Pulmonary embolism
- the great masquerader

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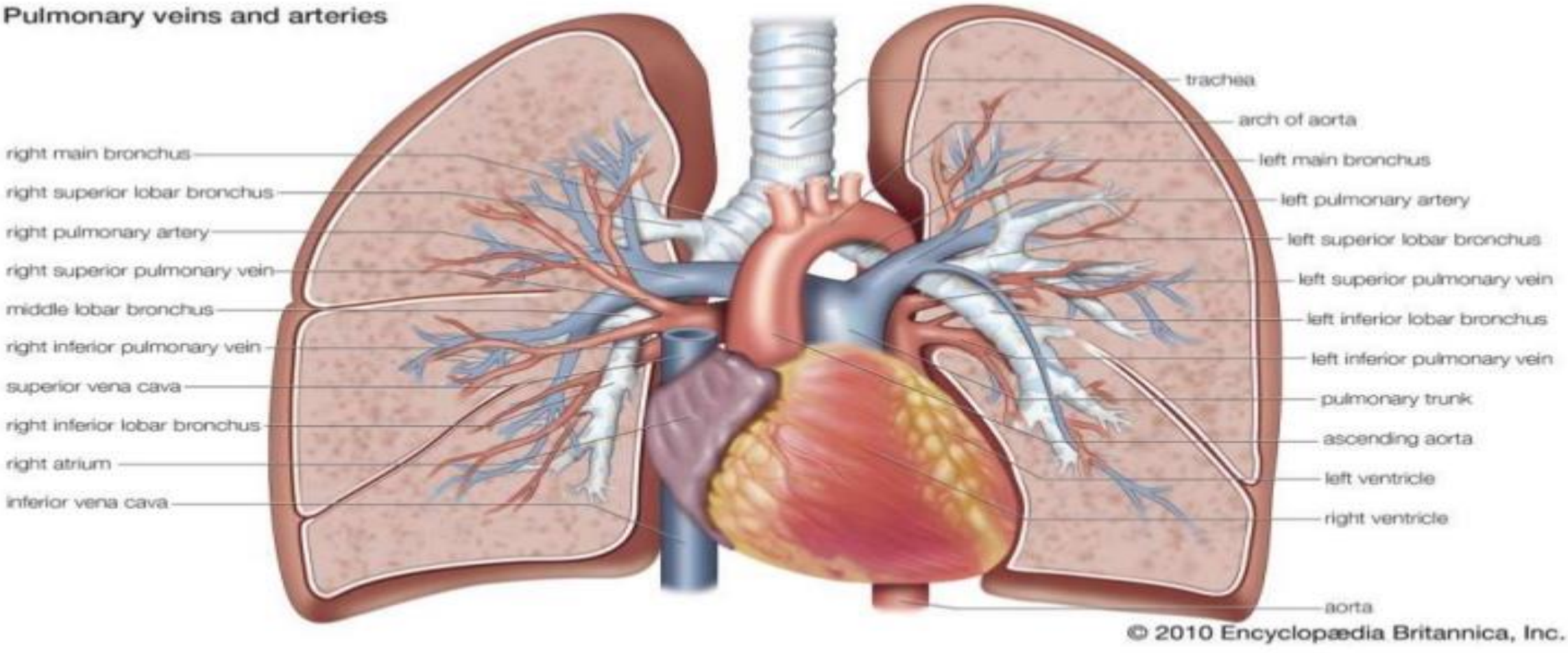
2016


Pulmonary veins and arteries
right main bronchus
right superior lobar bronchus
right pulmonary artery
right superior pulmonary vein
middle lobar bronchus
right inferior pulmonary vein
superior vena cava
right inferior lobar bronchus
right atrium
inferior vena cava
trachea
arch of aorta
left main bronchus
left pulmonary artery
left superior lobar bronchus
left superior pulmonary vein
left inferior lobar bronchus
left inferior pulmonary vein
pulmonary trunk
ascending aorta
left ventricle
right ventricle
aorta
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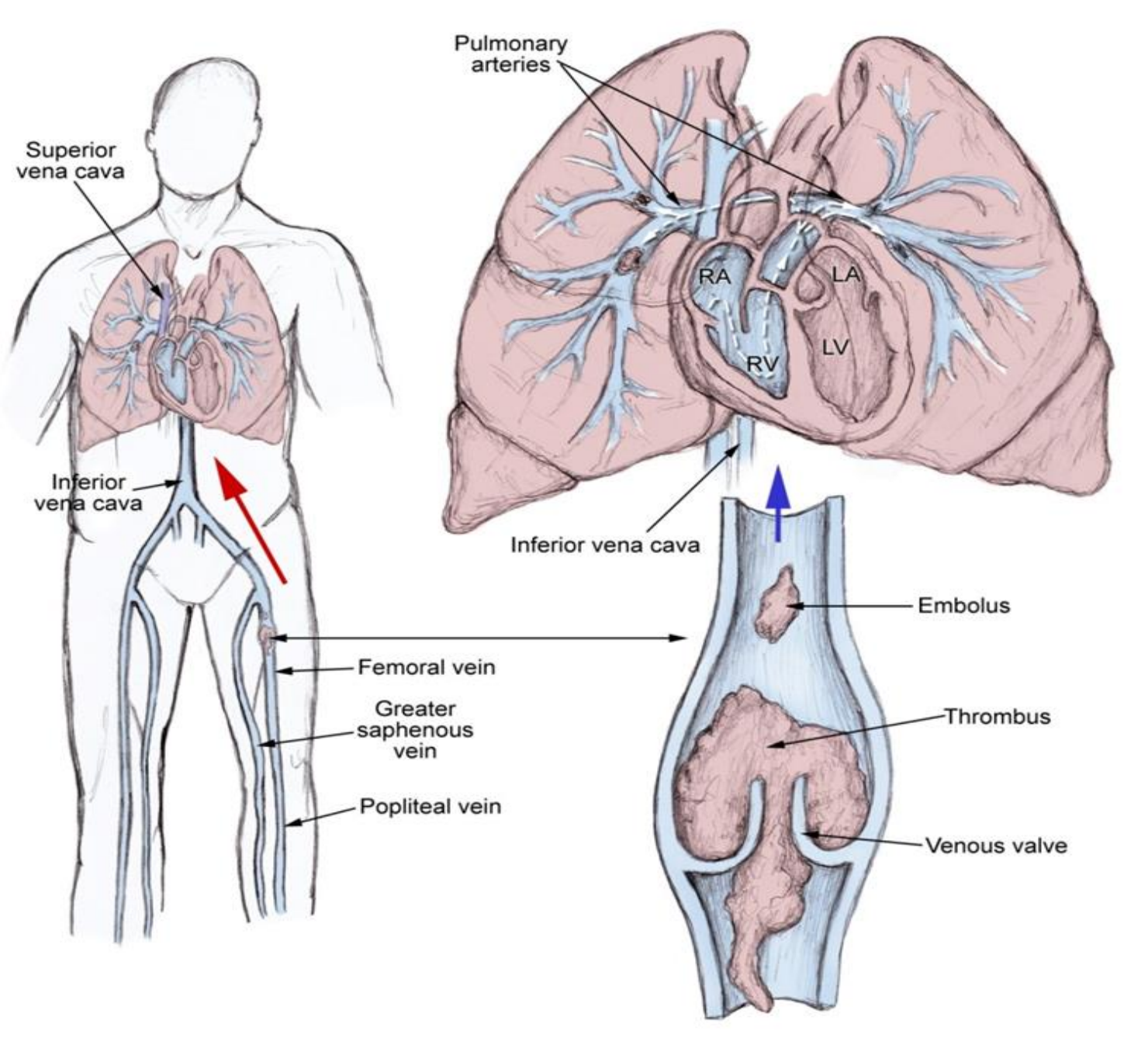

Pulmonary embolism (PE) is a blockage of the main artery of the lung or one of its branches by a substance that has travelled from elsewhere in the body through the bloodstream (embolism). PE most commonly results from deep vein thrombosis (a blood clot in the deep veins of the legs or pelvis) that breaks off and migrates to the lung, a process termed *venous thromboembolism* (VTE).

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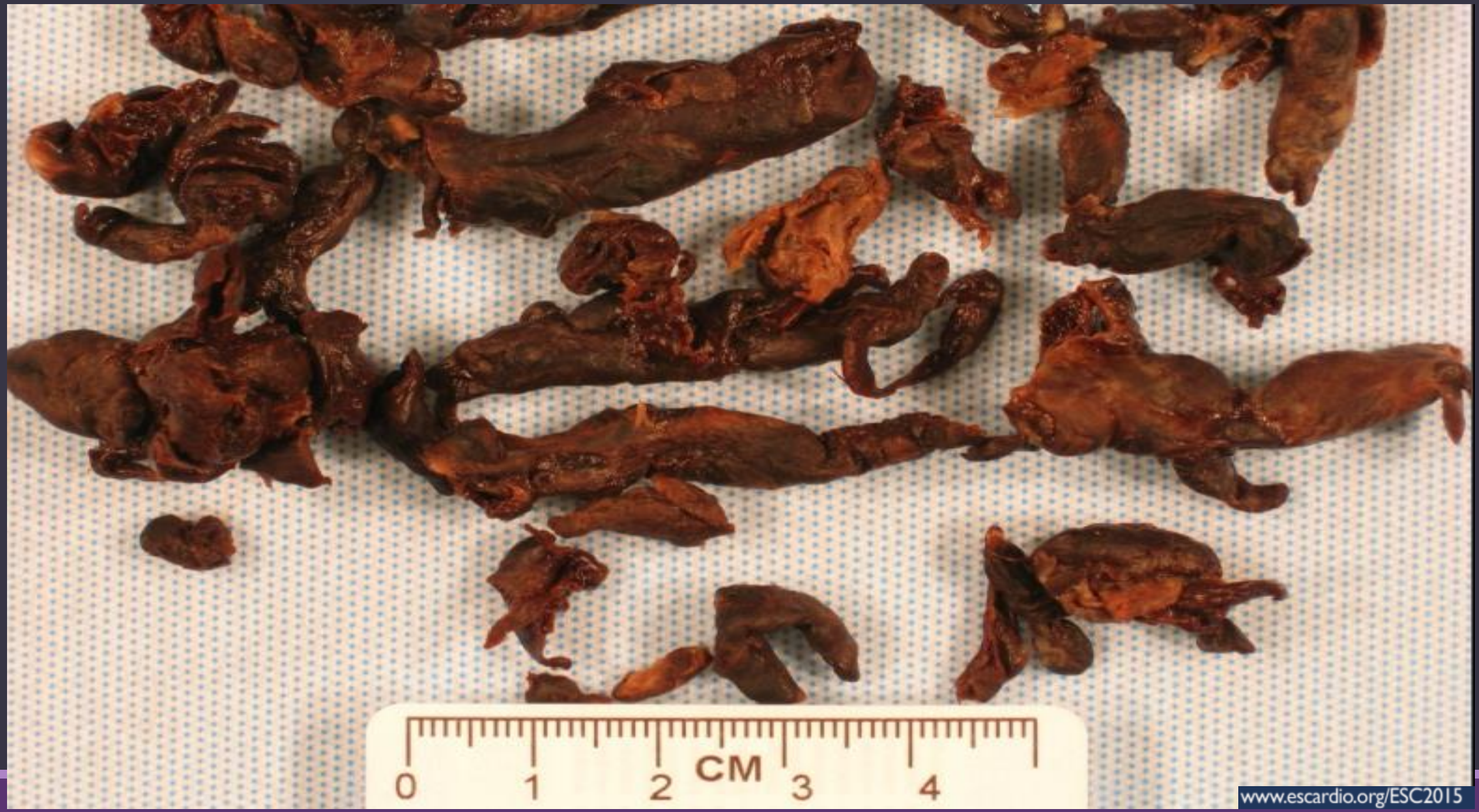
0
1
2
CM
3
4

CLASSIFICATION OF PULMONARY EMBOLISM

- **Massive PE**
accounts for 5-10% of cases

- **Submassive PE**
accounts for 20-25% of patients

- **Low-risk**
constitutes about 70-75% of cases

- dyspnea,
- syncope,
- hypotension,
- cyanosis

- RV dysfunction (right heart failure) despite
- normal systemic arterial pressure.

CLASSIFICATION OF PULMONARY EMBOLISM

Acute ⟷ **Chronic**

situated centrally within the vascular lumen or if it occludes a vessel (vessel cut - off sign)

it is eccentric and contiguous with the vessel wall, it reduces the arterial diameter by more than 50%, evidence of recanalization within the thrombus is present, and an arterial web is present.

Central ⟷ **Peripheral**

main pulmonary artery, the left and right main pulmonary arteries, the anterior trunk, the right and left interlobar arteries, the left upper lobe trunk, the right middle lobe artery, and the right and left lower lobe arteries

segmental and subsegmental arteries of the right upper lobe, the right middle lobe, the right lower lobe, the left upper lobe, the lingula, and the left lower lobe

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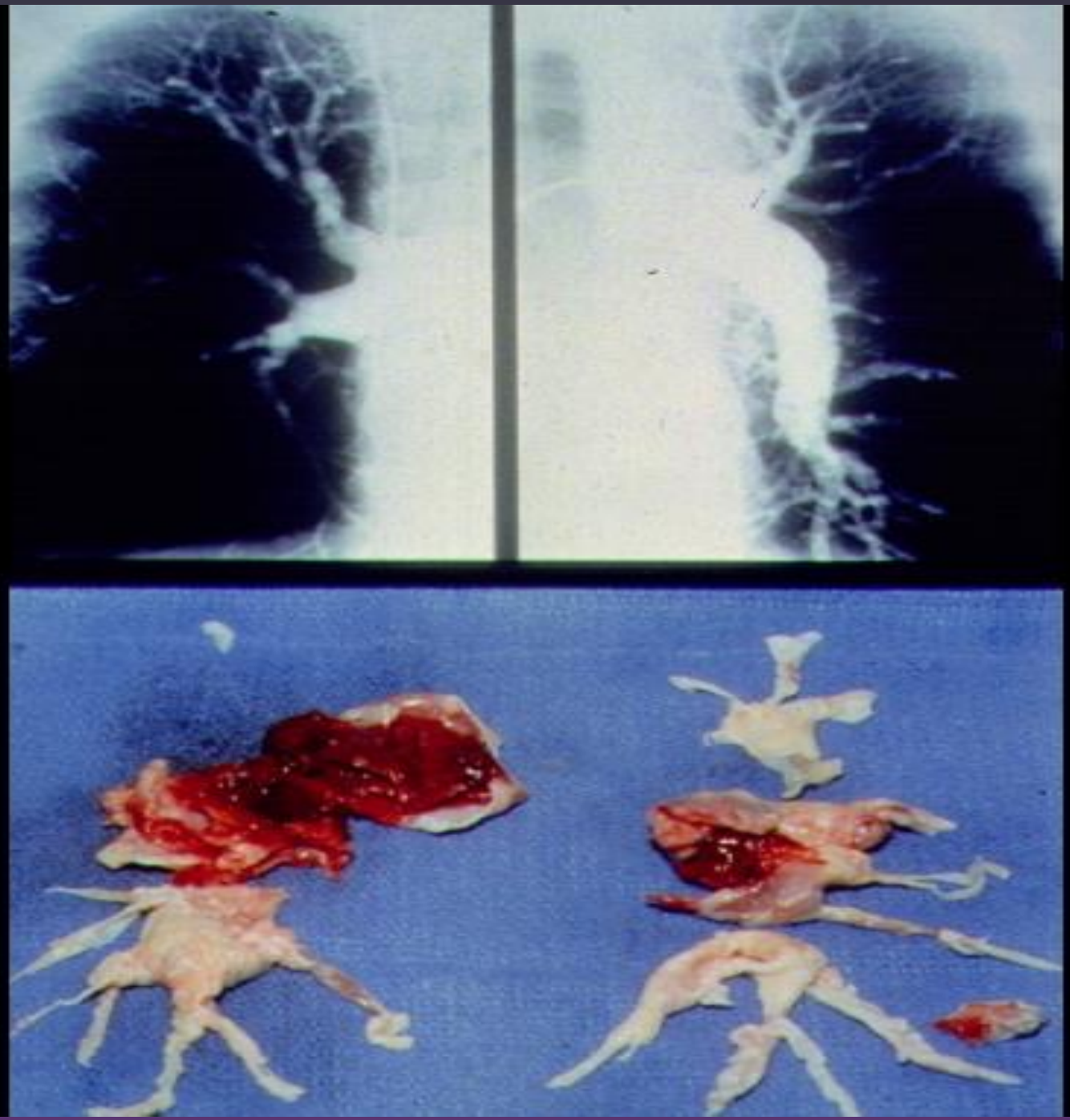
Acute

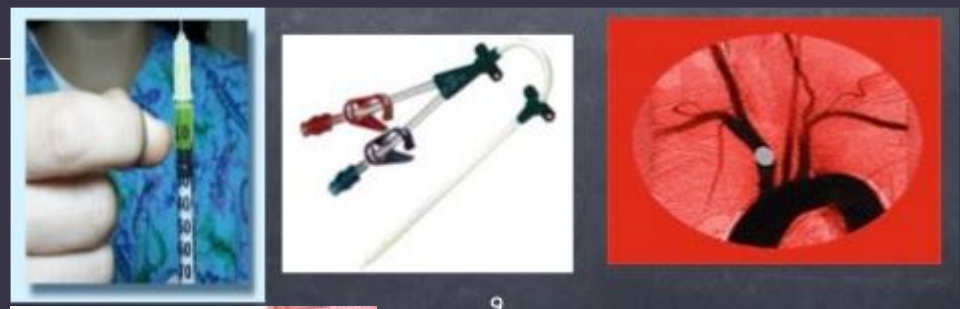
Central

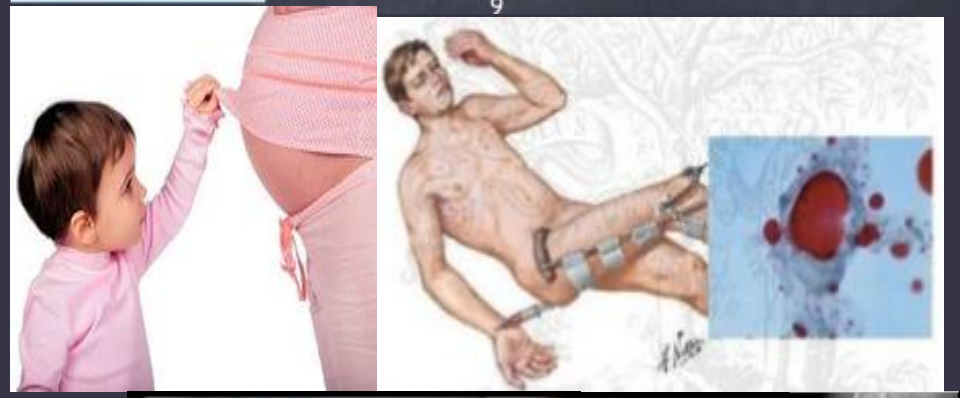
- Massive PE

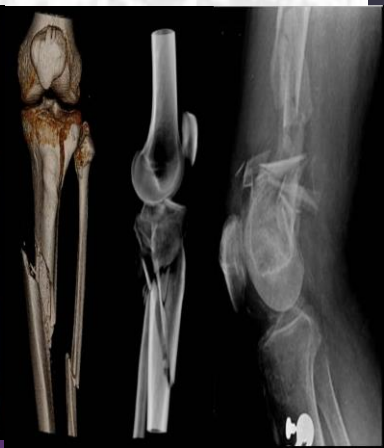


Predisposing factors of PULMONARY EMBOLISM

- Venous stasis
- Hypercoagulable states
- Immobilization
- Surgery and trauma
- Pregnancy
- Oral contraceptives and estrogen replacement
- Malignancy
- Warfarin (first few days of therapy)
- Central venous instrumentation - past 3 months
- Hereditary factors (Protein C deficiency, factor V Leiden, plasminogen activator abnormality etc.)
- Acute medical illness (AIDS (lupus anticoagulant), Behçet disease, myocardial infarction, systemic lupus erythematosus, polycythemia, ulcerative colitis etc.)







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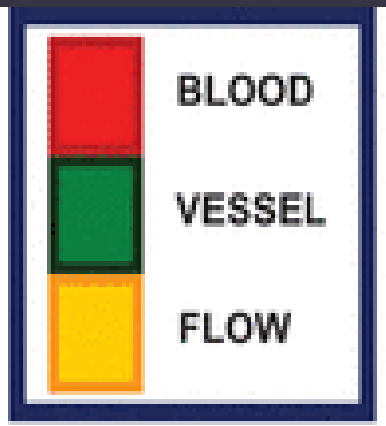
Virchow TRIAD

HYPERCOAGULABILITY

- Major surgery / trauma
- Malignancy
- Pregnancy (post-partum)
- Inherited thrombophilia
- Infection and sepsis
- Inflammatory Bowel Disease
- Autoimmune condition
- Estrogen therapy
- Inflammation
- Dehydration

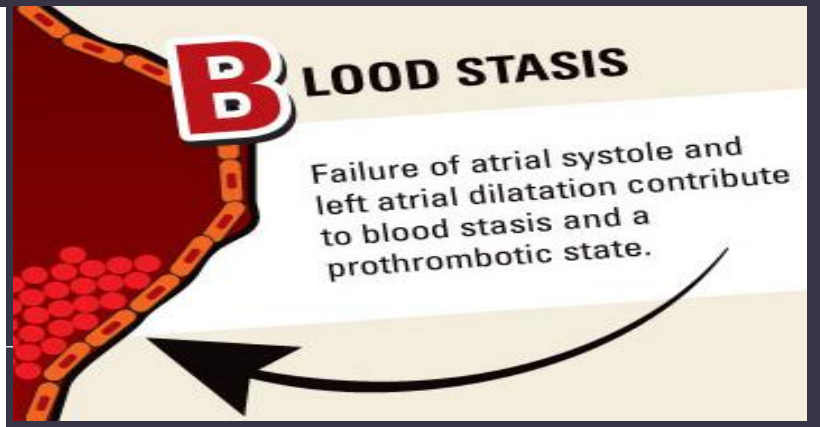


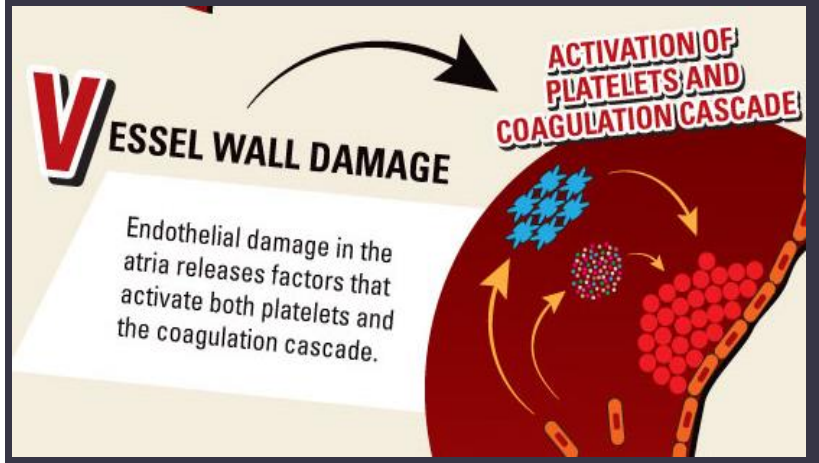
VASCULAR DAMAGE

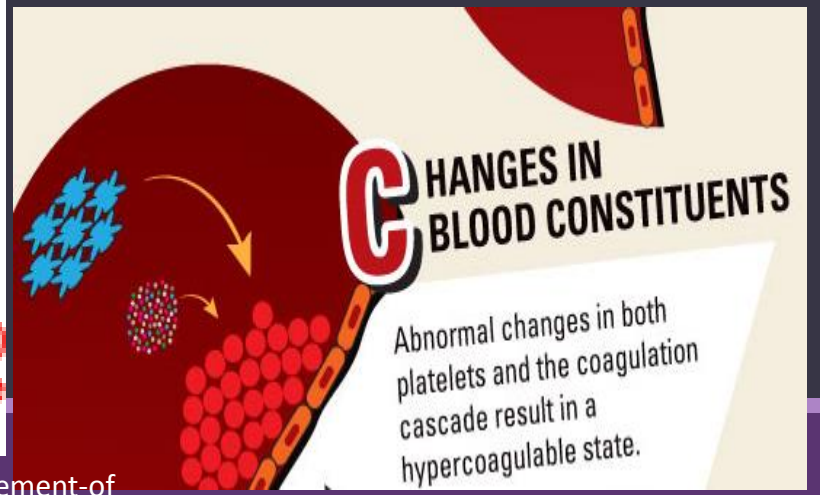
- Thrombophlebitis
- Cellulitis
- Atherosclerosis
- Indwelling catheter / heart valve
- Venepuncture
- Physical trauma, strain or injury
- Microtrauma to vessel wall

CIRCULATORY STASIS

- Immobility
- Venous obstruction (obesity, tumour, pregnancy)
- Varicose veins
- Atrial fibrillation or left ventricular dysfunction
- Congenital abnormalities affecting venous anatomy (e.g., May-Thurner and Paget-Schroëtter syndrome)
- Low heart rate (bradycardia) and low blood pressure







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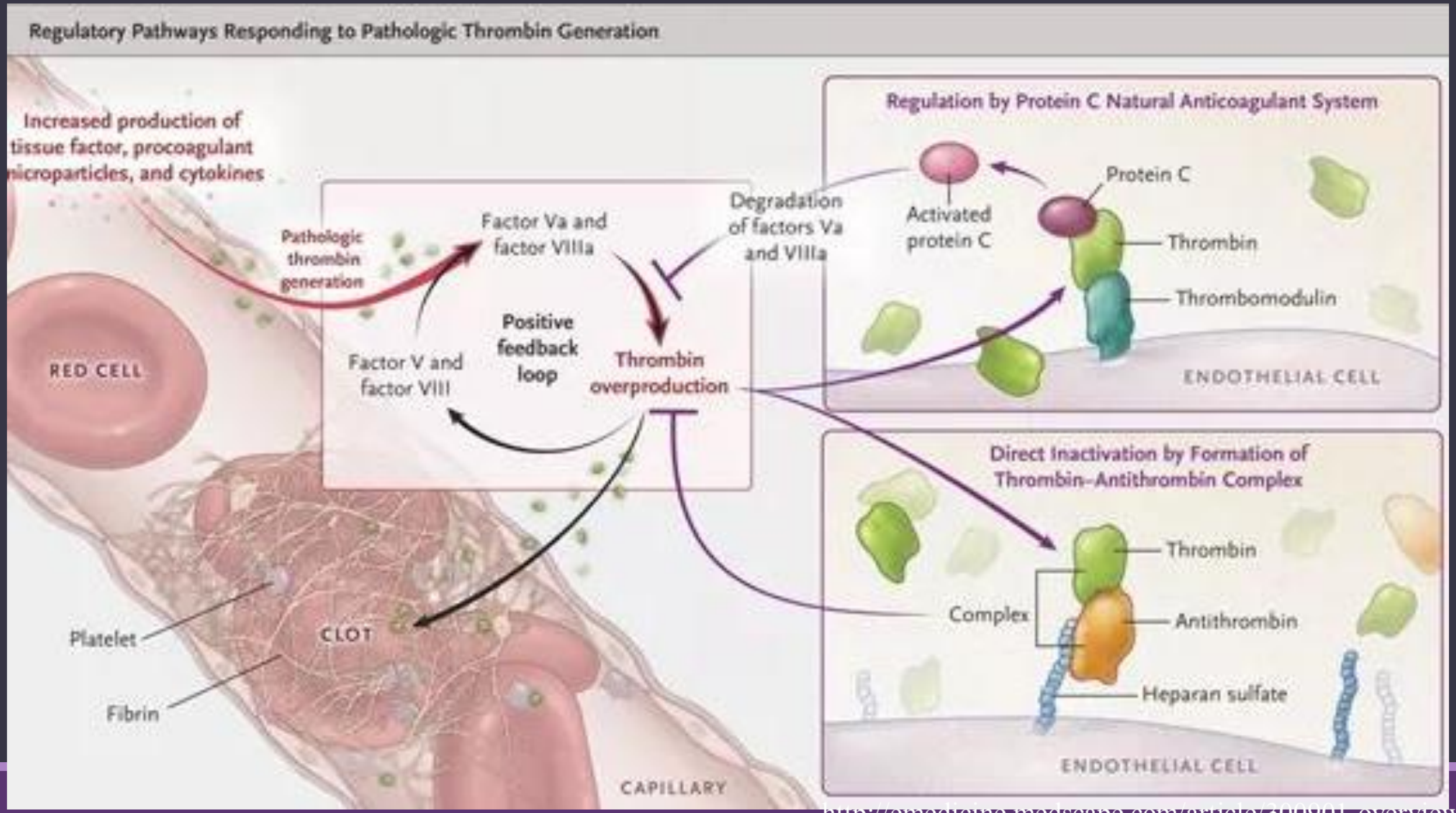

