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Lékařská fakulta
Univerzita Palackého v Olomouci

KOMPLEXNÍ KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC

# Akutní plicní embolie
# Co říkají nová doporučení ESC 2019

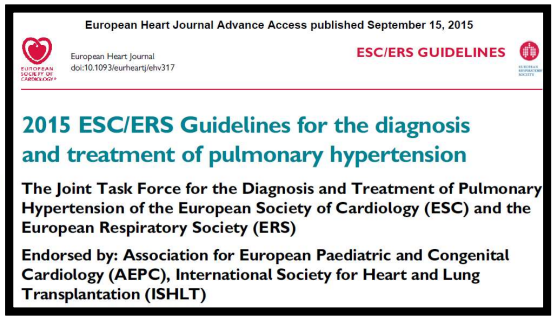
Martin Hutyra

# Deklarace konfliktu zájmů

| | Nemám konflikt zájmů | Mám konflikt zájmů | Specifikace konfliktu (vyjmenujte subjekty, firmy či instituce, se kterými Vaše spolupráce může vést ke konfliktu zájmů) |
|---|---|---|---|
| Zaměstnanecký poměr | ✓ | | |
| Vlastník / akcionář | ✓ | | |
| Konzultant | ✓ | | |
| Přednášková činnost | | ✓ | Roche, Actelion, AOP Orphan, MSD, Bayer, Novartis, Pfizer, Servier |
| Člen poradních sborů (advisory boards) | | ✓ | MSD |
| Podpora výzkumu / granty | | ✓ | IGA Ministerstvo zdravotnictví ČR, Institučí podpora FNOL/LF UP |
| Jiné honoráře (např. za klinické studie či registry) | ✓ | | |

ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–61
doi:10.1093/eurheartj/ehz405


European Heart Journal Advance Access published September 15, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv317

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)

ESC GUIDELINES

ESC Guidelines 25 YEARS

# 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS)

## The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC)

Konstantinides SV. Eur Respir J. **2019** Aug 31. pii: 1901647. doi: 10.1183/13993003.01647-**2019**.

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I. INTERNÍ KLINIKA KARDIOLOGICKÁ
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# Epidemiologie

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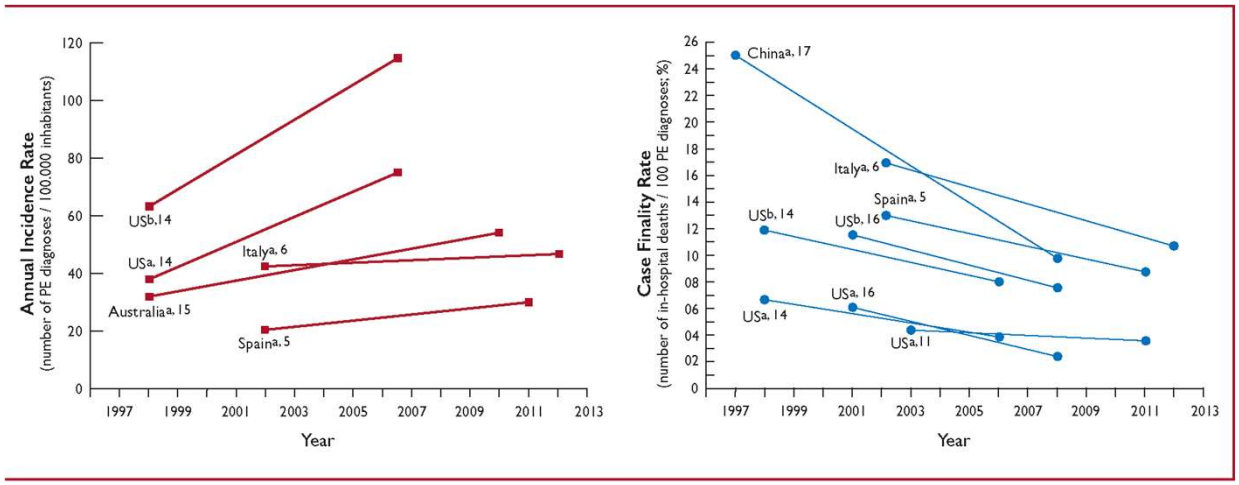



Trends in annual incidence rates (left panel) and case fatality rates (right panel) of pulmonary embolism.

**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

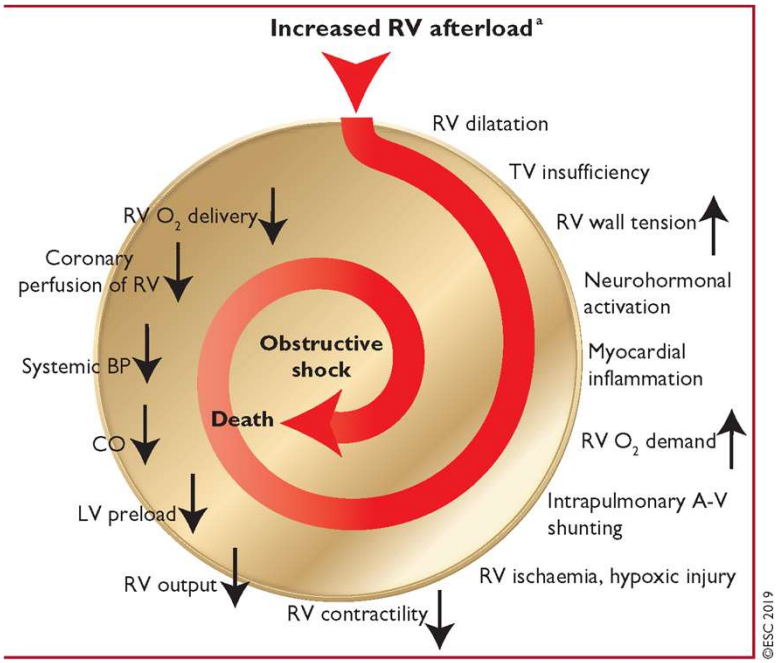
Závislost výskytu na věku a rizikových faktorech

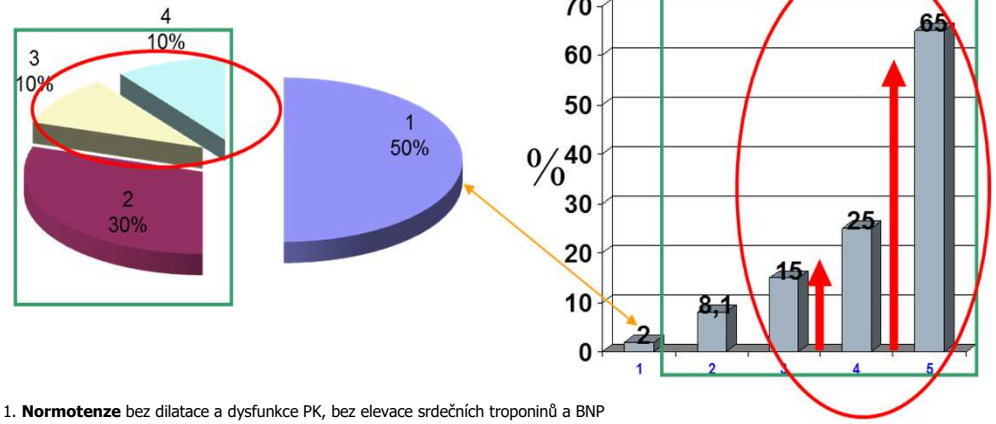
Jen 30-45% pacientů, kteří zemřeli v důsledku plicní embolie bylo adekvátně léčeno

Až 80% pacientů s rizikovými faktory tromboembolie je špatně diagnostikováno

# Patofyziologie a prognóza PE

Key factors contributing to haemodynamic collapse and death in acute pulmonary embolism




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**


Kasper W, Konstantinides S, Greibel A, et al. Management strategies and determinants of outcome in acute pulmonary embolism: results of a multicenter registry. J Am Coll Cardiol 1997;30:1165–71
Goldhaber SZ, Visani L, DeRosa M. for ICOPER. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet 1999; 353: 1386-9

# 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:

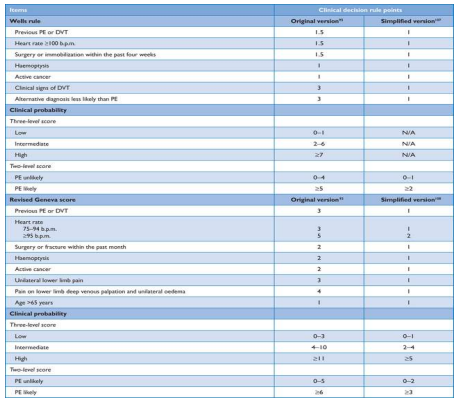
klinická pravděpodobnost

nízká 0-1 body

střední 2-6, vysoká ≥ 7

plicní embolie nepravděpodobná 0-4

pravděpodobná ≥ 5



| Items | Clinical decision rule points | |
|---|---|---|
| **Wells rule** | **Original version[41]** | **Simplified version[42]** |
| Previous PE or DVT | 1.5 | 1 |
| Heart rate >100 b.p.m. | 1.5 | 1 |
| Surgery or immobilization within the past four weeks | 1.5 | 1 |
| Haemoptysis | 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 | 2–6 | N/A |
| High | ≥7 | N/A |
| *Two-level score* | | |
| PE unlikely | 0–4 | 0–1 |
| PE likely | ≥5 | ≥2 |
| **Revised Geneva score** | **Original version[43]** | **Simplified version[44]** |
| Previous PE or DVT | 3 | 1 |
| Heart rate<br>75–94 b.p.m.<br>≥95 b.p.m. | 3<br>5 | 1<br>2 |
| Surgery or fracture within the past month | 2 | 1 |
| Haemoptysis | 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 |

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

Guo DJ. Chin Med J (Engl). 2015 Apr 20; 128(8): 1052–1057.

