Guidelines ESC/ERS 2019 for diagnosis and management of acute pulmonary embolism

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Facteurs prédisposants

Table 3 Predisposing factors for venous thromboembolism (data modified from Rogers *et al.*[23] and Anderson and Spencer[24])

Strong risk factors (OR > 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 VTE
Spinal cord injury
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)
In vitro fertilization
Oral contraceptive therapy
Post-partum period
Infection (specifically pneumonia, urinary tract infection, and HIV)
Inflammatory bowel disease
Cancer (highest risk in metastatic disease)
Paralytic stroke
Superficial vein thrombosis
Thrombophilia
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

HIV = human immunodeficiency virus; OR = odds ratio; VTE = venous thromboembolism.

Diagnostic

- La clinique /ECG
- Les scores cliniques: GENEVE REVISE/ Wells
- D dimeres
- Imagerie :

Rx Thorax

ETT /SCAN/ EDV

V/P Sinti SPECT V/P

Scores de probabilite

Table 5 The revised Geneva clinical prediction rule for pulmonary embolism

Items	Clinical decision rule points	
	Original version[91]	Simplified version[87]
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
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

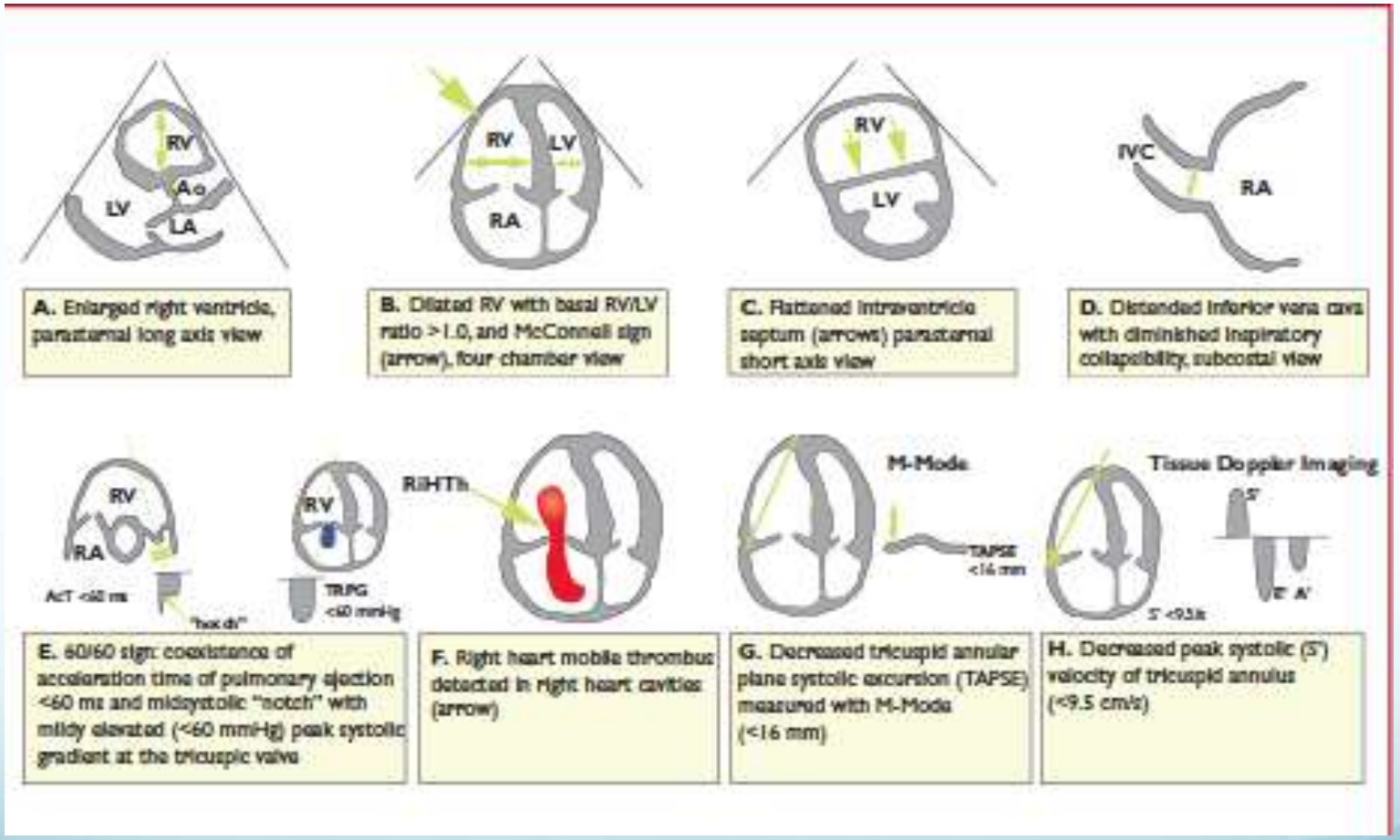
b.p.m. = beats per minute; DVT = deep vein thrombosis; PE = pulmonary embolism.

