2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

ESC
European Society of Cardiology

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

ESC European Society of Cardiology

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

Developed in collaboration with the European Respiratory Society (ERS)

Authors/Task Force Members: Stavros V. Konstantinides (Chairperson) (Germany/Greece), Guy Meyer (Co-Chairperson) (France), Cecilia Becattini (Italy), Héctor Bueno (Spain), Geert-Jan Geersing (Netherlands), Veli-Pekka Harjola (Finland), Menno V. Huisman (Netherlands), Marc Humbert[1] (France), Catriona Sian Jennings (United Kingdom), David Jiménez (Spain), Nils Kucher (Switzerland), Irene Marthe Lang (Austria), Mareike Lankeit (Germany), Roberto Lorusso (Netherlands), Lucia Mazzolai (Switzerland), Nicolas Meneveau (France), Fionnuala Ní Áinle (Ireland), Paolo Prandoni (Italy), Piotr Pruszczyk (Poland), Marc Righini (Switzerland), Adam Torbicki (Poland), Eric Van Belle (France), José Luis Zamorano (Spain).

[1] Representing the European Respiratory Society (ERS)

ESC Classes of recommendations

ESC
European Society of Cardiology

	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/ efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

ESC Levels of evidence

ESC
European Society of Cardiology

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

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

Table 1 Changes in recommendations 2014-2019

ESC European Society of Cardiology

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

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

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

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

Table 2 Main new recommendations 2019 (2)

ESC European Society of Cardiology

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

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

Table 2 Main new recommendations 2019 (3)

ESC European Society of Cardiology

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

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

Table 2 Main new recommendations 2019 (4)

ESC European Society of Cardiology

Chronic treatment and prevention of recurrence in patients without cancer	
Indefinite treatment with a VKA is recommended in patients with the 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 in patients with a persistent risk factor other than the antiphospholipid antibody syndrome.	IIa
Extended anticoagulation should be considered for patients with a minor transient/reversible risk factor for the index PE event.	IIa
Reduced dose of apixaban or rivaroxaban should be considered after the first 6 months.	IIa

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

Table 2 Main new recommendations 2019 (5)

ESC European Society of Cardiology

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

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

Table 2 Main new recommendations 2019 (6)

ESC European Society of Cardiology

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

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

Table 3 Predisposing factors for VTE (1)

Strong risk factors (OR >10)
Fracture of lower limb
Previous VTE
Spinal cord injury
Hospitalization for heart failure or atrial fibrillation/flutter (within previous 3 months)
Hip or knee replacement
Major trauma
Myocardial infarction (within previous 3 months)

VTE = venous thromboembolism.

Table 3 Predisposing factors for VTE (2)

Moderate risk factors (OR 2–9)
Arthroscopic knee surgery
Autoimmune diseases
Blood transfusion
Central venous lines
Intravenous catheters and leads
Chemotherapy
Congestive heart failure or respiratory failure
Erythropoiesis-stimulating agents
Hormone replacement therapy (depends on formulation)

VTE = venous thromboembolism.

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

Table 3 Predisposing factors for VTE (3)

Moderate risk factors (cont'd)
In vitro fertilization
Oral contraceptive therapy
Postpartum period
Infection (specifically pneumonia, urinary tract infection, and HIV)
Inflammatory bowel disease
Cancer (highest risk in metastatic disease)
Paralytic stroke
Superficial vein thrombosis
Thrombophilia

VTE = venous thromboembolism.

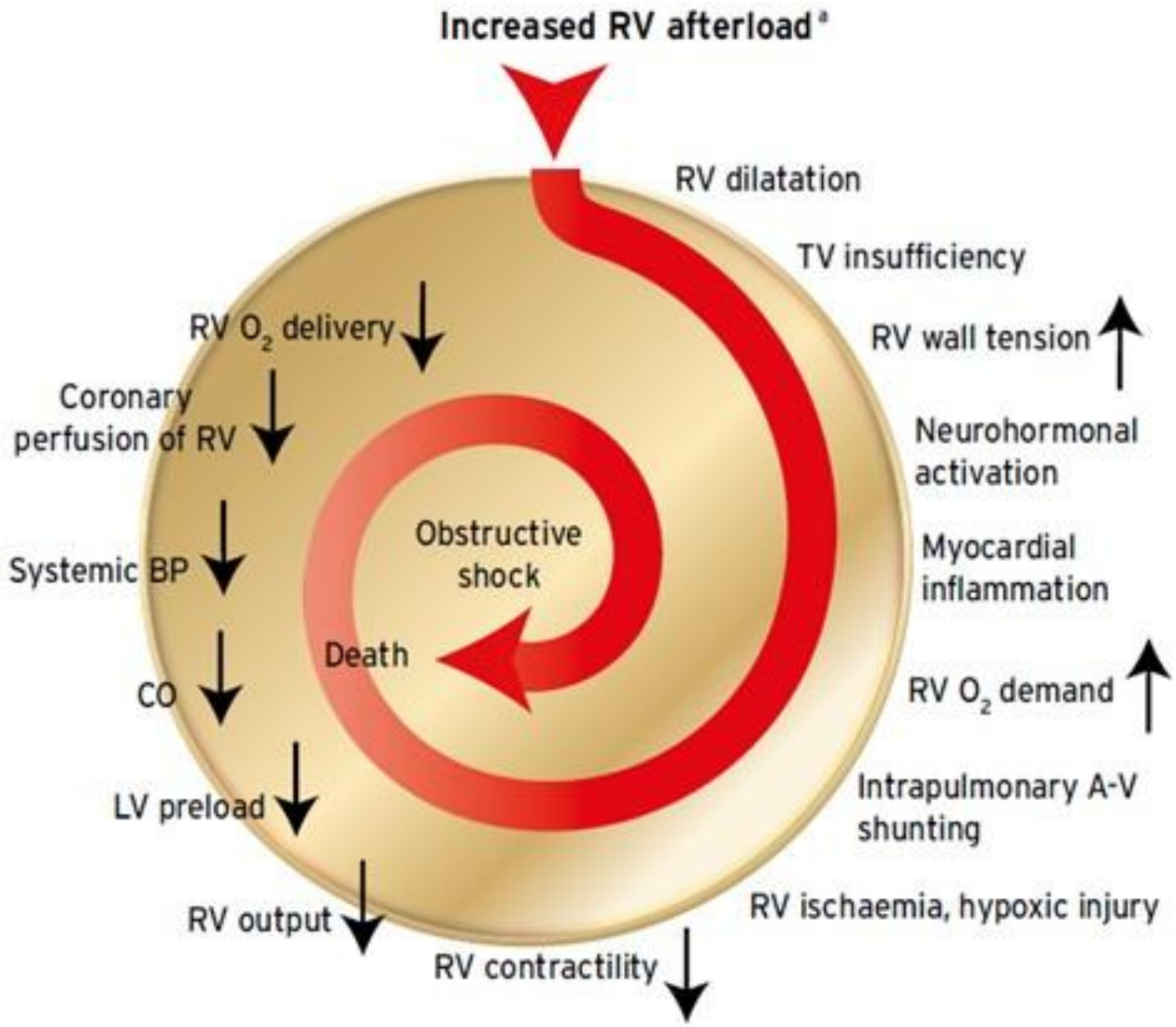
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 3 Predisposing factors for VTE (4)

Weak risk factors (OR <2)
Bed rest >3 days
Diabetes mellitus
Arterial hypertension
Immobility due to sitting (e.g. prolonged car or air travel)
Increasing age
Laparoscopic surgery (e.g. cholecystectomy)
Obesity
Pregnancy
Varicose veins

VTE = venous thromboembolism.

Figure 1 The spiral of haemodynamic collapse in acute PE



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

Table 4 Definition of haemodynamic instability

(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)	

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

Table 5 Revised Geneva clinical prediction rule for PE (1)

Items	Clinical decision rule points	
	Original version	Simplified version
Previous PE or DVT	3	1
Heart rate		
75–94 b.p.m.	3	1
≥95 b.p.m.	5	2
Surgery or fracture within the past month	2	1
Haemoptysis	2	1

DVT = deep vein thrombosis.

