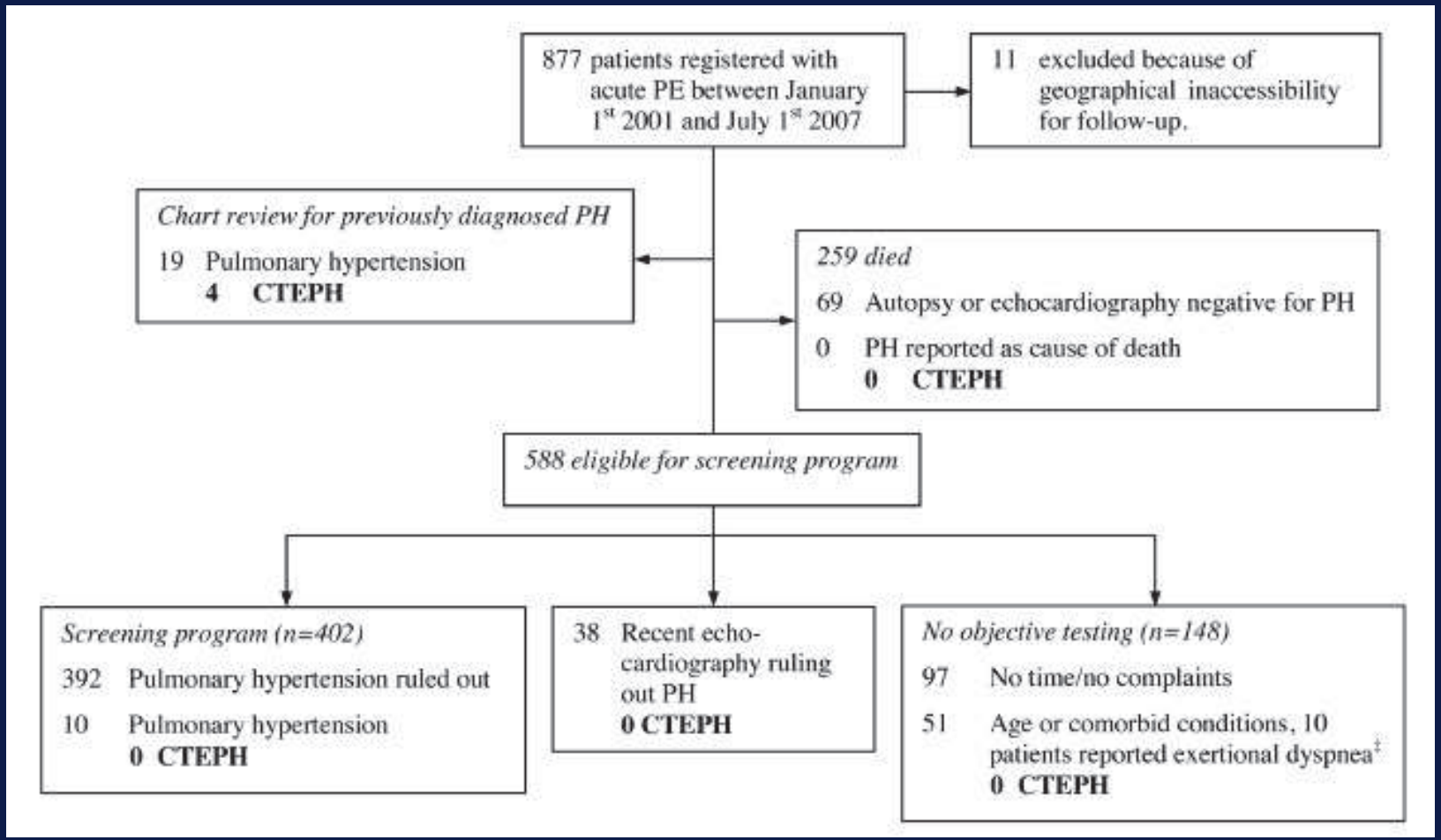






Prospective cardiopulmonary screening program to detect chronic thromboembolic pulmonary hypertension in patients after acute pulmonary embolism

Frederikus A. Klok,[1] Klaas W. van Kralingen,[2] Arie P.J. van Dijk,[3] Fenna H. Heyning[4], Hubert W. Vliegen,[5] and Menno V. Huisman[1]



Haematologica 2010;95:970-975

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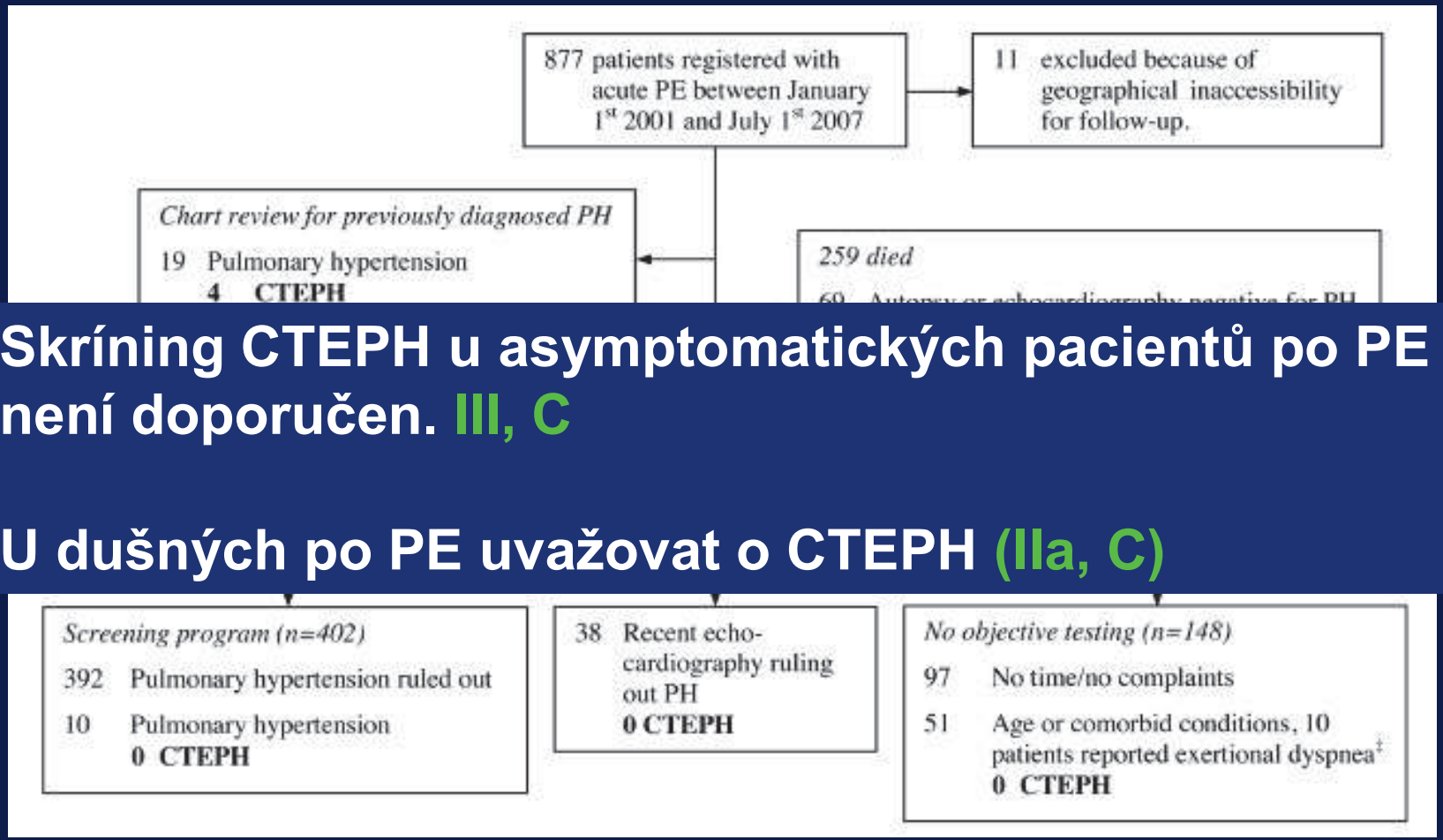


