Guidelines ESC 2019 – Plicní embolie

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Assessment of pre-test probability (cont'd)

Clinical prediction rules for pulmonary embolism (cont.)		
	Clinical decision rule points	
Revised Geneva score	**Original version**	**Simplified version**
Previous DVT or PE	3	1
Heart rate 75-94 b.p.m. ≥95 b.p.m.	 3 5	 1 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

Recommendations for diagnosis (3)

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Recommendations	Class	Level
D-dimer		
Plasma D-dimer measurement, preferably using a highly sensitive assay, is recommended in outpatients/emergency department patients with low or intermediate clinical probability, or PE-unlikely, to reduce the need for unnecessary imaging and irradiation.	I	A
As an alternative to the fixed D-dimer cut-off, a negative D-dimer test using an age-adjusted cut-off (age x 10 µg/L, in patients >50 years) should be considered for excluding PE in patients with low or intermediate clinical probability, or PE-unlikely.	IIa	B

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Recommendations for diagnosis (4)

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Recommendations	Class	Level
D-dimer (cont'd)		
As an alternative to the fixed or age-adjusted D-dimer cut-off, D-dimer levels adapted to clinical probability should be considered for excluding PE.	IIa	B
D-dimer measurement is not recommended in patients with high clinical probability, as a normal result does not safely exclude PE, even when using a highly sensitive assay.	III	A
CTPA		
It is recommended to reject the diagnosis of PE (without further testing) if CTPA is normal in a patient with low or intermediate clinical probability, or PE-unlikely.	I	A

CTPA = computed tomography pulmonary angiography.

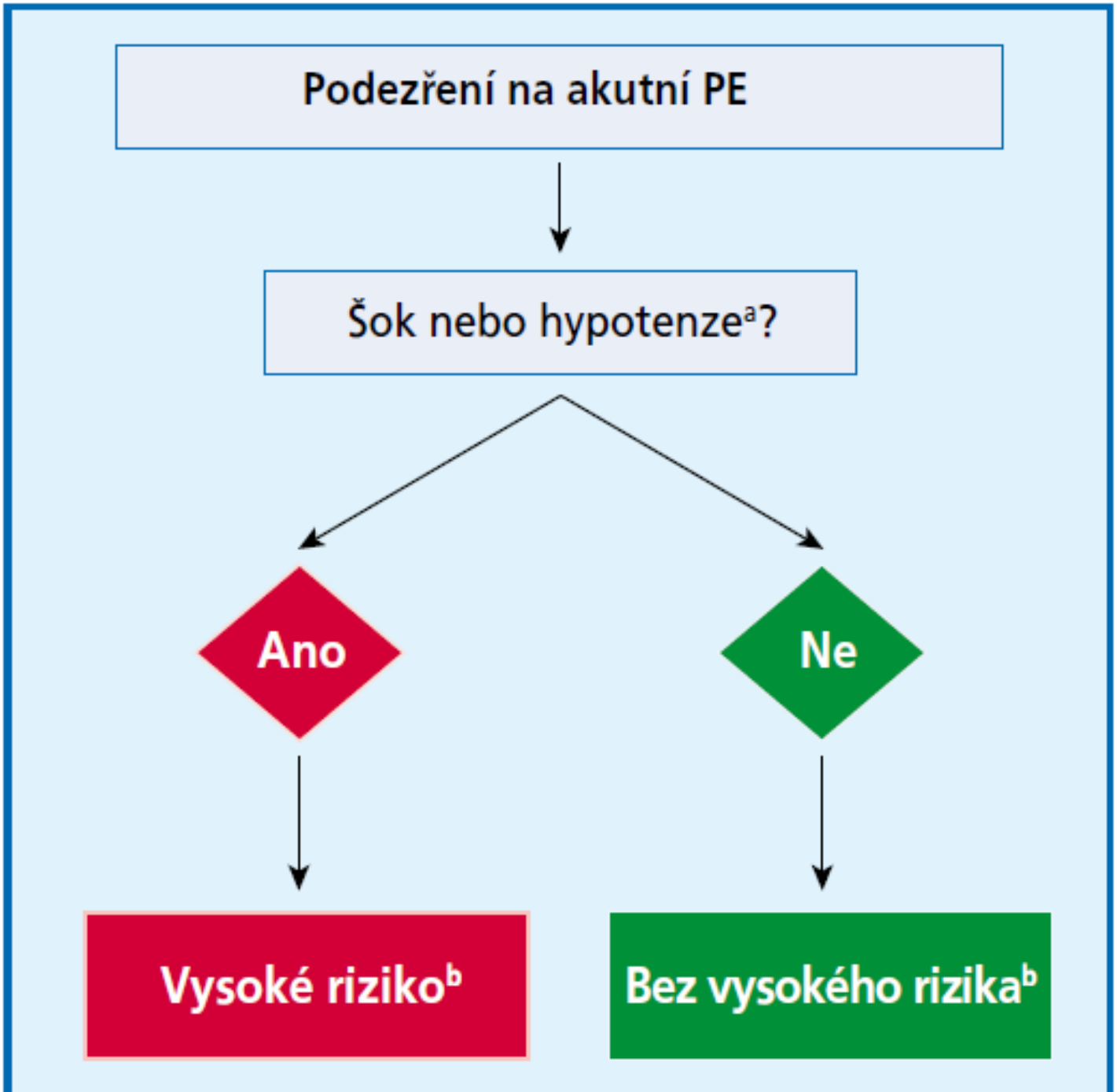
Podezření na akutní PE
Šok nebo hypotenze[a]?
Ano
Ne
Vysoké riziko[b]
Bez vysokého rizika[b]

Table 4 Definition of haemodynamic instability

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(1) Cardiac arrest	(2) Obstructive shock	(3) Persistent hypotension
Need for cardiopulmonary resuscitation	Systolic BP <90 mmHg, or vasopressors required to achieve a BP ≥90 mmHg despite adequate filling status	Systolic BP <90 mmHg, or systolic BP drop ≥40 mmHg, either lasting longer than 15 minutes and not caused by new-onset arrhythmia, hypovolaemia, or sepsis
	And	
	End-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)	

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Figure 2 TTE parameters of RV pressure overload (1)

A. Enlarged right ventricle, parasternal long axis view

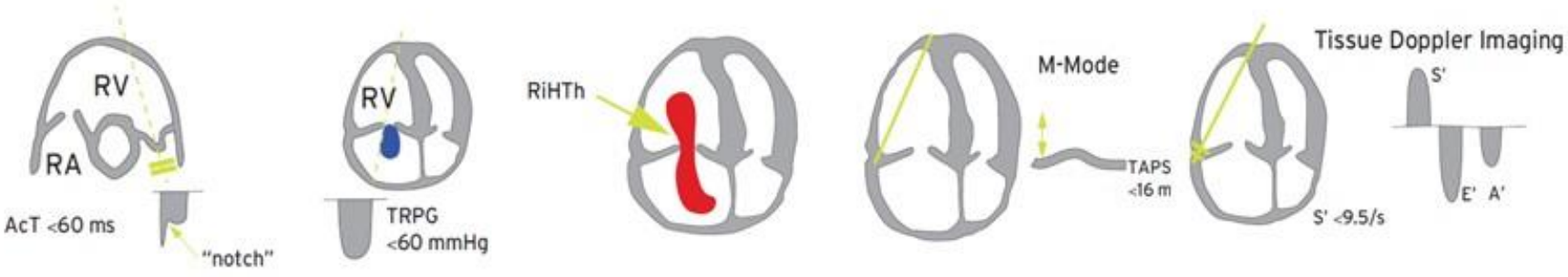
B. Dilated RV with basal RV/LV ratio >1.0, and McConnell sign (arrow), four chamber view

C. Flattened interventricular septum (arrows) parasternal short axis view

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

RV = right ventricular; TTE = transthoracic echocardiography/echocardiographic.