Table 5 Revised Geneva clinical prediction rule for PE (2)

	Original version	Simplified version
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

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

Table 5 Revised Geneva clinical prediction rule for PE (3)

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

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

Table 6 Imaging tests for diagnosis of PE (1)

	Strengths	Weaknesses/limitations
CTPA	• Readily available around the clock in most centres • Excellent accuracy • Strong validation in prospective management outcome studies • Low rate of inconclusive results (3–5%) • May provide alternative diagnosis if PE excluded • Short acquisition time	• Radiation exposure • Exposure to iodine contrast: – limited use in iodine allergy and hyperthyroidism – risks in pregnant and breast-feeding women – contraindicated in severe renal failure • Tendency to overuse because of easy accessibility • Clinical relevance of CTPA diagnosis of subsegmental PE unknown

CTPA = computed tomography pulmonary angiography.

Table 6 Imaging tests for diagnosis of PE (2)

V/Q = ventilation-perfusion; SPECT = single photon emission computed tomography.

	Strengths	Weaknesses/limitations
Planar V/Q scan	• Almost no contraindications • Relatively inexpensive • Strong validation in prospective management outcome studies	• Not readily available in all centres • Interobserver variability in interpretation • Results reported as likelihood ratios • Inconclusive in 50% of cases • Cannot provide alternative diagnosis
V/Q SPECT	• Almost no contraindications • Lowest rate of non-diagnostic tests (<3%) • High accuracy according to available data • Binary interpretation ("PE" vs "no PE")	• Variability of techniques • Variability of diagnostic criteria • Cannot provide alternative diagnosis • No validation in prospective management outcome studies
Pulmonary angiography	• Historical gold standard	• Invasive procedure • Not readily available in all centres

Table 6 Imaging tests for diagnosis of PE (3)

	Radiation issues
CTPA	• Radiation effective dose 3–10 mSv • Significant radiation exposure to young female breast tissue
Planar V/Q scan	• Lower radiation than CTPA, effective dose approximately 2 mSv
V/Q SPECT	• Lower radiation than CTPA, effective dose approximately 2 mSv
Pulmonary angiography	• Highest radiation, effective dose 10–20 mSv

CTPA = computed tomography pulmonary angiography; V/Q = ventilation-perfusion; SPECT = single photon emission computed tomography.

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

Table 7 Findings of pre-existing CTEPH on CTPA (1)

ESC
European Society of Cardiology

Direct vascular signs
Eccentric wall-adherent filling defect(s), which may calcify; different from the central filling defects within a distended lumen, which are the hallmark of acute PE
Abrupt tapering and truncation
Complete occlusion and pouch defects
Intimal irregularity
Linear intraluminal filling defects (intravascular webs and bands)
Stenosis and post-stenotic dilatation
Vascular tortuosity

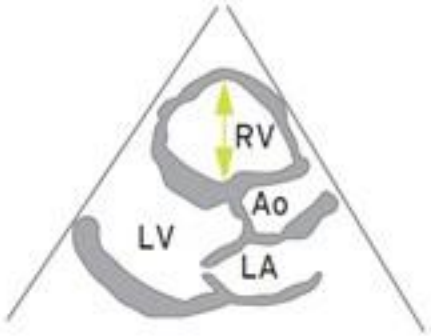
CTEPH = chronic thromboembolic pulmonary hypertension; CTPA = computed tomography pulmonary angiography.

Table 7 Findings of pre-existing CTEPH on CTPA (2)

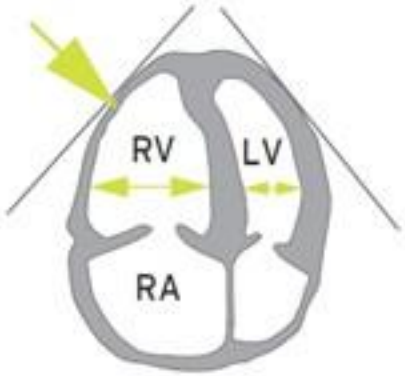
Indirect vascular signs
Significant RV hypertrophy, RA dilatation
Pericardial effusion
Dilatation of pulmonary artery (>29 mm in men and >27 mm in women) and/ or calcifications of pulmonary artery
Systemic collateral arterial supply (bronchial arterial collaterals towards pulmonary post-obstructive vessels)
Parenchymal changes
Mosaic attenuation of the lung parenchyma resulting in geographical variation in perfusion

CTEPH = chronic thromboembolic pulmonary hypertension; CTPA = computed tomography pulmonary angiography.

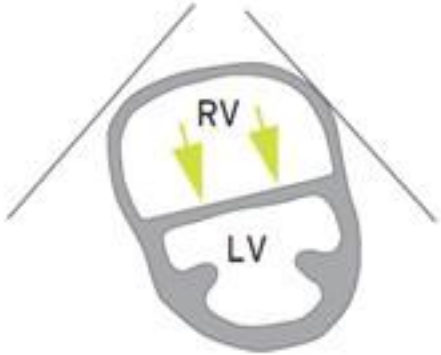
Figure 2 TTE parameters of RV pressure overload (1)



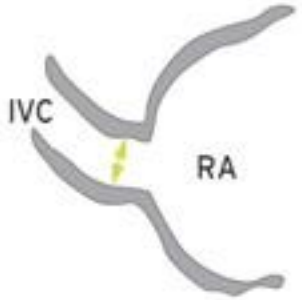
A. Enlarged right ventricle, parasternal long axis view



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

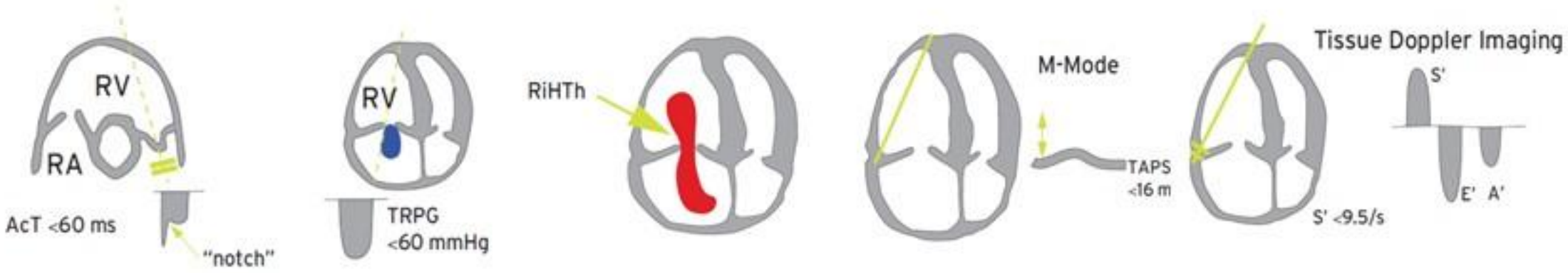


D. Distended inferior vena cava with diminished inspiratory collapsibility, subcostal view

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

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

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.

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

Recommendations for diagnosis (1)

Recommendations	Class	Level
Suspected PE with haemodynamic instability		
In suspected high-risk PE, as indicated by the presence of haemodynamic instability, bedside echocardiography or emergency CTPA (depending on availability and clinical circumstances) are recommended for diagnosis.	I	C
It is recommended that i.v. anticoagulation with UFH, including a weight-adjusted bolus injection, be initiated without delay in patients with suspected high-risk PE.	I	C

CTPA = computed tomography pulmonary angiography.

Recommendations for diagnosis (2)

Recommendations	Class	Level
Suspected PE without haemodynamic instability		
The use of validated criteria for diagnosing PE is recommended.	I	B
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE while diagnostic work-up is in progress.	I	C
Clinical evaluation		
It is recommended that the diagnostic strategy be based on clinical probability, assessed either by clinical judgement or by a validated prediction rule.	I	A

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

Recommendations for diagnosis (3)

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

Recommendations for diagnosis (4)

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.

