Pulmonary embolism

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Introduction

Hemostasis

Definition:

is the process of forming clots in the walls of damaged blood vessels and preventing blood loss, while maintaining blood in a fluid state within the vascular system.

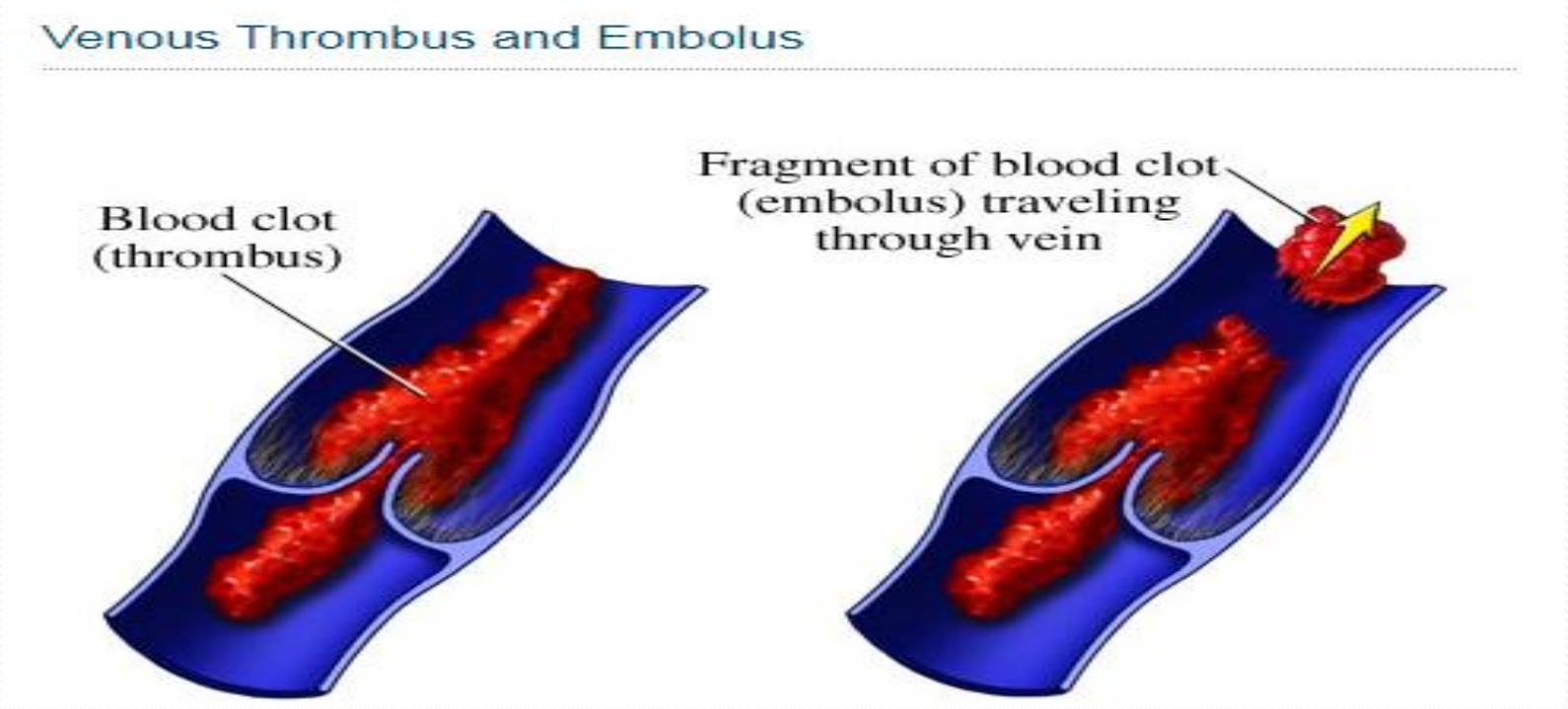
- Physiologic

Thrombosis

- The formation of an unwanted clot within a blood vessel.
- The most common abnormality of hemostasis.
- Pathologic

Thrombus vs. Embolus

- **Thrombus**: a clot that adheres to a vessel wall.
- **Embolus**: an intravascular clot that floats in the blood.