Figure 2 TTE parameters of RV pressure overload (2)



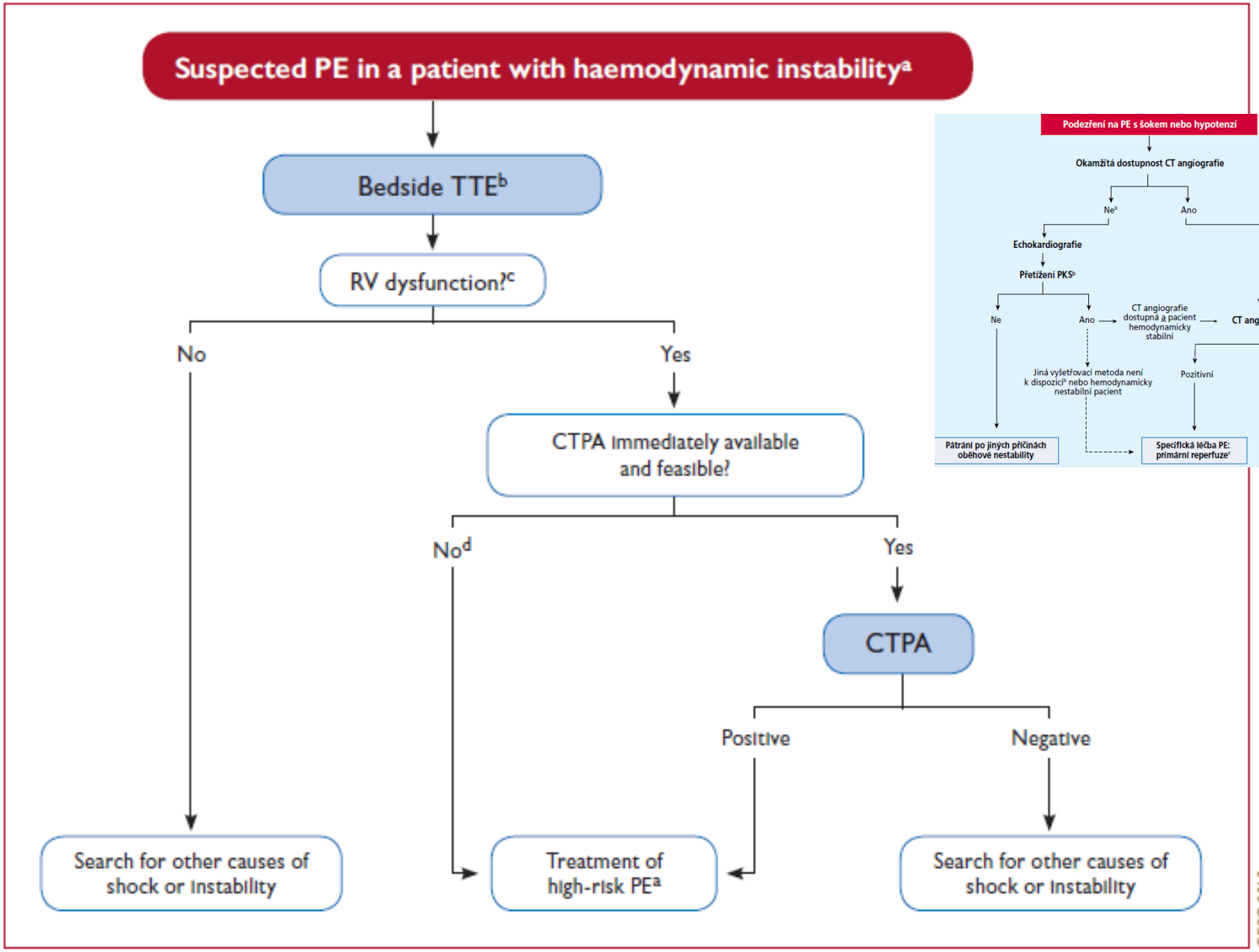
E. 60/60 sign: coexistence of acceleration time of pulmonary ejection <60 ms and midsystolic "notch" with mildy elevated (<60 mmHg) peak systolic gradient at the tricuspic valve

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)

RV = right ventricular; TTE = transthoracic echocardiography/echocardiographic.



In suspected high-risk PE, as indicated by the presence of haemodynamic instability, bedside echocardiography or emergency CTPA (depending on availability and clinical circumstances) is recommended for diagnosis.[169]

I C

Suspected PE in a patient without haemodynamic instability[a]

Assess clinical probability of PE
Clinical judgement or prediction rule[b]

Low or intermediate clinical probability, or PE unlikely

D-dimer test

Negative

No treatment[c]

Positive

CTPA

No PE

No treatment[c]

PE confirmed[d]

Treatment[c]

High clinical probability or PE likely

CTPA

No PE

No treatment[c] or investigate further[e]

PE confirmed[d]

Treatment[c]

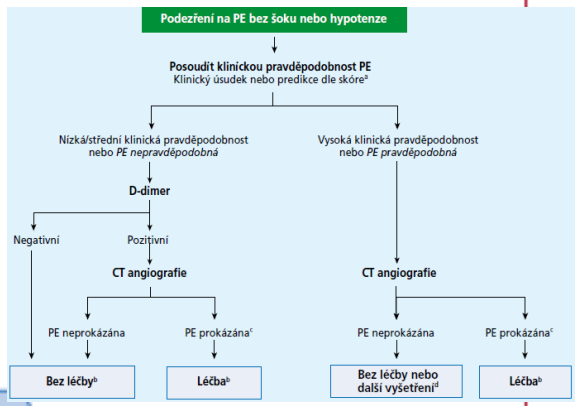


Table 9 Classification of PE based on early mortality risk

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Early mortality risk		Indicators of risk			
		Haemo-dynamic instability	Clinical parameters of PE severity/ comorbidity: PESI III–V or sPESI ≥1	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
High		+	(+)	+	(+)
Interme-diate	Intermediate–high	-	+	+	+
	Intermediate–low	-	+	One (or none) positive	
Low		-	-	-	Assessment optional; if assessed, negative

CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; TTE = transthoracic echocardiography.

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Index závažnosti PE (PESI – pulmonary embolism severity index)

Parametr	Zjednodušená verze
Věk	1 bod (pokud věk > 80 let)
Mužské pohlaví	–
Nádorové onemocnění	1 bod
Chronické srdeční selhání	1 bod
Chronické plicní onemocnění	
Srdeční frekvence ≥ 110 tepů/min	1 bod
Systolický krevní tlak < 100 mm Hg	1 bod
Dechová frekvence > 30 dechů/min	–
Teplota < 36 °C	–
Změněný duševní stav	–
Arteriální saturace oxyhemoglobinu < 90 %	1 bod

0 bodů - 30d riziko úmrtí 1 %

≥ 1 bod - 30d riziko úmrtí 10,9 %

Figure 5 Risk-adjusted management strategy for acute PE (1)

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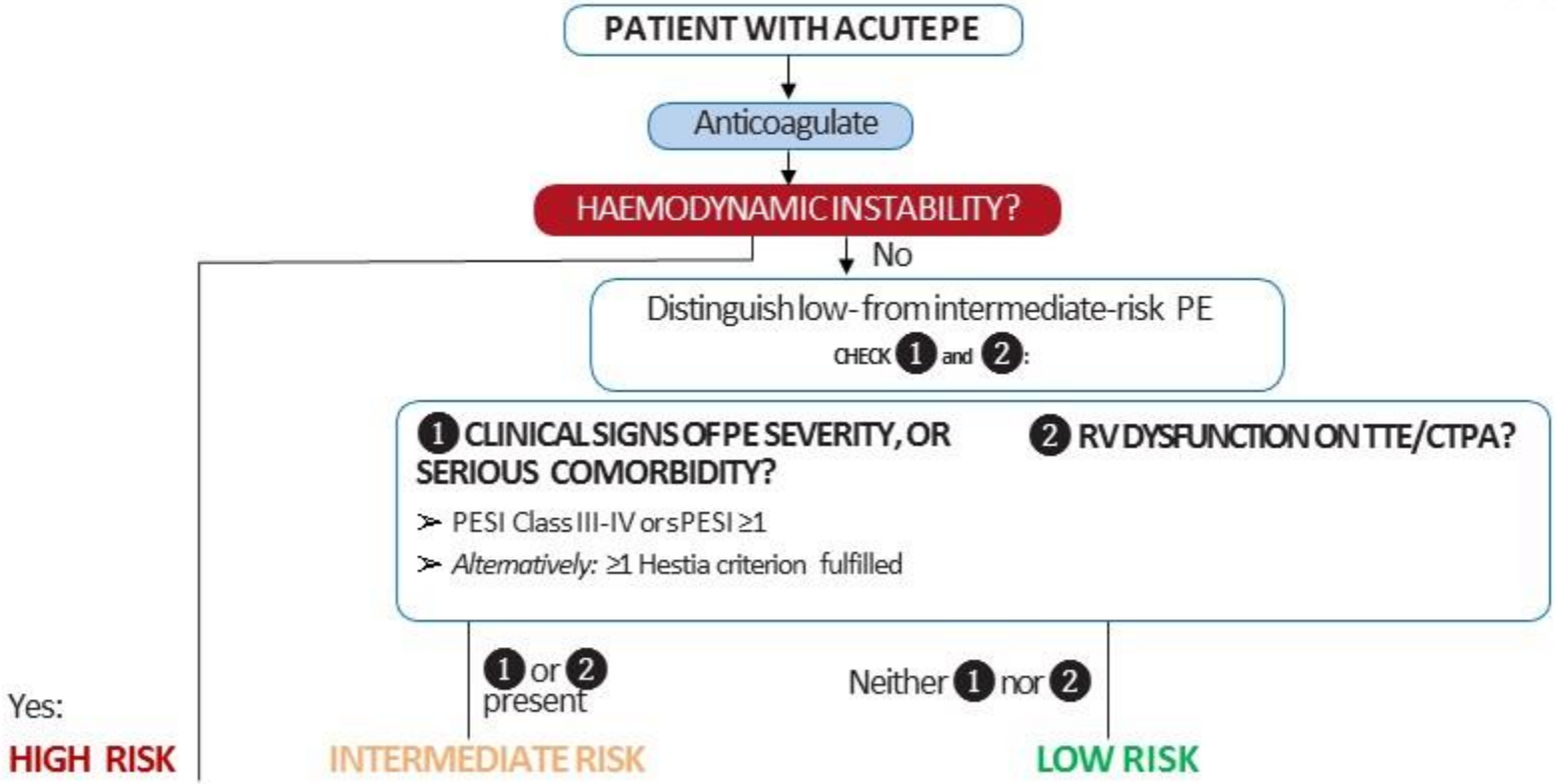

