

Od akutní plicní embolie k chronické tromboembolické plicní hypertenzi

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ESC GUIDELINES

2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC)

Endorsed by the European Respiratory Society (ERS)

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ESC/ERS GUIDELINES



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

The Joint 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: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)



I. INTERNÍ KLINIKA
KARDIOLOGIE
FAKULTNÍ NEMOCNICE OLMOUC

Epidemiologie

Prevalence 0,4% populace

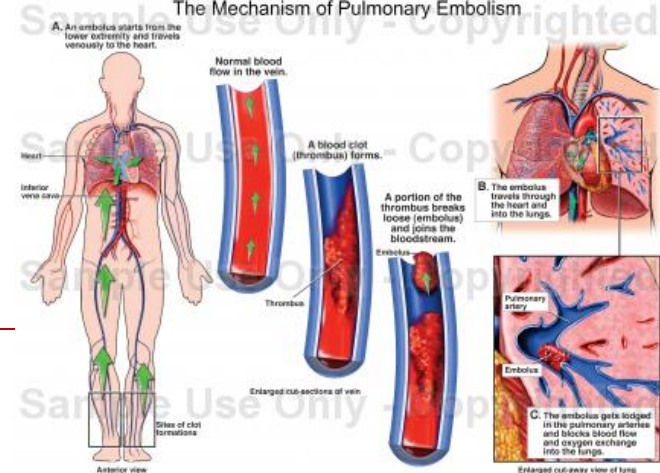
Incidence 100-200/100 000/1 rok

Autopsie 2356 (79% všech zemřelých z populace 200 tis.) s nálezem PE u 25% a u 18% jako hlavní příčina smrti

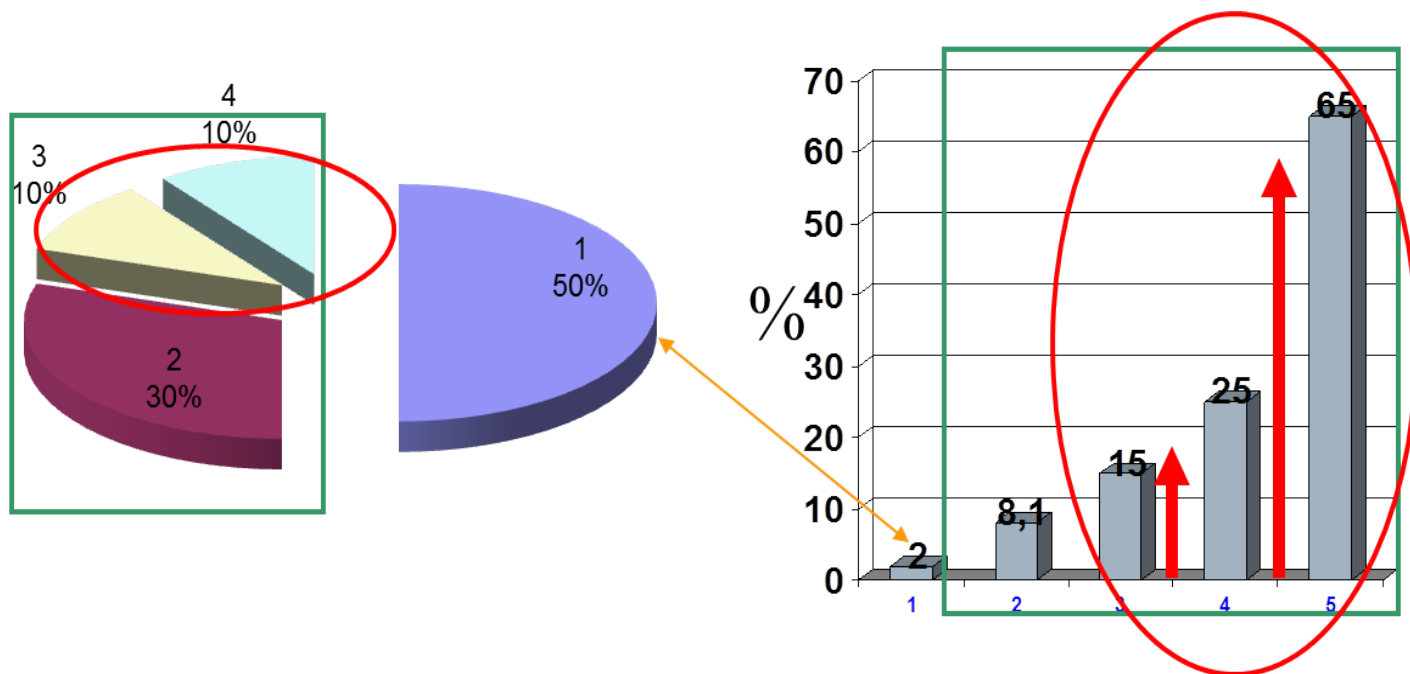
Závislost výskytu na věku a rizikových faktorech

Jen 30-45% pacientů, kteří zemřeli v důsledku plicní embolie bylo adekvátně léčeno

Až 80% pacientů s rizikovými faktory tromboembolie je špatně diagnostikováno



Prognóza



1. **Normotenze** bez dilatace a dysfunkce PK, bez elevace srdečních troponinů a BNP
2. **Normotenze s dilatací nebo dysfunkcí PK, plicní hypertenzí**, (elevace srdečních troponinů a BNP)
3. **Systémová hypotenze bez klinických známek šokové cirkulace** (pokles TKs<90 mmHg nebo pokles TKs>40 mmHg, bez nutnosti použití vazopresorů s výjimkou dobutaminu do maximální dávky 5 µg/kg/min)
4. **Kardiogenní obstrukční šok** s orgánovou hypoperfuzí a multiorgánovým selháním
5. Nutnost **iniciální kardiopulmonální resuscitace a náhlá srdeční smrt**

Klinická pravděpodobnost

Geneva skóre:

klinická pravděpodobnost
nízká 0-3 body
střední 4-10
vysoká ≥ 11

Predisponující faktory	
Věk nad 65 let	+1
Předchozí TEN	+3
Chirurgický výkon nebo trauma do 1 měsíce	+2
Malignita	+2
Symptomy	
Bolesti končetiny	+3
Hemoptýza	+2
Fyzikální vyšetření	
Srdeční frekvence	
75-95/min.	+3
>95/min.	+2
Asymetrický otok nebo bolestivost končetiny	+4

Wellsovo skóre:

klinická pravděpodobnost
nízká 0-1 body
střední 2-6, vysoká ≥ 7
plicní embolie nepravděpodobná 0-4
pravděpodobná ≥ 5

Predisponující faktory	
Předchozí TEN	+1,5
Recentní chirurgický výkon nebo imobilizace	+1,5
Malignita	+1,0
Symptomy	
Hemoptýza	+1,0
Fyzikální vyšetření	
Teplota frekvence > 100/min.	+1,5
Klinické známky hluboké žilní trombózy	+3,0
Klinické hodnocení	
Jiná diagnóza je méně pravděpodobná než PE	+3,0

Items	Original version ¹¹	Simplified version ¹²
Wells rule		
Previous PE or DVT	1.5	1
Heart rate ≥ 100 bpm	1.5	1
Surgery or immobilization within the past four weeks	1.5	1
Hemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Clinical probability		
Three-level score		
Low	0-1	N/A
Intermediate	2-4	N/A
High	≥ 7	N/A
Two-level score		
PE unlikely	0-4	0-1
PE likely	≥ 5	≥ 2
Revised Geneva score		
Previous PE or DVT	3	1
Heart rate		
75-94 bpm	3	1
≥ 95 bpm	5	2
Surgery or fracture within the past month	2	1
Hemoptysis	2	1
Active cancer	2	1
Unilateral lower limb pain	3	1
Pain on lower limb deep venous palpation and unilateral oedema	4	1
Age ≥ 65 years	1	1
Clinical probability		
Three-level score		
Low	0-3	0-1
Intermediate	4-10	2-4
High	≥ 11	≥ 5
Two-level score		
PE unlikely	0-5	0-2
PE likely	≥ 6	≥ 3

Performance of 4 Clinical Decision Rules in the Diagnostic Management of Acute Pulmonary Embolism A Prospective Cohort Study from the Prometheus Study Group

Ann Intern Med. 2011;154(11):709-718.

Table 4. Accuracy Indexes of the Clinical Decision Rules in Combination With a Normal D-Dimer Result in Patients With a Suspected Event*

Variable	Original Wells Rule (n = 796)	Simplified Wells Rule (n = 803)	RGS (n = 796)	Simplified RGS (n = 795)
Sensitivity†				
Number/number	190/191	191/192	188/189	187/188
Percentage (95% CI)	99.5 (97–100)	99.5 (97–100)	99.5 (97–100)	99.5 (97–100)
Specificity‡				
Number/number	183/605	177/611	184/607	189/607
Percentage (95% CI)	30 (27–34)	29 (25–33)	30 (27–34)	31 (28–34)
Negative predictive value§				
Number/number	183/184	177/178	184/185	189/190
Percentage (95% CI)	99.5 (97–100)	99.4 (97–100)	99.5 (97–100)	99.5 (97–100)

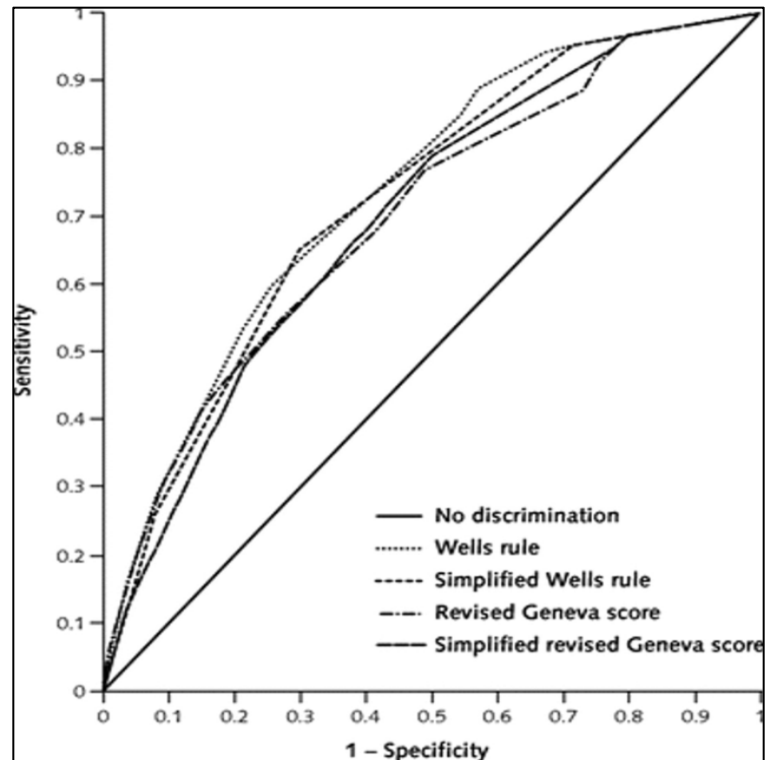
RGS = revised Geneva rule.

* Patients with a clinical decision rule indicating that PE was unlikely but in whom the D-dimer result was missing (protocol violation) were not included in this analysis; this number differed among the 4 clinical decision rules. Sensitivities did not differ among the 4 clinical decision rules in combination with D-dimer test. Specificity differed significantly between the Wells rule and the simplified Wells rule ($P = 0.031$) and the simplified Wells rule and the simplified RGS ($P = 0.017$). Other differences in specificity were not statistically significant.

† The number of patients correctly identified as having pulmonary embolism by the combination of clinical decision rules and D-dimer testing divided by the total number of patients with proven pulmonary embolism identified by computed tomography at the time of initial evaluation or venous thromboembolism at 3-mo follow-up.

‡ The number of patients correctly identified as not having pulmonary embolism by the combination of clinical decision rules and D-dimer testing divided by the total number of patients in whom pulmonary embolism was excluded by computed tomography at the time of initial evaluation or venous thromboembolism at 3-mo follow-up.

§ The number of patients correctly identified as not having pulmonary embolism by the combination of clinical decision rules and D-dimer testing divided by the total number of patients with the combination of clinical decision rule and D-dimer testing indicating that pulmonary embolism was excluded (i.e., pulmonary embolism and deep venous thrombosis).



Receiver-operating characteristic curves of the 4 clinical decision rules:

Area under the receiver-operating characteristic curves were 0.73 (95% CI, 0.69 to 0.77) for the Wells rule, 0.72 (CI, 0.68 to 0.76) for the simplified Wells rule, 0.70 (CI 0.65 to 0.74) for the revised Geneva score, and 0.69 (CI, 0.65 to 0.74) for the simplified revised Geneva score.

Ann Intern Med. 2011;154(11):709-718.

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Terminologie

	Hemodynamická nestabilita ^(a)	Echokardiografické markery dilatace, dysfunkce PK a PH [*]	Kardiomarkery	Léčebná strategie
Masivní (high risk, mortalita >15%)	+	+	+	Trombolýza nebo embolektomie
Submasivní (medium risk)	-	+/-	+/-	Antikoagulace nebo trombolýza
Neriziková (mortalita <3%)	-	-	-	Antikoagulace

Early mortality risk		Risk parameters and scores			
		Shock or hypotension	PESI class III-V or sPESI >1 ^a	Signs of RV dysfunction on an imaging test ^b	Cardiac laboratory biomarkers ^c
High		+	(+) ^d	+	(+) ^d
Intermediate	Intermediate-high	-	+	Both positive	
	Intermediate-low	-	+	Either one (or none) positive ^e	
Low		-	-	Assessment optional; if assessed, both negative ^e	



PESI – prognostická stratifikace

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Parameter	Original version ²¹⁴	Simplified version ²¹⁸
Age	Age in years	1 point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1 point
Chronic heart failure	+10 points	1 point
Chronic pulmonary disease	+10 points	
Pulse rate ≥ 110 b.p.m.	+20 points	1 point
Systolic blood pressure <100 mm Hg	+30 points	1 point
Respiratory rate >30 breaths per minute	+20 points	–
Temperature <36 °C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point
	Risk strata^a	
	<p>Class I: ≤ 65 points very low 30-day mortality risk (0–1.6%)</p> <p>Class II: 66–85 points low mortality risk (1.7–3.5%)</p> <p>Class III: 86–105 points moderate mortality risk (3.2–7.1%)</p> <p>Class IV: 106–125 points high mortality risk (4.0–11.4%)</p> <p>Class V: >125 points very high mortality risk (10.0–24.5%)</p>	<p>0 points= 30-day mortality risk 1.0% (95% CI 0.0%–2.1%)</p> <p>≥ 1 point(s)= 30-day mortality risk 10.9% (95% CI 8.5%–13.2%)</p>