Annals of Internal Medicine
ESTABLISHED IN 1927 BY THE AMERICAN COLLEGE OF PHYSICIANS

# Performance of 4 Clinical Decision Rules in the Diagnostic Management of Acute Pulmonary Embolism

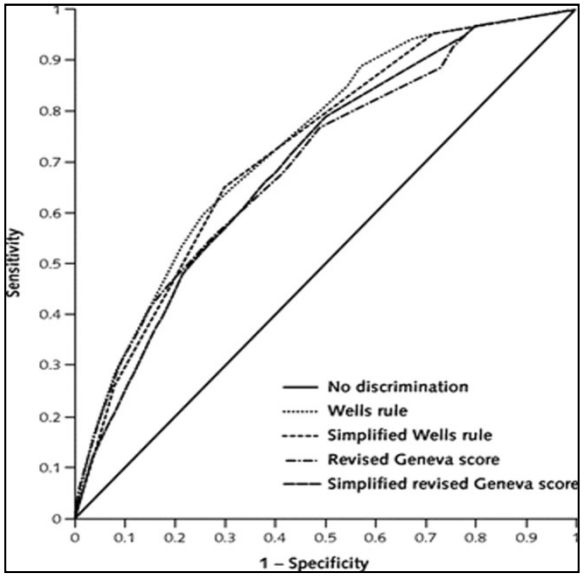
## A Prospective Cohort Study from the Promethius Study Group

**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.

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# PESI

| 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] | |
| | **Class I:≤65 points**<br>very low 30-day mortality risk (0–1.6%)<br>**Class II: 66–85 points**<br>low mortality risk (1.7–3.5%)<br><br>**Class III: 86–105 points**<br>moderate mortality risk (3.2–7.1%)<br>**Class IV: 106–125 points**<br>high mortality risk (4.0–11.4%)<br>**Class V: >125 points**<br>very high mortality risk (10.0–24.5%) | **0 points**= 30-day mortality risk 1.0% (95% CI 0.0%–2.1%)<br><br>**≥1 point(s)**= 30-day mortality risk 10.9% (95% CI 8.5%–13.2%) |

Konstantinides SV. Eur Respir J. **2019** Aug 31. pii: 1901647. doi: 10.1183/13993003.01647-**2019**.

# Klasifikace a riziková stratifikace

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| Early mortality risk | | Indicators of risk | | | |
|---|---|---|---|---|---|
| | | Haemodynamic instability[a] | Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥I | RV dysfunction on TTE or CTPA[b] | Elevated cardiac troponin levels[c] |
| High | | + | (+)[d] | + | (+) |
| Intermediate | Intermediate–high | - | +[e] | + | + |
| | Intermediate–low | - | +[e] | One (or none) positive | |
| Low | | - | - | - | Assesment optional; if assessed, negative |

BP = blood pressure; CTPA = computed tomography pulmonary angiography; H-FABP = heart-type fatty acid-binding protein; NT-proBNP = N-terminal pro B-type natriuretic peptide; PE = pulmonary embolism; PESI = Pulmonary Embolism Severity Index; RV = right ventricular; sPESI = simplified Pulmonary Embolism Severity Index; TTE = transthoracic echocardiogram.

[a] One of the following clinical presentations (*Table 4*): cardiac arrest, obstructive shock (systolic BP <90 mmHg or vasopressors required to achieve a BP ≥90 mmHg despite an adequate filling status, in combination with end-organ hypoperfusion), or persistent hypotension (systolic BP <90 mmHg or a systolic BP drop ≥40 mmHg for >15 min, not caused by new-onset arrhythmia, hypovolaemia, or sepsis).

[b] Prognostically relevant imaging (TTE or CTPA) findings in patients with acute PE, and the corresponding cut-off levels, are graphically presented in *Figure 3*, and their prognostic value is summarized in Supplementary Data *Table 3*.

[c] Elevation of further laboratory biomarkers, such as NT-proBNP ≥600 ng/L, H-FABP ≥6 ng/mL, or copeptin ≥24 pmol/L, may provide additional prognostic information. These markers have been validated in cohort studies but they have not yet been used to guide treatment decisions in randomized controlled trials.

[c] Haemodynamic instability, combined with PE confirmation on CTPA and/or evidence of RV dysfunction on TTE, is sufficient to classify a patient into the high-risk PE category. In these cases, neither calculation of the PESI nor measurement of troponins or other cardiac biomarkers is necessary.

[e] Signs of RV dysfunction on TTE (or CTPA) or elevated cardiac biomarker levels may be present, despite a calculated PESI of I–II or an sPESI of 0.[234] Until the implications of such discrepancies for the management of PE are fully understood, these patients should be classified into the intermediate-risk category.

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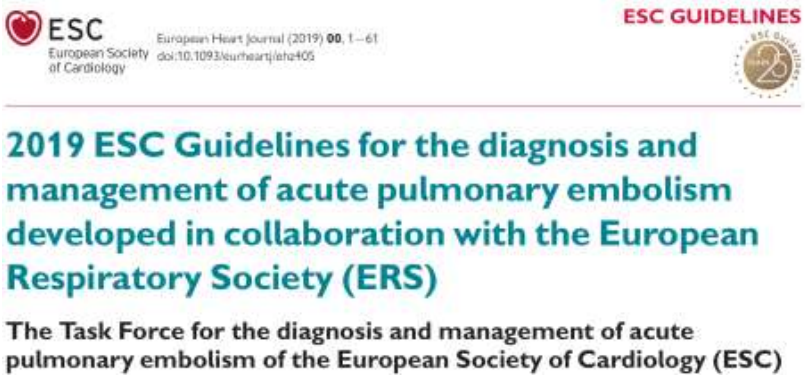
# Posun v ESC doporučení 2014 - 2019

| Recommendations | 2014 | 2019 |
|---|---|---|
| Rescue thrombolytic therapy is recommended for patients who deteriorate haemodynamically. | IIa | I |
| Surgical embolectomy or catheter-directed treatment should be considered as alternatives to rescue thrombolytic therapy for patients who deteriorate haemodynamically. | IIb | IIa |
| D-dimer measurement and clinical prediction rules should be considered to rule out PE during pregnancy or the post-partum period. | IIb | IIa |
| Further evaluation may be considered for asymptomatic PE survivors at increased risk for CTEPH. | III | IIb |

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# Diagnostický algoritmus

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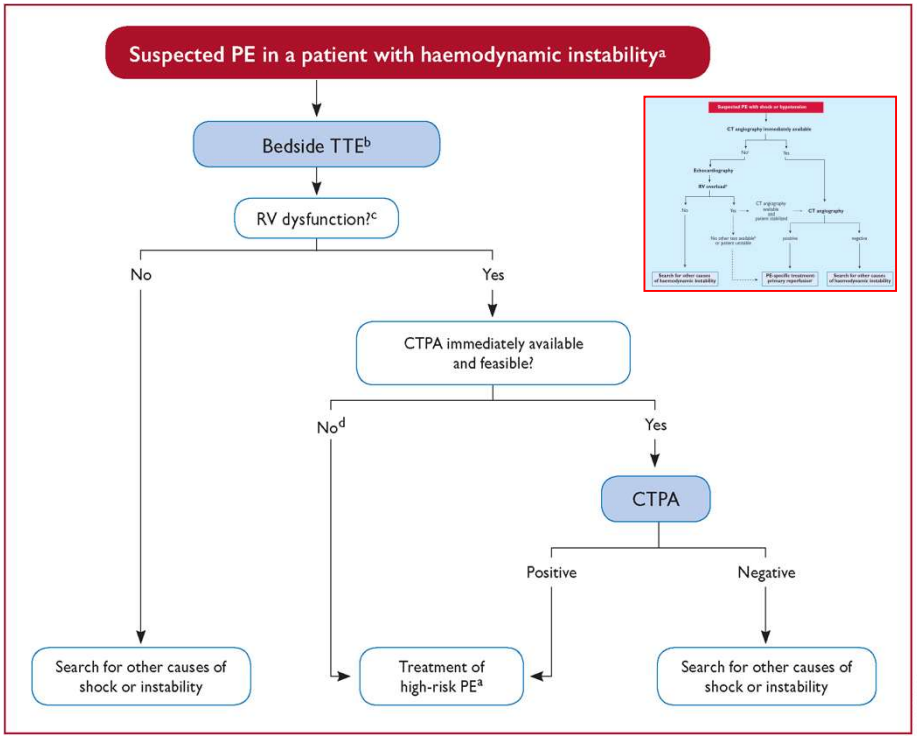


