Diagnosis and Management of Acute Pulmonary Embolism

The Task Force on Acute Pulmonary Embolism of the European Society of Cardiology

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Symptoms and signs reported in confirmed PE

Symptoms	Approximate prevalence
Dyspnoea	80%
Chest pain (pleuritic)	52%
Chest pain (substernal)	12%
Cough	20%
Syncope	19%
Haemoptysis	11%
Signs	**Approximate prevalence**
Tachypnoea (≥ 20/min)	70%
Tachycardia (> 100/min)	26%
Signs of DVT	15%
Cyanosis	11%
Fever (> 38·5 °C)	7%

Adapted from Miniati M, Prediletto R, Formichi B, Marini C, Di Ricco G, Tonelli L et al., Am J Respir Crit Care Med 1999; 159(3):864-871 and Stein PD, Saltzman HA, Weg JG., Am J Cardiol 1991; 68(17):1723-1724

Risk- and Severity-Adjusted Strategy

Severity of PE should be understood as an individual estimate of PE-related early mortality risk, rather than anatomic burden, shape and distribution of intrapulmonary emboli. Therefore current guidelines suggest replacing potentially misleading terms such as "massive, sub-massive, non-massive" with the estimated levels of risk of PE-related early death.

Principal markers useful for risk stratification

Clinical markers	Shock Hypotension*
Markers of RV dysfunction	RV dilatation, hypokinesis or pressure overload on echocardiography RV dilatation on spiral computed tomography BNP or NT-proBNP elevation Elevated right heart pressures at right heart catheterization
Markers of myocardial injury	Cardiac troponin T or I positive**

BNP - brain natruretic peptide, NT-proBNP - N-terminal proBNP
** Defined as a systolic blood pressure < 90 mmHg or a pressure drop of > 40 mmHg for > 15 minutes if not caused by new-onset arrhythmia, hypovolaemia or sepsis.*
*** Heart-type fatty-acids binding protein (H-FABP) is an emerging marker in this category, but still requires confirmation.*

Severity of Pulmonary Embolism

PE-related early MORTALITY RISK	RISK MARKERS		
	CLINICAL (Shock or hypotension)	RV Dysfunction	Myocardial injury
HIGH > 15%	+	(+)*	(+)*

Severity of Pulmonary Embolism

PE-related early MORTALITY RISK	RISK MARKERS		
	CLINICAL (Shock or hypotension)	RV Dysfunction	Myocardial injury
HIGH > 15%	+	(+)*	(+)*
NON HIGH			