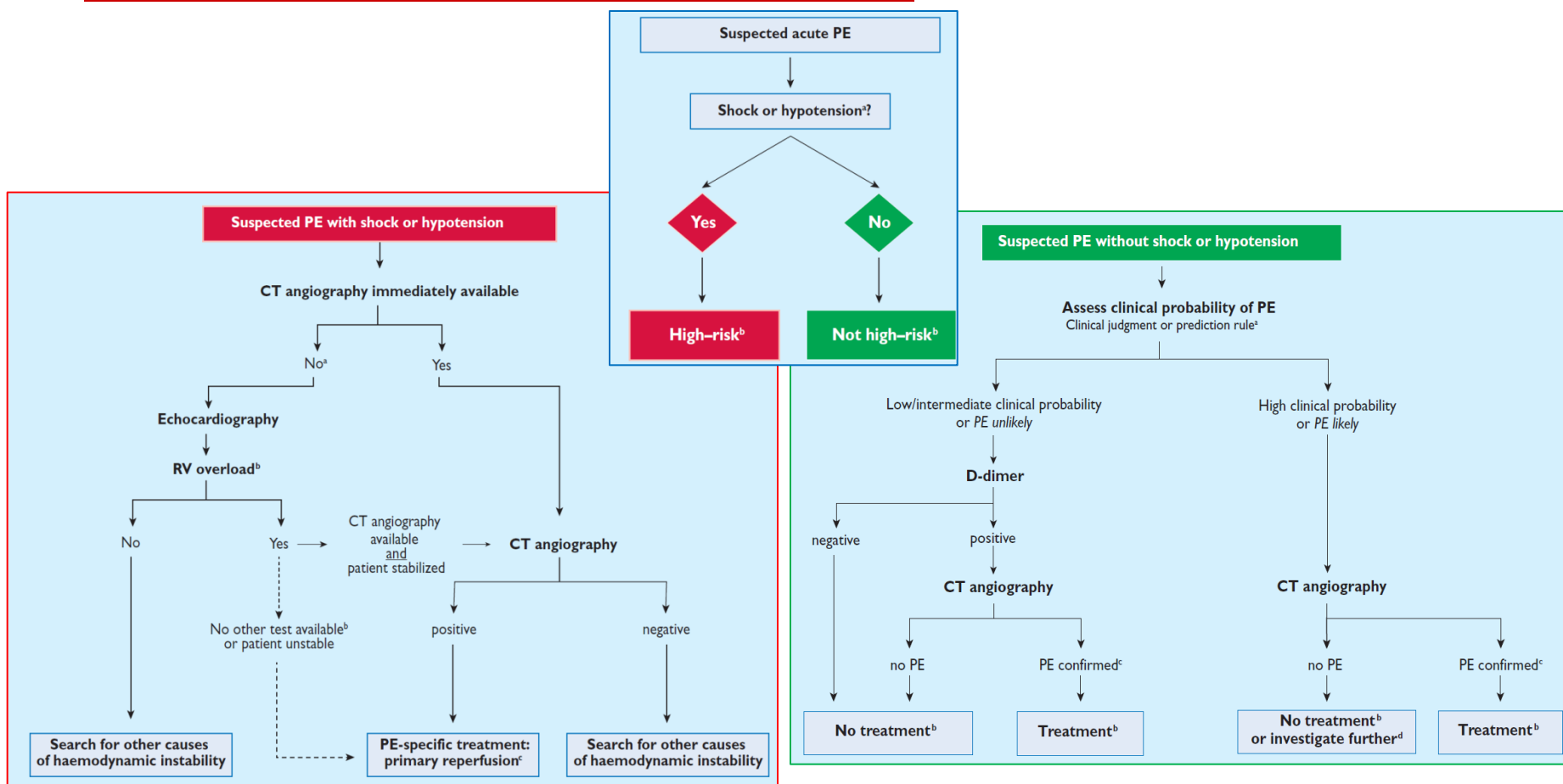


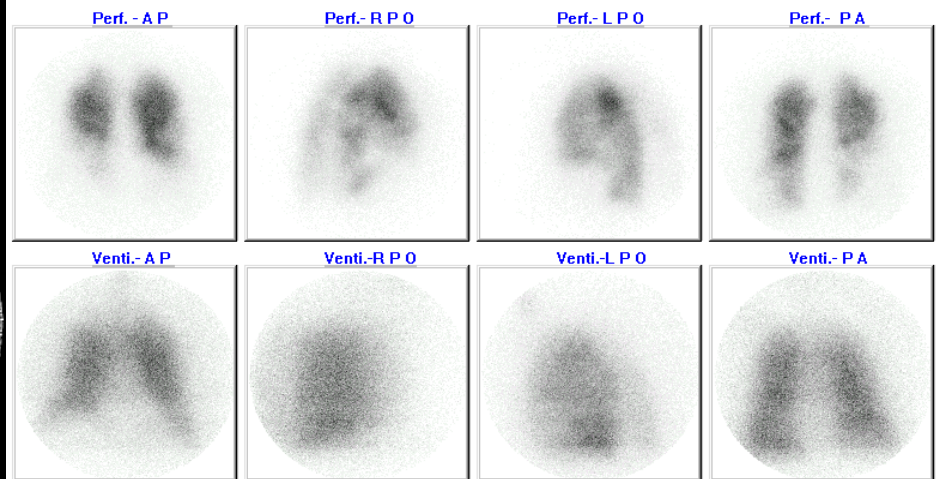
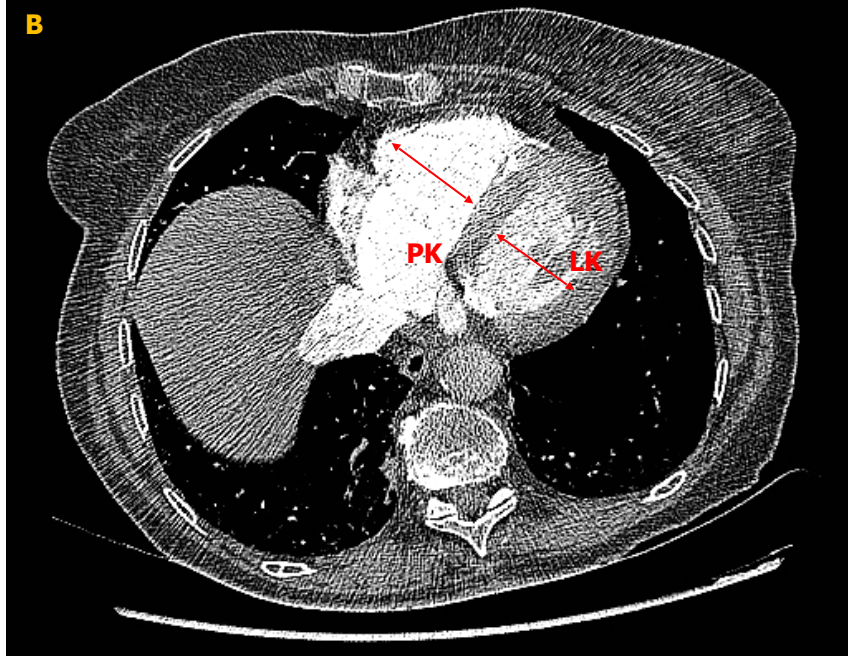
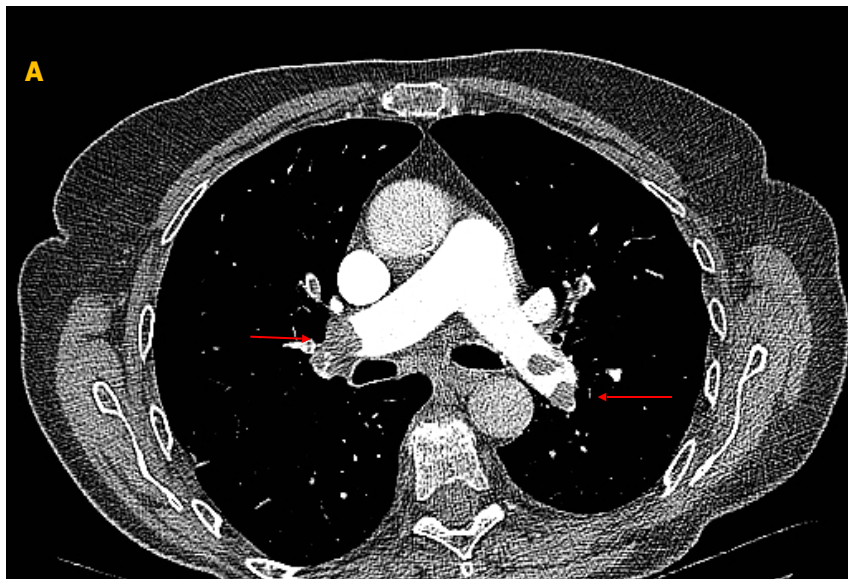
Diagnostika a riziková stratifikace

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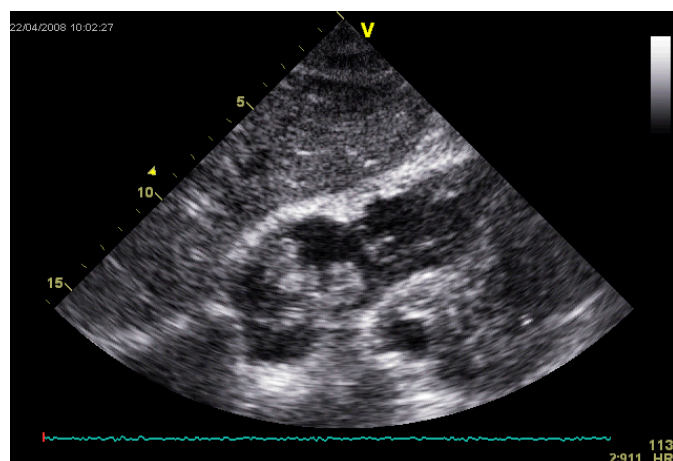
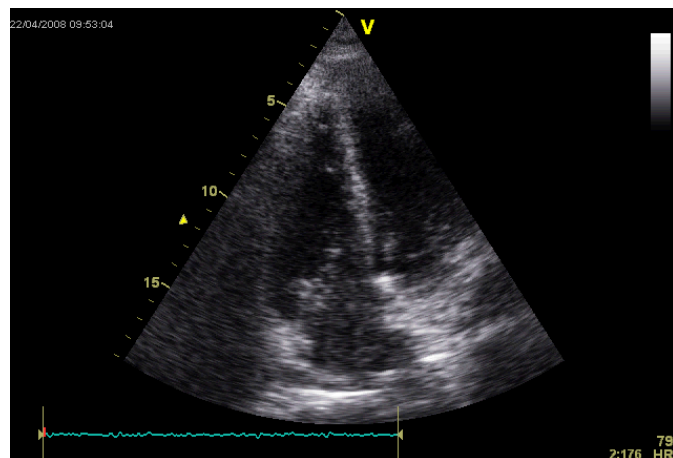
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Test or biomarker	Cut-off value	Sensitivity, % (95% CI)	Specificity, % (95% CI)	NPV, % (95% CI)	PPV, % (95% CI)	OR or HR (95% CI)	No. patients	Study design (reference)	Remarks
Echocardiography	Various criteria of RV dysfunction	74 (61–84)	54 (51–56)	98 (96–99)	8 (6–10)	2.4 (1.3–4.3)	1249	Meta-analysis ²²⁶	RV dysfunction on echocardiography or CT was one of the inclusion criteria in two randomized trials investigating thrombolysis in normotensive patients with PE. ^{252,253}
CT angiography	RV/LV ≥ 1.0	46 (27–66)	59 (54–64)	93 (89–96)	8 (5–14)	1.5 (0.7–3.4)	383	Meta-analysis ²²⁶	
	RV/LV ≥ 0.9	84 (65–94)	35 (30–39)	97 (94–99)	7 (5–10)	2.8 (0.9–8.2)	457	Prospective cohort ²²⁸	
BNP	75–100 pg/mL	85 (64–95)	56 (50–62)	98 (94–99)	14 (9–21)	6.5 (2.0–21)	261	Meta-analysis ²³²	The optimal cut-off value for PE has not been defined.
NT-proBNP	600 pg/mL	86 (69–95)	50 (46–54)	99 (97–100)	7 (5–19)	6.3 (2.2–18.3)	688	Prospective cohort ^{234e}	NT-proBNP <500 pg/mL was one of the inclusion criteria in a single-armed management trial investigating home treatment of PE. ²³⁷
Troponin I	Different assays/cut-off values ^c	NR	NR	NR	NR	4.0 (2.2–7.2)	1303	Meta-analysis ²³⁹	A positive cardiac troponin test was one of the inclusion criteria in a randomized trial investigating thrombolysis in normotensive patients with PE. ²⁵³
Troponin T	Different assays/cut-off values ^c	NR	NR	NR	NR	5.0 (1.7–14.4)	682	Meta-analysis ²³⁹	
	14 pg/mL ^d	87 (71–95)	42 (38–47)	98 (95–99)	9 (6–12)	5.0 (1.7–14.4)	526	Prospective cohort ^{76e}	
H-FABP	6 ng/mL	89 (52–99)	82 (74–89)	99 (94–99)	28 (13–47)	36.6 (4.3–304)	126	Prospective cohort ^{244e}	

Tranzientní tromby



Přítomny až u 4 (18)%
nemocných s plicní
embolií

Závažný nález indikující
trombolýzu

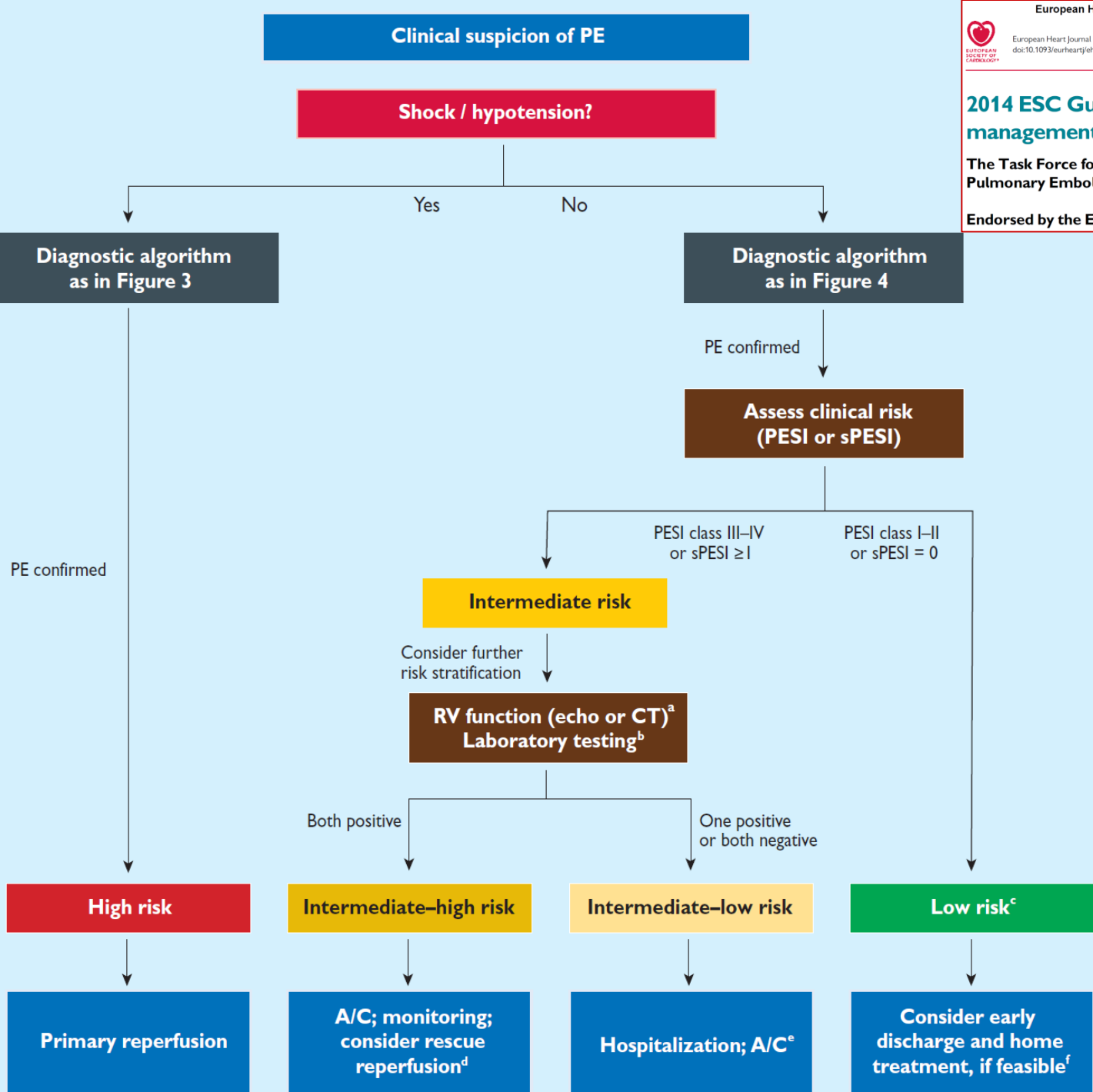
Při kontraindikaci (při
PFO z rizikem vzniku
paradoxní embolizace)
k embolektomii

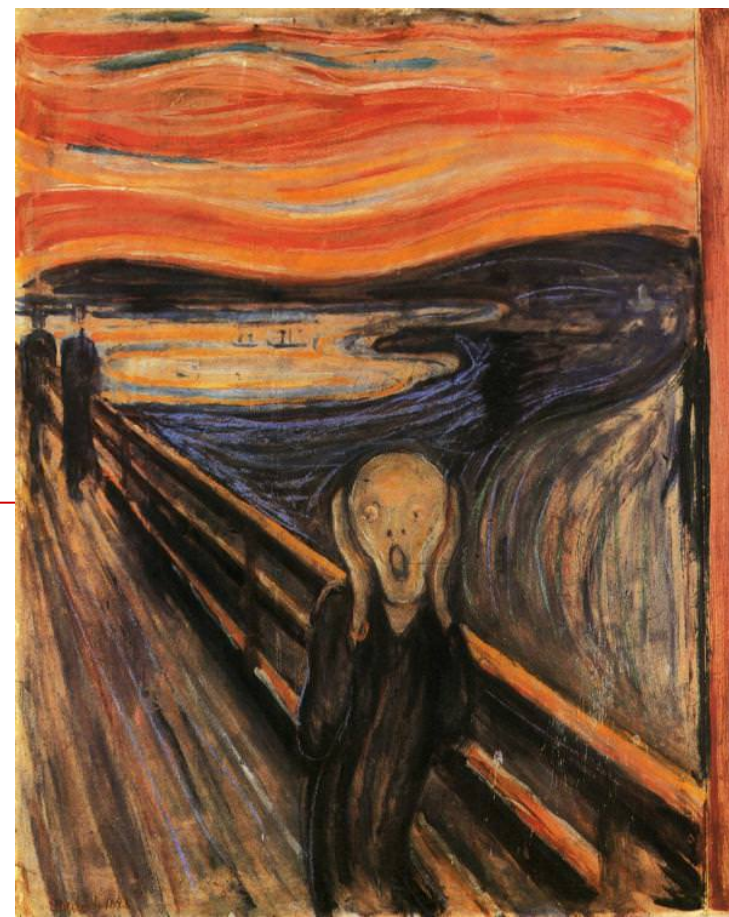


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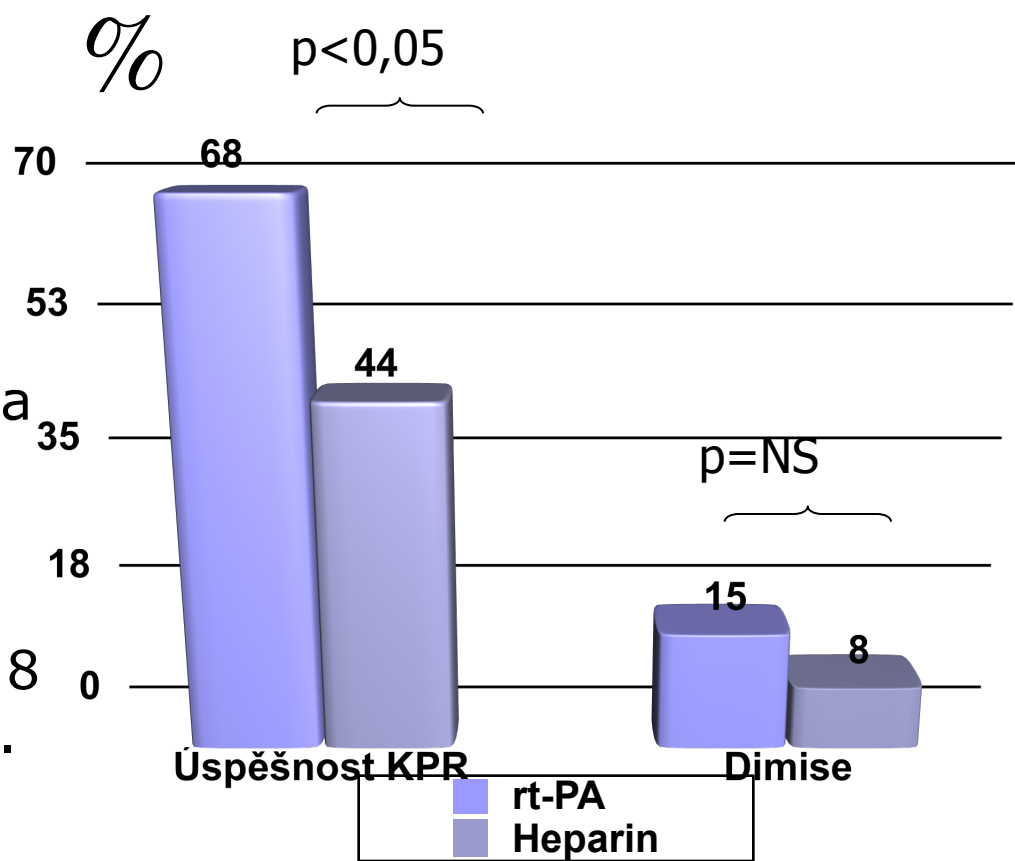




Masivní (high-risk) plicní embolie se
zástavou oběhu a KPR

Trombolýza při zástavě oběhu způsobené plicní embolií

- Prospektivní studie srovnávající **rt-PA** 50 mg/2 min. (n=40) + heparin i.v. s **konvenčním postupem** (n=50) u pacientů s masivní PE a >15 min. trvající oběhovou zástavou s nutností KPR
- 1 zachráněný život na 8 trombolyzovaných pac.