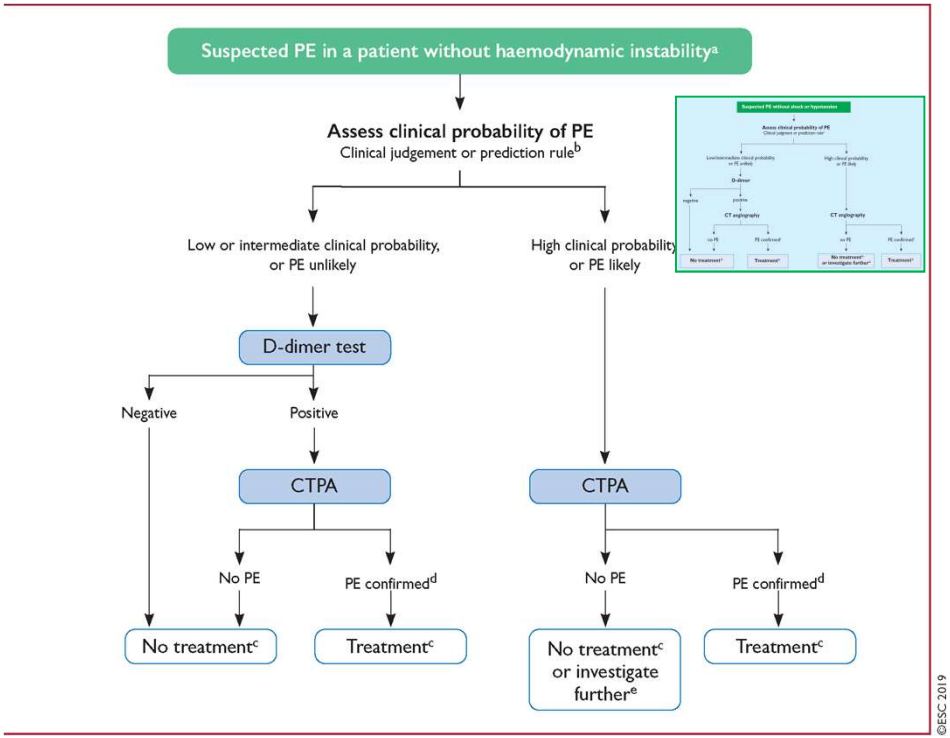


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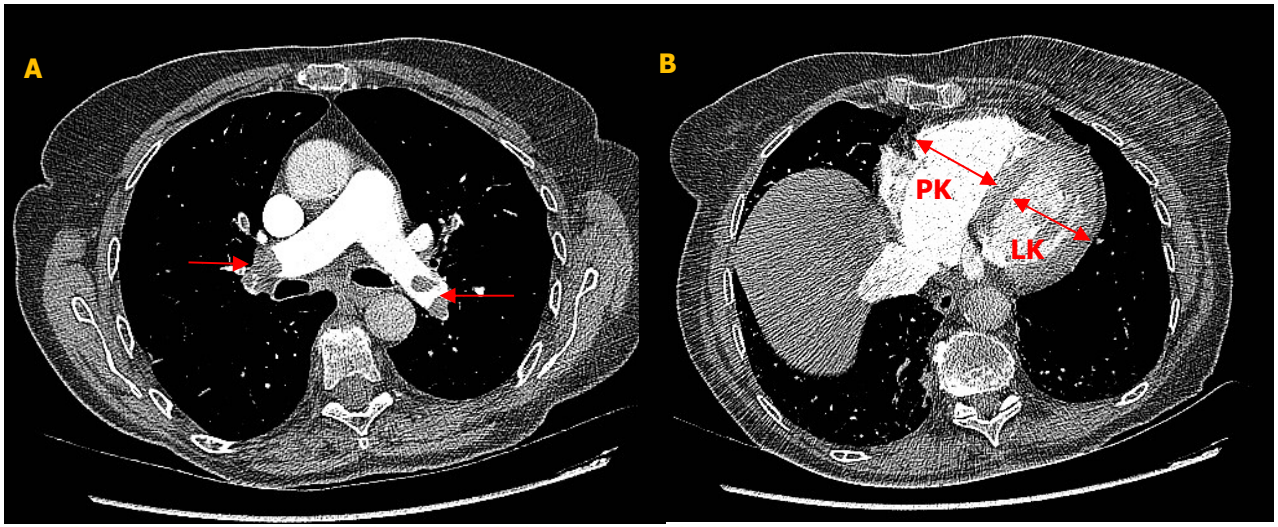
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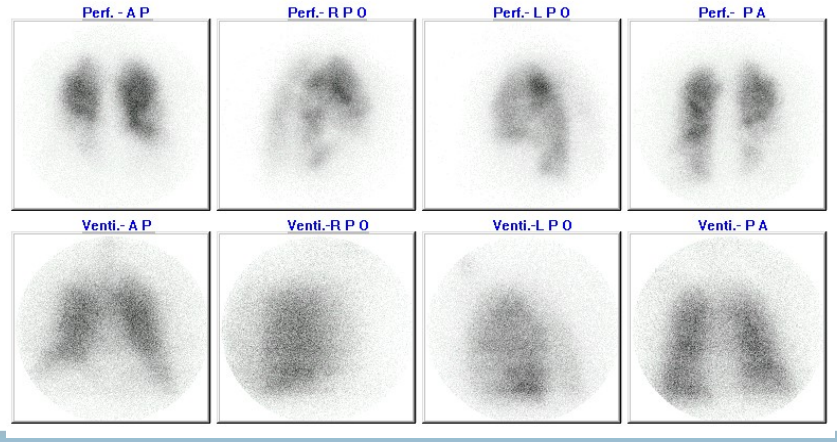
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# Echokardiografie v rizikové stratifikaci PE

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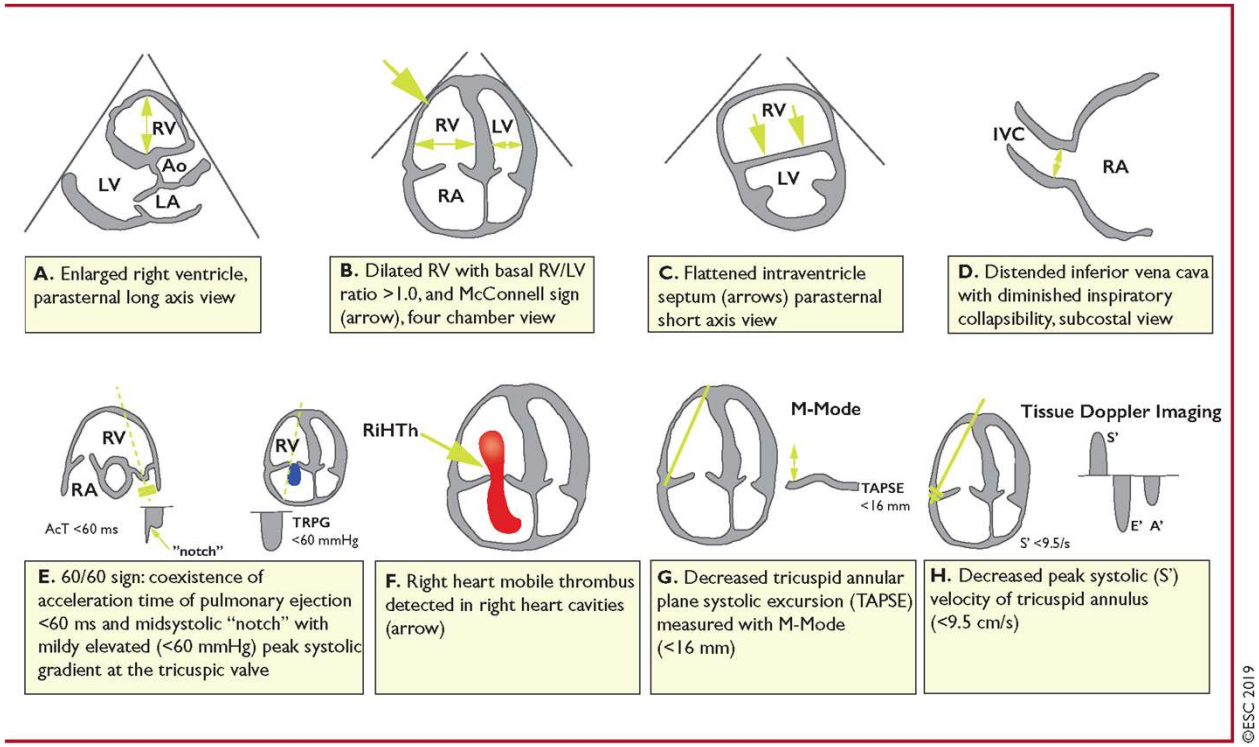


**A.** Enlarged right ventricle, parasternal long axis view

**B.** Dilated RV with basal RV/LV ratio >1.0, and McConnell sign (arrow), four chamber view

**C.** Flattened intraventricle septum (arrows) parasternal short axis view

**D.** Distended inferior vena cava with diminished inspiratory collapsibility, subcostal view

**E.** 60/60 sign: coexistence of acceleration time of pulmonary ejection <60 ms and midsystolic "notch" with mildy elevated (<60 mmHg) peak systolic gradient at the tricuspic valve

**F.** Right heart mobile thrombus detected in right heart cavities (arrow)

**G.** Decreased tricuspid annular plane systolic excursion (TAPSE) measured with M-Mode (<16 mm)

**H.** Decreased peak systolic (S') velocity of tricuspid annulus (<9.5 cm/s)



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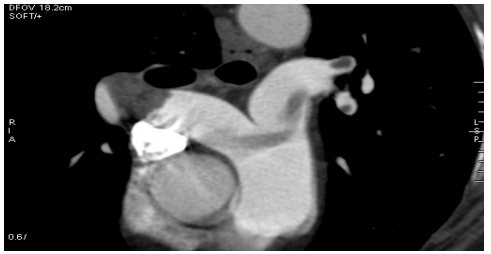
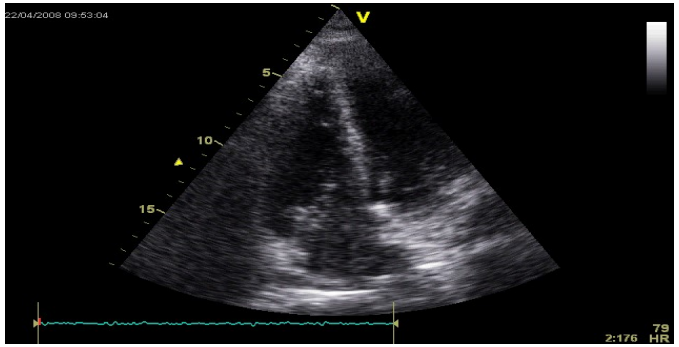
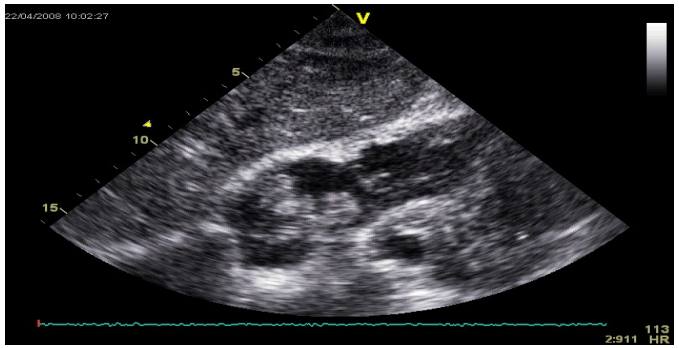
# Tranzientní tromby






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

Závažný nález indikující trombolýzu

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

Casazza F, Bongarzoni A. Prevalence and prognostic significance of right-sided cardiac mobile thrombi in acute massive pulmonary embolism. Am J Cardiol 1997; 79:1433-5
Chartier L, Bera J. et al. Free-Floating Thrombi in the right Heart: Diagnosis, management and prognostic indexes in 38 consecutive patients. Circulation 1999; 99: 2779-83

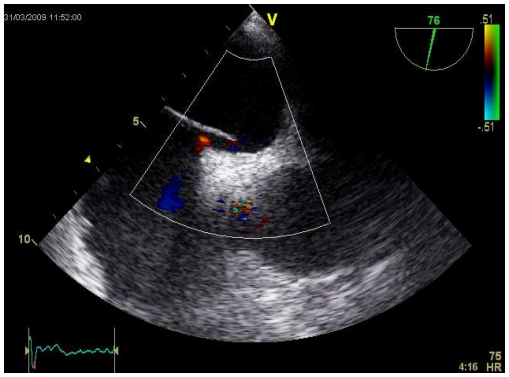
# PFO jako zdroj paradoxní embolizace

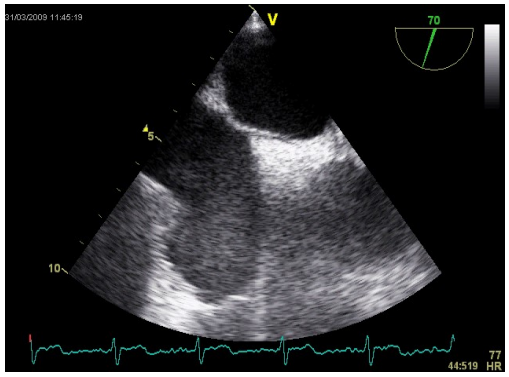
<u>Nemocní s PFO a plicní embolií mají:</u>