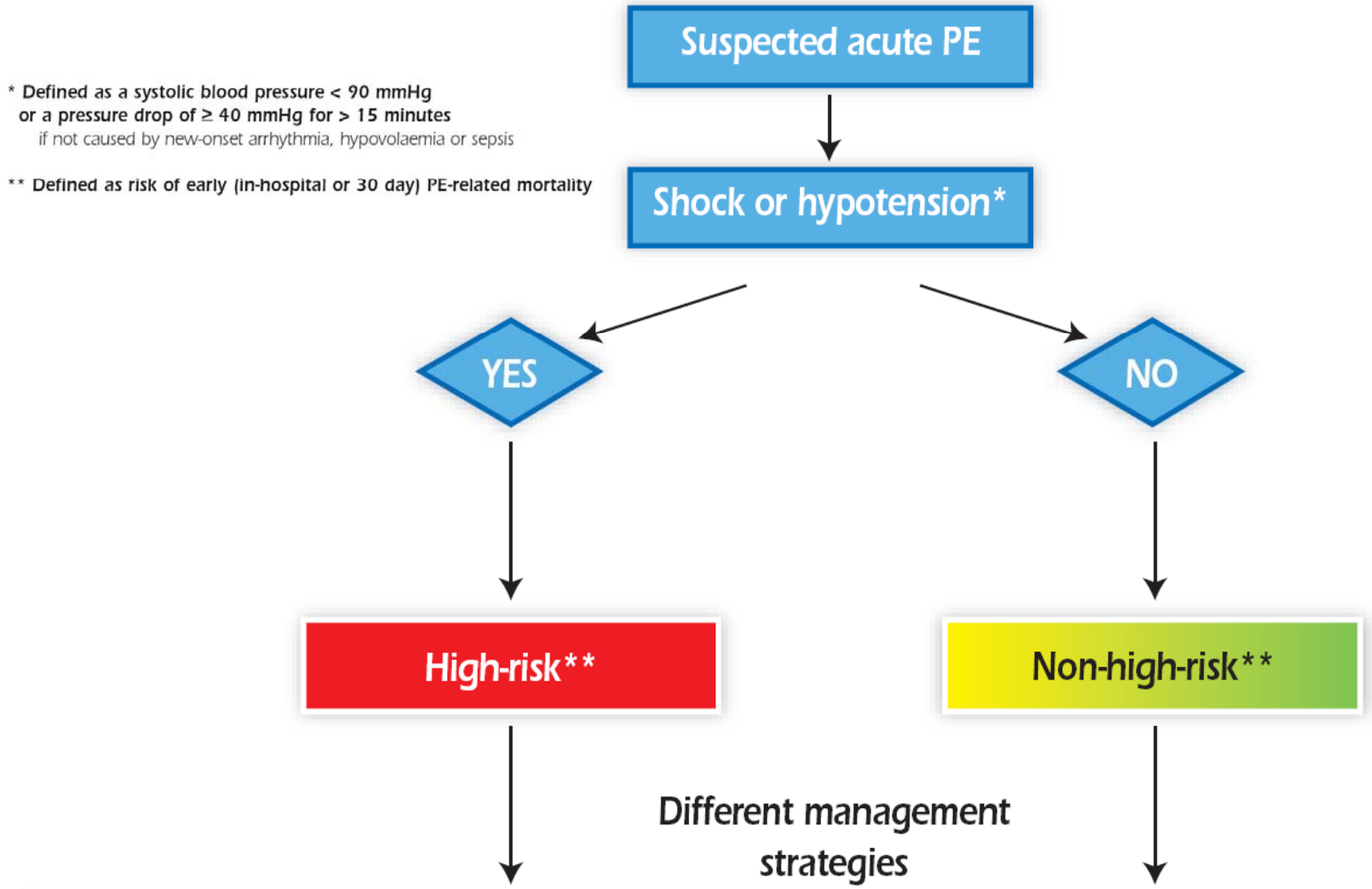
Severity of Pulmonary Embolism

PE-related early MORTALITY RISK		RISK MARKERS		
		CLINICAL (Shock or hypotension)	RV Dysfunction	Myocardial injury
HIGH > 15%		+	(+)*	(+)*
NON HIGH	Intermediate 3 - 15%	–		
	Low <1%	–		