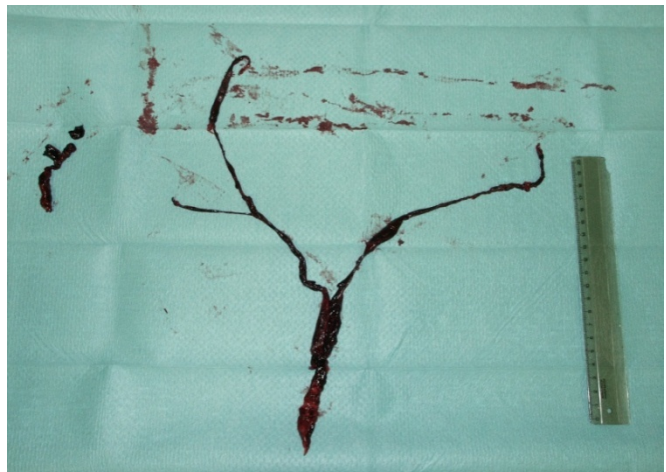
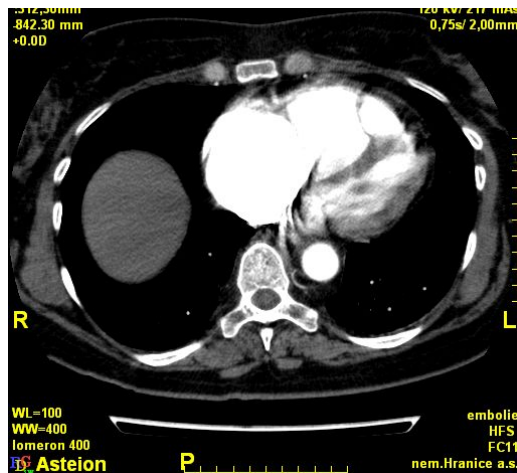
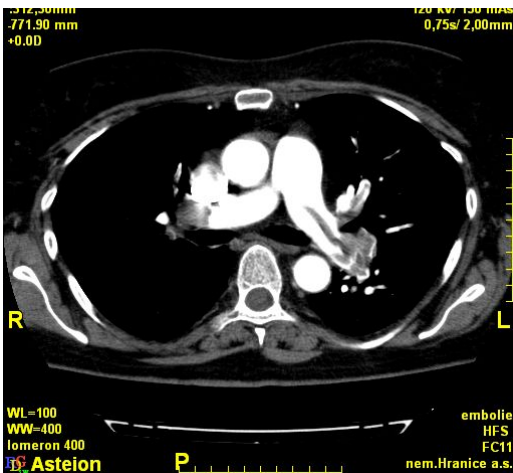


Masivní high-risk plicní embolie s hypotenzí a kardiogenním šokem

Trombolýza vs. heparin u „high-risk“ plicní embolie

- Jerjes-Sanchez, J Thromb Thrombolysis 1995;2:227–9

Study	Treatment regimens	No. of patients	Mortality, n (%)	Recurrence n (%)	Major haemorrhage,* n (%)	Comments
Jerjes-Sanchez et al.	STREPROKINÁZA vs.	4	0 (0%)	0	2 (4,3%)	
	HEPARIN	4	4 (100%)	NA	0	



Kontraindikace trombolýzy

Absolute contraindications^a

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in preceding 6 months
- Central nervous system damage or neoplasms
- Recent major trauma/surgery/head injury (within preceding 3 weeks)
- Gastrointestinal bleeding within the last month
- Known bleeding

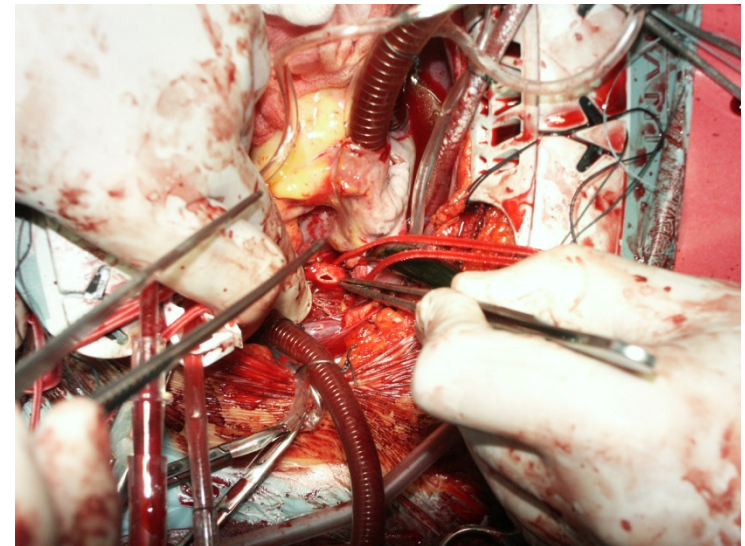
Relative contraindications

- Transient ischaemic attack in preceding 6 months
- Oral anticoagulant therapy
- Pregnancy or within 1 week post partum
- Non-compressible punctures
- Traumatic resuscitation
- Refractory hypertension (systolic blood pressure > 180 mmHg)
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer

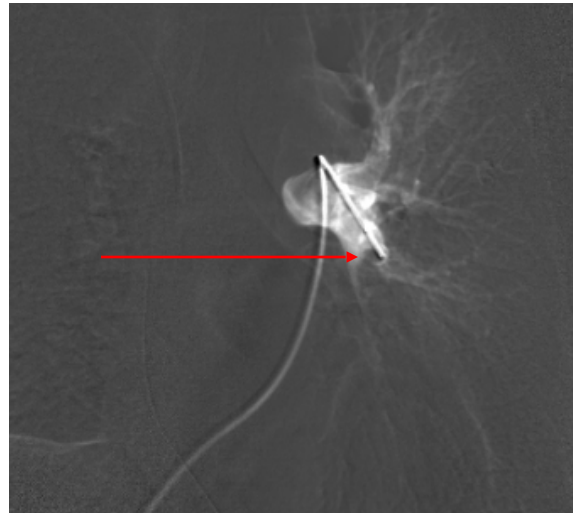
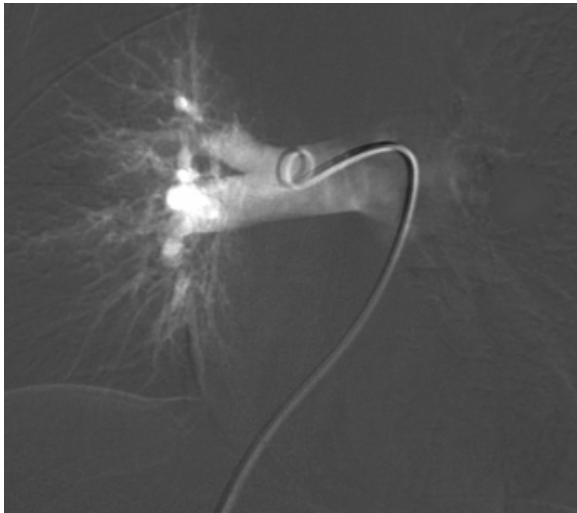
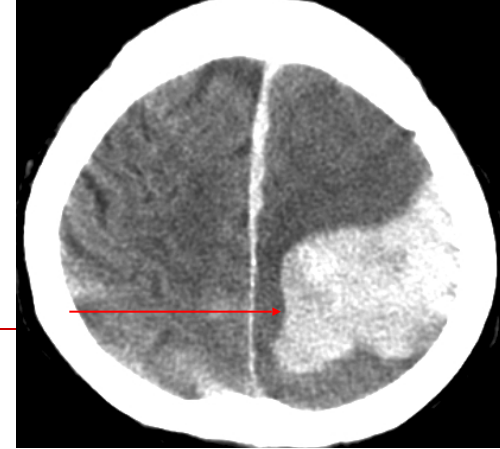


Embolektomie

- „Reperfuční – emboly odstraňující“ alternativa trombolýzy při kontraindikaci podání
- Srovnávací studie 23 pacientů v kardiogenním šoku léčených embolektomií a 24 léčených farmakologicky (TL) prokázala přežívání 77% proti 67% v konzervativně léčené skupině.



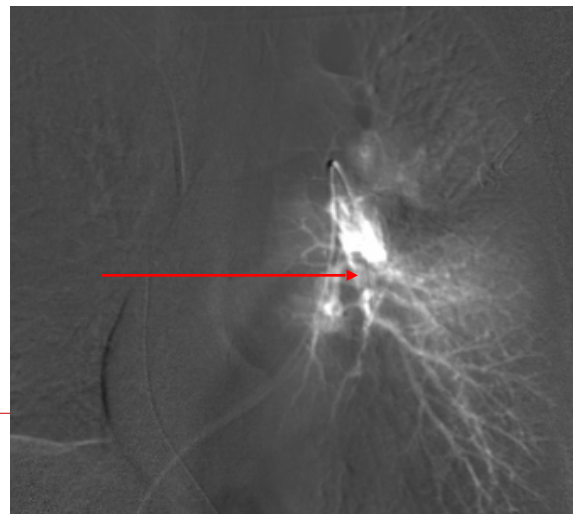
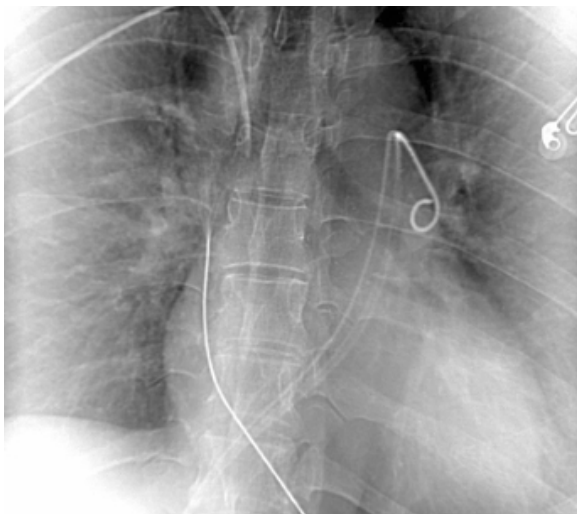
Katetrová fragmentace PE



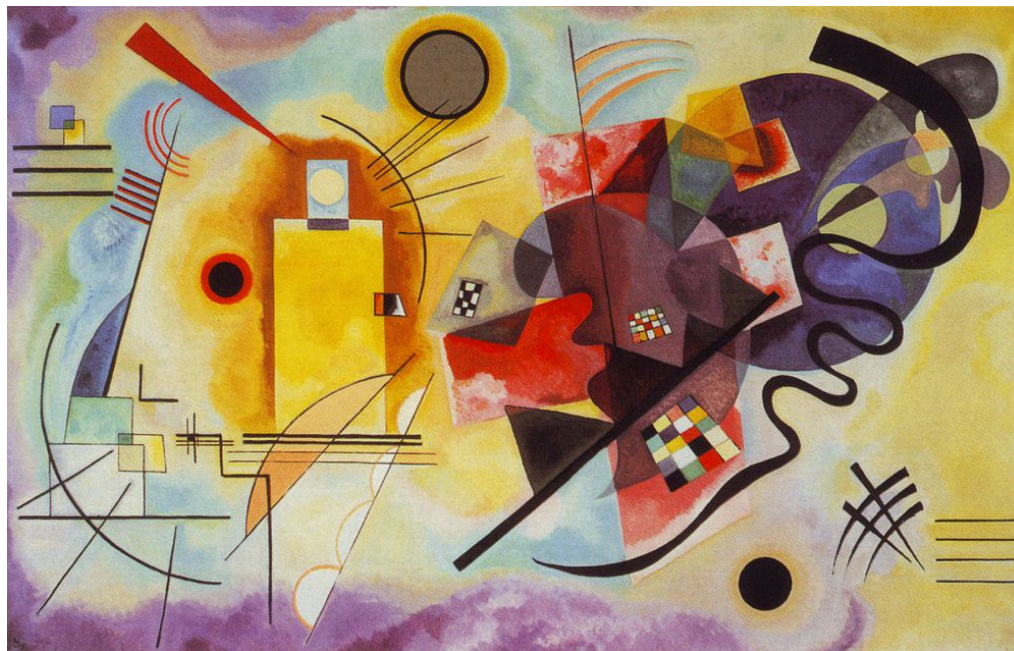
Při vysokém riziku závažné hemoragie

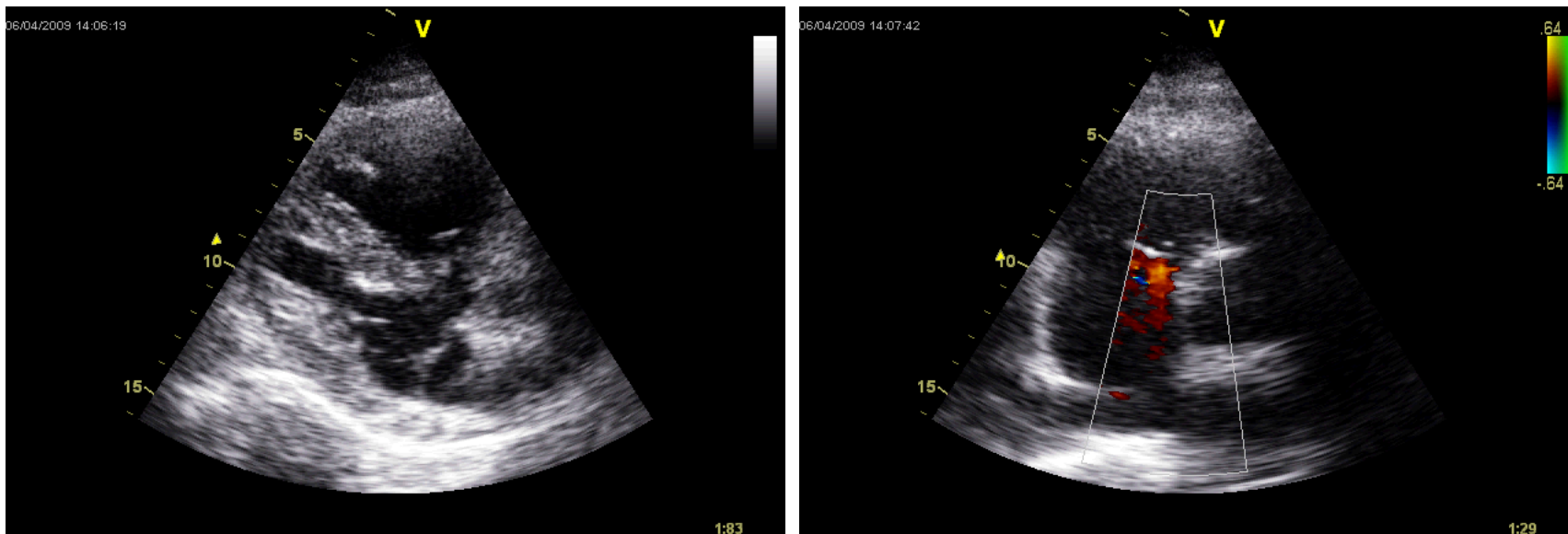
Prospektivní studie
konsekutivních pacientů s
dysfunkcí PK bez
kardiogenního šoku:
**mortalita 11% a zvýšení
srdečního výdeje u 91%**

Rescue metoda bez žádné
srovnávací studie



Submasivní - středně riziková plicní embolie





Normální systémový tlak, anamnéza synkopy (!), narůstající dušnost při léčbě LMWH, troponin T 0,24 $\mu\text{g/l}$, NT-proBNP 11375 ng/l, snížený srdeční výdej

MAPPET-2

Registr 1001 pacientů, 719 normotenzních pacientů s
dysfunkcí pravé komory

	Trombolýza (n=169)	Heparin (n=550)	Sign.
Mortalita	4,7%	11,1%	0,016
Recidiva	7,7%	18,7%	<0,001
Větší hemoragie	21,9%	7,8%	<0,001
Mozková hemoragie	1,2%	0,4%	NS

ORIGINAL ARTICLE

Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

Guy Meyer, M.D., Eric Vicaut, M.D., Thierry Danays, M.D., Giancarlo Agnelli, M.D., Cecilia Becattini, M.D., Jan Beyer-Westendorf, M.D., Erich Bluhmki, M.D., Ph.D., Helene Bouvaist, M.D., Benjamin Brenner, M.D., Francis Couturaud, M.D., Ph.D., Claudia Dellas, M.D., Klaus Empen, M.D., Ana Franca, M.D., Nazzareno Galiè, M.D., Annette Geibel, M.D., Samuel Z. Goldhaber, M.D., David Jimenez, M.D., Ph.D., Matija Kozak, M.D., Christian Kupatt, M.D., Nils Kucher, M.D., Irene M. Lang, M.D., Mareike Lankeit, M.D., Nicolas Meneveau, M.D., Ph.D., Gerard Pacouret, M.D., Massimiliano Palazzini, M.D., Antoniu Petris, M.D., Ph.D., Piotr Pruszczyk, M.D., Matteo Rugolotto, M.D., Aldo Salvi, M.D., Sebastian Schellong, M.D., Mustapha Sebbane, M.D., Bozena Sobkowicz, M.D., Branislav S. Stefanovic, M.D., Ph.D., Holger Thiele, M.D., Adam Torbicki, M.D., Franck Verschuren, M.D., Ph.D., and Stavros V. Konstantinides, M.D., for the PEITHO Investigators*

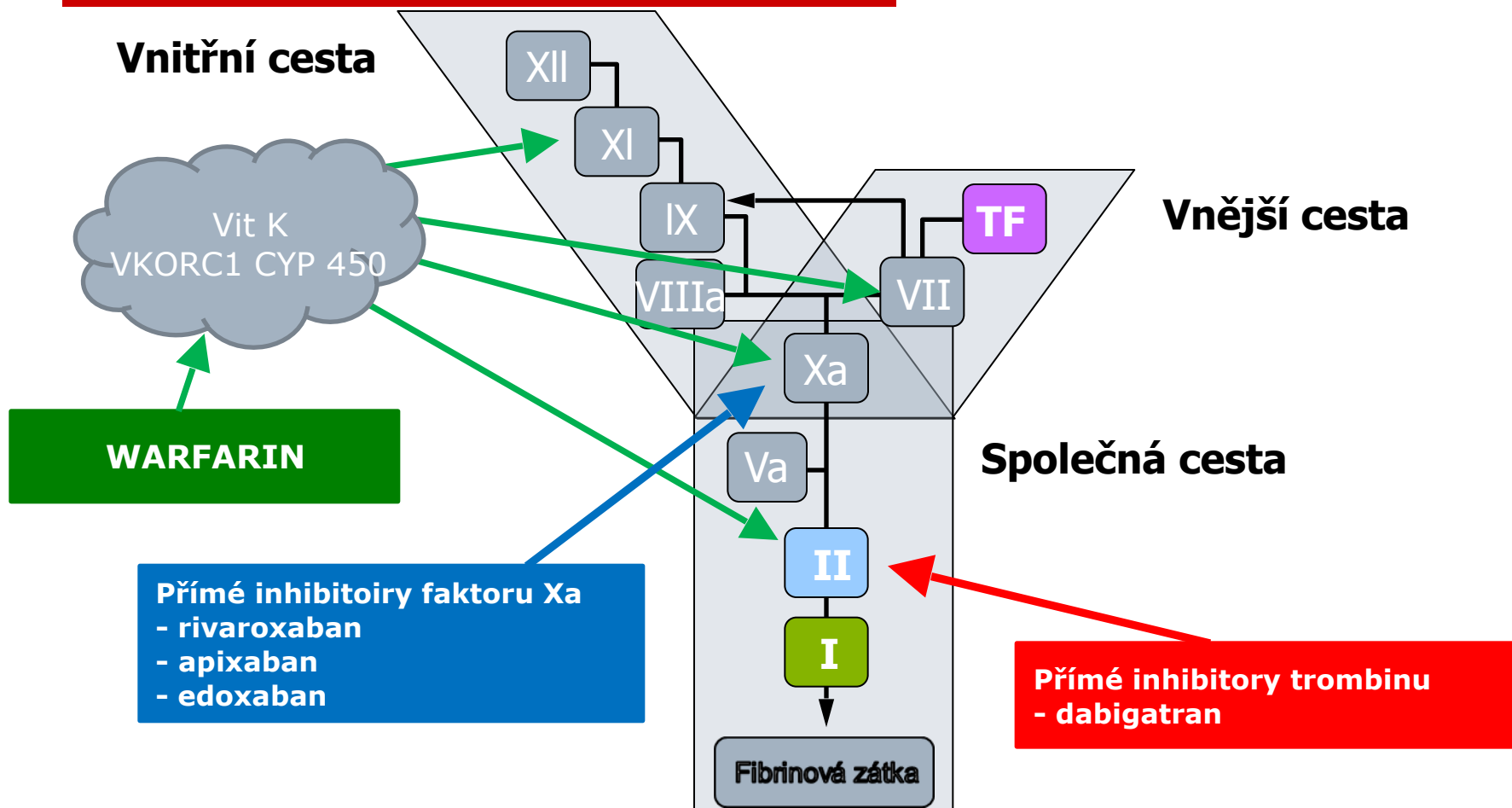
Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

