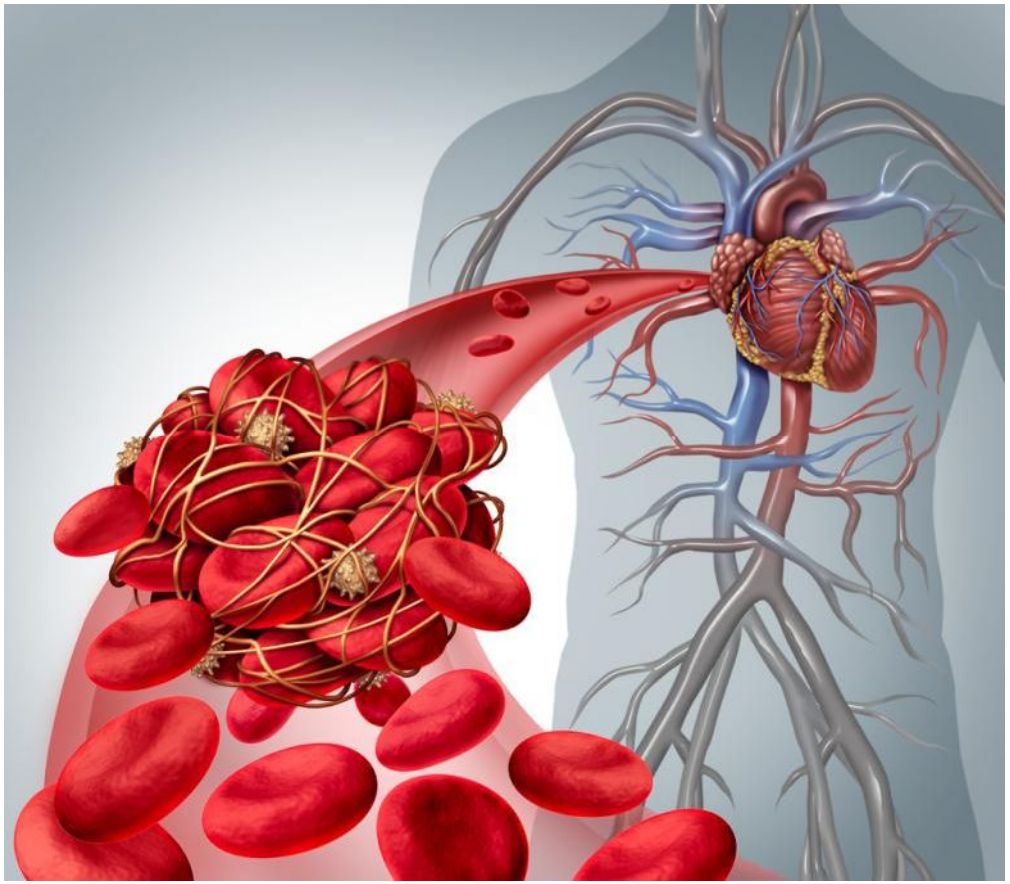
Acute Pulmonary Embolism



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ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS)

The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC)

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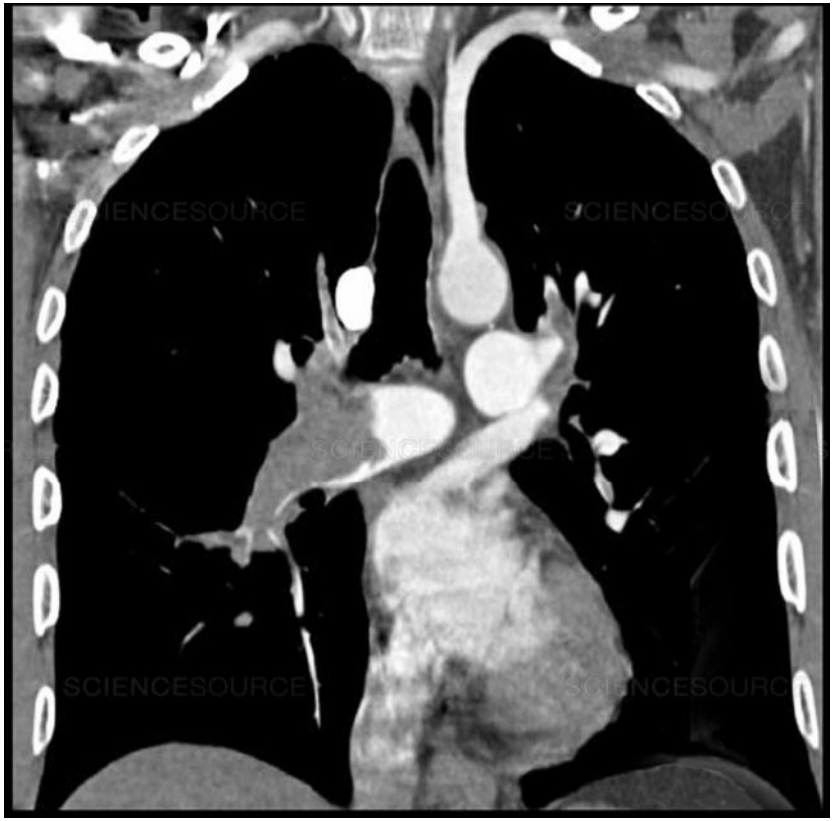
Definition of PE

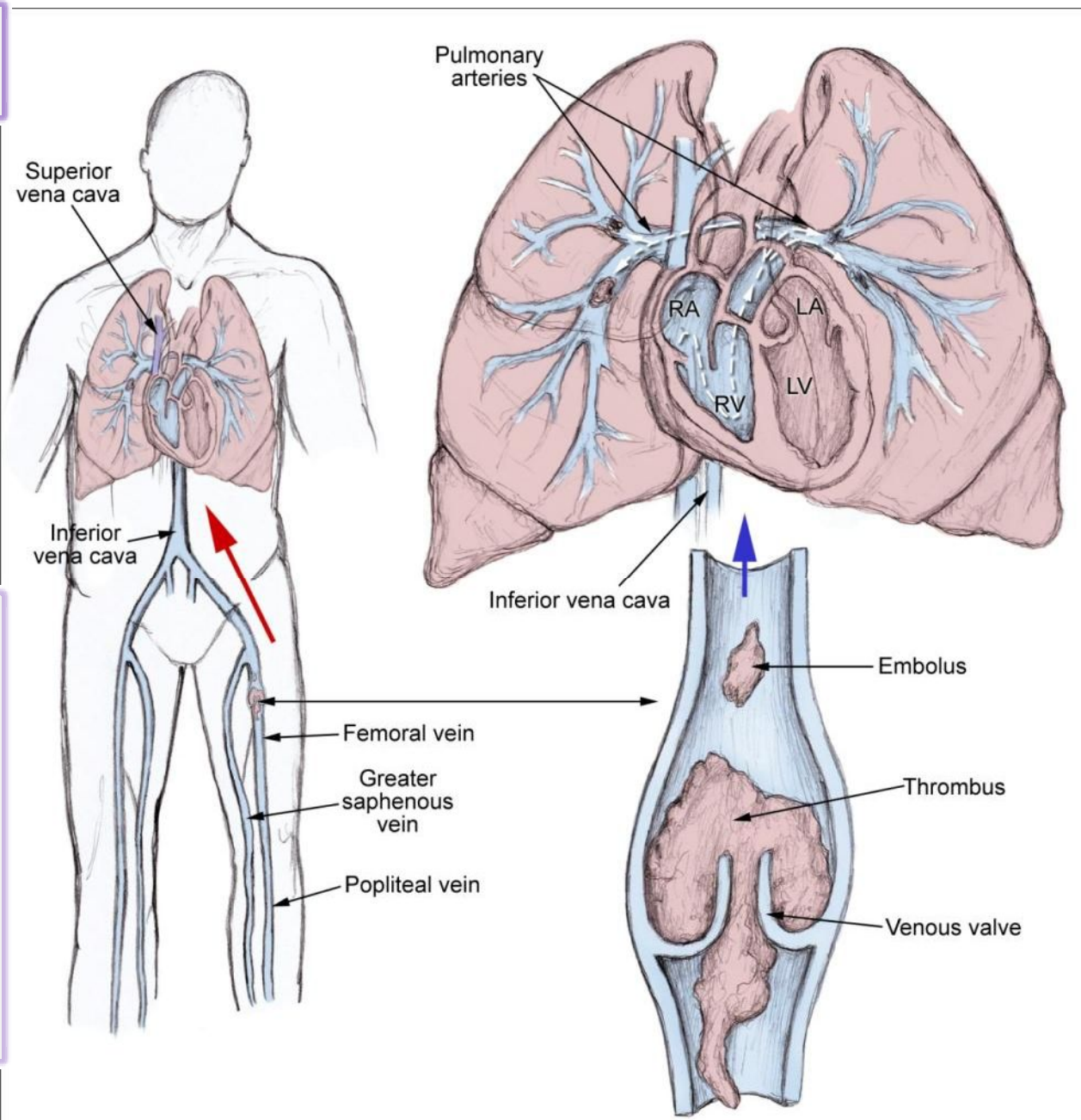
Obstruction of the **pulmonary artery** or **one** of its **branches** by ***material***

- **Thrombus**
- **Tumor**
- **Air**
- **Fat**



Most PE

Thrombi in the **deep venous system** of the **lower extremities**



Predisposing factors for **venous thromboembolism**

Rogers MA, Levine DA, Blumberg N, Flanders SA, Chopra V, Langa KM. Triggers of hospitalization for venous thromboembolism. Circulation 2012;125:20922099. 24. Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. Circulation 2003;107:I9I16

- **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**

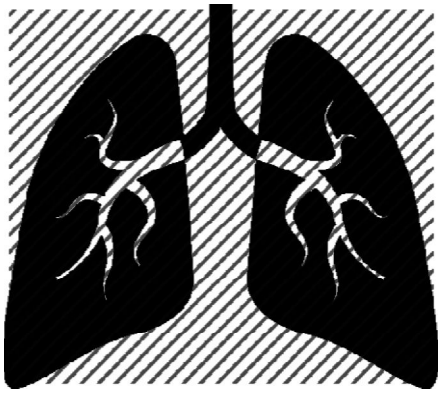
Rogers MA, Levine DA, Blumberg N, Flanders SA, Chopra V, Langa KM. Triggers of hospitalization for venous thromboembolism. Circulation 2012;125:20922099. 24. Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. Circulation 2003;107:I9I16

- **Strong risk factors** (OR > 10)

BTSH-pVTE

Rogers MA, Levine DA, Blumberg N, Flanders SA, Chopra V, Langa KM. Triggers of hospitalization for venous thromboembolism. Circulation 2012;125:20922099. 24. Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. Circulation 2003;107:I9I16

- **Moderate risk factors** (OR 29)
  - **Arthroscopic knee surgery**
  - **Autoimmune diseases**
  - **Inflammatory bowel disease**
  - **Congestive heart failure** or **respiratory failure**



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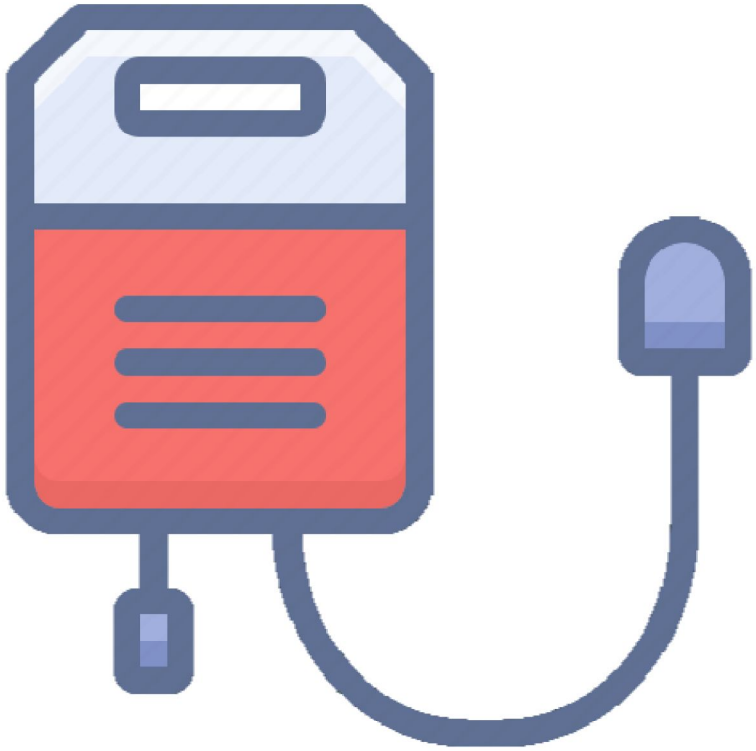
- **Moderate risk factors** (OR 29)
  - **Blood transfusion**
  - **Erythropoiesis-stimulating agents**



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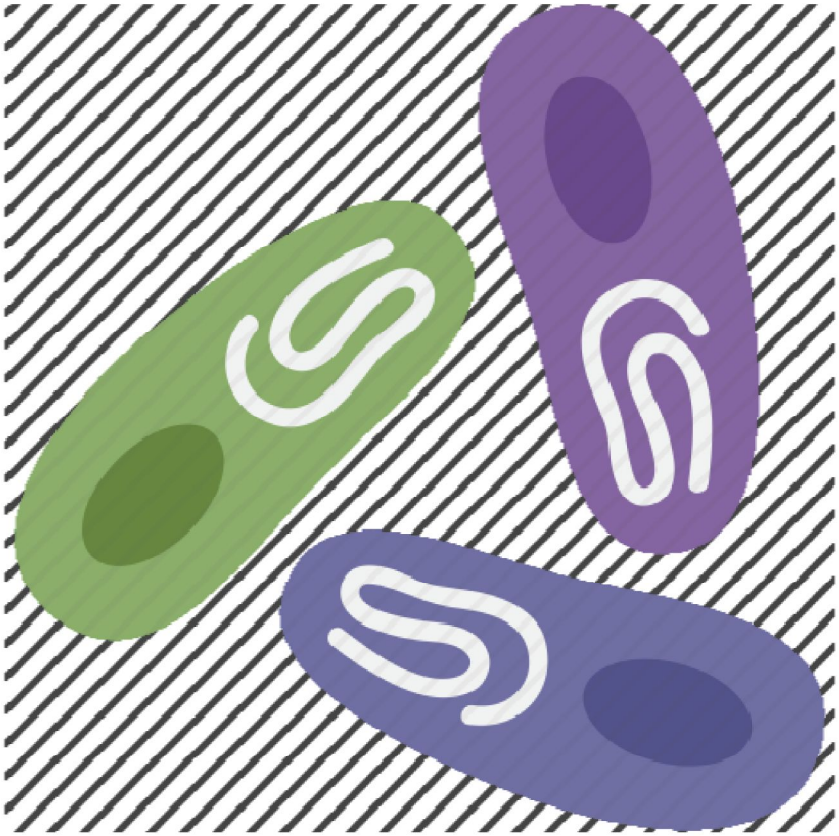
- **Moderate risk factors** (OR 29)
  - **Infection specifically**
    - **Pneumonia**
    - **Urinary tract infection**
    - **HIV**



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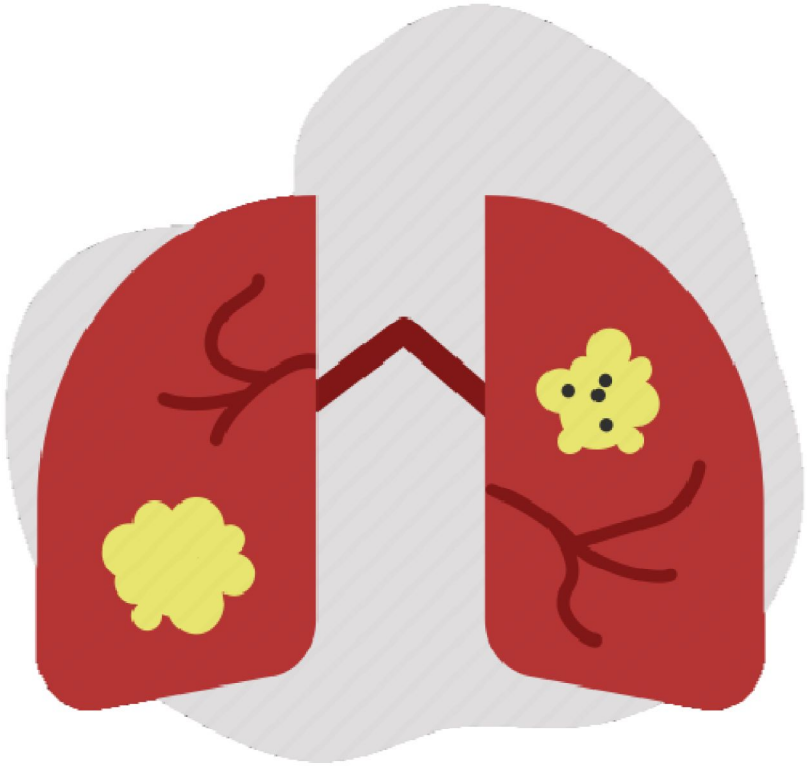
- **Moderate risk factors** (OR 29)
  - **Cancer** (highest risk in metastatic disease)
  - **Chemotherapy**
  - **Central venous lines**
  - **Intravenous catheters and leads**



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Moderate risk factors (OR 29)

- **Hormone replacement therapy (depends on formulation) (post-menopausal women)**
- **In vitro fertilization**
- **Oral contraceptive therapy**
- **Post-partum period**

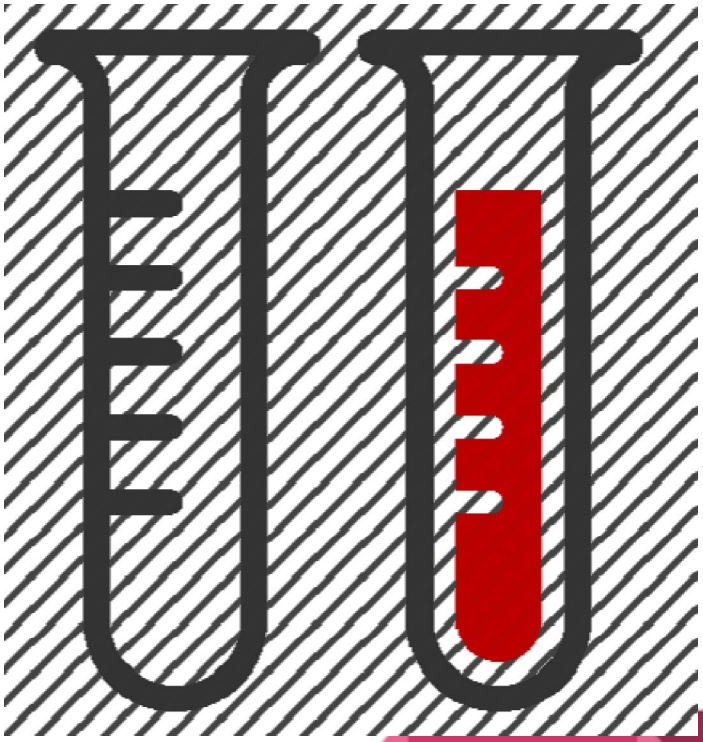
High *Estrogen* + *Progestogen* states

Rogers MA, Levine DA, Blumberg N, Flanders SA, Chopra V, Langa KM. Triggers of hospitalization for venous thromboembolism. Circulation 2012;125:20922099. 24. Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. Circulation 2003;107:I9I16

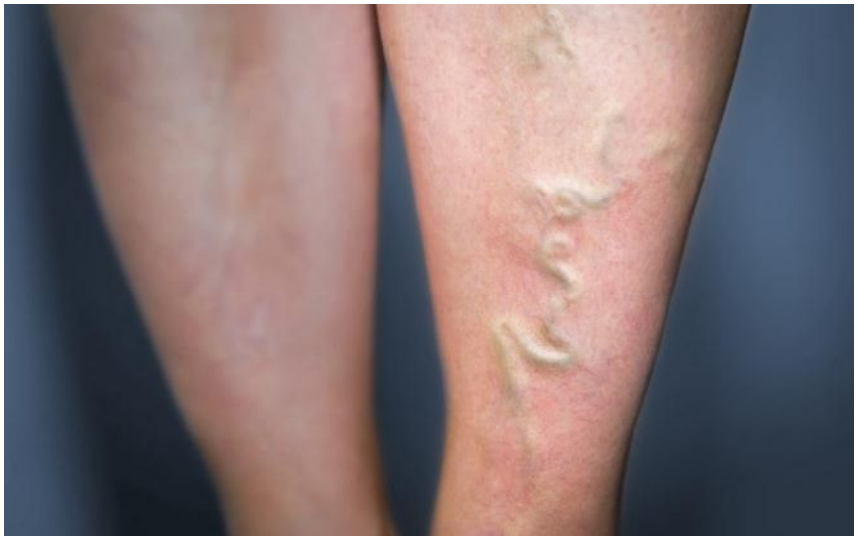
Moderate risk factors (OR 29)

Inherited thrombophilia

- *Factor V Leiden mutation*
- *Prothrombin gene mutation*
- *Protein S deficiency*
- *Protein C deficiency*
- *Antithrombin deficiency*
- *Rare disorders*
  - *Dysfibrinogenemia*



- **Moderate risk factors** (OR 29)
  - **Paralytic stroke**
  - **Superficial vein thrombosis**



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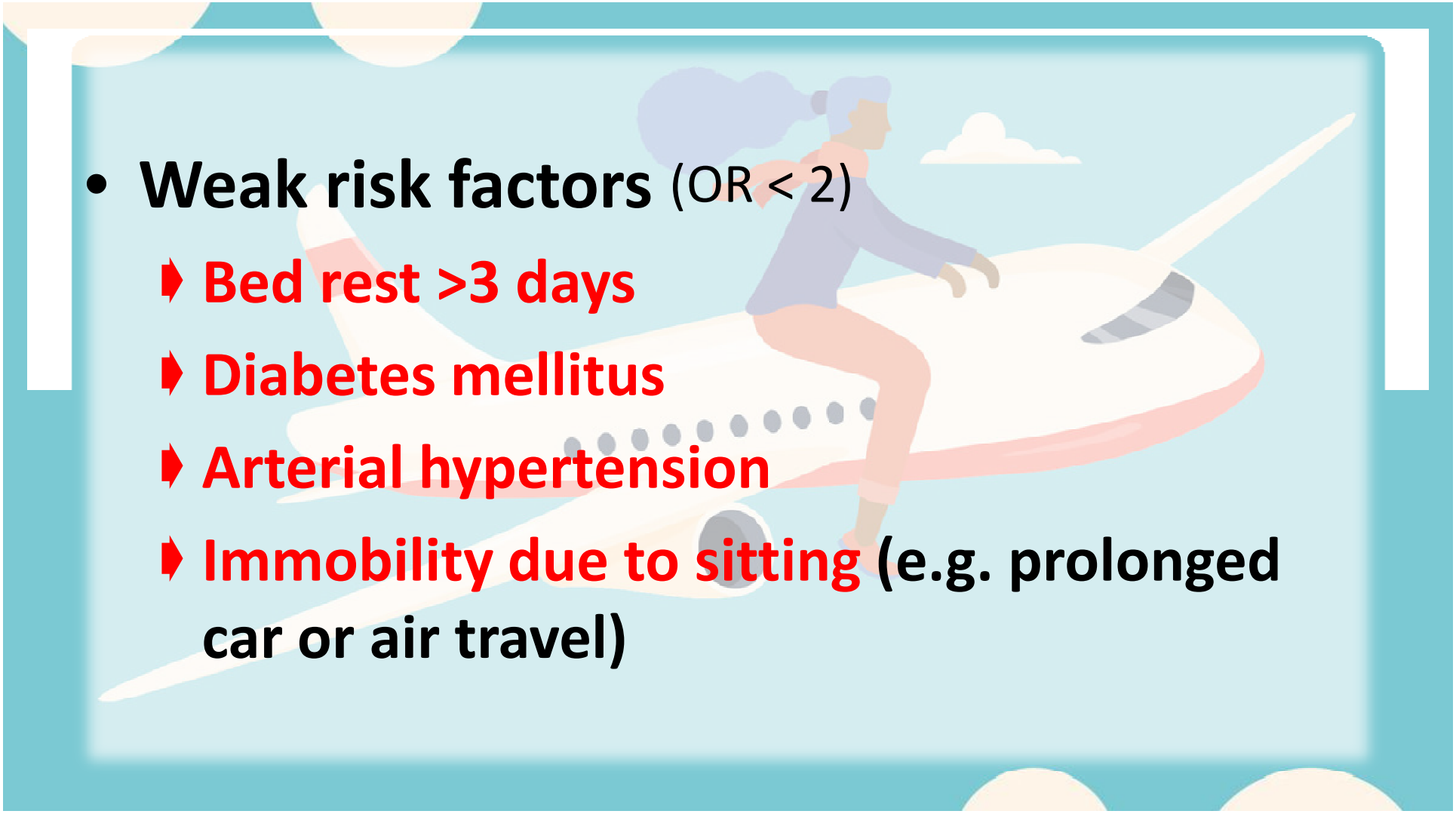
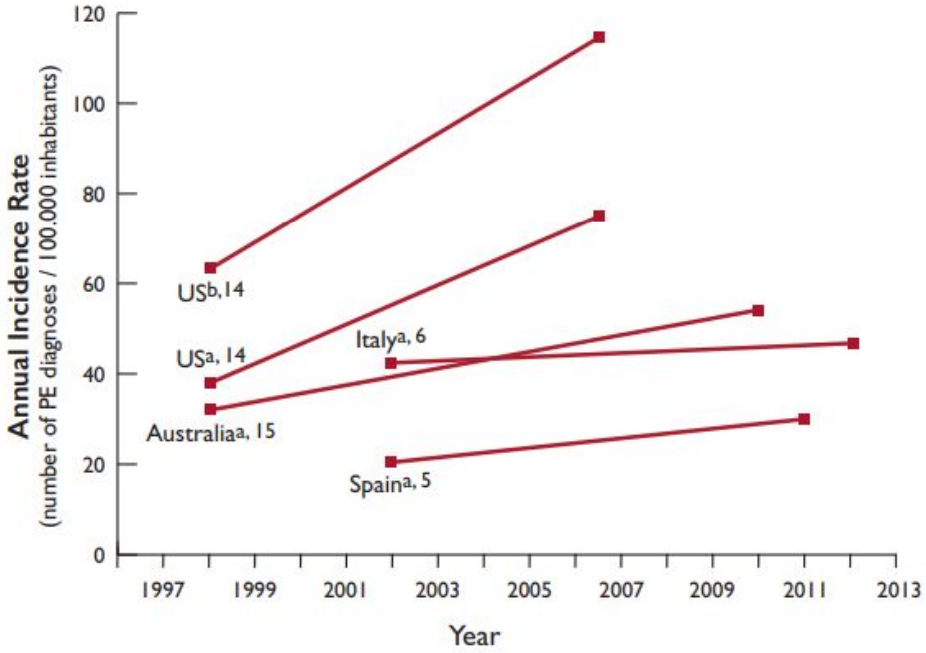


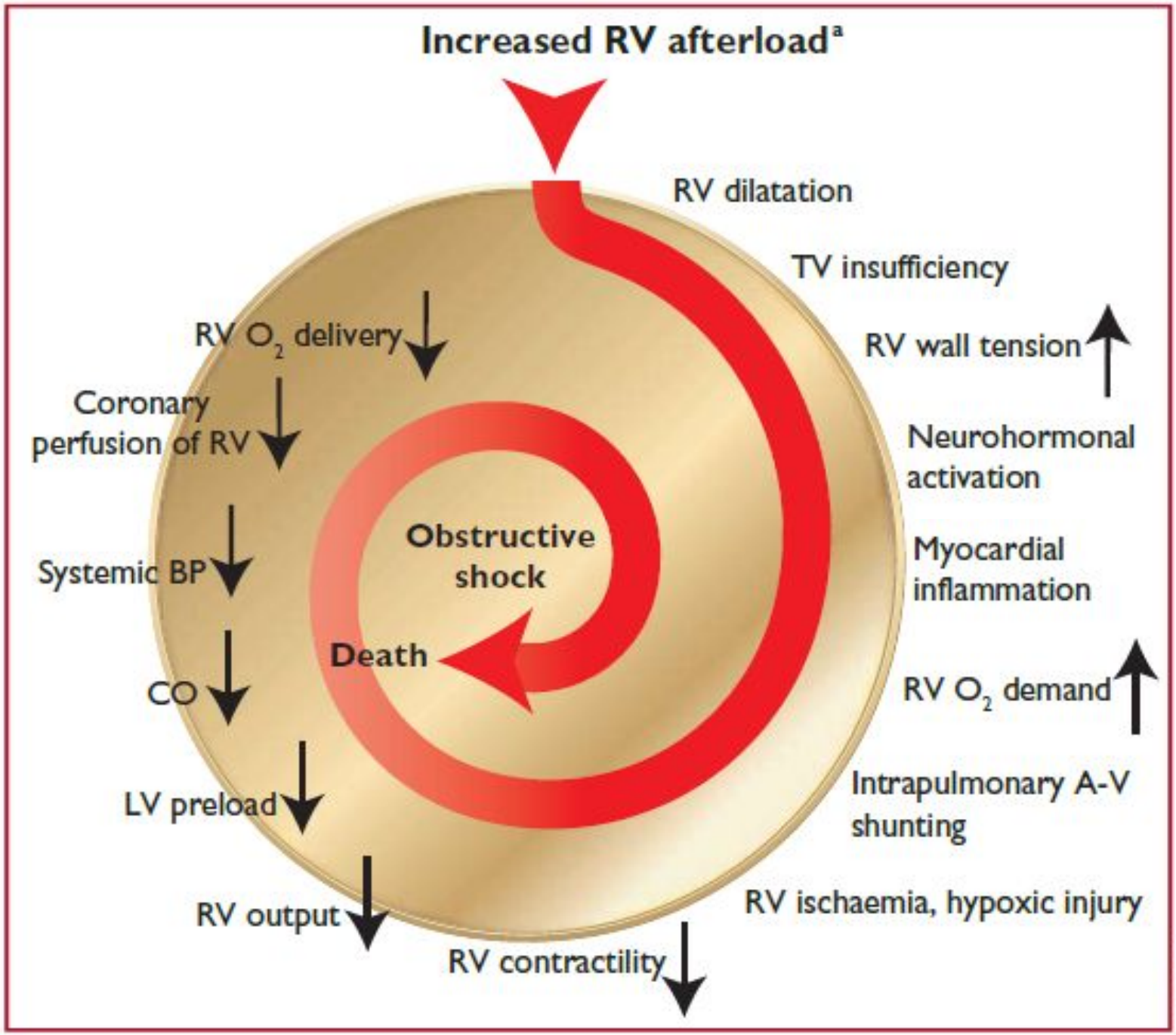
- **Weak risk factors** (OR < 2)
  - **Bed rest >3 days**
  - **Diabetes mellitus**
  - **Arterial hypertension**
  - **Immobility due to sitting (e.g. prolonged car or air travel)**

- **Weak risk factors** (OR < 2)
  - **Increasing age**
  - **Laparoscopic surgery** (e.g. cholecystectomy)
  - **Obesity**
  - **Pregnancy**
  - **Varicose veins**

Epidemiology of PE

↗Annual incidence rates




Increased RV afterload[a]
RV dilatation
TV insufficiency
RV wall tension
Neurohormonal activation
Myocardial inflammation
RV O_2 demand
Intrapulmonary A-V shunting
RV ischaemia, hypoxic injury
RV contractility
RV output
LV preload
CO
Systemic BP
Coronary perfusion of RV
RV O_2 delivery
Obstructive shock
Death
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Diagnosis

- Diagnosis
  - Clinical presentation
  - Assessment of clinical (pre-test) probability
  - D-dimer testing
  - Computed tomographic pulmonary angiography
  - Lung scintigraphy
  - Pulmonary angiography
  - Magnetic resonance angiography
  - Echocardiography
  - Compression ultrasonography
  - Computed tomography venography

Clinical Presentation

The **clinical signs** and **symptoms** of **acute PE** are ***non-specific***

Acute Dyspnoea

Central PE

↗ Dyspnoea

Underlying cardiac or **respiratory diseases**

Chest pain

Pleural irritation

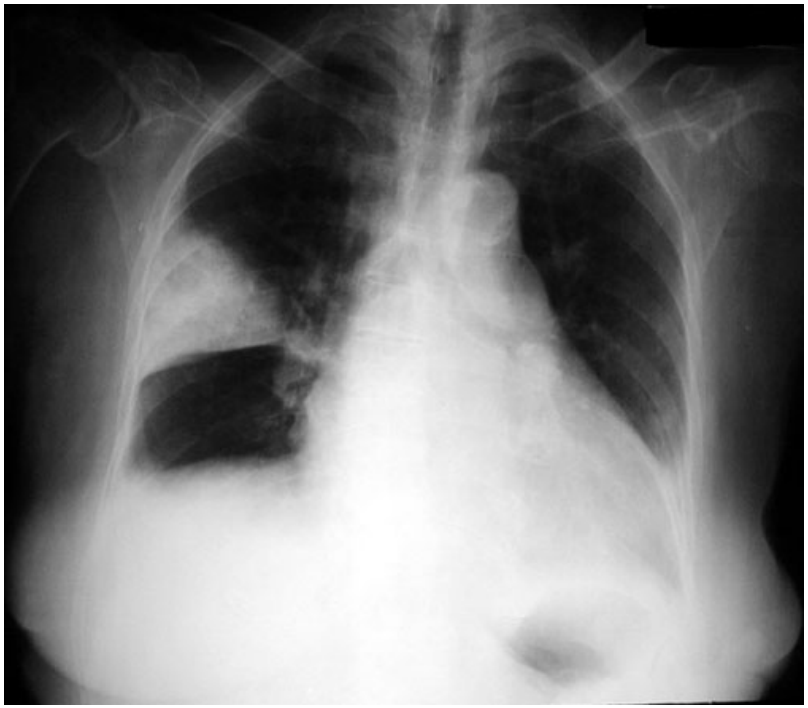
Distal PE

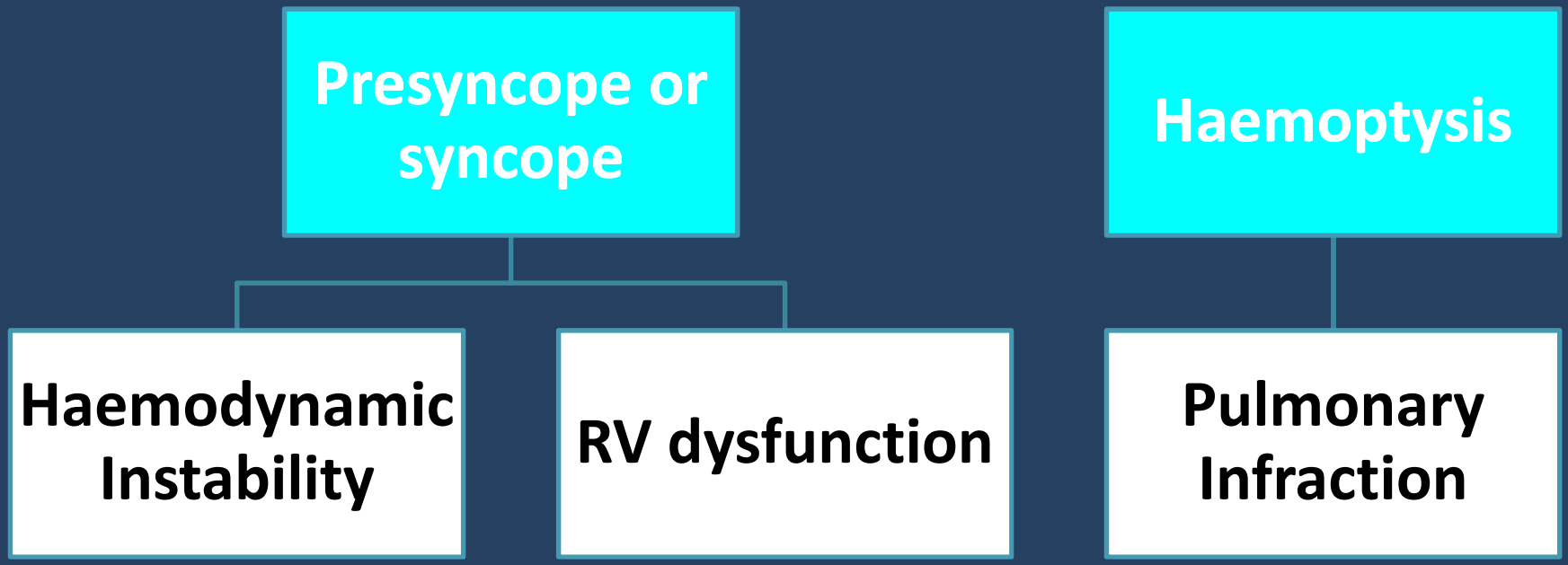
Pulmonary infraction

Central chest pain

Central PE

Rule out of Angina

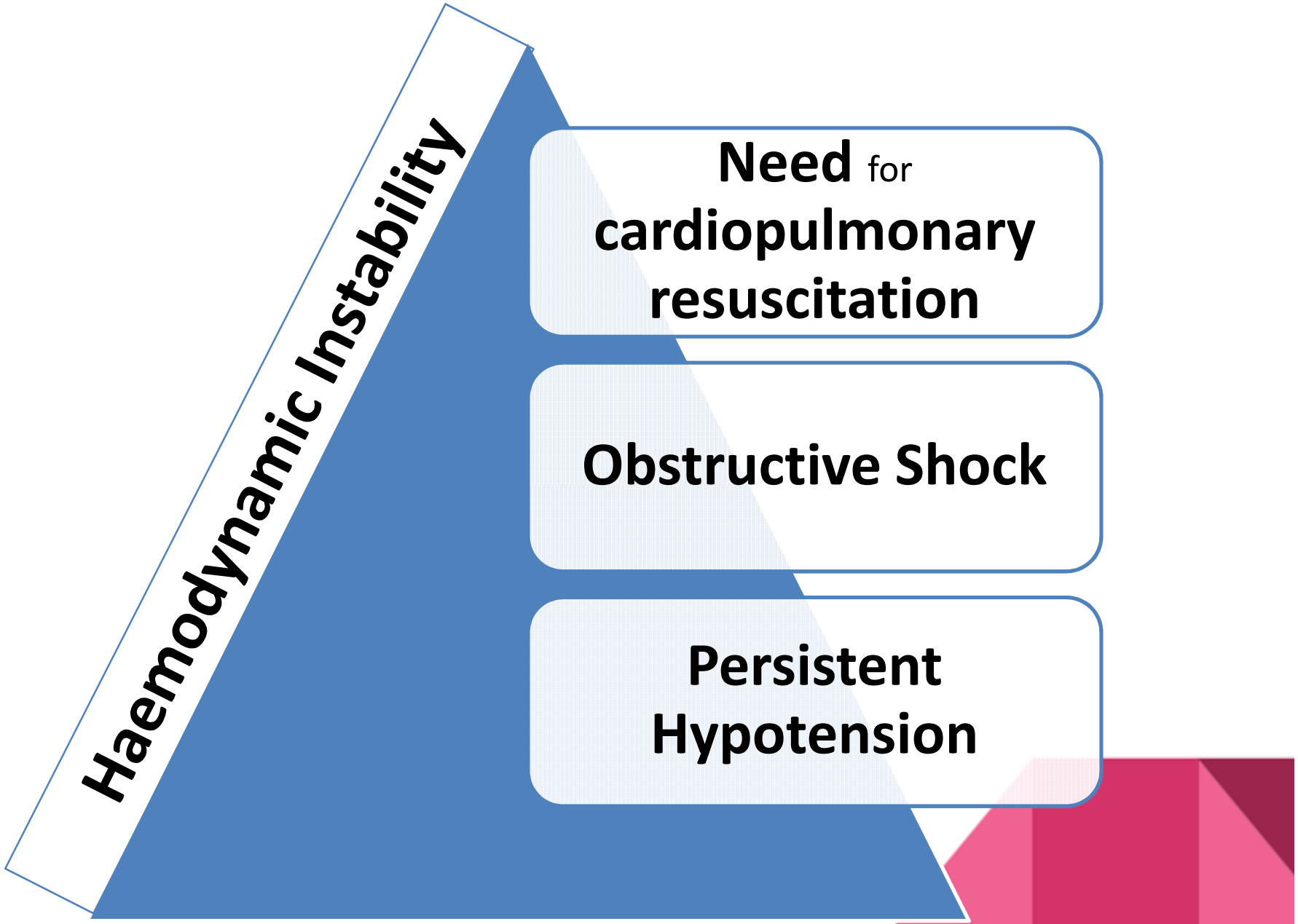



Presyncope or syncope
Haemoptysis
Haemodynamic Instability
RV dysfunction
Pulmonary Infraction

Haemodynamic Instability

Haemodynamic Instability

Acute high-risk pulmonary embolism


Haemodynamic Instability
Need for cardiopulmonary resuscitation
Obstructive Shock
Persistent Hypotension

(1) Cardiac Arrest

Need for **cardiopulmonary resuscitation**

2) Obstructive Shock

- **Systolic BP < 90** mmHg
- or **vasopressors required** to **achieve** a **BP ≥ 90** mmHg **despite adequate filling status**

And

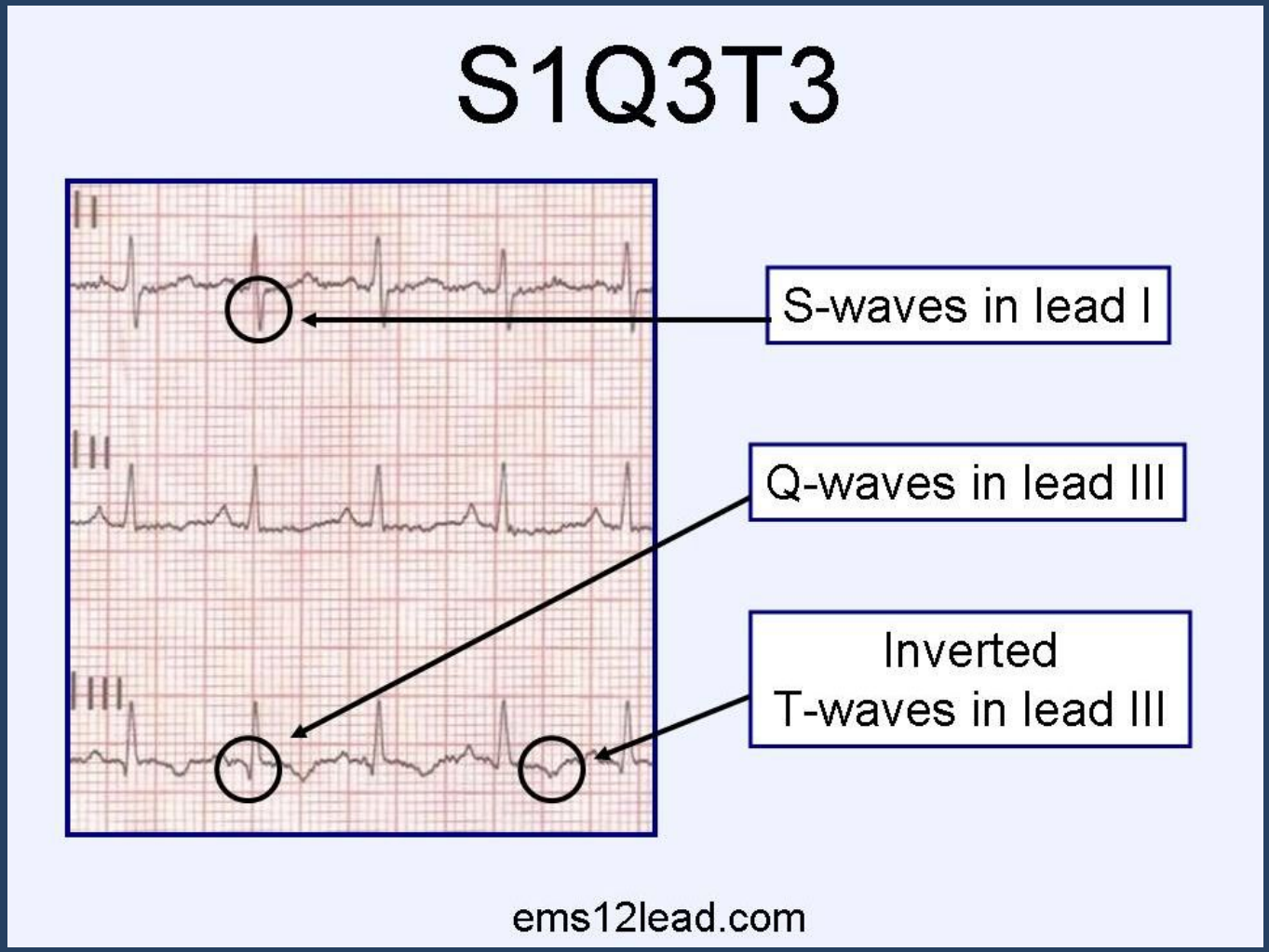
End-organ hypoperfusion

  - **Altered mental status**
  - **Cold, clammy skin**
  - **Oliguria/anuria**
  - **Increased serum lactate**

(3) Persistent Hypotension
Not caused by new-onset arrhythmia, hypovolaemia, or sepsis

- **Systolic BP < 90** mmHg
- OR **Systolic BP drop ≥ 40**mmHg**, lasting longer** than **15 min**

ECG : Pulmonary Embolism



- Diagnosis
  - Clinical presentation
  - Assessment of clinical (pre-test) probability

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

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.

Probability	Score
Traditional clinical probability assessment (Wells criteria)	
High	>6.0
Moderate	2.0 to 6.0
Low	<2.0

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.

Simplified clinical probability assessment (Modified Wells criteria)

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.

Simplified clinical probability assessment (Modified Wells criteria)	
PE likely	>4.0

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.

Simplified clinical probability assessment (Modified Wells criteria)	
PE likely	>4.0
PE unlikely	≤4.0

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.

- Diagnosis
  - Clinical presentation
  - Assessment of clinical (pre-test) probability
  - **D-dimer testing**

A **normal *D-dimer***

<500 ng/mL

The **specificity** of ***D-dimer*** **…** in **suspected PE**

- ⬇ **steadily** with **age** to **> 10%**
- in **patients >80 years** of **age**

D-dimer : **Cutoff value** in **ng/mL**

Age (if over 50 years) **x 10 = cutoff value** in **ng/mL**

For patients in whom the risk of PE is thought to be *Low* or *Intermediate*

- A Normal D-dimer (<500 ng/mL) could rule out PE (46%)
- and typically No further testing is required (with a failure rate of 1.5%)

Point-of-care

- **In these situations**
  - **PE could** be **ruled out** in **46%** of **patients with suspected PE**
  - **without proceeding** to **imaging tests** (with a failure rate of 1.5%)

- **Diagnosis**
  - **Clinical presentation**
  - **Assessment of clinical (pre-test) probability**
  - **D-dimer testing**
  - **Computed tomographic pulmonary angiography**

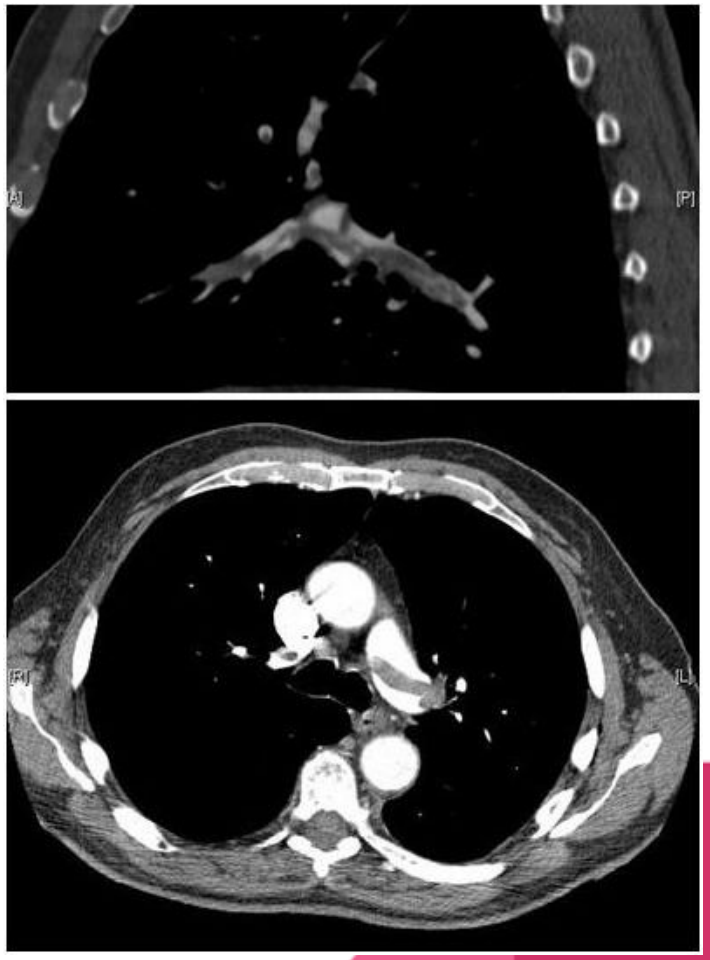
Computed tomographic pulmonary angiography (CTPA)

- Sensitivity
  - 83%
- Specificity
  - 96%

N Engl J Med 2006;354:23172327

CTPA : *most accurate* for the detection of

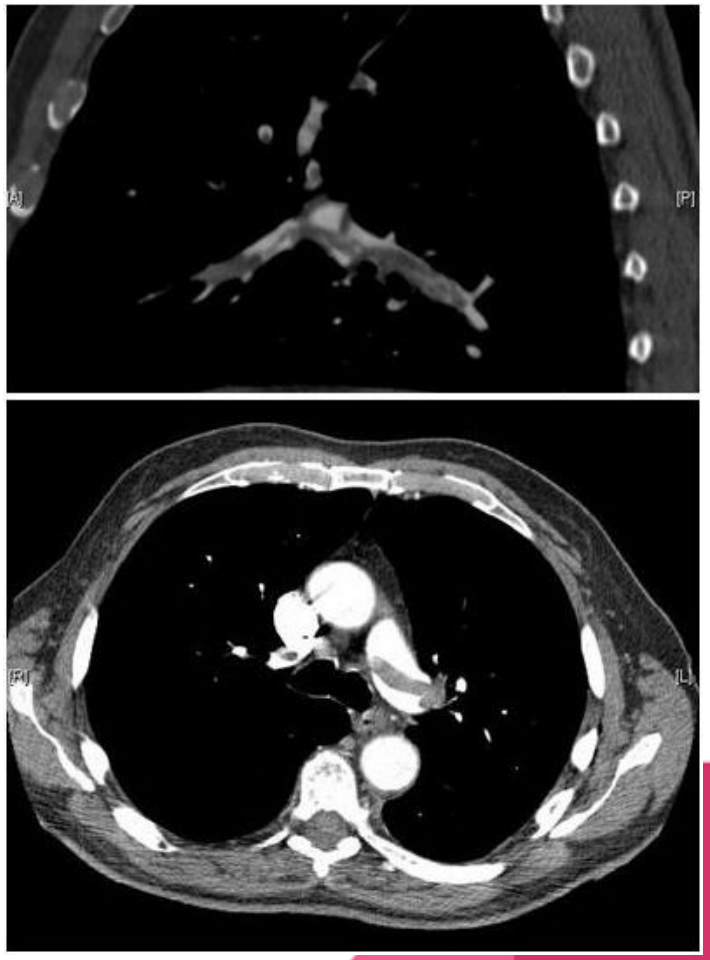
- Large
- Main
- Lobar
- Segmental PE



Quiroz R, Kucher N, Zou KH, et al. Clinical validity of a negative computed tomography scan in patients with suspected pulmonary embolism: a systematic review. JAMA 2005; 293:2012.

CTPA : Less Accurate for the detection of

- **Smaller, peripheral sub segmental PE**



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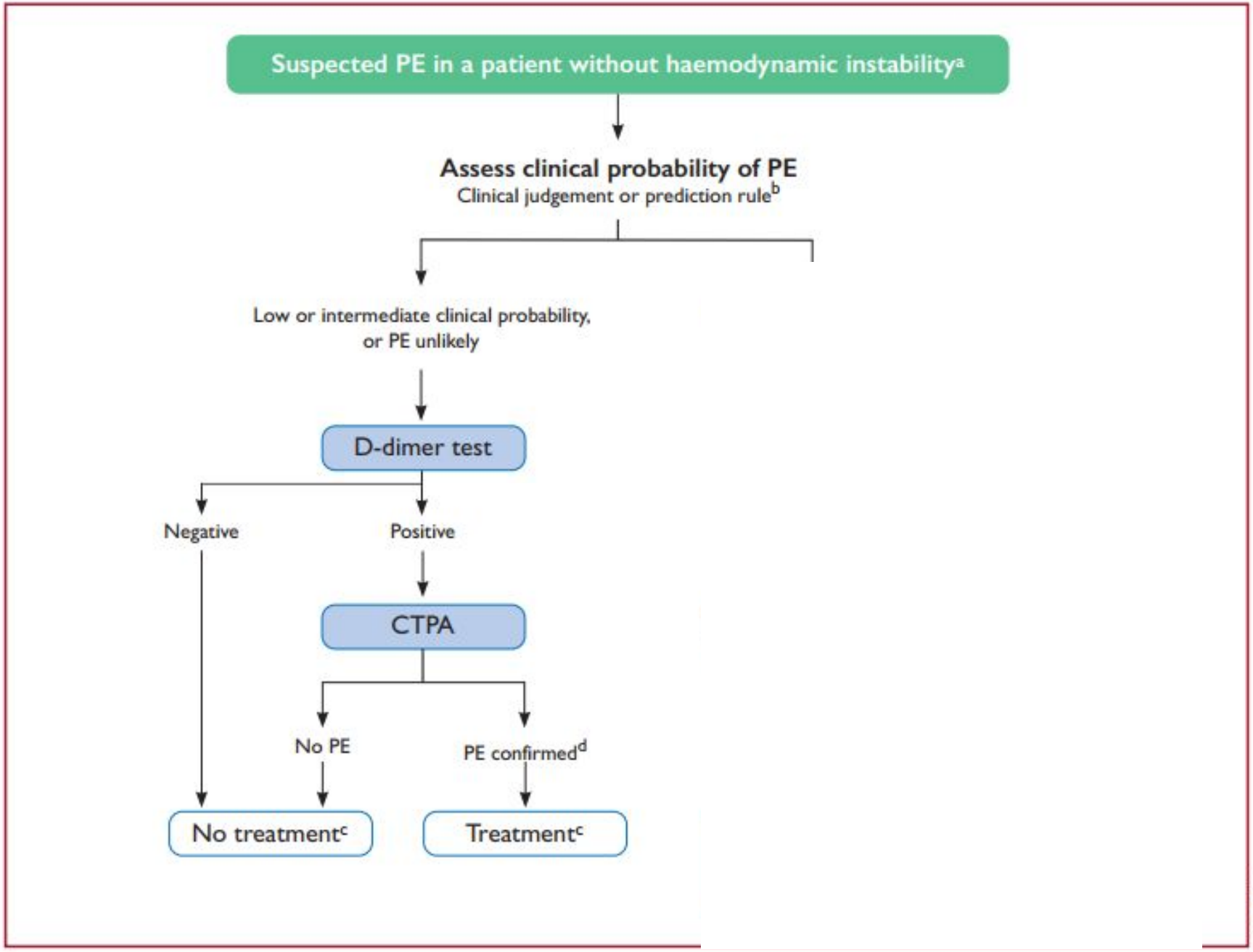
Suspected PE in a patient without haemodynamic instability[a]
Assess clinical probability of PE
Clinical judgement or prediction rule[b]
Low or intermediate clinical probability, or PE unlikely
D-dimer test
Negative
Positive
CTPA
No PE
PE confirmed[d]
No treatment[c]
Treatment[c]
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Scenario

Scenario…

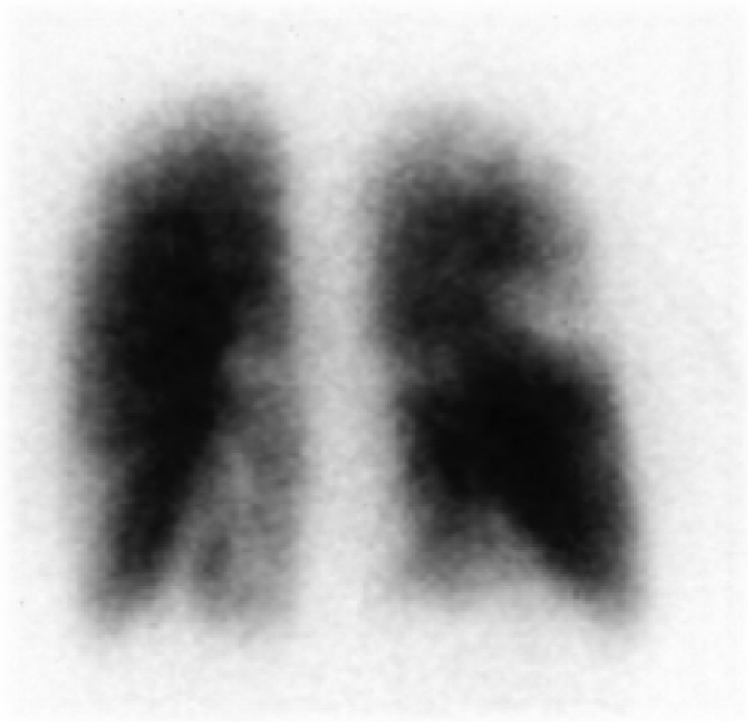
Weak risk factors
Unlikely PE

- A **40-year-old m… after returning from** a **distant journey**
- he **complains from severe right chest pain** with **mild breathlessness**:
  - **Di-dimer**
  - **CTPA**

- Diagnosis
  - Clinical presentation
  - Assessment of clinical (pre-test) probability
  - D-dimer testing
  - Computed tomographic pulmonary angiography
  - ***Lung scintigraphy***

V/Q scan

- **V** (technetium-99m)
- **Q** (xenon-133 gas) **scan**



Data from: PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA 1990; 263:2753.

The V/Q scan: application

- **Outpatients** with a **low clinical probability** and a **normal chest X-ray:**
  - In **young (particularly female) patients**
  - In **pregnant women**

Hutchinson BD, Navin P, Marom EM, et al. Overdiagnosis of Pulmonary Embolism by Pulmonary CT Angiography. AJR Am J Roentgenol 2015; 205:271.

The V/Q scan: application

- **History** of
  - **Contrast medium-induced anaphylaxis**

Hutchinson BD, Navin P, Marom EM, et al. Overdiagnosis of Pulmonary Embolism by Pulmonary CT Angiography. AJR Am J Roentgenol 2015; 205:271.

The V/Q scan: application

- In **patients** with **severe *Renal Failure***

Hutchinson BD, Navin P, Marom EM, et al. Overdiagnosis of Pulmonary Embolism by Pulmonary CT Angiography. AJR Am J Roentgenol 2015; 205:271.

V/Q scan results and **diagnosis** of ***pulmonary embolism***

V/Q Scan Result
High
Intermediate
Low
Normal or near normal

Data from: PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA 1990; 263:2753.

V/Q scan results and **diagnosis** of ***pulmonary embolism***

V/Q Scan Result	Clinical probability of emboli		
	High	**Intermediate**	**Low**
High			
Intermediate			
Low			
Normal or near normal			

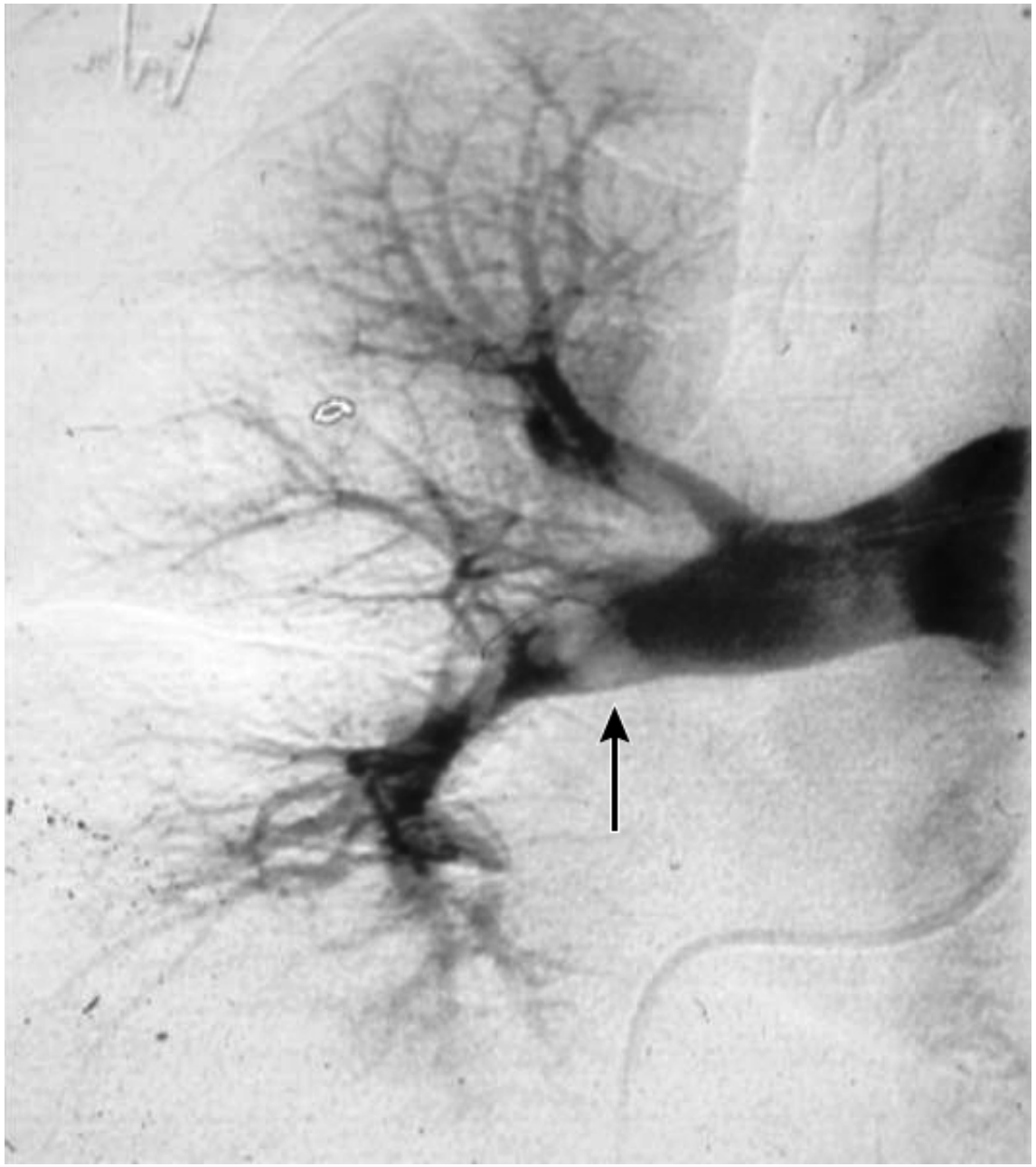
Data from: PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA 1990; 263:2753.

V/Q scan results and **diagnosis** of ***pulmonary embolism***

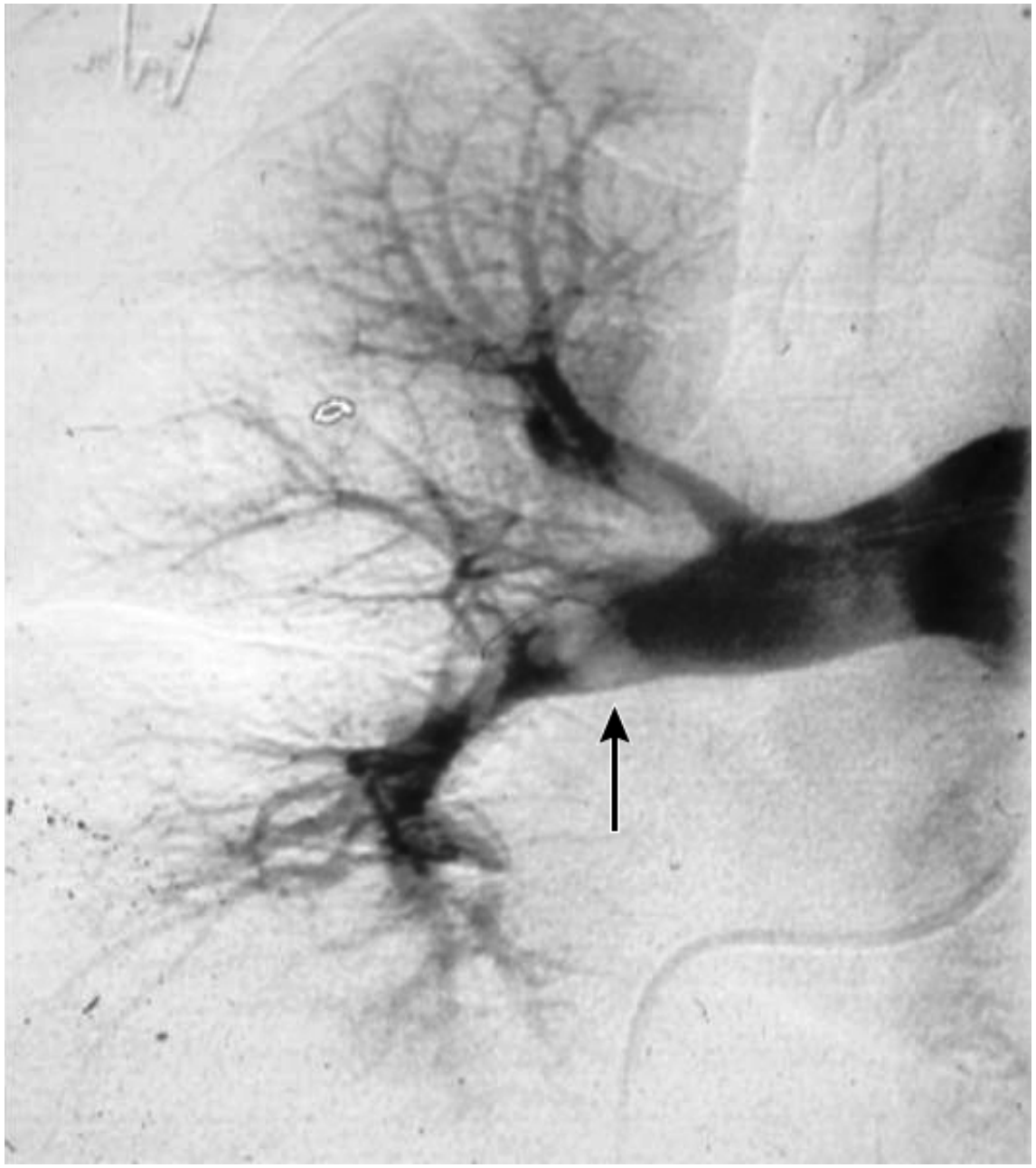
V/Q Scan Result	Clinical probability of emboli		
	High	Intermediate	Low
High	96%	88	56
Intermediate	66	28	16
Low	40	16	4%
Normal or near normal	0	6	2

Data from: PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA 1990; 263:2753.

- Diagnosis
  - Clinical presentation
  - Assessment of clinical (pre-test) probability
  - Avoiding overuse of diagnostic tests for pulmonary embolism
  - D-dimer testing
  - Computed tomographic pulmonary angiography
  - Lung scintigraphy
  - **Pulmonary angiography**

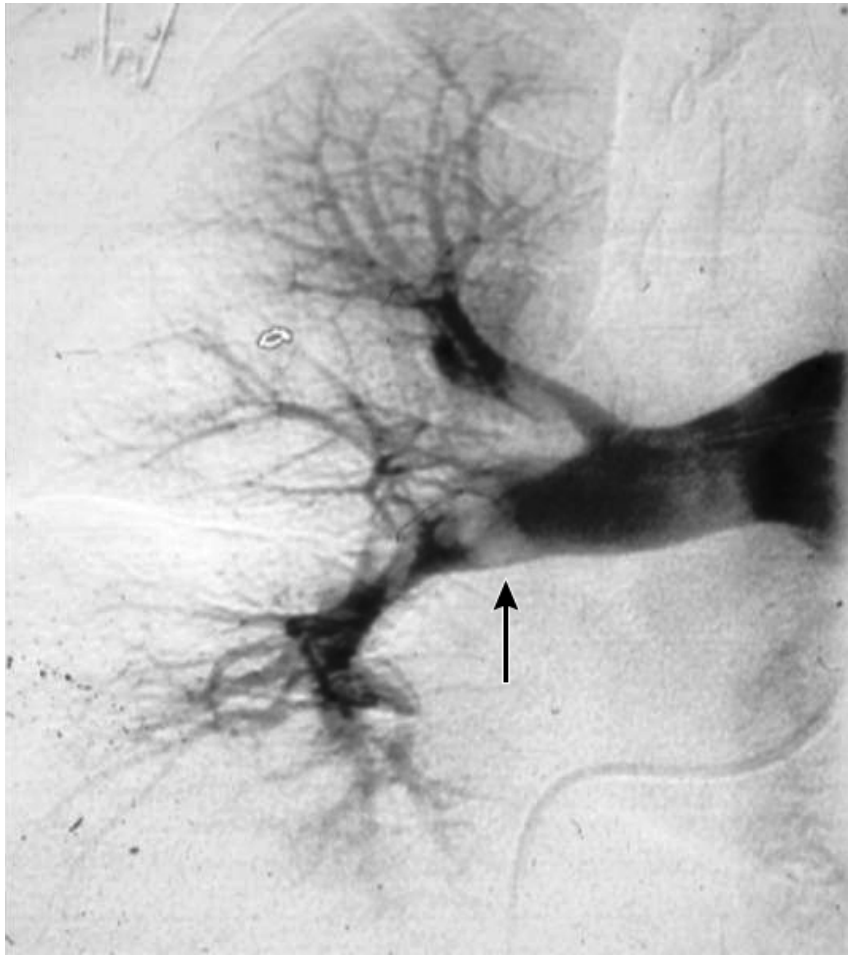


Was the **historical gold standard** for the **diagnosis** of **PE**



- **Pulmonary embolus**
- A **filling Defect (arrow)**

Indication of Pulmonary Angiography

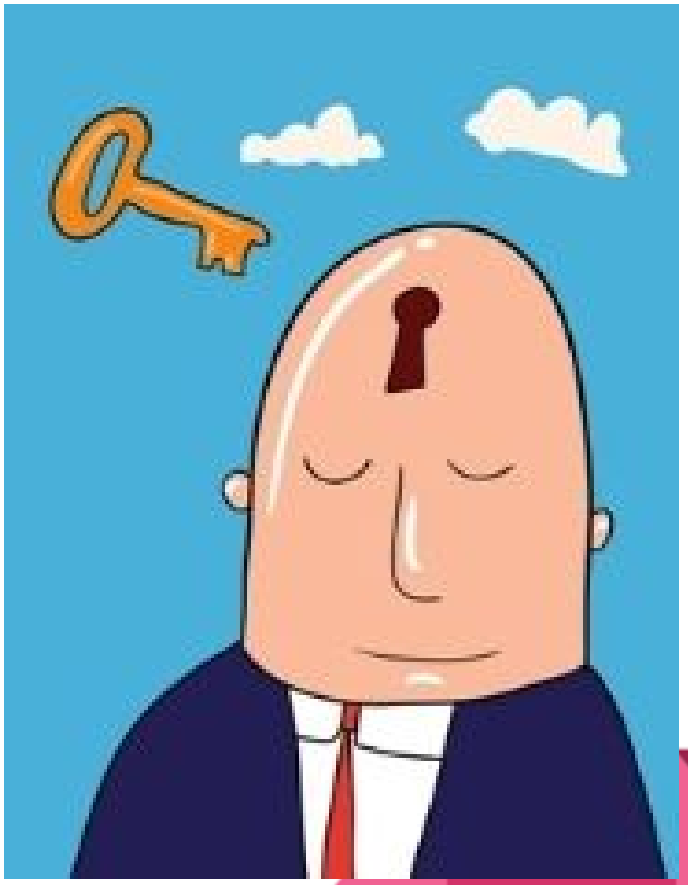


- A **high clinical probability** of **PE**
  - In **whom CTPA** or **V/Q scanning** is **nondiagnostic**
- And
- In **whom** a **diagnosis determines** an **important clinical decision**

- Diagnosis
  - Clinical presentation
  - Assessment of clinical (pre-test) probability
  - D-dimer testing
  - Computed tomographic pulmonary angiography
  - Lung scintigraphy
  - Pulmonary angiography
  - **Magnetic resonance angiography**

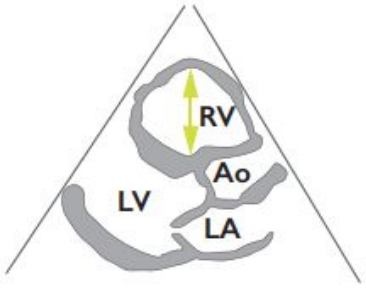
Magnetic resonance angiography

???

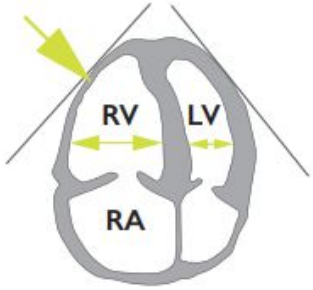


- Diagnosis
  - Clinical presentation
  - Assessment of clinical (pre-test) probability
  - Avoiding overuse of diagnostic tests for pulmonary embolism
  - D-dimer testing
  - Computed tomographic pulmonary angiography
  - Lung scintigraphy
  - Pulmonary angiography
  - Magnetic resonance angiography
  - **Echocardiography**

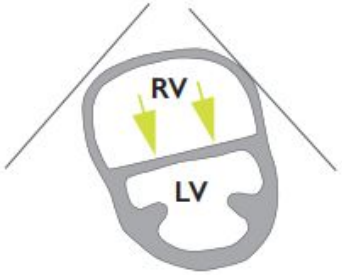
Echocardiography



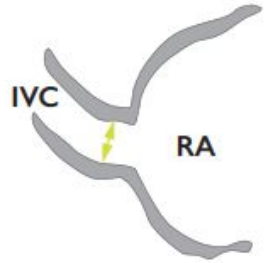
A. Enlarged right ventricle, parasternal long axis view



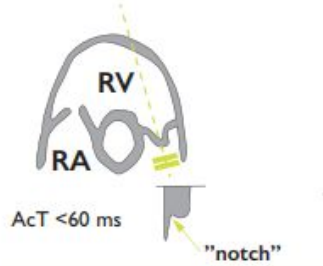
B. Dilated RV with basal RV/LV ratio >1.0, and McConnell sign (arrow), four chamber view

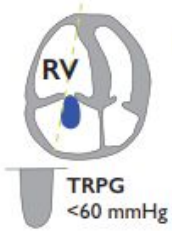


C. Flattened intraventricle septum (arrows) parasternal short axis view

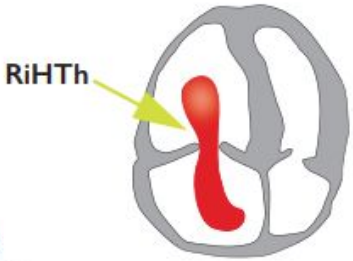


D. Distended inferior vena cava with diminished inspiratory collapsibility, subcostal view

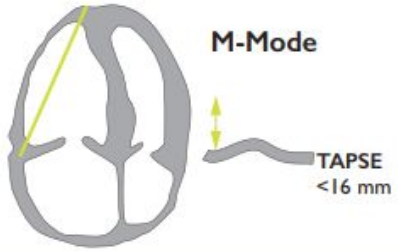




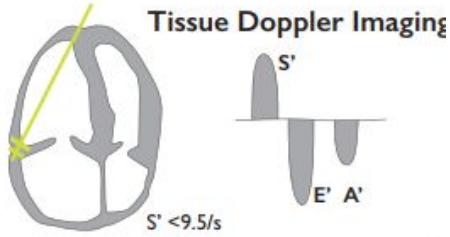
E. 60/60 sign: coexistence of acceleration time of pulmonary ejection <60 ms and midsystolic "notch" with mildy elevated (<60 mmHg) peak systolic gradient at the tricuspic valve



F. Right heart mobile thrombus detected in right heart cavities (arrow)



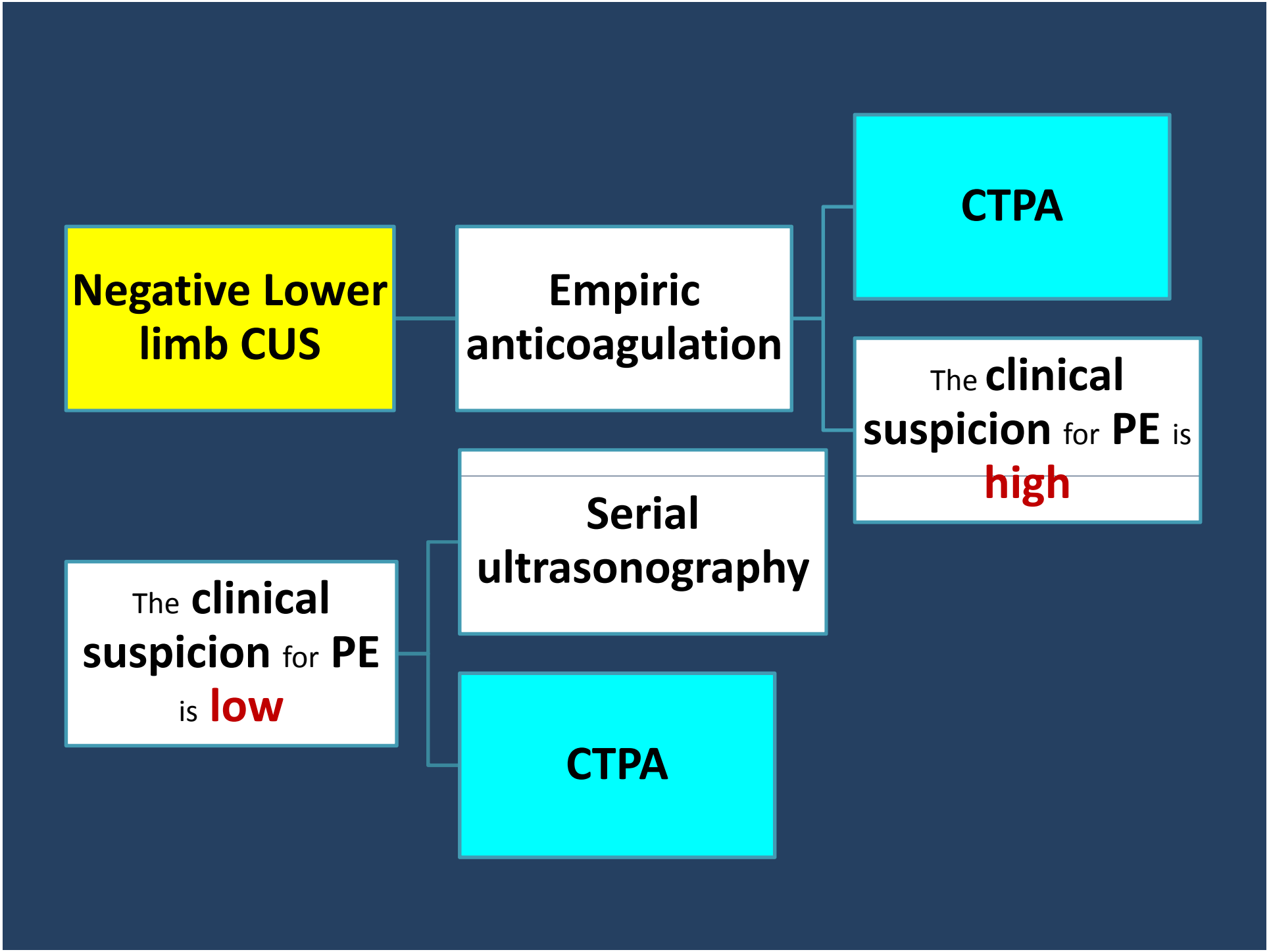
G. Decreased tricuspid annular plane systolic excursion (TAPSE) measured with M-Mode (<16 mm)



H. Decreased peak systolic (S') velocity of tricuspid annulus (<9.5 cm/s)

- **Diagnosis**
  - **Clinical presentation**
  - **Assessment of clinical (pre-test) probability**
  - **D-dimer testing**
  - **Computed tomographic pulmonary angiography**
  - **Lung scintigraphy**
  - **Pulmonary angiography**
  - **Magnetic resonance angiography**
  - **Echocardiography**
  - **Compression ultrasonography**

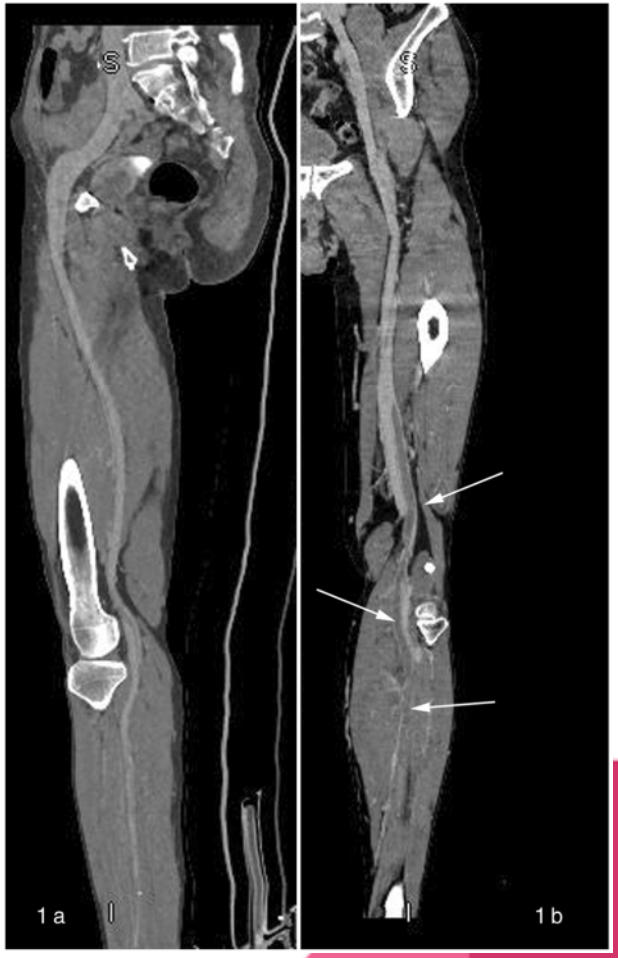
Lower limb CUS


Negative Lower limb CUS
Empiric anticoagulation
CTPA
The clinical suspicion for PE is high
The clinical suspicion for PE is low
Serial ultrasonography
CTPA

- **Diagnosis**
  - Clinical presentation
  - Assessment of clinical (pre-test) probability
  - D-dimer testing
  - Computed tomographic pulmonary angiography
  - Lung scintigraphy
  - Pulmonary angiography
  - Magnetic resonance angiography
  - Echocardiography
  - Compression ultrasonography
  - **Computed tomography venography**

Computed tomography venography

- The **added value** of **venous imaging** is **limited**
- Associated with ↗ ***Radiation*** **doses**



Pulmonary Embolism Severity Index

Mortality

Simplified pulmonary embolism severity index (sPESI)	
Clinical feature	**Points**
Age >80 years	**1**
History of cancer	**1**
Chronic cardiopulmonary disease	**1**

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Pulse ≥110/min	**1**
Systolic blood pressure <100 mmHg	**1**
Arterial oxygen saturation <90 percent	**1**

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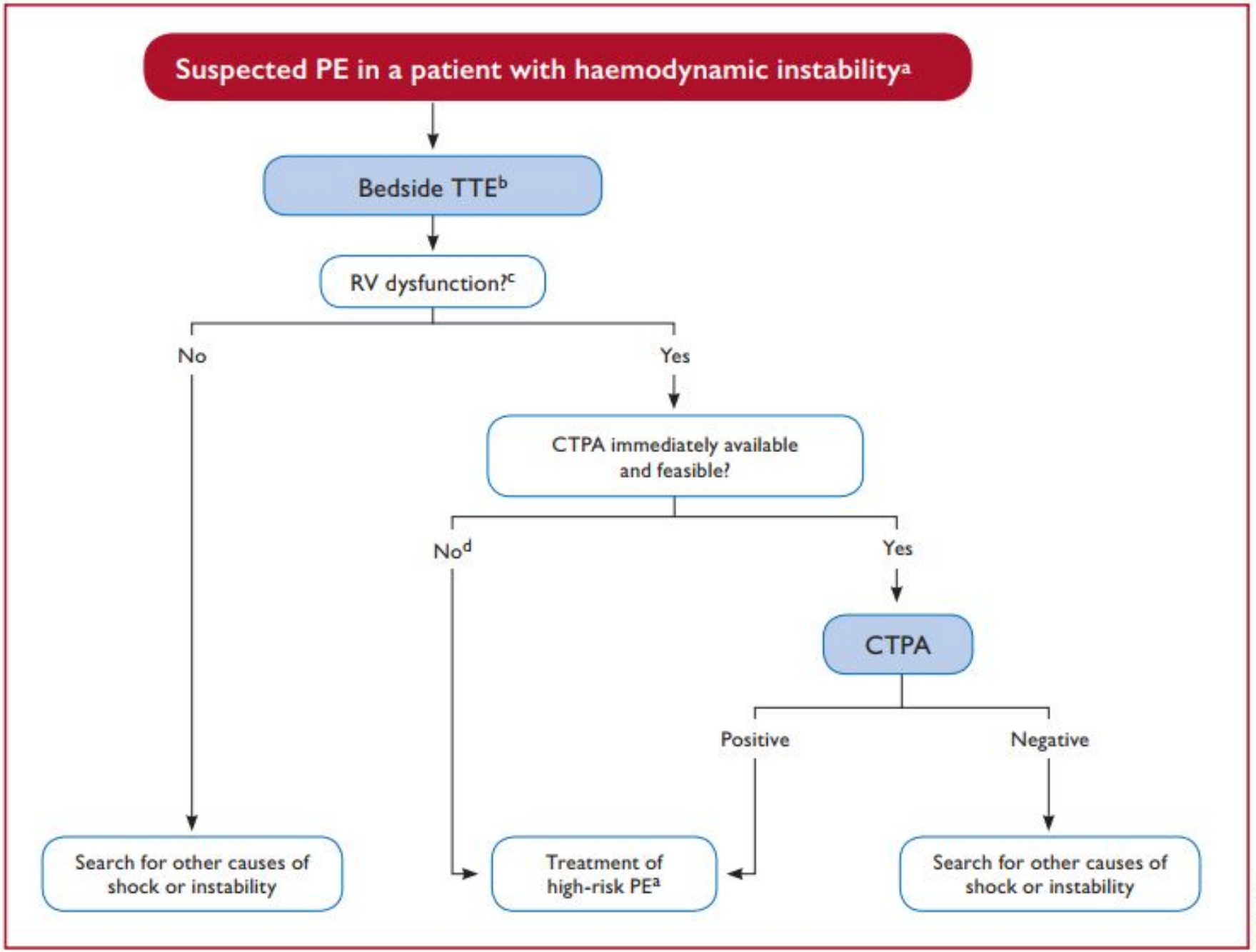
Systolic blood pressure <100 mmHg	**1**
Arterial oxygen saturation <90 percent	**1**
Low risk	**0**
High risk	**≥1**


Simplified pulmonary embolism severity index (sPESI)
Low risk
0
30 day
mortality risk 1.0%

Simplified pulmonary embolism severity index (sPESI)		
Low risk	**0**	**30 day mortality risk 1.0%**
High risk	**≥1**	**30 day mortality risk 10.9%**

Integrated risk-adapted diagnosis and management


Suspected PE in a patient with haemodynamic instability[a]
Bedside TTE[b]
RV dysfunction?[c]
No
Yes
CTPA immediately available and feasible?
No[d]
Yes
CTPA
Positive
Negative
Search for other causes of shock or instability
Treatment of high-risk PE[a]
Search for other causes of shock or instability
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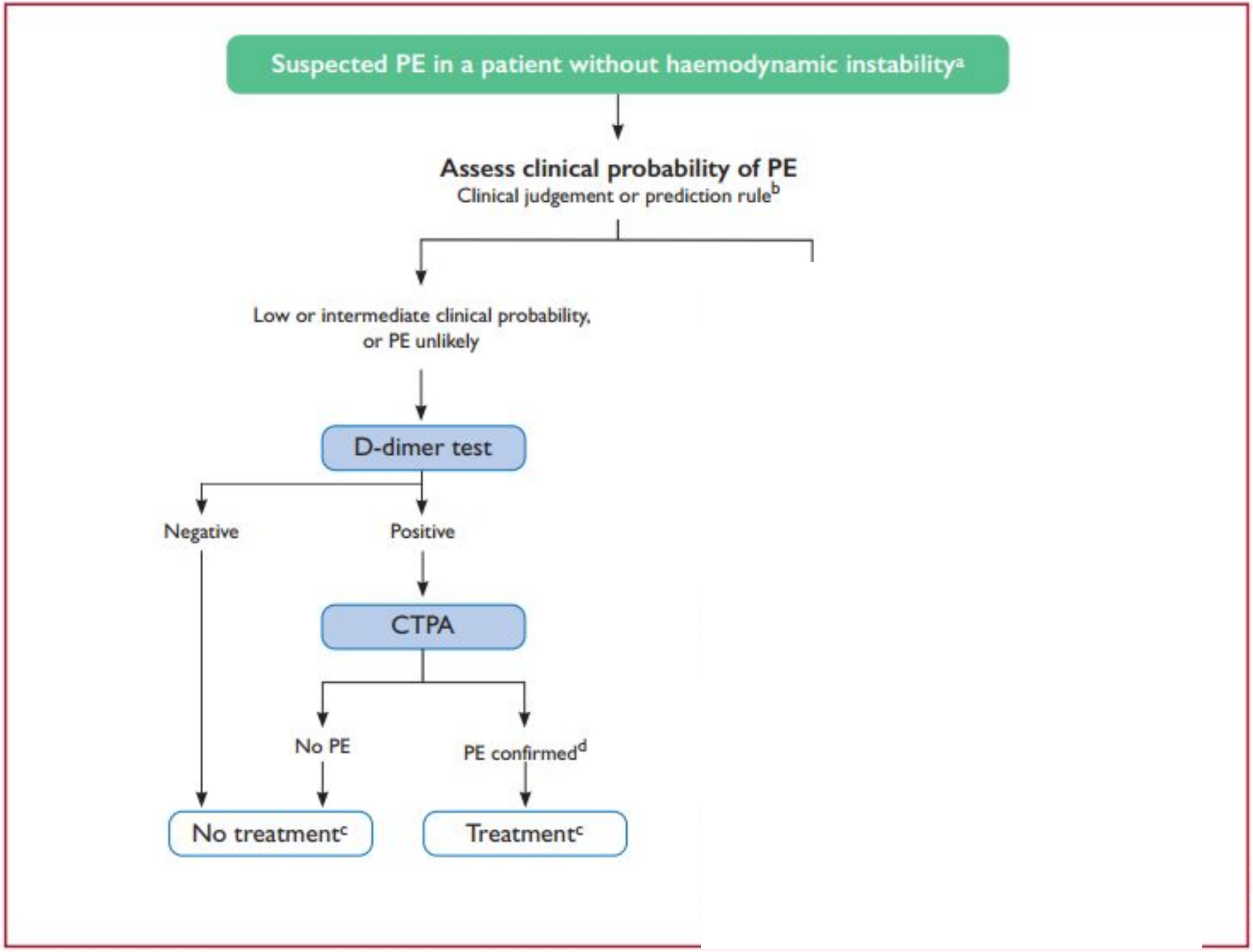
Suspected PE in a patient without haemodynamic instability[a]
Assess clinical probability of PE
Clinical judgement or prediction rule[b]
Low or intermediate clinical probability, or PE unlikely
D-dimer test
Negative
Positive
CTPA
No PE
PE confirmed[d]
No treatment[c]
Treatment[c]
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- **Pulmonary Embolism Rule-out Criteria (PERC)**
  - **Avoiding overuse** of **diagnostic tests** for **pulmonary embolism**

Pulmonary Embolism Rule-out Criteria (PERC)

1. Age < 50 years
2. Pulse < 100 beats per minute
3. SaO2 >94%
4. No unilateral leg swelling
5. No haemoptysis
6. No recent trauma or surgery
7. No history of VTE
8. No oral hormone use

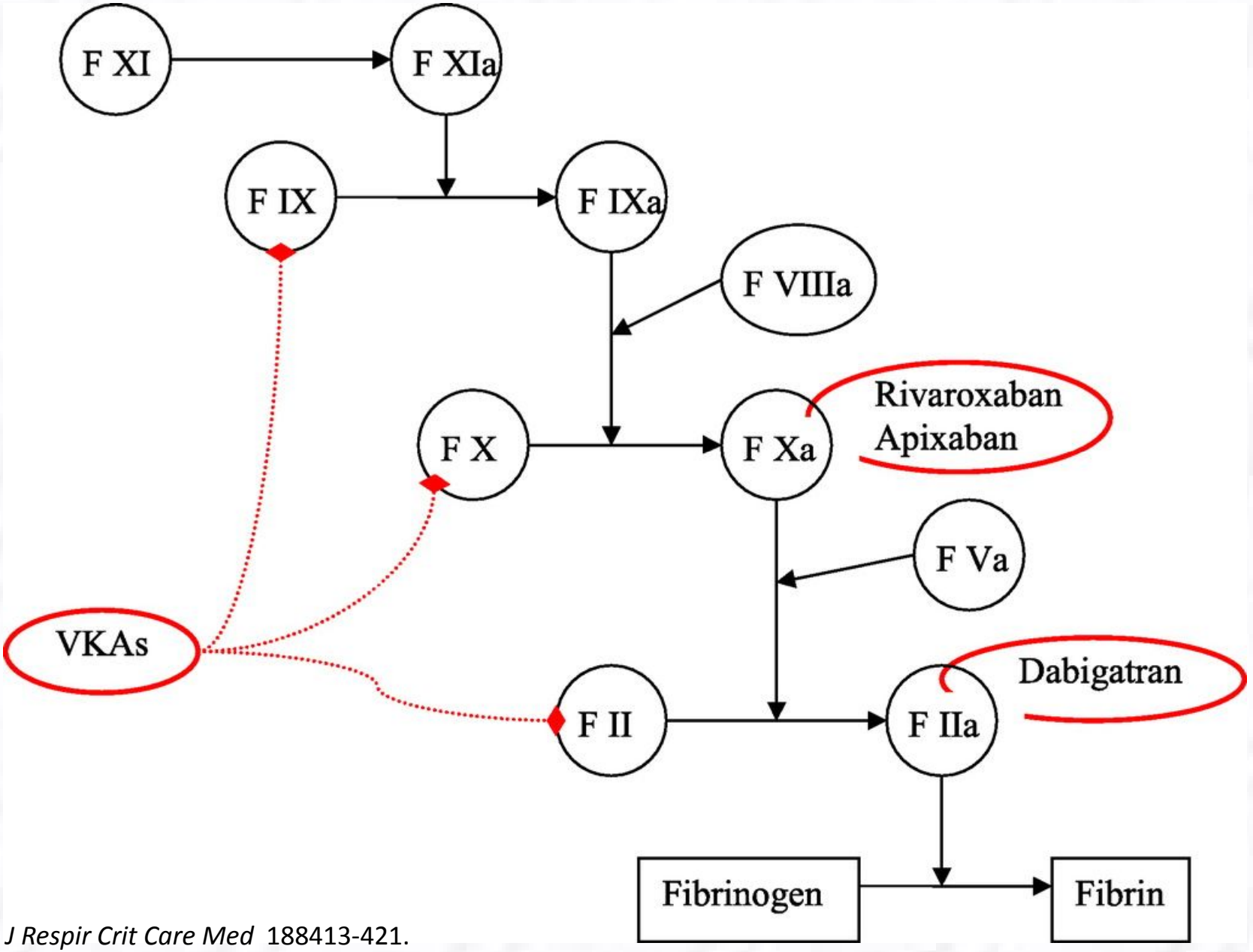
J Am Coll Cardiol 2011;57:700706

Treatment of PE

Treatment	Mechanism	Monitoring	Reversal Agent
Heparin	Binds AT III and factor Xa	PTT levels	Protamin
Enoxaparin	Binds factor xa >>> AT III	Factor Xa levels	Protamin
Fondaparinux	Binds AT III and factor Xa		

Treatment	Mechanism	Monitoring	Reversal Agent
	Blosck vitamin K		
Warfarin	epoxide: Slow desrease in factors II, VII, IX,X and thrombin inhibitor	INR	Vitamin k, FFP prothrombin complex

Treatment	Mechanism	Monitoring	Reversal Agent
Argatroban	Direct thrombin inhibitor	PTT	None
Dabigatran	Oral factor IIa inhibitor	None	None
Rivaroxaban	Oral factor Xa inhibitor	None	None



Am J Respir Crit Care Med 188413-421.

Treatment	Mechanism	Monitoring	Reversal Agent
Streptokinase Urokinase Tpa	Increased plasminogen. Plasmin, which breaks- down fibrin.	Non	Non
IVC filter	Placed when a contraindication exists to anticoagulation or if poor cardiopulmonary reserve after PE		Retrievable or permanent
Compression stocking	Reduces symptoms of post-thrombotic syndrome.		

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