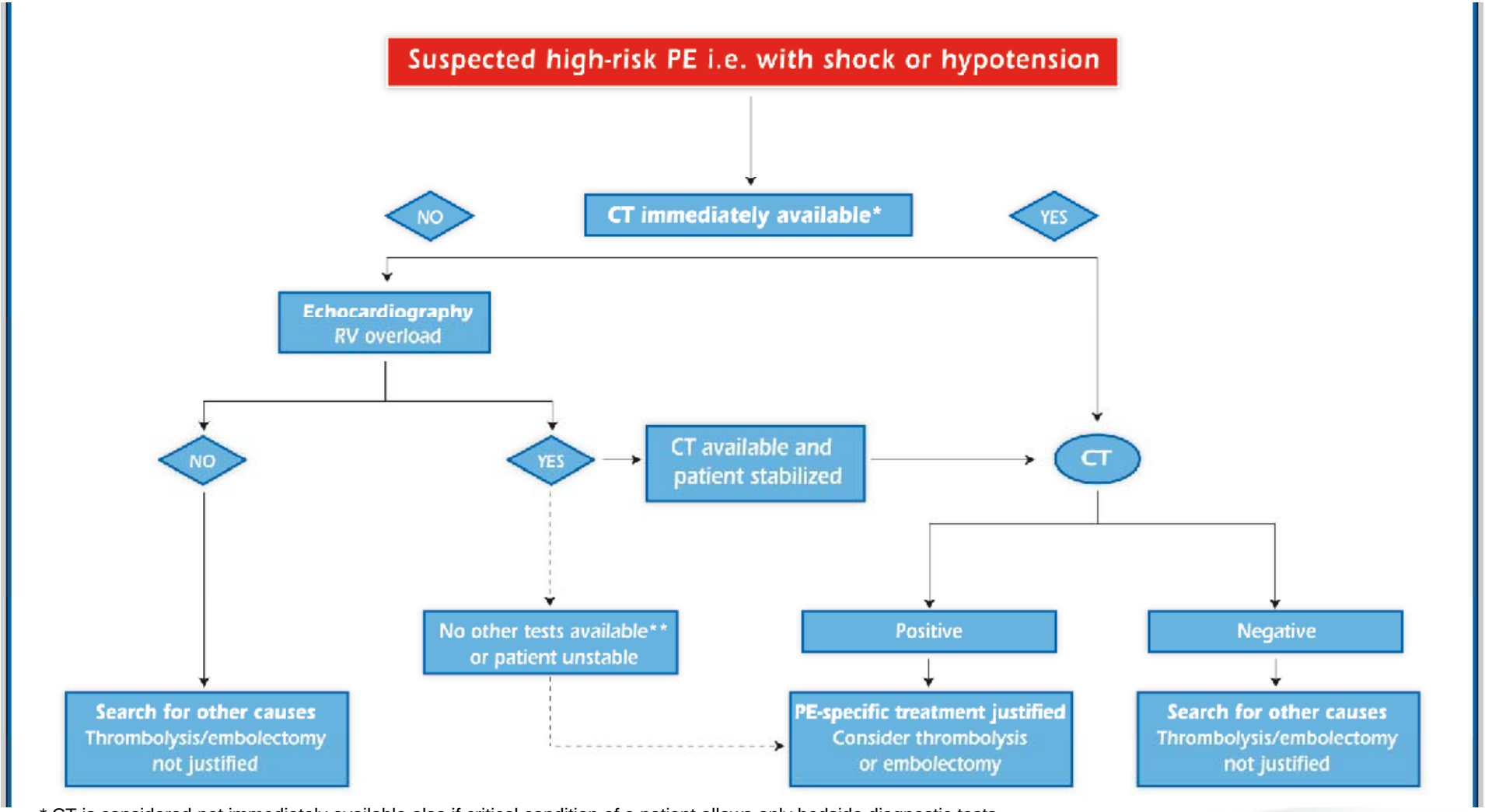
Risk-Adjusted Treatment Strategy

PE-related early MORTALITY RISK		RISK MARKERS		
		CLINICAL (Shock or hypotension)	RV Dysfunction	Myocardial injury
HIGH > 15%		+	(+)*	(+)*
NON HIGH	Intermediate 3 - 15%	–	+	+
			+	–
			–	+
	Low <1%	–	–	–