Recommendations for diagnosis (5)

Recommendations	Class	Level
CTPA (cont'd)		
It is recommended to accept the diagnosis of PE (without further testing) if CTPA shows a segmental or more proximal filling defect in a patient with intermediate or high clinical probability.	I	B
It should be considered to reject the diagnosis of PE (without further testing) if CTPA is normal in a patient with high clinical probability or PE-likely.	IIa	B
Further imaging tests to confirm PE may be considered in case of isolated subsegmental filling defects.	IIb	C
CT venography is not recommended as an adjunct to CTPA.	III	B

CTPA = computed tomography pulmonary angiography.

Recommendations for diagnosis (6)

ESC European Society of Cardiology

Recommendations	Class	Level
V/Q scintigraphy		
It is recommended to reject the diagnosis of PE (without further testing) if the perfusion lung scan is normal.	I	A
It should be considered to accept the diagnosis of PE (without further testing) if the V/Q scan yields high probability for PE.	IIa	B
A non-diagnostic V/Q scan should be considered as exclusion of PE when combined with a negative proximal CUS in patients with low clinical probability, or PE-unlikely.	IIa	B
V/Q SPECT		
V/Q SPECT may be considered for PE diagnosis.	IIb	B

V/Q = ventilation-perfusion; SPECT = single photon emission computed tomography.

Recommendations for diagnosis (7)

Recommendations	Class	Level
Lower-limb compression ultrasonography (CUS)		
It is recommended to accept the diagnosis of VTE (and PE) if a CUS shows a proximal DVT in a patient with clinical suspicion of PE.	I	A
If CUS shows only a distal DVT, further testing should be considered to confirm PE.	IIa	A
If a positive proximal CUS is used to confirm PE, assessment of PE severity should be considered to permit risk-adjusted management.	IIa	C
Magnetic resonance angiography (MRA)		
MRA is not recommended for ruling out PE.	III	A

DVT = deep vein thrombosis; VTE = venous thromboembolism.

Table 8 Original and simplified PESI (1)

Parameter	Original version	Simplified version
Age	Age in years	1point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1point
Chronic heart failure	+10 points	1point
Chronic pulmonary disease	+10 points	
Pulse rate ≥110b.p.m.	+20 points	1point
Systolic BP <100mmHg	+30 points	1point

BP = blood pressure; PESI = Pulmonary Embolism Severity Index.

Table 8 Original and simplified PESI (2)

Parameter	Original version	Simplified version
Respiratory rate >30 breaths per min	+20 points	–
Temperature <36 °C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1point

PESI = Pulmonary Embolism Severity Index.

Table 8 Original and simplified PESI (3)

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

PESI = Pulmonary Embolism Severity Index.

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

Table 9 Classification of PE based on early mortality risk

ESC European Society of Cardiology

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.

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

Recommendations for prognostic assessment (1)

ESC European Society of Cardiology

Recommendations	Class	Level
Initial risk stratification of suspected or confirmed PE – based on the presence of haemodynamic instability – is recommended to identify patients at high risk of early mortality.	I	B
In patients without haemodynamic instability, further stratification of patients with acute PE into an intermediate-risk and a low-risk category is recommended.	I	B
In patients without haemodynamic instability, use of clinical prediction rules integrating PE severity and comorbidity, preferably the PESI or sPESI, should be considered for risk assessment in the acute phase of PE.	IIa	B

(s)PESI = (simplified) Pulmonary Embolism Severity Index.

Recommendations for prognostic assessment (2)

Recommendations	Class	Level
Assessment of the RV by imaging methods or laboratory biomarkers should be considered even in the presence of a low PESI or a negative sPESI.	IIa	B
In patients without haemodynamic instability, use of validated scores combining clinical, imaging and laboratory PE-related prognostic factors may be considered to further stratify the severity of the acute PE episode.	IIb	C

(s)PESI = (simplified) Pulmonary Embolism Severity Index; RV = right ventricle.

Table 10 Treatment of RV failure in acute high-risk PE (1)

ESC European Society of Cardiology

Strategy	Properties and use	Caveats
Volume optimization		
Cautious volume loading, saline, or Ringer's lactate, up to 500 mL over 15–30 min	Consider in patients with normal-to-low central venous pressure (due, for example, to concomitant hypovolaemia)	Volume loading can overdistend the RV, worsen ventricular interdependence, and reduce CO

CO = cardiac output; RV = right ventricle/ventricular.

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

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

Vasopressors and inotropes		
Norepinephrine, 0.2–1.0 μg/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.

Table 10 Treatment of RV failure in acute high-risk PE (3)

Mechanical circulatory support		
Veno-arterial ECMO/ extracorporeal life support	Rapid short-term support combined with oxygenator	Complications with use over longer periods (>5–10 days), including bleeding and infections; no clinical benefit unless combined with surgical embolectomy; requires an experienced team

ECMO = extracorporeal membrane oxygenation; RV = right ventricular.

Table 11 LMWH and fondaparinux for PE (1)

	Dosage	Interval
Enoxaparin	1.0 mg/kg	Every 12 h
	Or	
	1.5 mg/kg	Once daily
Tinzaparin	175 U/kg	Once daily
Dalteparin	100 IU/kg	Every 12 h
	Or	
	200 IU/kg	Once daily

LMWH = low molecular weight heparin(s).

Table 11 LMWH and fondaparinux for PE (2)

	Dosage	Interval
Nadroparin	86 IU/kg	Every 12 h
	Or	
	171 IU/kg	Once daily
Fondaparinux	5 mg (body weight <50 kg);	Once daily
	7.5 mg (body weight 50–100 kg);	
	10 mg (body weight >100 kg)	

LMWH = low molecular weight heparin(s).

Table 12 Thrombolytic doses and contraindications (1)

ESC European Society of Cardiology

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	

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

Table 12 Thrombolytic doses and contraindications (2)

ESC European Society of Cardiology

Molecule	Regimen	Contraindications to fibrinolysis (cont'd)
Urokinase	4400 IU/kg as a loading dose over 10 min, followed by 4400 IU/kg/h over 12–24 h	**Relative** • Transient ischaemic attack in previous 6 months • Oral anticoagulation • Pregnancy or first postpartum week • Non-compressible puncture sites • Traumatic resuscitation • Refractory hypertension (systolic BP >180 mmHg) • Advanced liver disease • Infective endocarditis • Active peptic ulcer
	Accelerated regimen: 3 million IU over 2 h	

BP = blood pressure; IU = international units.

Recommendations for acute-phase treatment of high-risk PE[a] (1)

ESC European Society of Cardiology

Recommendations	Class	Level
It is recommended that anticoagulation with UFH, including a weight-adjusted bolus injection, be initiated without delay in patients with high-risk PE.[a]	I	C
Systemic thrombolytic therapy is recommended for high- risk PE.	I	B
Surgical pulmonary embolectomy is recommended for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.	I	C

[a] After haemodynamic stabilization of the patient, continue anticoagulation as in intermediate- or low-risk PE.
UFH = unfractionated heparin.

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

Recommendations for acute-phase treatment of high-risk PE (2)

ESC European Society of Cardiology

Recommendations	Class	Level
Percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.	IIa	C
Norepinephrine and/or dobutamine should be considered in patients with high-risk PE.	IIa	C
ECMO may be considered, in combination with surgical embolectomy or catheter-directed treatment, in patients with PE and refractory circulatory collapse or cardiac arrest.	IIb	C

ECMO = extracorporeal membrane oxygenation.

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

Recommendations for acute-phase treatment of intermediate- or low- risk PE (1)

ESC European Society of Cardiology

Recommendations	Class	Level
Initiation of anticoagulation		
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE, while diagnostic work-up is in progress.	I	C
If anticoagulation is initiated parenterally, LMWH or fondaparinux is recommended (over UFH) for most patients.	I	A
Oral anticoagulants		
When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a VKA.	I	A

NOAC = non-vitamin K antagonist oral anticoagulant; LMWH = low molecular weight heparin; VKA = vitamin K antagonist; UFH = unfractionated heparin.