SCORE DE WELLS		
	Version originale	Version simplifiée
Atcd d'EP ou TVP	1,5	1
Fr cardiaque ≥100 bpm	1,5	1
Chirurgie ou immobilisation durant les 4 sem	1,5	1
Hémptysie	1	1
Cancer évolutif	1	1
Signes cliniques de TVP	3	1
Autre diagnostic moins probable	3	1
Probabilité Clinque		
Score 3 niveaux		
Faible	0 – 1	-
Intermédiaire	2 – 6	-
Haute	≥7	-
Score 2 niveaux		
EP peu probable	0 – 4	0 – 1
EP probable	≥5	≥2

D DIMERES

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 those that are PE-unlikely, to reduce the need for unnecessary imaging and irradiation.[101–103,122,164,171,173,174]	I	A
As an alternative to the fixed D-dimer cut-off, a negative D-dimer test using an age-adjusted cut-off (age × 10 µg/L, in patients aged >50 years) should be considered for excluding PE in patients with low or intermediate clinical probability, or those that are PE-unlikely.[106]	IIa	B
As an alternative to the fixed or age-adjusted D-dimer cut-off, D-dimer levels adapted to clinical probability[f] should be considered to exclude PE.[107]	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.[175,176]	III	A

ETT



A. Enlarged right ventricle, parasternal long axis view

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

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

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

E. 60/60 sign: coexistence of acceleration time of pulmonary ejection <60 ms and midsystolic "notch" with mildly 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)

imagerie

Table 6 Imaging tests for diagnosis of pulmonary embolism

	Strengths	Weaknesses/limitations	Radiation issues[a]

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 breastfeeding women
		  ○ contraindicated in severe renal failure
		• Tendency to overuse because of easy accessibility
		• Clinical relevance of CTPA diagnosis of subsegmental PE unknown
			• Radiation effective dose 3–10 mSv[b]
			• Significant radiation exposure to young female breast tissue

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 if PE excluded	• Lower radiation than CTPA, effective dose ~2 mSv[b]
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 if PE excluded • No validation in prospective management outcome studies	• Lower radiation than CTPA, effective dose ~2 mSv[b]
Pulmonary angiography	• Historical gold standard	• Invasive procedure • Not readily available in all centres	• Highest radiation, effective dose 10–20 mSv[b]

IMAGERIE

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 who is PE-unlikely.[101,122,164,171]	I	A
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.[115]	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 who is PE-likely.[171]	IIa	B
Further imaging tests to confirm PE may be considered in cases of isolated subsegmental filling defects.[115]	IIb	C
CT venography is not recommended as an adjunct to CTPA.[115,164]	III	B
V/Q scintigraphy		
It is recommended to reject the diagnosis of PE (without further testing) if the perfusion lung scan is normal.[75,122,134,174]	I	A
It should be considered to accept that the diagnosis of PE (without further testing) if the V/Q scan yields high probability for PE.[134]	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 who are PE-unlikely.[75,122,174]	IIa	B
V/Q SPECT		
V/Q SPECT may be considered for PE diagnosis.[121,126–128]	IIb[d]	B
Lower-limb 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.[164,165]	I	A
If CUS shows only a distal DVT, further testing should be considered to confirm PE.[177]	IIa	B
If a positive proximal CUS is used to confirm PE, assessment of PE severity should be considered to permit risk-adjusted management.[178,179]	IIa	C
MRA		
MRA is not recommended for ruling out PE.[139,140]	III	A

Evaluation du risque

Repose sur

- les signes d'instabilité HD
- Signes en faveur de sévérité de L 'EP
- Elévation des biomarqueurs marqueurs d'ischemie: les troponines ou de dysfonction VD :BNP/NTproBNP
- Présence de dysfonction et dilatation VD a ETT ou au scanner

Table 7 Original and simplified Pulmonary Embolism Severity Index

Parameter	Original version[22,6]	Simplified version[22,9]
Age	Age in years	1 point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1 point
Chronic heart failure	+10 points	1 point
Chronic pulmonary disease	+10 points	
Pulse rate ≥110 b.p.m.	+20 points	1 point
Systolic BP <100 mmHg	+30 points	1 point
Respiratory rate >30 breaths per min	+20 points	–
Temperature <36°C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point
	Risk strata[a]	
	Class I: ≤65 points 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%)

BP = blood pressure; b.p.m. = beats per minute; CI = confidence interval.