Skríning CTEPH u asymptomatických pacientů po PE není doporučen. III, C

U dušných po PE uvažovat o CTEPH (IIa, C)

Haematologica 2010;95:970-975

LÉČBA CTEPH

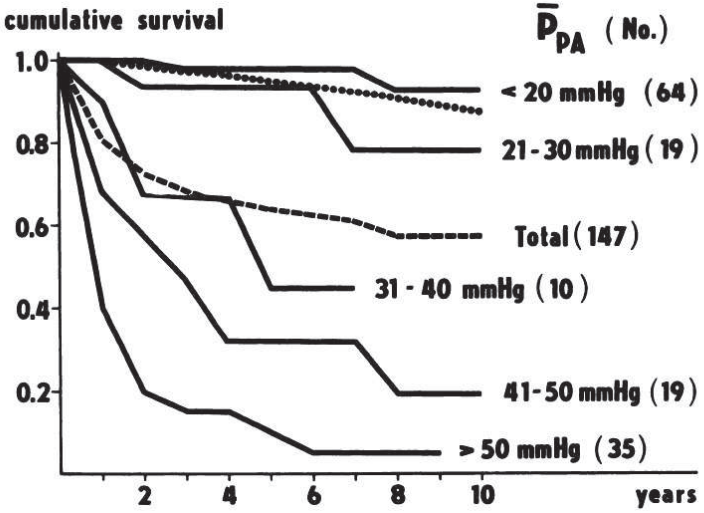
- **Doživotní antikoagulace (I, C)**
- **Posouzení operability multidisciplinárním teamem včetně chirurga (I, C)**
- **PEA v DHA je léčbou volby (I, C)**
- **U inoperabilní pacientů/pacientů s reziduální PH po PEA je doporučena léčba riociguatem (I, B)**
- **U inoperabilní pacientů/pacientů s reziduální PH po PEA je možná off-label léčba ostatními léky používanými u PAH (IIb, B)**

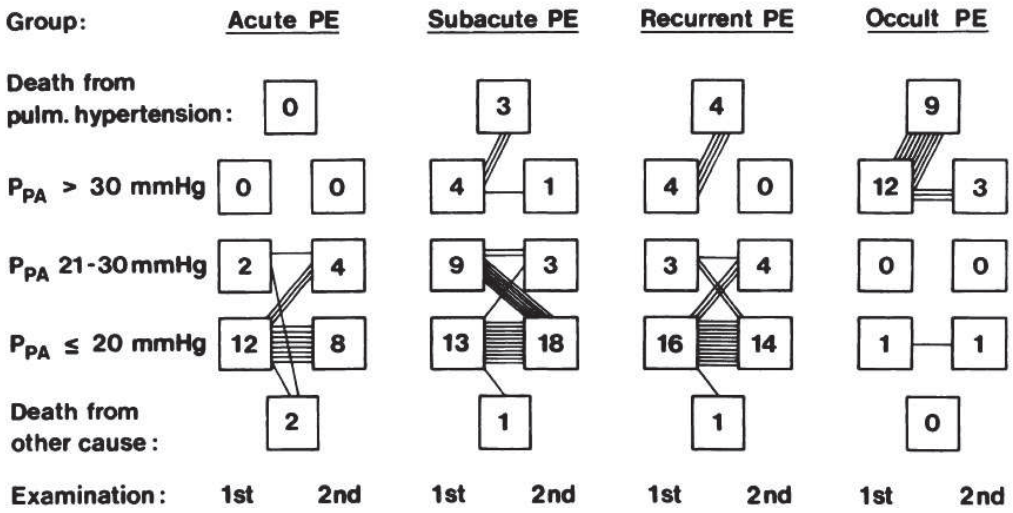
Eur Respir J 2015, 46(4):903-75

Longterm Follow-up of Patients with Pulmonary Thromboembolism*

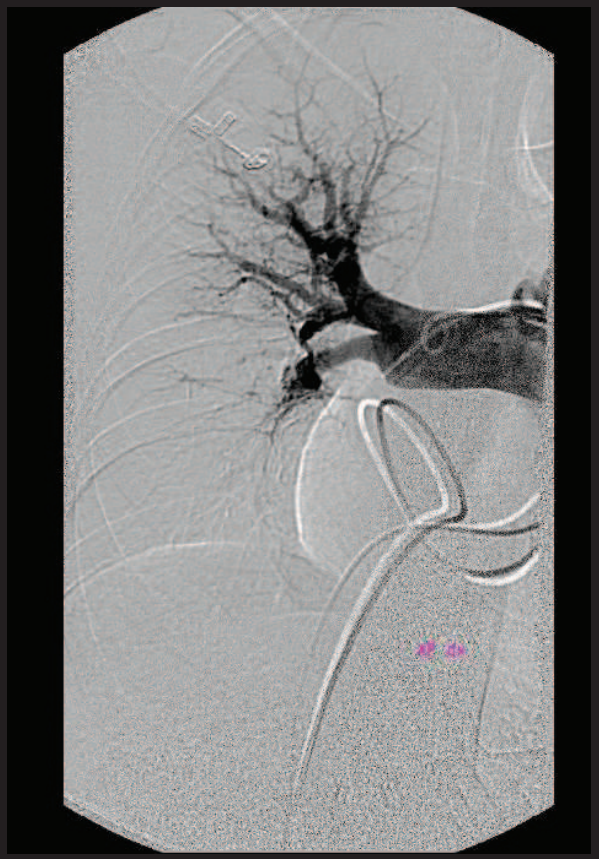
Late Prognosis and Evolution of Hemodynamic and Respiratory Data

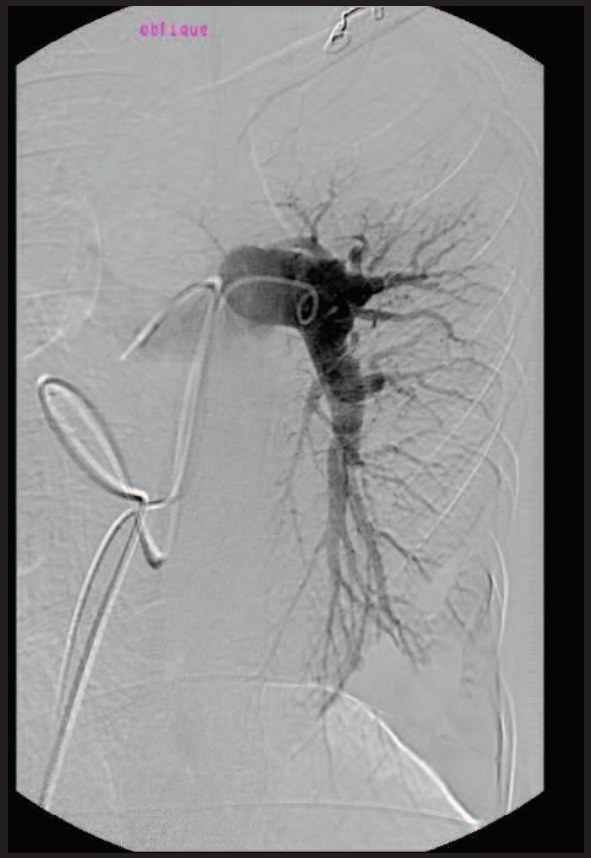
Martin Riedel, M.D.; Vladimír Stanek, M.D.; Jiri Widimsky, M.D.; and Ivo Prerovsky, M.D.