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Figure 5 Risk-adjusted management strategy for acute PE (2)

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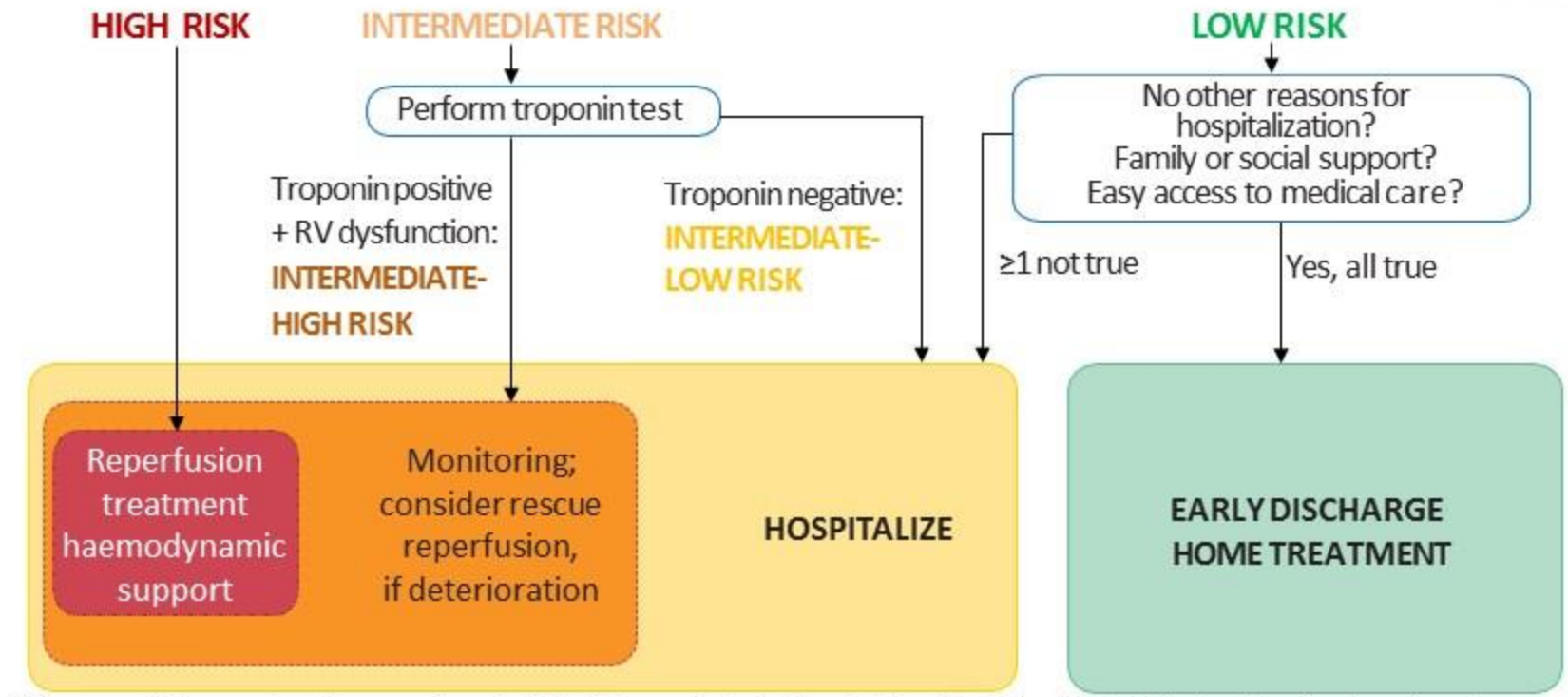

CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; RV = right ventricular; TTE = transthoracic echocardiography.

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Recommendations	Class	Level
Carefully selected patients with 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	A

Table 12 Thrombolytic doses and contraindications (1)

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Molecule	Regimen	Contraindications to fibrinolysis
Recombinant tissue-type plasminogen activator (rtPA)	100 mg over 2 h	**Absolute** • History of haemorrhagic stroke or stroke of unknown origin • Ischaemic stroke in previous 6 months • Central nervous system neoplasm • Major trauma, surgery, or head injury in previous 3 weeks • Bleeding diathesis • Active bleeding
	0.6 mg/kg over 15 min (maximum dose 50 mg)	
Streptokinase	250,000 IU as a loading dose over 30 min, followed by 100,000 IU/h over 12–24 h	
	Accelerated regimen: 1.5 million IU over 2 h	

ECMO – může být zváženo (II b) v kombinaci s chirurgickou embolektomií nebo katetrovou léčbou při zhroucení cirkulace nebo srdeční zástavě

Table 10 Treatment of RV failure in acute high-risk PE (2)

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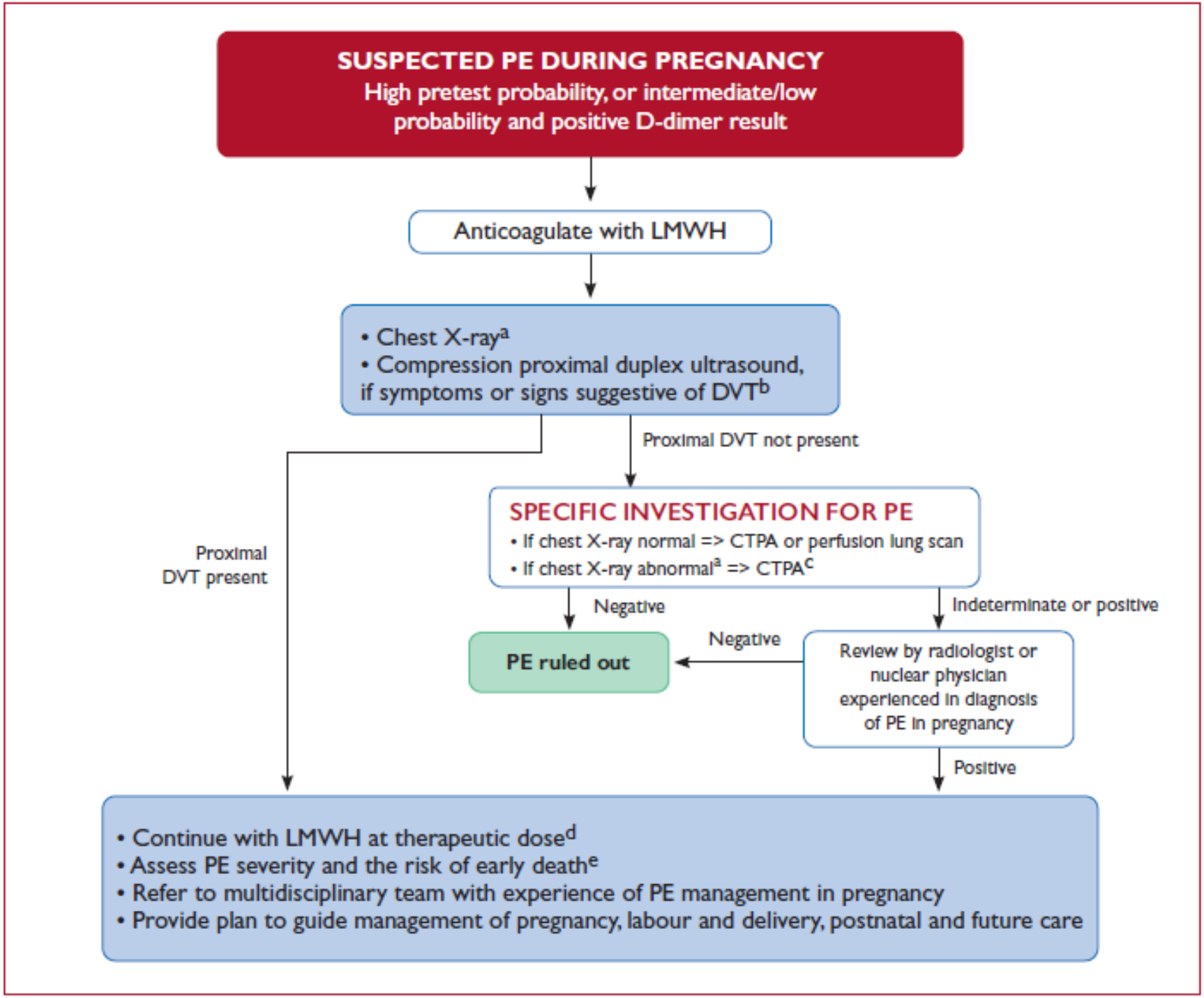
Vasopressors and inotropes		
Norepinephrine, 0.2–1.0μg/kg/min	Increases RV inotropy, systemic BP; promotes positive ventricular interactions; restores coronary perfusion gradient	Excessive vasoconstriction may worsen tissue perfusion
Dobutamine, 2–20 μg/kg/min	Increases RV inotropy, lowers filling pressures	May aggravate arterial hypotension if used alone, without a vasopressor; may trigger or aggravate arrhythmias