ThePulmonary Embolism Rule-out Criteria (PERC) eight clinical variables significantly associated with an absence of PE:

age < 50 years
pulse < 100 beats per minute;
SaO2 >94%;
no unilateral leg swelling;
no haemoptysis;
no recent trauma or surgery;
No history of VTE;
and no oral hormone use.

SAFE EXCLUSION OF PE IN PATIENTS WITH LOW CLINICAL PROBABILITY

Table 8 Classification of pulmonary embolism severity and the risk of early (in-hospital or 30 day) death

Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥1	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
High		+	(+)[d]	+	(+)
Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

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Table 4 Definition of haemodynamic instability, which delineates acute high-risk pulmonary embolism (one of the following clinical manifestations at presentation)

(1) Cardiac arrest	(2) Obstructive shock[68–70]	(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, lasting longer than 15 min 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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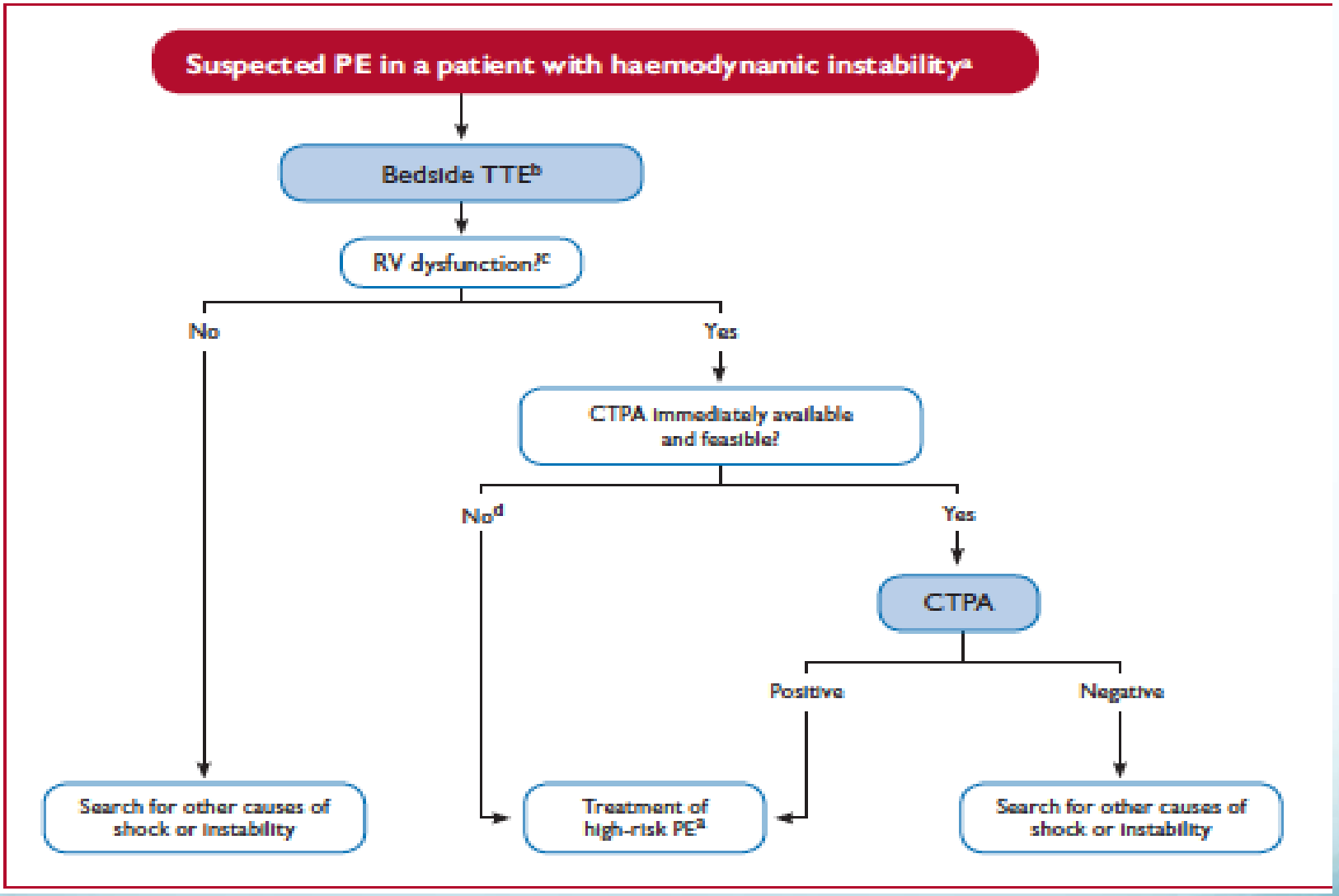
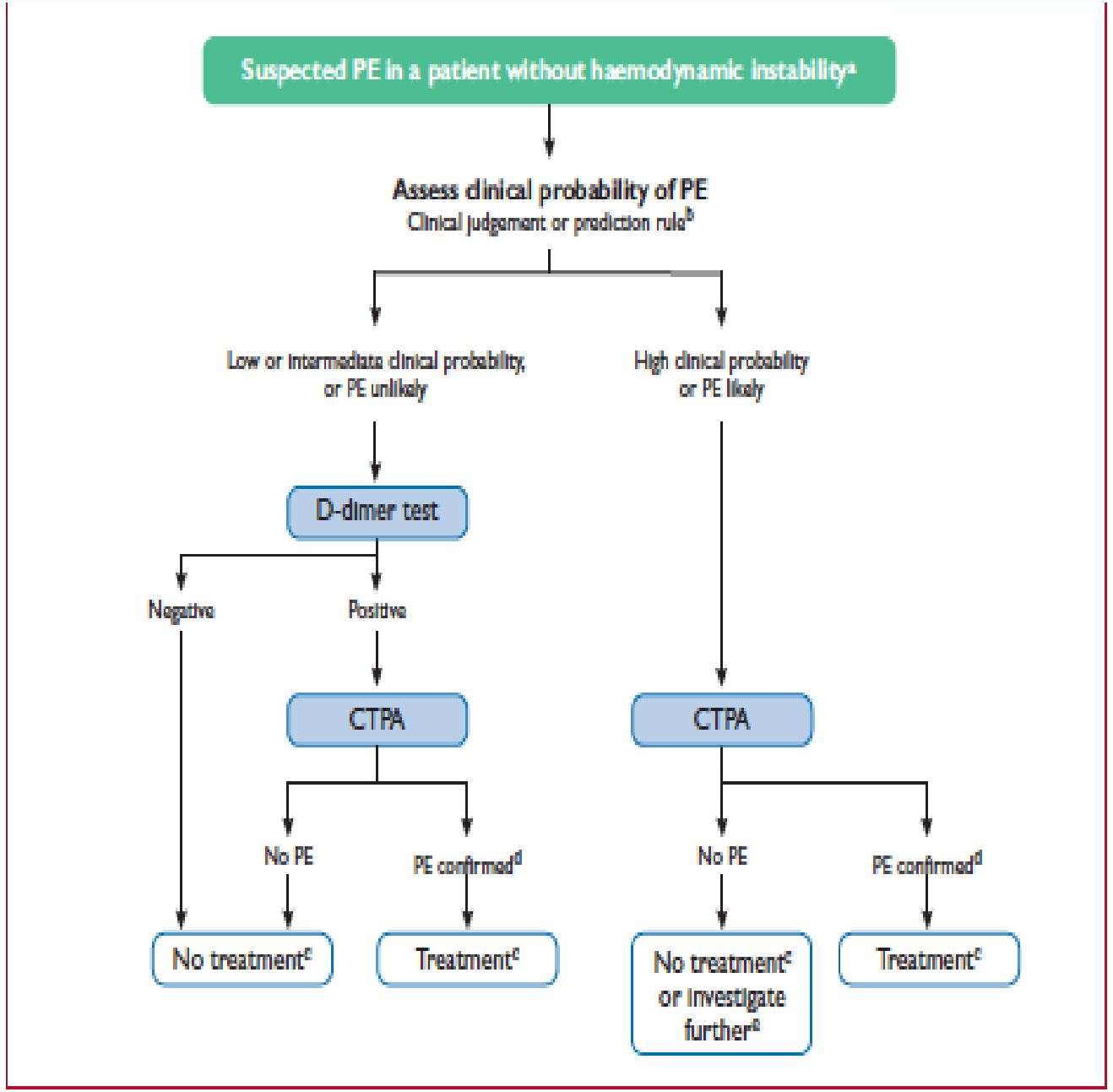
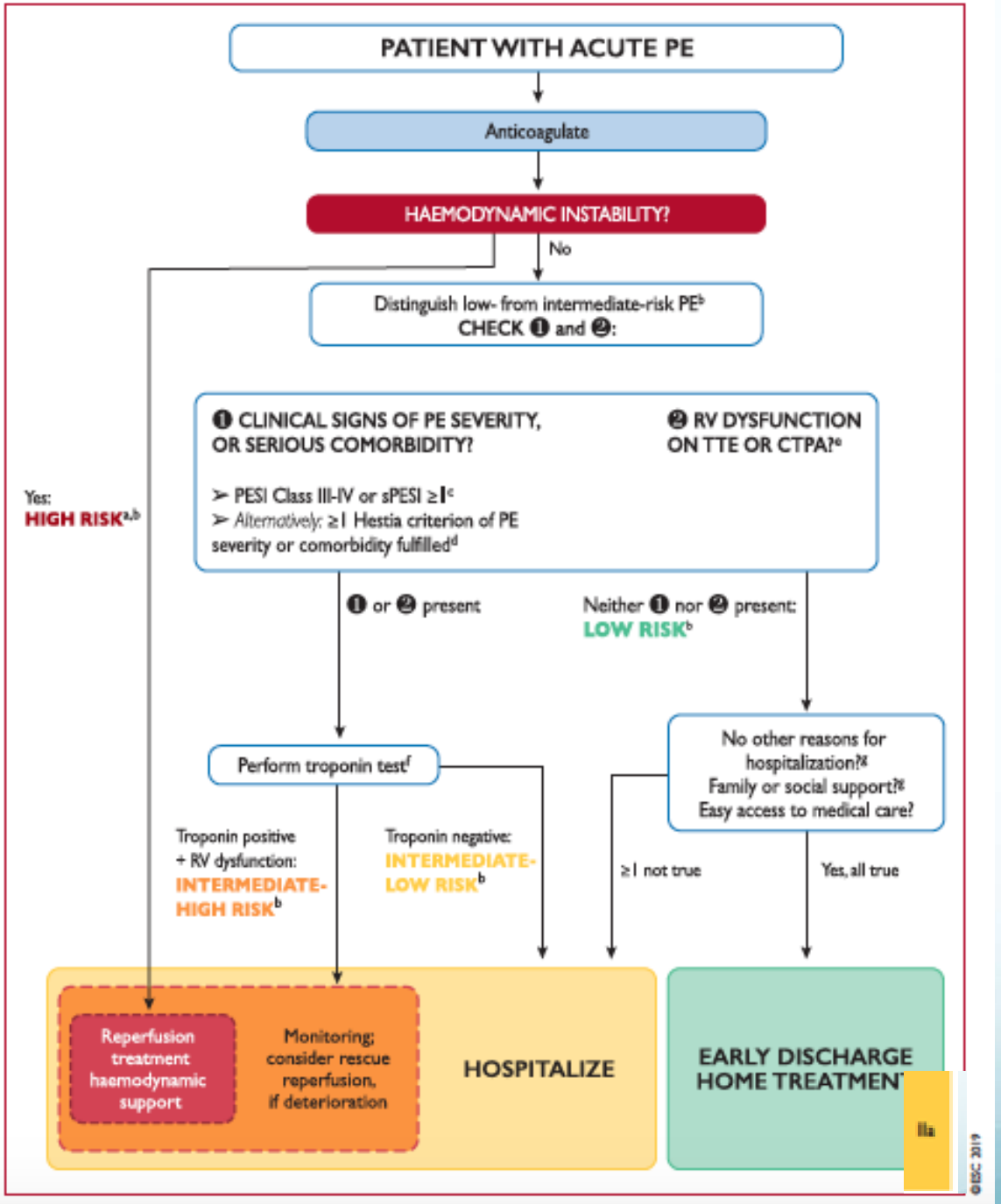
Algorithme de PEC