Riedel M, Stanek V, Widimsky J, Prerovsky I, *Chest* 1982, 81: 151-8

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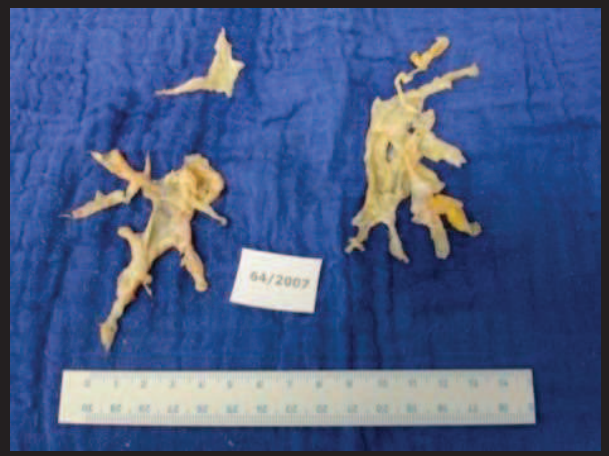
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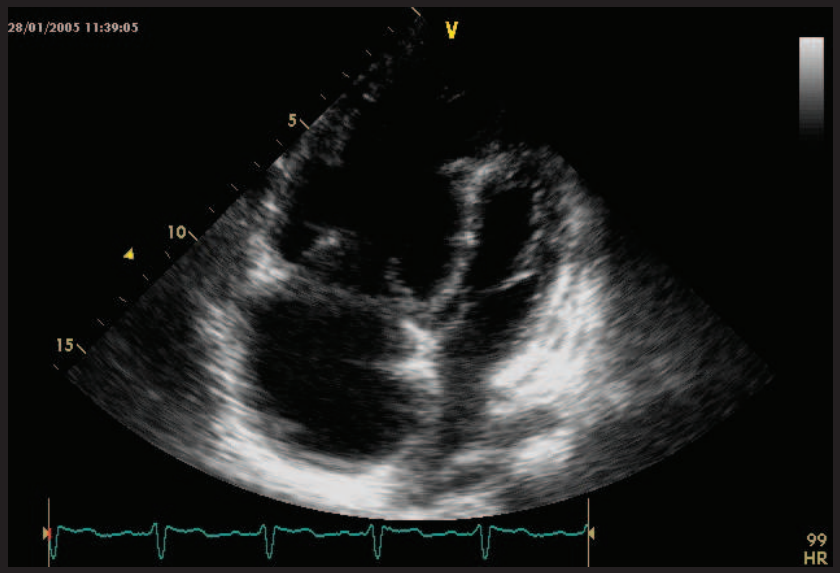
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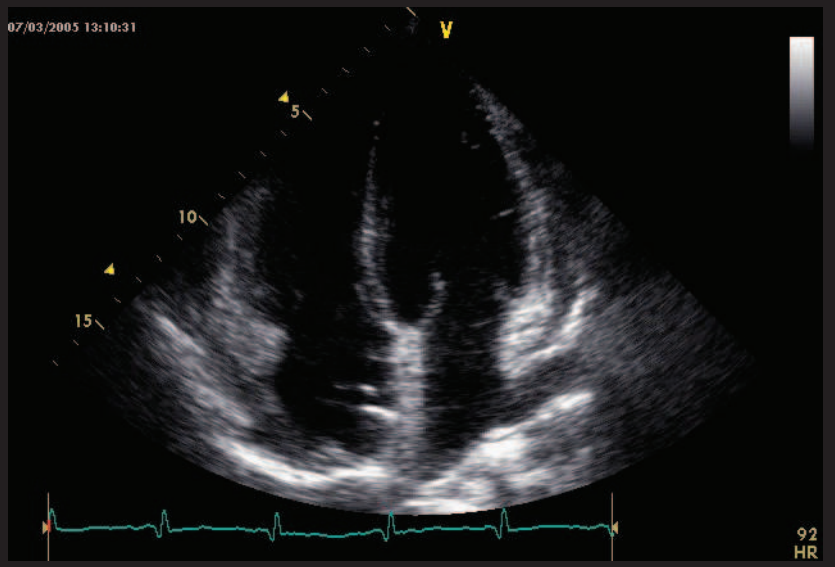
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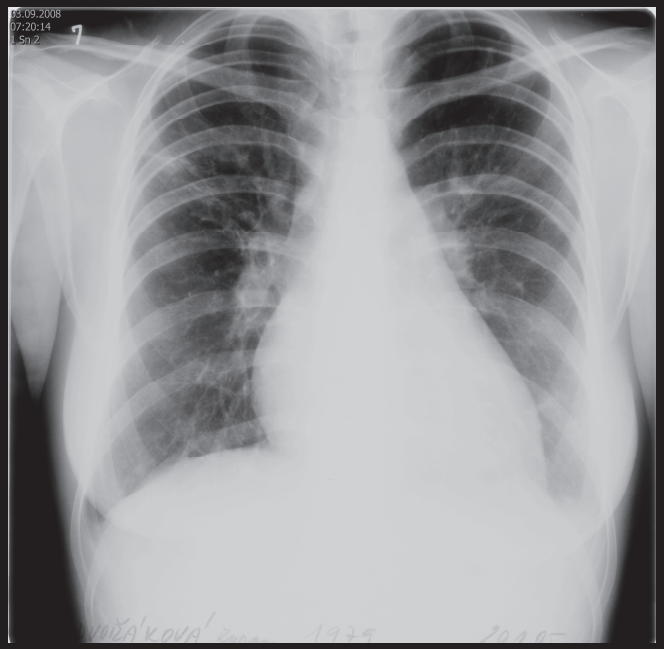
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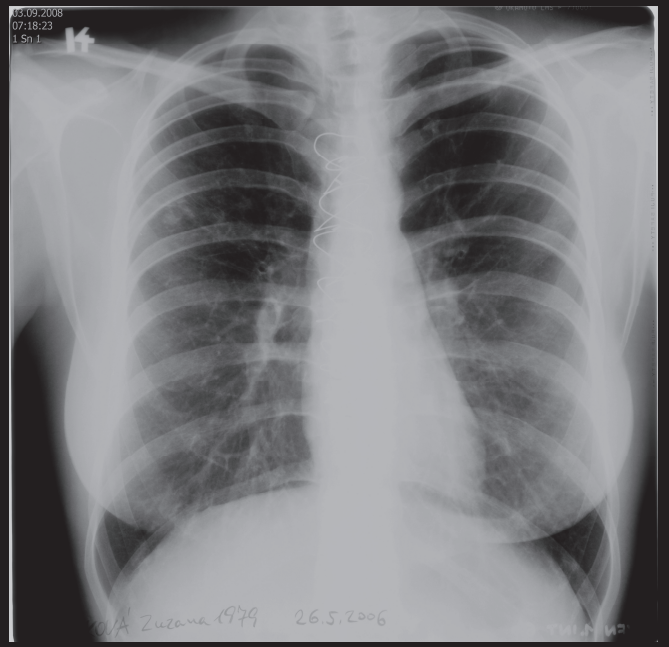
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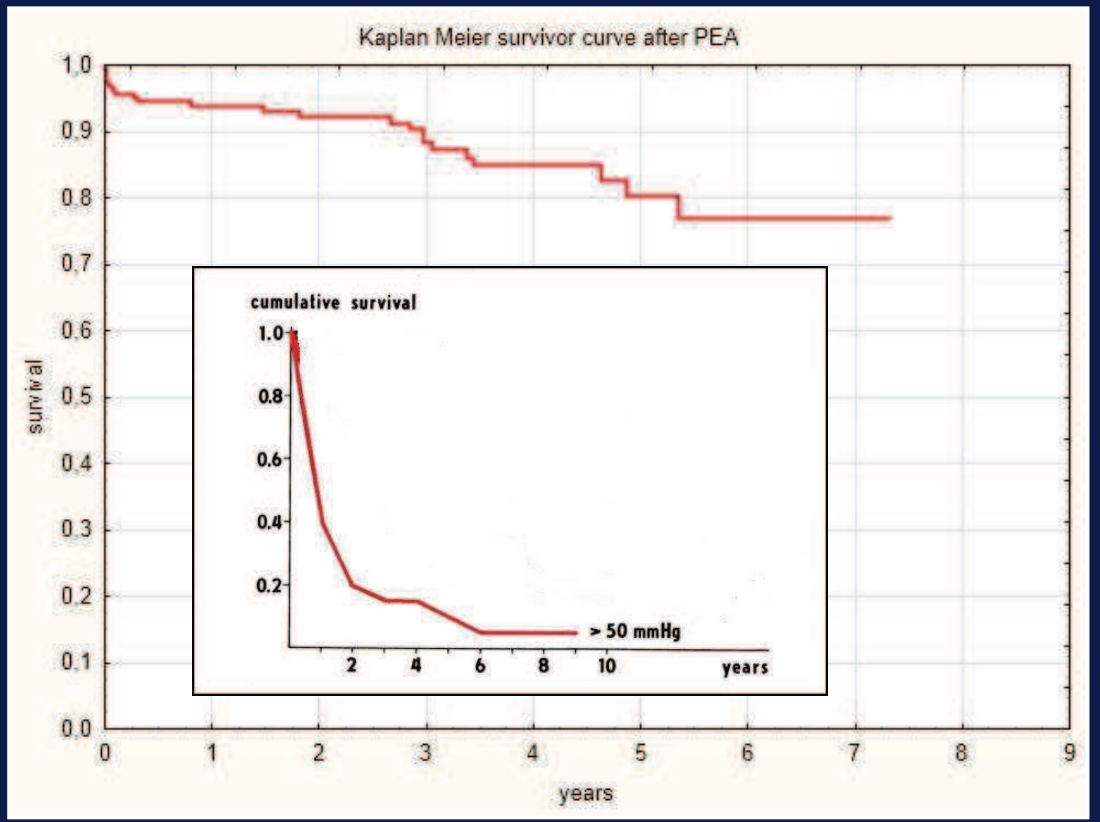
PŘEŽÍVÁNÍ PO PEA