BP = blood pressure; RV = right ventricular.

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)


SUSPECTED PE DURING PREGNANCY
High pretest probability, or intermediate/low probability and positive D-dimer result
Anticoagulate with LMWH
• Chest X-ray[a]
• Compression proximal duplex ultrasound, if symptoms or signs suggestive of DVT[b]
Proximal DVT not present
Proximal DVT present
SPECIFIC INVESTIGATION FOR PE
• If chest X-ray normal => CTPA or perfusion lung scan
• If chest X-ray abnormal[a] => CTPA[c]
Negative
Indeterminate or positive
PE ruled out
Negative
Review by radiologist or nuclear physician experienced in diagnosis of PE in pregnancy
Positive
• Continue with LMWH at therapeutic dose[d]
• Assess PE severity and the risk of early death[e]
• Refer to multidisciplinary team with experience of PE management in pregnancy
• Provide plan to guide management of pregnancy, labour and delivery, postnatal and future care

Predisposing factors for venous thromboembolism

Strong risk factors (odds ratio >10)
Fracture of lower limb
Hospitalization for heart failure or atrial fibrillation/flutter (within previous 3 months)
Hip or knee replacement
Major trauma
Myocardial infarction (within previous 3 months)
Previous venous thromboembolism
Spinal cord injury
Moderate risk factors (odds ratio 2-9)
Arthroscopic knee surgery
Auto-immune diseases
Blood transfusion
Central venous lines
Chemotherapy
Congestive heart or respiratory failure
Erythropoiesis-stimulating agents
Hormone replacement therapy (depends on formulation)
In vitro fertilization

Predisposing factors for VTE (cont'd)

Infection (specifically pneumonia, urinary tract infection and HIV)
Inflammatory bowel disease
Cancer (highest risk in metastatic disease)
Oral contraceptive therapy
Paralytic stroke
Postpartum period
Superficial vein thrombosis
Thrombophilia
Weak risk factors (odds ratio <2)
Bed rest >3 days
Diabetes mellitus
Hypertension
Immobility due to sitting (e.g. prolonged car or air travel)
Increasing age
Laparoscopic surgery (e.g. cholecystectomy)
Obesity
Pregnancy
Varicose veins

Table 11 Categorization of risk factors for venous thromboembolism based on the risk of recurrence over the long-term

Estimated risk for long-term recurrence[a]	Risk factor category for index PE[b]	Examples[b]
Low (<3% per year)	Major transient or reversible factors associated with >10-fold increased risk for the index VTE event (compared to patients without the risk factor)	• Surgery with general anaesthesia for >30 min • Confined to bed in hospital (only "bathroom privileges") for ≥3 days due to an acute illness, or acute exacerbation of a chronic illness • Trauma with fractures
Intermediate (3–8% per year)	Transient or reversible factors associated with ≤10-fold increased risk for first (index) VTE	• Minor surgery (general anaesthesia for <30 min) • Admission to hospital for <3 days with an acute illness • Oestrogen therapy/contraception • Pregnancy or puerperium • Confined to bed out of hospital for ≥3 days with an acute illness • Leg injury (without fracture) associated with reduced mobility for ≥3 days • Long-haul flight
	Non-malignant persistent risk factors	• Inflammatory bowel disease • Active autoimmune disease
	No identifiable risk factor	
High (>8% per year)		• Active cancer • One or more previous episodes of VTE in the absence of a major transient or reversible factor • Antiphospholipid antibody syndrome

Doba antikoagulace

Doporučení	Třída	Úroveň znalostí
≥ 3 měsíce všichni pacienti s PE	I	A
První PE + velký přechodný/reverzibilní RF – po 3 M ukončit	I	B
Dlouhodobá AK – rekurentní PE bez velkého RF nebo pro pacienty s antifosfolipidovým sy	I	B
Prodloužená (nad 3 M, indefinite..) 1. epizoda bez RF 1. epizoda s RF jiným než AF sy 1. epizoda PE s malým RF	IIa	C
Prodloužená AK u pacientů bez nádoru apixaban 2 x 2,5 mg nebo rivaroxaban 10 mg po 6 M	IIa	A

Table 1 Changes in recommendations 2014-2019

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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 postpartum period.	IIb	IIa
Further evaluation may be considered for asymptomatic PEsurvivors at increased risk for CTEPH.	III	IIb

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Table 2 Main new recommendations 2019 (2)

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Risk assessment	
Assessing the RV by imaging or laboratory biomarkers should be considered even in the presence of a low PESI or a sPESI of 0.	IIa
Validated scores combining clinical, imaging and laboratory prognostic factors may be considered to further stratify PE severity.	IIb

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Table 2 Main new recommendations 2019 (3)

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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

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Table 2 Main new recommendations 2019 (5)

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Pulmonary embolism in patients with cancer	
Edoxaban or rivaroxaban should be considered as an alternative to LMWH, with the exception of patients with gastrointestinal cancer.	IIa
Pulmonary embolism in pregnancy	
Amniotic fluid embolism should be considered in a pregnant or postpartum 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

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Table 2 Main new recommendations 2019 (6)

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

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Děkuji za pozornost

Table 13 Hestia exclusion criteria for outpatient management of PE (1)

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Criterion/question
Is the patient haemodynamically unstable?
Is thrombolysis or embolectomy necessary?
Active bleeding or high risk of bleeding?
More than 24 h of oxygen supply to maintain oxygen saturation >90%?
Is PE diagnosed during anticoagulant treatment?
Severe pain needing i.v. pain medication for more than 24 h?

If at least one of the questions is answered with „yes", the patient cannot be discharged early.

Table 13 Hestia exclusion criteria for outpatient management of PE (2)

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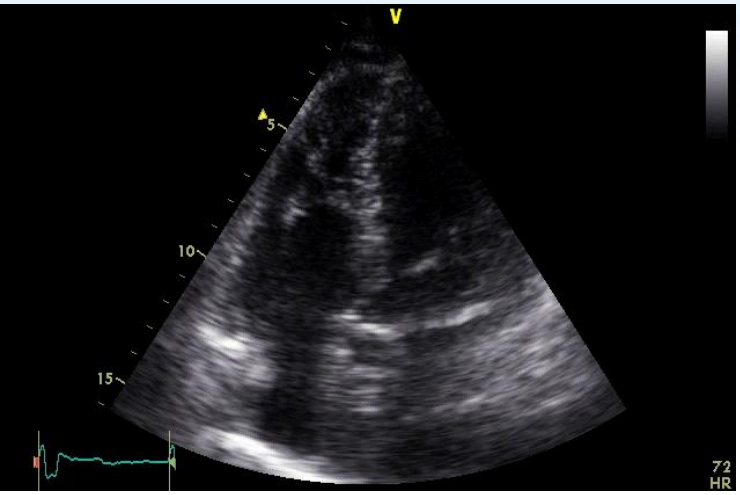
Medical or social reason for treatment in the hospital for more than 24 h (infection, malignancy, no support system)?
Does the patient have a CrCl of <30 mL/min?
Does the patient have severe liver impairment?
Is the patient pregnant?
Does the patient have a documented history of heparin-induced thrombocytopenia?