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
High clinical probability or PE likely
D-dimer test
Negative
Positive
CTPA
CTPA
No PE
PE confirmed[d]
No PE
PE confirmed[d]
No treatment[c]
Treatment[c]
No treatment[c] or investigate further[e]
Treatment[c]



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

6.6 Recommendations for acute-phase treatment of high-risk pulmonary embolism[a]

Recommendations	Class[b]	Level[c]
It is recommended that anticoagulation with UFH, including a weight-adjusted bolus injection, be initiated without delay in patients with high-risk PE.	I	C
Systemic thrombolytic therapy is recommended for high-risk PE.[282]	I	B
Surgical pulmonary embolectomy is recommended for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.[d 281]	I	C
Percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.[d]	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.[d 252]	IIb	C

ECMO = extracorporeal membrane oxygenation; PE = pulmonary

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6.7 Recommendations for acute-phase treatment of intermediate- or low-risk pulmonary embolism

Recommendations	Class[a]	Level[b]
Initiation of anticoagulation		
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE,[c] while diagnostic workup is in progress.	I	C
If anticoagulation is initiated parenterally, LMWH or fondaparinux is recommended (over UFH) for most patients.[262,309–311]	I	A
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.[260,261,312–314]	I	A
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.[315,316]	I	A
NOACs are not recommended in patients with severe renal impairment,[d] during pregnancy and lactation, and in patients with antiphospholipid antibody syndrome.[260,261,312–314]	III	C

Risque élevé==Thrombolyse==5joursHNF ==AOD

Risque intermédiaire== 2 a 3 jours HBPM =AOD

6.9 Recommendations for inferior vena cava filters

Recommendations	Class[a]	Level[b]
IVC filters should be considered in patients with acute PE and absolute contraindications to anticoagulation.	IIa	C
IVC filters should be considered in cases of PE recurrence despite therapeutic anticoagulation.	IIa	C
Routine use of IVC filters is not recommended.[302–304]	III	A

Risque de recurrence

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

Duree d'anticoagulation

8.4 Recommendations for the regimen and duration of anticoagulation after pulmonary embolism in patients without cancer

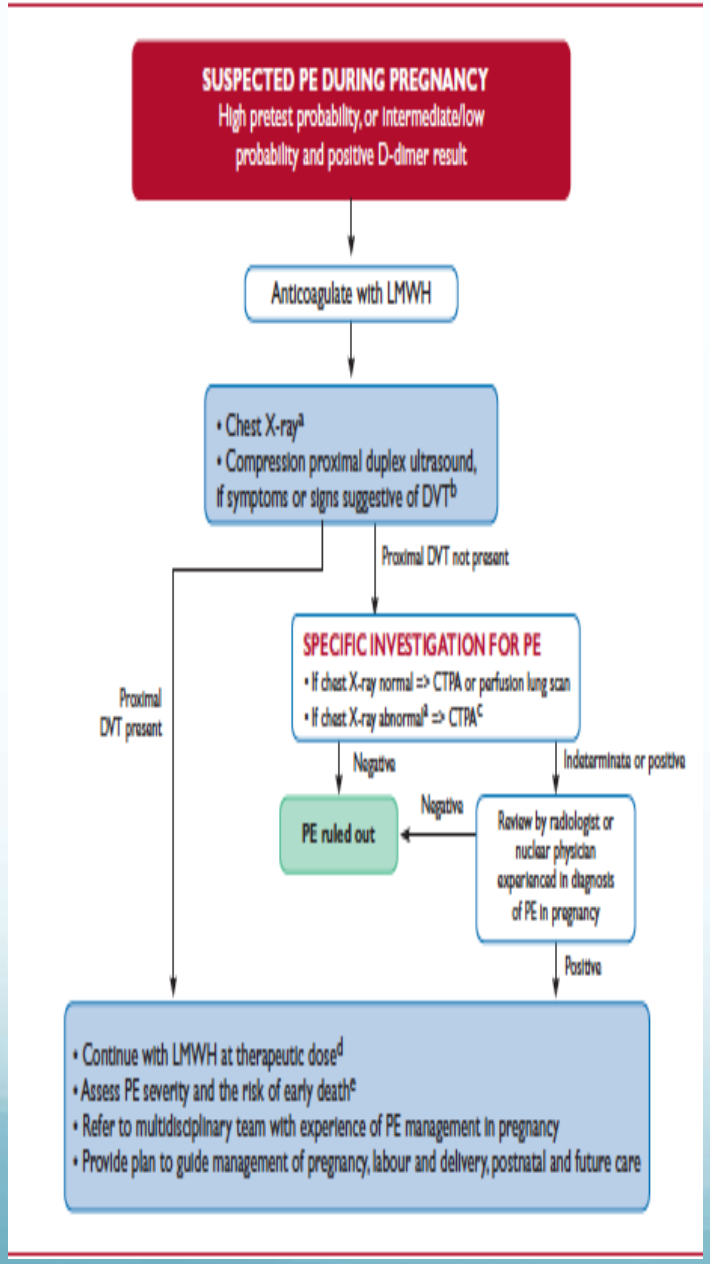
Recommendations	Class[a]	Level[b]
Therapeutic anticoagulation for ≥ 3 months is recommended for all patients with PE.[347]	I	A
Patients in whom discontinuation of anticoagulation after 3 months is recommended		
For patients with first PE/VTE secondary to a major transient/reversible risk factor, discontinuation of therapeutic oral anticoagulation is recommended after 3 months.[331,340,341]	I	B
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.[358]	I	B
Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with antiphospholipid antibody syndrome.[359]	I	B
Patients in whom extension of anticoagulation beyond 3 months should be considered[c,d]		
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE and no identifiable risk factor.[330,331,347,351–353]	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 antiphospholipid antibody syndrome.[330,352,353]	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.[330,331,352]	IIa	C
NOAC dose in extended anticoagulation[e]		
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.[352,353]	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.[355–357]	IIb	B
Follow-up of the patient under anticoagulation		
In patients who receive extended anticoagulation, it is recommended that their drug tolerance and adherence, hepatic and renal[f] function, and bleeding risk be reassessed at regular intervals.[359]	I	C