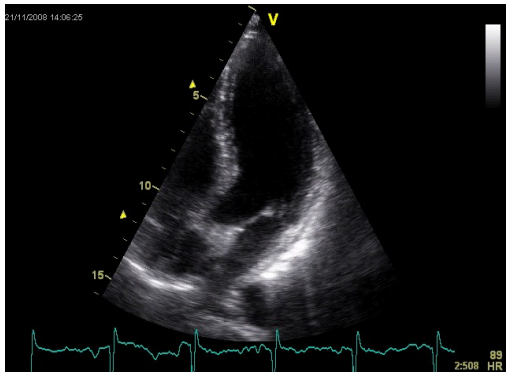
Vyšší riziko mortality (33% vs. 14%)

Vyšší výskyt ischemické CMP (13% vs. 2%)

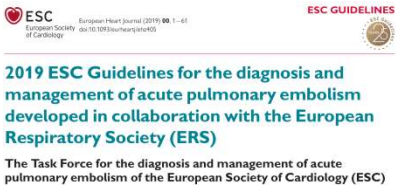
Vyšší incidenci periferní arteriální embolizace (15% vs. 0%)







# Nová ESC doporučení 2019




| **Diagnosis** | |
|---|---|
| A D-dimer test, using an age-adjusted cut-off or adapted to clinical probability, should be considered as an alternative to the fixed cut-off level. | **IIa** |
| If a positive proximal CUS is used to confirm PE, risk assessment should be considered to guide management. | **IIa** |
| V/Q SPECT may be considered for PE diagnosis. | **IIb** |
| **Risk assessment** | |
| Assessment of the RV by imaging or laboratory bio-markers should be considered, even in the presence of a low PESI or a sPESI of 0. | **IIa** |
| Validated scores combining clinical, imaging, and labo-ratory prognostic factors may be considered to fur-ther stratify PE severity. | **IIb** |

Konstantinides SV. Eur Respir J. **2019** Aug 31. pii: 1901647. doi: 10.1183/13993003.01647-**2019**.

KOMPLEXNÍ KARDIOVASKULÁRNÍ CENTRUM

Lékařská fakulta Univerzity Palackého v Olomouci

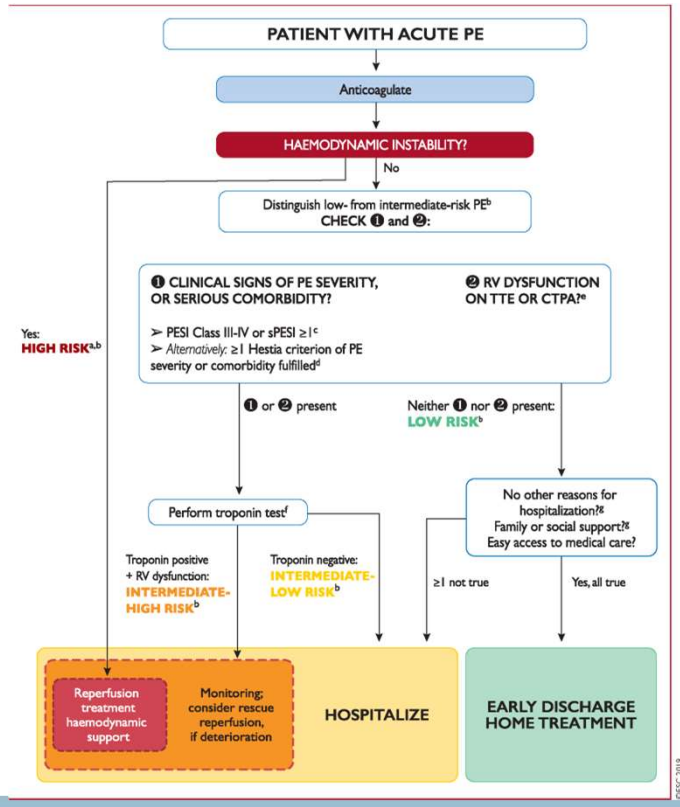
I. INTERNÍ KLINIKA KARDIOLOGICKÁ
FAKULTNÍ NEMOCNICE OLOMOUC

# Management PE

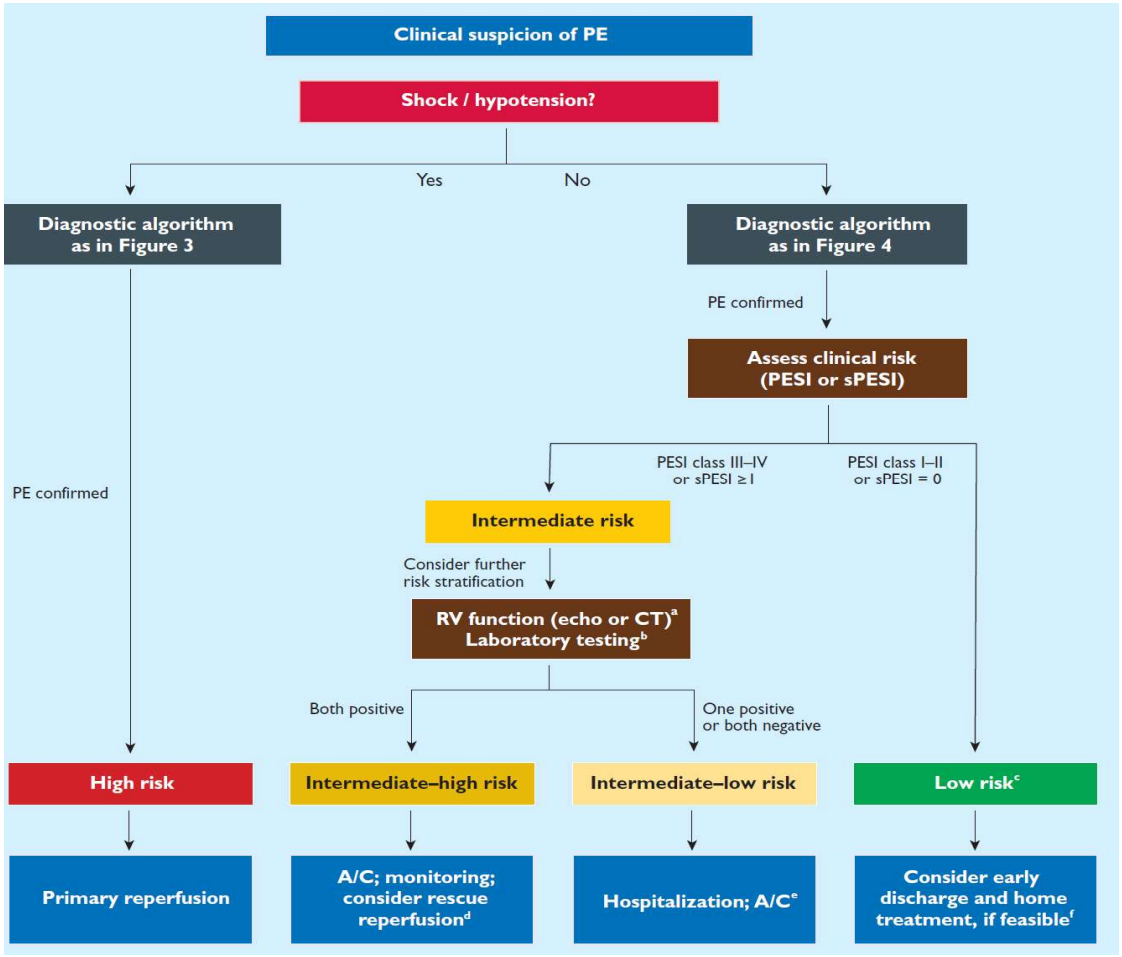
ESC European Heart Journal (2019) 00, 1–61 doi:10.1093/eurheartj/ehz405
ESC GUIDELINES

**2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS)**

The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC)




Risk-adjusted management strategy for acute pulmonary embolism. CTPA = computed tomography pulmonary angiography/angiogram; PE = pulmonary embolism; PESI = Pulmonary Embolism Severity Index; RV = right ventricular; sPESI = simplified Pulmonary Embolism Severity Index; TTE = transthoracic echocardiogram.




European Heart Journal Advance Access published August 29, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu283

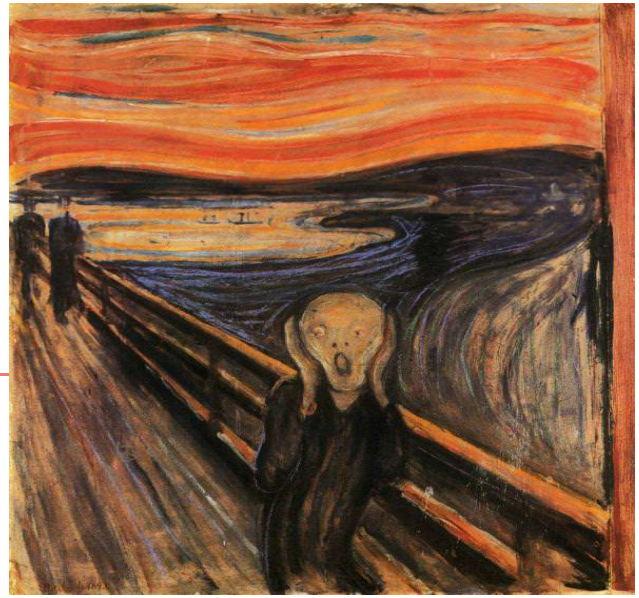
ESC GUIDELINES

# 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)**

Konstantinides SV. Eur Respir J. **2019** Aug 31. pii: 1901647. doi: 10.1183/13993003.01647-**2019**.