Initial Risk Stratification

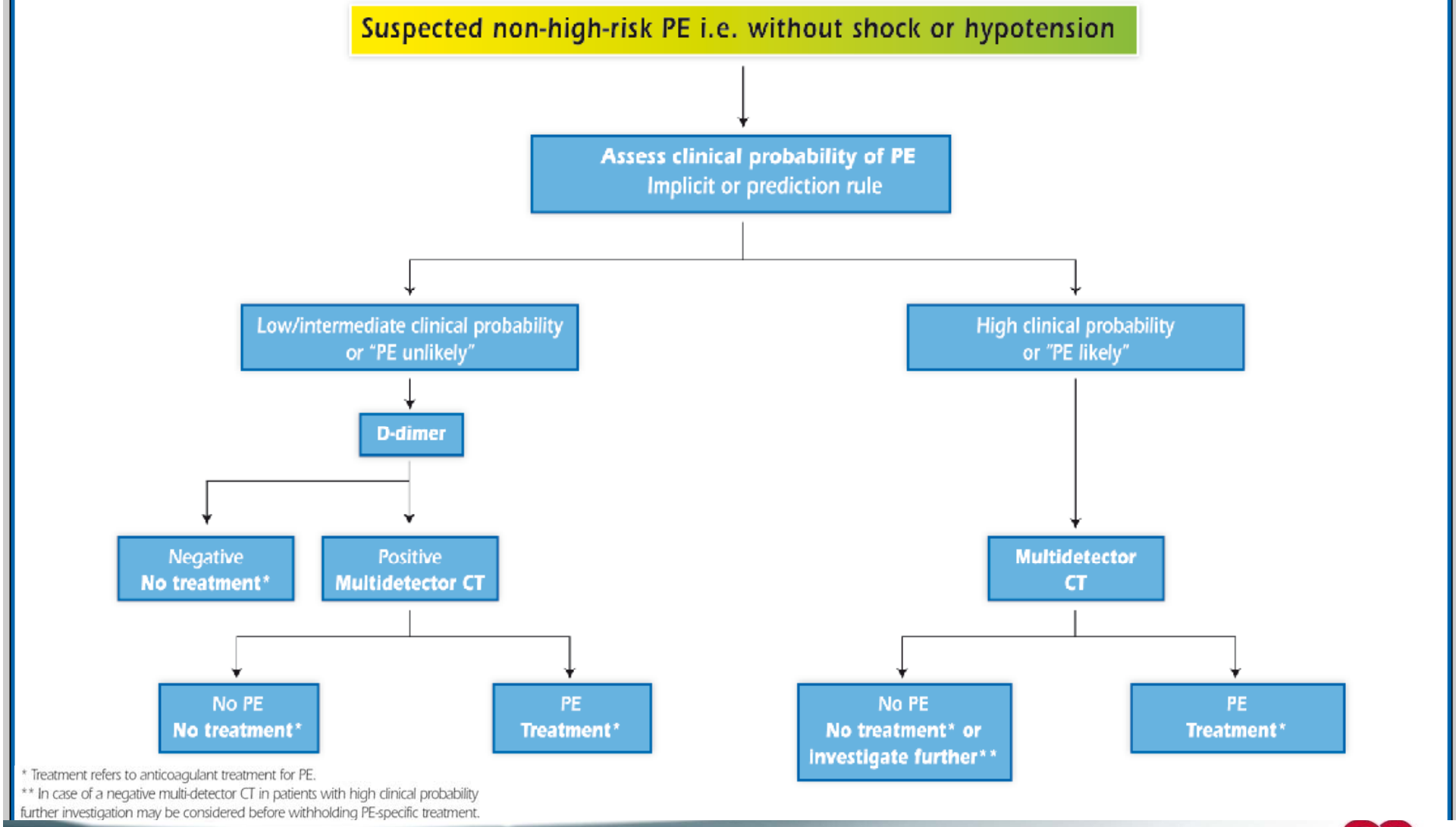


Diagnostic Assessment (1)



* CT is considered not immediately available also if critical condition of a patient allows only bedside diagnostic tests.
** Note that transesophageal echocardiography may detect thrombi in the pulmonary arteries in a significant proportion of patients with RV overload and PE ultimately confirmed at spiral CT and that confirmation of DVT with bedside CUS might also help in decision making.

Diagnostic Assessment (2)



Wells score

Variables	Points
Predisposing factors	
Previous PE or DVT	+1.5
Recent surgery or immobilization	+1.5
Cancer	+1
Symptoms	
Haemoptysis	+1
Clinical signs	
Heart rate > 100 beats per minute	+1.5
Clinical signs of DVT	+3
Clinical judgment	
Alternative diagnosis less likely than PE	+3
Clinical probability (2-level)	**Total**
PE unlikely	0-4
PE likely	> 4

Wells score

Variables	Points
Predisposing factors	
Previous PE or DVT	+1.5
Recent surgery or immobilization	+1.5
Cancer	+1
Symptoms	
Haemoptysis	+1
Clinical signs	
Heart rate > 100 beats per minute	+1.5
Clinical signs of DVT	+3
Clinical judgment	
Alternative diagnosis less likely than PE	+3
Clinical probability (3-level)	**Total**
Low	0 to 1
Intermediate	2 to 6
High	≥ 7

Revised Geneva score

Variables	Points
Predisposing factors	
Age > 65 years	+1
Previous DVT or PE	+3
Surgery or fracture within one month	+2
Active malignancy	+2
Symptoms	
Unilateral lower limb pain	+3
Haemoptysis	+2
Clinical signs	
Heart rate	
75 to 94 beats per minute	+3
≥ 95 beats per minute	+5
Pain on lower limb deep vein at palpation and unilateral oedema	+4
Clinical probability	**Total**
Low	0 to 3
Intermediate	4 to 10
High	≥ 11

Validated diagnostic criteria for patients without shock and hypotension according to clinical probability

Non-high-risk PE

Valid criterion (no further testing required): +, color green.
Invalid criterion (further testing mandatory): –, color red.
Controversial criterion (further testing to be considered); ±, color orange.
* Non diagnostic lung scan: low or intermediate probability lung scan according to the PIOPED (Prospective Investigation On Pulmonary Embolism Diagnosis study) classification.