Outcome	Tenecteplase (N=506)	Placebo (N=499)	Odds Ratio (95% CI)	P Value
Primary outcome — no. (%)	13 (2.6)	28 (5.6)	0.44 (0.23–0.87)	0.02
Death from any cause	6 (1.2)	9 (1.8)	0.65 (0.23–1.85)	0.42
Hemodynamic decompensation	8 (1.6)	25 (5.0)	0.30 (0.14–0.68)	0.002
Time between randomization and primary efficacy outcome — days	1.54±1.71	1.79±1.60		
Recurrent pulmonary embolism between randomization and day 7 — no. (%)	1 (0.2)	5 (1.0)	0.20 (0.02–1.68)	0.12
Fatal	0	3 (0.6)		
Nonfatal	1 (0.2)	2 (0.4)		
Other in-hospital complications and procedures — no. (%)				
Mechanical ventilation	8 (1.6)	15 (3.0)		
Surgical embolectomy	1 (0.2)	2 (0.4)		
Catheter thrombus fragmentation	1 (0.2)	0 (0.0)		
Vena cava interruption	5 (1.0)	1 (0.2)		
Thrombolytic treatment other than study medication	4 (0.8)	23 (4.6)		
Death from any cause between randomization and day 30 — no. (%)	12 (2.4)	16 (3.2)	0.73 (0.34–1.57)	0.42
Patient still hospitalized at day 30 — no. (%)	59 (11.7)	50 (10.0)		
Rehospitalization between randomization and day 30 — no. (%)	22 (4.4)	15 (3.0)		

Table 4. Safety Outcomes in the Intention-to-Treat Population.*

Outcome	Tenecteplase (N=506) no. (%)	Placebo (N=499)	Odds Ratio (95% CI)	P Value
Bleeding between randomization and day 7				
Major extracranial bleeding	32 (6.3)	6 (1.2)	5.55 (2.3–13.39)	<0.001
Minor bleeding	165 (32.6)	43 (8.6)		
Major bleeding†	58 (11.5)	12 (2.4)		
Stroke between randomization and day 7				
Ischemic stroke	12 (2.4)	1 (0.2)	12.10 (1.57–93.39)	0.003
Hemorrhagic stroke‡	2 (0.4)	0		
Serious adverse events between randomization and day 30	10 (2.0)	1 (0.2)		
Serious adverse events between randomization and day 30	55 (10.9)	59 (11.8)	0.91 (0.62–1.34)	0.63

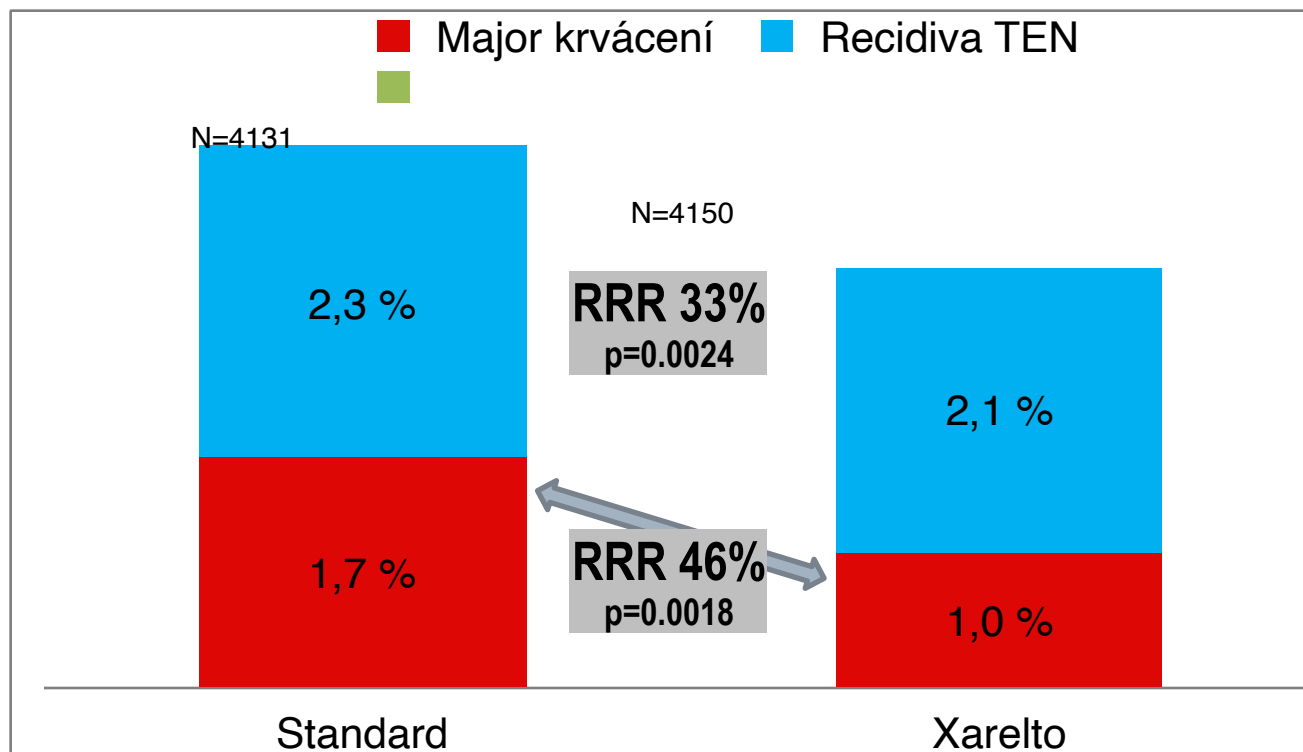
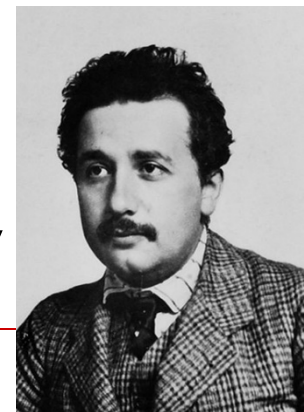
Koagulační kaskáda



NOAC/DVT a PE - přehled

	Rivaroxaban	Dabigatran	Apixaban	Edoxaban
klin. studie	EINSTEIN (-PE, -DVT, -Ext)	RE-COVER	AMPLIFY	HOKUSAI-VTE
dávkování	15 mg 2x denně (první 3T), 20 mg 1x denně	LMWH 5dní, poté 150 mg 2x denně	10 mg 2x denně (prvních 7D), poté 5mg 2x denně	LMWH 5dní, poté 60 mg 1x denně
rekurence TEN	NI (HR 1,12)	NI (2,4% vs. 2,1%)	NI (2,3% vs. 2,7%)	NI (3,2% vs. 3,5%)
„major“ krvácení	NI (10,3% vs. 11,4%)	NI (1,6 vs. 1,9%)	SUP (0,6% vs. 1,8%)	SUP (8,5% vs. 10,3%)
„major“ krvácení + klin. relevantní krvácení	SUP (1,1 % vs 2,2%)	NI	SUP (4,3% vs. 9,7%)	-

EINSTEIN DVT a PE - výsledky

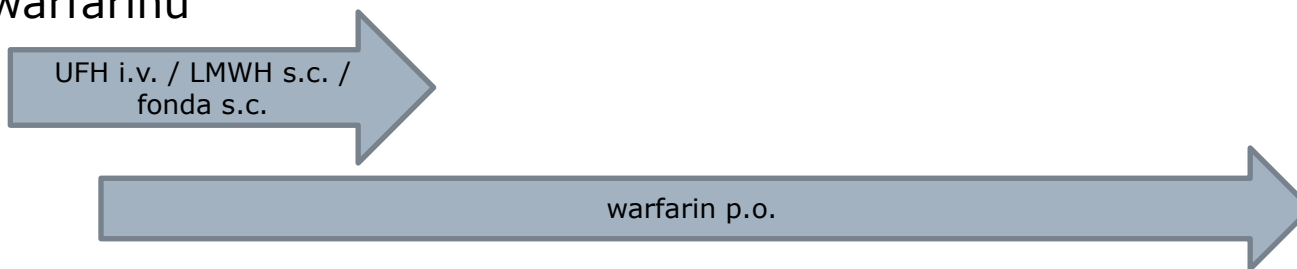


Recidiva TEN: Kompozit symptomatické rekurentní HŽT, symptomatické PE (fatální nebo nefatální), úmrtí asociovaného s TEN a progresse trombózy

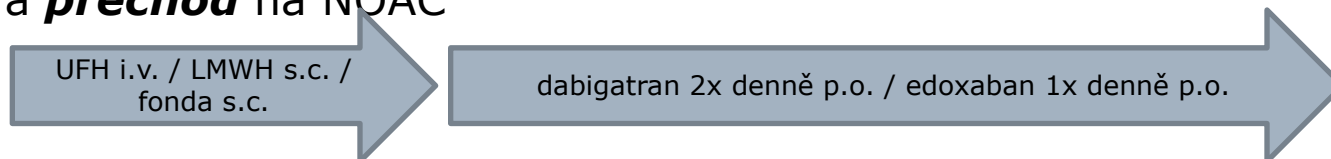
Buller H, Oral Rivaroxaban for the Treatment of Symptomatic Venous Thromboembolism: A Pooled Analysis of the EINSTEIN DVT and EINSTEIN PE Studies, ASH 2012, <https://ash.confex.com/ash/2012/webprogram/Paper51556.html>

Terapeutická schémata

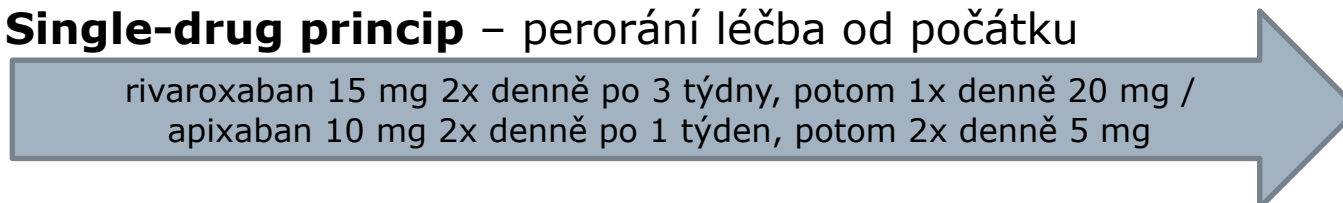
- **Klasické schéma – překrytí** parenterálního antikoagulantia a warfarinu



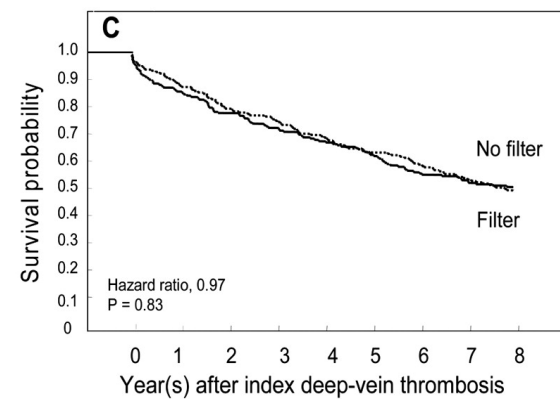
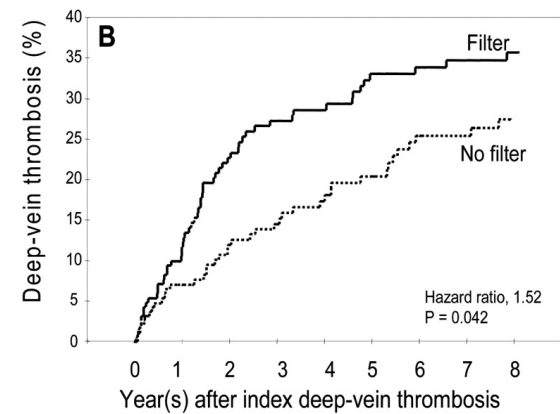
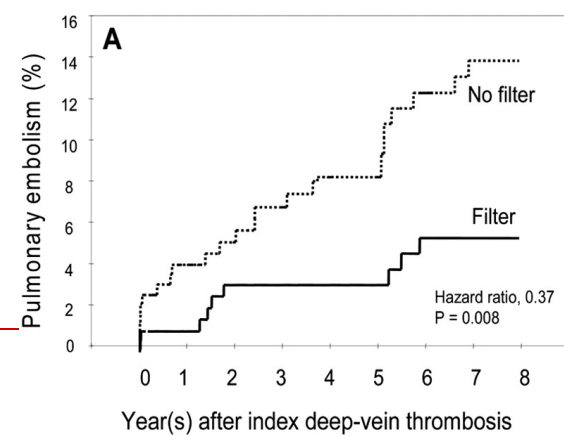
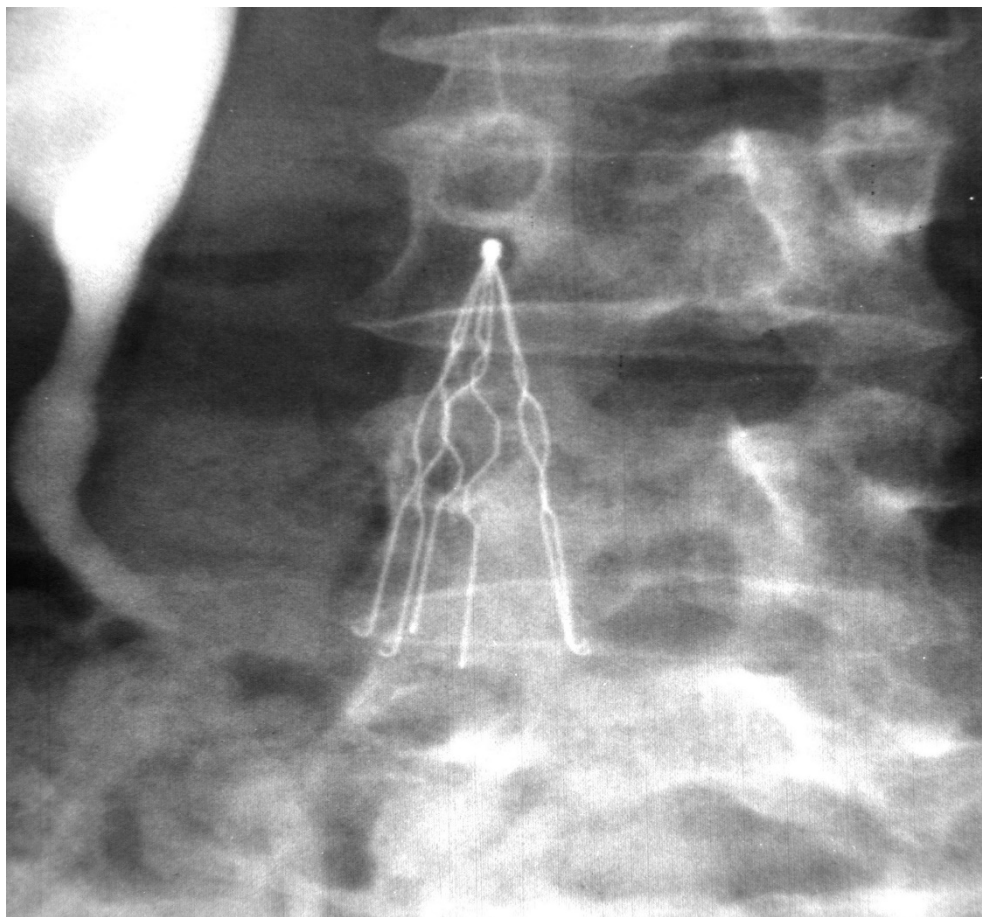
- **Sekvenční podávání – zahájení léčby** parenterálním antikoagulantem a **přechod** na NOAC



- **Single-drug princip – perorální léčba od počátku**



Kavální filtry?