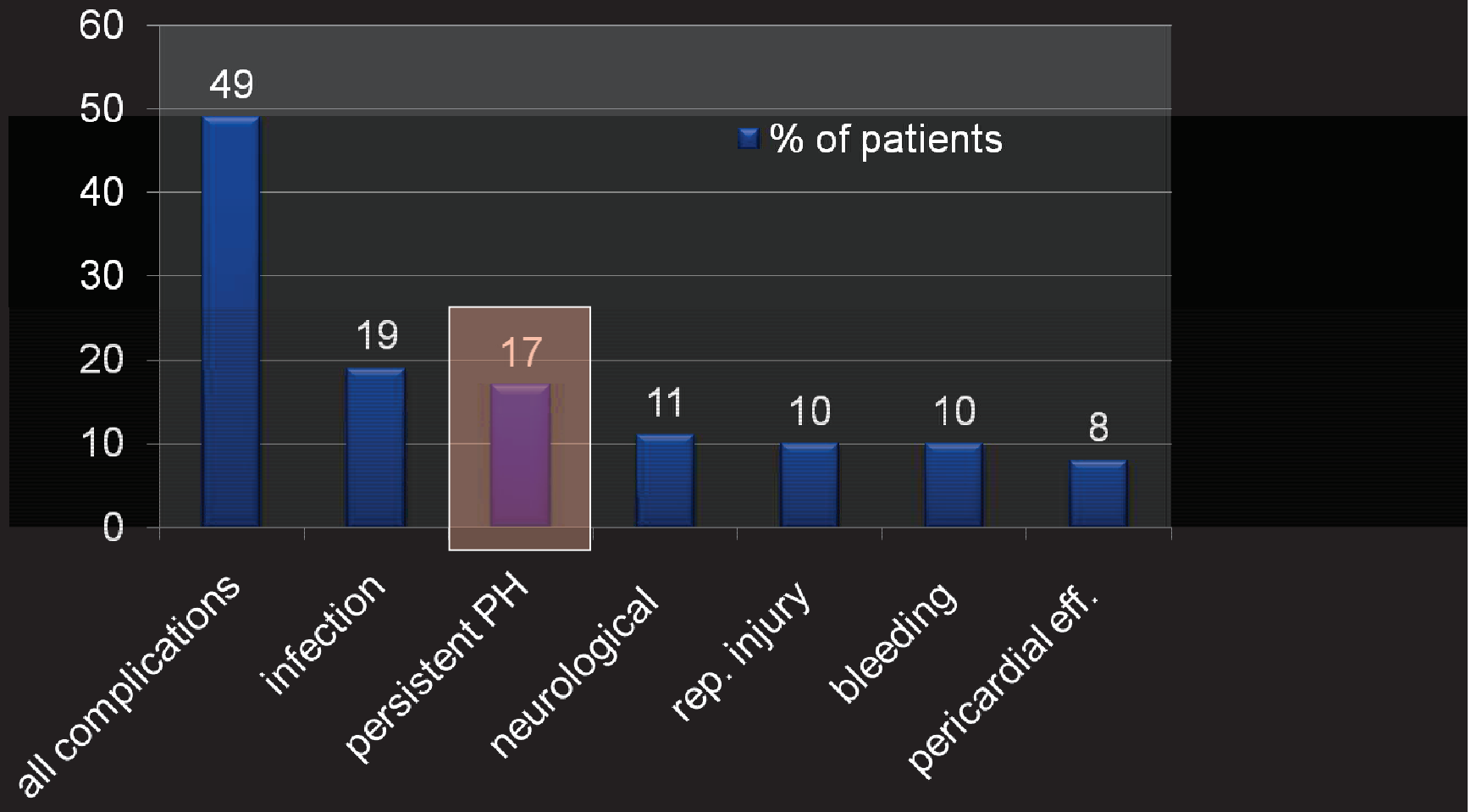
VFN Praha, 2004-2013, n=197

- **Časná hospitalizační mortalita 4,8%**
- **Dlouhodobé přežívání:**
  - 1 rok: 94%
  - 3 roky: 90%
  - 5 let: 80%