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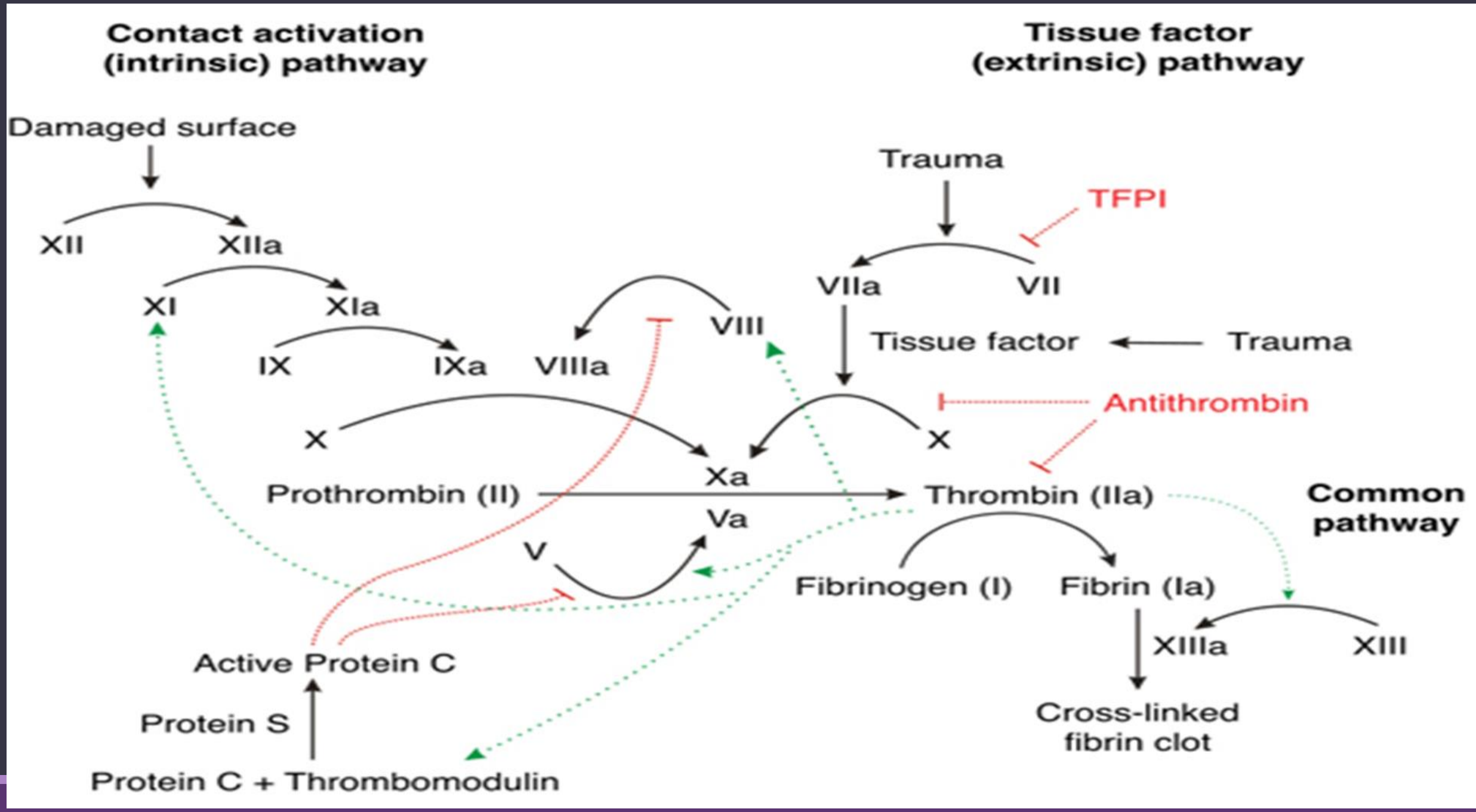
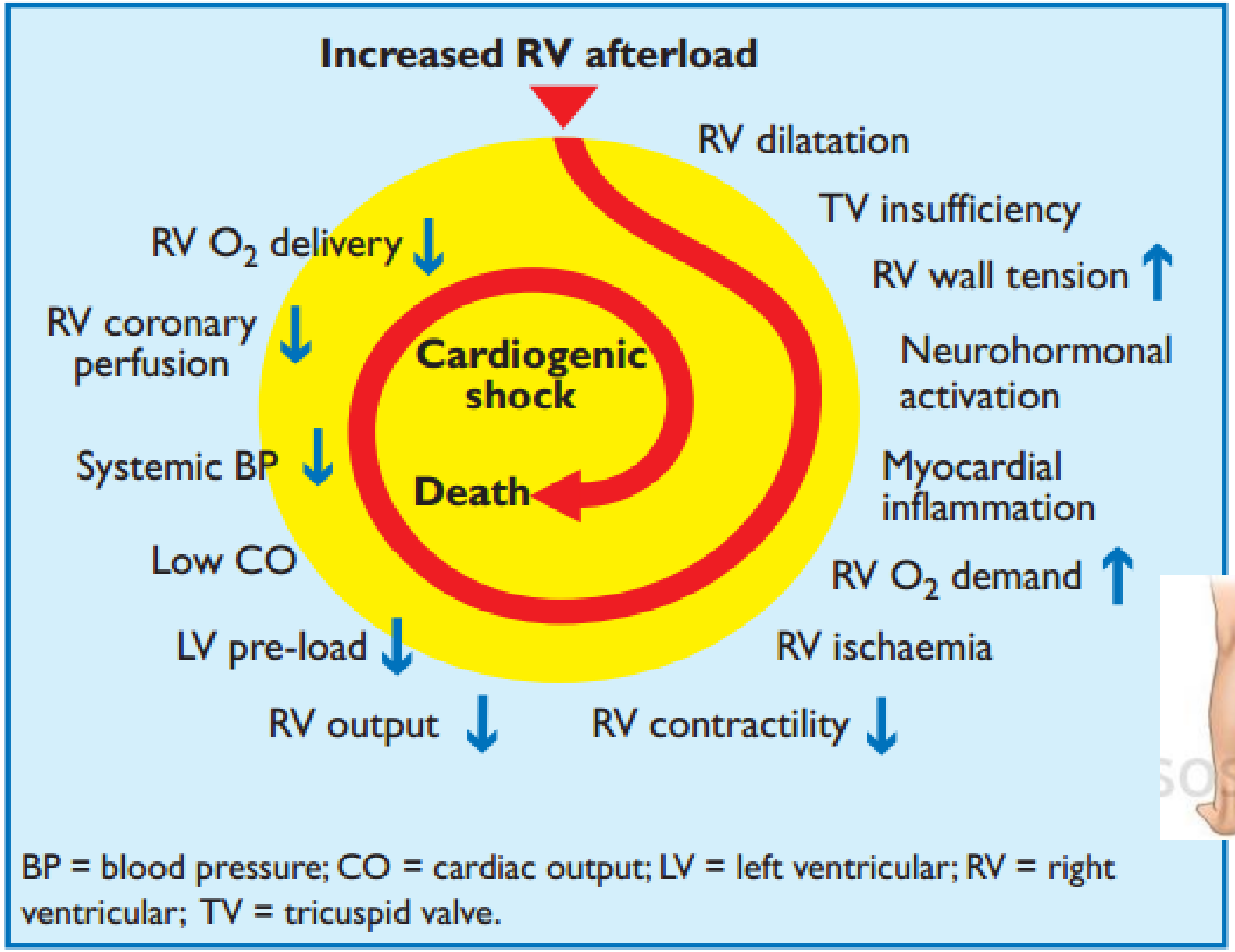
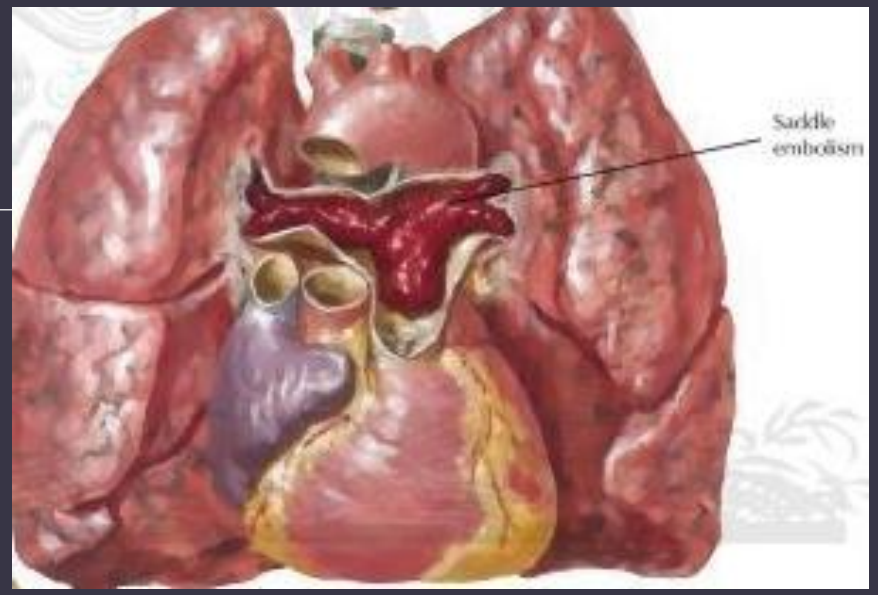


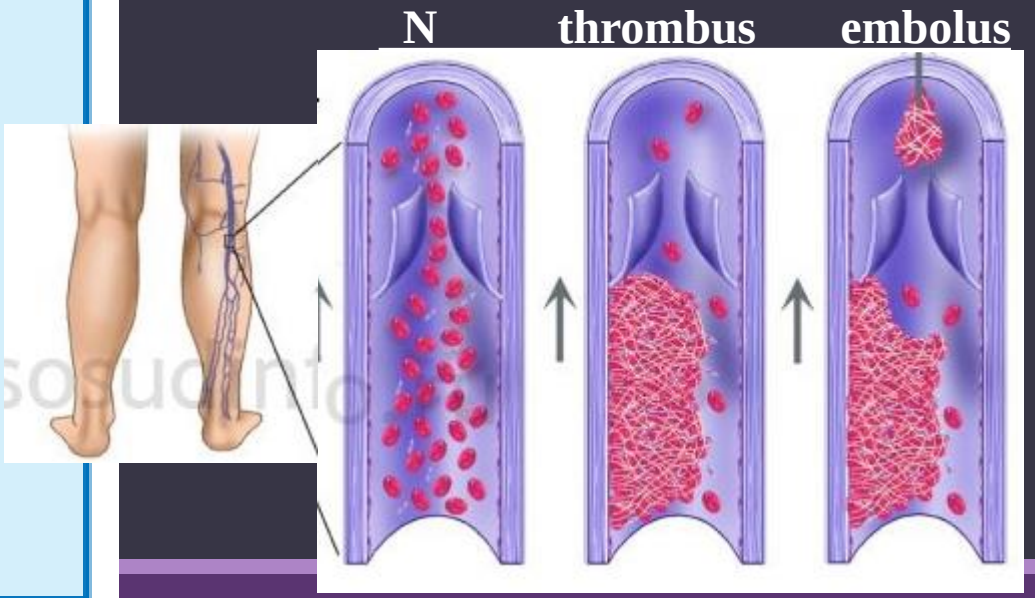
http://reference.medscape.com/features/slideshow/pulmonary-embolism?src=wnl_ref_clinfo&uac=200127DN&impID=886985&faf=1#page=14

PULMONARY EMBOLISM: Pathophysiology



BP = blood pressure; CO = cardiac output; LV = left ventricular; RV = right ventricular; TV = tricuspid valve.





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PULMONARY EMBOLISM: clinical picture

- Abrupt onset of pleuritic chest pain
- Shortness of breath
- Hypoxia
- Seizures
- Syncope
- Abdominal pain
- Fever
- Productive cough
- Wheezing
- Decreasing level of consciousness
- New onset of atrial fibrillation
- Hemoptysis
- Flank pain
- Delirium (in elderly patients)

Feature	PE confirmed (*n* = 1880)	PE not confirmed (*n* = 528)
Dyspnoea	50%	51%
Pleuritic chest pain	39%	28%
Cough	23%	23%
Substernal chest pain	15%	17%
Fever	10%	10%
Haemoptysis	8%	4%
Syncope	6%	6%
Unilateral leg pain	6%	5%
Signs of DVT (unilateral extremity swelling)	24%	18%

DVT = deep vein thrombosis.

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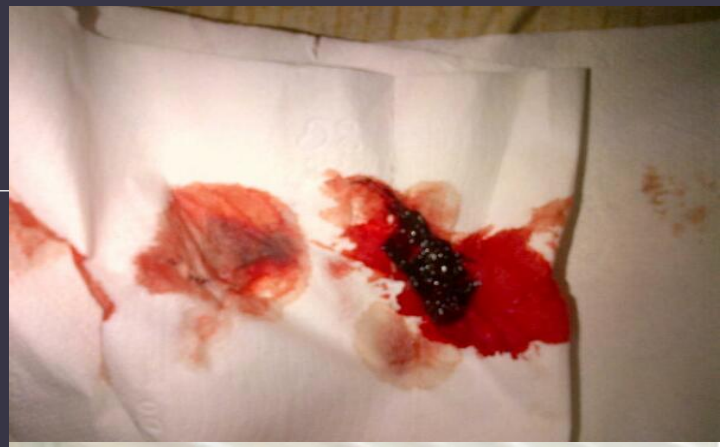
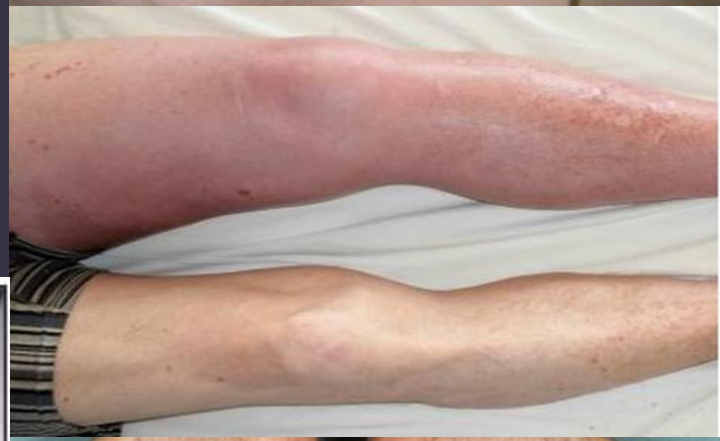
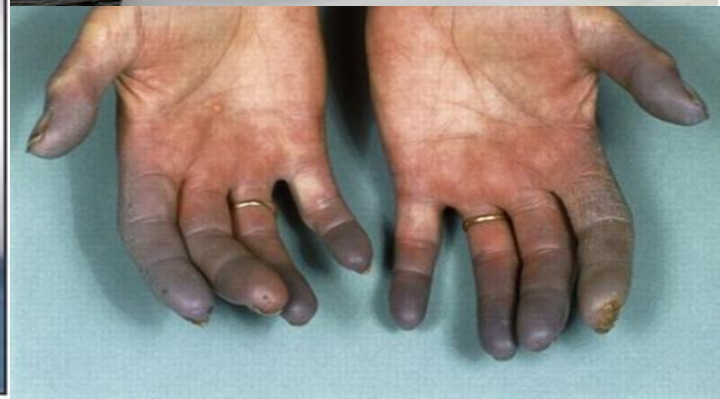
PULMONARY EMBOLISM: Physical Examination

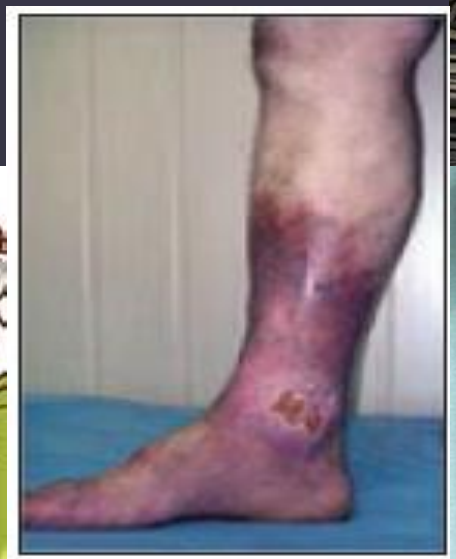
Physical signs:

- Tachypnea (RR>16/min) - 96%
- Rales - 58%
- Accentuated second heart sound - 53%
- Tachycardia (heart rate >100/min) - 44%
- Fever (temperature >37.8°C) - 43%
- Diaphoresis - 36%
- S_3 or S_4 gallop - 34%
- Clinical signs and symptoms of thrombophlebitis - 32%
- Lower extremity edema - 24%
- Cardiac murmur - 23%
- Cyanosis - 19%









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PULMONARY EMBOLISM: Physical Examination

may be grouped into 4 categories as follows:

- Massive pulmonary infarction
- Acute pulmonary infarction
- Acute embolism without infarction
- Multiple pulmonary emboli or thrombi

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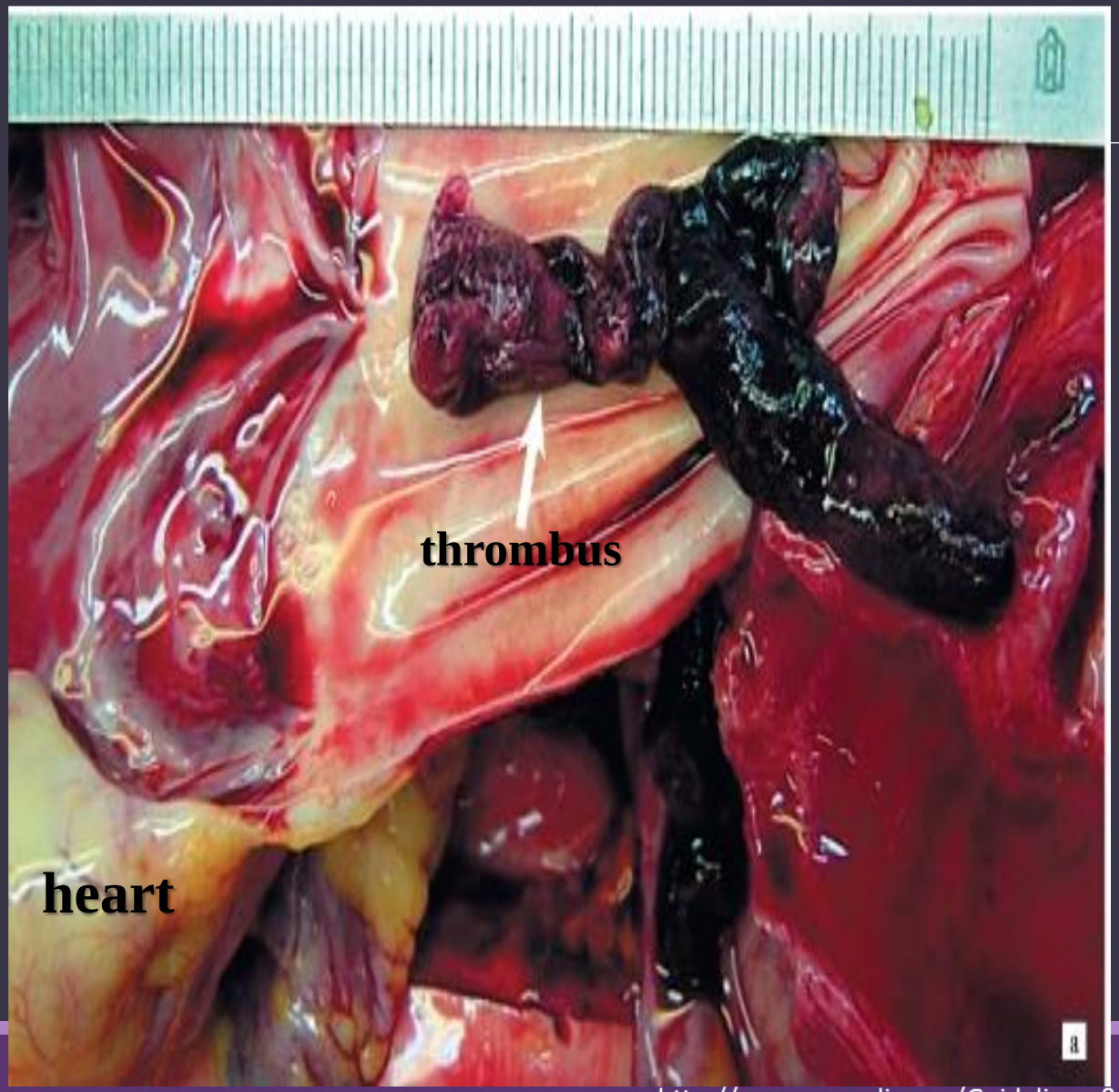
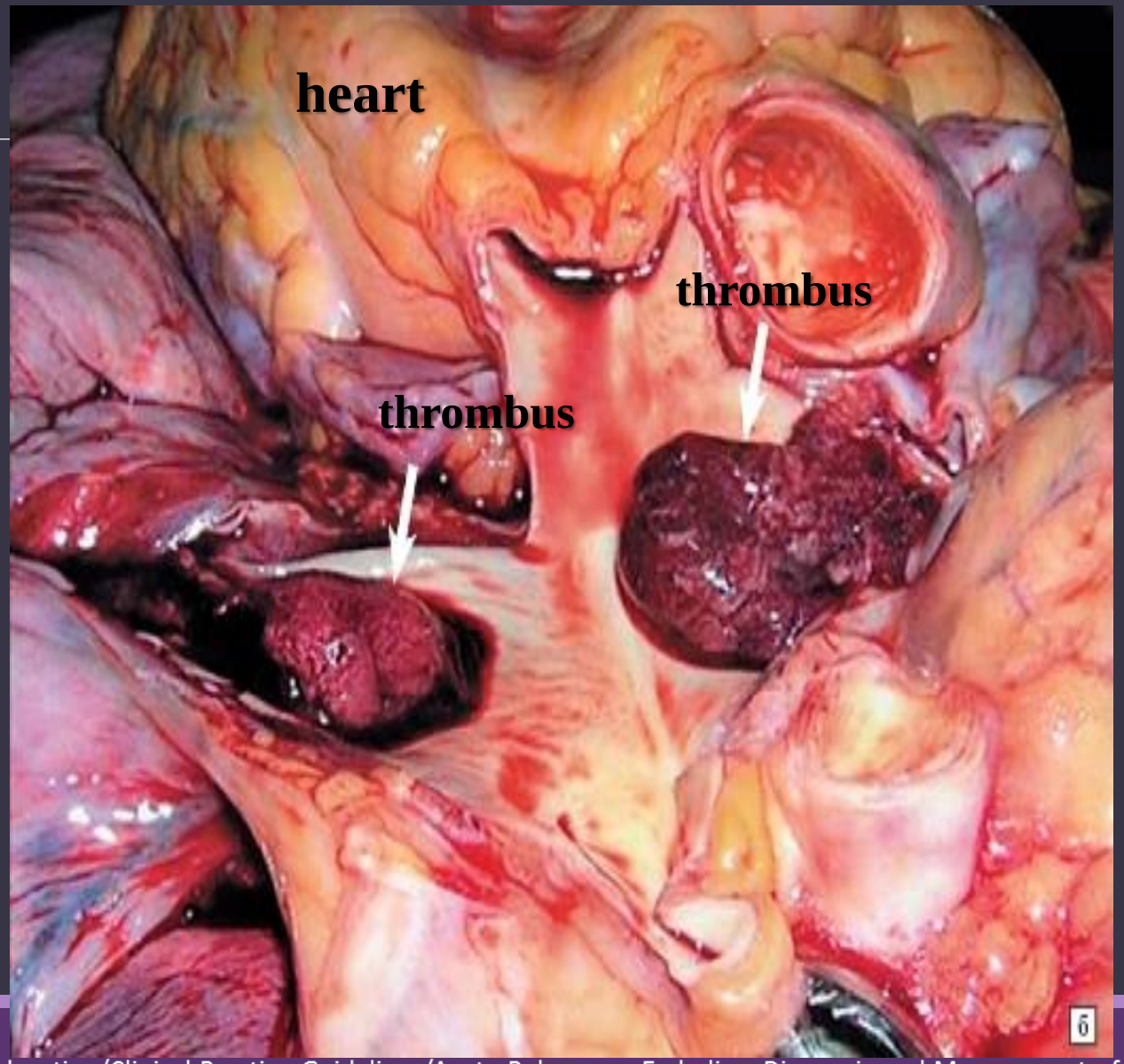
PULMONARY EMBOLISM: massive





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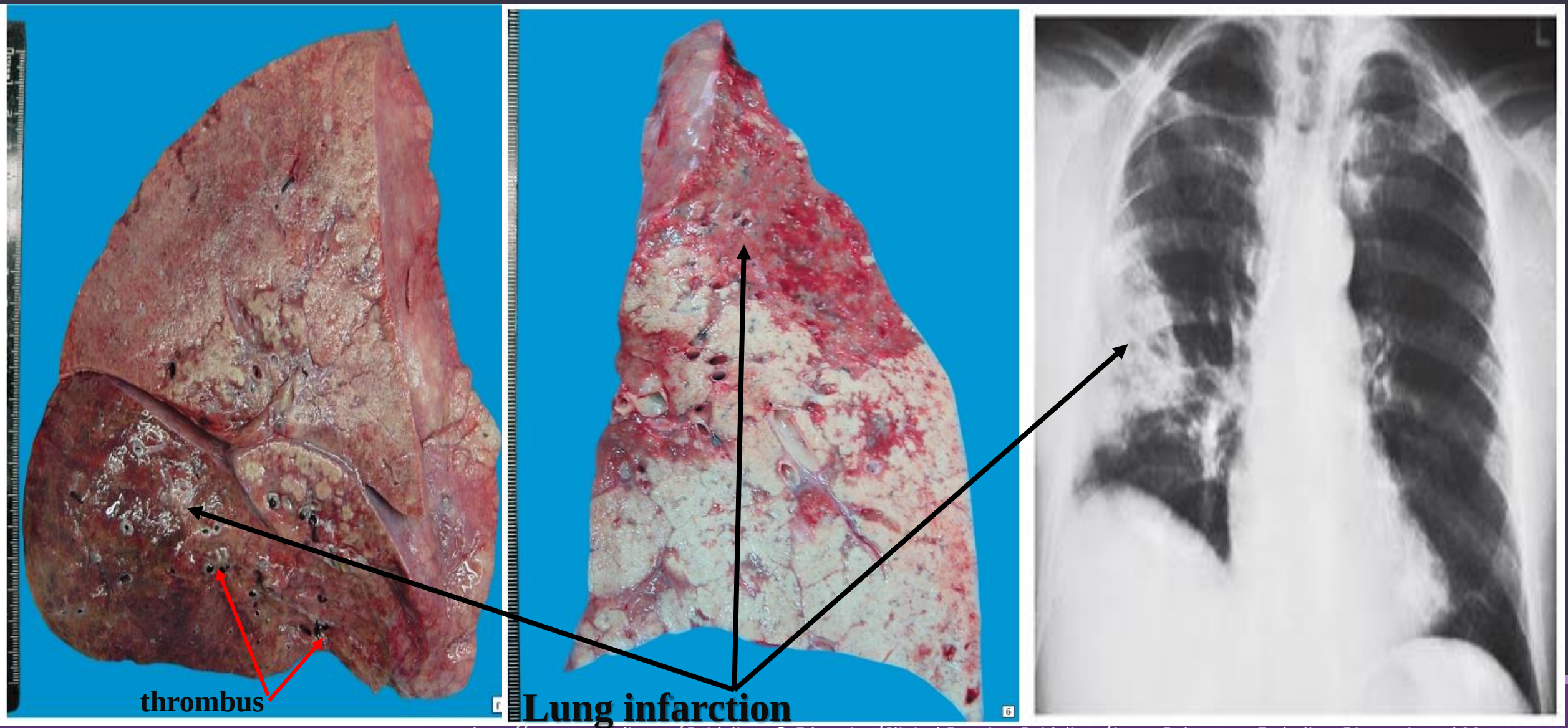
PULMONARY EMBOLISM: acute pulmonary infarction