Recommendations for acute-phase treatment of intermediate- or low- risk PE (2)

ESC European Society of Cardiology

Recommendations	Class	Level
Oral anticoagulants		
When patients are treated with a VKA, overlapping with parenteral anticoagulation is recommended until an INR of 2.5 (range 2.0–3.0) is reached.	I	A
NOACs are not recommended in patients with severe renal impairment, during pregnancy and lactation, and in patients with the antiphospholipid antibody syndrome.	III	C

INR = International Normalized Ratio; NOAC(s) = non-vitamin K antagonist oral anticoagulant(s); VKA = vitamin K antagonist.

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

Recommendations for acute-phase treatment of intermediate- or low- risk PE (3)

ESC European Society of Cardiology

Recommendations	Class	Level
Reperfusion treatment		
Rescue thrombolytic therapy is recommended for patients with haemodynamic deterioration on anticoagulation treatment.	I	B
As an alternative to rescue thrombolytic therapy, surgical embolectomy or percutaneous catheter- directed treatment should be considered for patients with haemodynamic deterioration on anticoagulation treatment.	IIa	C
Routine use of primary systemic thrombolysis is not recommended in patients with intermediate- or low-risk PE.	III	B

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

Recommendations for multidisciplinary PE teams

Recommendations	Class	Level
Set-up of a multidisciplinary team and programme for management of high-risk and (in selected cases) intermediate-risk PE should be considered, depending on the resources and expertise available in each hospital.	IIa	C

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

Recommendations for inferior vena cava (IVC) filters

ESC European Society of Cardiology

Recommendations	Class	Level
IVC filters should be considered in patients with acute PE and absolute contraindications to anticoagulation.	IIa	C
IVC filters should be considered in case of PE recurrence despite therapeutic anticoagulation.	IIa	C
Routine use of IVC filters is not recommended.	III	A

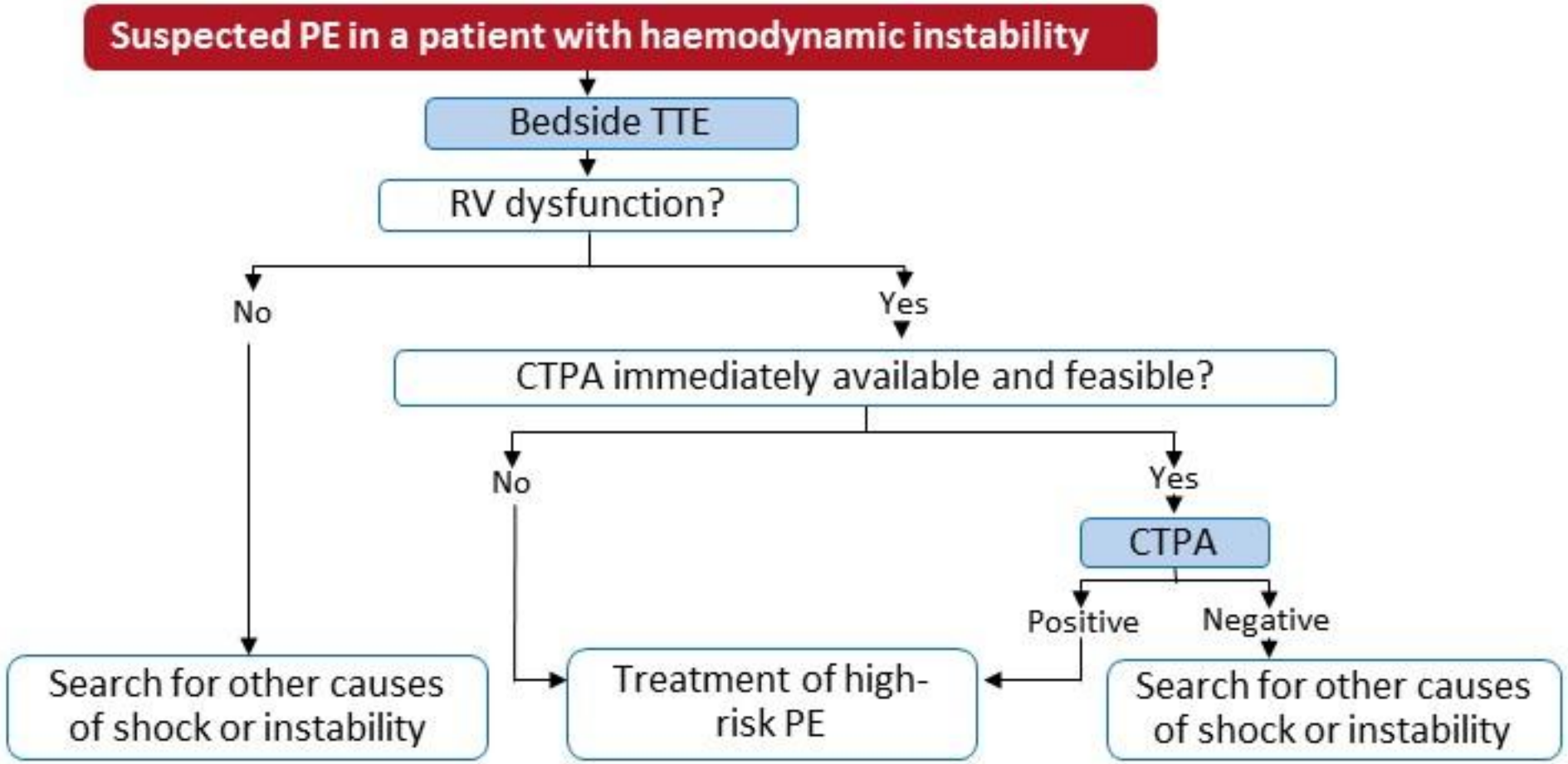
2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for early discharge, home treatment

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

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

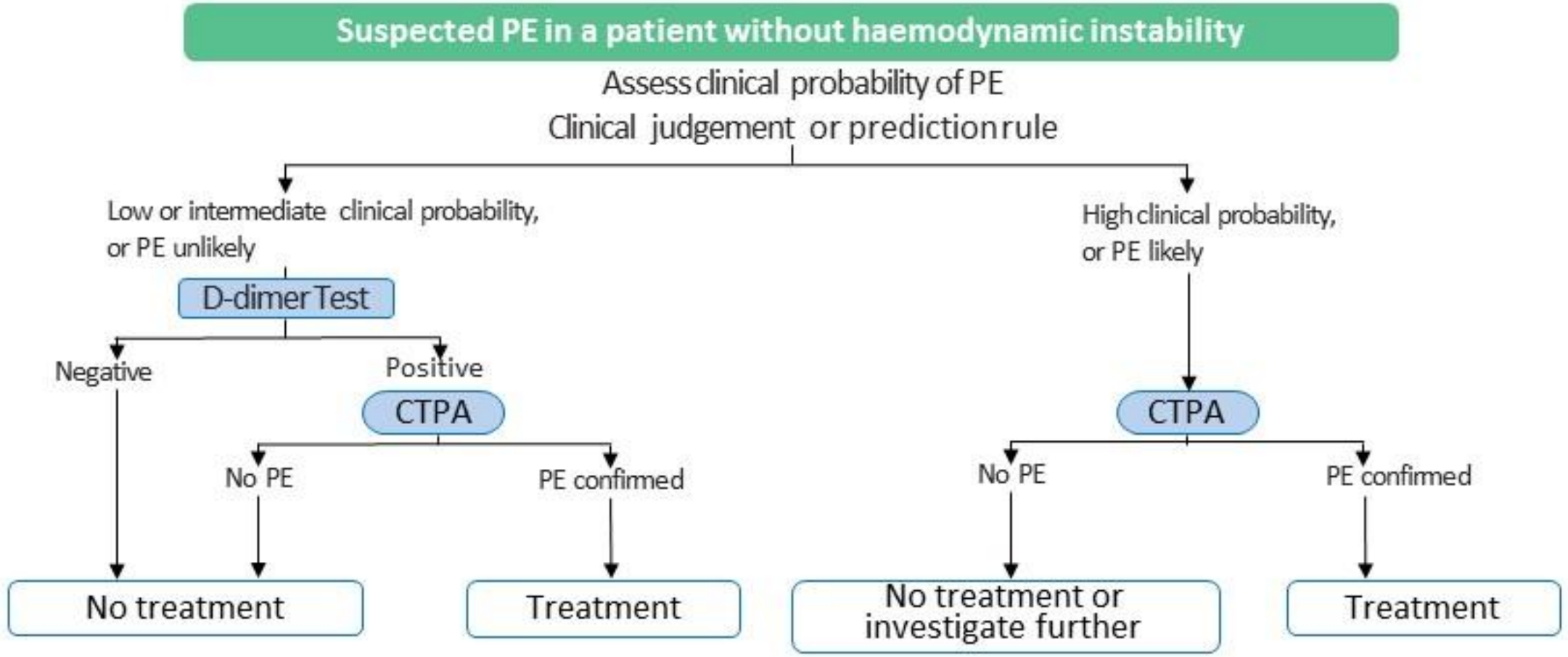
Figure 3 Diagnostic algorithm for suspected high-risk PE