INTERNATIONAL EUROPEAN CTEPH REGISTRY

SURGICAL COMPLICATIONS

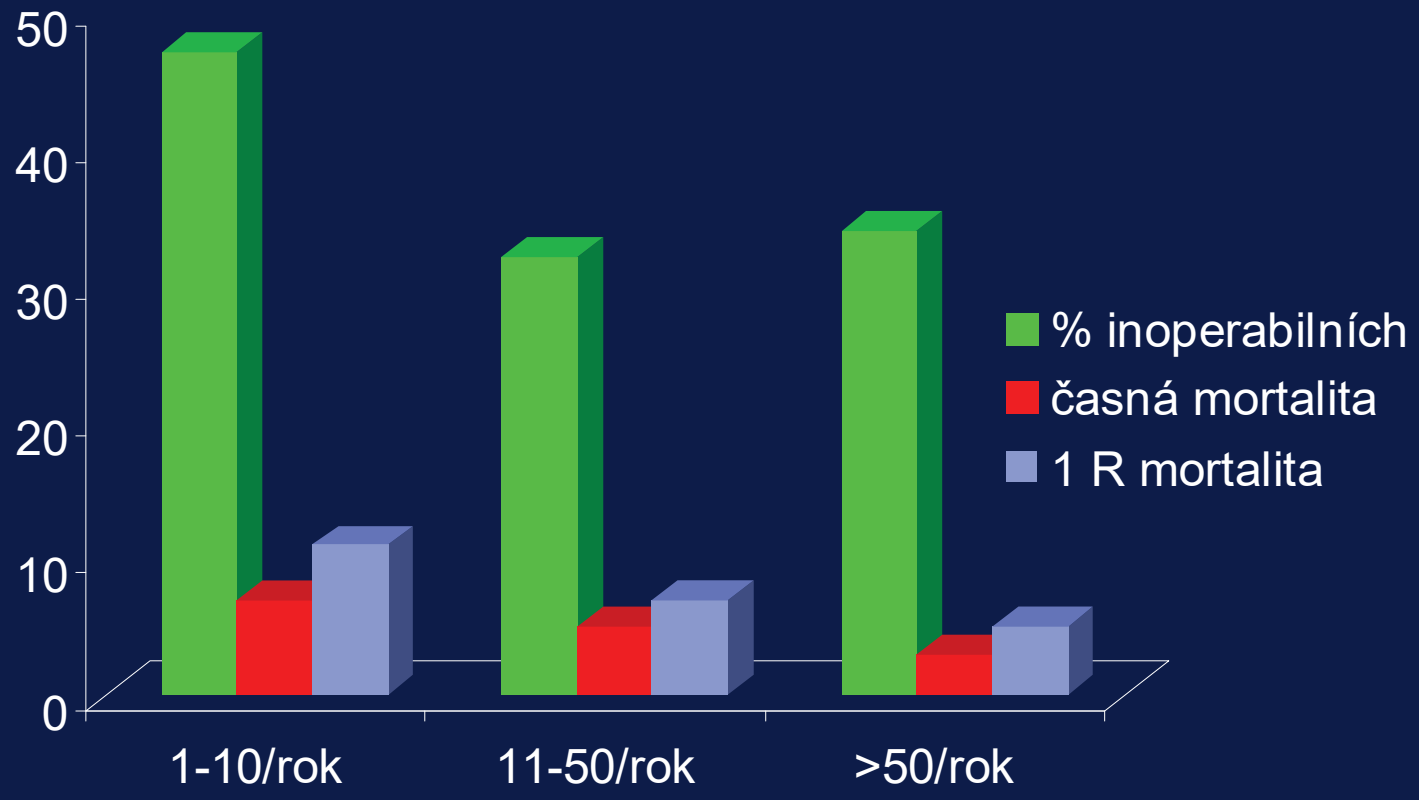


Delcroix M et al., *Am. J. Respir. Crit. Care Med.*.2010; 181: A1941

Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Results From an International Prospective Registry

Joanna Pepke-Zaba, MD; Marion Delcroix, MD; Irene Lang, MD; Eckhard Mayer, MD; Pavel Jansa, MD; David Ambroz, MD; Carmen Treacy, BSc; Andrea M. D'Armini, MD; Marco Morsolini, MD; Repke Snijder, MD; Paul Bresser, MD; Adam Torbicki, MD; Bent Kristensen, MD; Jerzy Lewczuk, MD; Iveta Simkova, MD; Joan A. Barberà, MD; Marc de Perrot, MD; Marius M. Hoeper, MD; Sean Gaine, MD; Rudolf Speich, MD; Miguel A. Gomez-Sanchez, MD; Gabor Kovacs, MD; Abdul Monem Hamid, MD; Xavier Jaïs, MD; Gérald Simonneau, MD



Circulation 2011, 124 (Nov)

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N=679, nově diagnostikovaní pro CTEPH (2007-2009)

16 evropských zemí + Kanada

62.9 % operabilní, 56.8 % operováno

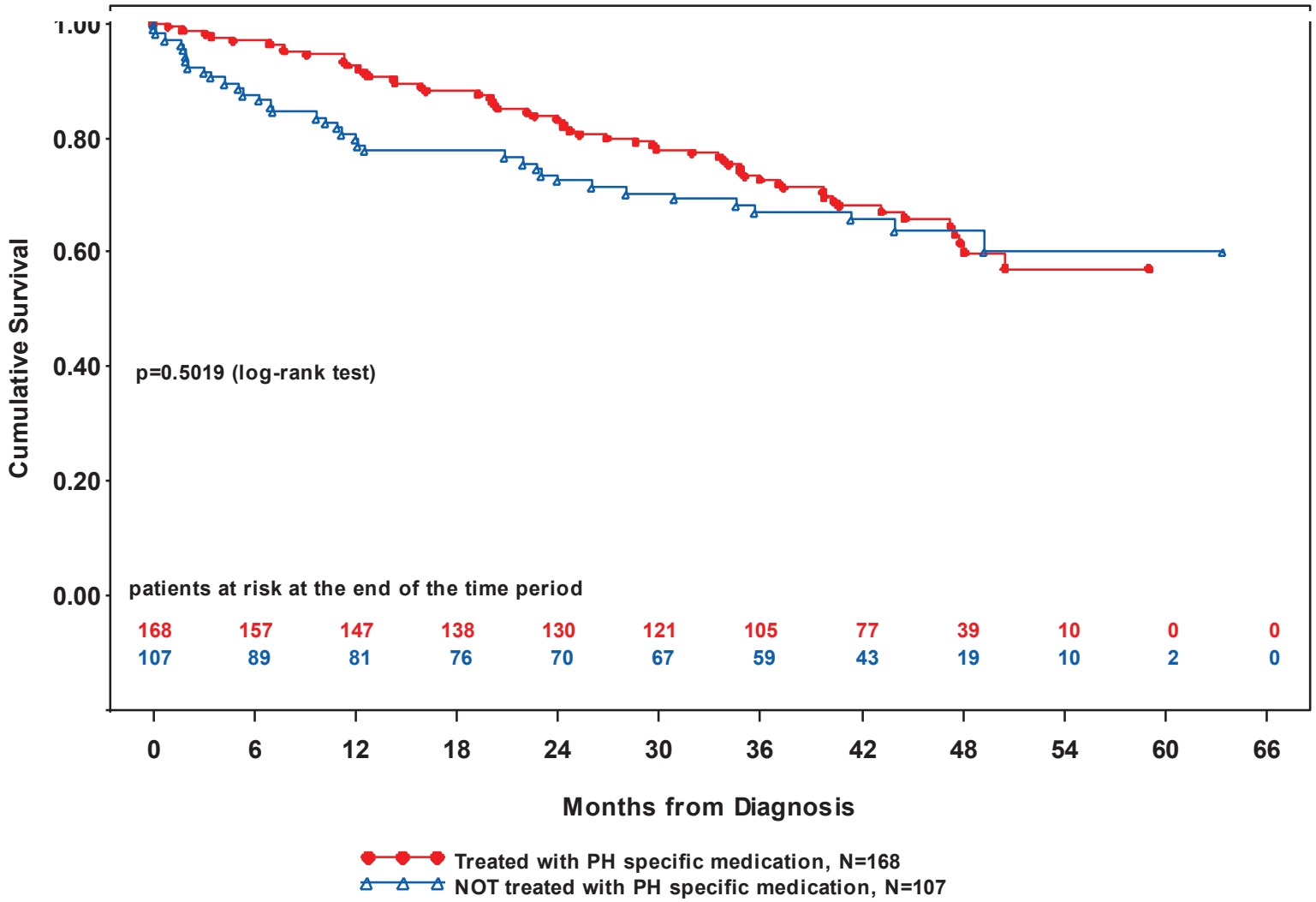
	All Patients (n=679)	Operable Patients* (n=427)	Nonoperable Patients* (n=247)	*P* (Exploratory)
PAH-targeted therapy, % (n)	37.9 (676)	28.3 (427)	53.8 (247)	<0.0001
Phosphodiesterase type V inhibitor, %	17.5	16.2	19.4	0.2923
Endothelin receptor antagonist, %	21.7	12.2	37.7	<0.0001
Prostacyclin analogue, %	2.7	1.6	4.5	0.0443
Combination therapies, %	4.0	1.6	7.7	0.0002