Exclusion of pulmonary embolism

Diagnostic criterion	Clinical probability of PE		
	Low	Intermediate	High
Normal pulmonary angiogram	+	+	+
D-dimer			
Negative result, highly sensitive assay	+	+	–
Negative result, moderately sensitive assay	+	–	–
V/Q scan			
Normal lung scan	+	+	+
Non-diagnostic lung scan*	+	–	–
Non-diagnostic lung scan* and negative proximal CUS	+	+	±
Chest CT angiography			
Normal single-detector CT and negative proximal CUS	+	+	±
Normal multi-detector CT alone	+	+	±

appropriate

inappropriate

No definitive data

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Validated diagnostic criteria for patients without shock and hypotension according to clinical probability

Non-high-risk PE

Valid criterion (no further testing required): +, color green.
Invalid criterion (further testing mandatory): –, color red.
Controversial criterion (further testing to be considered); ±, color orange.

Confirmation of pulmonary embolism

Diagnostic criterion	Clinical probability of PE		
	Low	Intermediate	High
Pulmonary angiogram showing PE	+	+	+
High probability V/Q scan	±	+	+
CUS showing a proximal DVT	+	+	+
Chest CT angiography			
Single or multi-detector helical CT scan showing PE (at least segmental)	±	+	+
Single or multi-detector helical CT scan showing sub-segmental PE	±	±	±

Comprehensive Risk Stratification

Recommendations	Class [a]	Level [b]
▪ Initial risk stratification of suspected and/or confirmed PE based on the presence of shock and hypotension is recommended to distinguish between patients with high and non-high risk of PE related early mortality	I	B
▪ In non-high-risk PE patients, further stratification to an intermediate or low-risk PE subgroup based on the presence of imaging or biochemical markers of RV dysfunction and myocardial injury should be considered	IIa	B

Initial Treatment

Recommendations	Class [a]	Level [b]
▪ Anticoagulation with UFH should be initiated without delay in patients with high-risk PE	I	A
▪ Systemic hypotension should be corrected to prevent progression of RV failure and death due to PE	I	C
▪ Vasopressive drugs are recommended for hypotensive patients with PE	I	C
▪ Dobutamine and dopamine may be used in patients with PE, low cardiac output and normal blood pressure	IIa	B
▪ Aggressive fluid challenge is not recommended	III	B
▪ Oxygen should be administered to patients with hypoxaemia	I	C
▪ Thrombolytic therapy should be used in patients with high-risk PE presenting with cardiogenic shock and/or persistent arterial hypotension	I	A
▪ Surgical pulmonary embolectomy is a recommended therapeutic alternative in patients with high-risk PE in whom thrombolysis is absolutely contraindicated or has failed	I	C
▪ Catheter embolectomy or fragmentation of proximal pulmonary arterial clots may be considered as an alternative to surgical treatment in high-risk patients when thrombolysis is absolutely contraindicated or has failed	IIb	C

Approved thrombolytic regimens for pulmonary embolism

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
Urokinase	4,400 IU/kg as a loading dose over 10 min, followed by 4,400 IU/Kg/h over 12-24 h
→	Accelerated regimen: 3 million IU over 2 h
rtPA →	100 mg over 2 h; or
	0.6 mg/kg over 15 min (maximum dose 50 mg)

Contra-indications to thrombolytic therapy

Absolute contra-indications*:

- 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)
- Gastro-intestinal bleeding within the last month
- Known bleeding

Relative contra-indications

- 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 mm Hg)
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer

Relative in life-threatening PE

High-risk PE

Recommendations	Class [a]	Level [b]
▪ Anticoagulation with UFH should be initiated without delay in patients with high-risk PE	I	A
▪ Systemic hypotension should be corrected to prevent progression of RV failure and death due to PE	I	C
▪ Vasopressive drugs are recommended for hypotensive patients with PE	I	C
▪ Dobutamine and dopamine may be used in patients with PE, low cardiac output and normal blood pressure	IIa	B
▪ Aggressive fluid challenge is not recommended	III	B
▪ Oxygen should be administered to patients with hypoxaemia	I	C
▪ Thrombolytic therapy should be used in patients with high-risk PE presenting with cardiogenic shock and/or persistent arterial hypotension	I	A
▪ Surgical pulmonary embolectomy is a recommended therapeutic alternative in patients with high-risk PE in whom thrombolysis is absolutely contraindicated or has failed	I	C
▪ Catheter embolectomy or fragmentation of proximal pulmonary arterial clots may be considered as an alternative to surgical treatment in high-risk patients when thrombolysis is absolutely contraindicated or has failed	IIb	C