CTPA = computed tomography pulmonary angiography; RV = right ventricular; TTE = transthoracic echocardiography

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

Figure 4 Diagnostic algorithm for suspected PE without haemodynamic instability

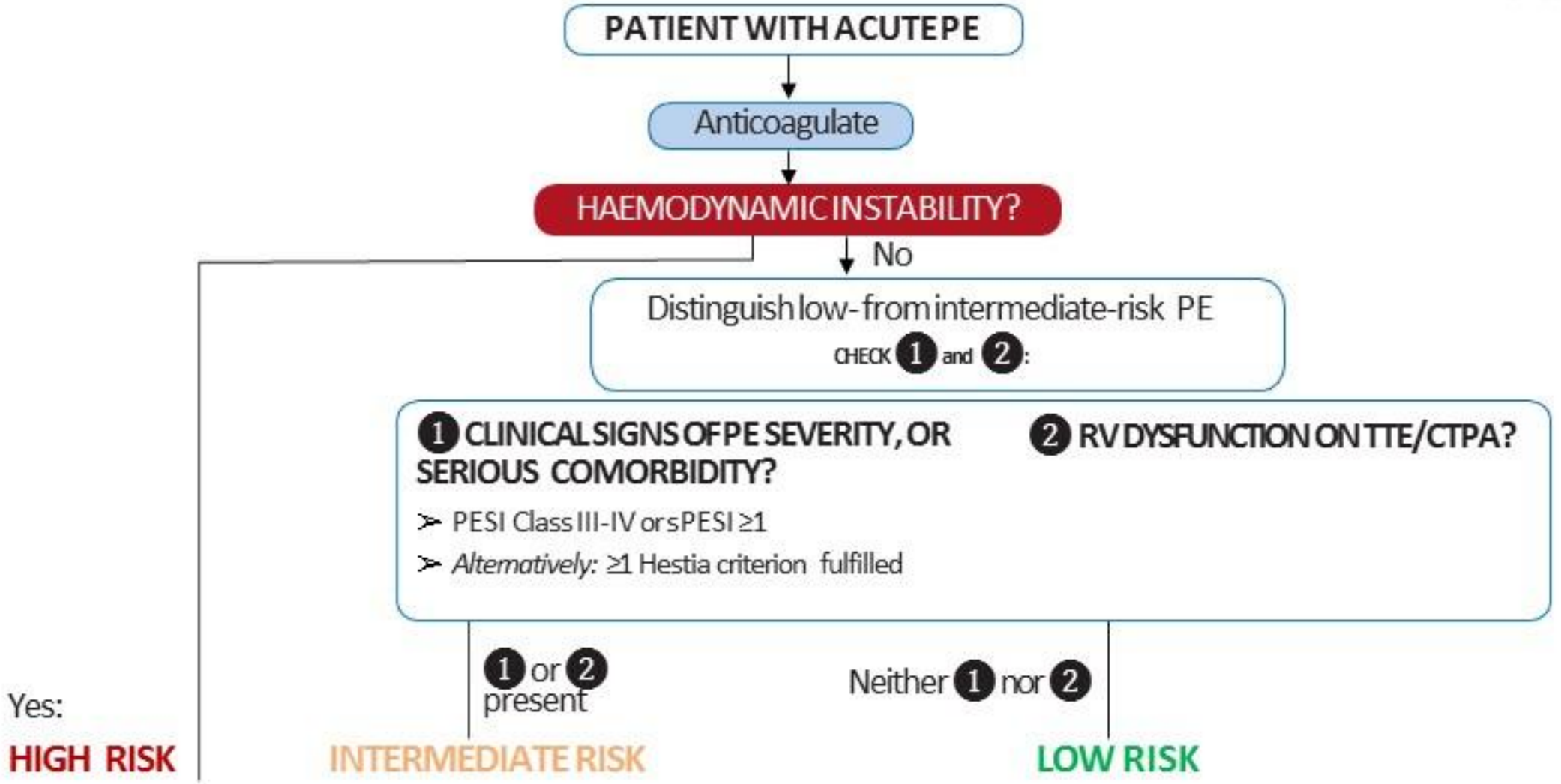


CTPA = computed tomography pulmonary angiography

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

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

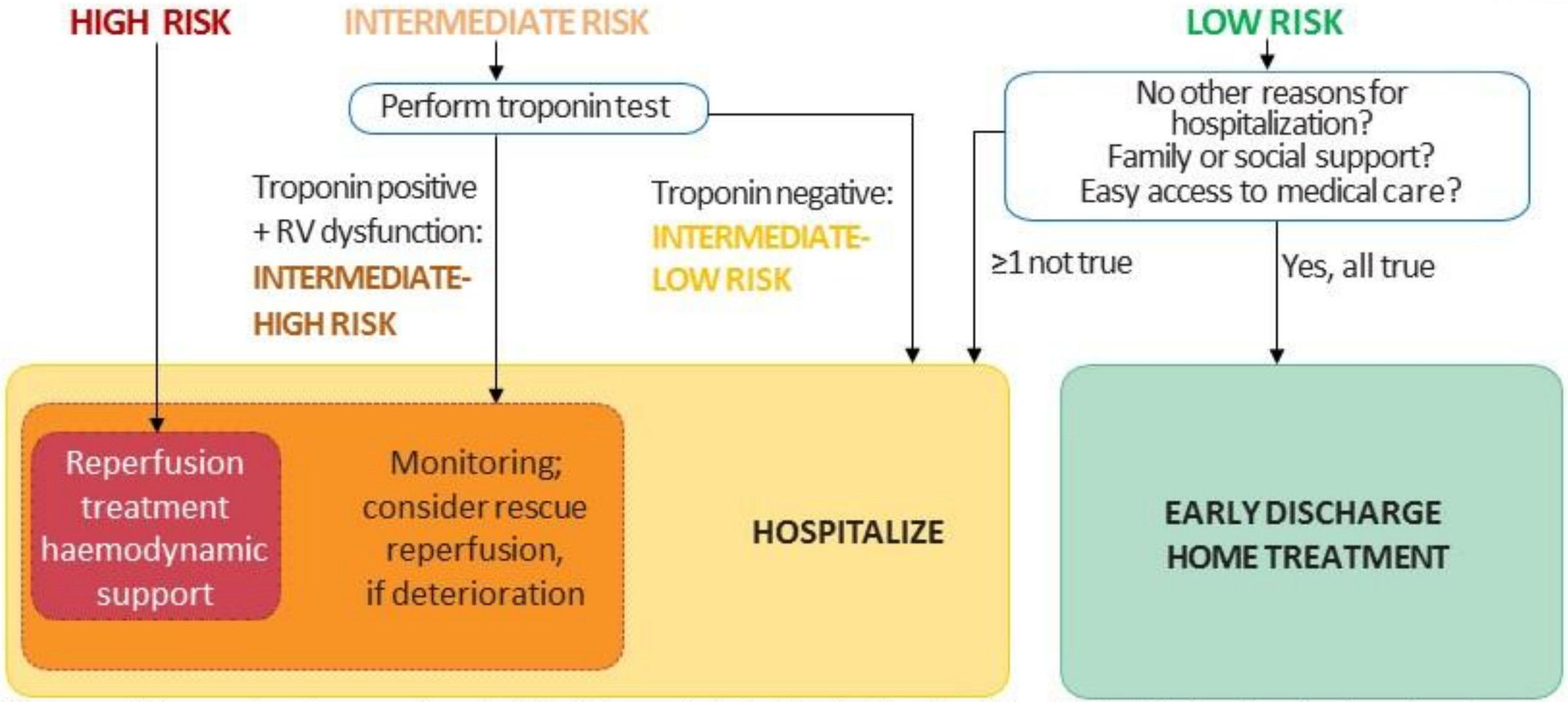
ESC European Society of Cardiology



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

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

ESC European Society of Cardiology



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

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

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

ESC
European Society of Cardiology

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.