P values from Fisher exact test. (n): patients with assessment. PAH indicates pulmonary arterial hypertension.
*Five patients had no data on operability.

Circulation 2011, 124 (Nov)

INTERNATIONAL EUROPEAN CTEPH REGISTRY

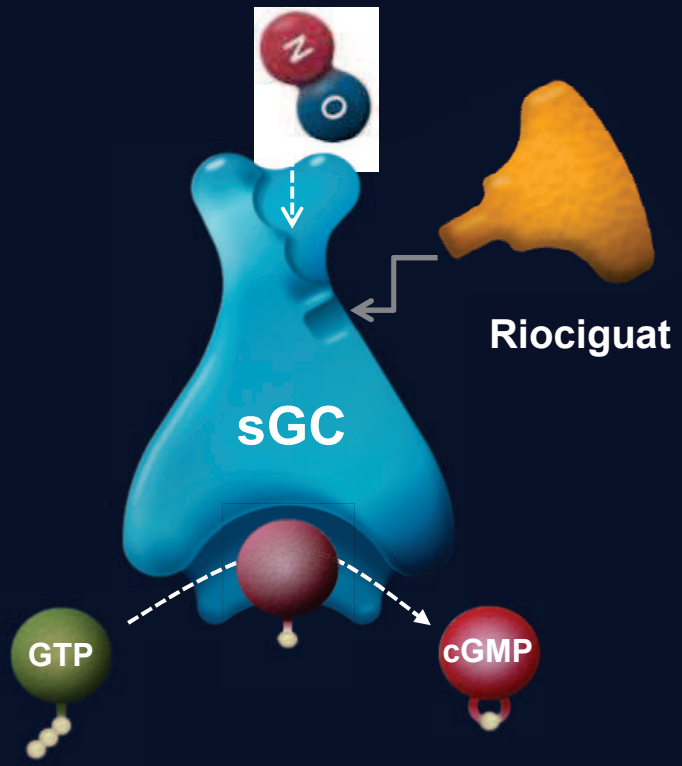
INOPERABILNÍ, FARMAKOLOGICKY LÉČENÍ VS NELÉČENÍ

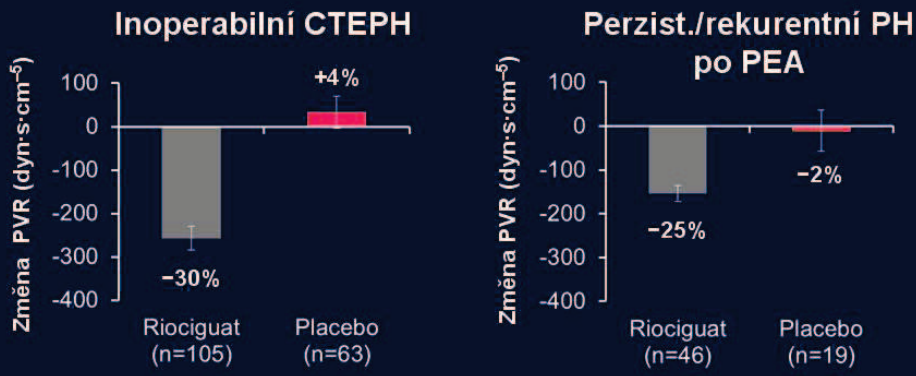


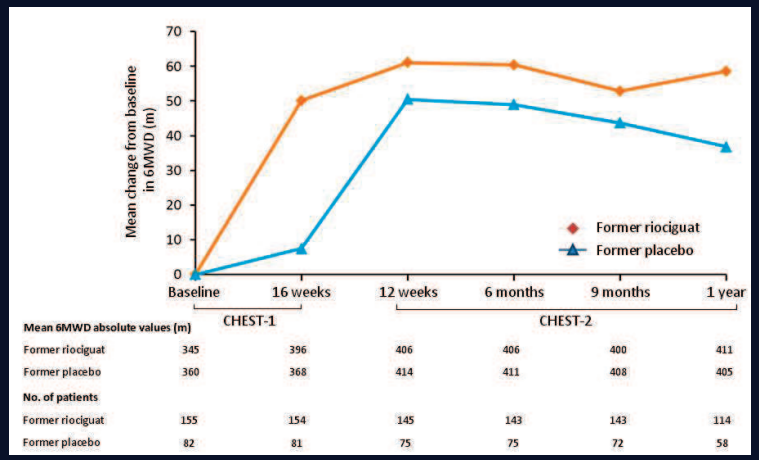
Simonneau et al, *ATS 2013*

Riociguat for the Treatment of Chronic Thromboembolic Pulmonary Hypertension

Hossein-Ardeschir Ghofrani, M.D., Andrea M. D'Armini, M.D., Friedrich Grimminger, M.D., Marius M. Hoeper, M.D., Pavel Jansa, M.D., Nick H. Kim, M.D., Eckhard Mayer, M.D., Gerald Simonneau, M.D., Martin R. Wilkins, M.D., Arno Fritsch, Ph.D., Dieter Neuser, M.D., Gerrit Weimann, M.D., and Chen Wang, M.D., for the CHEST-1 Study Group*







Mean 6MWD absolute values (m)						
Former riociguat	345	396	406	406	400	411
Former placebo	360	368	414	411	408	405
No. of patients						
Former riociguat	155	154	145	143	143	114
Former placebo	82	81	75	75	72	58