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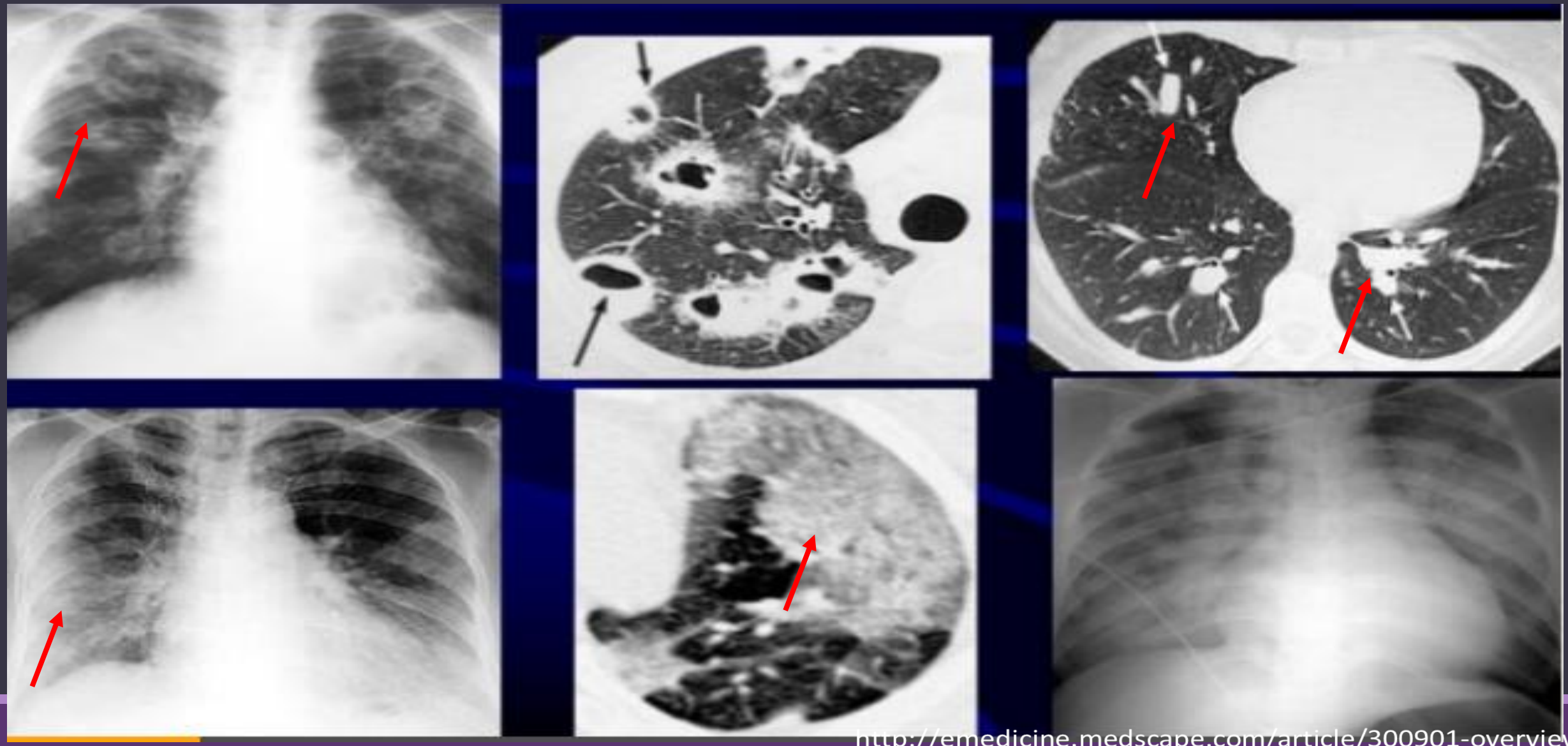
PULMONARY EMBOLISM: acute embolism without infarction



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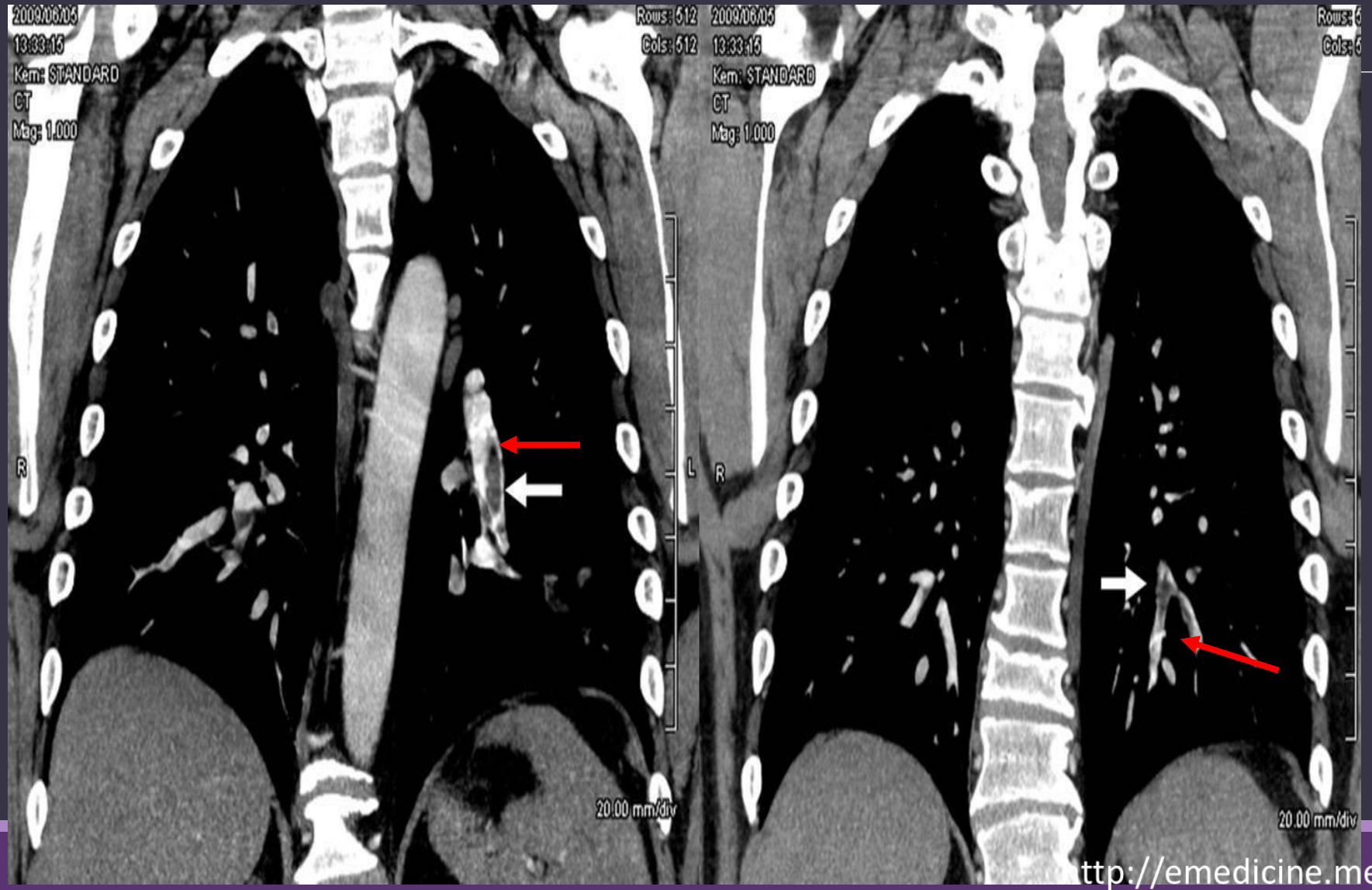
PULMONARY EMBOLISM: multiple pulmonary emboli or thrombi



These two coronal CT images are of the same patient who presented with dyspnea, chest pain, and mild core pulmonale. The chest CT angiogram reveals multiple PE (arrows) as was suspected by clinical observations. Pulmonary emboli were found in several secondary, tertiary, and distal branches of the pulmonary arteries.

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PULMONARY EMBOLISM: Assessment of clinical probability

Items	Clinical decision rule points	
Wells rule (Canadian Pulmonary Embolism Score)	**Original version[95]**	**Simplified version[107]**
Previous PE or DVT	1.5	1
Heart rate ≥100 b.p.m.	1.5	1
Surgery or immobilization within the past four weeks	1.5	1
Haemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Clinical probability		
Three-level score		
Low	0–1	N/A
Intermediate	2–6	N/A
High	≥7	N/A
Two-level score		
PE unlikely	0–4	0–1
PE likely	≥5	≥2

American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP)

Revised Geneva score	Original version[93]	Simplified version[108]
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

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PULMONARY EMBOLISM: D-dimer testing

- D-dimer testing is most reliable for excluding pulmonary embolism in younger patients who have no associated comorbidity or history of venous thromboembolism and whose symptoms are of short duration
- it is of questionable value in patients who are older than 80 years, who are hospitalized, who have cancer, or who are pregnant, because nonspecific elevation of D-dimer concentrations is common in such patients

Using D-dimer Assay

- In combination with low pretest clinical probability test is highly predictive for withholding anticoagulant therapy.
- D-dimer measurement alone cannot be accurately used to determine the presence of absence of VTE or PE.
- Only ELISA and whole blood assays such as Simpli-RED have accuracy for clinical reliability.
- Specificity is sufficiently diminished in elderly and some types of comorbid states like leukocytosis, anemia, etc.
- Used in parallel with clinical test D-dimer can guide clinical diagnosis, limit invasive and serial testing for VTE/PE.

- D-dimer testing should not be used when the clinical probability of pulmonary embolism is high

Conditions Associated with D-Dimer Production

- Acute myocardial infarction
- Acute stroke
- Advanced age
- Connective tissue diseases
- Disseminated intravascular coagulation (DIC)
- Heart failure
- Hemorrhaging
- Infection (moderate to severe)
- Malignancy
- Postoperative
- Pregnancy
- Renal failure
- Sickle cell crisis
- Trauma
- Venous thrombosis

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Potentially useful laboratory tests in patients with suspected pulmonary embolism include:

- D-dimer testing
- Ischemia-modified albumin level
- White blood cell count
- Arterial blood gases
- Markers of myocardial injury - serum troponin and liptin levels
- Markers of right ventricular dysfunction - brain natriuretic peptide

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Laboratory tests and biomarkers

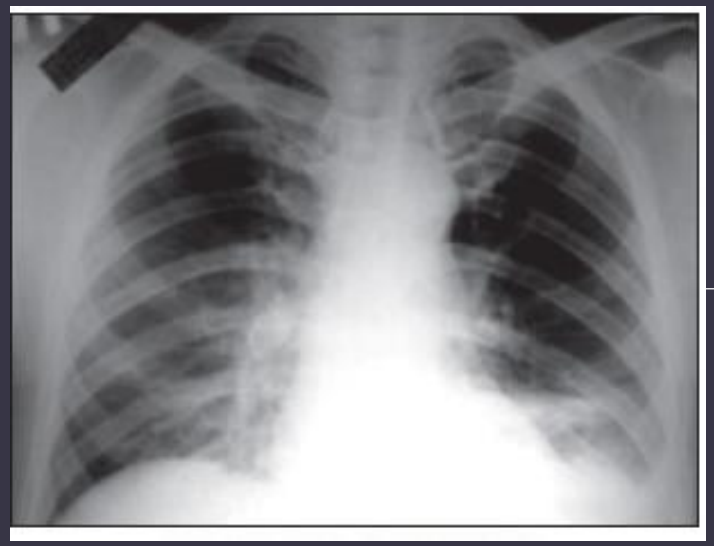
Markers of right ventricular dysfunction

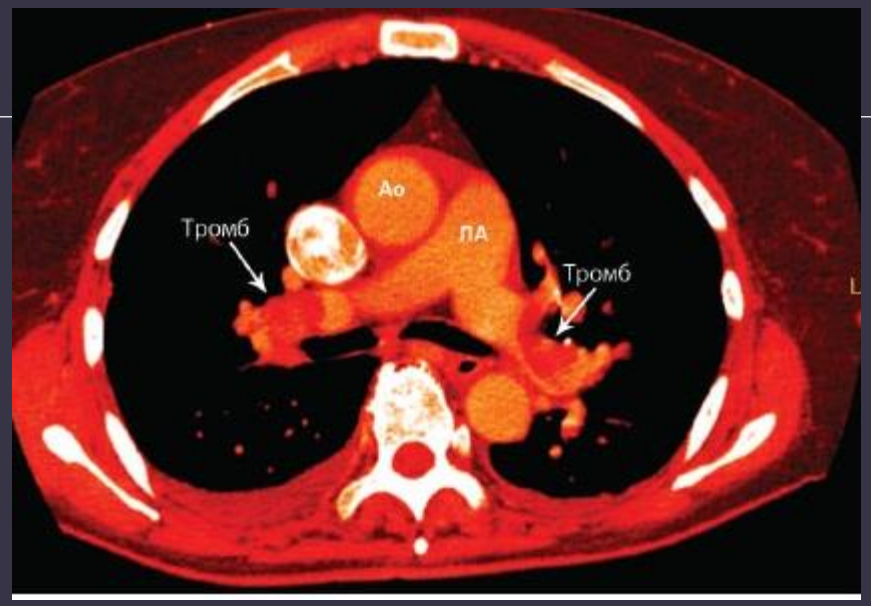
In normotensive patients with PE, the positive predictive value of elevated BNP or NT-proBNP concentrations for early mortality is low. Haemodynamically stable patients with low NT-proBNP levels may be candidates for early discharge and outpatient treatment

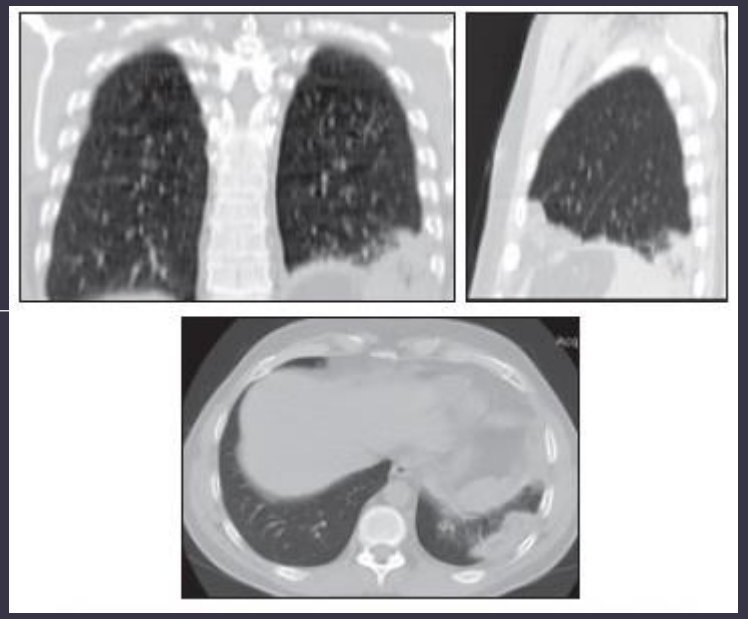
Markers of myocardial injury

Elevated plasma troponin concentrations on admission have been reported in connection with PE and were associated with worse prognosis (troponin T concentrations >14 pg/mL).

Elevated serum creatinine levels and a decreased (calculated) glomerular filtration rate are related to 30-day all-cause mortality in acute PE.



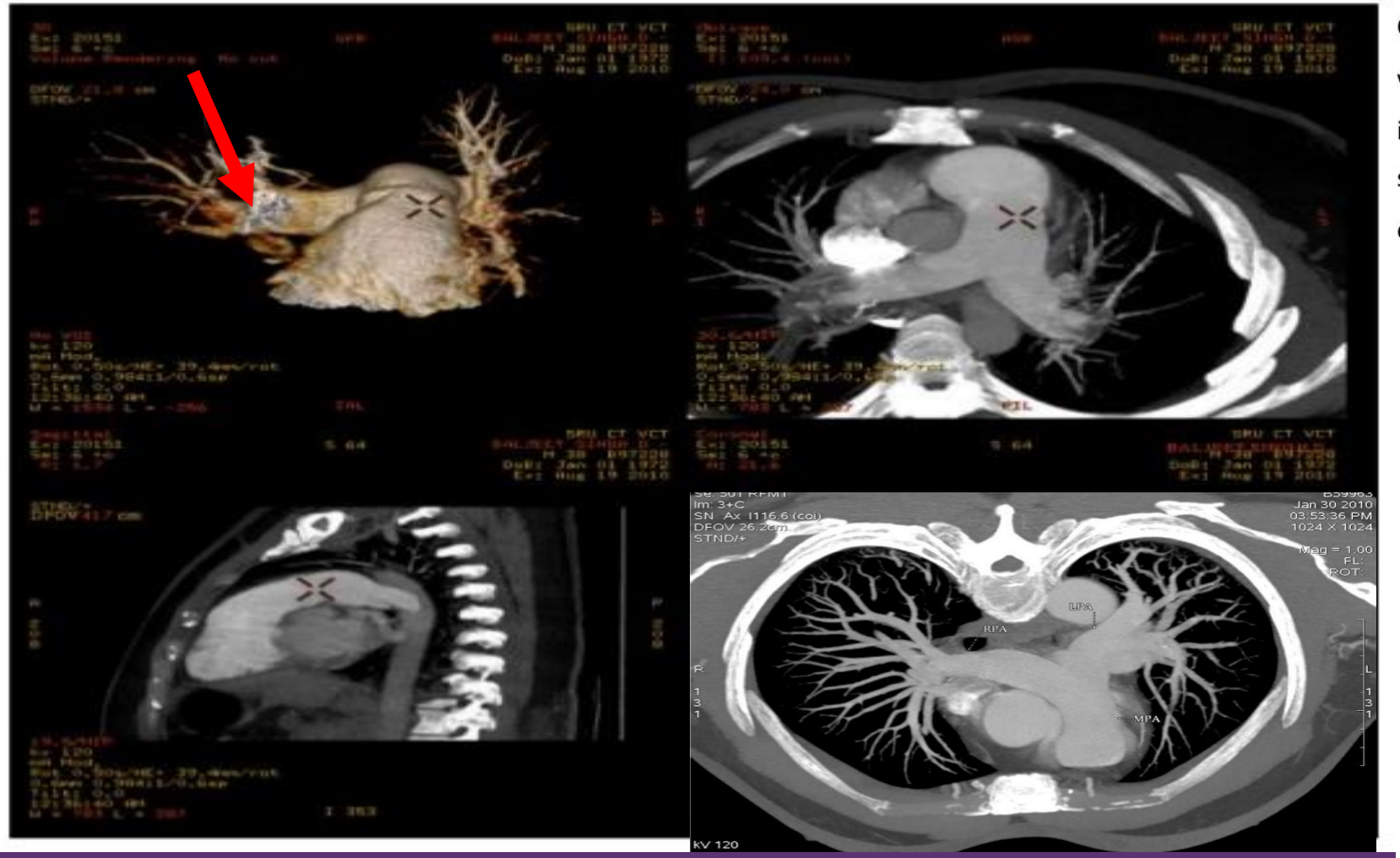




Imaging studies that aid in the diagnosis of pulmonary embolism

PULMONARY EMBOLISM: computed tomographic pulmonary angiography

is the initial imaging modality of choice for stable patients with suspected pulmonary embolism.



CTPA was introduced in the 1990s as an alternative to ventilation/perfusion scanning, which relies on radionuclide imaging of the blood vessels of the lung. It is regarded as a highly sensitive and specific test for pulmonary embolism.

Indications for Pulmonary CT Angiogram

- Clinical, laboratory, or radiologic finding suggestive of PE.
- Cardiac or lung disease excludes nuclear V/Q scan.
- Unsatisfactory V/Q scan, or inconclusive.
- Immediate diagnosis of PE is needed.
- Chest x-ray is not sufficiently clear to perform V/Q scan.
- Pulmonary hypertension secondary to PE.
- Prior history of PE with current symptoms.

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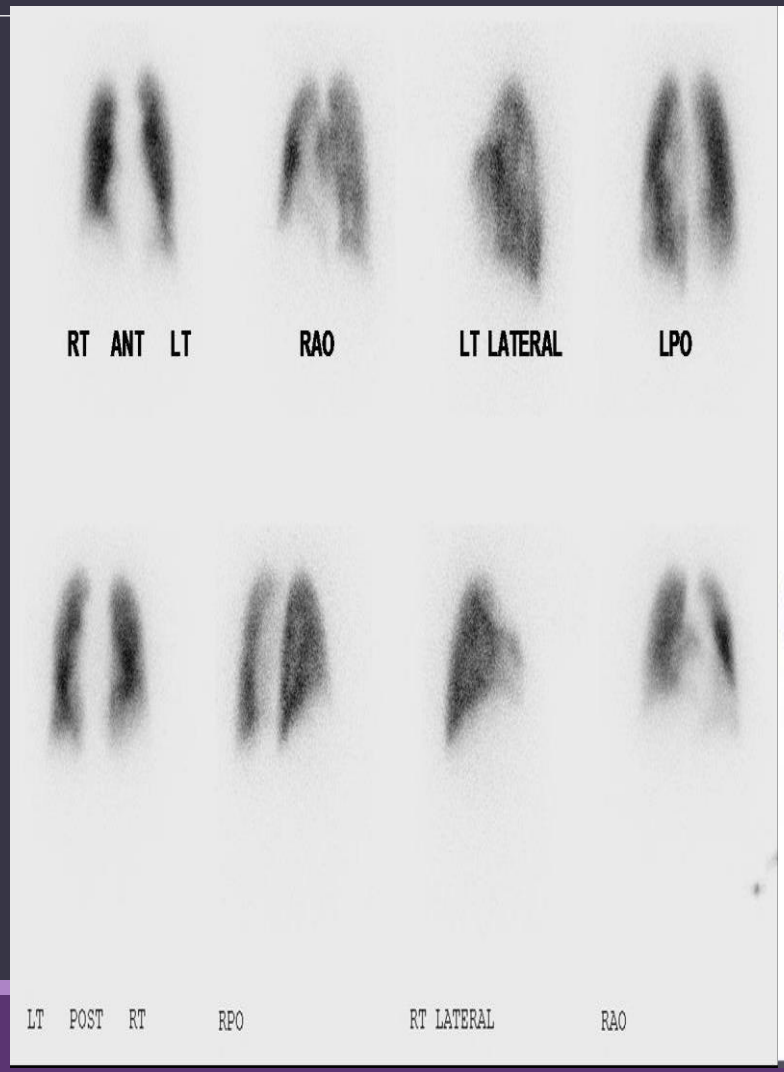
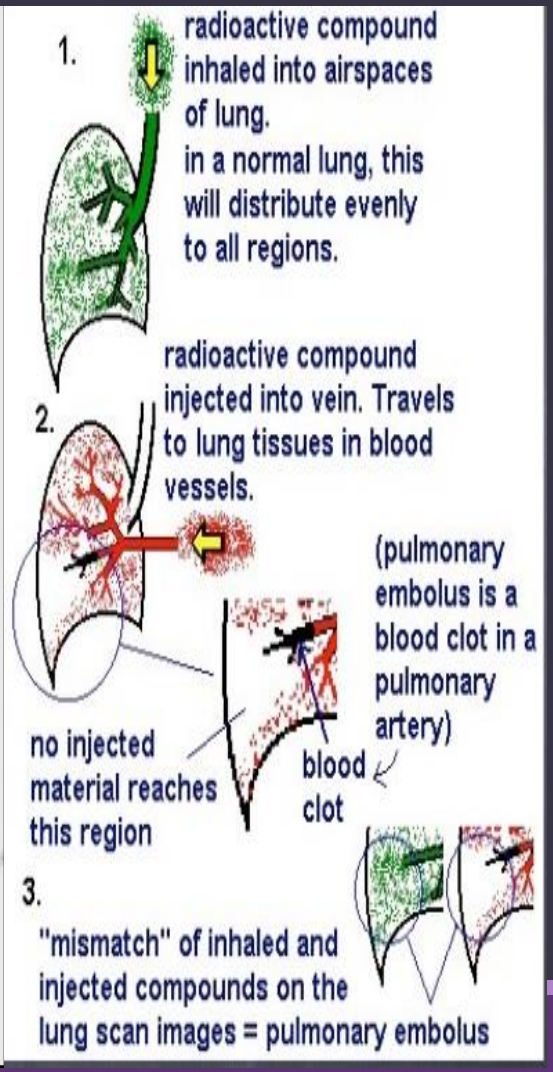
PULMONARY EMBOLISM: Lung scintigraphy

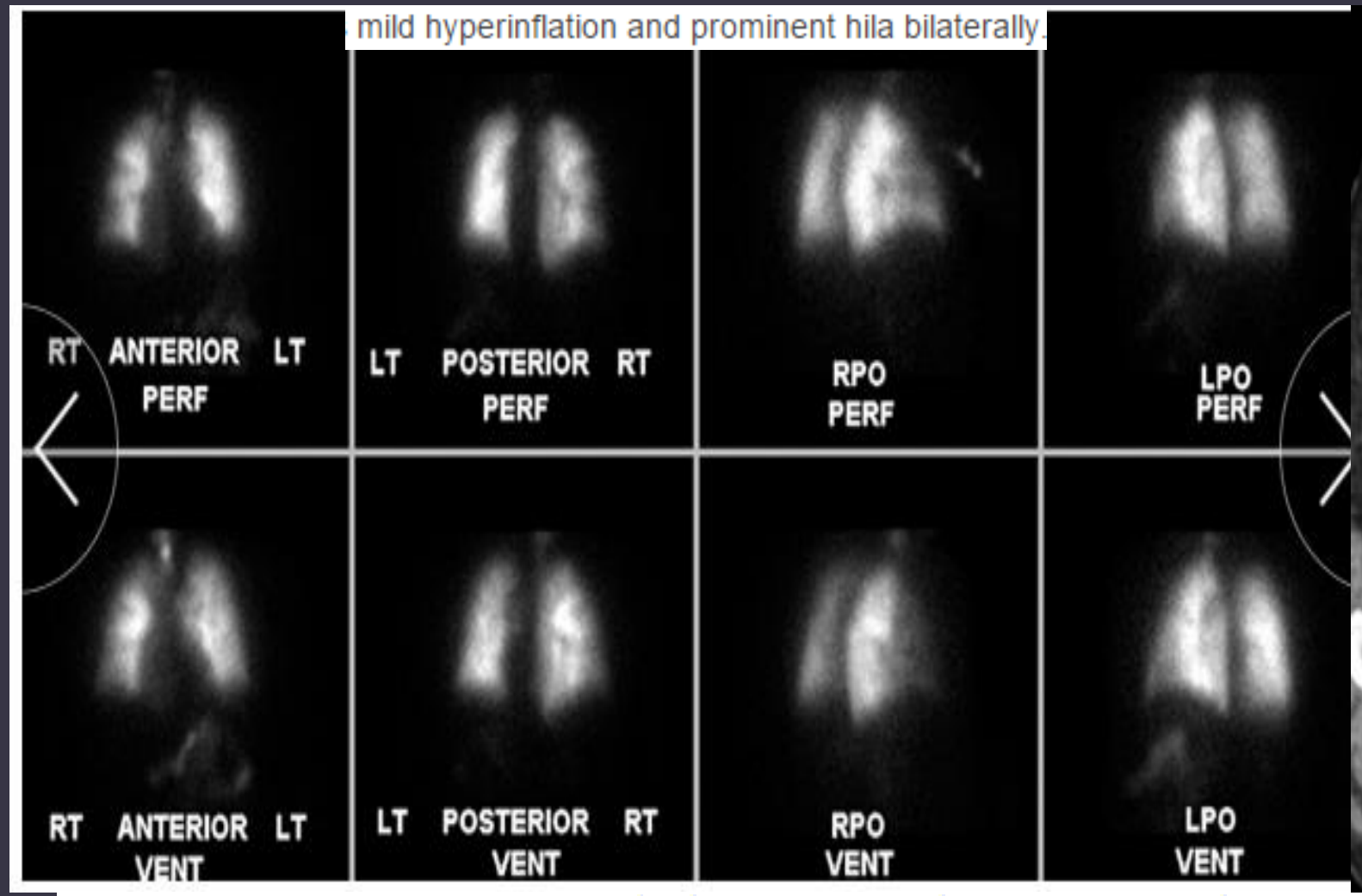
with multiple tracers such as xenon-133 gas, Tc-99m-labelled aerosols, or Tc-99m-labelled carbon microparticles (Technegas)

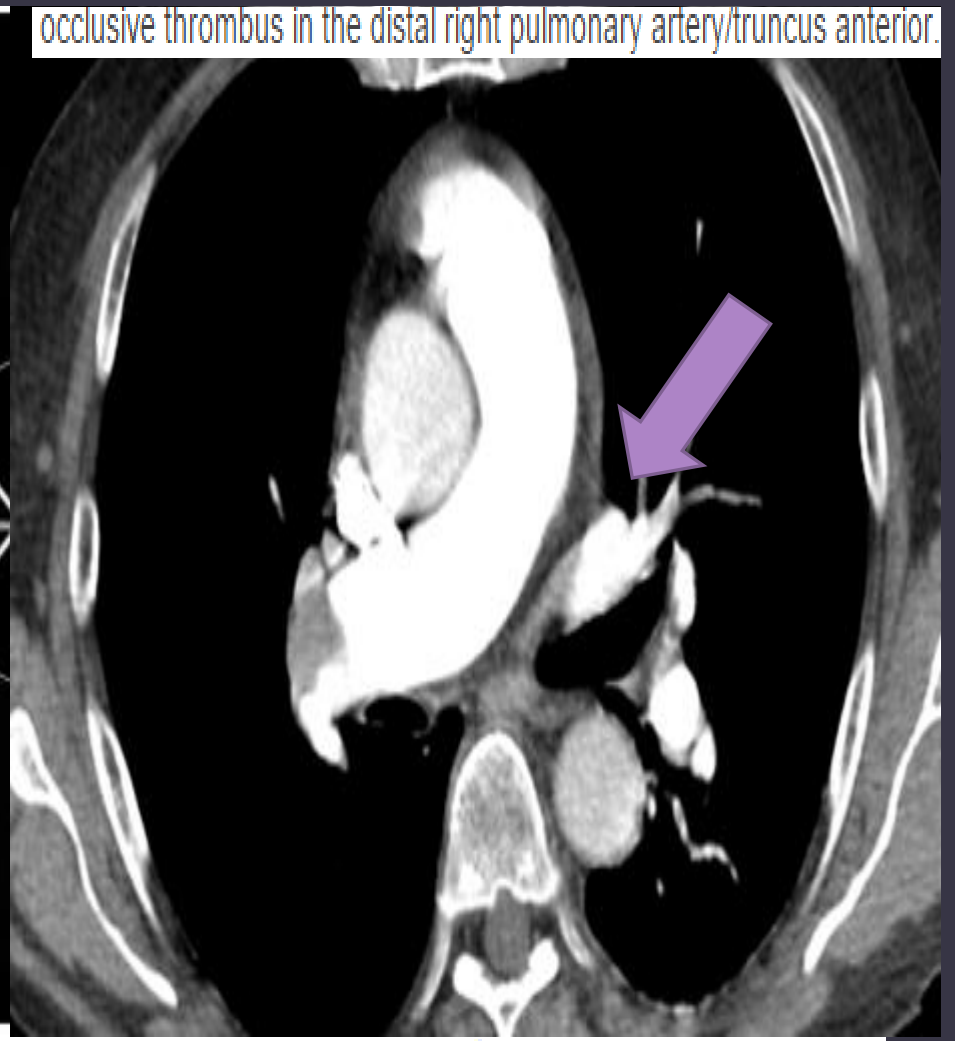
The high-probability criteria are as follows:

- Two large (>75% of a segment) segmental perfusion defects without corresponding ventilation or chest radiographic abnormalities
- One large segmental perfusion defect and 2 moderate (25-75% of a segment) segmental perfusion defects without corresponding ventilation or radiographic abnormalities
- Four moderate segmental perfusion defects without corresponding ventilation or chest radiographic abnormalities
- The intermediate-probability criteria are as follows:
- One moderate to fewer than 2 large segmental perfusion defects without corresponding ventilation or chest radiographic abnormalities
- Corresponding V/Q defects and radiographic parenchymal opacity in lower lung zone
- Single moderate matched V/Q defects with normal chest radiographic findings
- Corresponding V/Q and chest radiography small pleural effusion
- Difficult to categorize as normal, low, or high probability









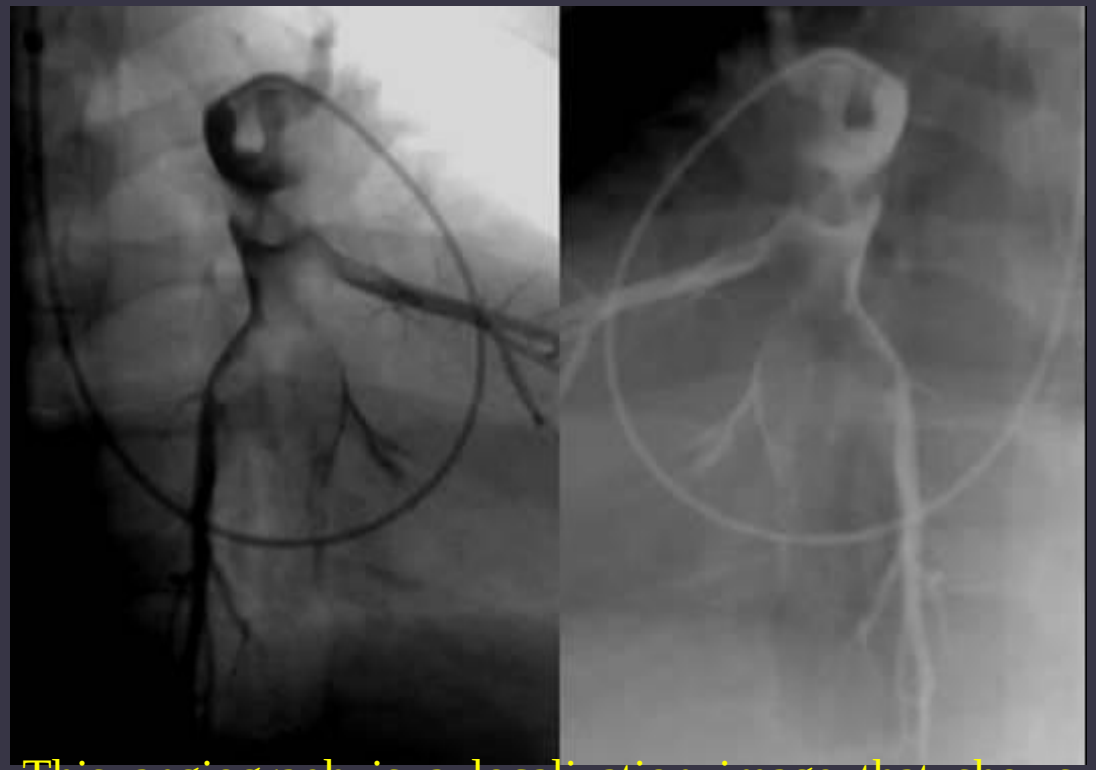
A 74-year-old man comes to the office with a complaint of mild dyspnea on exertion and a dry cough for the past few months. He has a 60-pack-year history of smoking and quit smoking 3 months ago after a transient episode of dyspnea. He has rare wheezing, no hemoptysis, and no orthopnea, and he denies experiencing leg swelling or pain. On examination at the office, the patient has no rales or wheezing and is normotensive. However, his oxygen saturation is 89%. D-dimer level is 802 ng/mL.

http://reference.medscape.com/features/slideshow/pulmonary-embolism?src=wnl_ref_clinfo&uac=200127DN&impID=886985&faf=1#page=21

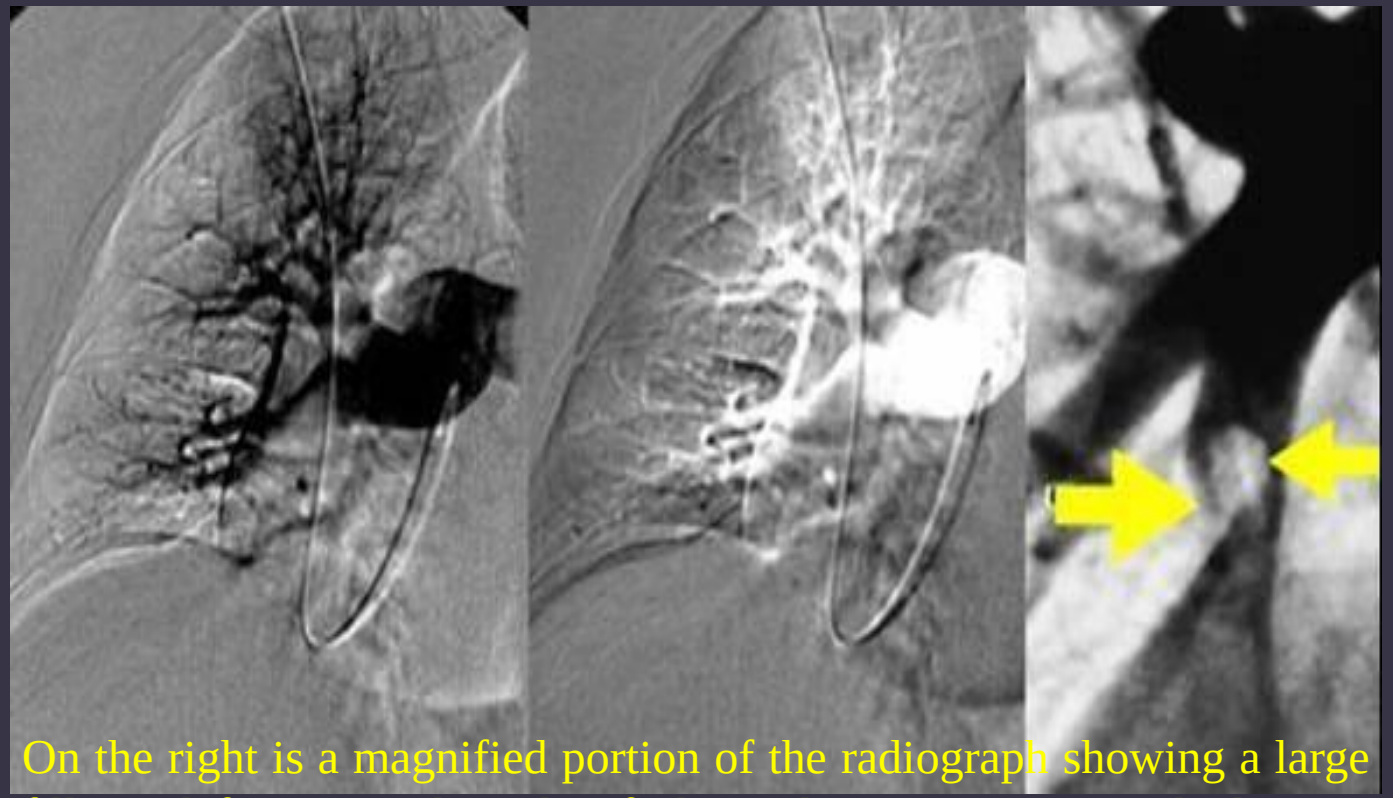
PULMONARY EMBOLISM: pulmonary angiography

http://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

- Interluminal defect or cutoff sign
- 'Court of Last Resort'
- Less radiation and less dye than CT



This angiograph is a localization image that shows placement of the pigtail catheter in the pulmonary artery for selective angiography. The radiograph on the left is the positive image and on the right the negative image.



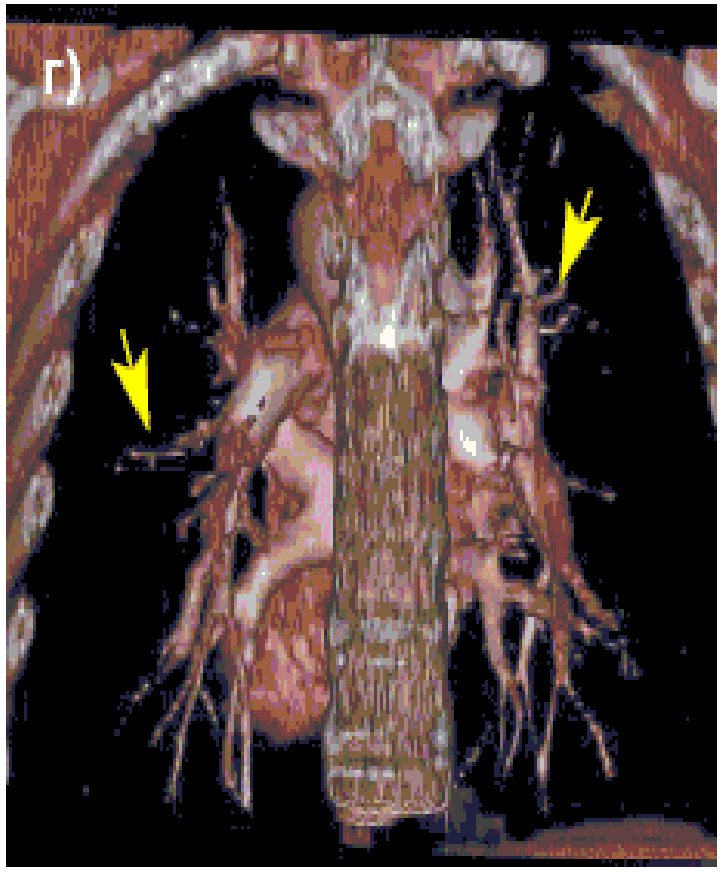
On the right is a magnified portion of the radiograph showing a large filling defect in a branch of the pulmonary artery, which is a pulmonary embolus (arrows). This patient presented with ah clinical history of chest pain, advanced peripheral vascular disease, diabetic, smoker, and hypertension.

http://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

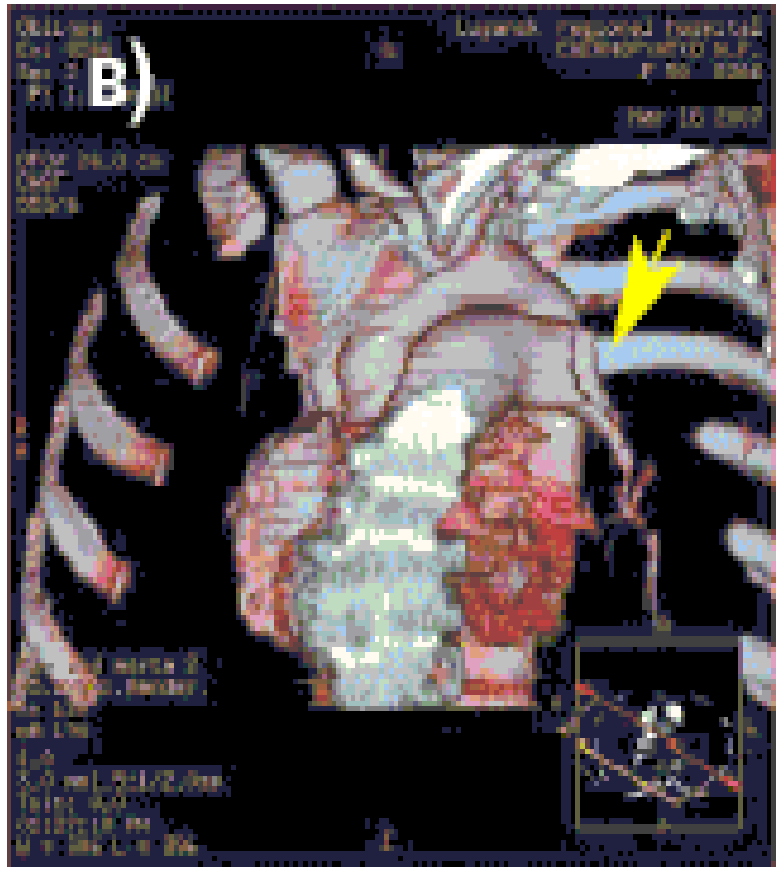
PULMONARY EMBOLISM: magnetic resonance angiography

Magnetic resonance angiography is performed following intravenous administration of gadolinium.

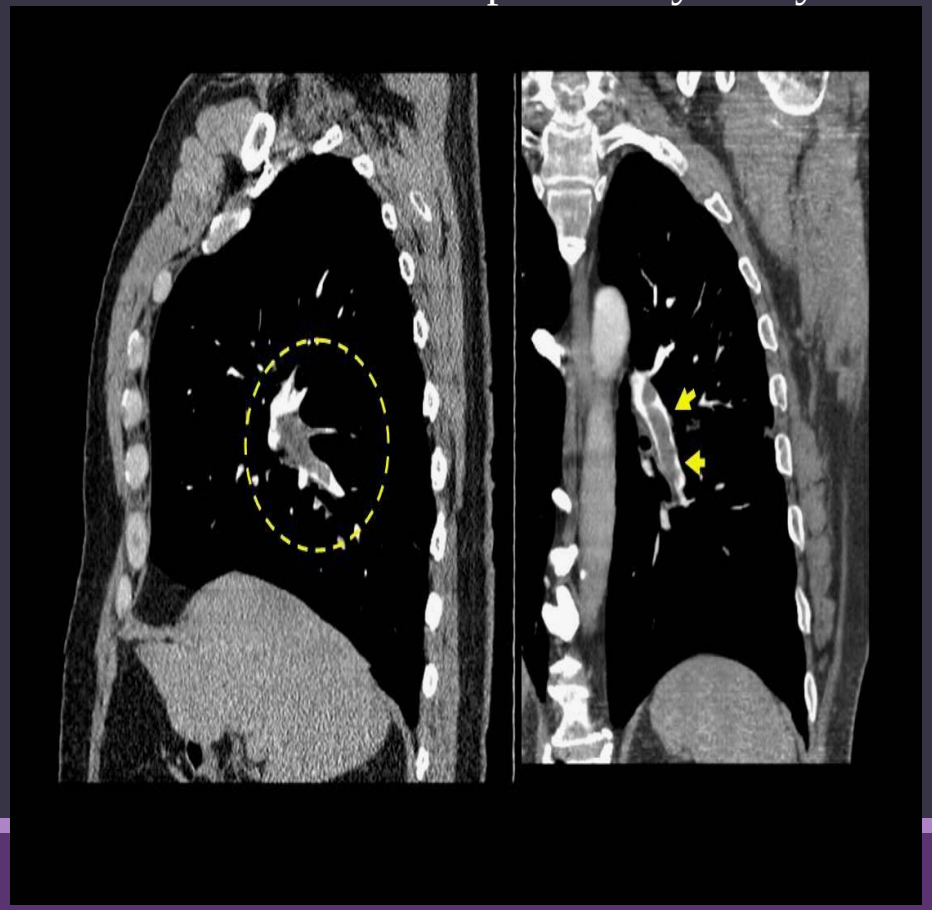
Emboli in the left and right main pulmonary arteries



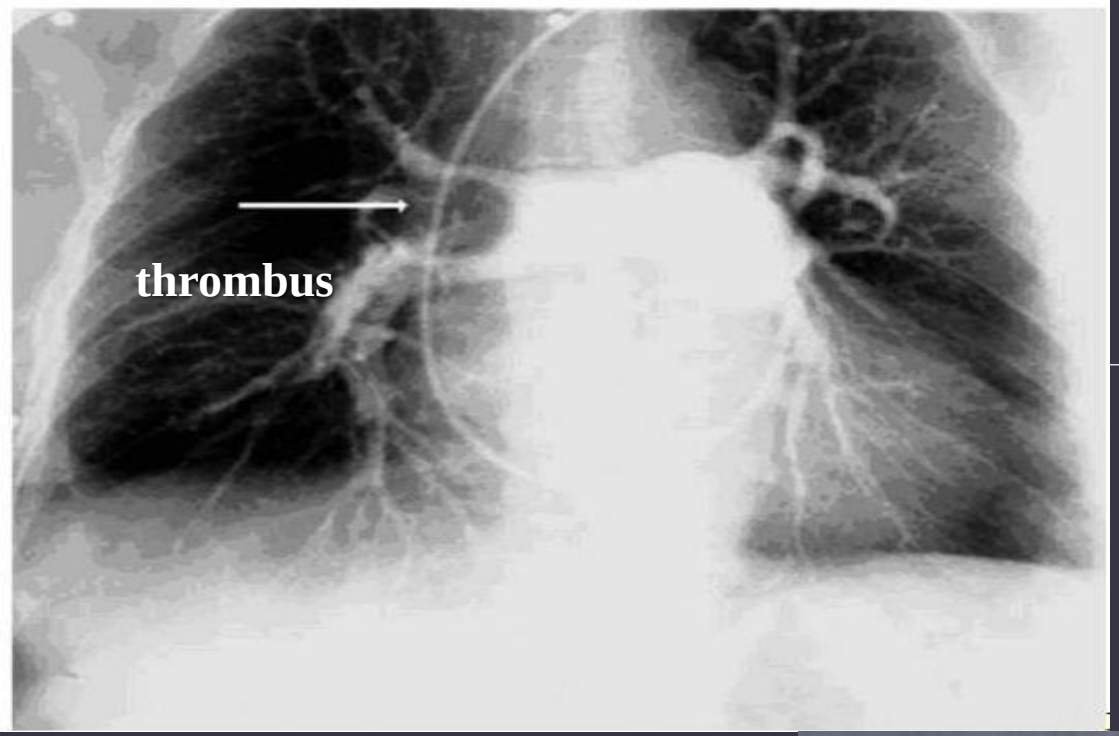
Embolus in the left main pulmonary artery

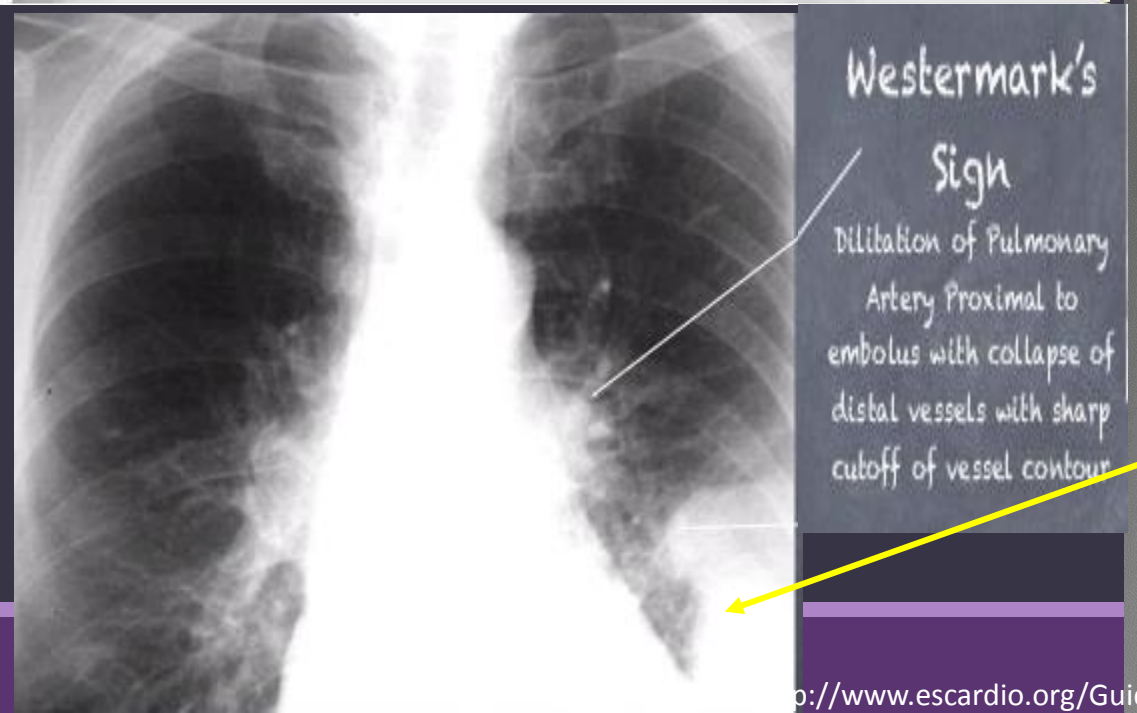


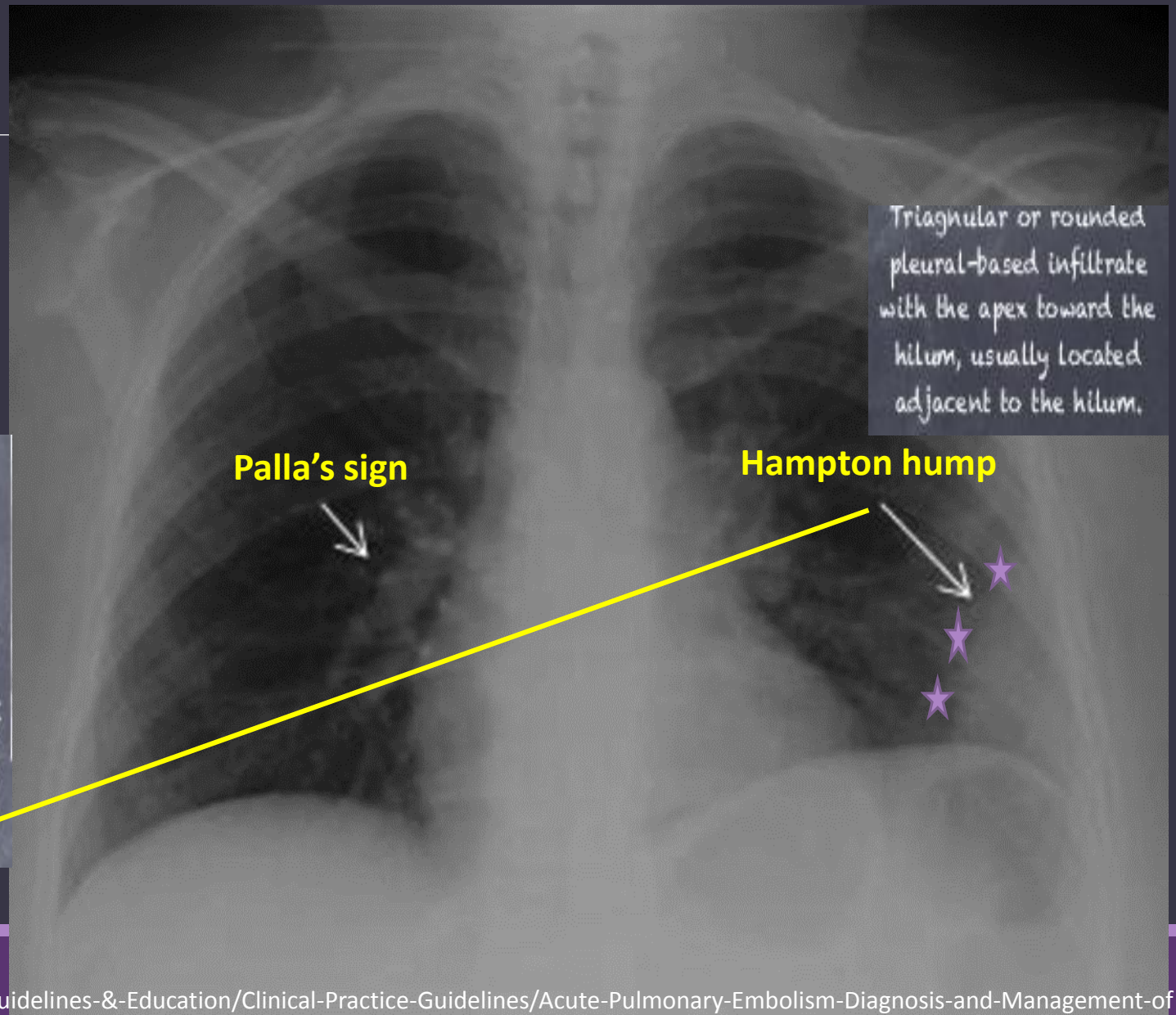
A large pulmonary embolus in the left main branch of the pulmonary artery



ray





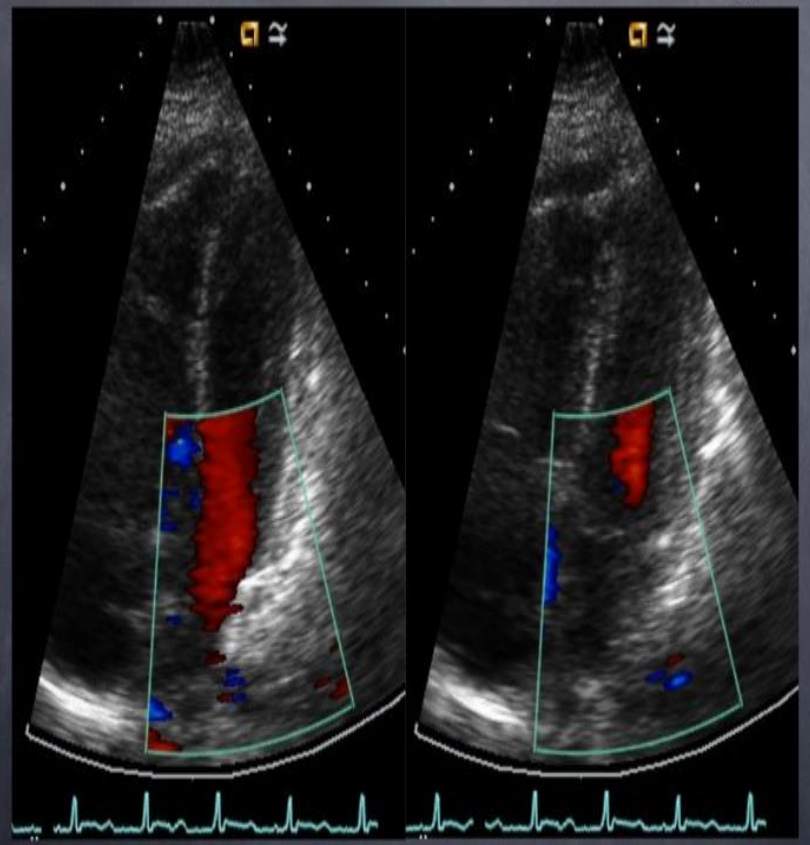


p://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

http://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

PULMONARY EMBOLISM: Echocardiography

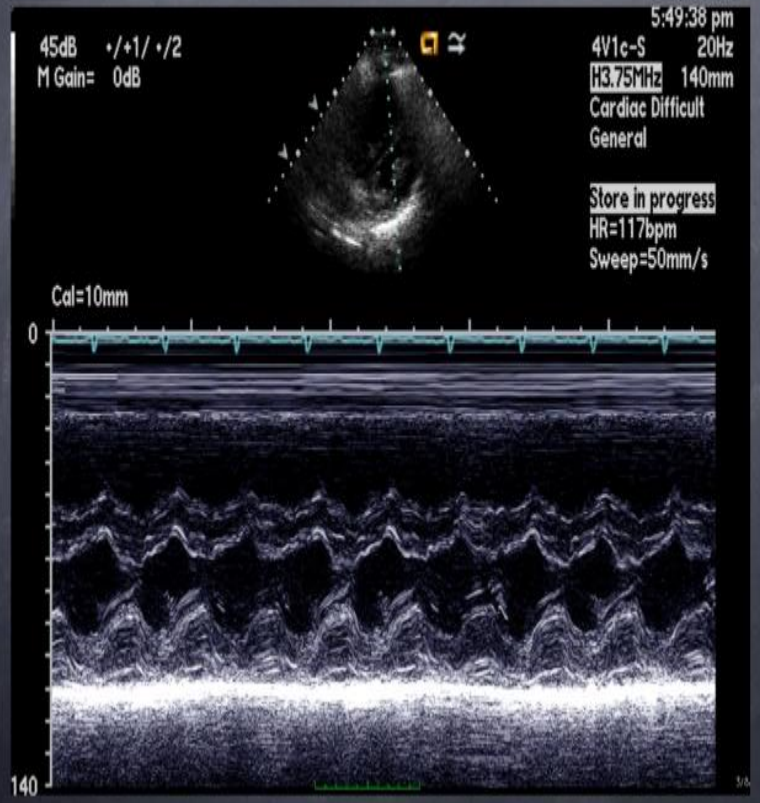
Echo - McConnell's Sign



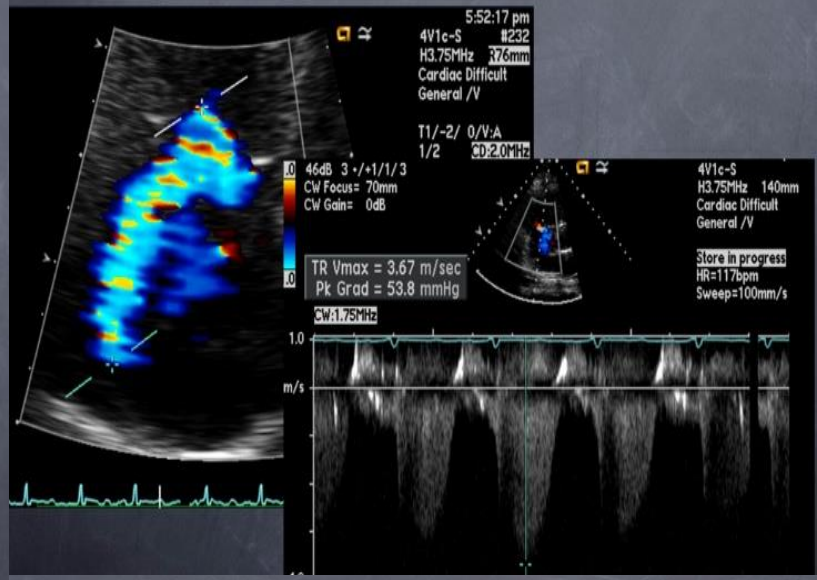
McConnell M.V., Solomon S.D., Rayan M.E., Come P.C., Goldhaber S.Z., Lee R.T.
Regional right ventricular dysfunction detected by echocardiography in acute pulmonary embolism.
Am J Cardiol 1996;78(4):469-473

on depressed contractility of the RV free wall compared with the RV apex

Echo - D-Shaped Septum Paradoxical Septal Motion



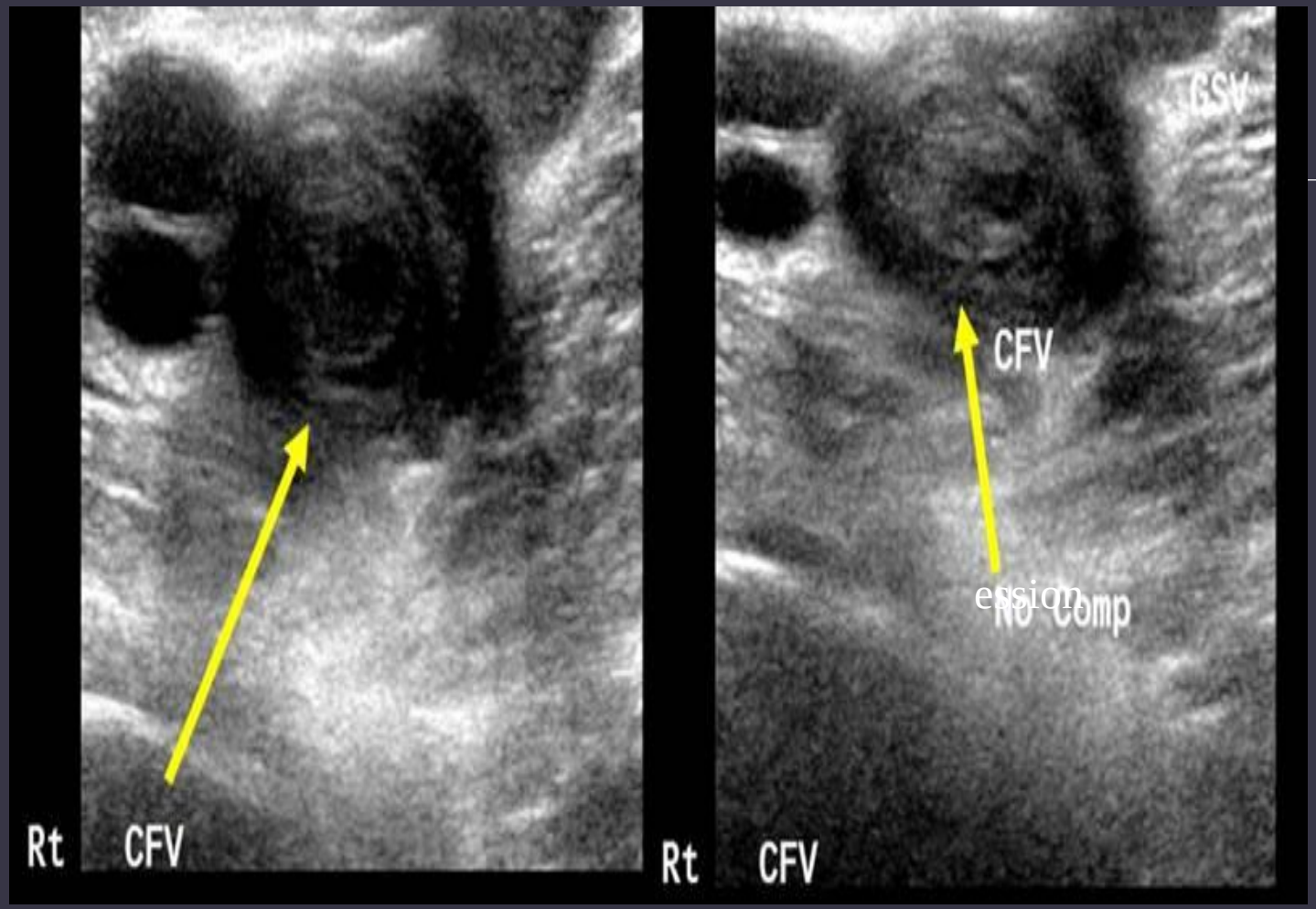
Echo - Severe TR - Severe RV Systolic

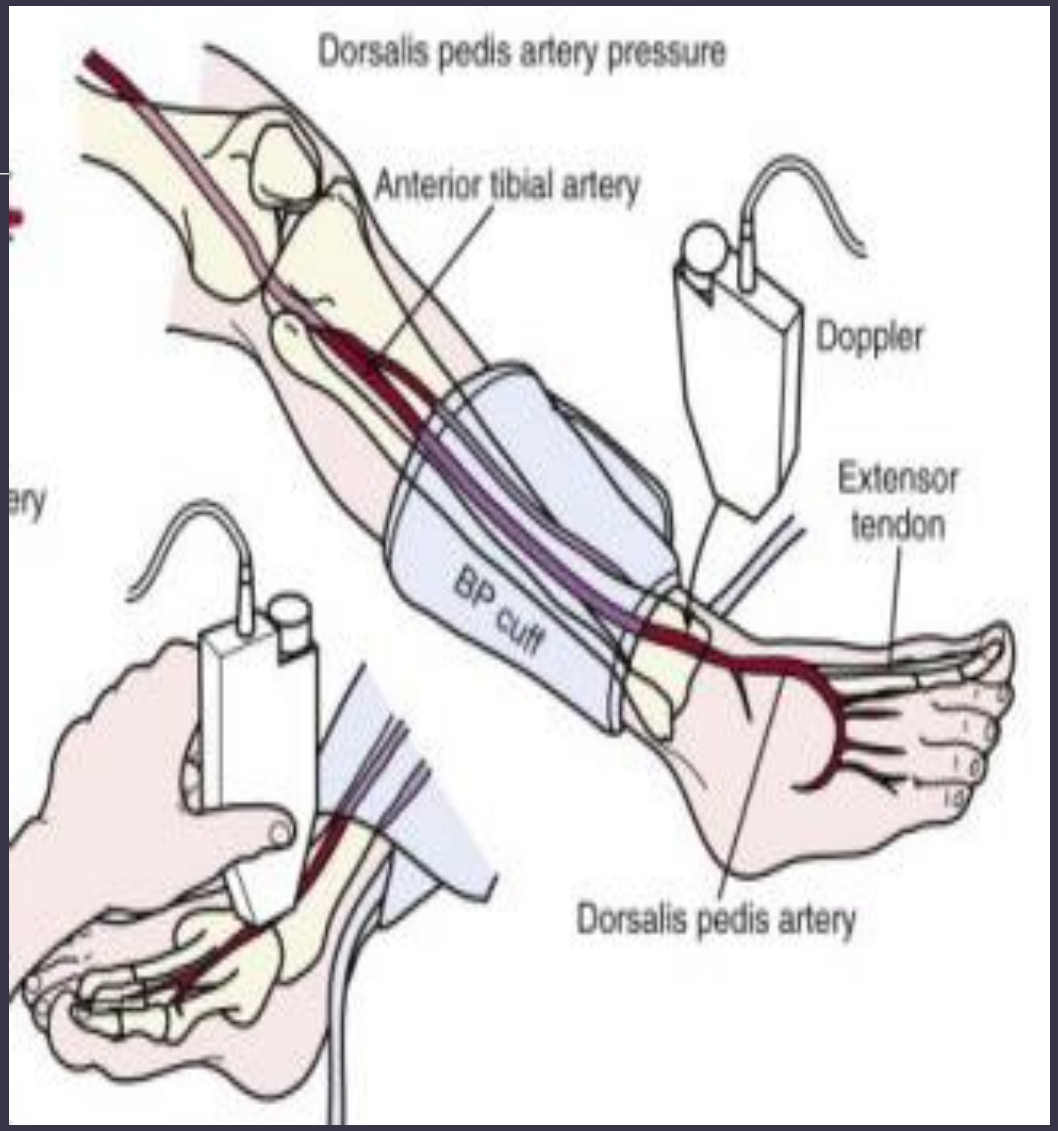


2/3 Echo Criteria = 56% Sensitivity & 90% Specificity

- RV Hypokinesis
- RVEDD > 27 mm (without RV Hypertropy)
- TR Velocity > 2.7 m/sec

PULMONARY EMBOLISM: compression Venous ultrasonography



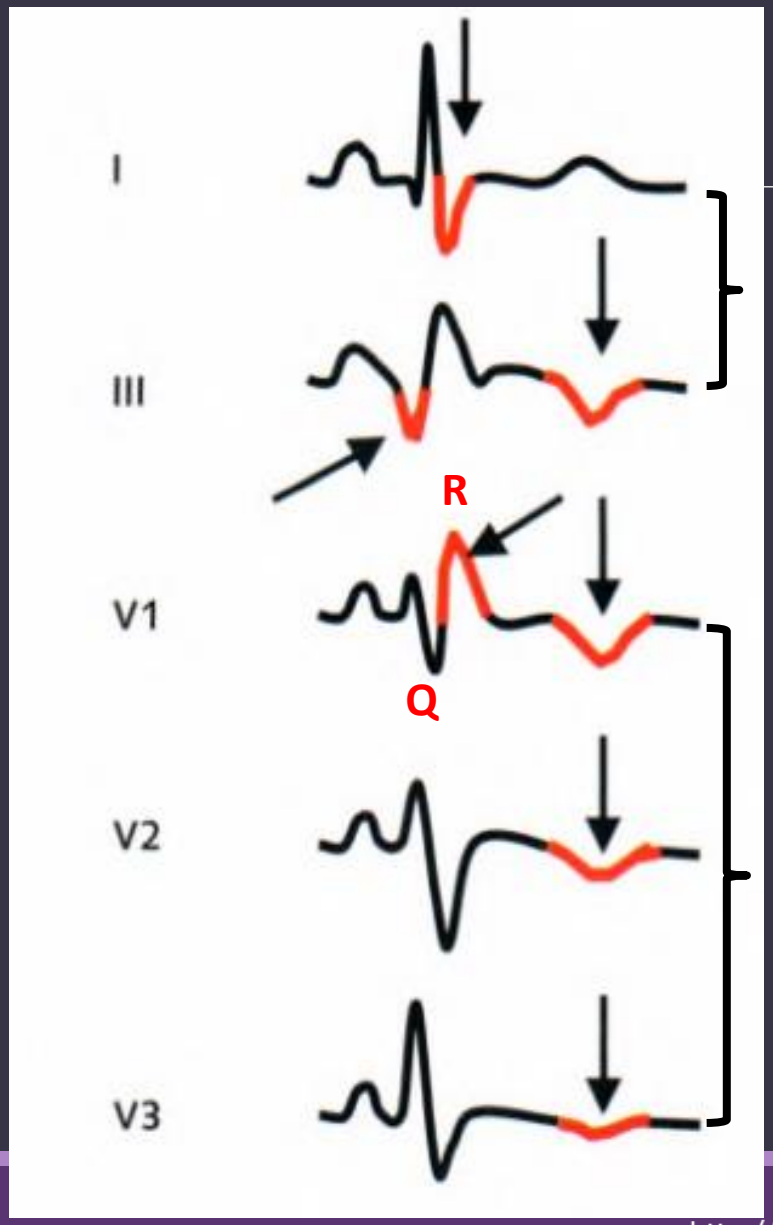


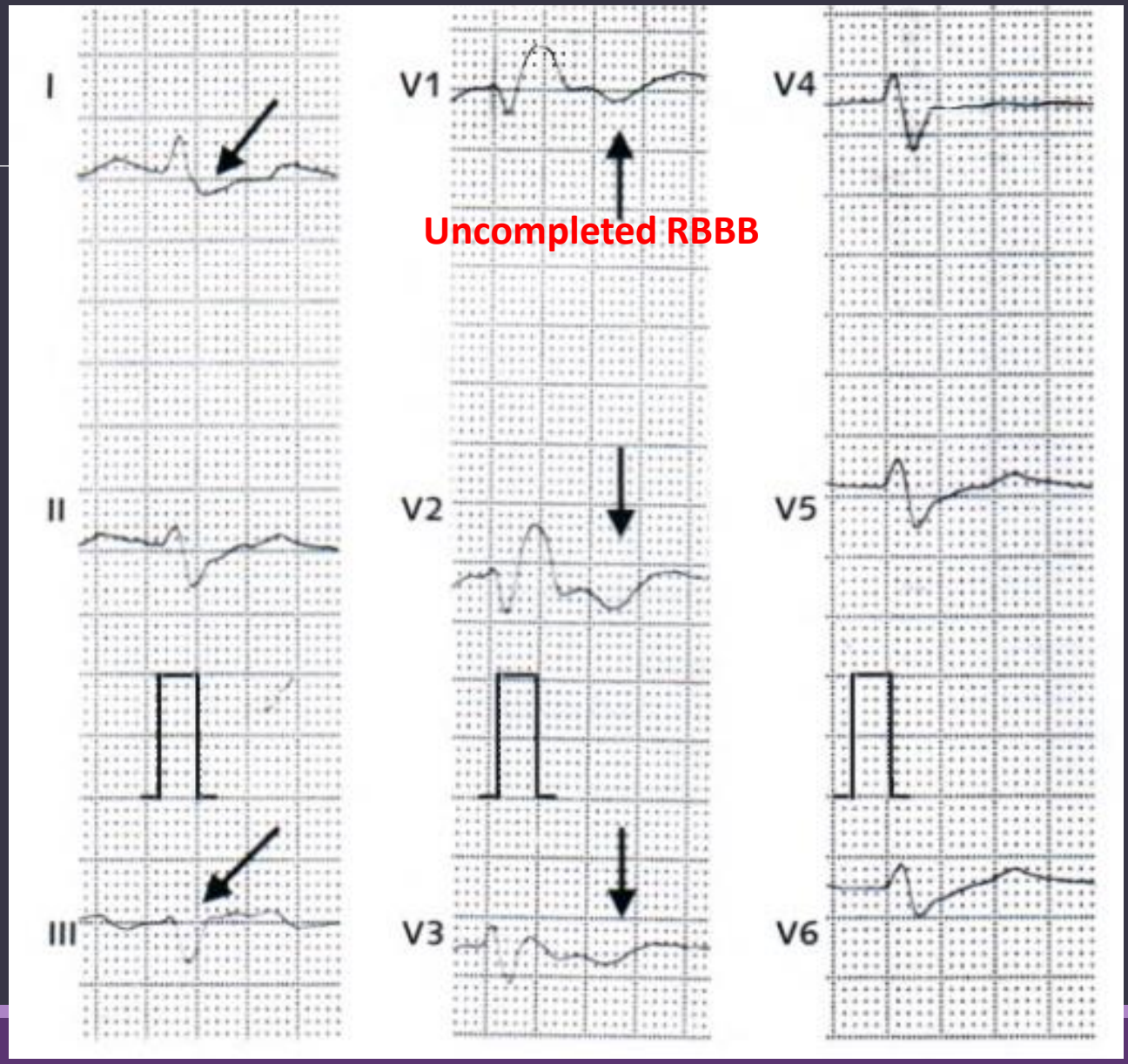
two crossection ultrasound images through the right common femoral vein (CFV) show a large nonocclusive thrombus in the vessel lumen (yellow arrow). The image on the left shows the common femoral vein prior to compression being applied with a large clot within it

http://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

PULMONARY EMBOLISM: ECG

50 MM/S





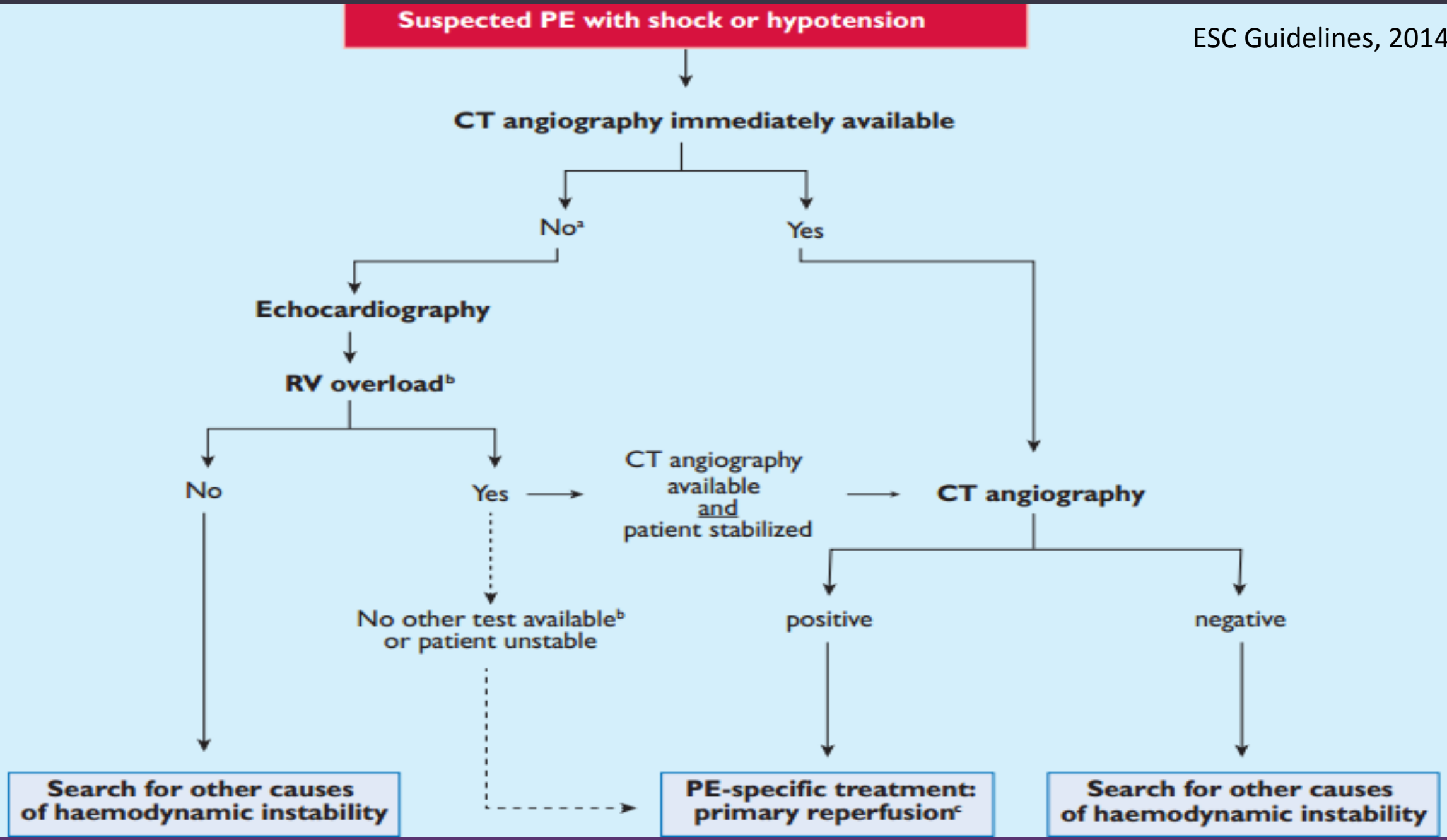
http://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

PULMONARY EMBOLISM: differential diagnoses

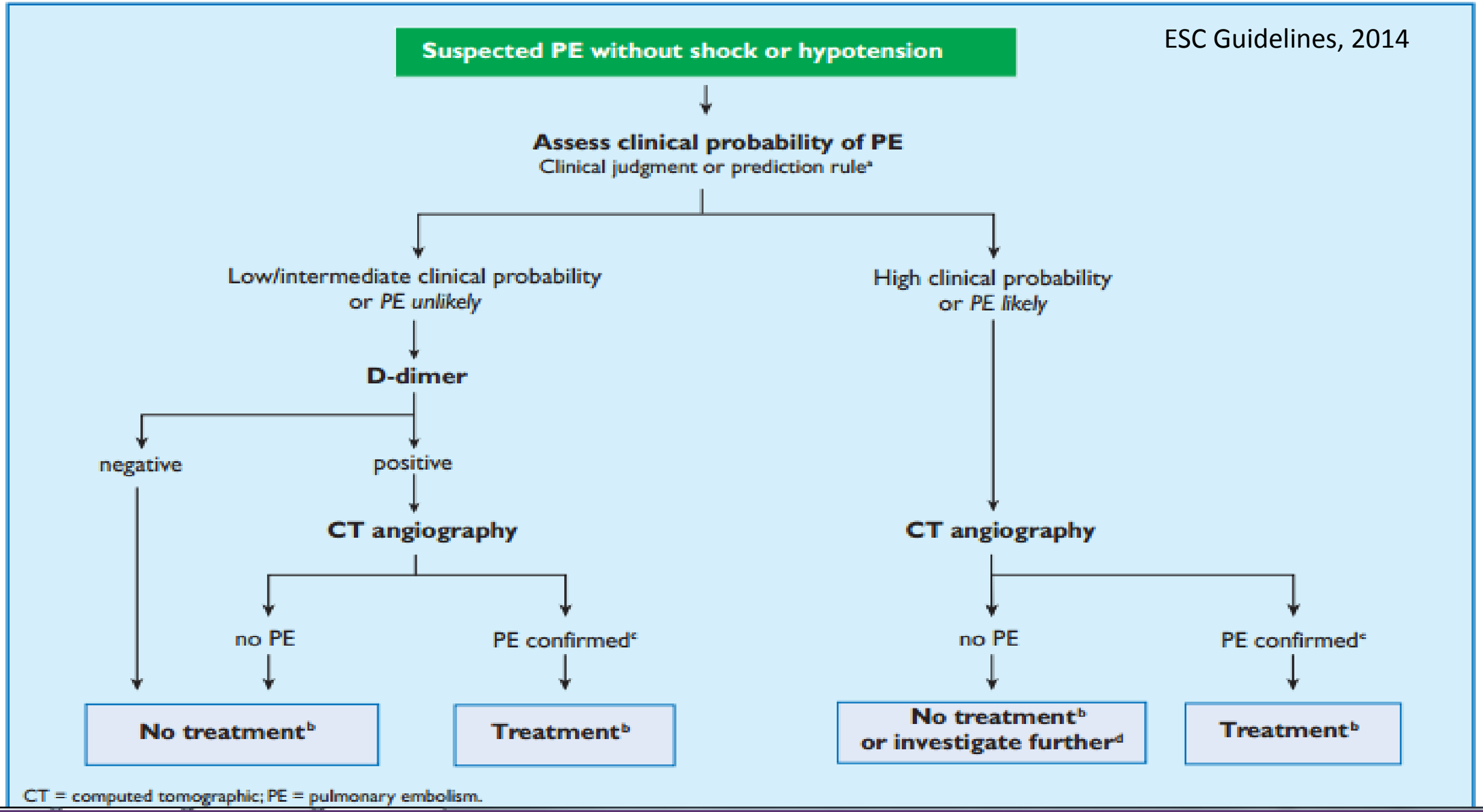
- Musculoskeletal pain
- Pleuritis
- Pericarditis
- Salicylate intoxication
- Hyperventilation
- Silicone pulmonary embolism
- Lung trauma
- Mediastinitis, acute
- Sickle cell disease

http://emedicine.medscape.com/article/300901-overview

ESC Guidelines, 2014

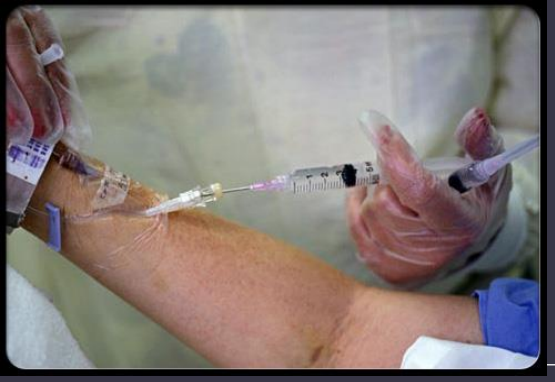


ESC Guidelines, 2014



CT = computed tomographic; PE = pulmonary embolism.

http://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of



PULMONARY EMBOLISM:

Treatment in the acute phase

- Haemodynamic and respiratory support
- Anticoagulation
- Thrombolytic treatment
- Surgical embolectomy
- Percutaneous catheter-directed treatment
- Venous filters
- Early discharge and home treatment

http://emedicine.medscape.com/article/300901-overview

Haemodynamic and respiratory support

Acute RV failure with resulting low systemic output is the leading cause of death in patients with high-risk PE.

- Use of vasopressors is often necessary, in parallel with (or while waiting for) pharmacological, surgical, or interventional reperfusion treatment. Norepinephrine appears to improve RV function via a direct positive inotropic effect, while also improving RV coronary perfusion by peripheral vascular alpha-receptor stimulation and the increase in systemic BP.
- Vasodilators decrease pulmonary arterial pressure and pulmonary vascular resistance, but the main concern is the lack of specificity of these drugs for the pulmonary vasculature after systemic (intravenous) administration.
- Hypoxaemia is usually reversed with administration of oxygen. When mechanical ventilation is required, care should be taken to limit its adverse haemodynamic effects. In particular, the positive intrathoracic pressure induced by mechanical ventilation may reduce venous return and worsen RV failure in patients with massive PE. Low tidal volumes (approximately 6 mL/kg lean body weight) should be used in an attempt to keep the end-inspiratory plateau pressure <30 cm H2O.

Anticoagulation

In patients with acute PE, anticoagulation is recommended, with the objective of preventing both early death and recurrent symptomatic or fatal VTE. The standard duration of anticoagulation should cover at least 3 months.

Diagnostic investigations should not delay empirical anticoagulant therapy. Thrombolytic therapy should be used in patients with acute pulmonary embolism who have hypotension (systolic blood pressure< 90 mm Hg) who do not have a high bleeding risk and in selected patients with acute pulmonary embolism not associated with hypotension who have a low bleeding risk and whose initial clinical presentation or clinical course suggests a high risk of developing hypotension. Long-term anticoagulation is critical to the prevention of recurrence of DVT or pulmonary embolism, because even in patients who are fully anticoagulated, DVT and pulmonary embolism can and often do recur.

Anticoagulation medications include the following:

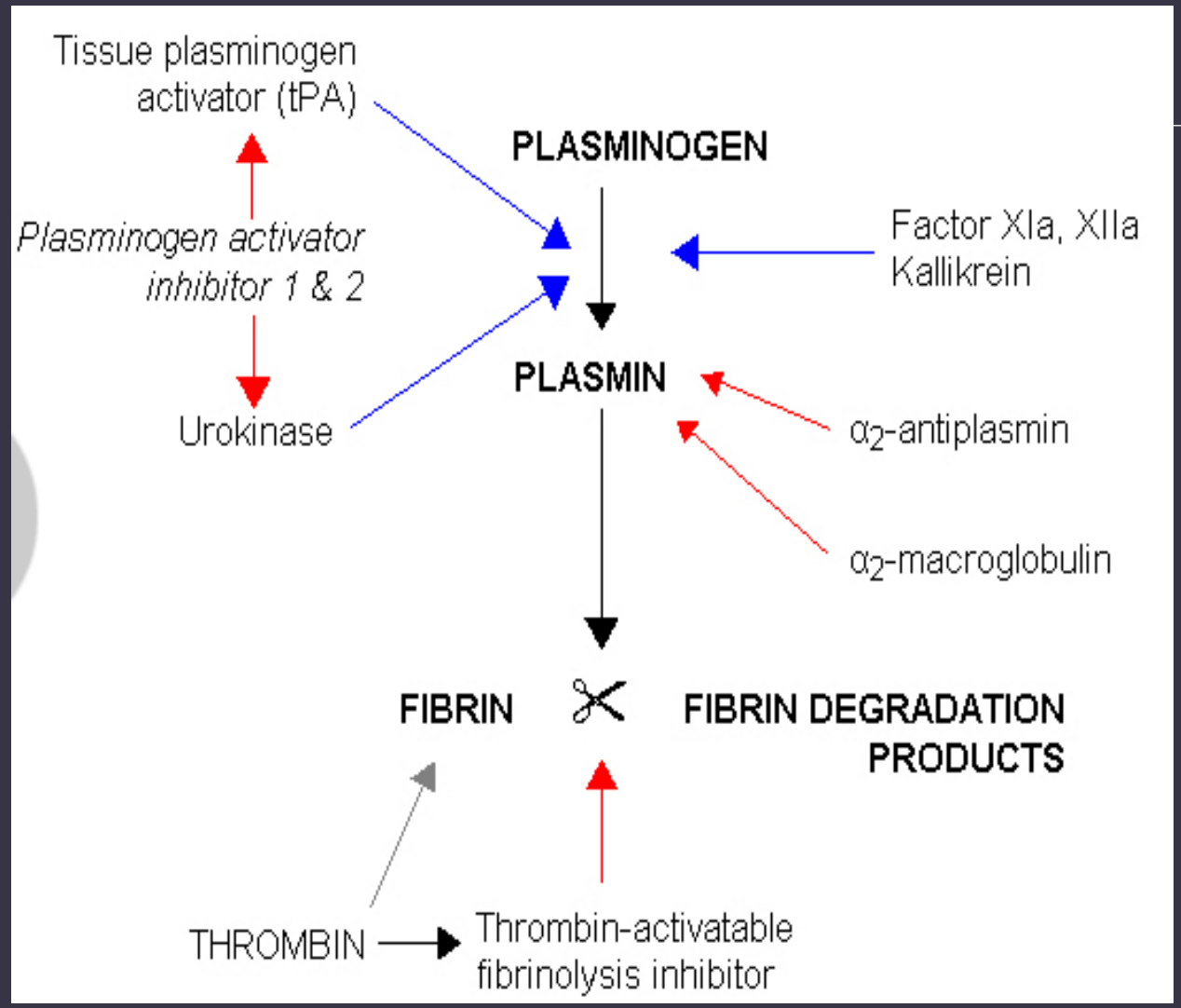
- Unfractionated heparin
- Low-molecular-weight heparin
- Factor Xa Inhibitors
- Fondaparinux
- Warfarin

Thrombolytic agents used in managing pulmonary embolism include the following:

- Alteplase
- Reteplase
- Urokinase
- Streptokinase

two approaches to thrombolysis.

The first is systemic thrombolysis followed by anticoagulation (shock). The second is catheter-directed thrombolysis.

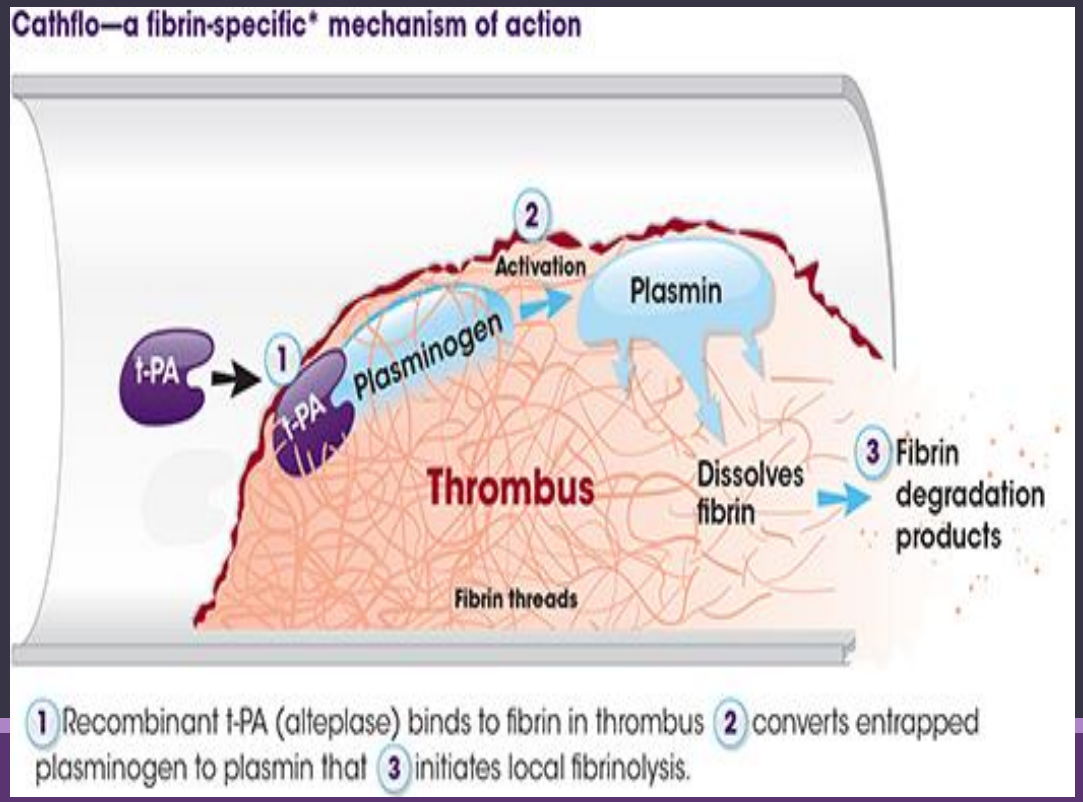


- Thrombolytic therapy should be used in patients with acute PE associated with hypotension (systolic BP < 90 mm HG), who do not have a high bleeding risk
- Thrombolytic therapy is suggested in select patients with acute PE not associated with hypotension and with a low bleeding risk whose initial clinical presentation or clinical course after starting anticoagulation suggests a high risk of developing hypotension
- Assessment of PE severity, prognosis, and risk of bleeding dictate whether thrombolytic therapy should be started. Thrombolytic therapy is not recommended for most patients with acute PE not associated with hypotension

http://reference.medscape.com/features/slideshow/pulmonary-embolism?src=wnl_ref_clinfo&uac=200127DN&impID=886985&faf=1#page=4

Thrombolytics

Thrombolysis is indicated for hemodynamically unstable patients with pulmonary embolism. Thrombolysis dramatically improves acute cor pulmonale. Thrombolytic therapy has replaced surgical embolectomy as the treatment for hemodynamically unstable patients with massive pulmonary embolism. Fibrinolytic regimens currently in common use for pulmonary embolism include 2 forms of recombinant tPA, alteplase and reteplase, along with urokinase and streptokinase.



Alteplase usually is given as a front-loaded infusion over 90 or 120 minutes.

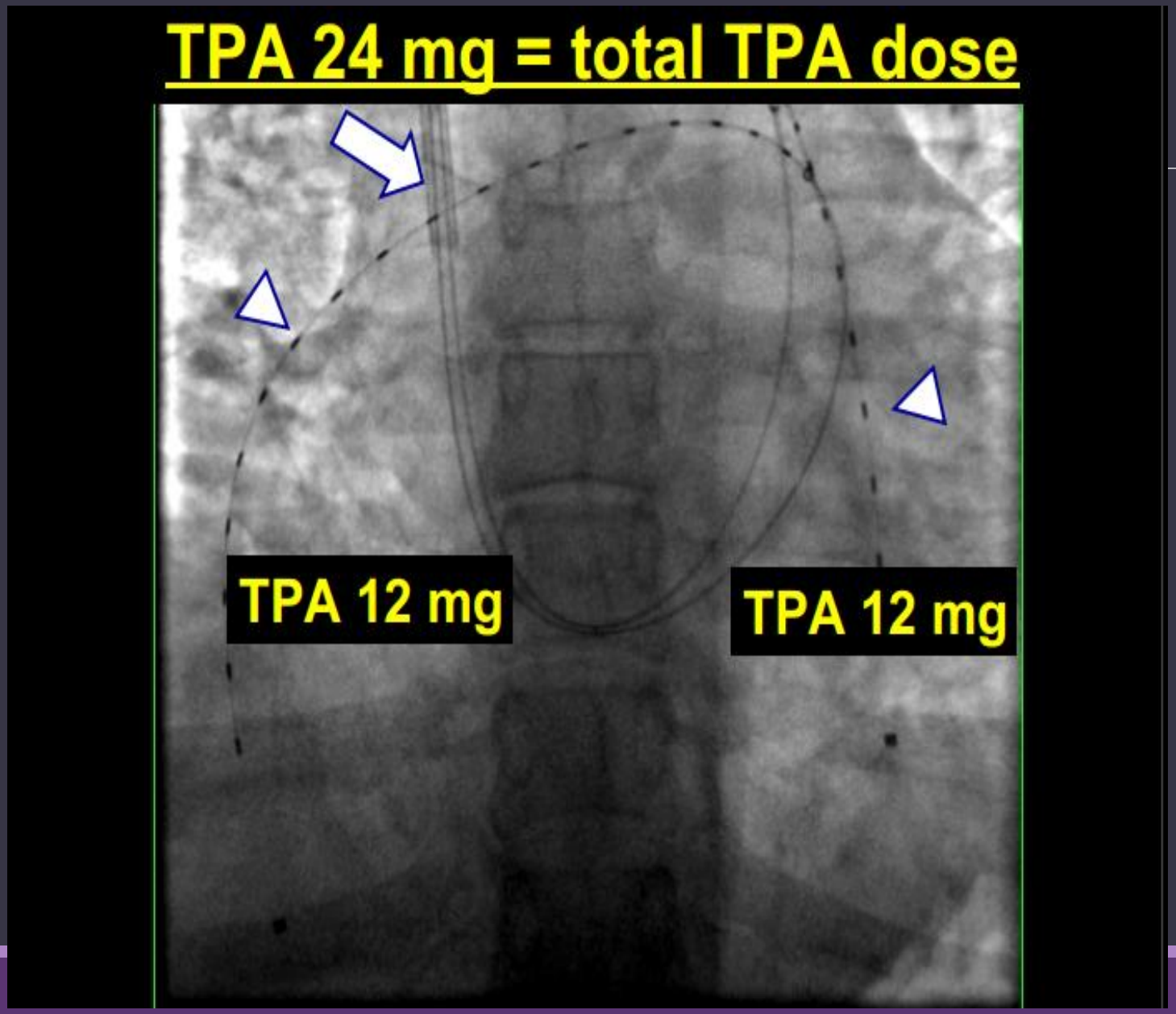
Urokinase and streptokinase usually are given as infusions over 24 hours or more.

Reteplase is a new-generation thrombolytic with a longer half-life; it is given as a single bolus or as 2 boluses administered 30 minutes apart.

Reteplase and alteplase are preferred for patients with pulmonary embolism

Streptokinase is least desirable of all the fibrinolytic agents because antigenic problems and other adverse reactions

Percutaneous catheter-directed treatment



For patients with absolute contraindications to thrombolysis, interventional options include:

(i) thrombus fragmentation with pigtail or balloon catheter,

(ii) rheolytic thrombectomy with hydrodynamic catheter devices,

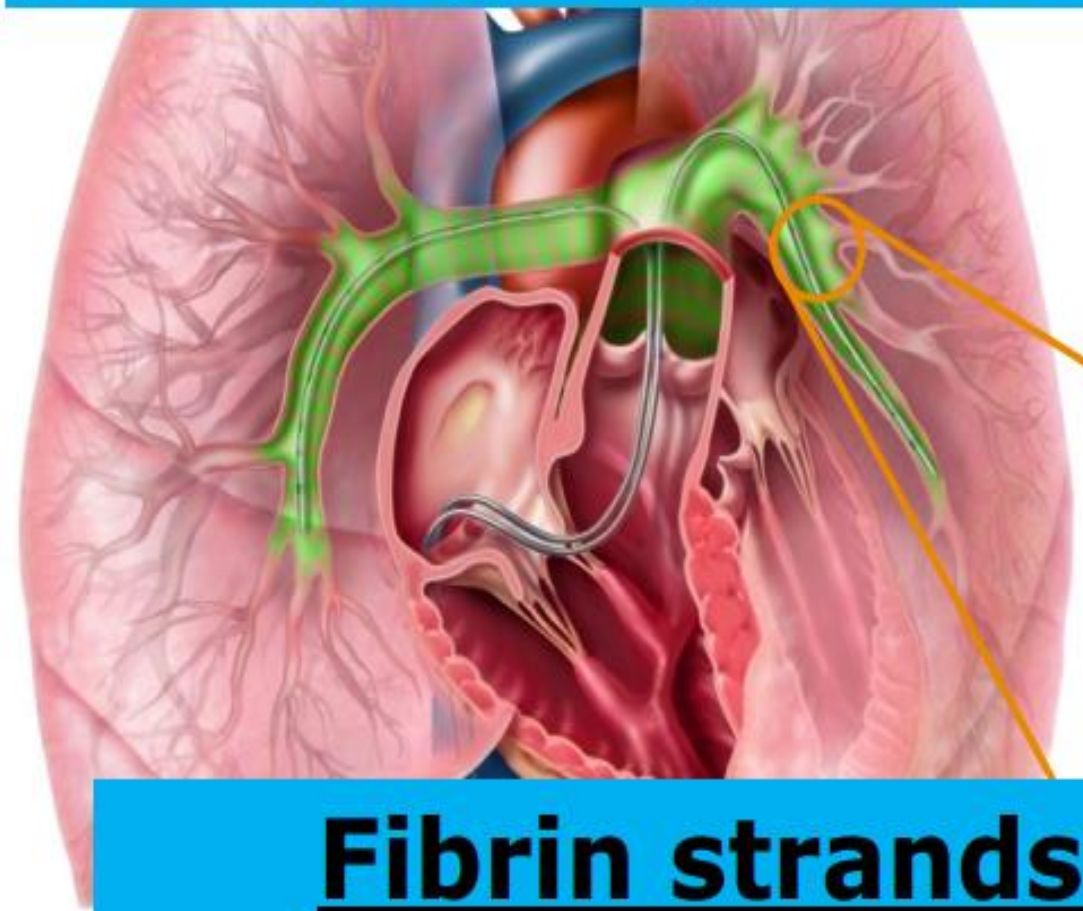
(iii) suction thrombectomy with aspiration catheters and

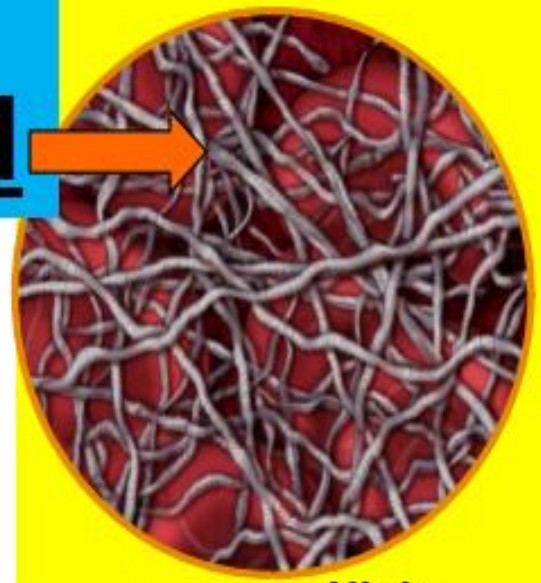
(iv) rotational thrombectomy.

On the other hand, for patients without absolute contraindications to thrombolysis, catheter-directed thrombolysis or pharmacomechanical thrombolysis are preferred approaches.

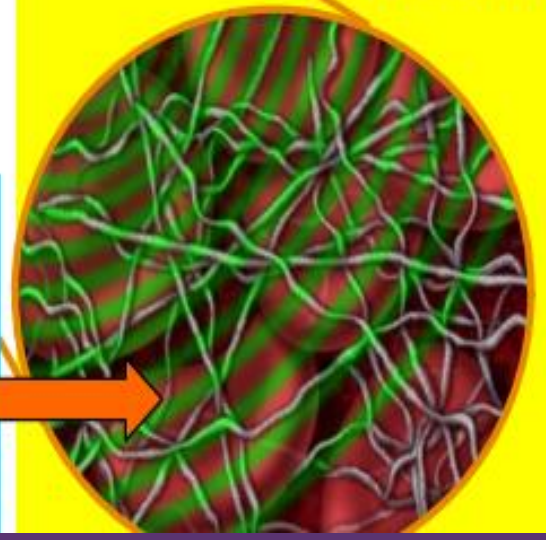
Catheter-directed, Ultrasound-facilitated thrombolysis

Fibrin strands:
Thick, Tightly Packed

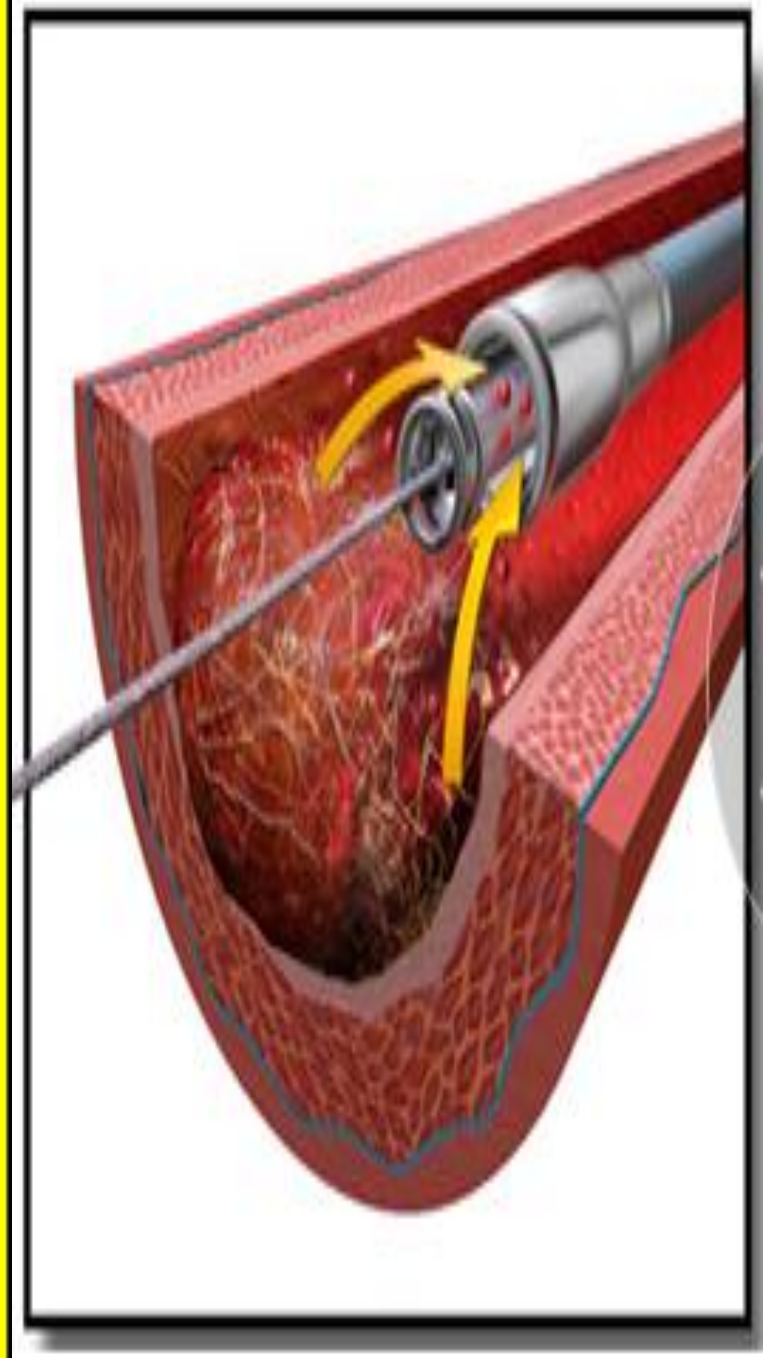




High frequency, low power ultrasound



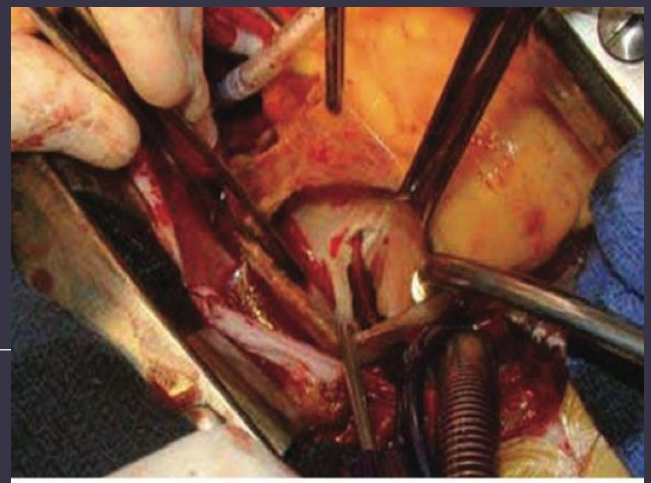
Fibrin strands:
Thin, Spread Out;
"Thrombus Conditioning"

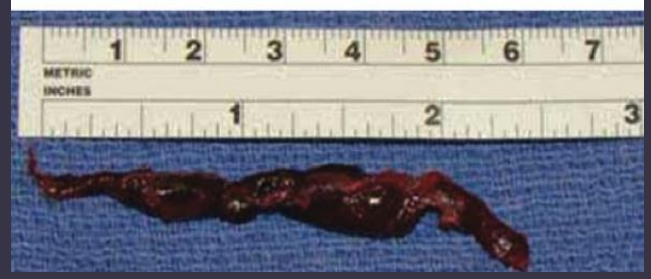


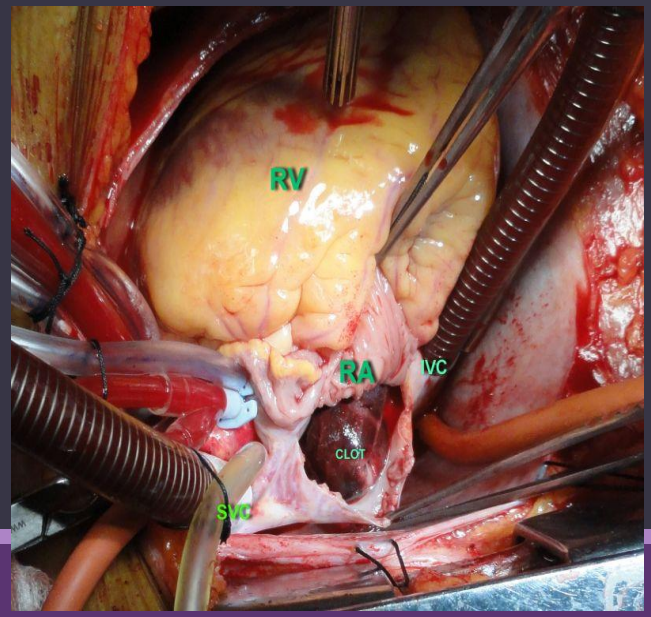
Surgical embolectomy

The first successful surgical pulmonary embolectomy was performed in 1924, several decades before the introduction of medical treatment for PE.

Following rapid transfer to the operating room and induction of anaesthesia and median sternotomy, normothermic cardiopulmonary bypass should be instituted.
Aortic cross-clamping and cardioplegic cardiac arrest should be avoided. With bilateral PA incisions, clots can be removed from both pulmonary arteries down to the segmental level under direct vision.
Prolonged periods of post-operative cardiopulmonary bypass and weaning may be necessary for recovery of RV function.







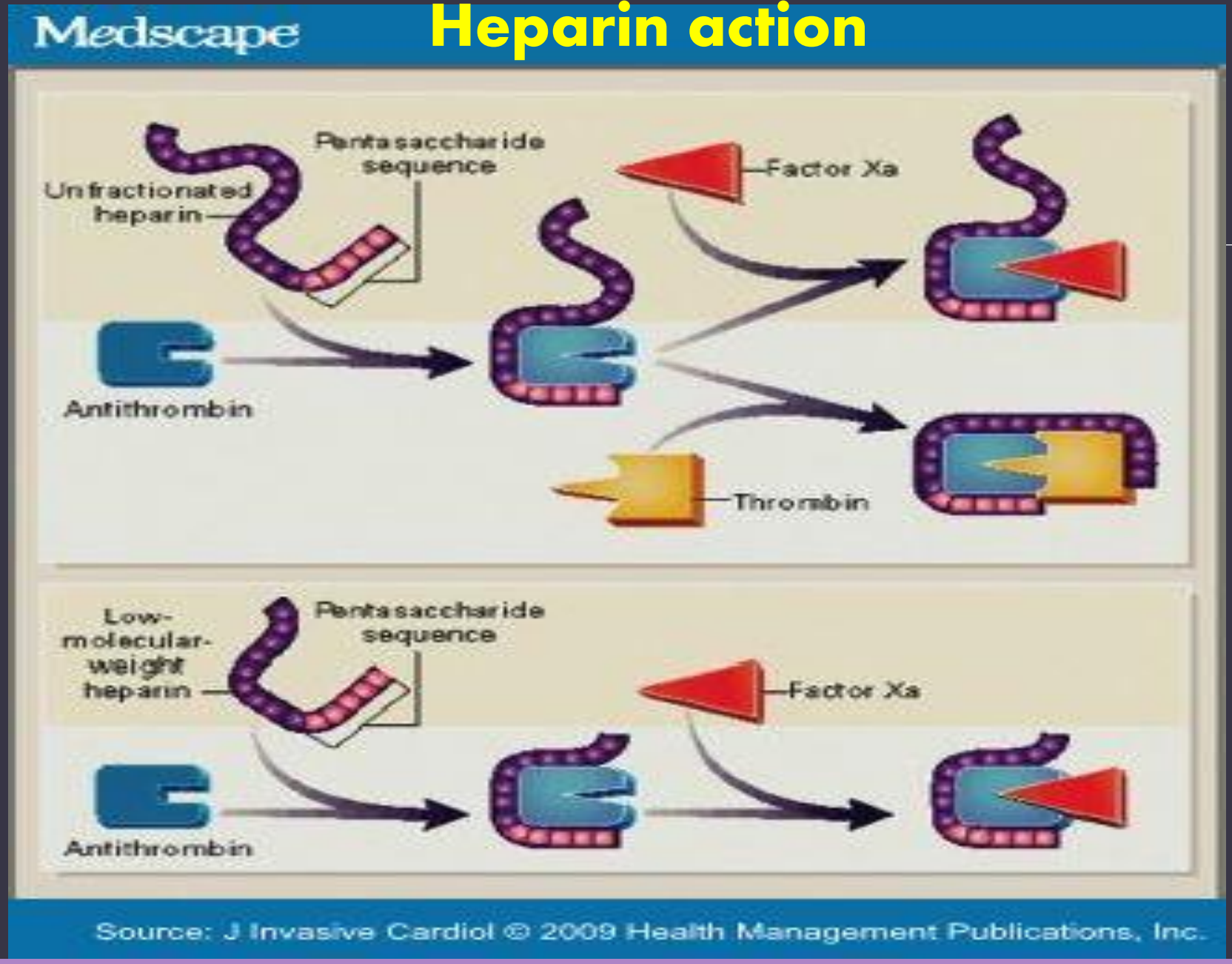
Parenteral anticoagulation

In patients with high or intermediate clinical probability for PE, parenteral anticoagulation should be initiated whilst awaiting the results of diagnostic tests. Immediate anticoagulation can be achieved with parenteral anticoagulants such as intravenous UFH, subcutaneous low-molecular-weight heparin (LMWH),or subcutaneous fondaparinux. UFH is recommended for patients in whom primary reperfusion is considered, as well as for those with serious renal impairment (creatinine clearance < 30 mL/min), or severe obesity. LMWH or fondaparinux are preferred over UFH for initial anticoagulation in PE.

Low-molecular-weight heparins and pentasaccharide (fondaparinux) approved for the treatment of pulmonary embolism

	Dosage	Interval
Enoxaparin	1.0 mg/kg or 1.5 mg/kg[a]	Every 12 hours Once daily[a]
Tinzaparin	175 U/kg	Once daily
Dalteparin	100 IU/kg[b] or 200 IU/kg[b]	Every 12 hours[b] Once daily[b]
Nadroparin[c]	86 IU/kg or 171 IU/kg	Every 12 hours 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

Heparin action



Heparin major anticoagulant effect by inactivating thrombin and activated factor X (factor Xa) through an antithrombin (AT)-dependent mechanism. Heparin binds to AT through a high-affinity pentasaccharide, which is present on about a third of heparin molecules. For inhibition of thrombin, heparin must bind to both the coagulation enzyme and AT, whereas binding to the enzyme is not required for inhibition of factor Xa.

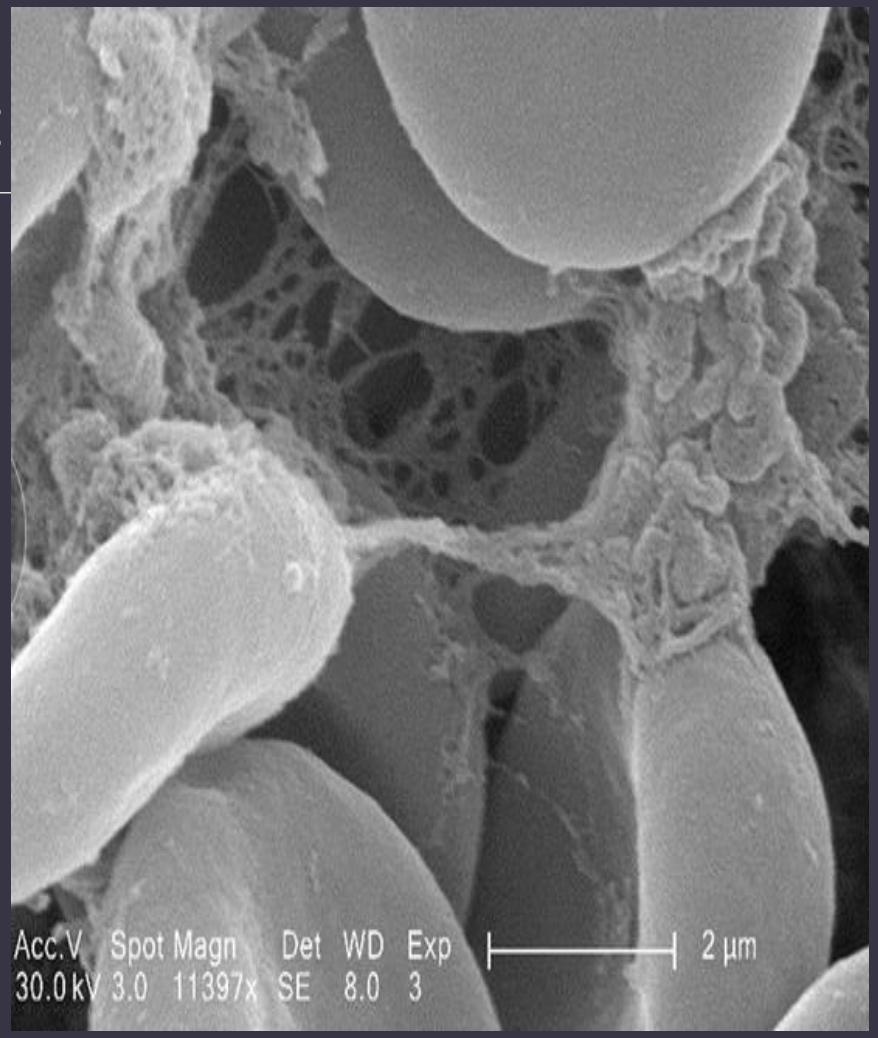
Unfractionated heparin infusion should be stopped during administration of streptokinase or urokinase

http://www.medscape.com/viewarticle/715597_2?sa=X&ved=0CB0Q9QEwBGoVChMI5u_X-s3zxgIVBV0sCh2HGQZD

Available oral anticoagulants include:

- vitamin K antagonists (warfarin),
- direct thrombin inhibitors (dabigatran),
- direct factor Xa inhibitors (rivaroxaban)

Oral anticoagulants should be initiated as soon as possible, and preferably on the same day as the parenteral anticoagulant. VKAs have been the ‘gold standard’ in oral anticoagulation for more than 50 years.

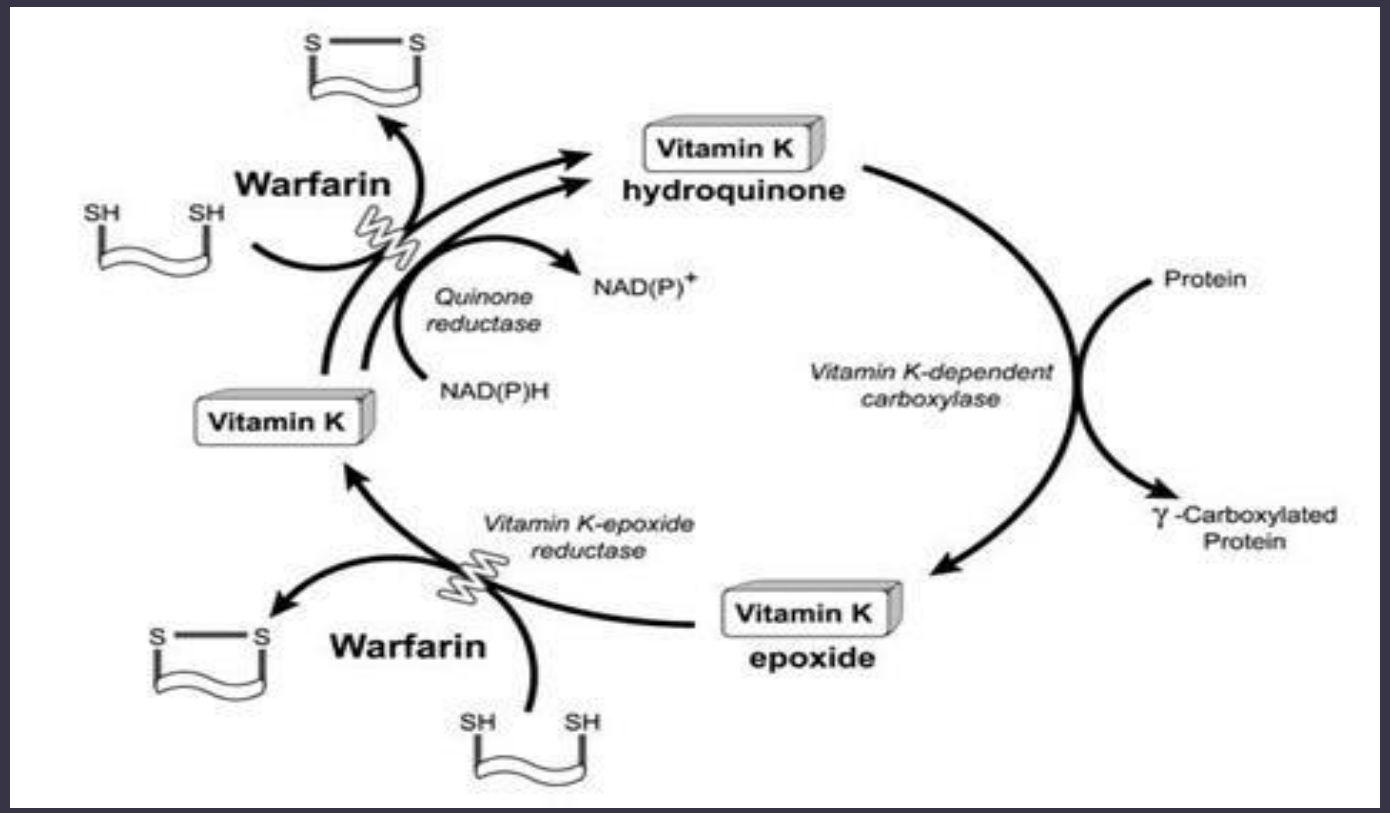


(The image shows red blood cells enmeshed in a fibrinous matrix in the process of clot formation.)

http://reference.medscape.com/features/slideshow/pulmonary-embolism?src=wnl_ref_clinfo&uac=200127DN&implD=886985&faf=1#page=4

vitamin K antagonists (warfarin)

The anticoagulant effect of warfarin is mediated by the inhibition of vitamin K–dependent factors, which are II, VII, IX, and X. The peak effect does not occur until 36-72 hours after drug administration, and the dosage is difficult to titrate. A prothrombin time ratio is expressed as an INR and is monitored to assess the adequacy of warfarin therapy. The recommended therapeutic range for venous thromboembolism is an INR of 2-3. This level of anticoagulation markedly reduces the risk of bleeding without the loss of effectiveness.

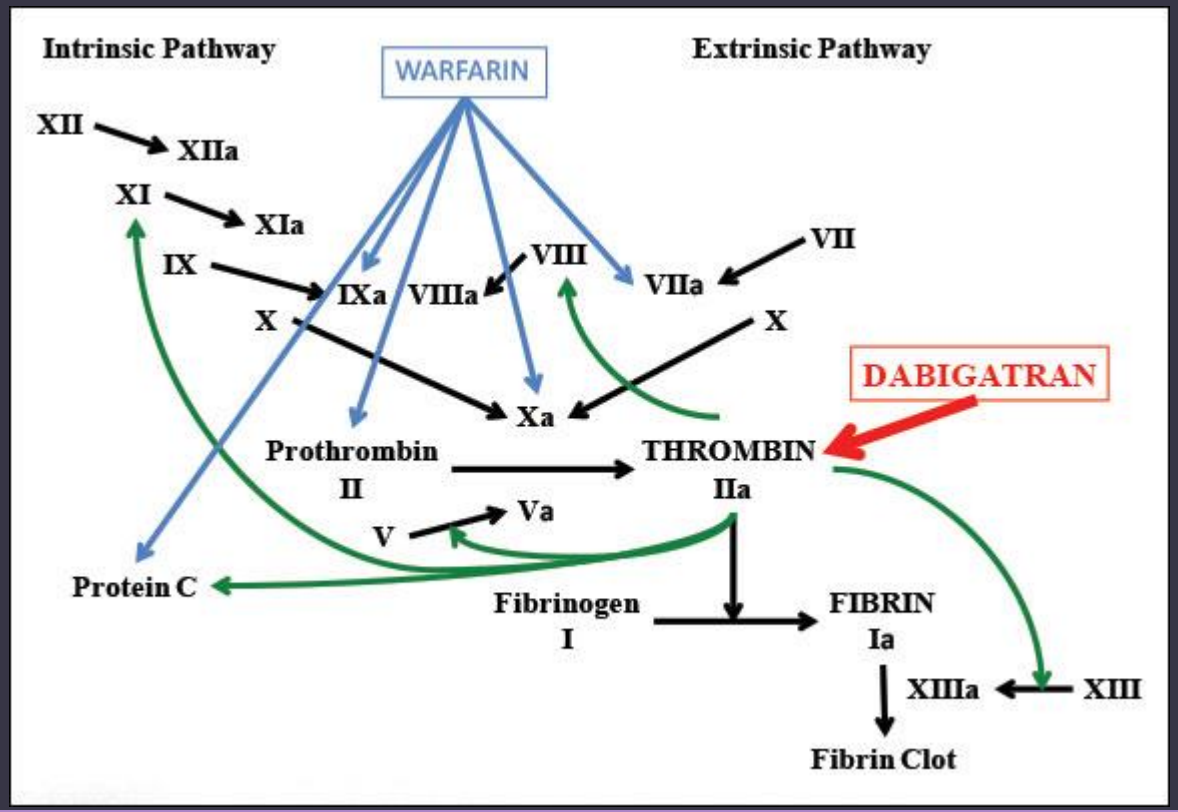


Warfarin can be started at a dose of 10 mg in younger (e.g. ,60 years of age), otherwise healthy outpatients, and at a dose of 5 mg in older patients and in those who are hospitalized. The daily dose is adjusted according to the INR over the next 5–7 days, aiming for an INR level of 2.0–3.0.

https://sciphu.files.wordpress.com/2008/11/vitamin-k-cycle.jpg

Direct thrombin inhibitors (dabigatran)

Dabigatran etexilate is a competitive reversible non-peptide antagonist of thrombin. Thrombin is a multifunctional enzyme which converts fibrinogen to fibrin, cross-linking fibrin monomers via activation of factor XIII and augmenting further thrombin production via the activation of factors V and VIII. It also activates platelets, generates anticoagulant activity via activation of protein C and initiates numerous cellular processes including wound healing.



Indicated for treatment of deep vein thrombosis (DVT) and pulmonary embolus (PE) in patients who have been treated with a parenteral anticoagulant for 5-10 days

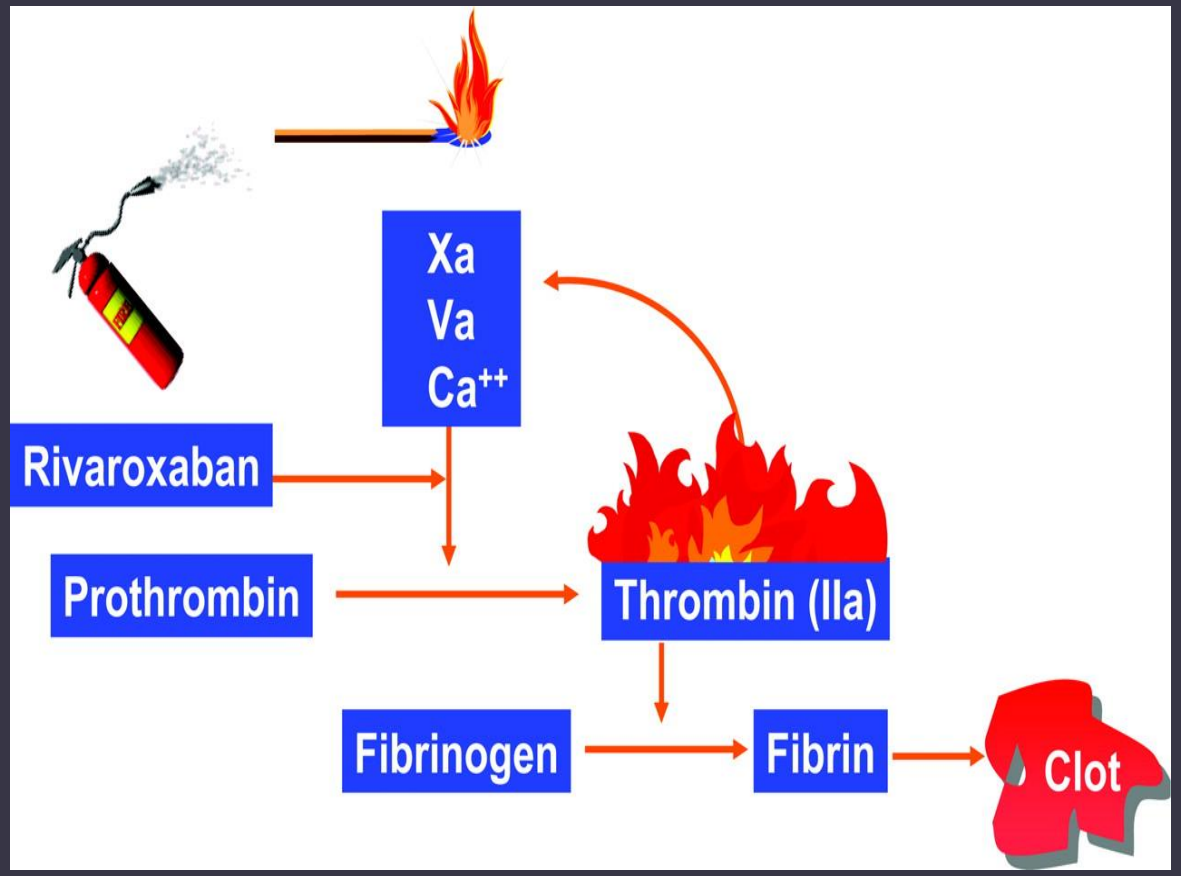
Also indicated to reduce the risk of recurrence of DVT and PE in patients who have been previously treated

- CrCl >30 mL/min: 150 mg PO BID
- CrCl ≤30 mL/min or on dialysis: Dosage recommendations cannot be provided
- CrCl <50 mL/min with concomitant use of P-gp inhibitors: Avoid co-administration

http://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

Direct factor Xa inhibitors (rivaroxaban)

Rivaroxaban is a competitive reversible antagonist of activated factor X (Xa). Factor Xa is the active component of the prothrombinase complex that catalyses conversion of prothrombin (factor II) to thrombin (factor IIa).



Treatment of DVT and PE	15 mg TWICE DAILY	with food for first 21 days
	▼ ON DAY 22 TRANSITION TO ▼	
	20 mg ONCE DAILY	with food, at approximately the same time each day for remaining treatment
Reduce risk of recurrent DVT and PE	20 mg ONCE DAILY	with food, at approximately the same time each day

CONTRAINDICATIONS:

- Active pathological bleeding
- Severe hypersensitivity reaction

http://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

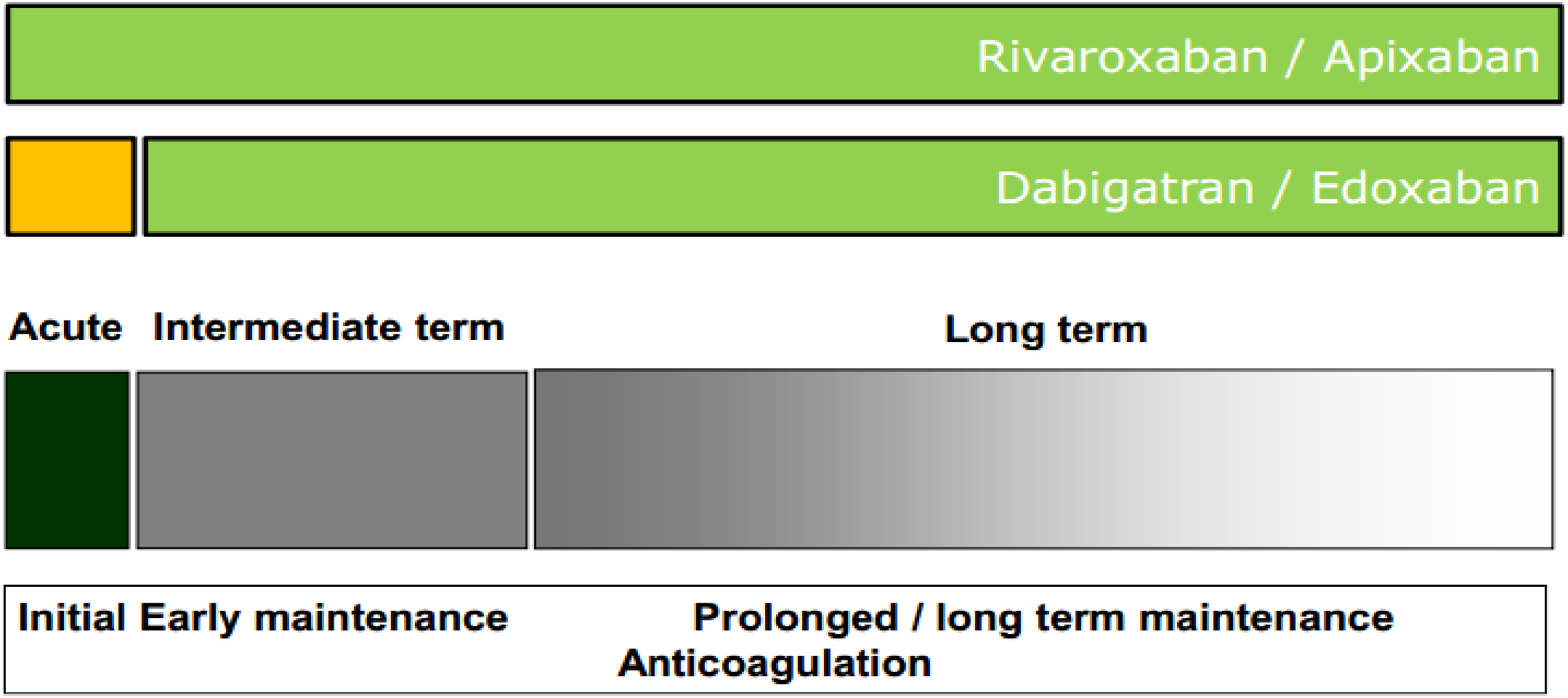
Recommended durations of therapy for different clinical situations are as follows[8]:

- First episode of provoked PE - Provide 3 months of anticoagulation
- First episode of nonprovoked PE - Provide 3 months of anticoagulation, then assess the risk of bleeding; if there is a low-to-moderate risk of bleeding, provide anticoagulation indefinitely
- Recurrence of PE - Provide 3 months of anticoagulation, then reassess; if there is a low-to-moderate risk of bleeding, provide anticoagulation indefinitely

http://reference.medscape.com/features/slideshow/pulmonary-embolism?src=wnl_ref_clinfo&uac=200127DN&impID=886985&faf=1#page=4

Therapy of low risk PE

Krankenhaus
Dresden-Friedrichstadt

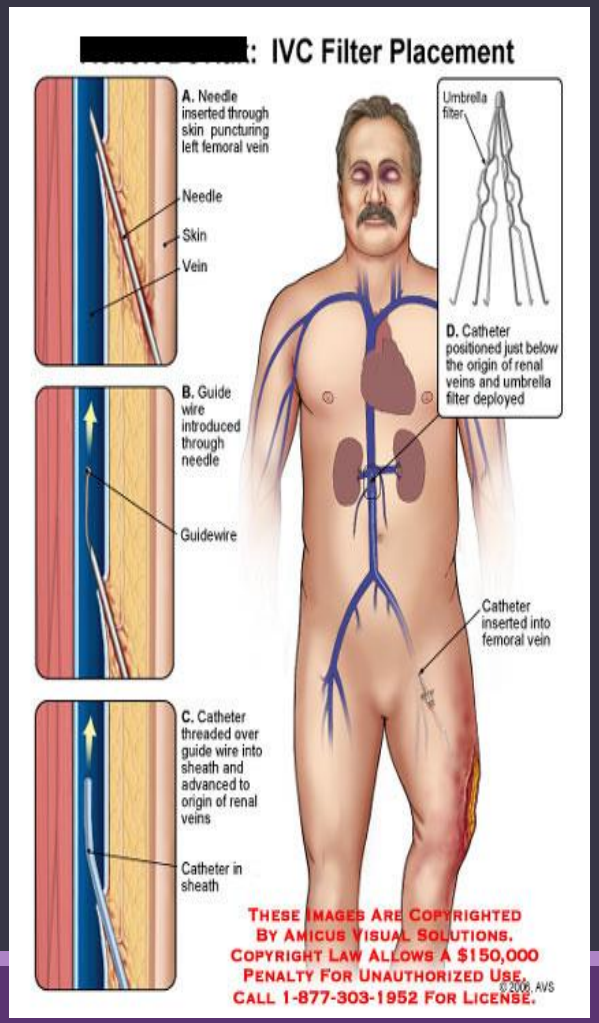


ADVANCED PE THERAPIES

1. **Systemic** full-dose thrombolysis:
   100 mg/2h TPA (FDA: 1990)
   Tenecteplase (PEITHO): (NEJM 2014)
2. **Catheter-directed**, Ultrasound-facilitated thrombolysis ≤ 24 mg TPA
(ULTIMA: Circulation 2014; 129: 479)
(SEATTLE II: JACC CV Intervent 2015)
3. Open surgical embolectomy
4. IVC Filter

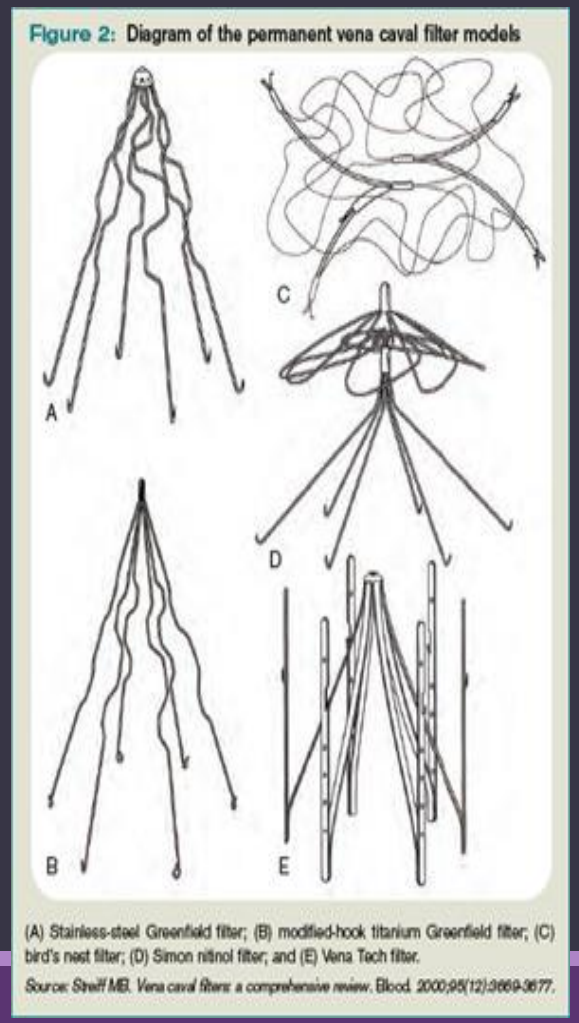
Vena Cava Filters

The current grade 1B recommendation is that patients with acute PE should not routinely receive vena cava filters in addition to anticoagulants. An ideal IVC filter should be easily and safely placed using a percutaneous technique, biocompatible and mechanically stable, and able to trap emboli without causing occlusion of the vena cava



INDICATED FOR:

- Patients with acute venous thromboembolism who have an absolute contraindication to anticoagulant therapy (eg, recent surgery, hemorrhagic stroke, significant active or recent bleeding)
- Patients with massive PE who survived but in whom recurrent embolism invariably will be fatal
- Patients who have objectively documented recurrent venous thromboembolism, adequate anticoagulant therapy notwithstanding



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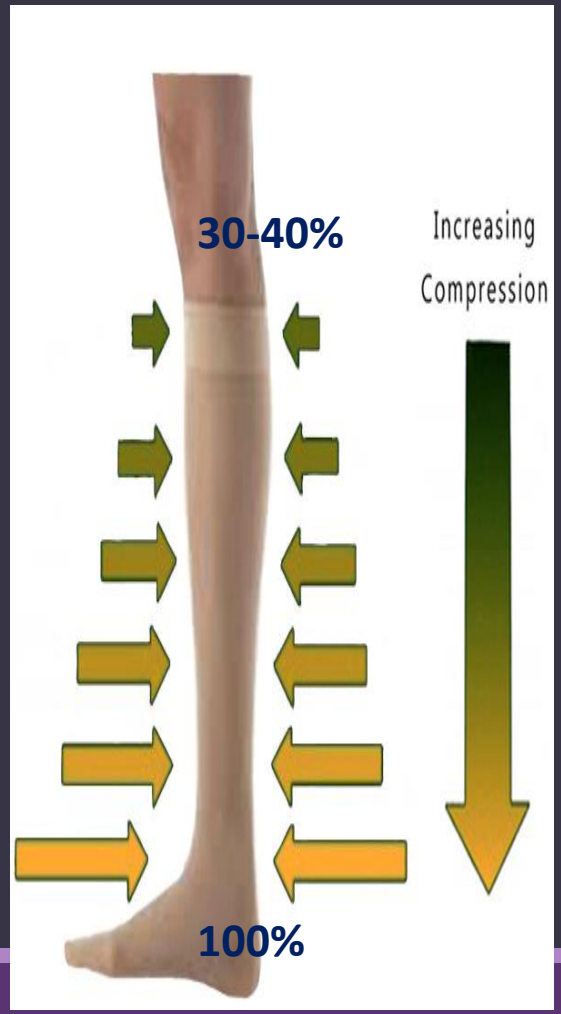
Supportive Care

Compression stockings

For patients who have had a proximal DVT, the use of elastic compression stockings provides a safe and effective adjunctive treatment that can limit postphlebitic syndrome. Stockings with a pressure of 30-40 mm Hg at the ankle, worn for 2 years following diagnosis, are recommended (grade 2B) to reduce the risk of postphlebitic syndrome.



Additional support therapies

- Dopamine and dobutamine are the usual inotropic agents.
- Mechanical ventilation may be necessary to provide respiratory support and as adjunctive therapy for a failing circulatory system.
- Transfusion with packed red blood cells (either simple or exchange) improves oxygenation immediately.
- IV fluids may help or may hurt the patient who is hypotensive.

http://www.escardio.org/Guidelines-&-Education/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

Pulmonary Embolism in Pregnancy

The risk of venous thromboembolism is increased during pregnancy and the postpartum period. Pulmonary embolism is the leading cause of death in pregnancy. DVT and pulmonary embolism are common during all trimesters of pregnancy and for 6-12 weeks after delivery.

- The diagnostic approach to patients with pulmonary embolism should be exactly the same in a pregnant patient as in a nonpregnant one.
- A nuclear perfusion lung scan is safe in pregnancy, as is a chest CT scan.
- If the patient has a low pretest probability for pulmonary embolism and a normal D-dimer test result, clinical exclusion from further investigations is recommended.
- When the suspicion is high, the patients should have bilateral leg Doppler assessment.
- If the results are negative, CT pulmonary angiography is the next step.
- *Heparin and fibrinolysis* are safe in pregnancy. Warfarin is contraindicated, because it crosses the placental barrier.
- Therapeutic treatment with unfractionated heparin or LMWH during pregnancy, with anticoagulation continuing for 4-6 weeks postpartum and for a total of at least 6 months.
- Pregnant women who are in a hypercoagulable state or who have had previous venous thromboembolism -prophylactic anticoagulation during pregnancy.

Complications of PE

- Sudden cardiac death
- Obstructive shock
- Pulseless electrical activity
- Atrial or ventricular arrhythmias
- Secondary pulmonary arterial hypertension
- Cor pulmonale

- Severe hypoxemia
- Right-to-left intracardiac shunt
- Lung infarction
- Pleural effusion
- Paradoxical embolism
- Heparin-induced thrombocytopenia
- Thrombophlebitis

Chronic thromboembolic pulmonary hypertension

Chronic thromboembolic pulmonary hypertension has been reported to be a long-term complication of PE, with a reported cumulative incidence of 0.1–9.1% within the first two years after a symptomatic PE event

Inadequate anticoagulation, large thrombus mass, residual thrombi, and recurrence of VTE

↓

a pulmonary vascular remodelling process modified by infection, inflammation, circulating and vascular-resident progenitor cells, thyroid hormone replacement, or malignancy

↓

Hypercoagulation, ‘sticky’ red blood cells, high platelet counts, and ‘uncleavable’ fibrinogen, pulmonary microvascular disease

↓

development of CTEPH

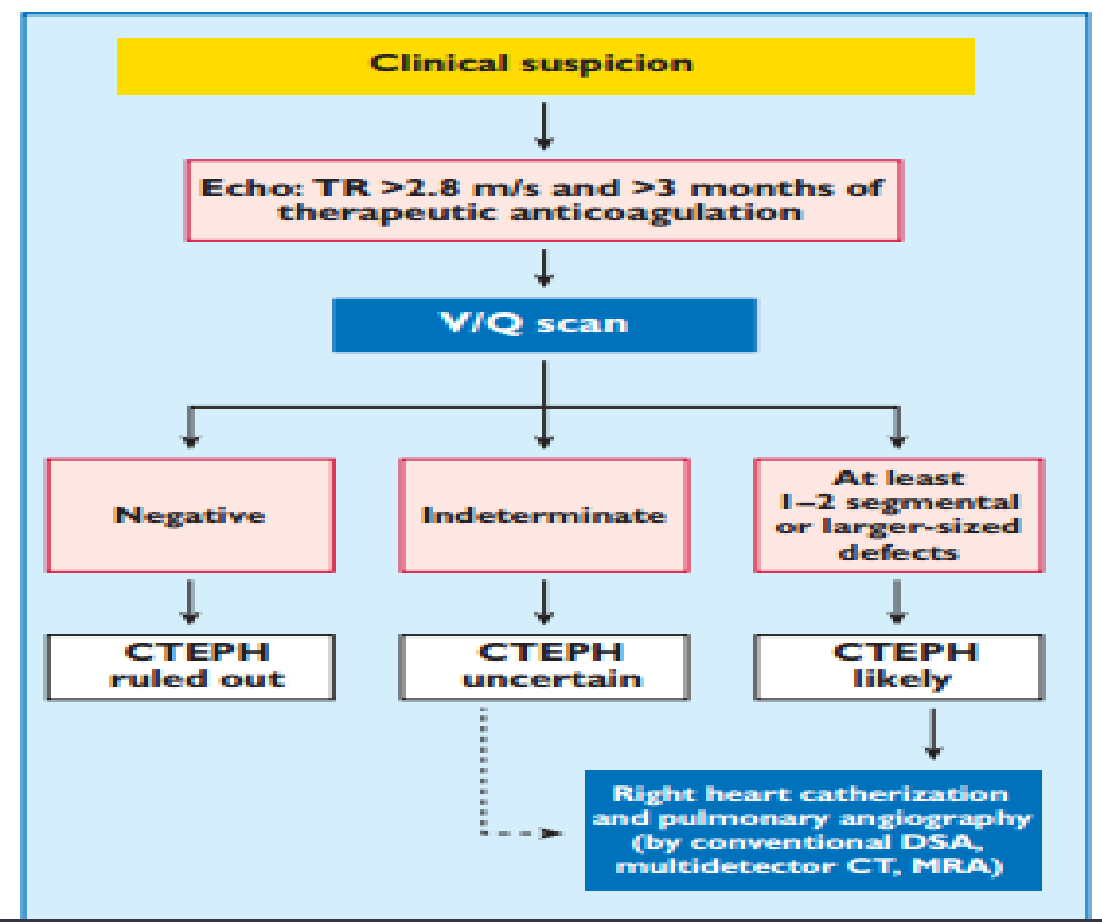
Chronic thromboembolic pulmonary hypertension

The diagnosis of CTEPH is based on findings obtained after at least 3 months of effective anticoagulation, in order to discriminate this condition from ‘sub-acute’ PE. These findings are:

† mean pulmonary arterial pressure ≥25 mm Hg, with pulmonary

arterial wedge pressure ≤15 mm Hg;

† at least one (segmental) perfusion defect detected by perfusion lung scan, or pulmonaryarteryobstruction seen by MDCT angiography or conventional pulmonary cineangiography.



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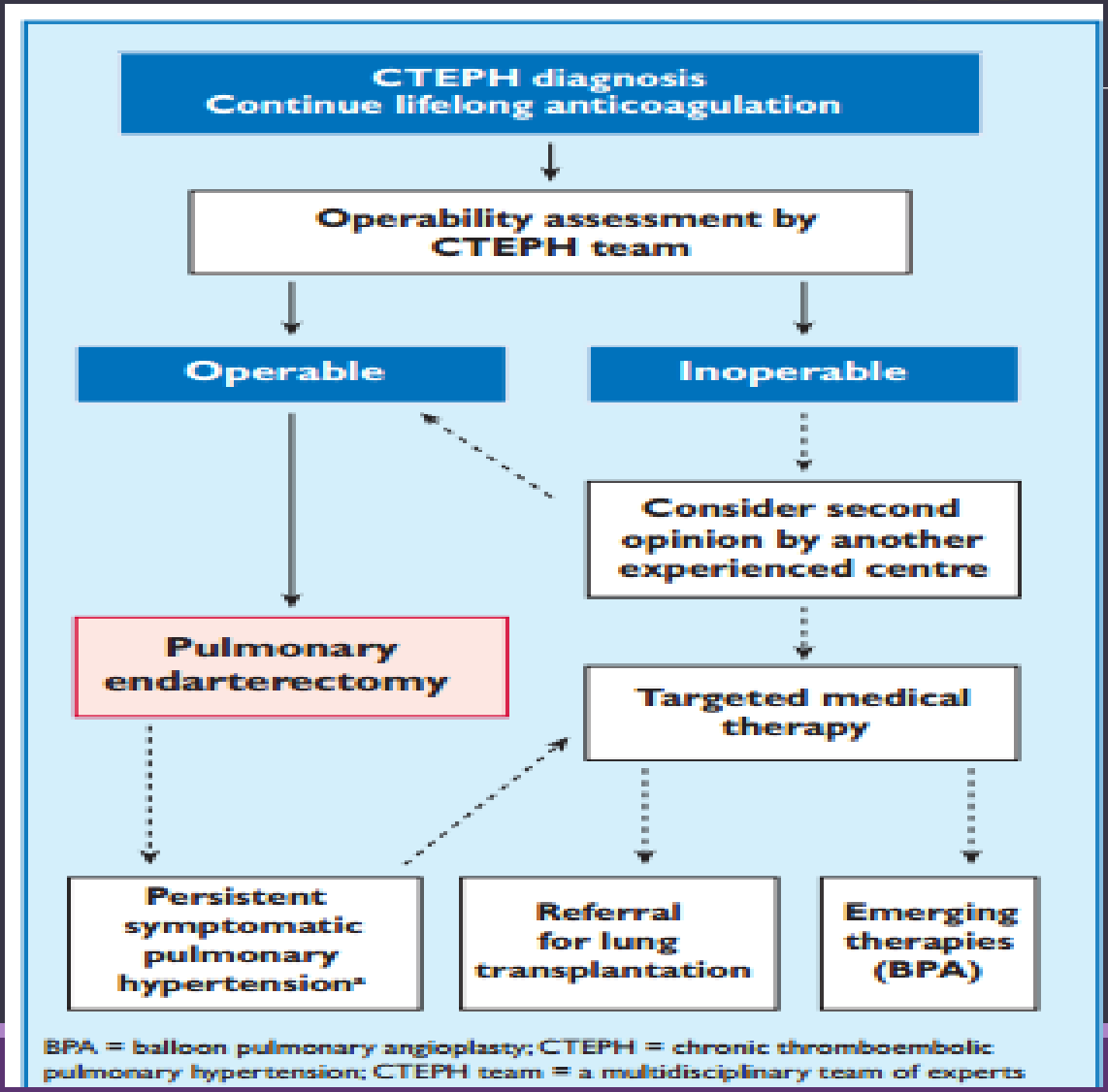
Chronic thromboembolic pulmonary hypertension



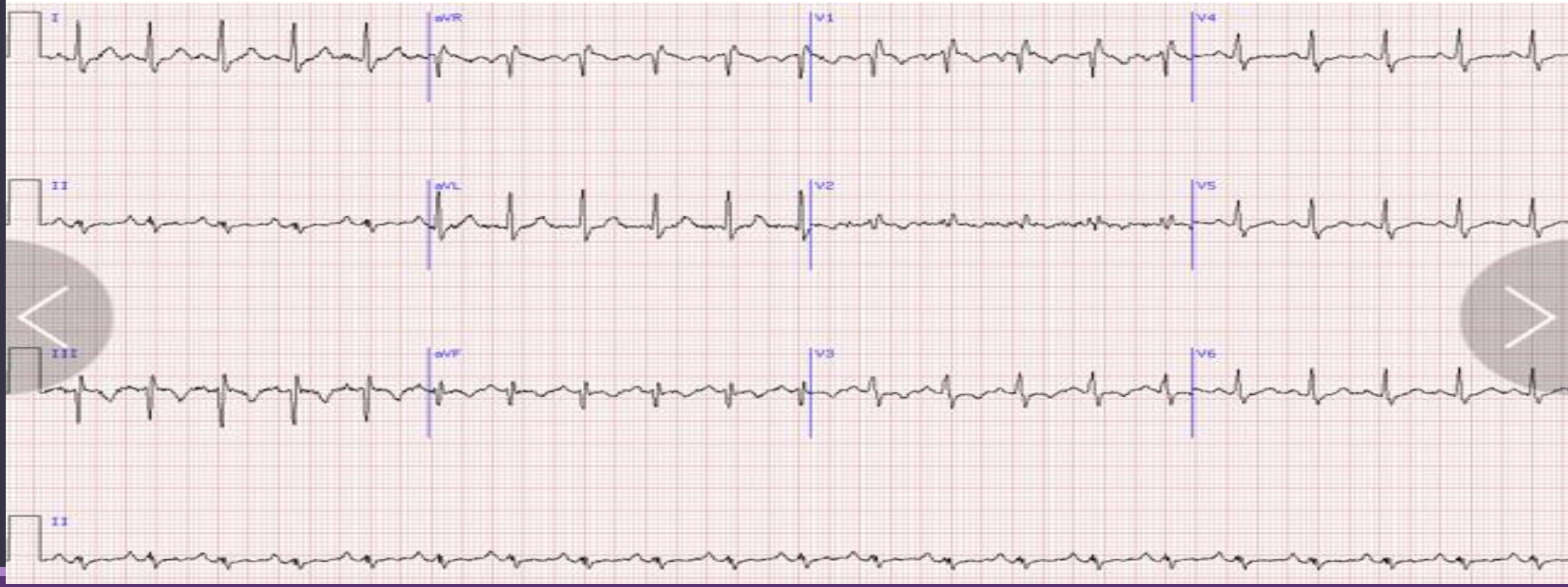
Pulmonary endarterectomy (PEA) is the treatment of choice for the disease.

Patients who do not undergo surgery, or suffer from persistent or residual pulmonary hypertension after PEA, face a poor prognosis.

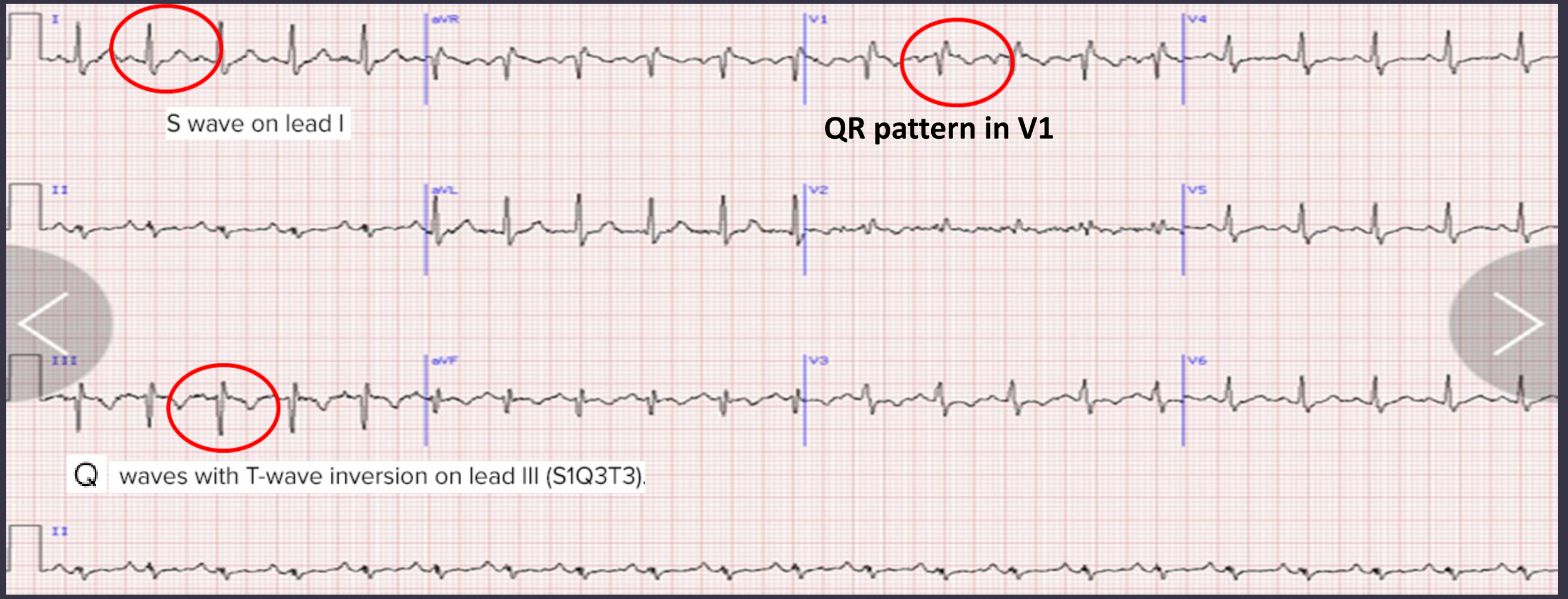
Advances in balloon pulmonary angioplasty are continuing in an attempt to make this technique a therapeutic alternative for selected patients with non-operable CTEPH

CLINICAL CASE

A previously healthy 60-year-old woman who has traveled from London to San Francisco has a near-syncope at the airport around 1 hour after arrival, and 911 is called. Her blood pressure (BP) is 89/52 mm Hg, her heart rate (HR) is 124 beats/min, her respiratory rate (RR) is 24 breaths/min, and her oxygen saturation on pulse oximetry is 90%. At the time of the paramedics' arrival, the patient is conscious. She states that she has no chest pain, but she feels dizzy while lying down. The paramedics administer a bolus of normal saline, obtain an electrocardiogram (ECG), and transport the patient to a hospital. After administration of 1 L of normal saline and the passage of 30 minutes, her BP has returned to normal.



In the ECG shown in the slide, what are the findings on leads I and III, and what is their relevance to PE?



Answer: The key findings on these two leads are an S wave on lead I and Q waves with T-wave inversion on lead III (S1Q3T3). The common ECG changes seen in acute PE are as follows:

- Nonspecific T-wave and ST-segment changes in 70% of cases[4]
- Right ventricular strain, strain including new incomplete right bundle-branch block (RBBB) and S1Q3T3, in 10% of cases[5]
- Poor prognostic ECG signs, including new RBBB, atrial fibrillation (AF), bradycardia, inferior Q-waves, anterior ST-segment changes, and T-wave inversions[6]

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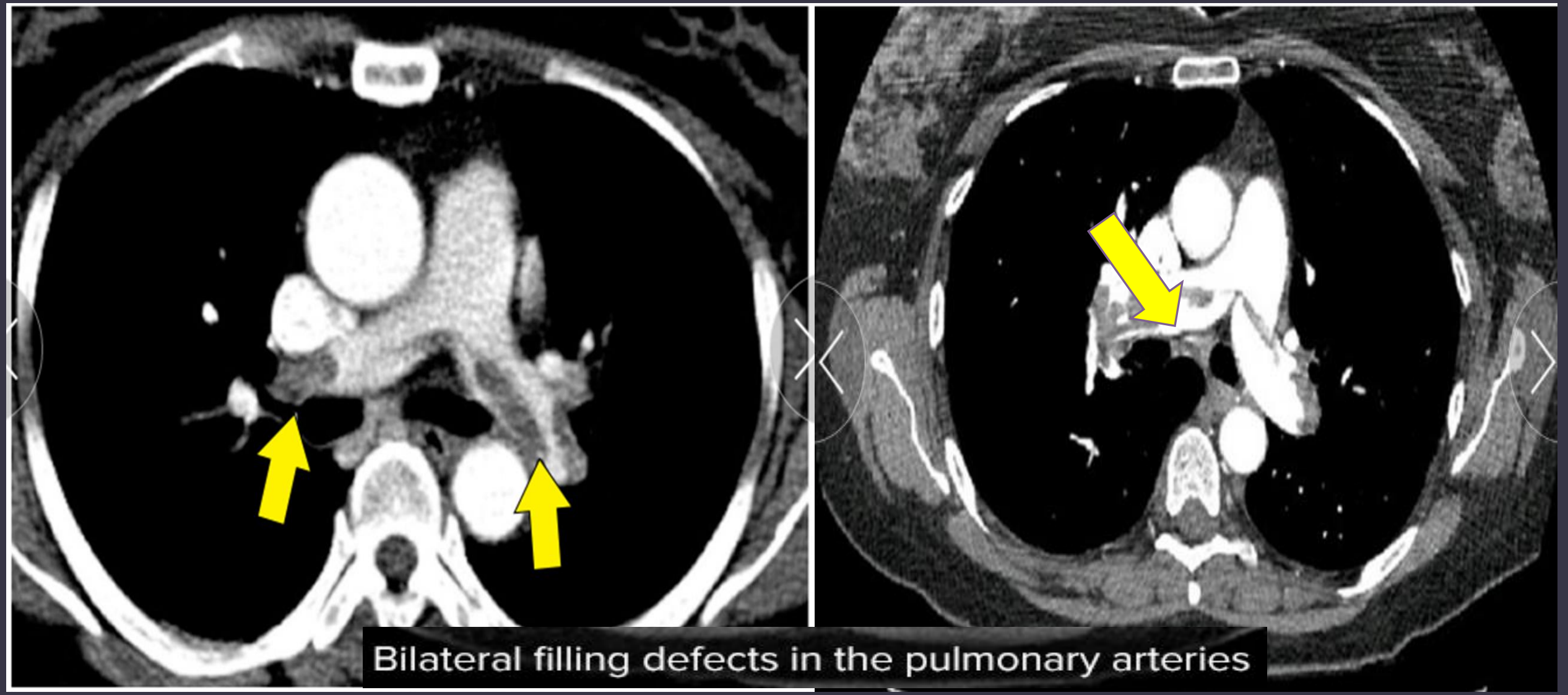
The D-dimer level is measured and determined to be higher than 10,000 ng/mL



CT venography reveals the presence of deep vein thrombosis (DVT) in the right leg. The patient's BP declines again to 89/62 mm Hg, and her heart rate is now 110 beats/min. Her oxygen saturation is 92%.

DIAGNOSIS?

Acute massive unstable Pulmonary Embolism (unstable when systolic BP remains below 90 mm Hg for more than 15 minutes or when vasopressors are required)

TREATMENT OPTIONS?

The treatment options for hemodynamically unstable PE consist of thrombolysis and thrombectomy.

Thrombectomy was performed

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Goodbye!