CANCER

8.6 Recommendations for the regimen and the duration of anticoagulation after pulmonary embolism in patients with active cancer

Recommendations	Class[a]	Level[b]
For patients with PE and cancer, weight-adjusted subcutaneous LMWH should be considered for the first 6 months over VKAs.[360–363]	IIa	A
Edoxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.[366]	IIa	B
Rivaroxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.[367]	IIa	C
For patients with PE and cancer, extended anticoagulation (beyond the first 6 months)[c] should be considered for an indefinite period or until the cancer is cured.[370]	IIa	B
In patients with cancer, management of 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.[376,377]	IIa	B

Grossesse



9.5 Recommendations for pulmonary embolism in pregnancy

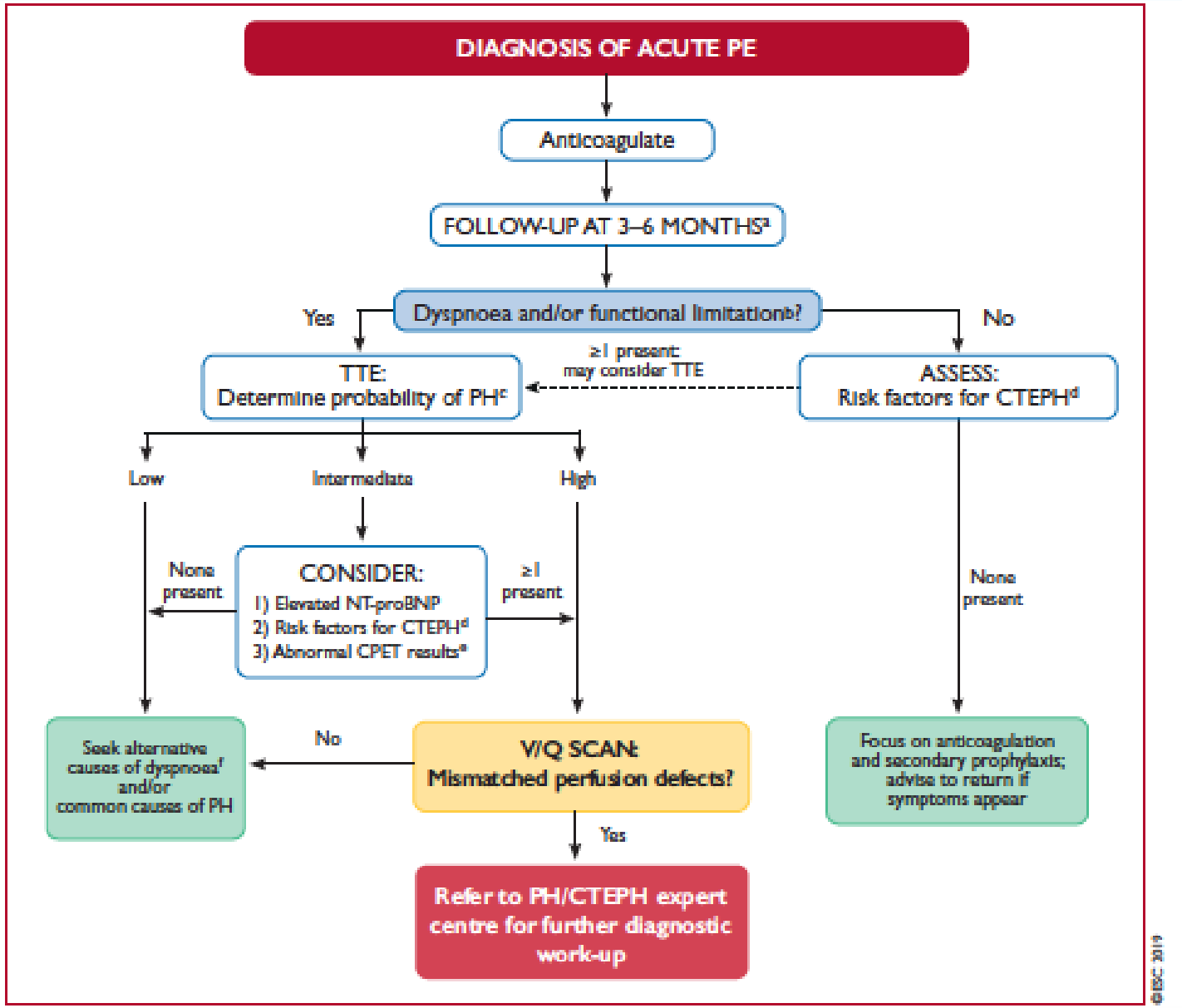
Recommendations	Class[a]	Level[b]
Diagnosis		
Formal diagnostic assessment with validated methods is recommended if PE is suspected during pregnancy or in the post-partum period.[388,391]	I	B
D-dimer measurement and clinical prediction rules should be considered to rule out PE during pregnancy or the post-partum period.[388,391]	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.[389]	IIa	B
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.[385,386]	IIa	C
Treatment		
A 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.[408,410]	I	B
Thrombolysis or surgical embolectomy should be considered for pregnant women with high-risk PE.[421]	IIa	C
Insertion of a spinal or epidural needle is not recommended, unless ≥24 h have passed since the last therapeutic dose of LMWH.	III	C
Administration of LMWH is not recommended within 4 h 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 post-partum woman with otherwise unexplained cardiac arrest, sustained hypotension, or respiratory deterioration, especially if accompanied by disseminated intravascular coagulation.[422,425,426]	IIa	C

HTAP post EP

Table 13 Risk factors and predisposing conditions for chronic thromboembolic pulmonary hypertension[447–449]

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[a]	History of splenectomy
CTPA findings suggestive of pre-existing chronic thromboembolic disease[b]	Thrombophilic disorders, particularly antiphospholipid antibody syndrome and high coagulation factor VIII levels
	Non-O blood group
	Hypothyroidism treated with thyroid hormones
	History of cancer
	Myeloproliferative disorders
	Inflammatory bowel disease
	Chronic osteomyelitis

CTEPH = Chronic thromboembolic pulmonary hypertension; CTPA = computed tomographic pulmonary angiography; DVT = deep vein thrombosis; i.v. = intravenous; LV =


DIAGNOSIS OF ACUTE PE
Anticoagulate
FOLLOW-UP AT 3–6 MONTHS[a]
Dyspnoea and/or functional limitation[b]?
Yes
No
TTE:
Determine probability of PH[c]
≥1 present:
may consider TTE
ASSESS:
Risk factors for CTEPH[d]
Low
Intermediate
High
None present
CONSIDER:
1) Elevated NT-proBNP
2) Risk factors for CTEPH[d]
3) Abnormal CPET results[e]
≥1 present
None present
Seek alternative causes of dyspnoea[f] and/or common causes of PH
No
V/Q SCAN:
Mismatched perfusion defects?
Yes
Refer to PH/CTEPH expert centre for further diagnostic work-up
Focus on anticoagulation and secondary prophylaxis; advise to return if symptoms appear
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