NEJM 2013, 369: 319-329

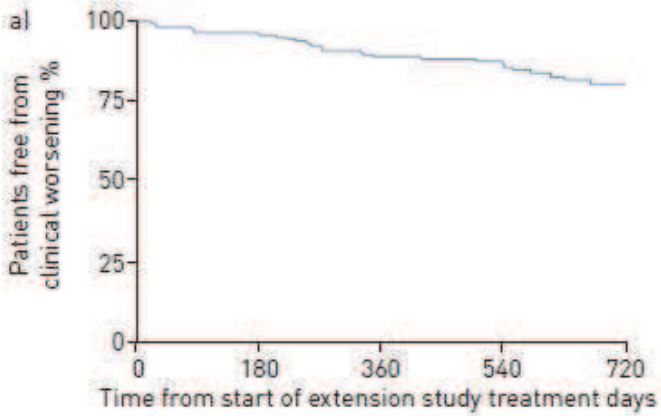
DALŠÍ CÍLOVÉ UKAZATELE CHEST-1

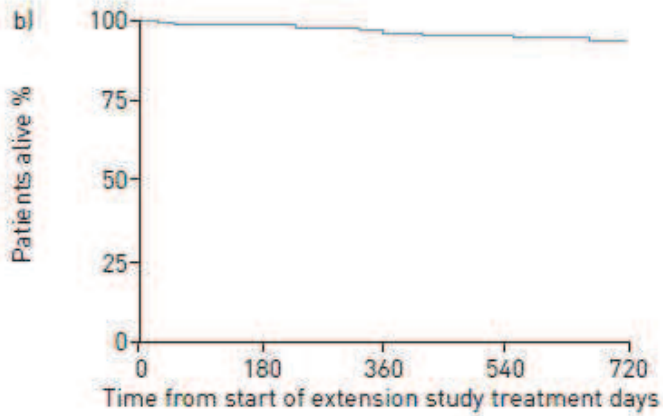
Parametr	Riociguat	Placebo	Δ (95% CI)	Riociguat vs placebo; p
NT-proBNP, pg/mL	−291±171	+76±1447	−444	<0.0001
WHO FC, zlepšení/stac./zhoršení(%)	33/62/5	15/78/7	—	0.0026
TTCW, n (%)	4 (2)	5 (6)	—	0.1724
Borgův stupeň dušnosti	−0.8±2	+0.2±2	—	0.0035
EQ-5D	+0.06±0.2	−0.08±0.34	0.13	<0.0001

Ghofrani et al. *NEJM* 2013, 369: 319-312

Riociguat for the treatment of chronic thromboembolic pulmonary hypertension: a long-term extension study (CHEST-2)

Gérald Simonneau[1], Andrea M. D'Armini[2], Hossein-Ardeschir Ghofrani[3,4], Friedrich Grimminger[3], Marius M. Hoeper[5], Pavel Jansa[6], Nick H. Kim[7], Chen Wang[8], Martin R. Wilkins[9], Arno Fritsch[10], Neil Davie[10], Pablo Colorado[11] and Eckhard Mayer[12]





Patients who reached time point without clinical worsening n	237	218	155	96	65
Patients with clinical worsening n	0	10	24	28	34

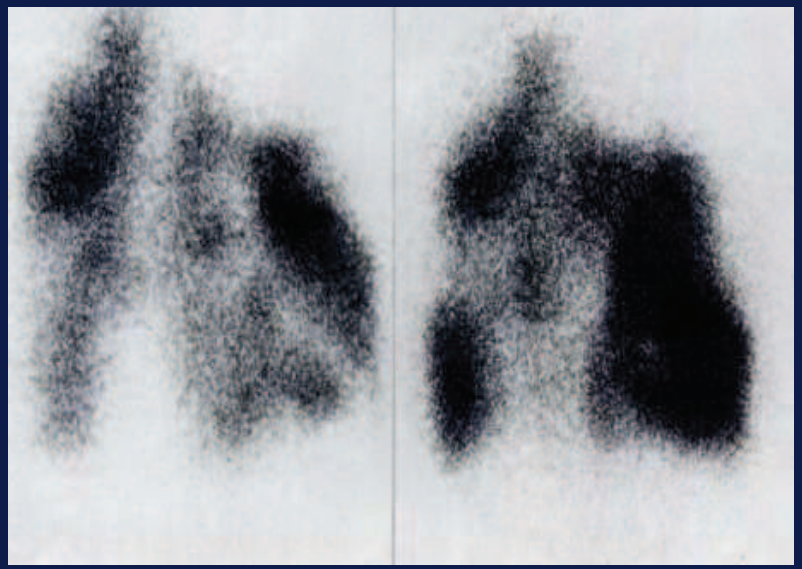
Patients alive at time point n	237	223	166	105	74
Deaths n	0	3	6	8	10

Eur Respir J 2015; 45: 1293–1302

Balloon Angioplasty in the Treatment of Pulmonary Hypertension Caused by Pulmonary Embolism*

Jan A. I. Voorburg, M.D.; Volkert Manger Cats, M.D.; Beert Buis, M.D.; and Albert V. G. Bruschke, M.D., F.C.C.P.