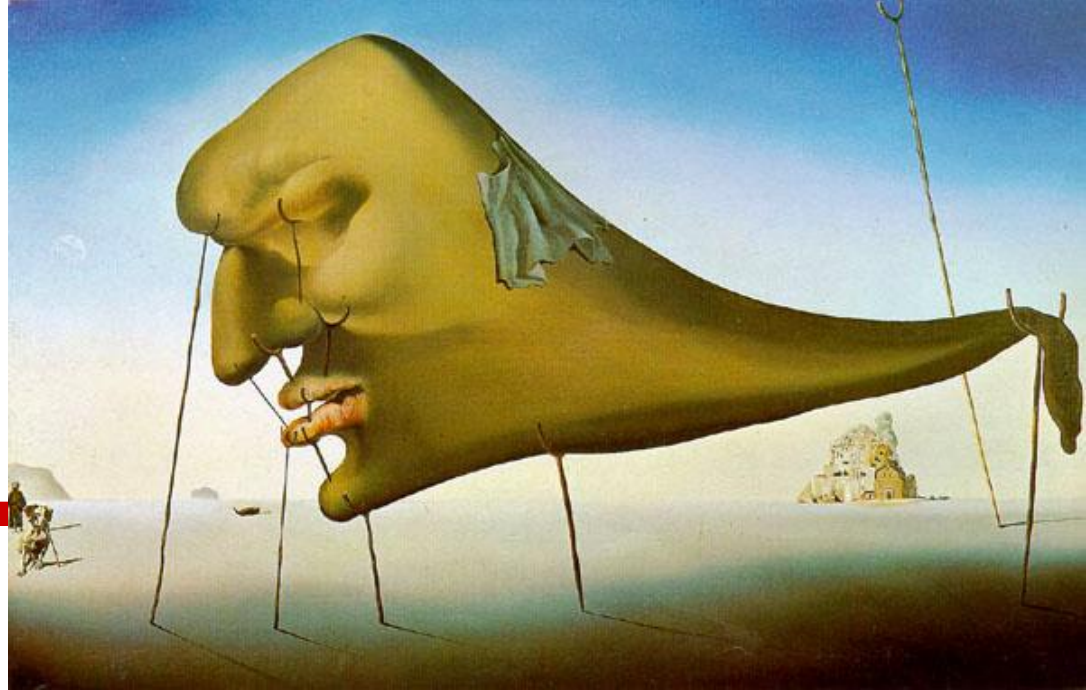


Recommendations	Class ^a	Level ^b	Ref ^c
PE with shock or hypotension (high-risk)			
It is recommended that intravenous anticoagulation with UFH be initiated without delay in patients with high-risk PE.	I	C	
Thrombolytic therapy is recommended.	I	B	168
Surgical pulmonary embolectomy is recommended for patients in whom thrombolysis is contraindicated or has failed. ^d	I	C	313
Percutaneous catheter-directed treatment should be considered as an alternative to surgical pulmonary embolectomy for patients in whom full-dose systemic thrombolysis is contraindicated or has failed. ^d	IIa	C	

Recommendations	Class ^a	Level ^b	Ref ^c
PE without shock or hypotension (intermediate-or low-risk)^d			
Anticoagulation: combination of parenteral treatment with VKA			
Initiation of parenteral anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE while diagnostic work-up is in progress.	I	C	352
LMWH or fondaparinux is the recommended form of acute phase parenteral anticoagulation for most patients.	I	A	273, 274, 281, 353
In parallel to parenteral anticoagulation, treatment with a VKA is recommended, targeting an INR of 2.5 (range 2.0–3.0).	I	B	352, 354
Anticoagulation: new oral anticoagulants			
As an alternative to the combination of parenteral anticoagulation with a VKA, anticoagulation with rivaroxaban (15 mg twice daily for 3 weeks, followed by 20 mg once daily) is recommended.	I	B	296

As an alternative to the combination of parenteral anticoagulation with a VKA, anticoagulation with apixaban (10 mg twice daily for 7 days, followed by 5 mg twice daily) is recommended.	I	B
As an alternative to VKA treatment, administration of dabigatran (150 mg twice daily, or 110 mg twice daily for patients ≥80 years of age or those under concomitant verapamil treatment) is recommended following acute-phase parenteral anticoagulation.	I	B ^e
As an alternative to VKA treatment, administration of edoxaban* is recommended following acute-phase parenteral anticoagulation.	I	B
New oral anticoagulants (rivaroxaban, apixaban, dabigatran, edoxaban) are not recommended in patients with severe renal impairment. ^f	III	A

Reperfusion treatment		
Routine use of primary systemic thrombolysis is not recommended in patients not suffering from shock or hypotension.	III	B
Close monitoring is recommended in patients with intermediate-high risk PE to permit early detection of haemodynamic decompensation and timely initiation of 'rescue' reperfusion therapy.	I	B
Thrombolytic therapy should be considered for patients with intermediate-high-risk PE and clinical signs of haemodynamic decompensation.	IIa	B
Surgical pulmonary embolectomy may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high. ^g	IIb	C
Percutaneous catheter-directed treatment may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high. ^g	IIb	B
Early discharge and home treatment		
Patients with acute low-risk PE should be considered for early discharge and continuation of treatment at home if proper outpatient care and anticoagulant treatment can be provided.	IIa	B

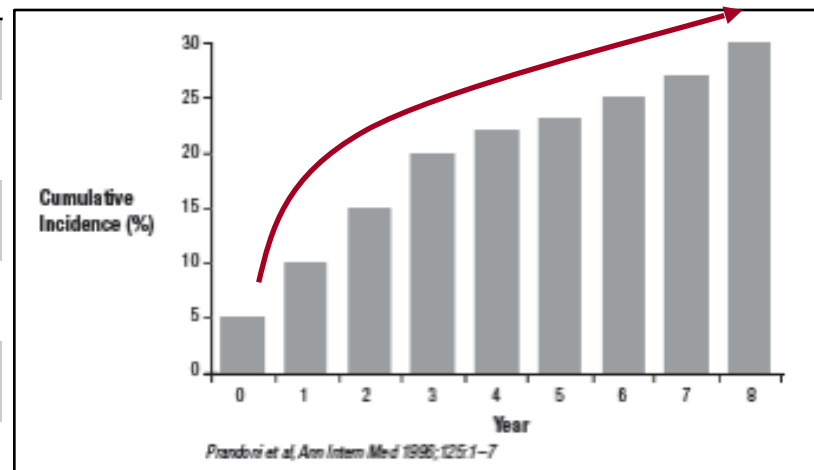


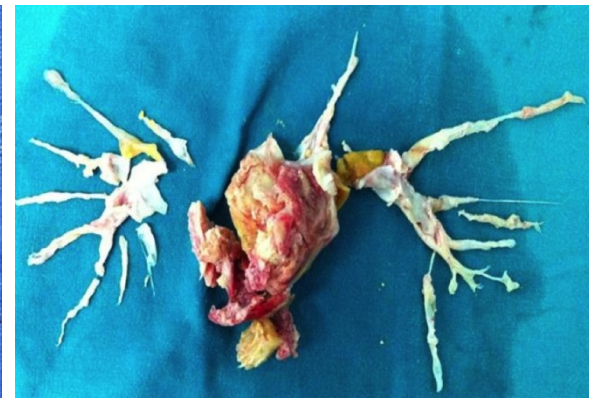
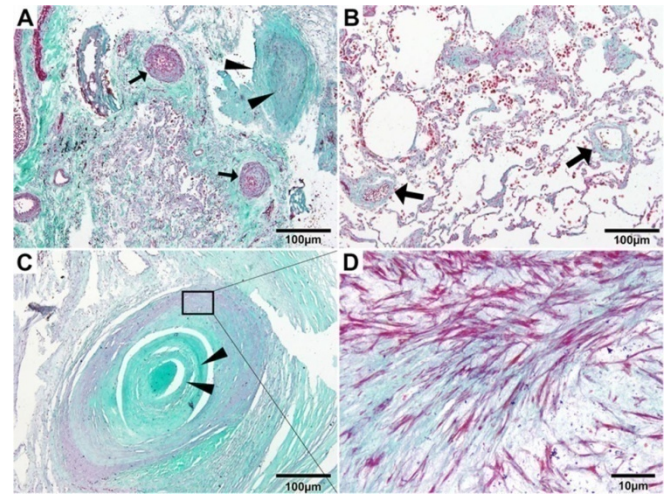
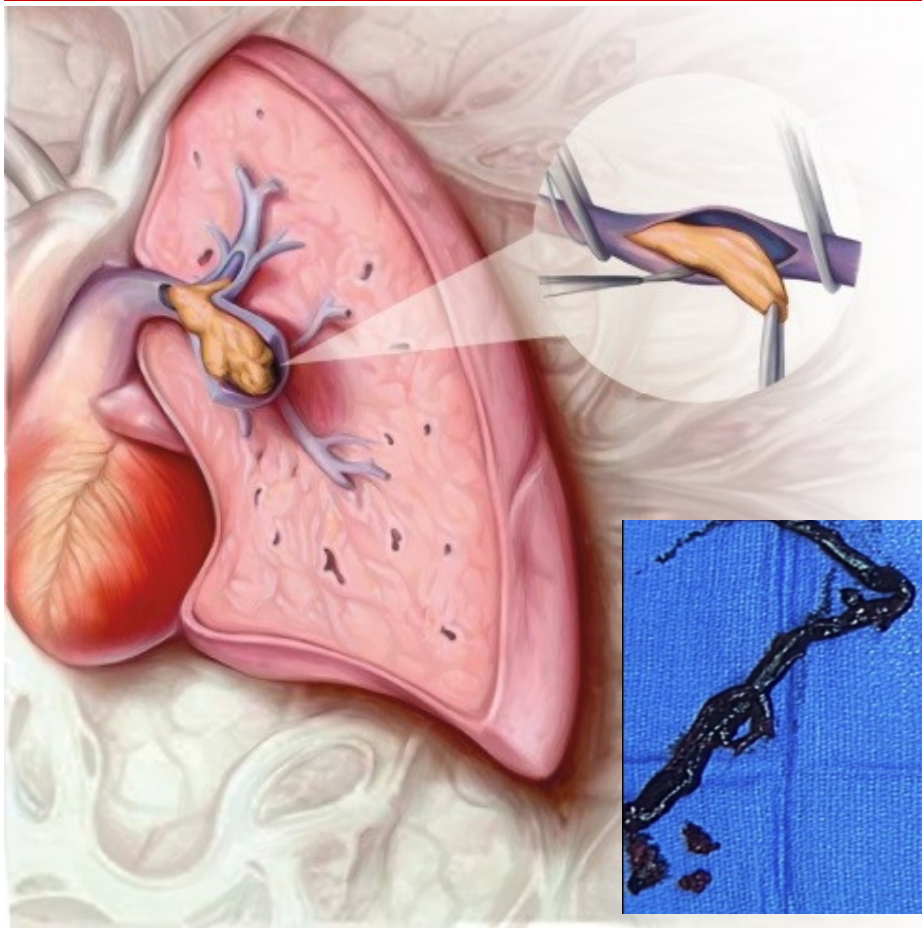
Plicní embolie:

Co nastává po akutní fázi onemocnění?

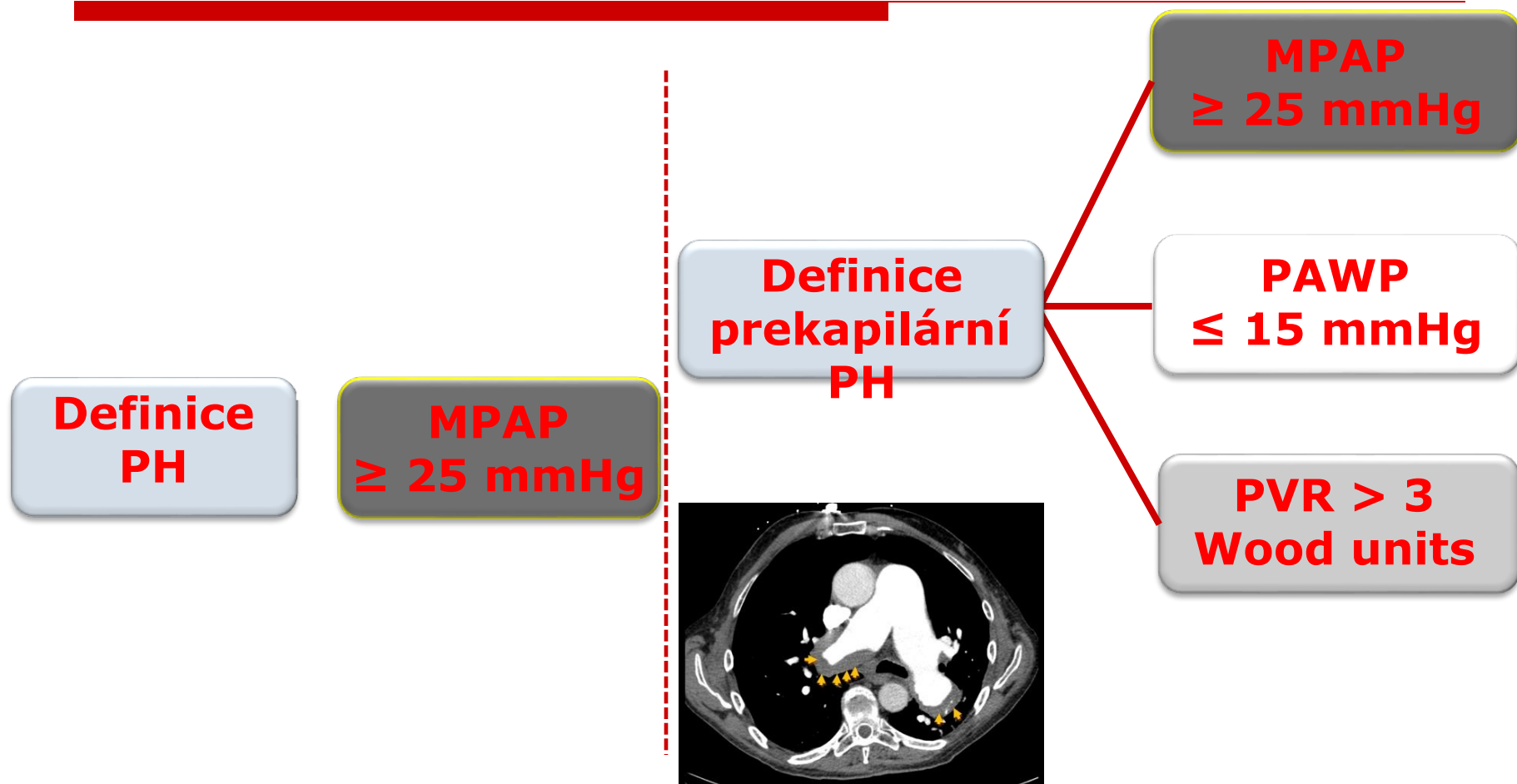
Rekurence

	Kumulativní incidence	Roční incidence
2 týdny	2%	55%
3 měsíce	6.4%	30%
6 měsíce	8%	18%
2 roky	17%	8.5%
5 roky	24%	4.8%
8 roky	30%	3.8%





Hemodynamická definice plicní hypertenze/CTEPH



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

Updated Clinical Classification of Pulmonary Hypertension

Gerald Simonneau, MD,* Michael A. Gatzoulis, MD, PhD,† Ian Adatia, MD,‡
 David Celermajer, MD, PhD,§ Chris Denton, MD, PhD,|| Ardeschir Ghofrani, MD,¶
 Miguel Angel Gomez Sanchez, MD,# R. Krishna Kumar, MD,** Michael Landzberg, MD,††
 Roberto F. Machado, MD,‡‡ Horst Olschewski, MD,§§ Ivan M. Robbins, MD,||||
 Rogério Souza, MD, PhD¶¶

Plicní hypertenze - definice a klasifikace

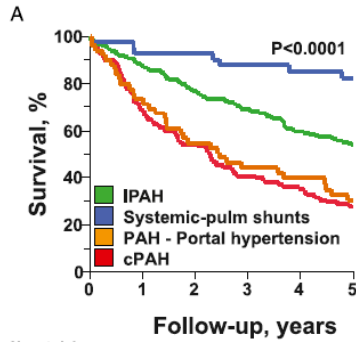
Definition	Characteristics	Clinical group(s) ^b
Pulmonary hypertension (PH)	Mean PAP ≥ 25 mmHg	All
Pre-capillary PH	Mean PAP ≥ 25 mmHg PWP ≤ 15 mmHg CO normal or reduced ^c	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	Mean PAP ≥ 25 mmHg PWP > 15 mmHg CO normal or reduced ^c	2. PH due to left heart disease
Passive	TPG ≤ 12 mmHg	
Reactive (out of proportion)	TPG > 12 mmHg	

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

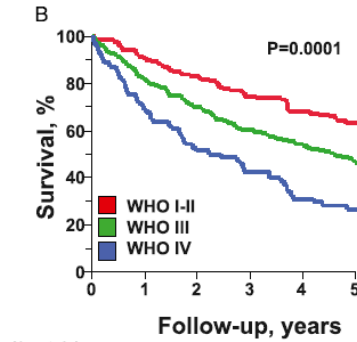
Prevalence of PAH in at risk populations
 CHD: 4–15%
 Systemic sclerosis: 8–10%
 Portal hypertension: 0.5–10%
 HIV: 0.5%
 Sickle cell disease: 2%
 BMPR2 mutation carriers: 20%

1. Pulmonary arterial hypertension
 - 1.1 Idiopathic PAH
 - 1.2 Heritable PAH
 - 1.2.1 BMPR2
 - 1.2.2 ALK-1, ENG, SMAD9, CAV1, KCNK3
 - 1.2.3 Unknown
 - 1.3 Drug and toxin induced
 - 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 diseases
 - 1.4.5 Schistosomiasis
- 1' Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis
- 1'' Persistent pulmonary hypertension of the newborn (PPHN)
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
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
4. Chronic thromboembolic pulmonary hypertension (CTEPH)
5. Pulmonary hypertension with unclear multifactorial mechanisms
 - 5.1 Hematologic disorders: chronic hemolytic anemia, 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: tumoral obstruction, fibrosing mediastinitis, chronic renal failure, segmental PH

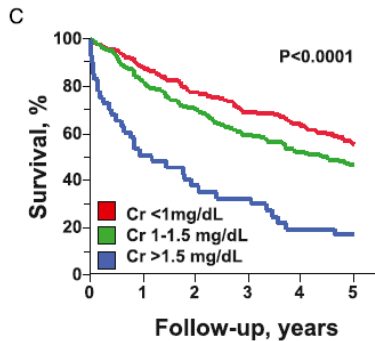
Plicní hypertenze - prognóza



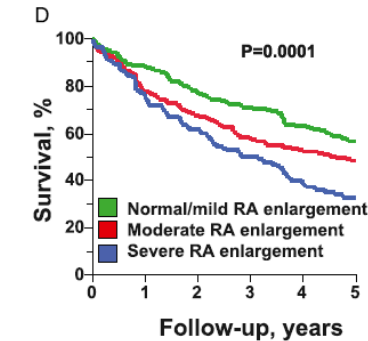
No. at risk	0	1	2	3	4	5
Shunts	43	39	38	35	34	32
IPAH	272	231	198	174	143	121
PoPH	51	35	27	21	18	13
cPAH	114	77	60	45	38	28