If at least one of the questions is answered with „yes", the patient cannot be discharged early.
CrCl = creatinine clearance.

Echokardiografie

- není doporučena u hemodynamicky stabilních, normotenzních pacientů s podezřením na PE (senzitivita cca 50 %)
- dif. dg. oběhové nestability, dušnosti, bolestí na hrudi a ↑ kardiomarkerů (šok + stavy s podobným obrazem jako PE)
- diagnostika při podezření na „high risk“ PE
- riziková stratifikace u nemocných s akutní PE
- echokardiografie by měla být provedena před dimisí u všech nemocných s PE s vysokým nebo (vyšším) středním rizikem (sledování účinnosti léčby)

ECHO nálezy u PE



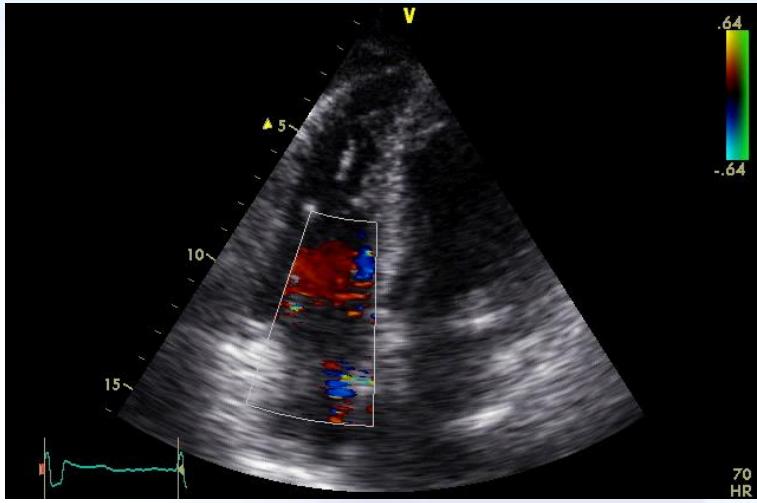
rozšíření PKS

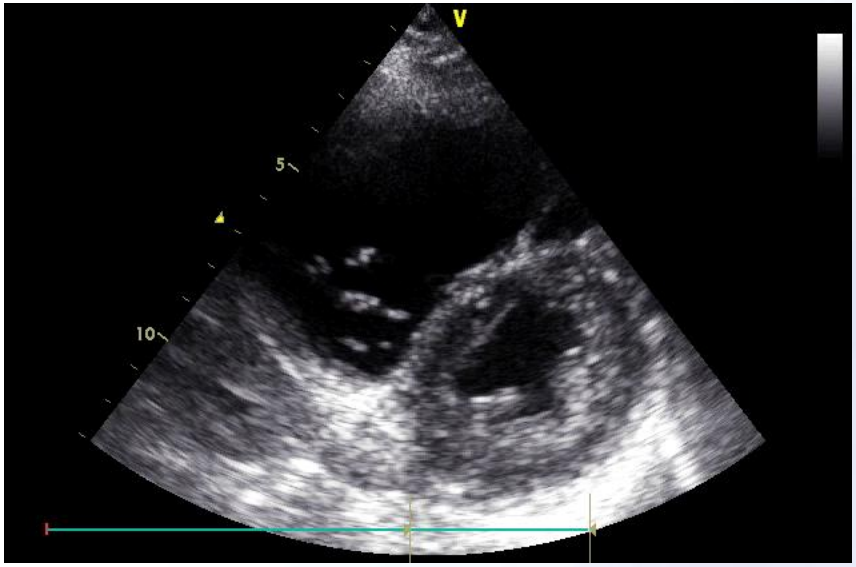
↑ PKS/LKS

dysf-ce PKS

Mc Connelovo zn

trikuspid. reg.