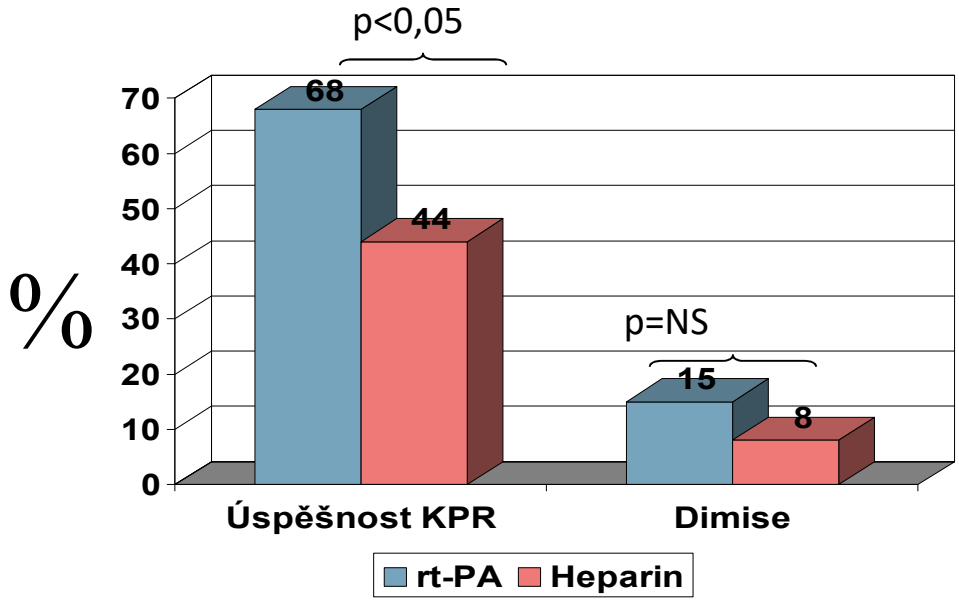


# Masivní (high-risk) plicní embolie se zástavou oběhu a KPR

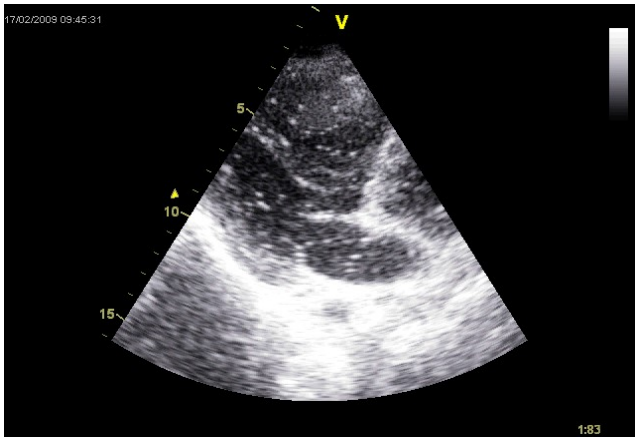
I. INTERNÍ KLINIKA
KARDIOLOGIE
FAKULTNÍ NEMOCNICE OLOMOUC

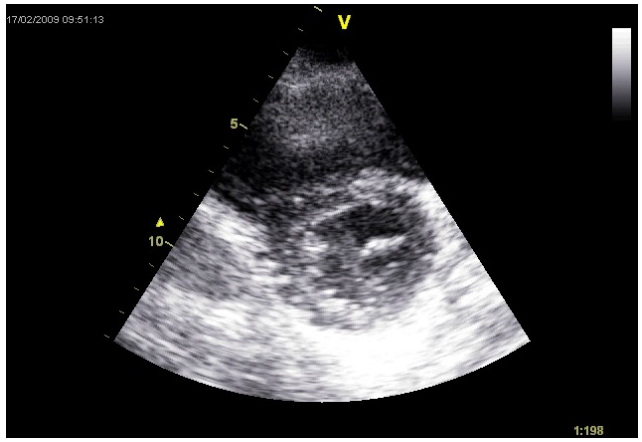
# Trombolýza při zástavě oběhu způsobené plicní embolií

- 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.



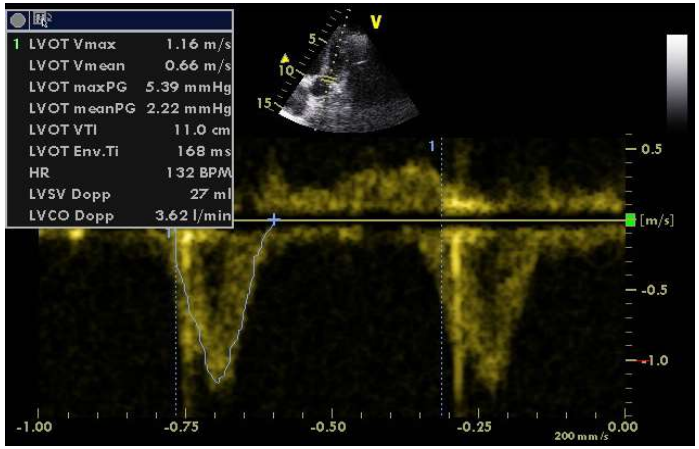

Bottiger BW. Efficacy and safety of thrombolytic therapy after initially unsuccessful cardiopulmonary resuscitation: a prospective clinical trial. Lancet 2001;357:1583–5

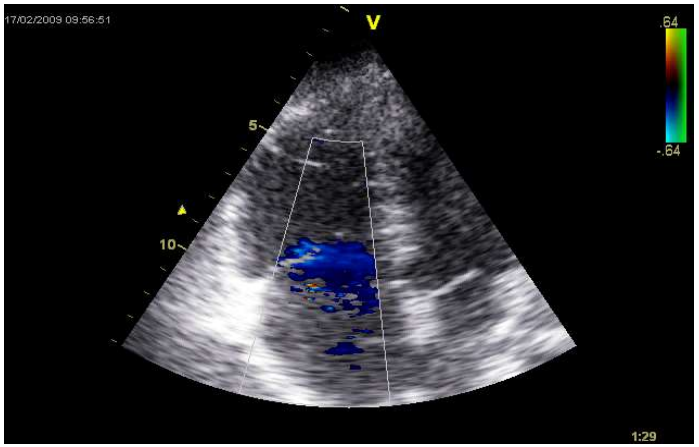



## ECMO Maquet

## LUCAS CPR Chest Compression System


1 LVOT Vmax 1.16 m/s
LVOT Vmean 0.66 m/s
LVOT maxPG 5.39 mmHg
LVOT meanPG 2.22 mmHg
LVOT VTI 11.0 cm
LVOT Env.Ti 168 ms
HR 132 BPM
LVSV Dopp 27 ml
LVCO Dopp 3.62 l/min
V
5
10
15
0.5
[m/s]
-0.5
-1.0
-1.00
-0.75
-0.50
-0.25
0.00
200 mm/s


17/02/2009 09:56:51
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.64
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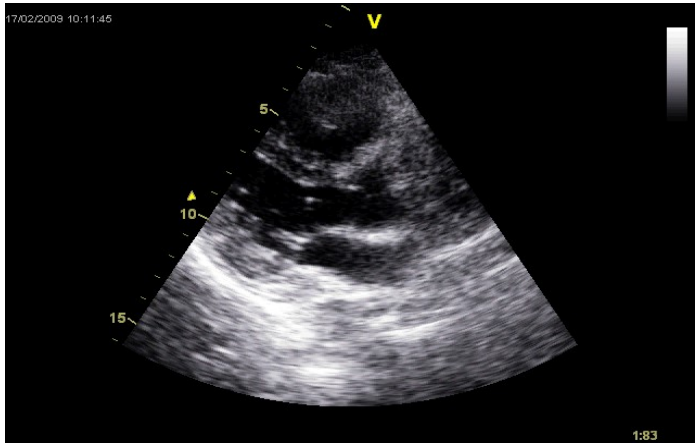
1:29


17/02/2009 10:11:45
V
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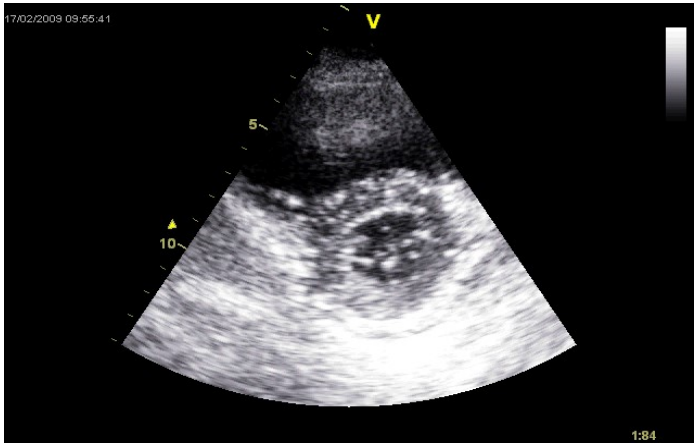
10
15
1:83


17/02/2009 09:55:41
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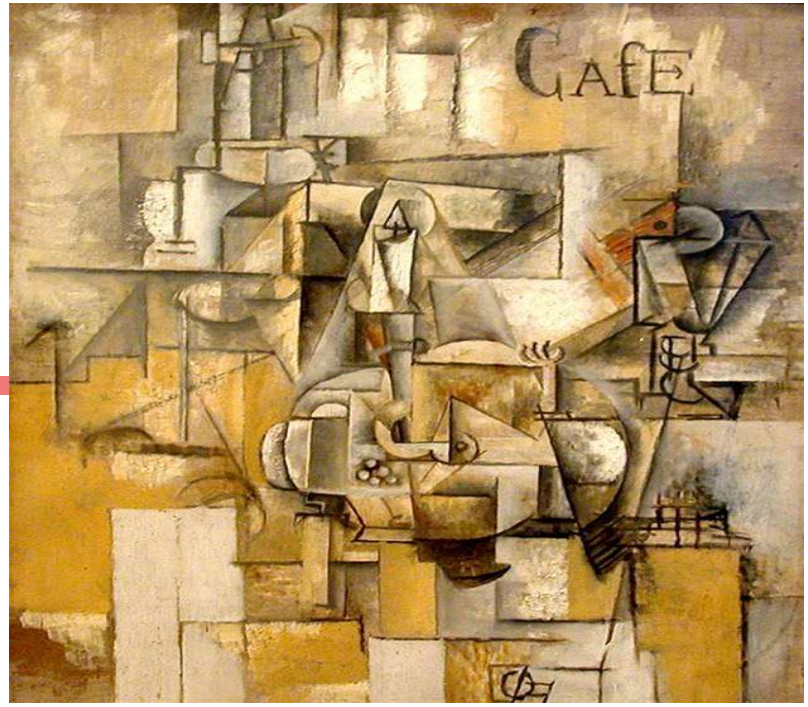