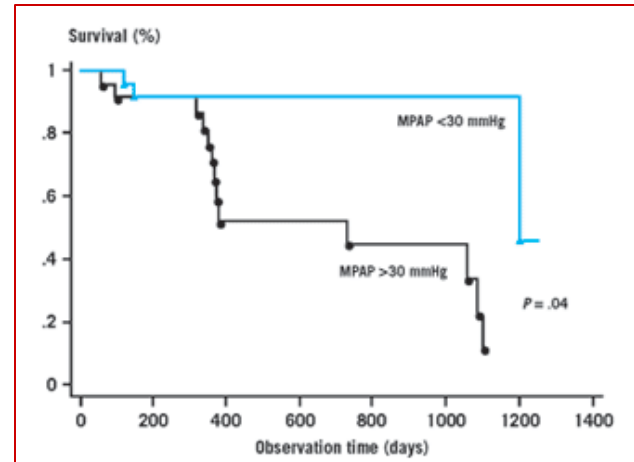
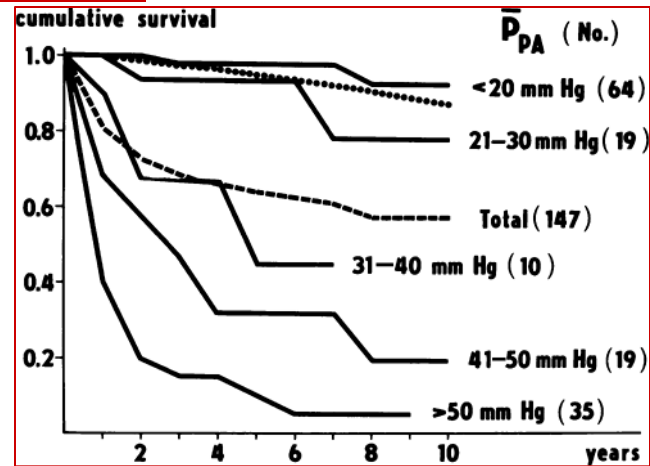
No. at risk	0	1	2	3	4	5
FC I-II	139	119	107	95	86	71
FC III	268	213	180	151	127	108
FC IV	77	52	38	31	22	18



No. at risk	0	1	2	3	4	5
<1	184	157	136	121	103	86
1-1.5	249	198	167	139	118	99
>1.5	41	21	15	12	8	6



No. at risk	0	1	2	3	4	5
Mild	186	158	134	121	106	90
Mod.	187	143	122	102	89	78
Severe	111	84	69	54	40	29



Epidemiologie CTEPH

Parameters	Japanese Registry ¹²	International Registry ⁵	University of California–San Diego Pulmonary Endarterectomy Registry ⁹⁰
No. of patients	519	679	2700
Sex, % male	28.1	50.1	49.7
Age, y	67 (53, 75)*	63 (51, 72)*	52 (40, 63)* (8–88)†
World Health Organization class, % I/II/III/IV	5.2/41.9/47.7/5.2	0.7/17.8/68.6/12.8	1.5/9.7/80.3/8.6
History of deep vein thrombosis, %	50.4	56.1	49.2
History of acute pulmonary embolism, %	37.2	74.8	70.6
Coagulopathies, %	11.7	31.9	30.1
Mean pulmonary arterial pressure, mm Hg, median	38 (33, 46)*	47 (38, 55)*	46 (38, 53)*
Pulmonary vascular resistance, dyne-s/cm ⁵ , median	621 (439, 916)*	709 (480, 988)*	814 (476, 1018)*
Pulmonary endarterectomy, %	13.9	56.8	100
Inferior vena cava filter, %	26.9	12.4	>90
PAH-targeted therapy, %	52.2	37.9‡	37.0‡

CTEPH indicates chronic thromboembolic pulmonary hypertension; and PAH, pulmonary arterial hypertension.
 *Medians and quartiles (quartile 1, quartile 3).
 †Range.
 ‡Preoperative treatments.

No. of Patients With Acute Pulmonary Embolism	Average Observation Time After Acute Event, mo	Cumulative Incidence of CTEPH, %
325	16.3	4.6
744	14	8.3
110	24	9.1
877	34	0.57
110	36	2.7
239	36	0.4
700	26	4.7
91	6–12	8.8
259	46	1.0
834	25	1.0
314	94.3	3.8
78	12	5.0

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 Bressler, 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

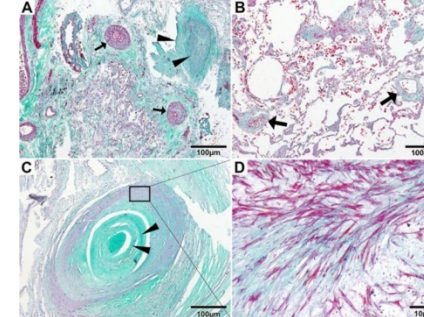
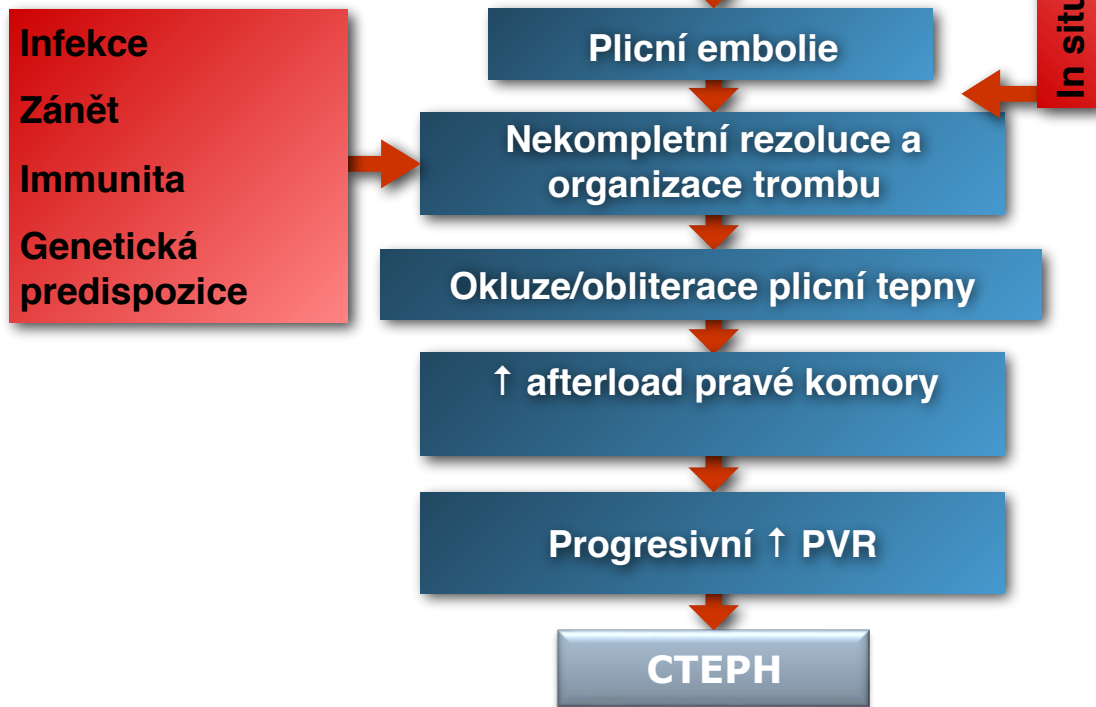


Table 2. Patients' History of Venous Thromboembolism

	All Patients (n=679)	Operable Patients* (n=427)	Nonoperable Patients* (n=247)	P (Exploratory)
Confirmed previous acute PE, % (n)	74.8 (678)	77.5 (427)	70.0 (247)	0.0344
PE diagnosed more than once, % (n)	32.8 (469)	35.0 (303)	28.8 (163)	0.2145
Size of previous PE reported as massive, % (n)	40.8 (240)	47.1 (155)	29.4 (85)	0.0090
Confirmed previous DVT, % (n)	56.1 (426)	60.4 (280)	49.0 (143)	0.0295
Acute PE and DVT, % (n)	55.4 (413)	59.3 (270)	48.9 (141)	0.0477
Acute PE no DVT, % (n)	42.6 (413)	39.3 (270)	48.2 (141)	0.0926
Thrombolytic treatment, % (n)	14.4 (404)	18.5 (265)	6.6 (137)	0.0009
Vena cava filter implanted, % (n)	12.4 (491)	13.7 (322)	10.2 (166)	0.3139

P values from Fisher exact test. (n): patients with assessment. DVT indicates deep vein thrombosis; PE, pulmonary embolism.

*5 patients had no data on operability.



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

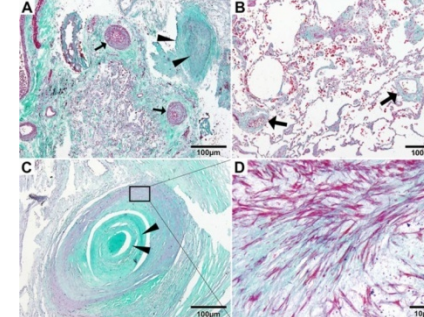
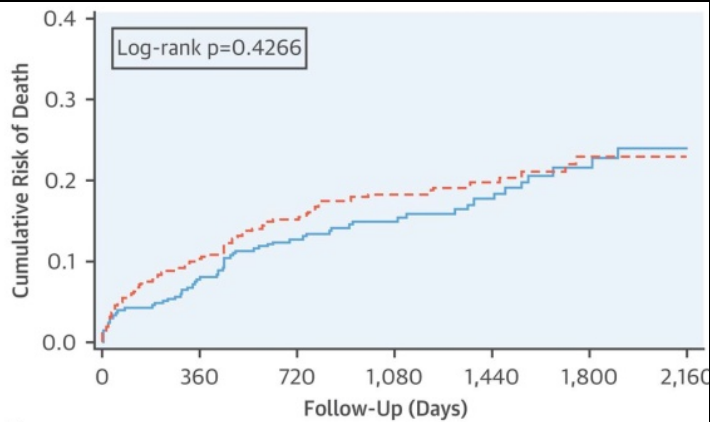


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	All Patients (n=679)	Operable Patients* (n=427)	Nonoperable Patients* (n=247)	P (Exploratory)
Confirmed	74.8 (678)	77.5 (427)	70.0 (247)	0.0344



N at risk	0	360	720	1,080	1,440	1,800	2,160
Placebo	350	316	299	188	120	71	38
Tenecteplase	359	317	299	198	129	69	35

— Placebo — Tenecteplase

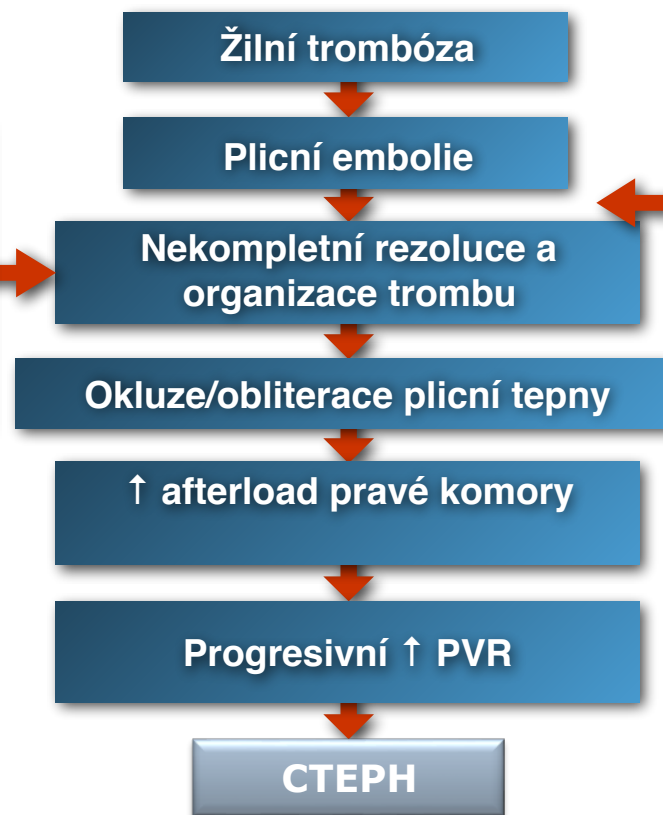
Konstantinides, S.V. et al. J Am Coll Cardiol. 2017;69(12):1536-44.

implanted, % (n)

P values from Fisher exact test. (n): patients with assessment. DVT indicates deep vein thrombosis; PE, pulmonary embolism.

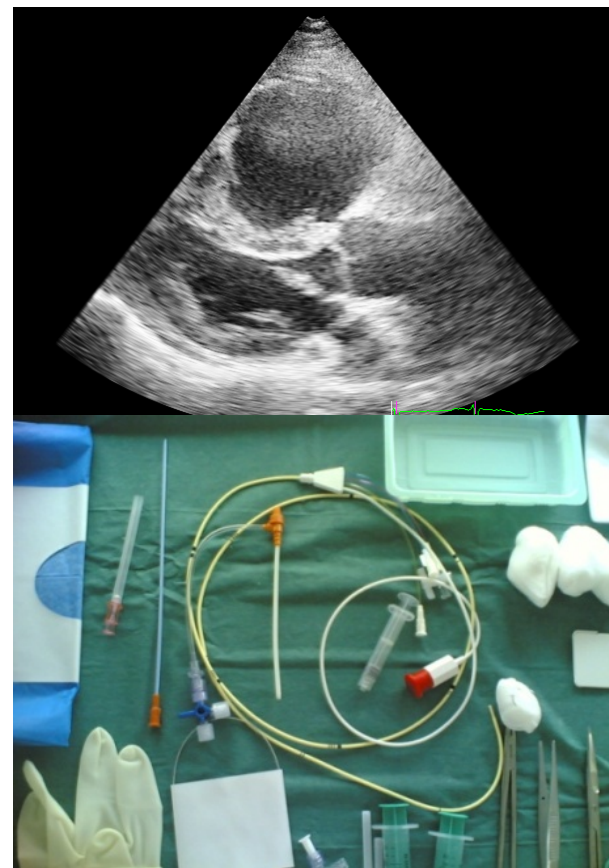
*5 patients had no data on operability.

**Infekce
Zánět
Immunita
Genetická
predispozice**



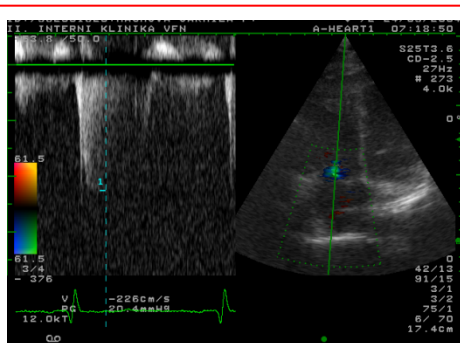
Plicní hypertenze - screening po plicní embolii

Recommendations	Class ^a	Level ^b	Ref. ^c
Interventional BPA may be considered in patients who are technically non-operable or carry an unfavourable risk:benefit ratio for PEA	IIb	C	57, 444–446, 448
Screening for CTEPH in asymptomatic survivors of PE is currently not recommended	III	C	417

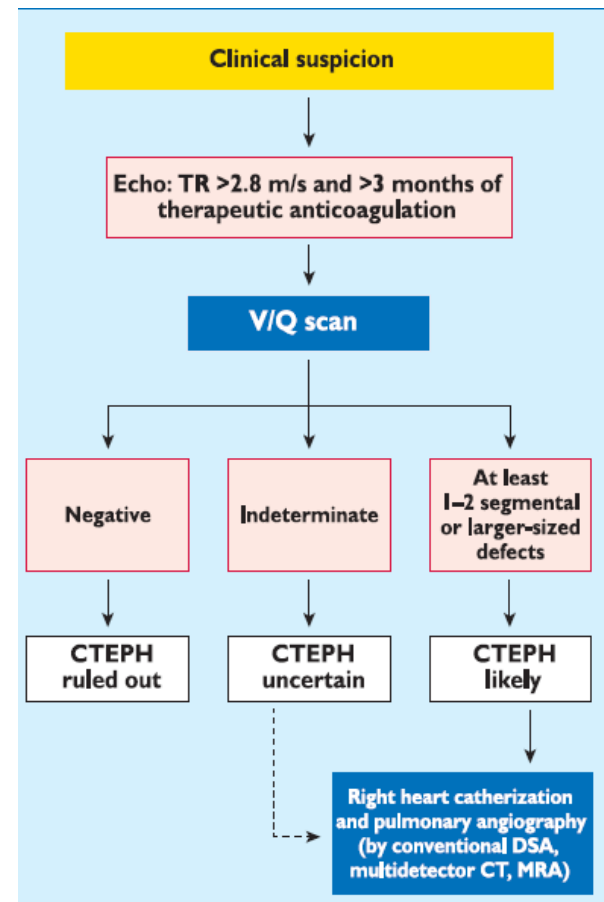
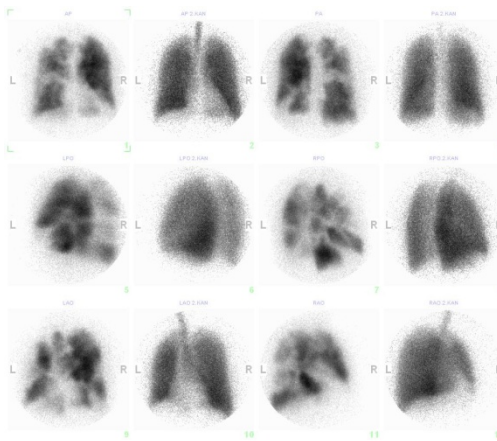


1. SCREENING

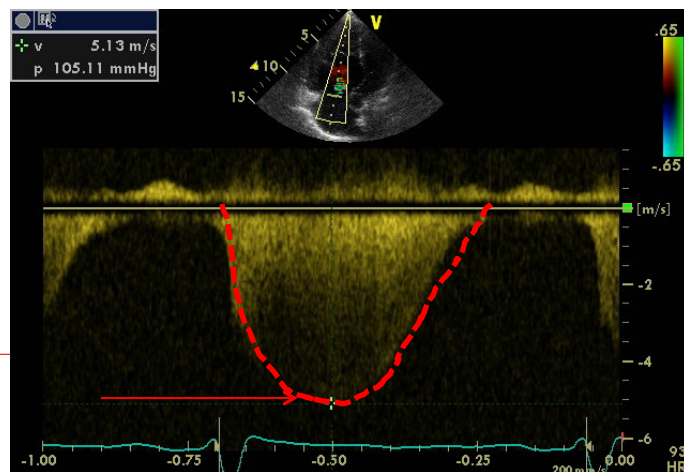
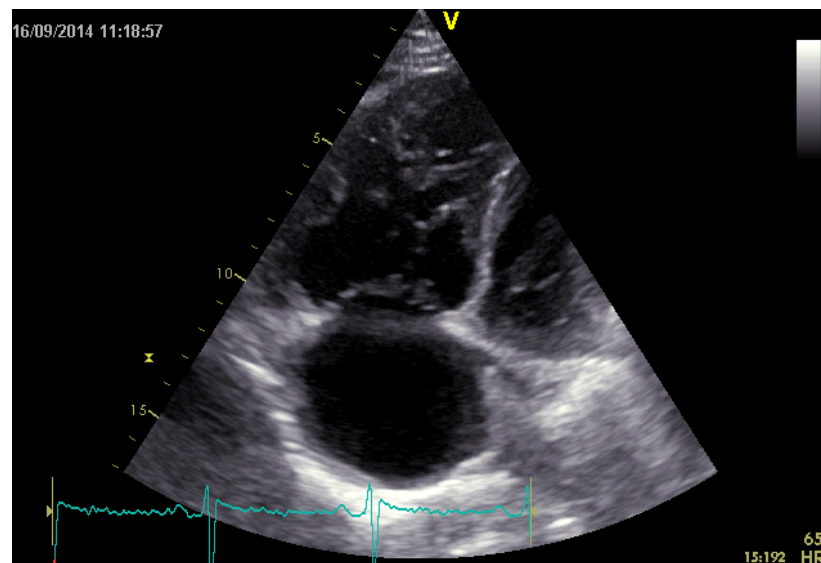
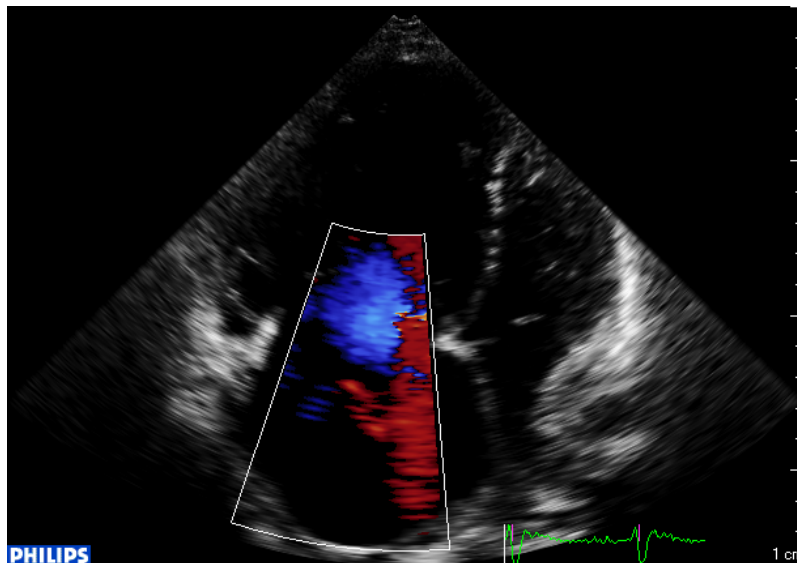
■ Echokardiografie