D-shape, hyperdynamická LKS

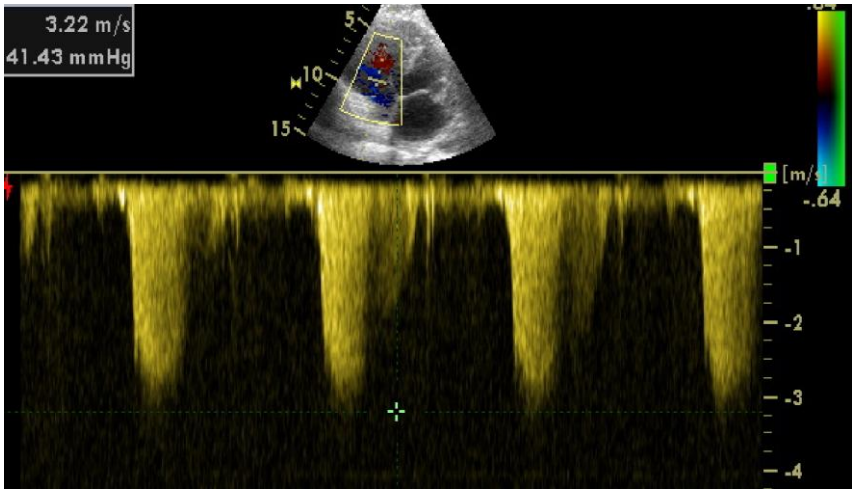
diastolická dysf-ce LKS

ECHO nálezy u PE

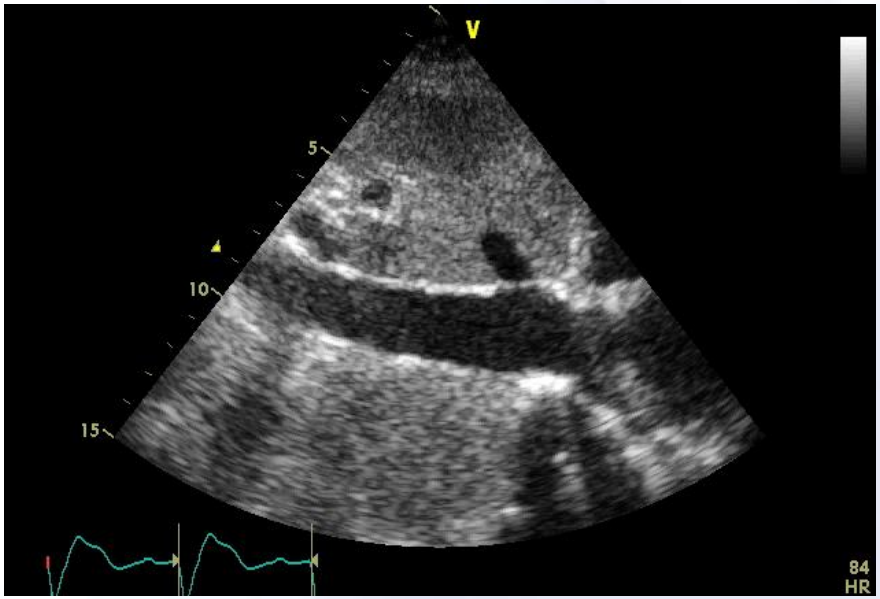
plicní hypertenze

trikusp. reg. tok . > 2.5 m/s

3,2 m/s
41mmHg

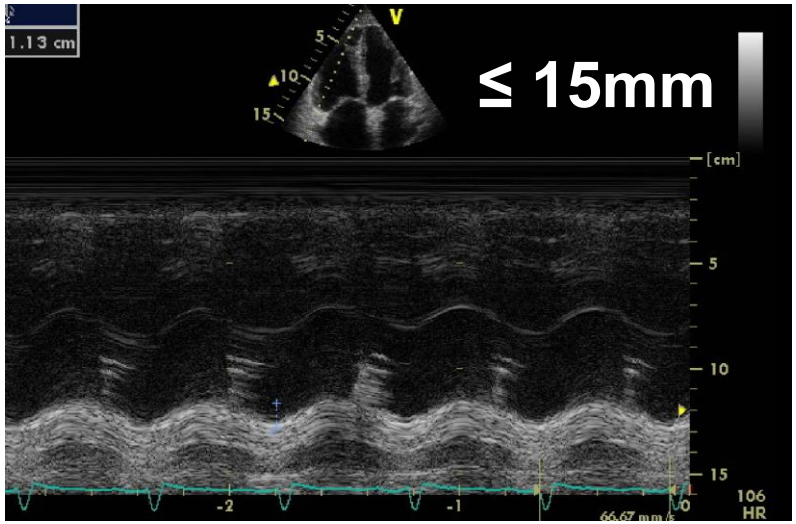


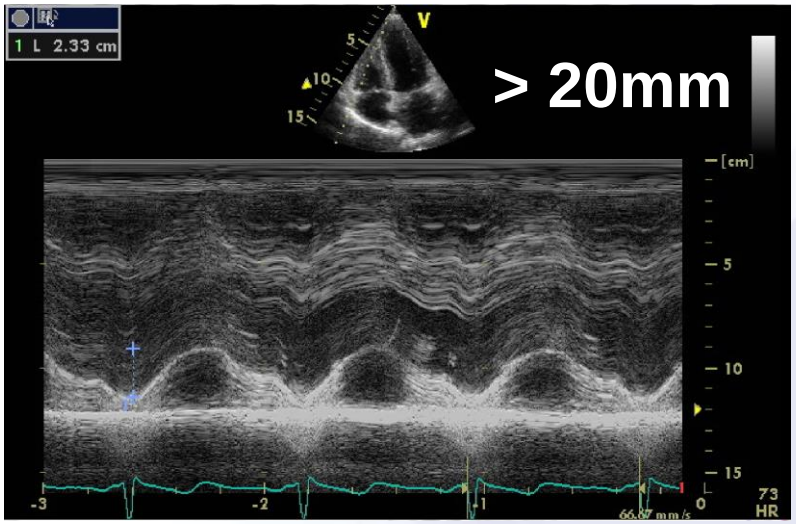
rozšíření a ↓ kolaps DDŽ



TAPSE

- účinnější prediktor časné mortality než PK/LK, aj.