# Masivní high-risk plicní embolie s hypotenzí a kardiogenním šokem

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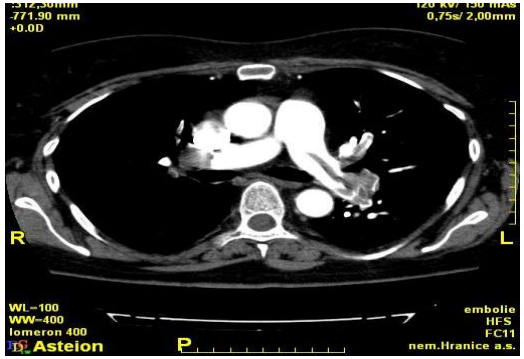
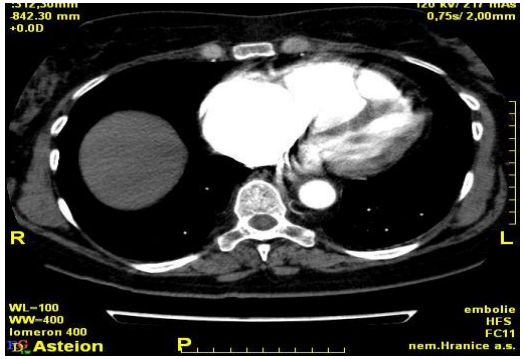
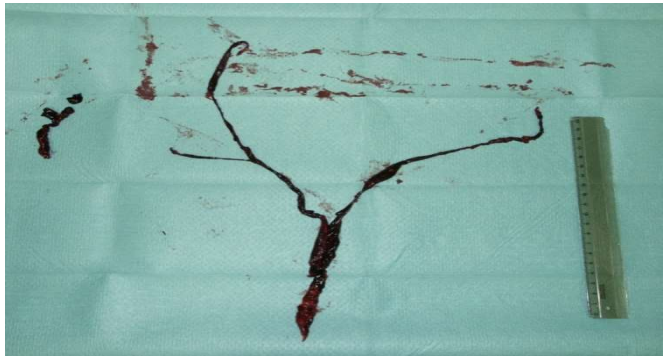
# Trombolýza vs. heparin u „high-risk“ plicní embolie

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

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



# Kontraindikace trombolýzy

Absolute contraindications[a]

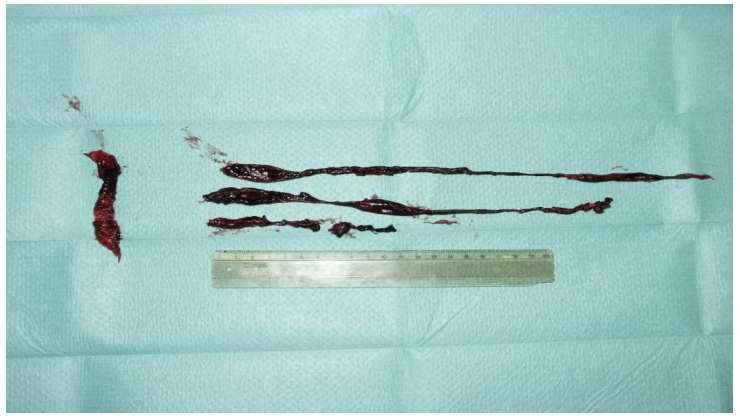
- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in preceding 6 months
- Central nervous system damage or neoplasms
- Recent major trauma/surgery/head injury (within preceding 3 weeks)
- Gastrointestinal bleeding within the last month
- Known bleeding

Relative contraindications

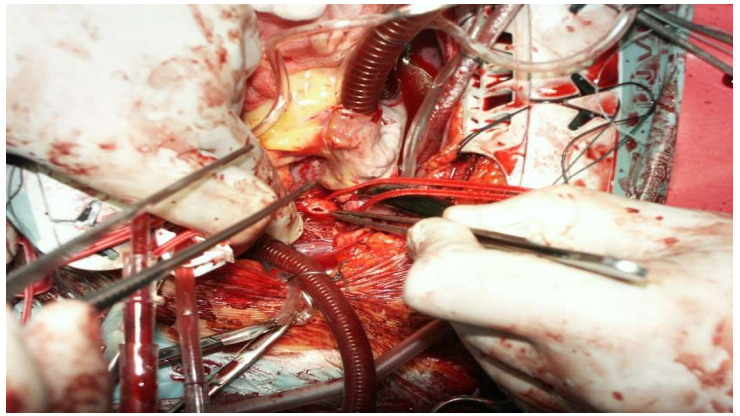
- Transient ischaemic attack in preceding 6 months
- Oral anticoagulant therapy
- Pregnancy or within 1 week post partum
- Non-compressible punctures
- Traumatic resuscitation
- Refractory hypertension (systolic blood pressure >180 mmHg)
- Advanced liver disease
- Infective endocarditis
- Active peptic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

# Embolektomie

•„Reperfuzní – emboly odstraňující“ alternativa trombolýzy při kontraindikaci podání

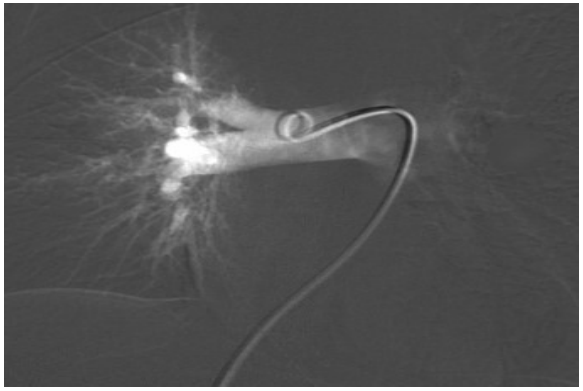


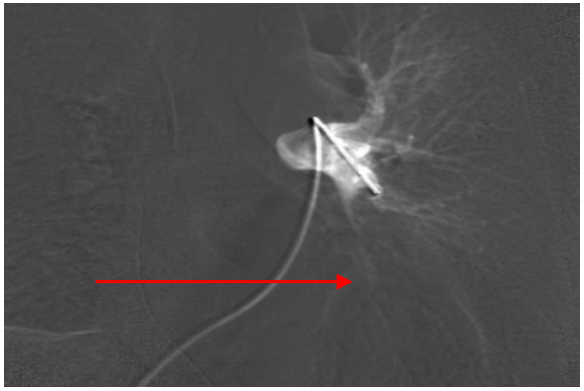
•Srovnávací studie 23 pacientů v kardiogenním šoku léčených embolektomií a 24 léčených farmakologicky (TL) prokázala přežívaní 77% proti 67% v konzervativně léčené skupině.

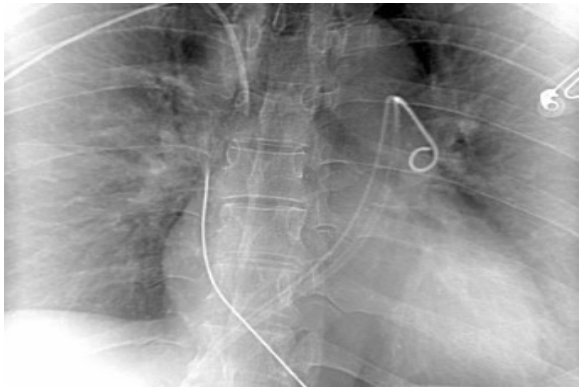


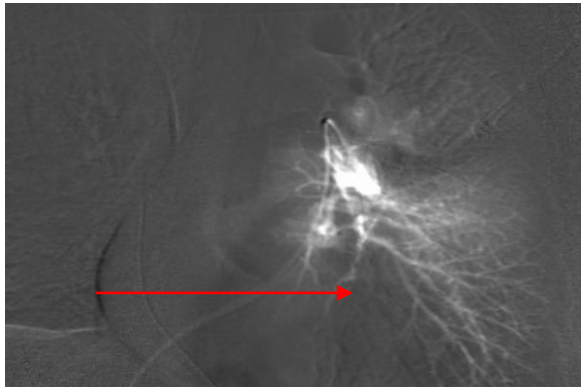
Clark D, Abrams L. Pulmonary embolectomy. A 25-year experience. J Thorac Cardiovasc Surg 1986;92:442–5.
Doerge H, Schoendole T, Voss M, et al. Surgical therapy for fulminant pulmonary embolism: early and late results. Thorac Cardiovasc Surg1999;47:9–13.
Gulba D, Schmid C, Borst H, et al. Medical compared to surgical treatment ofmassive pulmonary embolism. Lancet 1994;343:576–7.

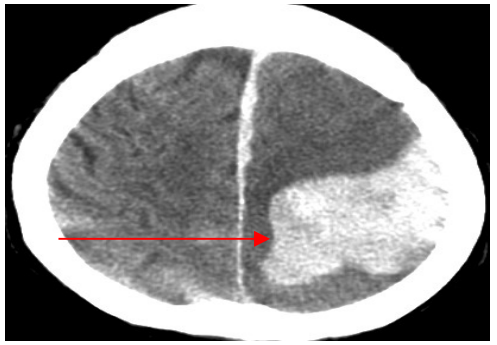
# Katetrová fragmentace PE











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

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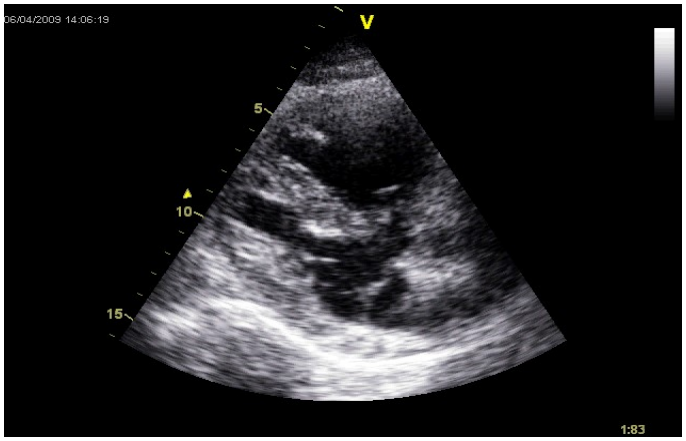
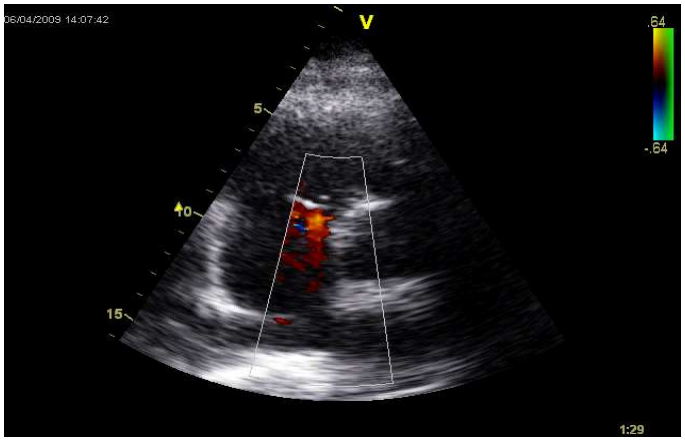



Normální systémový tlak, anamnéza synkopy (!), narůstající dušnost při léčbě LMWH, troponin T 0,24 μg/l, NT-proBNP 11375 ng/l, snížený srdeční výdej

# 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 |

# MAPPET 3

Dvojitě slepá randomizovaná studie u pacientů se „submasivní“ PE srovnávající rt-PA 100 mg a heparin i.v.