■ Scintigrafie plic



Echokardiografie - klíčové screeningové vyšetření



Morfologie a funkce pravé komory

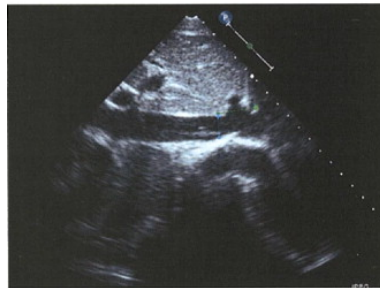
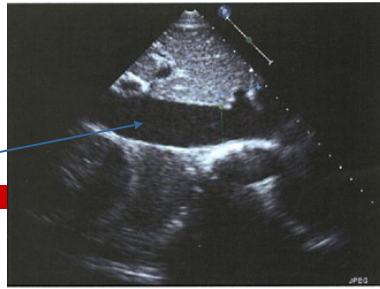


European Heart Journal – Cardiovascular Imaging (2015) **16**, 233–271
doi:10.1093/ehjci/jev014

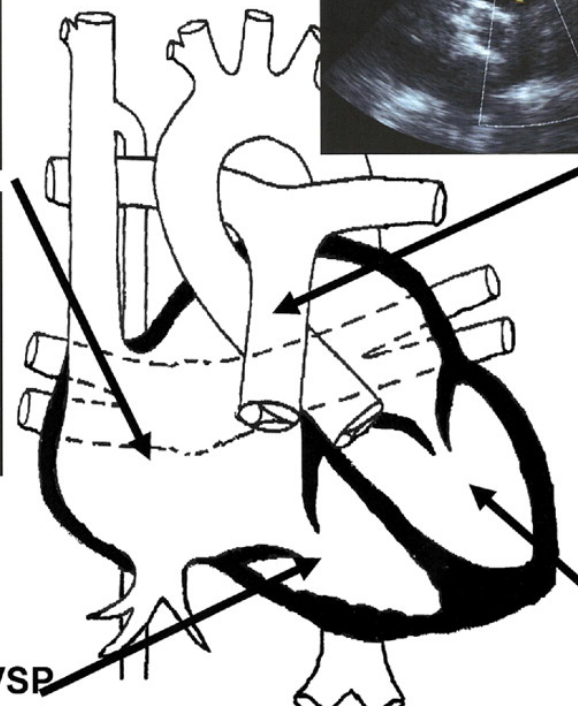
POSITION PAPER

Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

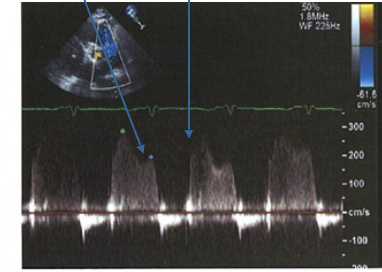
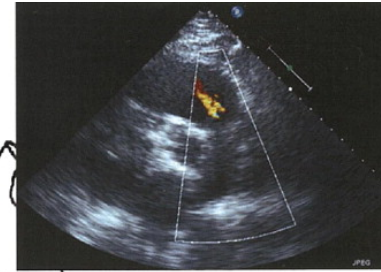
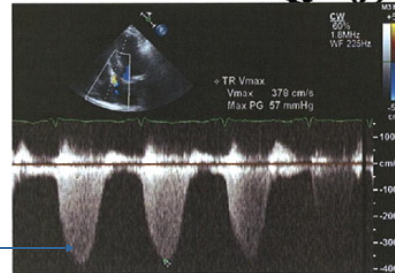
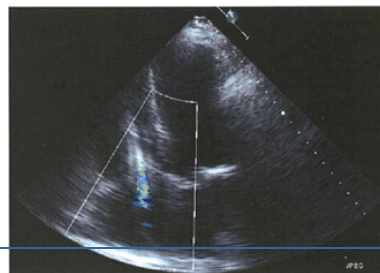
Maximální gradient regurgitace na pulmonální chlopní (PR) predikuje střední tlak v plicnici (**MAP**) .
 Endiastolický gradient pulmonální regurgitace predikuje diastolický tlak v plicnici (**DAP**) .



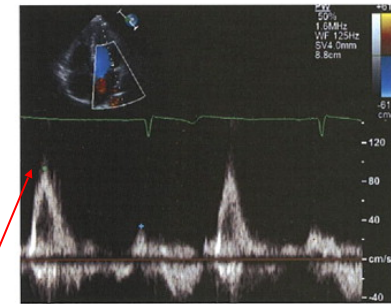
A. IVCCI--RAP



B. TR Vel.--RVSP



C. PR Vel.--PAPm, PAPd



D. E/E'--PCWP

Dolní dutá žíla (**IVC**) , její rozměr a stupeň inspiračního kolapsu predikují tlak v pravé síni (**RAP resp. CVT**):

IVC <1.2 cm a kolaps 100% = RAP 0 mmHg

IVC 1.2-1.7 cm s >50% kolapsem = RAP 0-5 mmHg

IVC >1.7 cm s >50% kolapsem = RAP 6-10 mmHg; <50% kolapsem = RAP 10-15 mmHg

IVC >1.7 cm s 0% kolapsem = RAP >15 mmHg

Vrcholová systolická rychlost jetu trikuspidální regurgitace (**TR**) predikuje systolický tlak v plicnici (**SAP**):

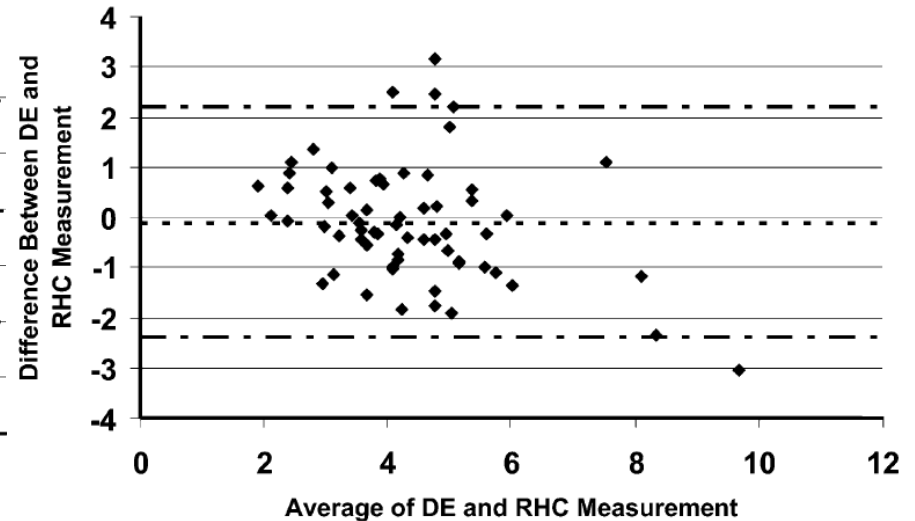
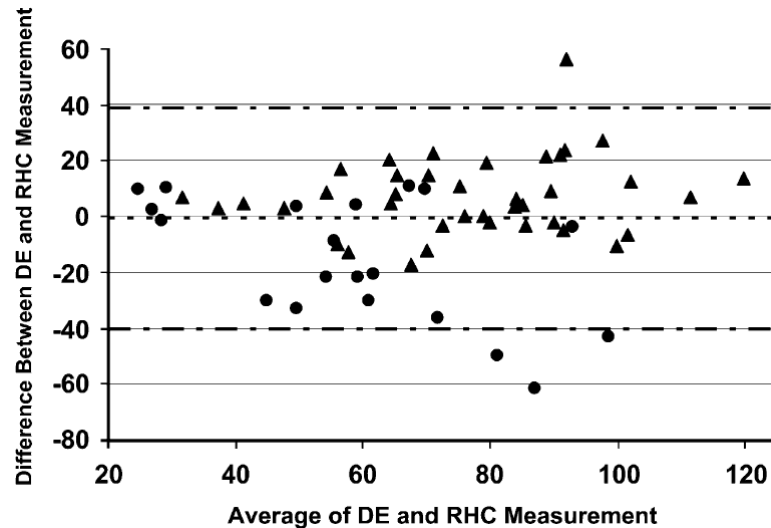
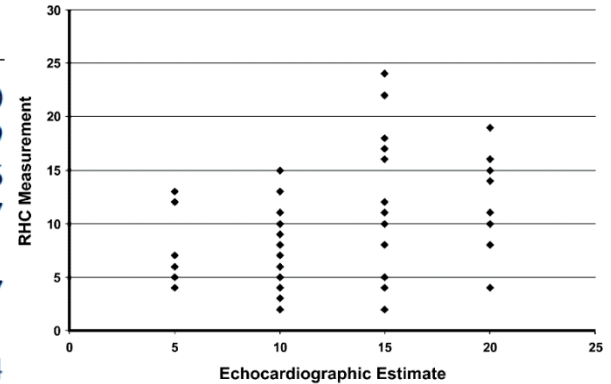
Poměr vrcholové systolické rychlosti časného mitrálního toku (E)/časná diastolická rychlost mitrálního anulu Em (**E/Em**) <8 nebo >15 přesně predikuje **PCWP** <15 mmHg resp. >15 mmHg.

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



Micah R. Fisher et al. Am J Respir Crit Care Med 2009, Vol 179, pp 615–621,



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

The Joint 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: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)

Peak tricuspid regurgitation velocity (m/s)	Presence of other echo 'PH signs' ^a	Echocardiographic probability of pulmonary hypertension
≤2.8 or not measurable	No	Low
≤2.8 or not measurable	Yes	Intermediate
2.9–3.4	No	
2.9–3.4	Yes	High
>3.4	Not required	

PLICNÍ HYPERTENZE NEPRAVDĚPODOBŇÁ

Rychlost trikuspidální regurgitace ≤ 2.8 m/s

Odhad PASP ≤36 mmHg

Bez přítomnosti hypertrofie, normální morfologie a systolická funkce pravé komory

PLICNÍ HYPERTENZE MOŽNÁ

Rychlost trikuspidální regurgitace ≤ 2.8 m/s

Odhad PASP ≤36 mmHg

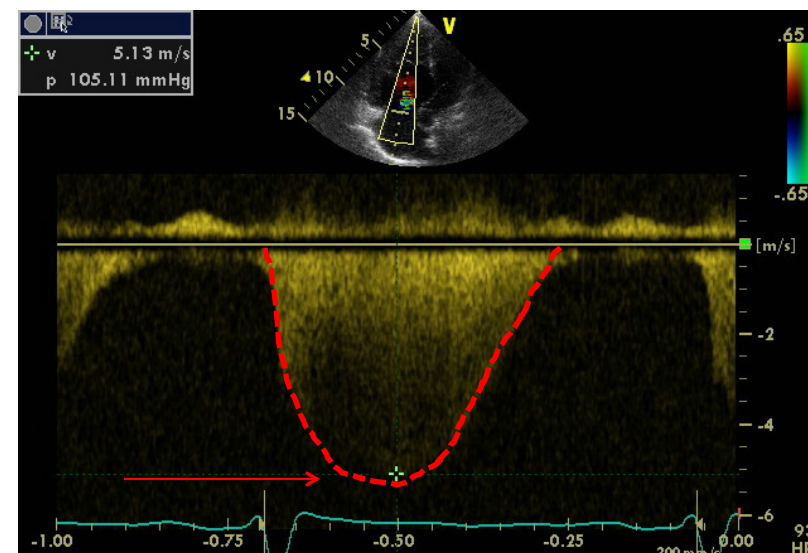
Suspektní hypertrofie, dilatace a/nebo systolická dysfunkce pravé komory

PLICNÍ HYPERTENZE PRAVDĚPODOBŇÁ

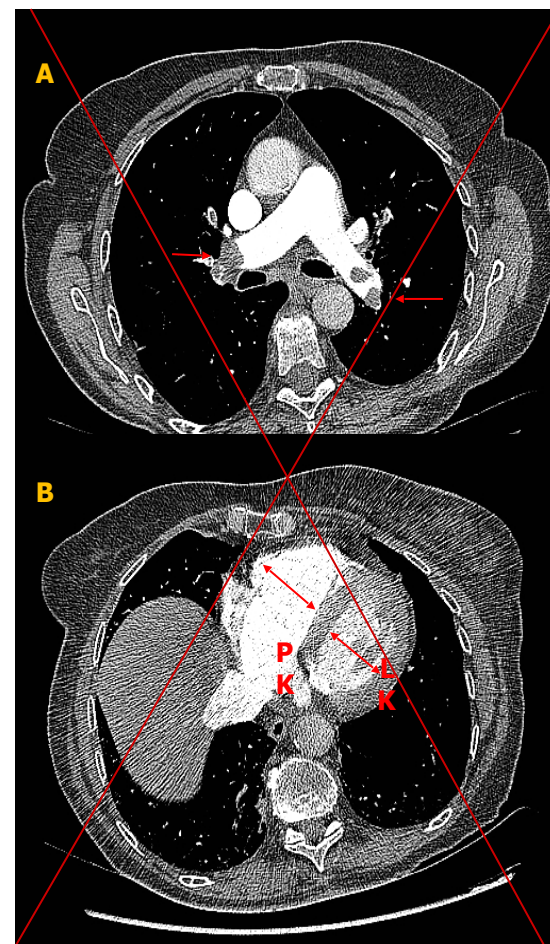
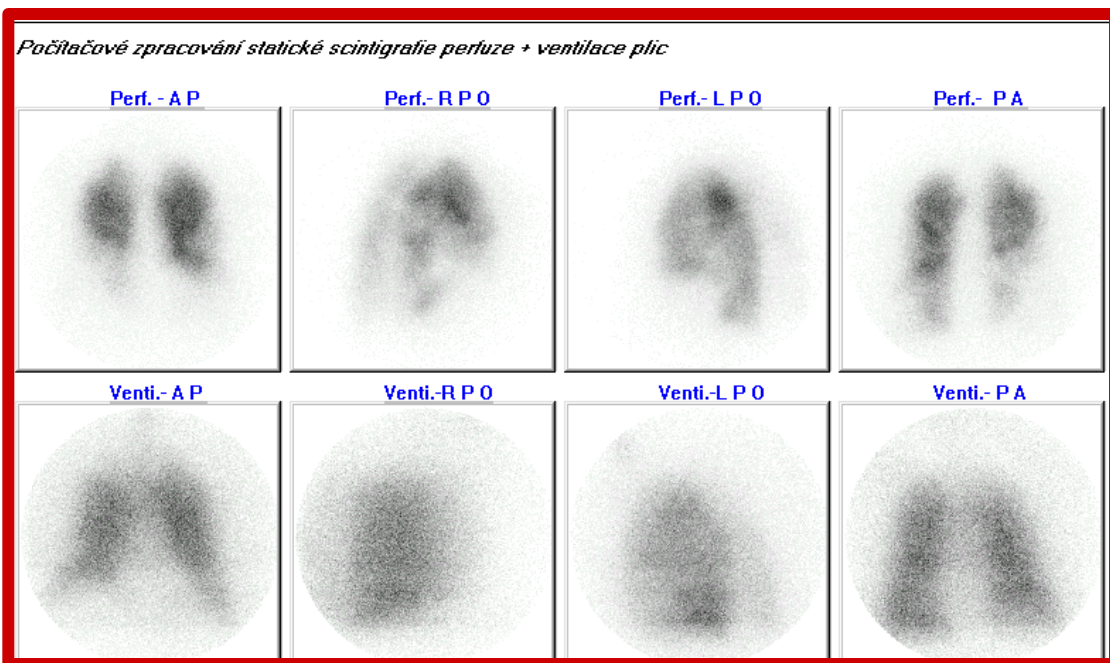
Rychlost trikuspidální regurgitace > 2.8 m/s

Odhad PASP >36 mmHg

Evidence/absence přítomnosti hypertrofie, dilatace a systolické dysfunkce pravé komory



Scintigrafie plic – screeningová zobrazovací metoda



Ventilation–Perfusion Scintigraphy Is More Sensitive than Multidetector CTPA in Detecting Chronic Thromboembolic Pulmonary Disease as a Treatable Cause of Pulmonary Hypertension

Nina Tunariu¹, Simon J.R. Gibbs^{2,3}, Zarni Win⁴, Wendy Gin-Sing², Alison Graham¹, Philip Gishen¹, and Adil AL-Nahhas^{3,4}