411 iniciálně normotenz. pac. s APE

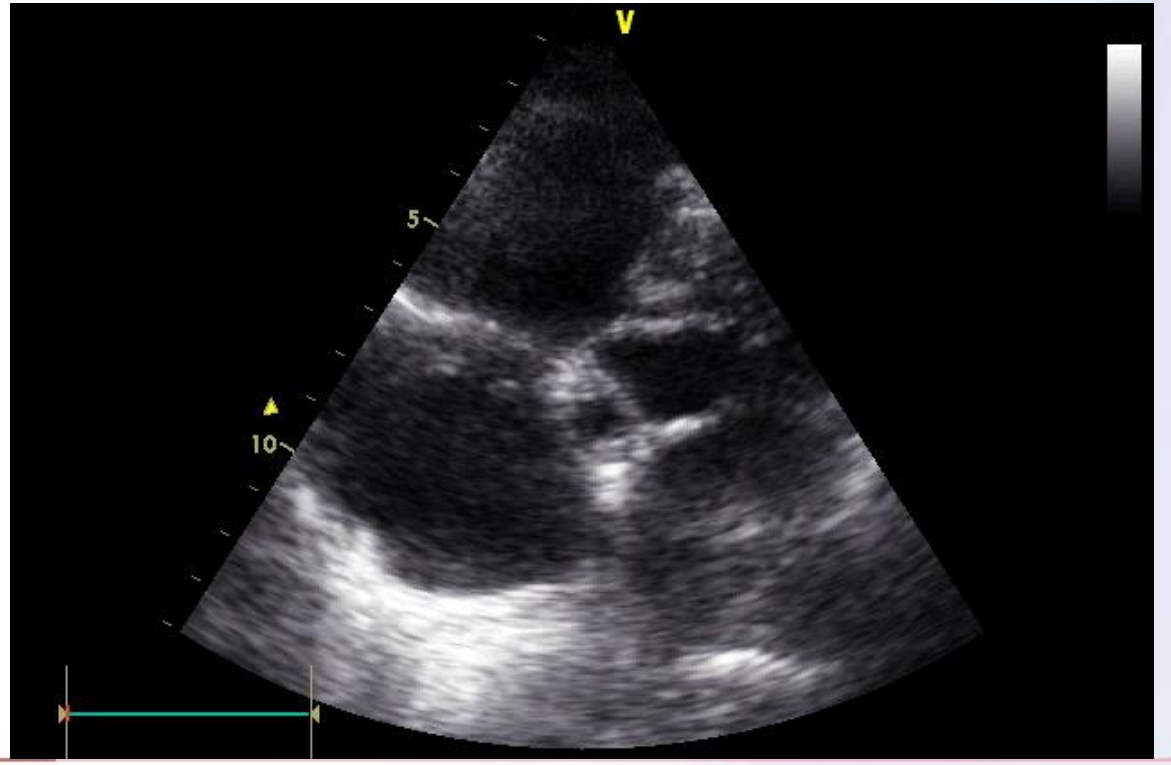
21 % riziko smrti / „rescue“ trombolýzy

žádná smrt / „rescue“ trombolýza

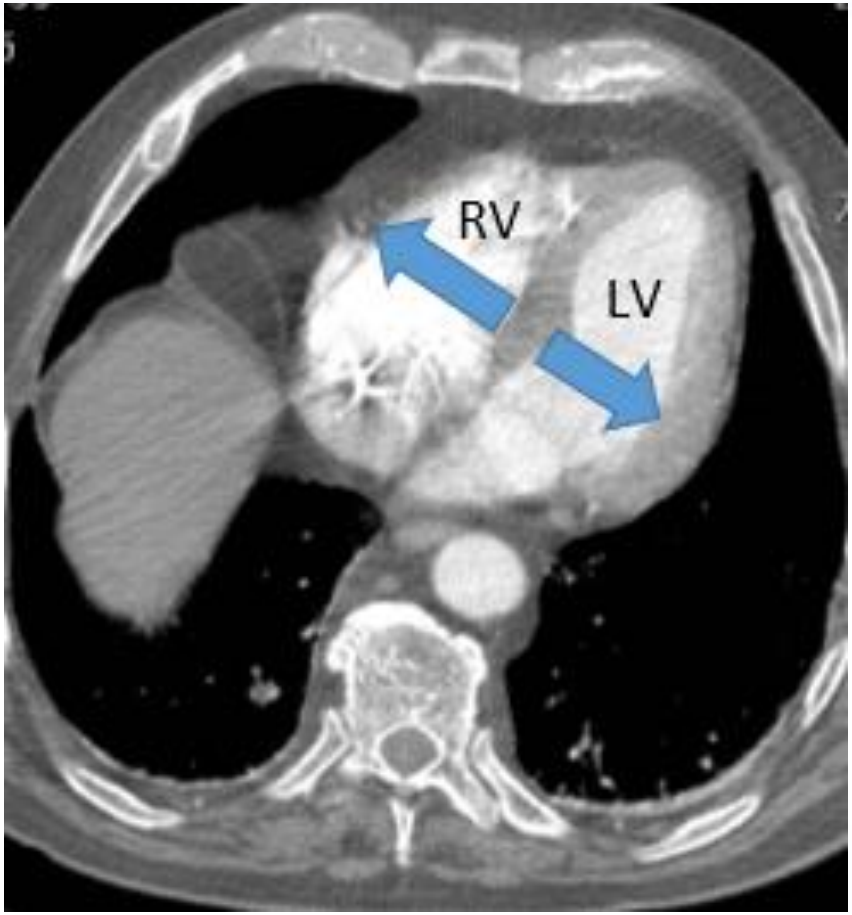
Pruszczyk P et al., JACC, 2014

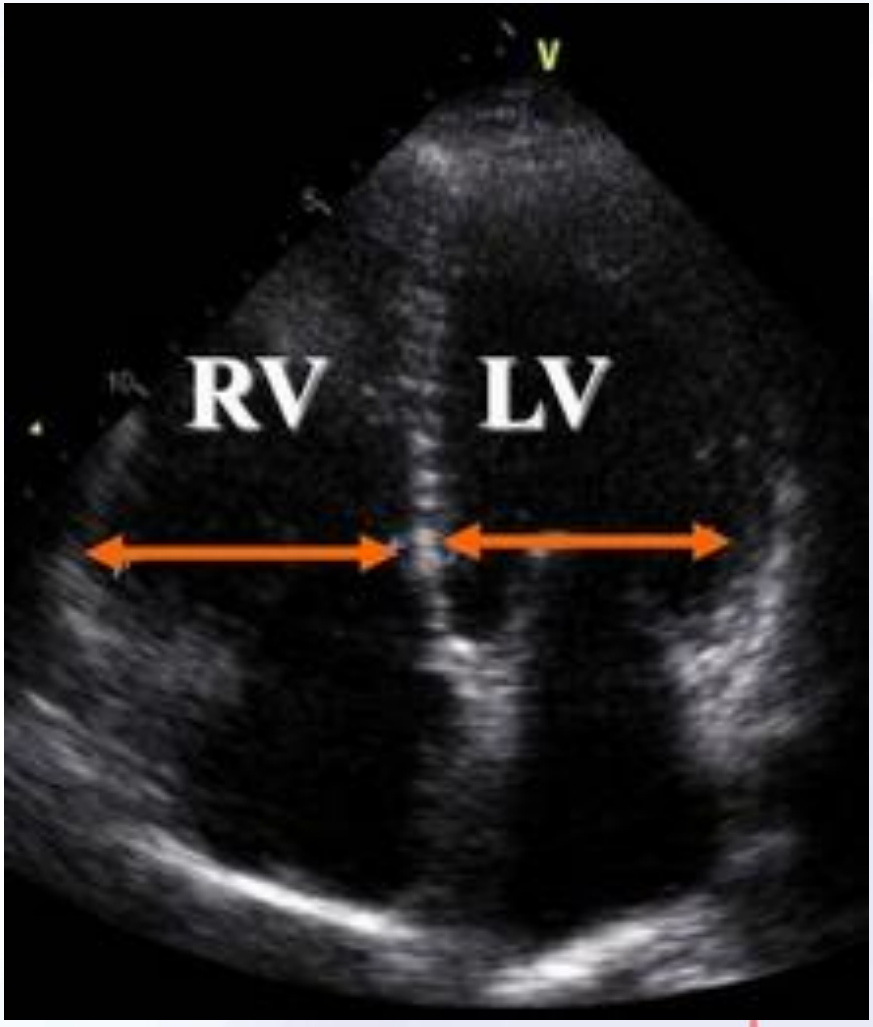
Mobilní pravostranné tromby

- potvrzují dg. PE
- ↑ časná mortalita
- u neselekt. PE < 4 %
- u PE na JIP až 18 %



Torbicki et al., JACC 2003





RV/LV EDD > 1,0

Figure 7 Follow-up strategy and diagnostic work-up for long-term sequelae of PE (1)

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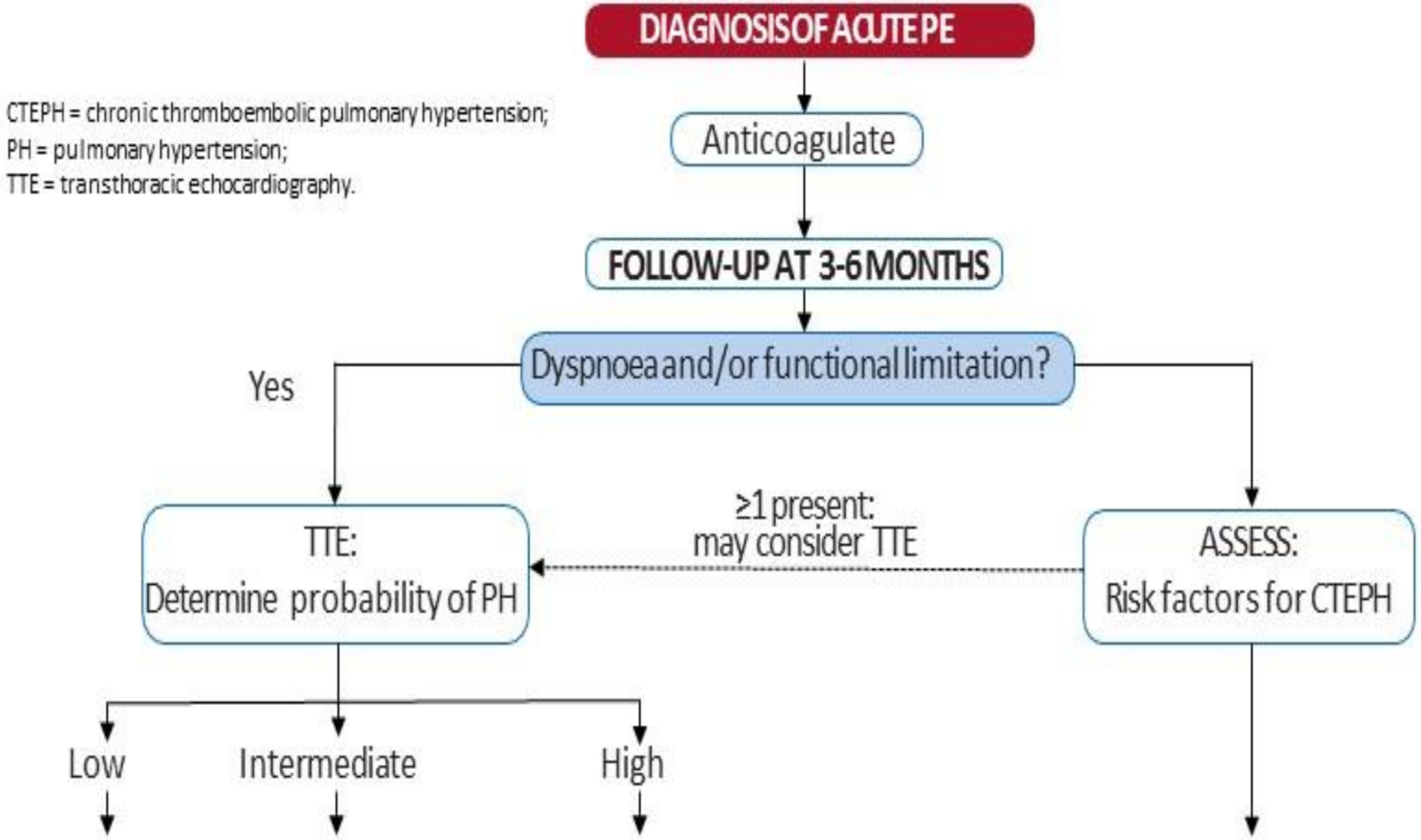

CTEPH = chronic thromboembolic pulmonary hypertension;
PH = pulmonary hypertension;
TTE = transthoracic echocardiography.

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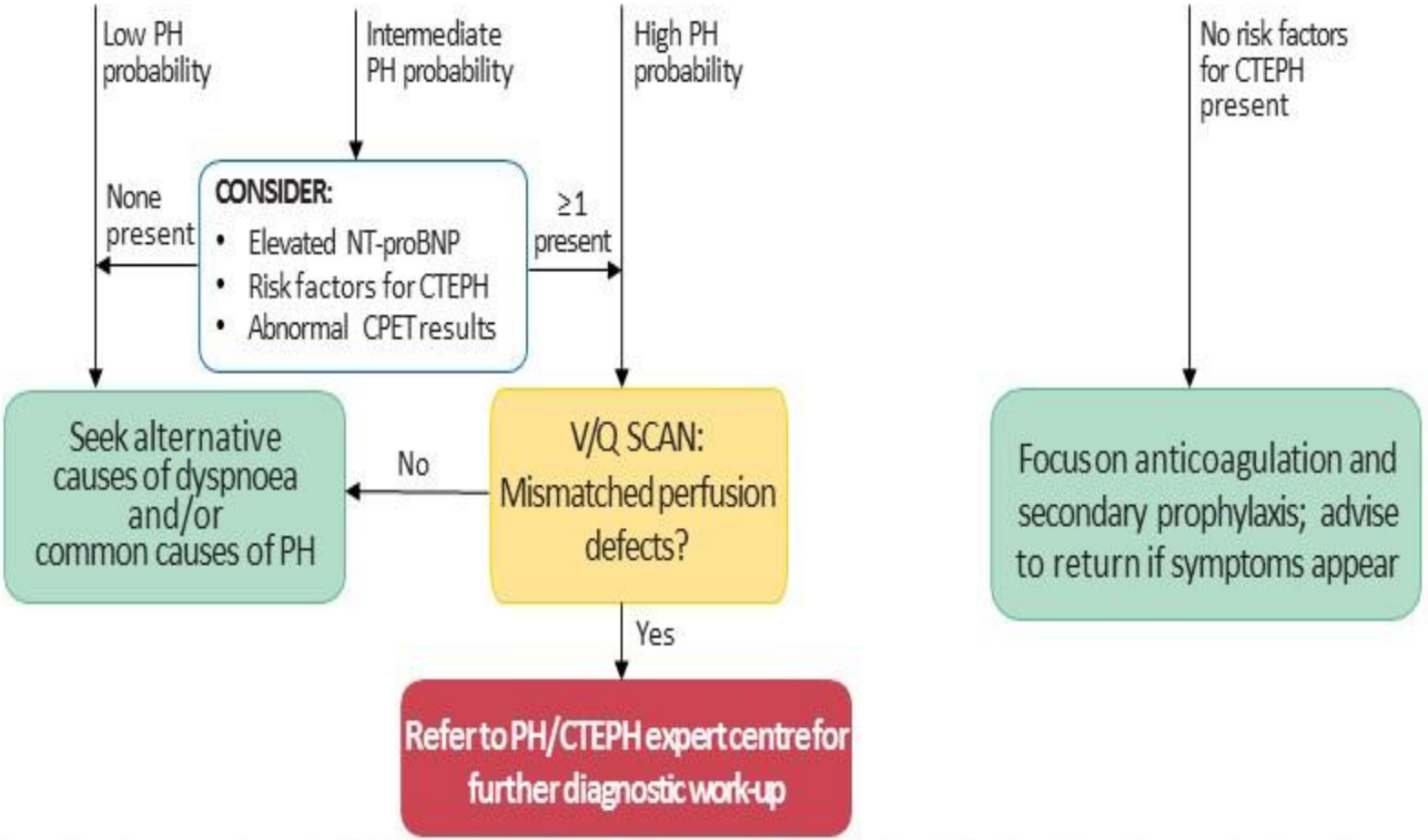
Figure 7 Follow-up strategy and diagnostic work-up for long-term sequelae of PE (2)



CPET = cardiopulmonary exercise testing; CTEPH = chronic thromboembolic pulmonary hypertension; NT-proBNP = N-terminal pro B-type natriuretic peptide; PH = pulmonary hypertension; V/Q = ventilation/perfusion.