| | t-PA (n=118) | Hep. (n=138) | Sign. |
|---|---|---|---|
| ***Mortalita a eskalace*** | **11%** | **24,6%** | **0,006** |
| Mortalita | 3,4% | 2,2% | NS |
| ***Eskalace terapie*** | **10,2%** | **24,6%** | **<0,004** |
| Sekundární trombolýza | 7,6% | 23,2% | <0,001 |
| Vazopresory | 2,5% | 5,8% | NS |
| Intubace a UPV | 2,5% | 2,2% | NS |
| KPR | 0% | 0,7% | NS |
| Embolektomie | 0% | 0,7% | NS |

Konstantinides S. A randomized trial comparing alteplase plus heparin with heparin alone in patients with acute major pulmonary embolism. NEJM 2002;347:1143-50

The NEW ENGLAND JOURNAL of MEDICINE

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) | | |

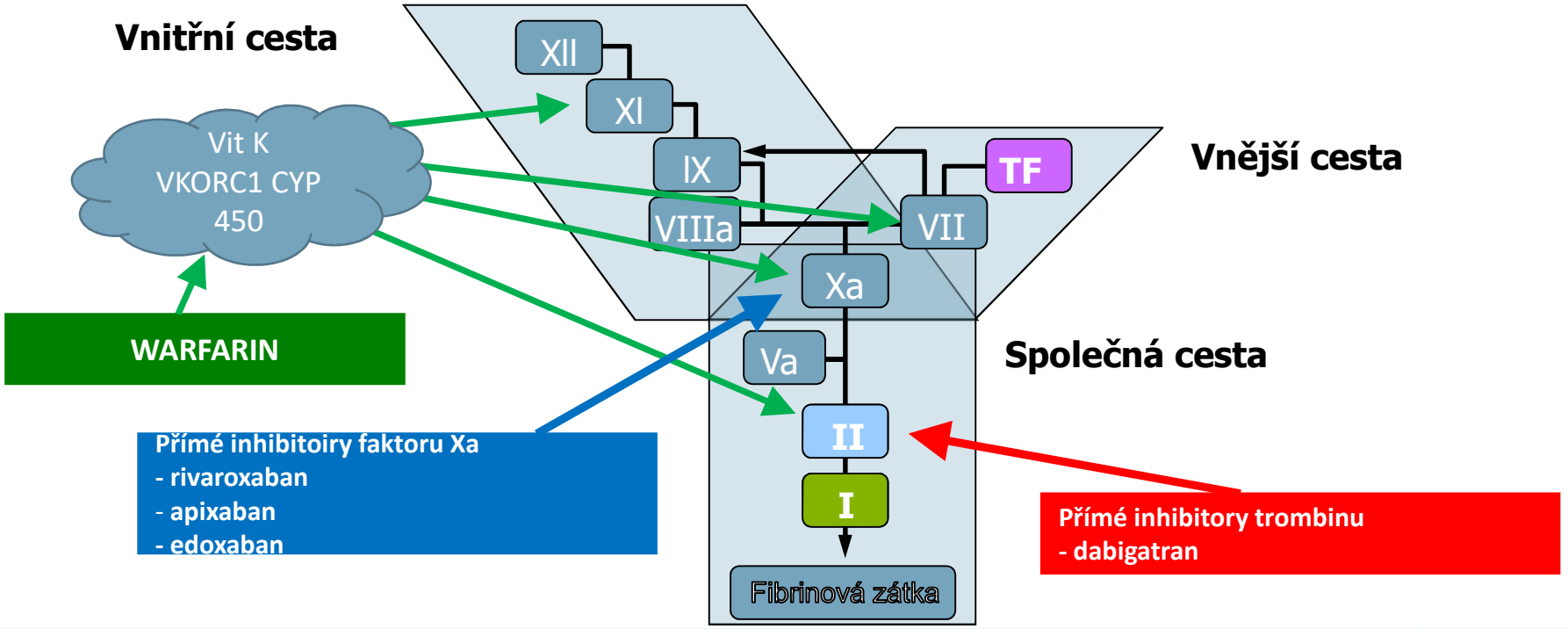
ORIGINAL ARTICLE

Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

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

| Outcome | Tenecteplase (N=506) | Placebo (N=499) | Odds Ratio (95% CI) | P Value |
|---|---|---|---|---|
| | *no. (%)* | | | |
| 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 | 12 (2.4) | 1 (0.2) | 12.10 (1.57–93.39) | 0.003 |
| Ischemic stroke | 2 (0.4) | 0 | | |
| Hemorrhagic stroke‡ | 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 |

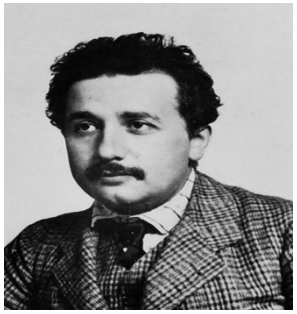
# Koagulační kaskáda

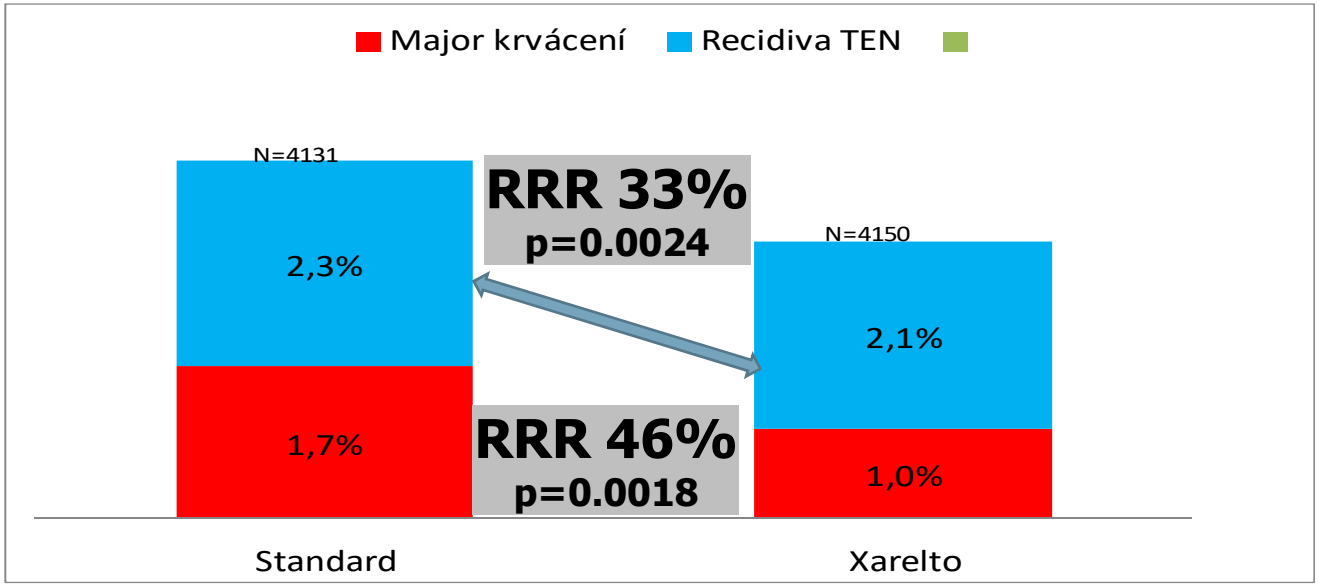




Převzato z Ansell J. J Thromb Haemost. 2007;5(suppl1):60-64.
Guyton AC, Hall JE. Hemostasis and blood coagulation. In: Textbook of Medical Physiology. 10th ed. Philadelphia, PA: WB Saunders Co; 2000:419-429.
Moake JL. Hemostasis. In: Porter RS, Kaplan JL, Homeier BP, eds. The Merck Manual Online

# EINSTEIN DVT a PE - výsledky



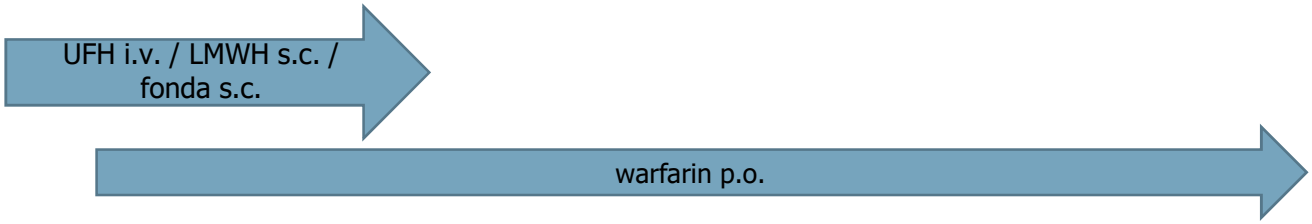



**Recidiva TEN:** Kompozit symptomatické rekurentní HŽT, symptomatické PE (fatální nebo nefatální), úmrtí asociovaného s TEN a progrese trombózy

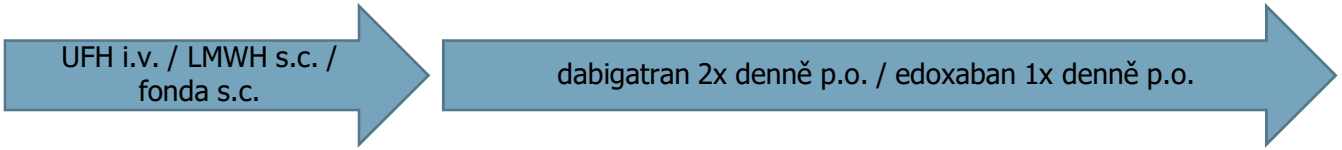
Buller H, Oral Rivaroxaban for the Treatment of Symptomatic Venous Thromboembolism: A Pooled Analysis of the EINSTEIN DVT and EINSTEIN PE Studies, ASH 2012, https://ash.confex.com/ash/2012/webprogram/Paper51556.html

# Terapeutické schémata

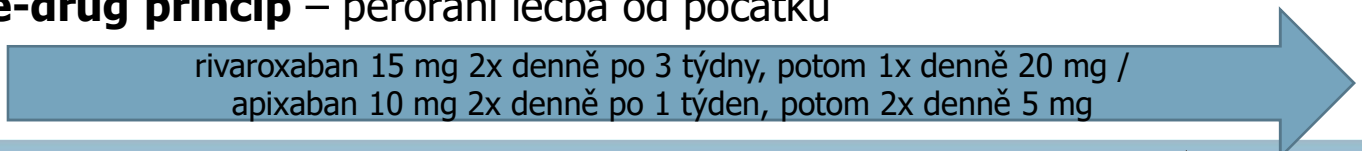
**Klasické schéma** – ***překrytí*** parenterálního antikoagulancia a warfarinu




**Sekvenční podávání** – zahájení léčby parenterálním antikoagulanciem a ***přechod*** na NOAC




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




SPC warfarin; SPC Pradaxa; SPC Xarelto; SPC Eliquis

# Nová ESC doporučení 2019

ESC European Heart Journal (2019) 00, 1–61 doi:10.1093/eurheartj/ehz405
ESC GUIDELINES

**2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS)**

The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC)

| Treatment in the acute phase | |
|---|---|
| When oral anticoagulation is initiated in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is the recommended form of anticoagulant treatment. | I |
| Set-up of multidisciplinary teams for management of high-risk and selected cases of intermediate-risk PE should be considered, depending on the resources and expertise available in each hospital. | IIa |
| ECMO may be considered, in combination with surgical embolectomy or catheter-directed treatment, in refractory circulatory collapse or cardiac arrest. | IIb |

| Chronic treatment and prevention of recurrence | |
|---|---|
| Indefinite treatment with a VKA is recommended for patients with antiphospholipid antibody syndrome. | I |
| Extended anticoagulation should be considered for patients with no identifiable risk factor for the index PE event. | IIa |
| Extended anticoagulation should be considered for patients with a persistent risk factor other than antiphospholipid antibody syndrome. | IIa |
| Extended anticoagulation should be considered for patients with a minor transient/reversible risk factor for the index PE event. | IIa |
| A reduced dose of apixaban or rivaroxaban should be considered after the first 6 months. | IIa |

Konstantinides SV. Eur Respir J. **2019** Aug 31. pii: 1901647. doi: 10.1183/13993003.01647-**2019**.