Non-high-risk PE

Recommendations	Class [a]	Level [b]
✓ ▪ Anticoagulation should be initiated without delay in patients with high or intermediate clinical probability of PE while diagnostic work-up is still ongoing	I	C
✓ ▪ Use of LMWH or fondaparinux is the recommended form of initial treatment for most patients with non-high-risk PE	I	A
✓ ▪ In patients at high bleeding risk and in those with severe renal dysfunction UFH with an aPTT target range of 1.5 – 2.5 times normal is a recommended form of initial treatment	I	C
✓ ▪ Initial treatment with UFH, LMWH or fondaparinux should be continued for at least 5 days and may be replaced by Vit K antagonists only after achieving target INR levels for at least 2 consecutive days	I I	A C
✓ ▪ Routine use of thrombolysis in non–high-risk PE patients is not recommended, but it may be considered in selected patients with intermediate-risk PE	IIb	B
✓ ▪ Thrombolytic therapy should not be used in patients with low-risk PE	III	B

Subcutaneous regimens of low molecular-weight heparins and fondaparinux approved for the treatment of PE

	Dosage	Interval
Enoxaparin	1.0 mg/kg or 1.5 mg/kg*	Every 12 h Once daily*
Tinzaparin	175 U/kg	Once daily
Fondaparinux	5 mg (body weight < 50 kg); 7.5 mg (body weight 50-100 kg); 10 mg (body weight > 100 kg)	Once daily

** Once-daily injection of enoxaparin at the dosage of 1.5 mg/kg is approved for inpatient (hospital) treatment of PE in the United States and in some, but not all, European countries.*

Subcutaneous regimens of low molecular-weight heparins and fondaparinux approved for the treatment of PE

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In patients with cancer Dalteparin is approved for extended treatment of symptomatic VTE (proximal DVT and/or PE), at an initial dose of 200 IU/kg s.c. once daily (see drug labeling for details). Other LMWH approved for the treatment of DVT are sometimes used also in PE.

Inferior Vena Cava Filters for PE

Recommendation	Class	Level
✓ IVC filters may be used when there are absolute contraindications to anticoagulation and a high risk of recurrence	**IIb**	**B**
✓ The routine use of IVC filters in patients with PE is not recommended	**III**	**B**

Long Term Treatment

Recommendations	Class [a]	Level [b]
▪ For patients with PE secondary to a transient (reversible) risk factor, treatment with a VKA is recommended for 3 months	I	A
▪ For patients with unprovoked PE, treatment with a VKA is recommended for at least 3 months	I	A
▪ Patients with a first episode of unprovoked PE and low bleeding risk, and in whom stable anticoagulation can be achieved, may be considered for long-term oral anticoagulation	IIb	B
▪ For patients with a second episode of unprovoked PE, long-term treatment is recommended	I	A
▪ In patients who receive long-term anticoagulant treatment, the risk-benefit ratio of continuing such treatment should be reassessed at regular intervals	I	C
▪ For patients with PE and cancer, LMWH should be considered for the first 3 to 6 months after this period, anticoagulant therapy with VKA or LMWH should be continued indefinitely, or until the cancer is considered cured	IIa I	B C
▪ In patients with PE, the dose of VKA should be adjusted to maintain a target INR of 2.5 (INR range, 2.0 to 3.0) regardless of treatment duration	I	A

Estimated radiation absorbed by foetus in procedures for diagnosing PE

Test	Estimated radiation	
	µGy	mSv
Chest radiography	< 10	0.01
Perfusion lung scan with Technetium-99m labelled albumin (1–2mCi)	60 - 120	0.06 - 012
Ventilation lung scan	200	0.2
CT angiography		
1st trimester	3 - 20	0.003 - 0.02
2nd trimester	8 - 77	0.008 - 0.08
3rd trimester	51 - 130	0.051 - 0.13
Pulmonary angiography by femoral access	2210 - 3740	2.2 - 3.7
Pulmonary angiography by brachial access	< 500	< 0.5

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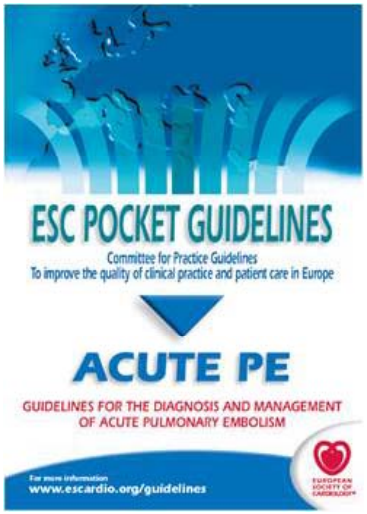

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ESC Task Force

Section Editors Meetting
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