♀ 30 let, CTEPH
3 intervence na 4 tepnách, 2x reperfúzní edém

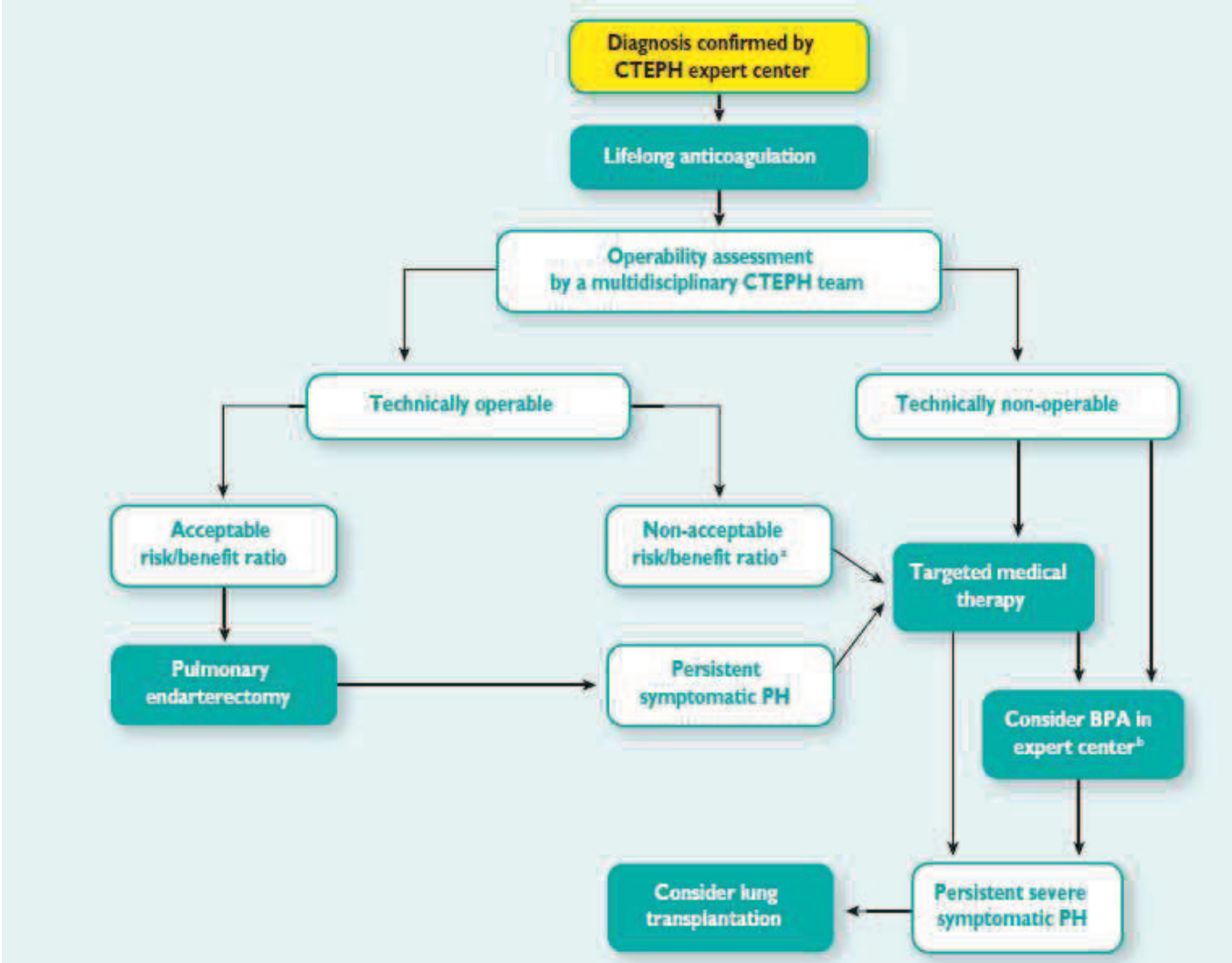


	Before	After
Right Atrium (mean), mm Hg	4-10 (6)	0-5 (2)
Pulmonary Artery (mean), mm Hg	90/25 (46)	78/13 (35)
Wedge (mm Hg)	5	5
Aorta (mm Hg)	105/60 (75)	134/68 (90)
Ratio Ao/PA pressures	1.63	2.57
Venous saturation(%)	65	67.5
Arterial saturation (%)	91	95
Cardiac output* (ml/min)	4770	4510
PVR (dynes·s·$^{-5}$)	688	532
SVR (dynes·s·$^{-5}$)	1157	1561

*Cardiac output only measured at rest. PA = pulmonary artery; Ao = aorta; PVR = pulmonary vascular resistance; SVR = systemic vascular resistance.

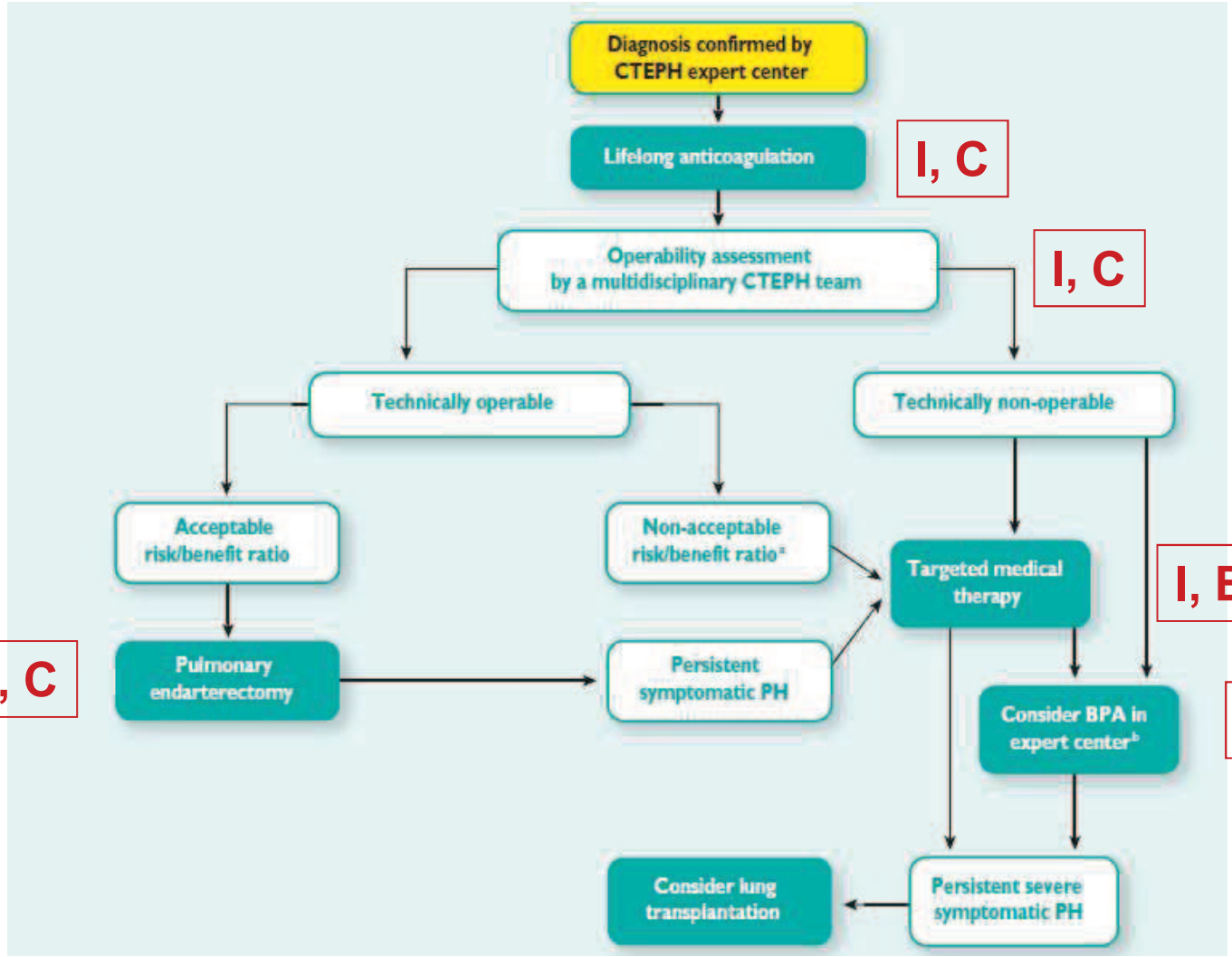
Chest 1998, 94: 1249-53

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



Eur Respir J 2015, 46(4):903-75

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



Eur Respir J 2015, 46(4):903-75

SHRNUTÍ

- CTEPH je relativně častou chronickou komplikací PE
- V detekci CTEPH je rozhodující ECHO a V/Q scinti plic
- Skríning asymptomatických není doporučen
- Doživotní antikoagulace
- Specifická léčba – CTEPH team včetně chirurga
  - a) PEA
  - b) farmakoterapie (riociguat)
  - c) PTPA, Tx plic

ÚČEL DOPORUČENÍ

- **NEJSOU** učebnicí diagnostiky a léčby chorob centrální cirkulace
- **NEJSOU** návodem k použití diagnostických a terapeutických metod
- **SNAŽÍ SE BÝ**T průvodcem strategiemi diagnostiky a léčby syndromu PH na základě současného medicínského poznání
- **JSOU nástrojem pro jasnou demarkaci nevhodných postupů vedoucích k možným katastrofám s fatálními konci**