**Vascular Medicine**

## Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

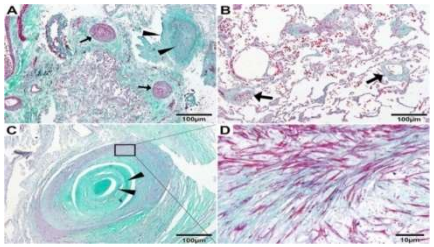
### Results From an International Prospective Registry

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

**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.




**Infekce**

**Zánět**

**Immunita**

**Genetická predispozice**

**Žilní trombóza**

**Plicní embolie**

**In situ trombózy**

**Nekompletní rezoluce a organizace trombu**

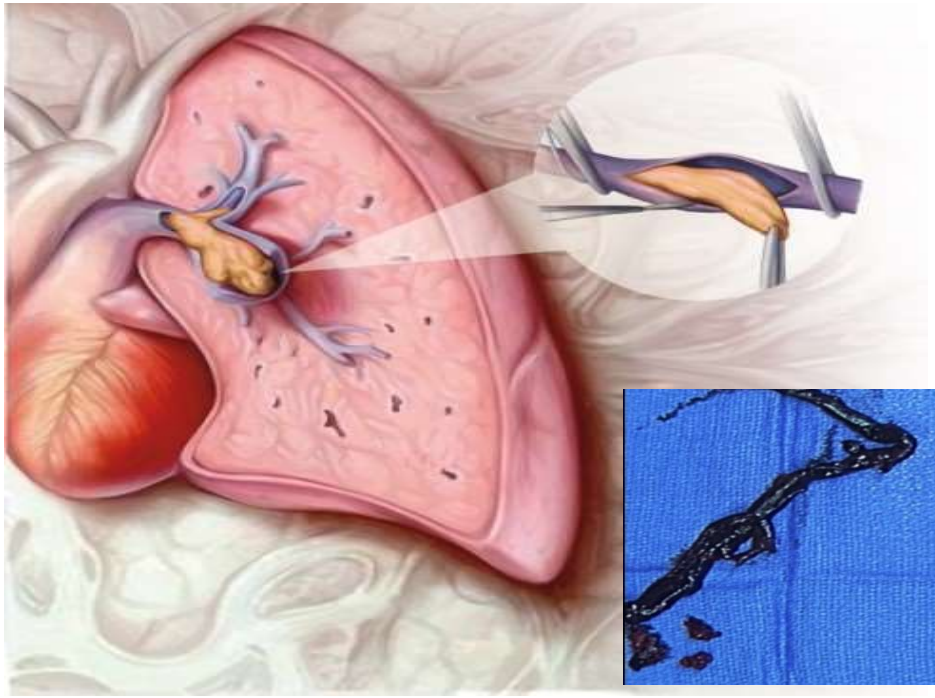
**Okluze/obliterace plicní tepny**

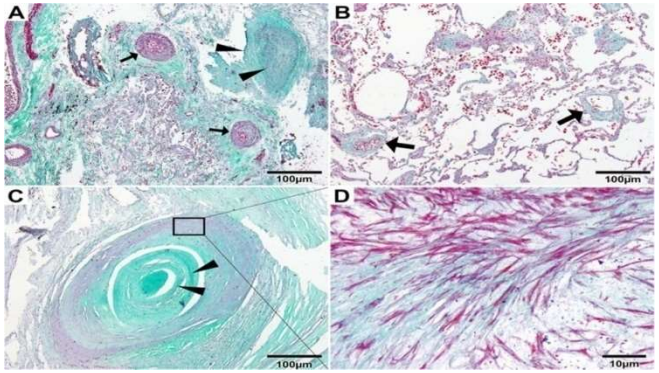
**↑ afterload pravé komory**

**Progresivní ↑ PVR**

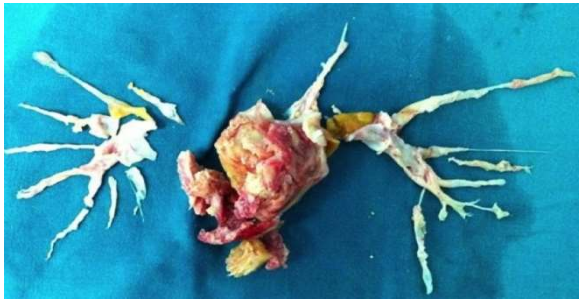
**CTEPH**

Zaba et al. Chronic thrombormbolic pulmonary hypertension. Circ. 2011;124(18):1973-1981




A
B
C
D
100μm
100μm
100μm
10μm





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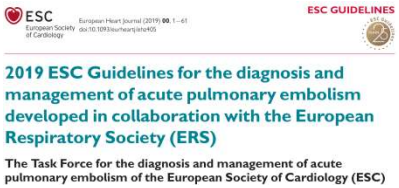
| PE in cancer | |
|---|---|
| Edoxaban or rivaroxaban should be considered as an alternative to LMWH, with the exception of patients with gastrointestinal cancer. | IIa |
| **PE in pregnancy** | |
| Amniotic fluid embolism should be considered in a pregnant or post-partum woman, with unexplained haemodynamic instability or respiratory deterioration, and disseminated intravascular coagulation. | IIa |
| Thrombolysis or surgical embolectomy should be considered for pregnant women with high-risk PE. | IIa |
| NOACs are not recommended during pregnancy or lactation. | III |

| Post-PE care and long-term sequelae | |
|---|---|
| Routine clinical evaluation is recommended 3–6 months after acute PE. | I |
| An integrated model of care is recommended after acute PE to ensure optimal transition from hospital to ambulatory care. | I |
| It is recommended that symptomatic patients with mismatched perfusion defects on a V/Q scan >3 months after acute PE are referred to a pulmonary hypertension/CTEPH expert centre, taking into account the results of echocardiography, natriuretic peptide, and/or cardiopulmonary exercise testing. | I |

*Mezi kontraindikace podání rivaroxabanu patří, mimo jiné, i léze nebo stavy, které jsou považovány za významné riziko závažného krvácení. Může mezi ně patřit přítomnost maligních nádorů s vysokým rizikem krvácení*

Konstantinides SV. Eur Respir J. **2019** Aug 31. pii: 1901647. doi: 10.1183/13993003.01647-**2019**.

# Key massages




1. In patients presenting with **haemodynamic instability**, perform bedside TTE as a fast, immediate step to differentiate suspected high-risk PE from other acute life-threatening situations.
2. If you suspect acute PE, institute **anticoagulation therapy as soon as possible**, while the diagnostic workup is ongoing, unless the patient is bleeding or has absolute contraindications to this therapy.
3. Use recommended, **validated diagnostic algorithms for PE**, including standardized assessment of (pre-test) clinical probability and D-dimer testing. They help to avoid unnecessary, expensive, and potentially harmful imaging tests and exposure to ionizing radiation.
4. If the CTPA report suggests single subsegmental PE, consider the **possibility of a false-positive finding**. Discuss the findings again with the radiologist and/or seek a second opinion to avoid misdiagnosis, and unnecessary, potentially harmful anticoagulation treatment.
5. Confirmation of PE in a patient, without haemodynamic instability, must be followed by **further risk assessment** involving clinical findings, evaluation of the size and/or function of the RV, and laboratory biomarkers as appropriate. This information will help you to decide on the need for reperfusion treatment or monitoring for patients at elevated risk, or consider the option of early discharge and continuation of anticoagulation on an ambulatory basis for patients at low risk.

6. As soon as you diagnose (or strongly suspect) high-risk PE, select the best **reperfusion option** (systemic thrombolysis, surgical embolectomy, or catheter-directed treatment) considering the patient's risk profile, and the resources and expertise available at your hospital. For patients with intermediate–high-risk PE, reperfusion is not first-line treatment, but you should prospectively plan the management strategy with your team to have a contingency plan ready if the situation deteriorates.

**7.** **Prefer anticoagulation with a NOAC** over the 'traditional' LMWH–VKA regimen unless the patient has contraindication(s) to this type of drug.

8. Always remember that, with the exception of acute PE provoked by a strong transient/reversible risk factor, there is a lifelong risk of VTE recurrence after a first episode of PE. Consequently, re-examine the patient after the first 3 – 6 months of anticoagulation, weigh the benefits vs. risks of continuing treatment, **and decide on the extension and dose of anticoagulant therapy**, also considering the patient's preference. Remember to recommend regular follow-up examinations, e.g. at yearly intervals.

9. If you suspect PE in a **pregnant patient**, consider diagnostic pathways and algorithms including CTPA or V/Q lung scan, which can be used safely during pregnancy.

10. After acute PE, **patients should not be lost to follow-up**. Apart from checking for possible signs of VTE recurrence, cancer, or bleeding complications of anticoagulation, ask the patient if there is persisting or new-onset dyspnoea or functional limitation. If yes, implement a staged diagnostic workup to exclude CTEPH or chronic thromboembolic disease, and to detect/treat comorbidity or 'simple' deconditioning. Follow-up imaging is not routinely recommended in an asymptomatic patient, but it may be considered in patients with risk factors for development of CTEPH.


# DĚKUJEME ZA POZORNOST

FAKULTNÍ NEMOCNICE OLOMOUC

KOMPLEXNÍ
KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC