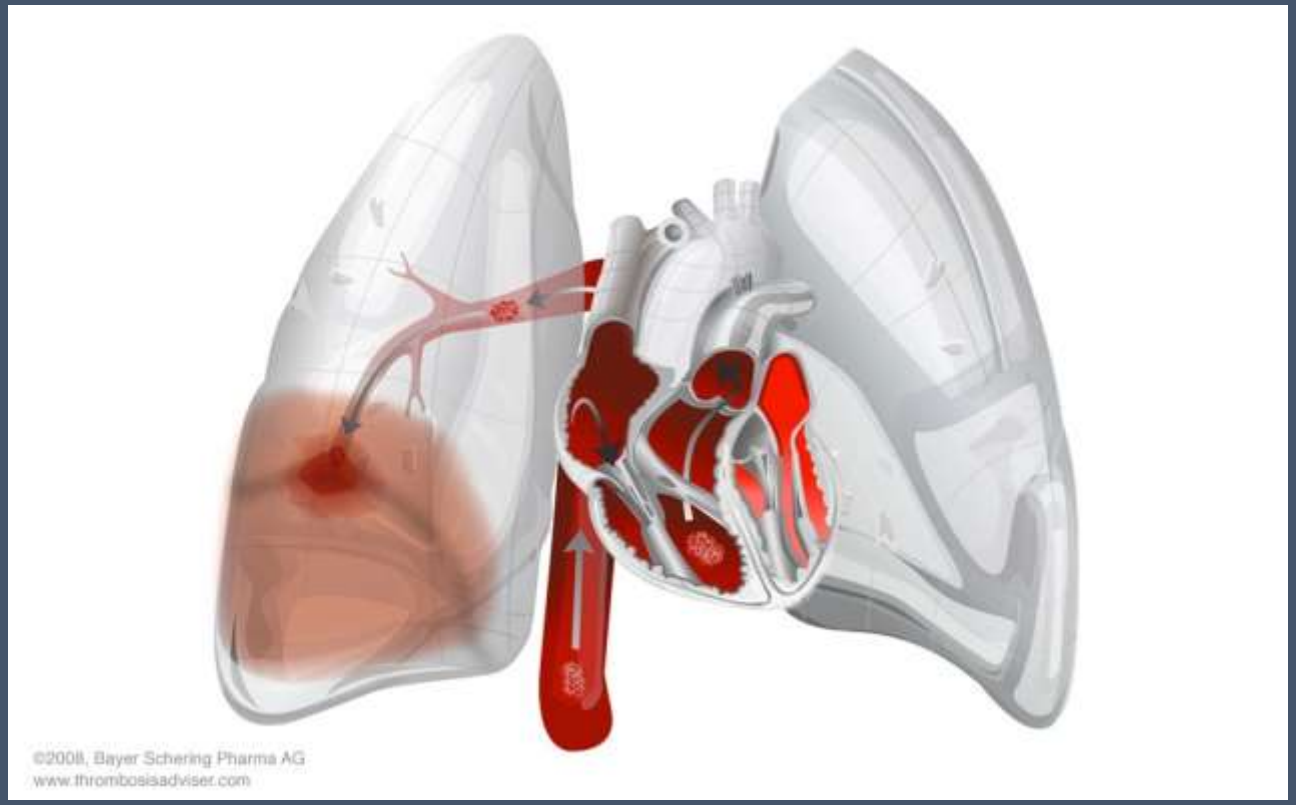


MANAGEMENT OF PULMONARY EMBOLISM IN PRIMARY CARE

Dr Priti Rath
MD,MRCPI,DME,DS&CVS,FRCP(Lon)

Objectives-

- Review the incidence, symptoms and presenting signs of PE
- Learn about clinical prediction models
- Different diagnostic methods and diagnostic algorithms.

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.

Incidence-

- The true incidence of PE is unknown and is suspected to be underestimated
- annual incidence of venous thromboembolism is approximately 2 in 1000 of the general population and the annual incidence of diagnosed pulmonary embolism in the UK has been reported as 7–8 per 10,000 people.
- Approximately one third of patients with symptomatic VTE manifest pulmonary embolism (PE), whereas two thirds manifest deep vein thrombosis (DVT) alone.
- It is estimated to be between 0.5% to 3% in the general population
- Mortality from PE is estimated to be 0.1%

Table 3 Predisposing factors for VTE (1)

ESC
European Society of Cardiology

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)

ESC
European Society of Cardiology

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.

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

Table 3 Predisposing factors for VTE (3)

ESC
European Society of Cardiology

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.

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

Table 3 Predisposing factors for VTE (4)

ESC
European Society of Cardiology

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.

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

Presentation-

Most Common Symptoms

- Dyspnea at rest or with exertion (73 %)
- Pleuritic pain (44 %)
- Cough (34 %)
- >2-pillow orthopnea (28 %)
- Calf or thigh pain (44 %)
- Calf or thigh swelling (41 %),
- Wheezing (21 %)

Most Common Signs

- Tachypnea (54 %)
- Tachycardia (24 %)
- Rales (18 %),
- Decreased breath sounds (17 %),
- Accentuated pulmonic component of the second heart sound (15 %)
- Jugular venous distension (14 %)

Determining the clinical probability of pulmonary embolism

Wells criteria and modified Wells criteria: clinical assessment for pulmonary embolism

Clinical symptoms of DVT (leg swelling, pain with palpation)	3.0
Other diagnosis less likely than pulmonary embolism	3.0
Heart rate >100	1.5
Immobilization (≥3 days) or surgery in the previous four weeks	1.5
Previous DVT/PE	1.5
Hemoptysis	1.0
Malignancy	1.0
Probability	**Score**
Traditional clinical probability assessment (Wells criteria)	
High	>6.0
Moderate	2.0 to 6.0
Low	<2.0
Simplified clinical probability assessment (Modified Wells criteria)	
PE likely	>4.0
PE unlikely	≤4.0

DVT: deep vein thrombosis; PE: pulmonary embolism.

Data from van Belle A, Buller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. JAMA 2006; 295:172.

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

ESC European Society of Cardiology

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)

ESC European Society of Cardiology

	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)

ESC
European Society of Cardiology

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

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

The pulmonary embolism rule out criteria (PERC rule)*

Age <50 years
Heart rate <100 bpm
Oxyhemoglobin saturation ≥95%
No hemoptysis
No estrogen use
No prior DVT or PE
No unilateral leg swelling
No surgery/trauma requiring hospitalization within the prior four weeks

DVT: deep venous thrombosis; PE: pulmonary embolus; bpm: beats per minute.

* This rule is only valid in patients with a low clinical probability of PE (gestalt estimate <15 percent). In patients with a low probability of PE who fullfil all eight criteria, the likelihood of PE is low and no further testing is required. All other patients should be considered

Table 6 Imaging tests for diagnosis of PE (1)

ESC European Society of Cardiology

	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.

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

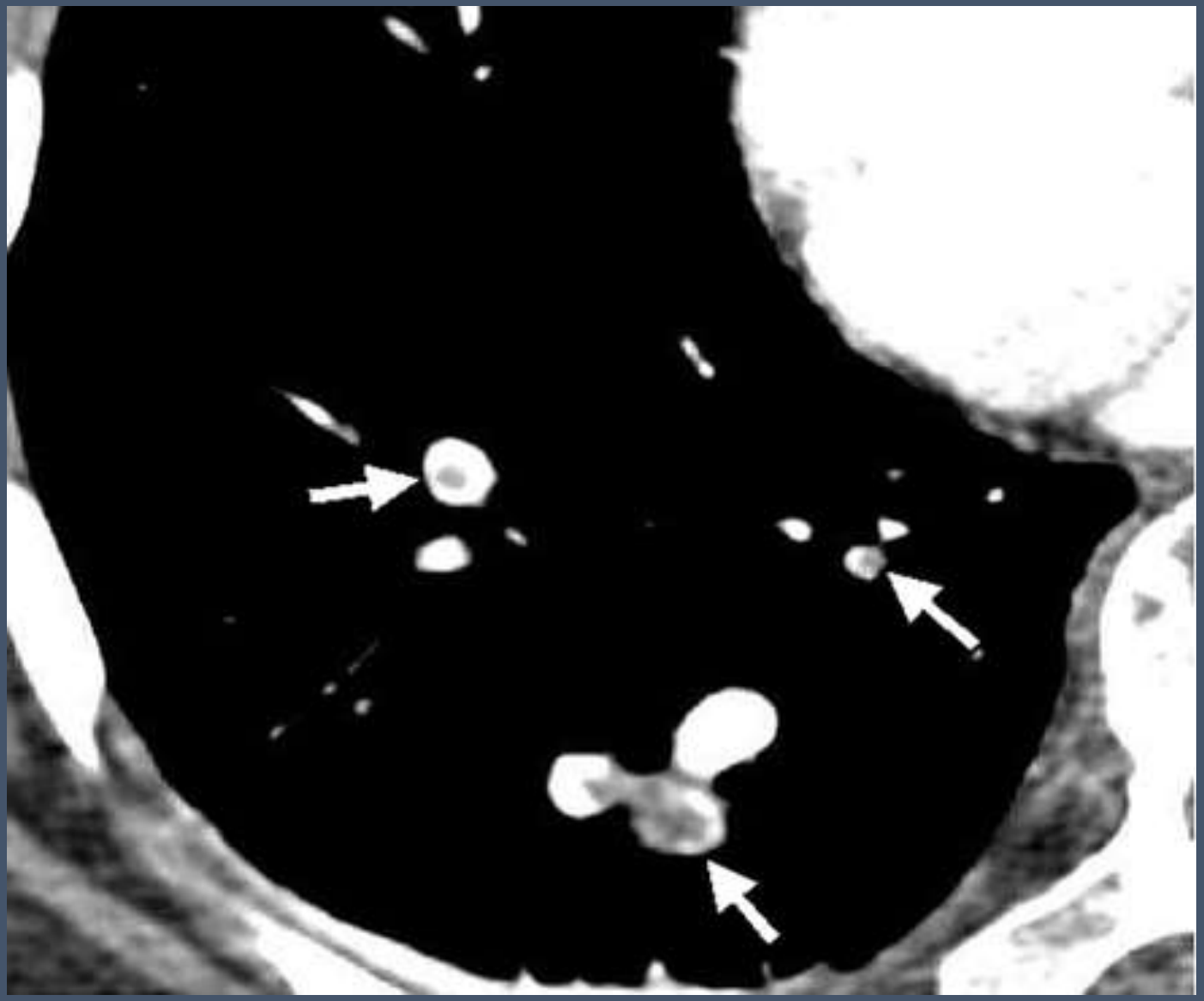


Table 6 Imaging tests for diagnosis of PE (2)

ESC European Society of Cardiology

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

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

Table 6 Imaging tests for diagnosis of PE (3)

ESC European Society of Cardiology

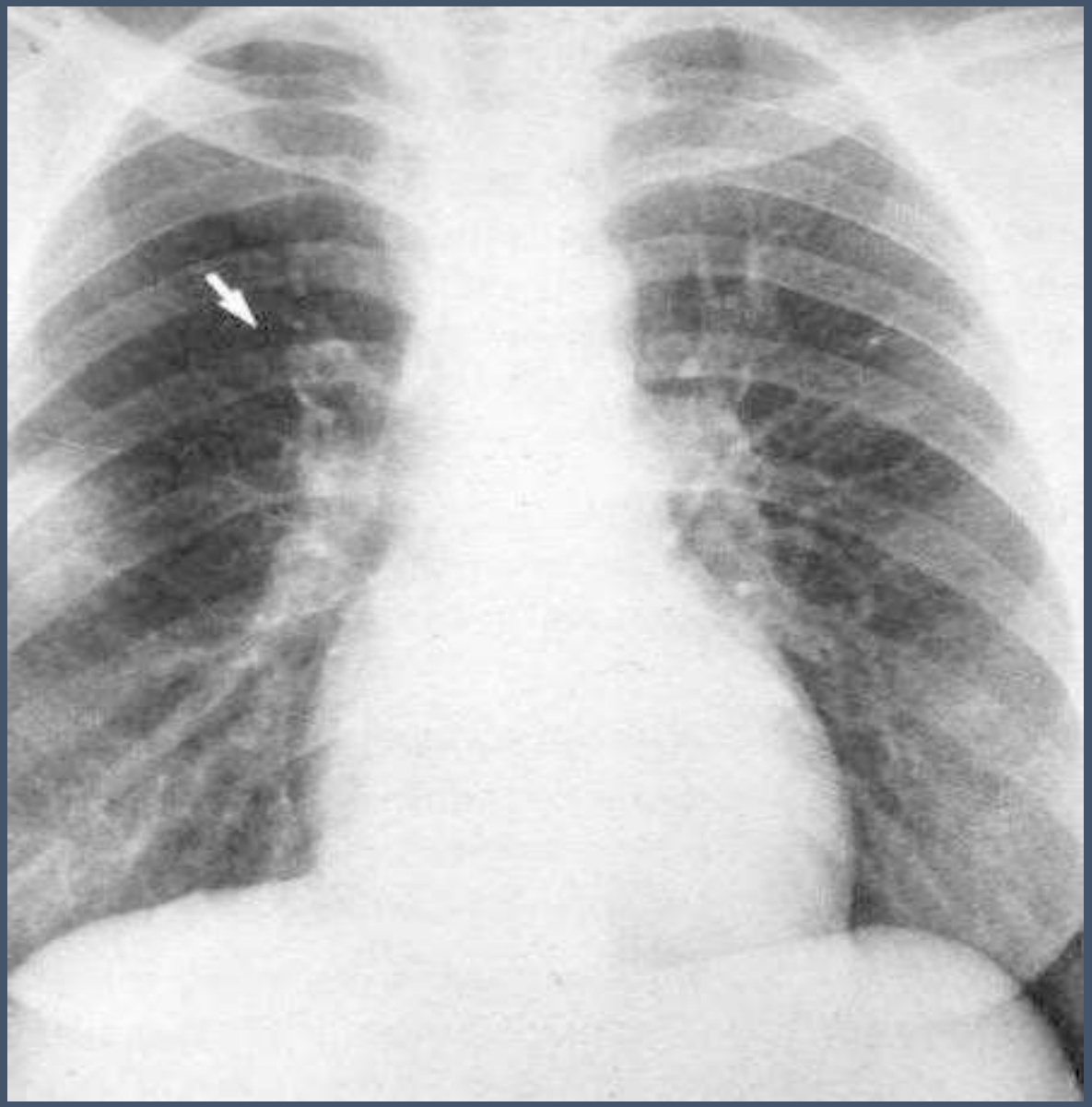
	Radiation issues
CTPA	• Radiation effective dose 3–10 mSv • Significant radiation exposure to young female breast tissue
Planar V/Q scan	• Lower radiation than CTPA, effective dose approximately 2 mSv
V/Q SPECT	• Lower radiation than CTPA, effective dose approximately 2 mSv
Pulmonary angiography	• Highest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

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

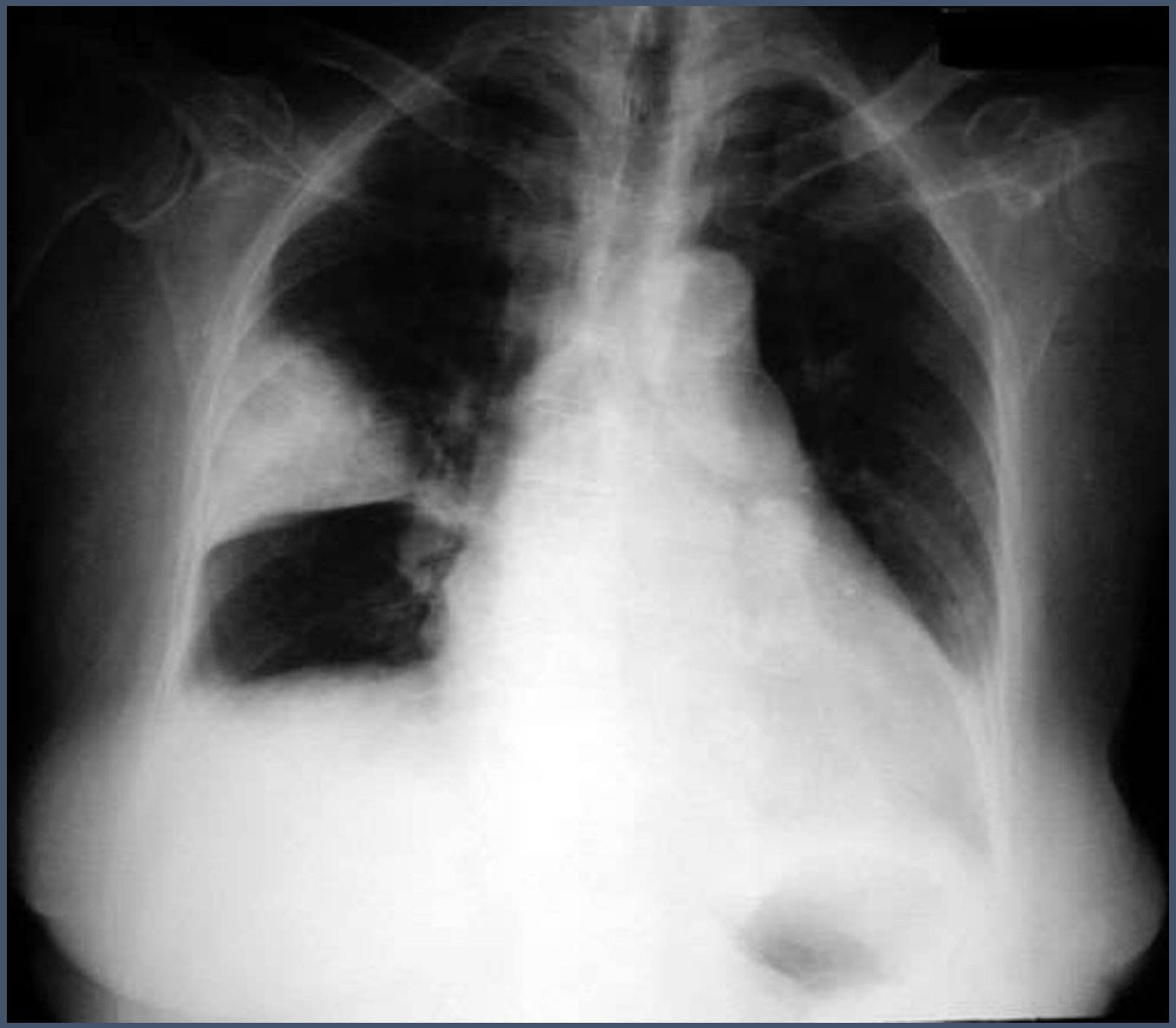
Chest Radiography-

- Not a sensitive or specific test for the diagnosis of PE.
- Atelectasis, Pleural effusion, or a pulmonary parenchymal abnormality is noted most commonly

Radiographic Signs – Westermark Sign



Radiographic Signs – Hamptons Hump



EKG in Pulmonary Embolism

- Most commonly sinus tachycardia, with possible nonspecific ST/T wave changes
- Only 10% of patients can have the S1Q3T3 so not reliable
- Other EKG abnormalities including atrial arrhythmias, right bundle branch block, inferior Q-waves, and precordial T-wave inversion and ST-segment changes, are associated with a poor prognosis.

Recommendations for diagnosis (1)

ESC European Society of Cardiology

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)

ESC
European Society of Cardiology

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)

D-Dimer-

- Elevated in thrombosis, malignancy, pregnancy, elderly, hospitalized patients
- Role in low or moderate probability for PE
  - Normal results can rule out PE
  - Estimated 3 month risk of thromboembolism with negative D-dimer is 0.14%
- No Role in high probability patients → proceed to CT, negative d-dimer can miss up to 15% of patients in this group

D-dimer in elderly patients: variable cut-off?

- New cut-off value proposed based on retrospective analysis of 2 cohorts including 5132 consecutive patients with suspected PE
- **New D-dimer cut-off value:**
  - ≤ 50 years-old 500 ng/mL
  - > 50 years-old Patient age X 10
    (e.g. 78-year-old patient, cut-off 780 ng/mL)

- Age-adjusted cut-off would increase the diagnostic yield of D-dimer by 10% (from 25 to 35% of all patients tested)

Douma et al., BMJ 2010;340:c1475

Recommendations for diagnosis (3)

ESC
European Society of Cardiology

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

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

Recommendations for diagnosis (7)

ESC
European Society of Cardiology

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)

ESC
European Society of Cardiology

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	1 point

PESI = Pulmonary Embolism Severity Index.

Table 8 Original and simplified PESI (3)

ESC
European Society of Cardiology

	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.

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)

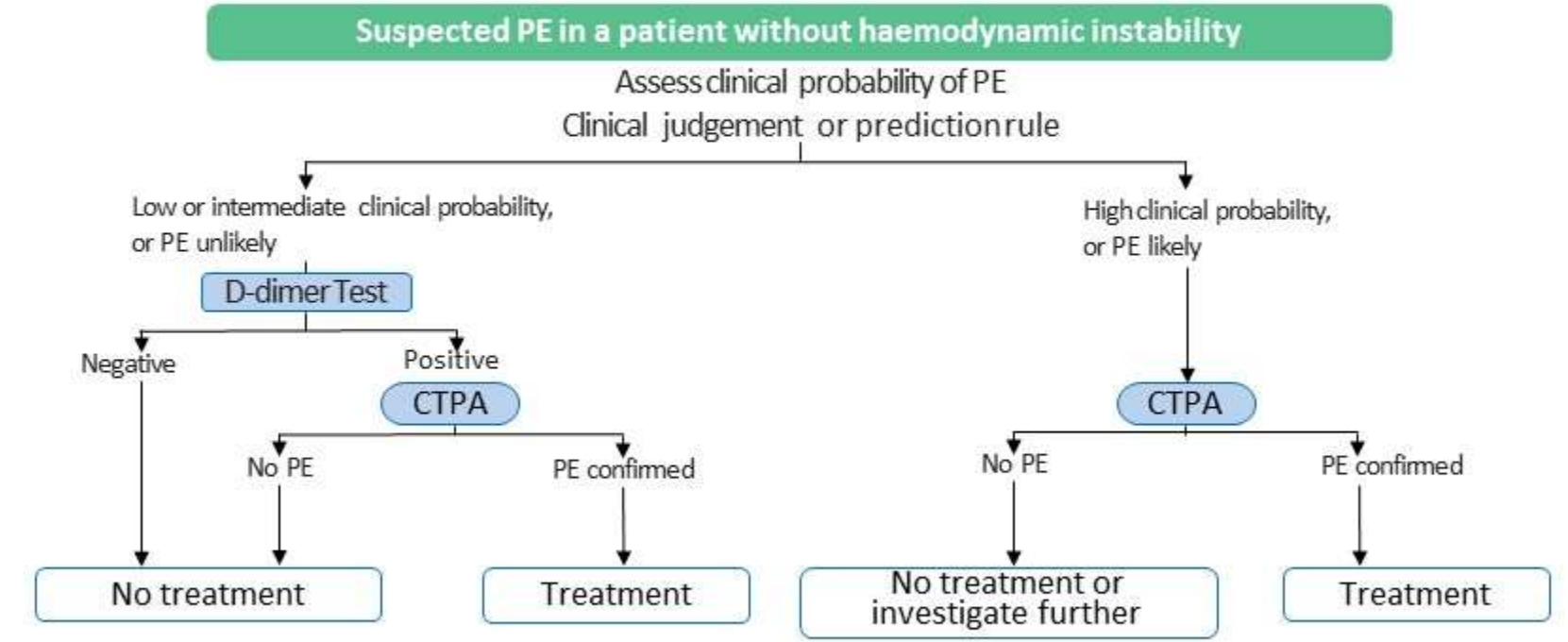
ESC European Society of Cardiology

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.

Figure 4 Diagnostic algorithm for suspected PE without haemodynamic instability

ESC
European Society of Cardiology

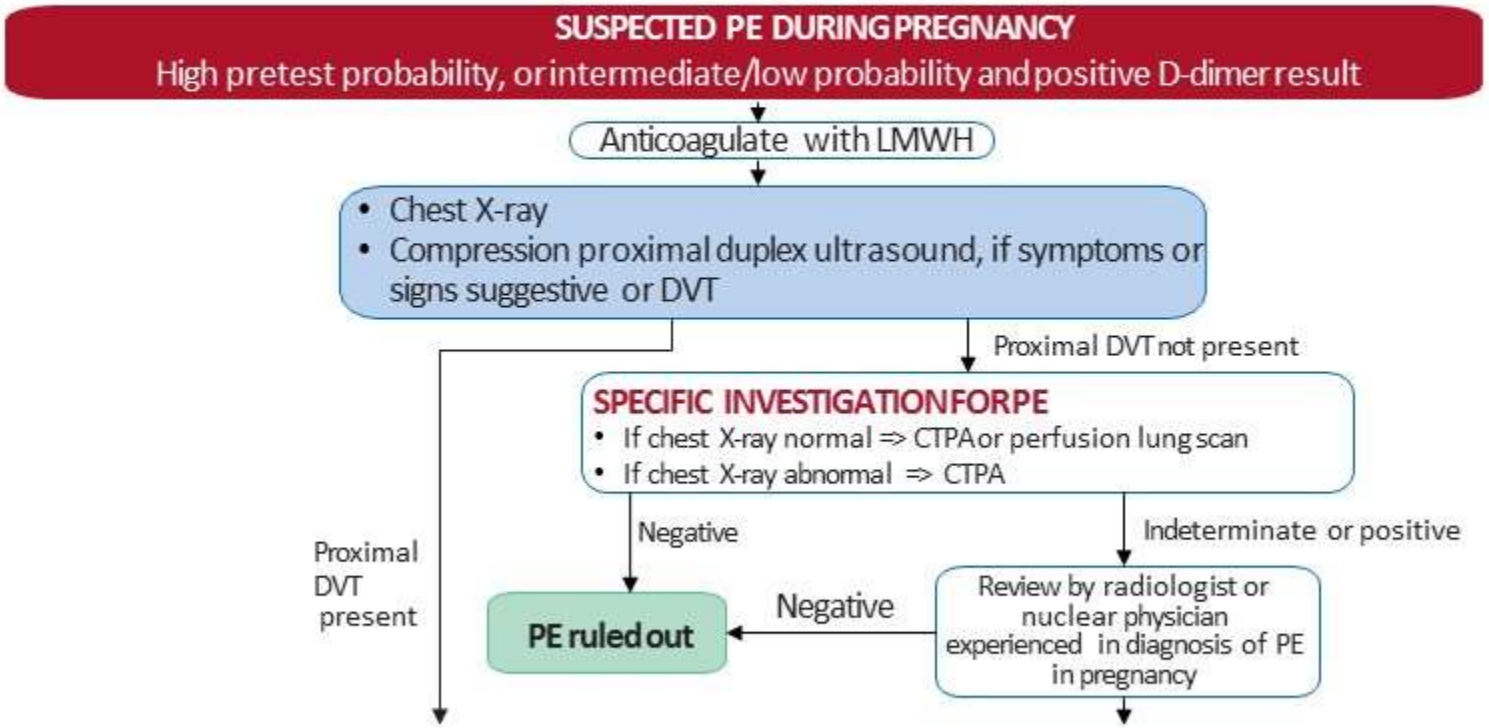


CTPA = computed tomography pulmonary angiography

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

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

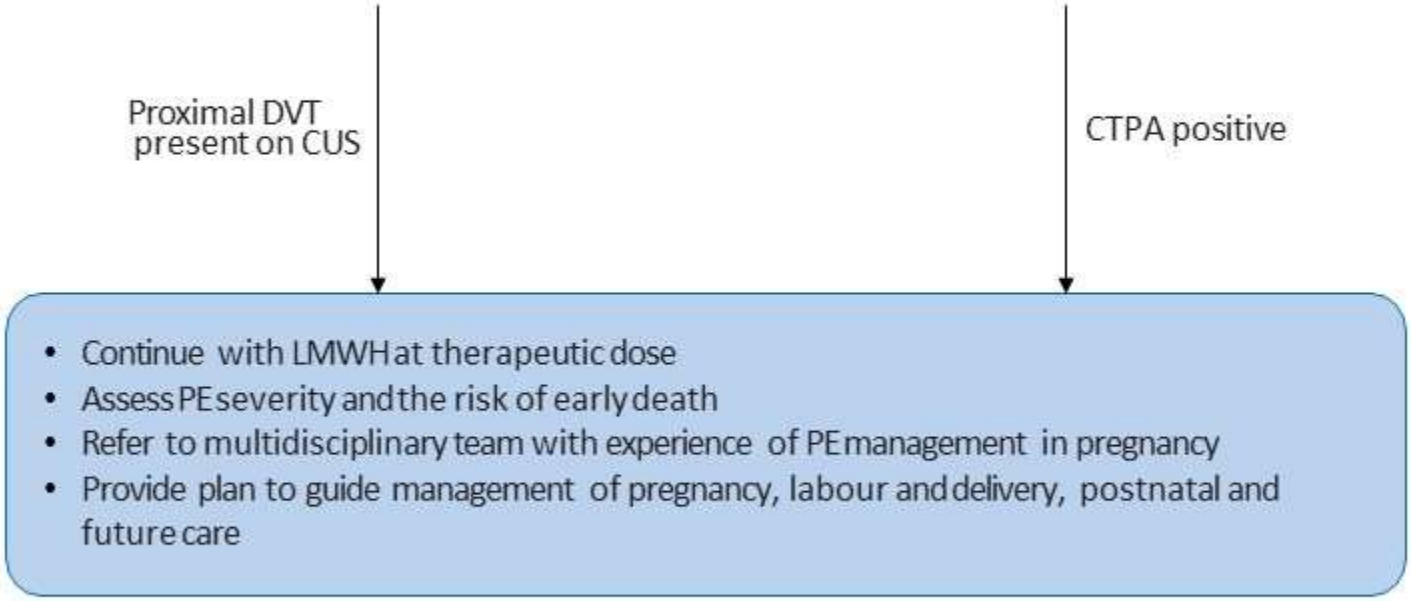
ESC European Society of Cardiology



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

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

Figure 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.

Recommendations for pulmonary embolism in pregnancy (1)

ESC European Society of Cardiology

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.

Recommendations for pulmonary embolism in pregnancy (2)

ESC European Society of Cardiology

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.

Summary and Recommendations

- *Consider your patient's risk factors for pulmonary embolism*
- *The clinical presentation of acute pulmonary embolism is variable and nonspecific*
- *Follow a diagnostic algorithm that combines clinical probability score, d-dimer and imaging*

References-

1.Diagnosis of thrombosis and Pulmonary Embolism H.Bounameaux.Geneva 2015
2.ESC Guidelines on Pulmonary embolism 2019.

Thank you

If you have any questions please send an email to pritirath@hotmail.com