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

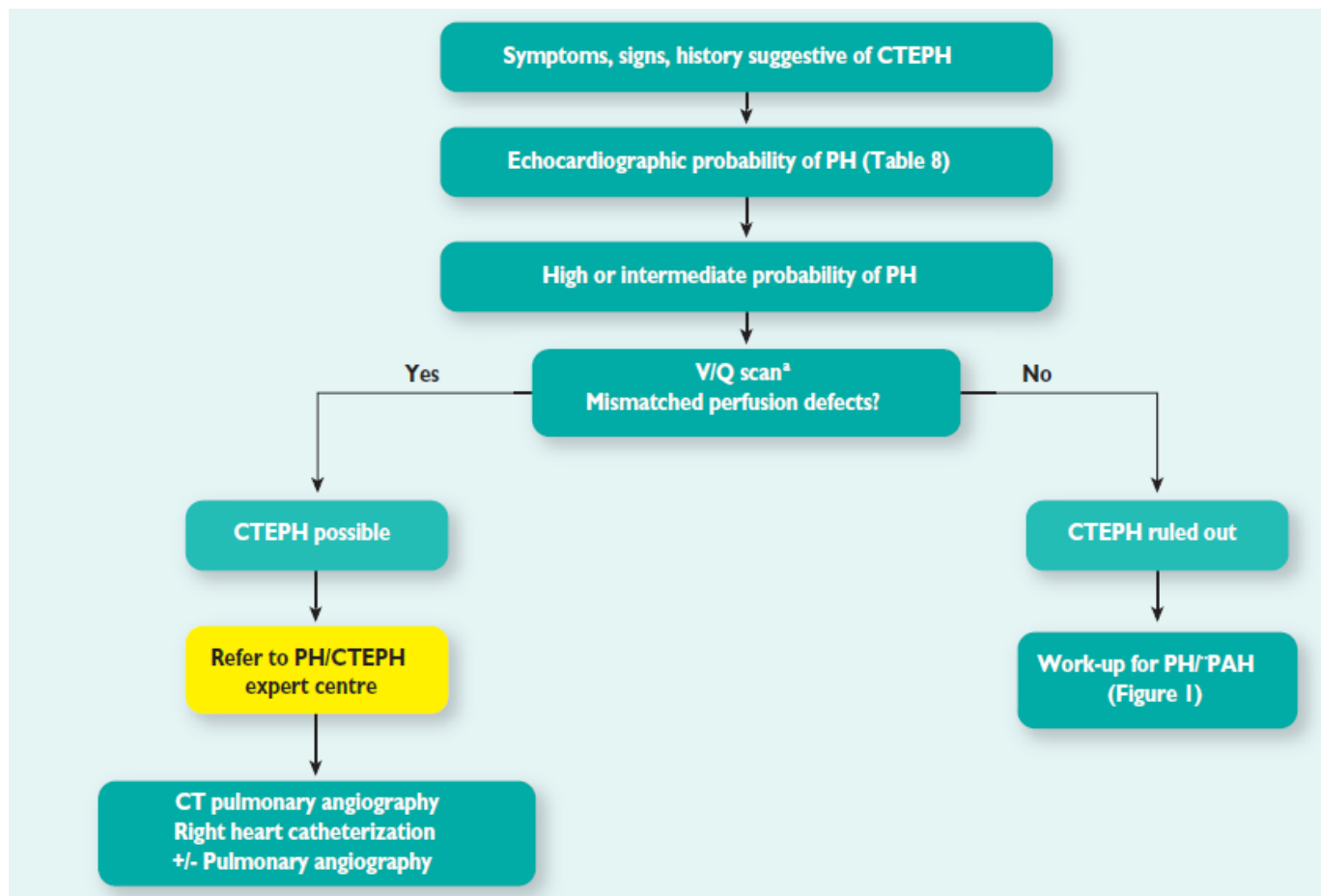


Group	V/Q			CTPA	
	Low probability	Intermediate probability	High probability	Negative	Positive
A (n = 78)	2	1	75	38	40
B (n = 149)	134	7	8	148	1

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

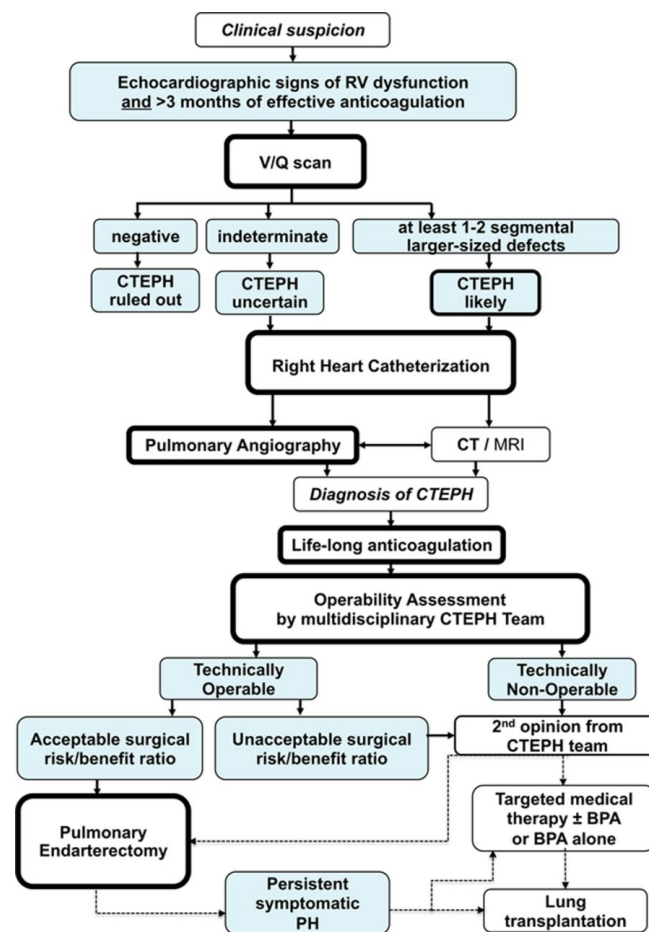
The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

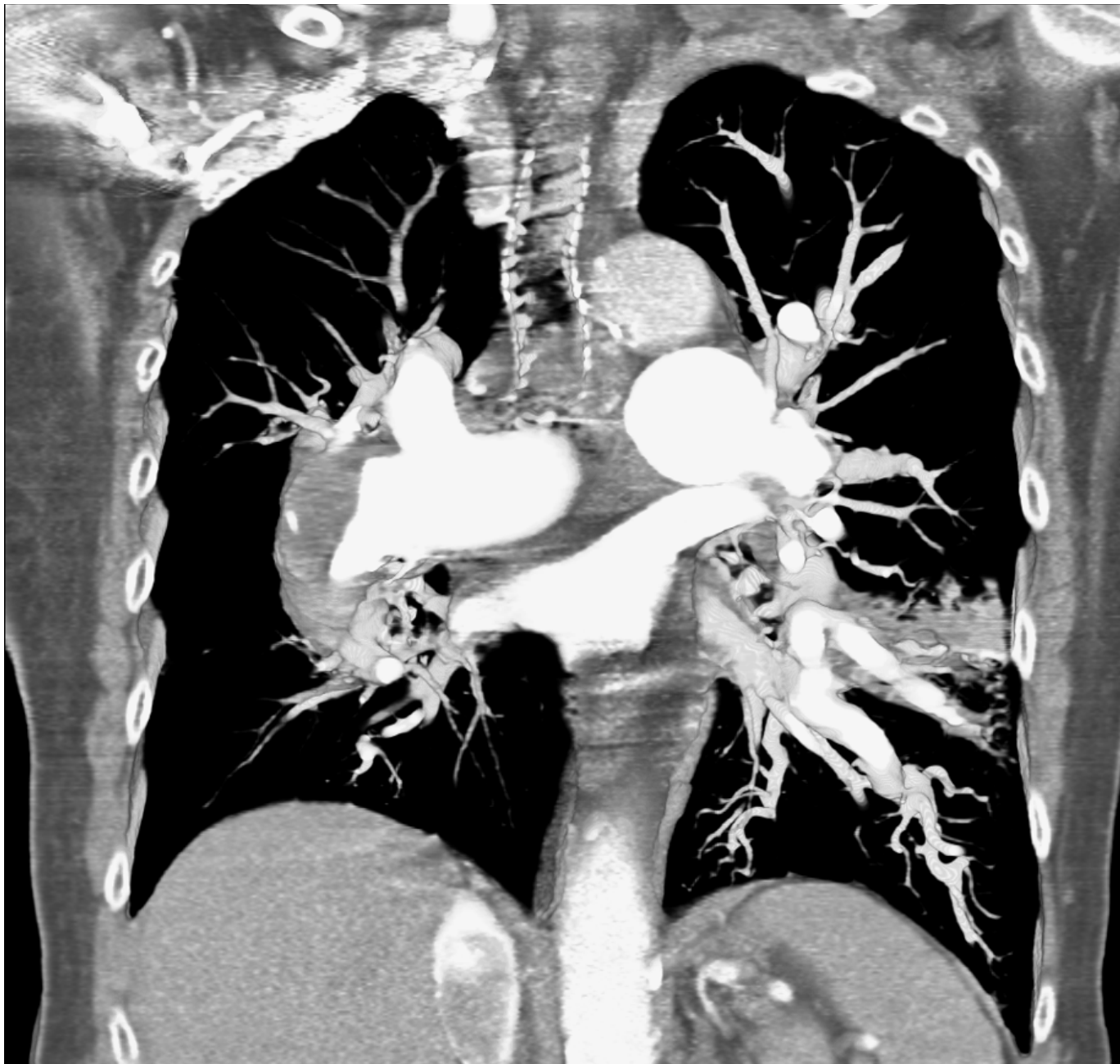
Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)



2. KONFIRMACE A EVALUACE

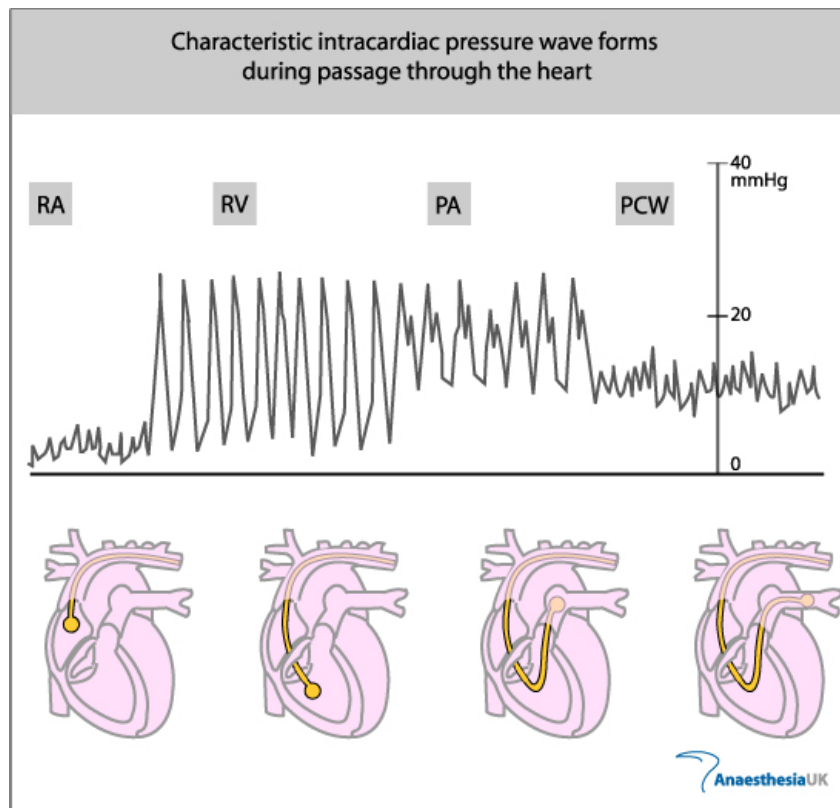
- **CTA, (MRI)**
- **PSK + hemodynamické vyšetření**
- **Angiografie plicnice**
- **Angiografie B-P kolaterál**
- **Identifikace periferní remodelace**

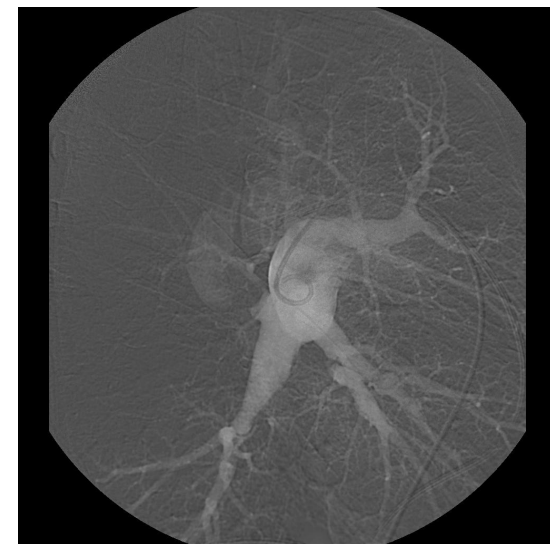
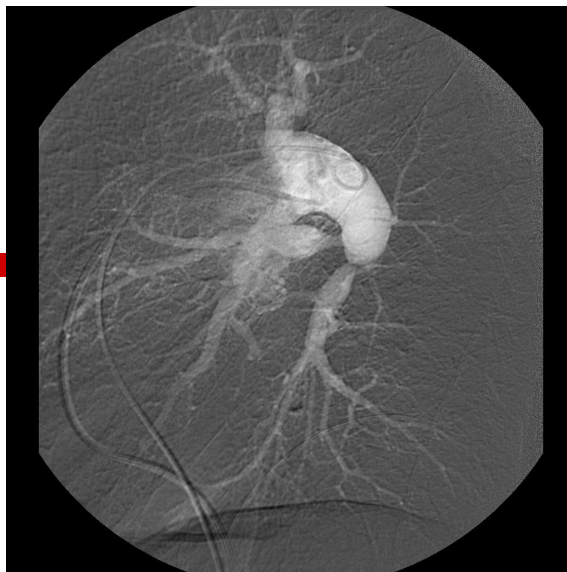
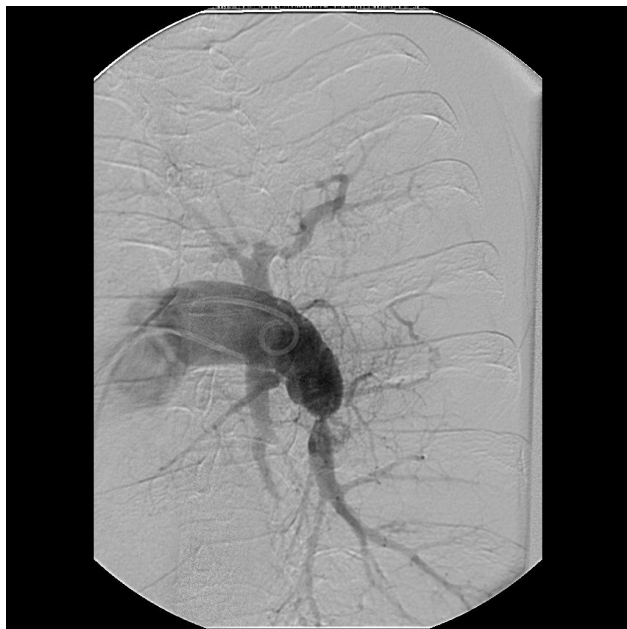




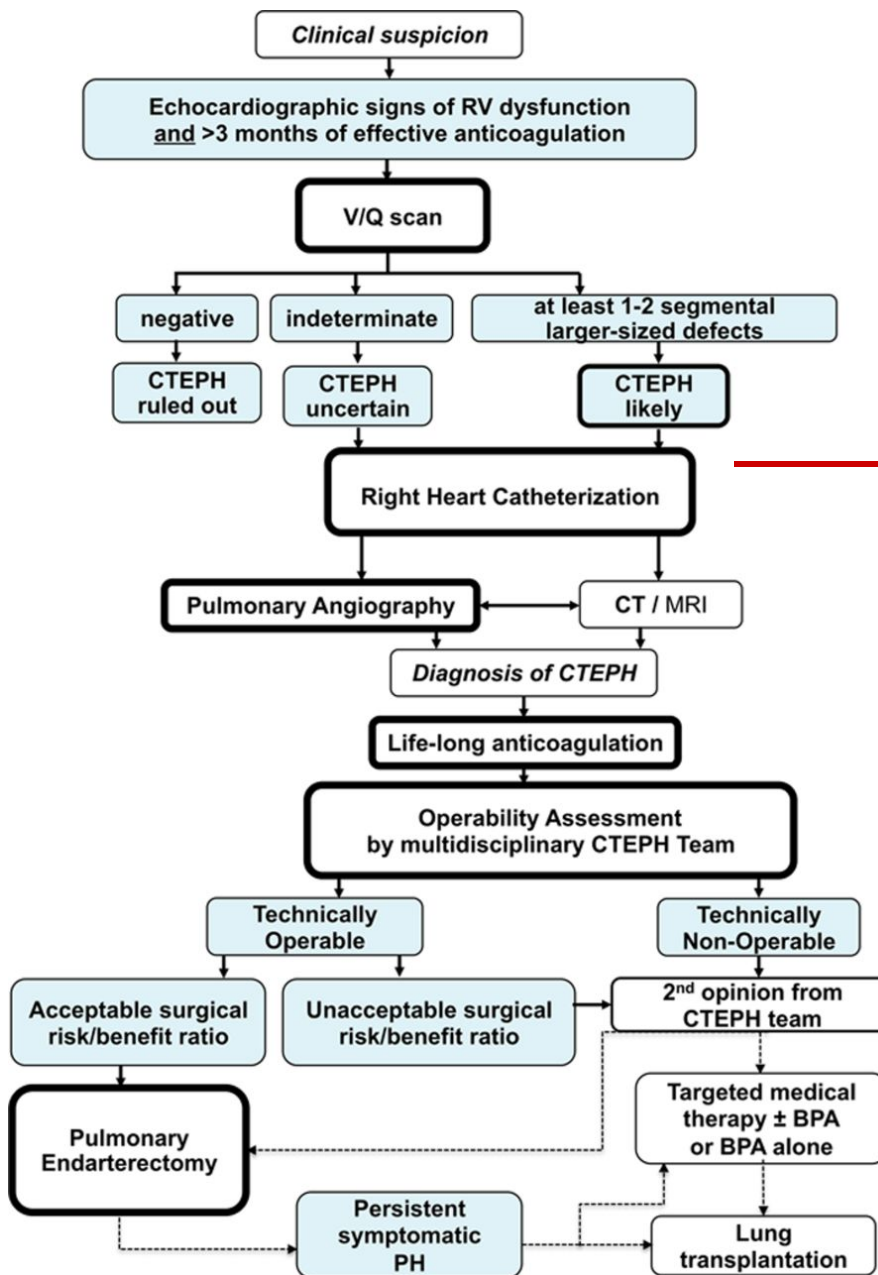
Obrázky poskytnuty laskavostí doc. Jansy

Pravostranná katetrizace - hemodynamika





Obrázky poskytnuty laskavostí doc. Jansy



Koho odeslat k evaluaci CTEPH?

- **symptomatický** pacient (námahová dušnost)
- (většinou) po předchozí **žilní tromboze/plicní embolii**
- s přetrvávajícími symptomy a PH při adekvátně vedené **antikoagulační léčbě**
- v rozumném **biologickém stavu**
- bez (velmi) četných **komorbidit**
- s možnou nebo pravděpodobnou **PREKAPILÁRNÍ PLICNÍ HYPERTENZÍ** na **echokardiografii**.
- s pozitivní **plicní scintigrafii**
- screening u **rizikových symptomatických populací**