Recommendations for the regimen and duration of anticoagulation after PE in patients *without* cancer (4)

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Recommendations	Class	Level
NOAC dose in extended anticoagulation		
If extended oral anticoagulation is decided after PE in a patient without cancer, a reduced dose of the NOACs apixaban (2.5 mg *b.i.d.*) or rivaroxaban (10 mg *o.d.*) should be considered after 6 months of therapeutic anticoagulation.	IIa	A
Extended treatment with alternative antithrombotic agents		
In patients who refuse to take or are unable to tolerate any form of oral anticoagulants, aspirin or sulodexide may be considered for extended VTE prophylaxis.	IIb	B

NOAC(s) = non-vitamin K antagonist oral anticoagulant(s); VTE = venous thromboembolism.

Recommendations for the regimen and the duration of anticoagulation after PE in patients with active cancer (1)

ESC European Society of Cardiology

Recommendations	Class	Level
For patients with PE and cancer, weight-adjusted subcutaneous LMWH should be considered for the first 6 months over VKAs.	IIa	A
Edoxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.	IIa	B
Rivaroxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.	IIa	C

LMWH = low molecular weight heparin; VKA(s) = vitamin K antagonist(s).

Recommendations for the regimen and the duration of anticoagulation after PE in patients with active cancer (2)

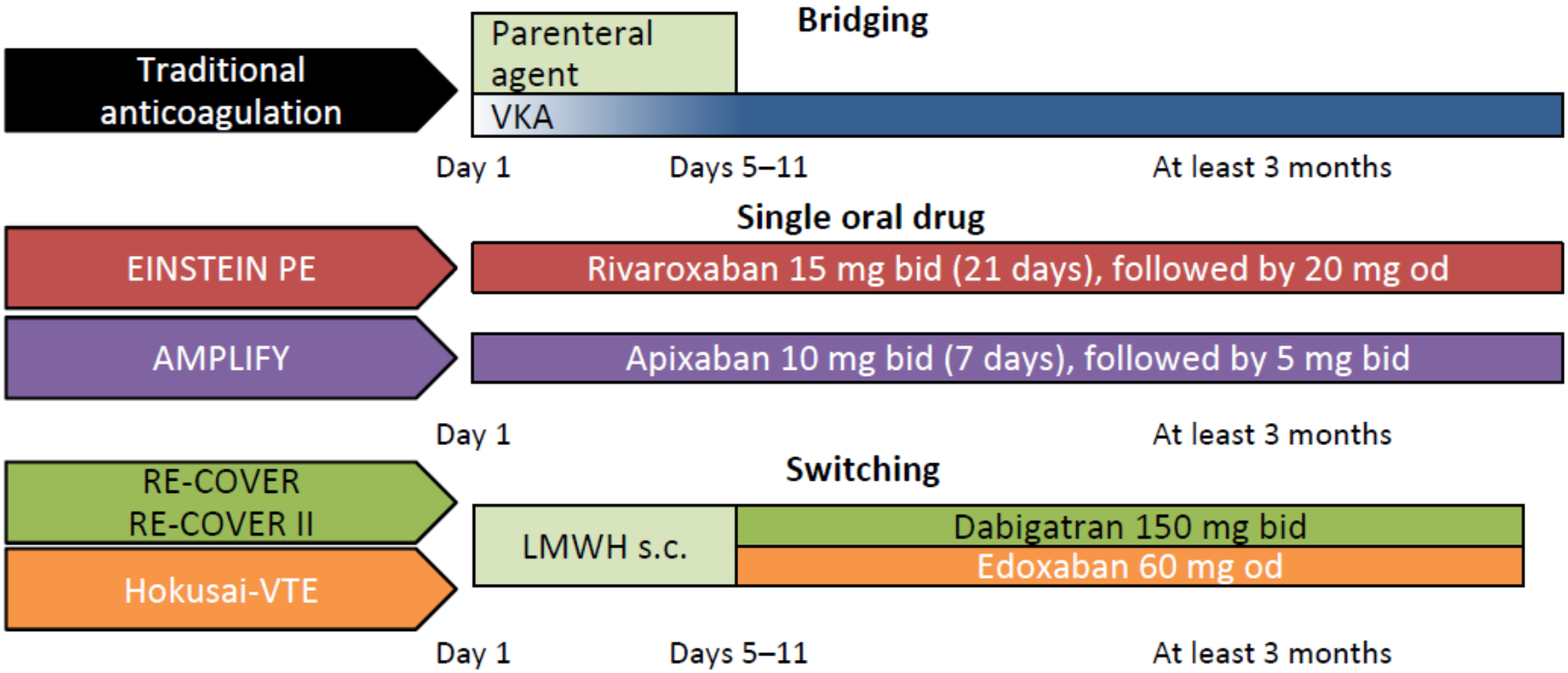
ESC European Society of Cardiology

Recommendations	Class	Level
For patients with PE and cancer, extended anticoagulation (beyond the first 6 months) should be considered for an indefinite period or until the cancer is cured.	IIa	B
In patients with cancer, managing incidental PE in the same manner as symptomatic PE should be considered, if it involves segmental or more proximal branches, multiple subsegmental vessels, or a single subsegmental vessel in association with proven DVT.	IIa	B

DVT = deep vein thrombosis

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Direct oral anticoagulants



Walter RJ, Curr Med Res Opin 2014

Akutní plicní embolie – diagnostika

anamneza + fyzikální vyšetření ► klin. pravděpodobnost

Lab (Astrup, D-dimer, srdeční markery)

EKG

RTG

CT angio , (plicní angiografie)

V/Q scinti

Kompresní žilní ultrasonografie DK

ECHO

(MR)

Doporučení III – Doporučení pro léčbu v akutní fázi		
Doporučení	**Třída[a]**	**Úroveň[b]**
PE bez šoku nebo hypotenze (se středním nebo nízkým rizikem)[c]		
Antikoagulace: nová perorální antikoagulancia		
Jako alternativa kombinace parenterální antikoagulace s VKA je doporučena antikoagulace rivaroxabanem (15 mg dvakrát denně po dobu tří týdnů, následně 20 mg jednou denně).	I	B
Jako alternativa kombinace parenterální antikoagulace s VKA je indikována antikoagulace apixabanem (10 mg dvakrát denně po dobu sedmi dní, následně 5 mg dvakrát denně).	I	B
Jako alternativa se po parenterální antikoagulaci v akutní fázi doporučuje podávání dabigatranu (150 mg dvakrát denně nebo 110 mg dvakrát denně u pacientů ve věku ≥ 80 nebo pacientů užívajících verapamil).	I	B[d]
Jako alternativa VKA je po parenterální antikoagulaci v akutní fázi doporučeno podávání edoxabanu.*	I	B
Pacientům s těžkým renálním postižením se nedoporučuje podávat nová perorální antikoagulancia (rivaroxaban, apixaban, dabigatran, edoxaban).[e]	III	A

Table 2 Main new recommendations 2019 (1)

ESC
European Society of Cardiology

Diagnosis	
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

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Plicní scintigrafie

- defekt perfuze segmentárního tvaru bez korelátu na ventilační scinti
- senzitivita 85% planární záznam, 97% SPECT
- negativní nález 100% vylučuje PE

- limitace u nemocných s chron. kardiopulmonálním onemocněním

Význam scinti plic v diagnostice PE (vždy vážit přínos pro pacienta vs. riziko)

- (není-li dostupné kvalitní CT angio)
- nízká klinická pravděpodobnost a normální RTG
- u mladých žen, v těhotenství
- alergie na kontrastní látku
- renální insuf. (GF<30ml/min.)
- pacient s myelomem a paraproteinémií