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

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

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.

Table 14 Risk factors for long-term VTE recurrence (1)

ESC European Society of Cardiology

Estimated risk for long-term recurrence	Risk factor category for index PE	Examples
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

VTE = venous thromboembolism.

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

Table 14 Risk factors for long-term VTE recurrence (2)

Estimated risk for long-term recurrence	Risk factor category for index PE	Examples
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

VTE = venous thromboembolism.

Table 14 Risk factors for long-term VTE recurrence (3)

Estimated risk for long-term recurrence	Risk factor category for index PE	Examples
	Non-malignant persistent risk factors	• Leg injury (without fracture) associated with reduced mobility for ≥3 days • Long-haul flight • Inflammatory bowel disease • Active autoimmune disease
	No identifiable risk factor	

VTE = venous thromboembolism.

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

Table 14 Risk factors for long-term VTE recurrence (4)

Estimated risk for long-term recurrence	Risk factor category for index PE	Examples
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

VTE = venous thromboembolism.

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

Recommendations for the regimen and duration of anticoagulation after PE in patients *without* cancer (1)

ESC European Society of Cardiology

Recommendations	Class	Level
Therapeutic anticoagulation for at least 3 months is recommended for all patients with PE.	I	A
Patients in whom discontinuation of anticoagulation after 3 months is recommended		
For patients with first PE/VTE secondary to a major transient/reversible risk factor, discontinuation of therapeutic oral anticoagulation is recommended after 3 months.	I	B

VTE = venous thromboembolism.

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

Recommendations for the regimen and duration of anticoagulation after PE in patients *without* cancer (2)

ESC European Society of Cardiology

Recommendations	Class	Level
Patients in whom extension of anticoagulation beyond 3 months is recommended		
Oral anticoagulant treatment of indefinite duration is recommended for patients presenting with recurrent VTE (that is, with at least one previous episode of PE or DVT) not related to a major transient or reversible risk factor.	I	B
Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with the antiphospholipid antibody syndrome.	I	B

DVT = deep vein thrombosis; VKA = vitamin K antagonist.

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

Recommendations for the regimen and duration of anticoagulation after PE in patients *without* cancer (3)

ESC European Society of Cardiology

Recommendations	Class	Level
Patients in whom extension of anticoagulation beyond 3 months should be considered		
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE and no identifiable risk factor.	IIa	A
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a persistent risk factor other than the antiphospholipid antibody syndrome.	IIa	C
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a minor transient or reversible risk factor.	IIa	C

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

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

ESC European Society of Cardiology

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 duration of anticoagulation after PE in patients *without* cancer (5)

Recommendations	Class	Level
Follow-up of the patient under anticoagulation		
In patients who receive extended anticoagulation, it is recommended to reassess drug tolerance and adherence, hepatic and renal function, and the bleeding risk at regular intervals.	I	C

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

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).

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

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)

Table 15 Estimated radiation absorbed in procedures used for diagnosing PE

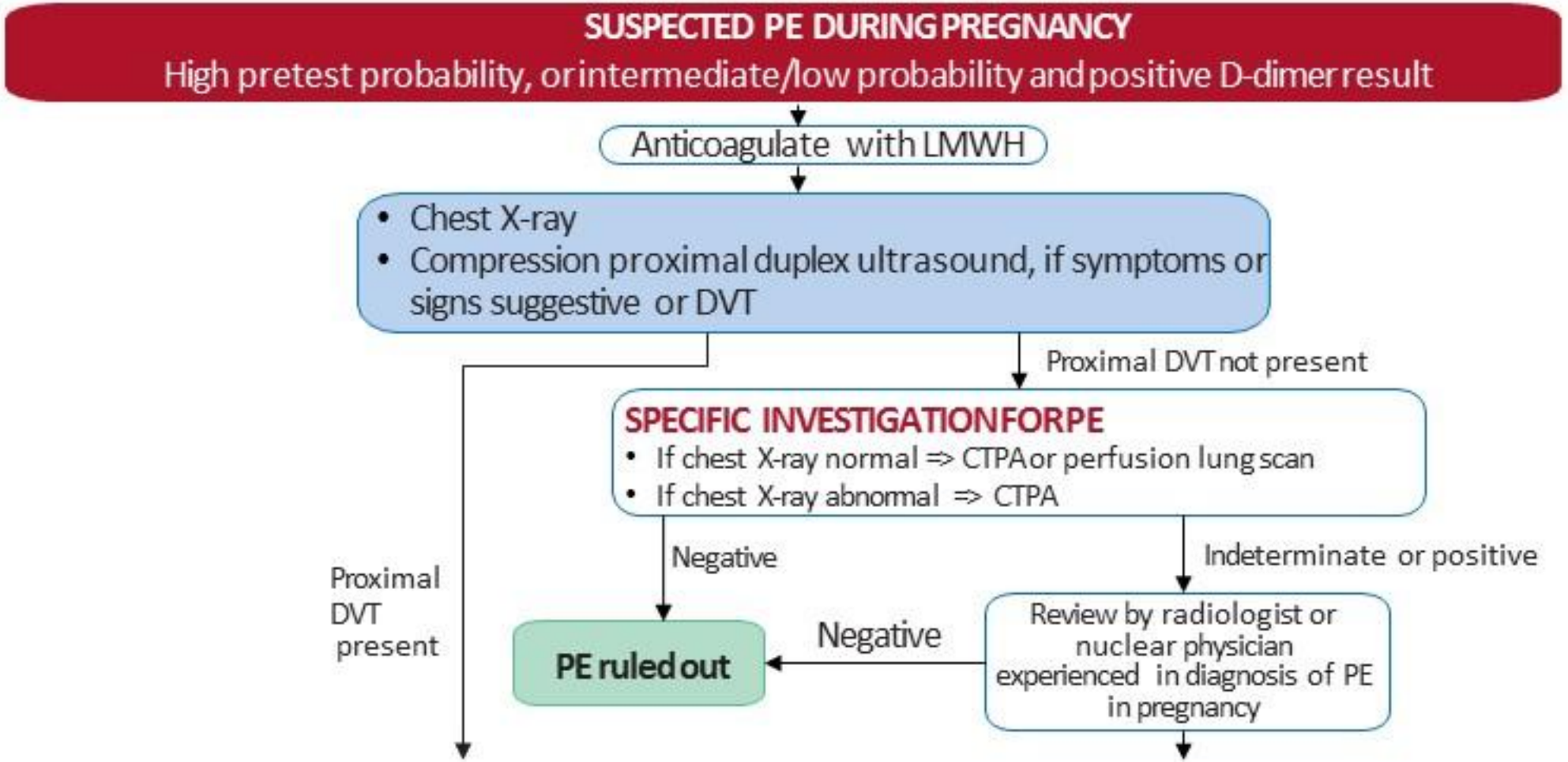
ESC European Society of Cardiology

Test	Estimated foetal radiation exposure (mGy)	Estimated maternal radiation exposure to breast tissue (mGy)
Chest X-ray	<0.01	<0.1
Perfusion lung scan with technetium-99m labelled albumin		
Low dose: ~40 MBq	0.02–0.20	0.16–0.5
High dose: ~200 MBq	0.20–0.60	1.2
Ventilation lung scan	0.10–0.30	<0.01
CTPA	0.05–0.5	3–10

CTPA = computed tomography pulmonary angiography.

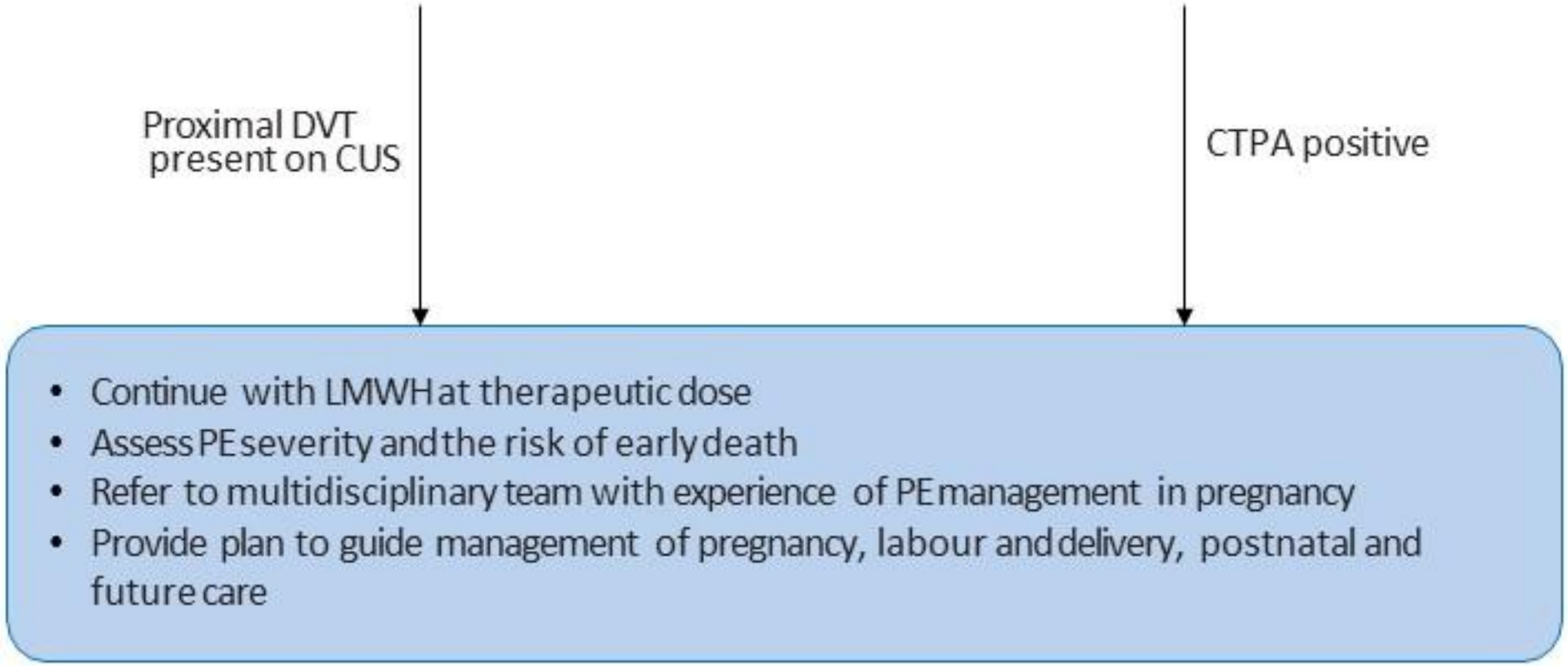
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Figure 6 Diagnostic work-up for suspected PE during pregnancy and up to 6 weeks postpartum (1)



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

Figure 6 Diagnostic work-up for suspected PE during pregnancy and up to 6 weeks postpartum (2)



CTPA = computed tomography pulmonary angiography; CUS = compression venous ultrasound; DVT = deep vein thrombosis; LMWH = low molecular weight heparin.

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

Recommendations for pulmonary embolism in pregnancy (1)

Recommendations	Class	Level
Diagnosis		
Formal diagnostic assessment with validated methods is recommended if PE is suspected during pregnancy or in the postpartum period.	I	B
D-dimer measurement and clinical prediction rules should be considered to rule out PE during pregnancy or the postpartum period.	IIa	B
In a pregnant patient with suspected PE (particularly if she has symptoms of DVT), venous CUS should be considered to avoid unnecessary irradiation.	IIa	B

CUS = compression venous ultrasound; 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)

Recommendations for pulmonary embolism in pregnancy (2)

Recommendations	Class	Level
Perfusion scintigraphy or CTPA (with a low-radiation dose protocol) should be considered to rule out suspected PE in pregnant women; CTPA should be considered as the first- line option if the chest X-ray is abnormal.	IIa	C
Treatment		
Therapeutic, fixed dose of LMWH based on early pregnancy body weight is the recommended therapy for PE in the majority of pregnant women without haemodynamic instability.	I	B
Thrombolysis or surgical embolectomy should be considered for pregnant women with high-risk PE.	IIa	C

CTPA = computed tomography pulmonary angiography; LMWH = low molecular weight heparin.

Recommendations for pulmonary embolism in pregnancy (3)

Recommendations	Class	Level
It is not recommended to insert a spinal or epidural needle unless at least 24 hours have passed since the last therapeutic dose of LMWH.	III	C
It is not recommended to administer LMWH within 4 hours of removal of an epidural catheter.	III	C
NOACs are not recommended during pregnancy or lactation.	III	C
Amniotic fluid embolism		
Amniotic fluid embolism should be considered in a pregnant or postpartum woman with otherwise unexplained cardiac arrest, sustained hypotension, or respiratory deterioration, especially if accompanied by disseminated intravascular coagulation.	IIa	C

LMWH = low molecular weight heparin; NOAC(s) = non-vitamin K antagonist oral anticoagulant(s).

Table 16 Risk factors, predisposing conditions for CTEPH (1)

ESC European Society of Cardiology

Findings related to the acute PE event (obtained at PE diagnosis)	Concomitant chronic diseases and conditions predisposing to CTEPH (documented at PE diagnosis or at 3–6-month follow-up)
Previous episodes of PE or DVT	Ventriculo-atrial shunts
Large pulmonary arterial thrombi on CTPA	Infected chronic i.v. lines or pacemakers
Echocardiographic signs of PH/RV dysfunction	History of splenectomy
CTPA findings suggestive of pre-existing chronic thromboembolic disease	Thrombophilic disorders, particularly antiphospholipid antibody syndrome and high coagulation factor VIII levels

CTEPH = chronic thromboembolic pulmonary hypertension; CTPA = computed tomography pulmonary angiography; DVT = deep vein thrombosis; PH = pulmonary hypertension; RV = right ventricular.

Table 16 Risk factors, predisposing conditions for CTEPH (2)

ESC European Society of Cardiology

Findings related to the acute PE event (obtained at PE diagnosis)	Concomitant chronic diseases and conditions predisposing to CTEPH (documented at PE diagnosis or at 3–6-month follow-up)
	Non-O blood group
	Hypothyroidism treated with thyroid hormones
	History of cancer
	myeloproliferative disorders
	Inflammatory bowel disease
	Chronic osteomyelitis

CTEPH = chronic thromboembolic pulmonary hypertension.

Recommendations for follow-up after acute PE (1)

ESC European Society of Cardiology

Recommendations	Class	Level
Routine clinical evaluation of patients 3–6 months after the acute PE episode is recommended.	I	B
An integrated model of patient care after PE (involving hospital specialists, appropriately qualified nurses, and primary care physicians) is recommended to ensure optimal transition from hospital to community care.	I	C
In symptomatic patients with mismatched perfusion defects persisting on V/Q scan beyond 3 months after acute PE, referral to a PH/CTEPH expert centre is recommended, after taking into account the results of echocardiography, natriuretic peptide levels and/or cardiopulmonary exercise testing.	I	C

CTEPH = chronic thromboembolic pulmonary hypertension; PH = pulmonary hypertension; V/Q = ventilation/perfusion.

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

Recommendations for follow-up after acute PE (2)

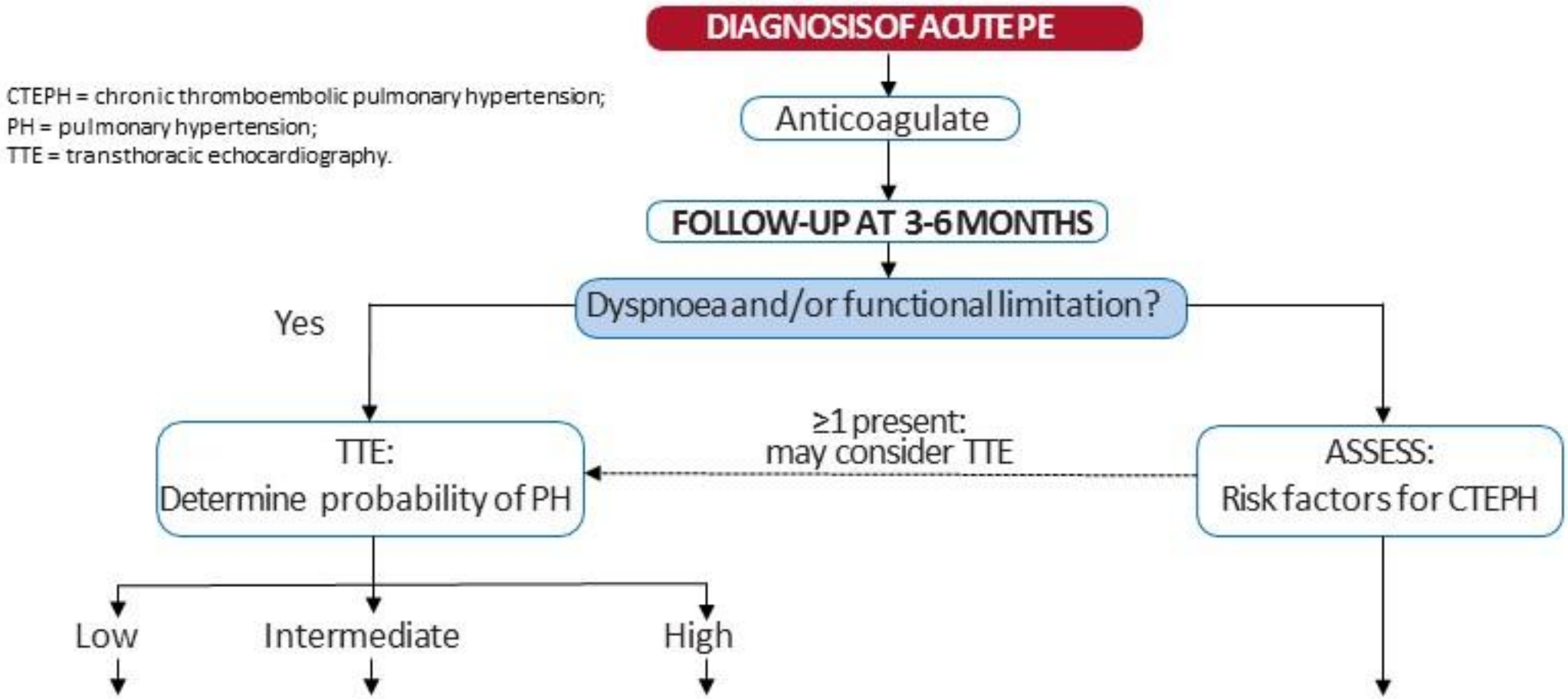
ESC European Society of Cardiology

Recommendations	Class	Level
Further diagnostic evaluation should be considered in patients with persistent or new-onset dyspnoea/exercise limitation after PE.	IIa	C
Further diagnostic evaluation may be considered in asymptomatic patients with risk factors for CTEPH.	IIb	C

CTEPH = chronic thromboembolic pulmonary hypertension.

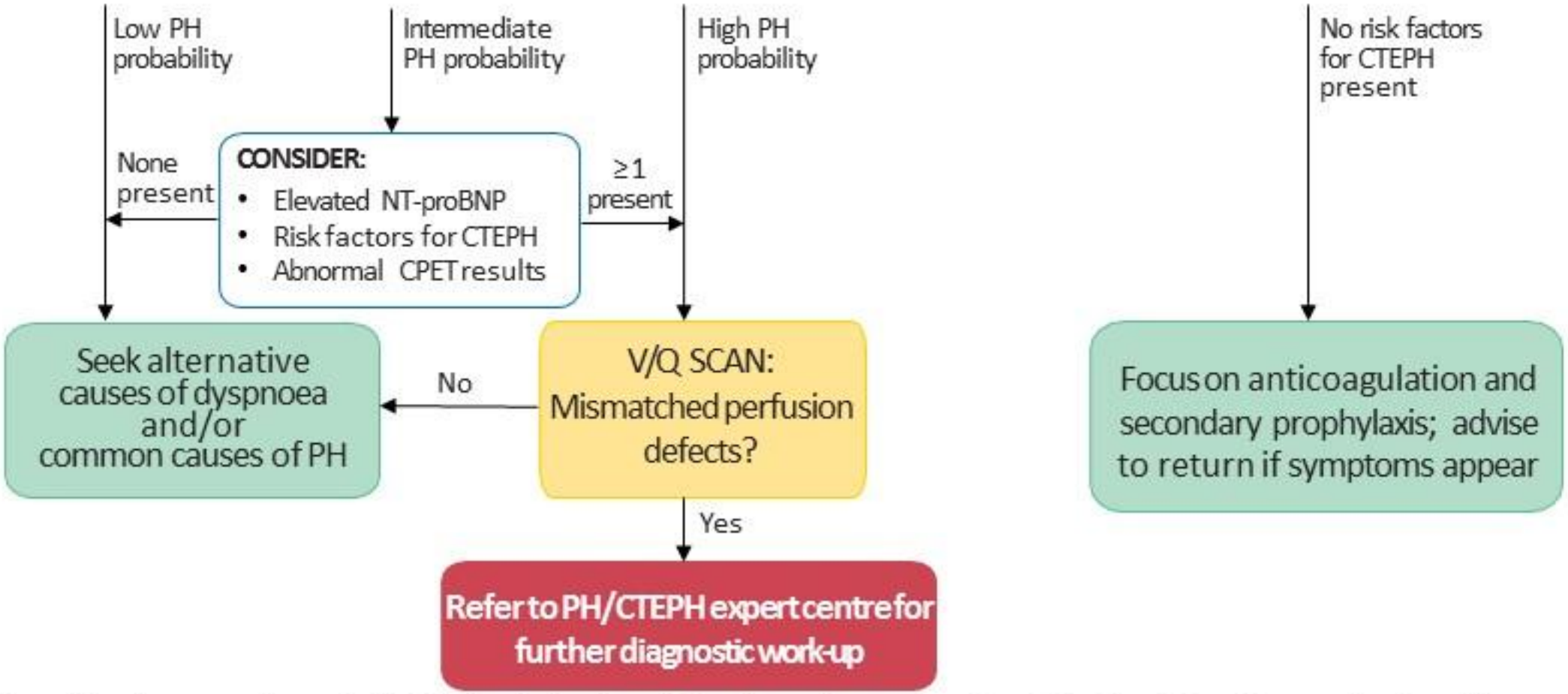
2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

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



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

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.

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

Acute PE

Guidelines for the Diagnosis and Management of Acute Pulmonary Embolism

ESC
European Society of Cardiology

www.escardio.org/guidelines

Full Text

ESC Pocket Guidelines App

and much more...

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

ESC Pocket Guidelines App

Anytime - Anywhere

- **All ESC Pocket Guidelines**
- **Over 145 interactive tools**
  - **Algorithms**
  - **Calculators**
  - **Charts & Scores**
- **Summary Cards & Essential Messages**
- **Online & Offline**

Learn more in the Guidelines area

www.escardio.org/guidelines

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

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