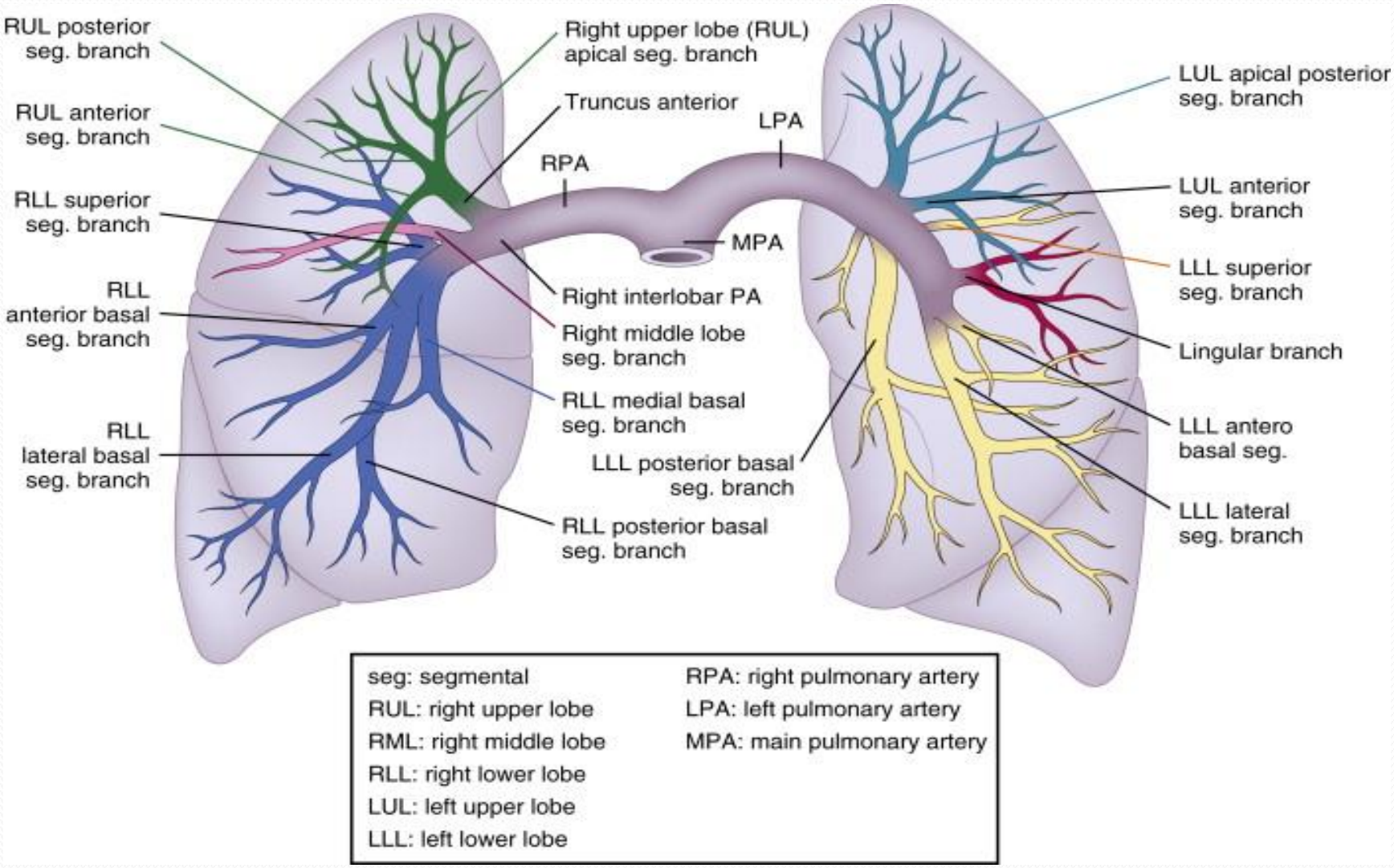
Pulmonary embolism (PE)

Definition:

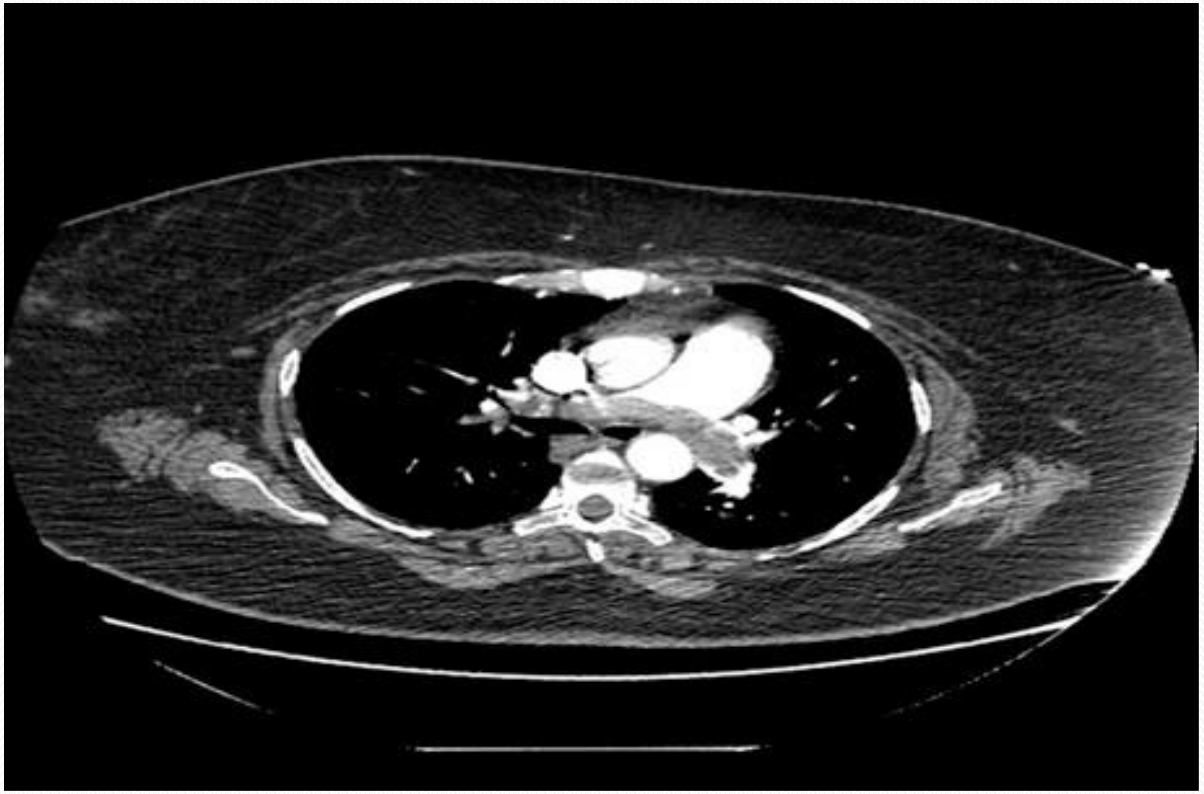
is a blockage of pulmonary artery by a substance that has moved from elsewhere in the body through the bloodstream. Most pulmonary emboli are multiple, more commonly in the lower lobes.

Venous thromboembolism (VTE) encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE).

Pulmonary artery anatomy



A saddle pulmonary embolism is described as a clot located in the main pulmonary artery that traverses the right and left pulmonary arteries.



Lobar, segmental, and subsegmental PEs: are clots located in the branches of the pulmonary artery corresponding to the anatomical lung segment.

Pulmonary Infarction : The pathological changes which develop in the lung as a result of pulmonary embolism.

Epidemiology

a.PE is the third most common cause of death among hospitalized patients.

b.PE is present in 60-80% of patients with DVT.

c. Acute **PE** is the most serious clinical presentation of VTE.

d. The epidemiology of **PE** is difficult to determine because it may remain asymptomatic, or its diagnosis may be an incidental finding, in some cases, the first presentation of PE may be sudden death.

.The incidence of **PE** also is age-dependent, with increasing incidence of death with advancing age

The percentages of the different subtypes of PE:

Massive PE: 5-10%

Sub massive PE: 20-25%

Low-risk PE: ~70%

Sources of emboli

(80%–95%) of PE occur as a result of thrombus originating in the lower extremity: **deep veins of the calf** , **the popliteal** and **femoral veins**.

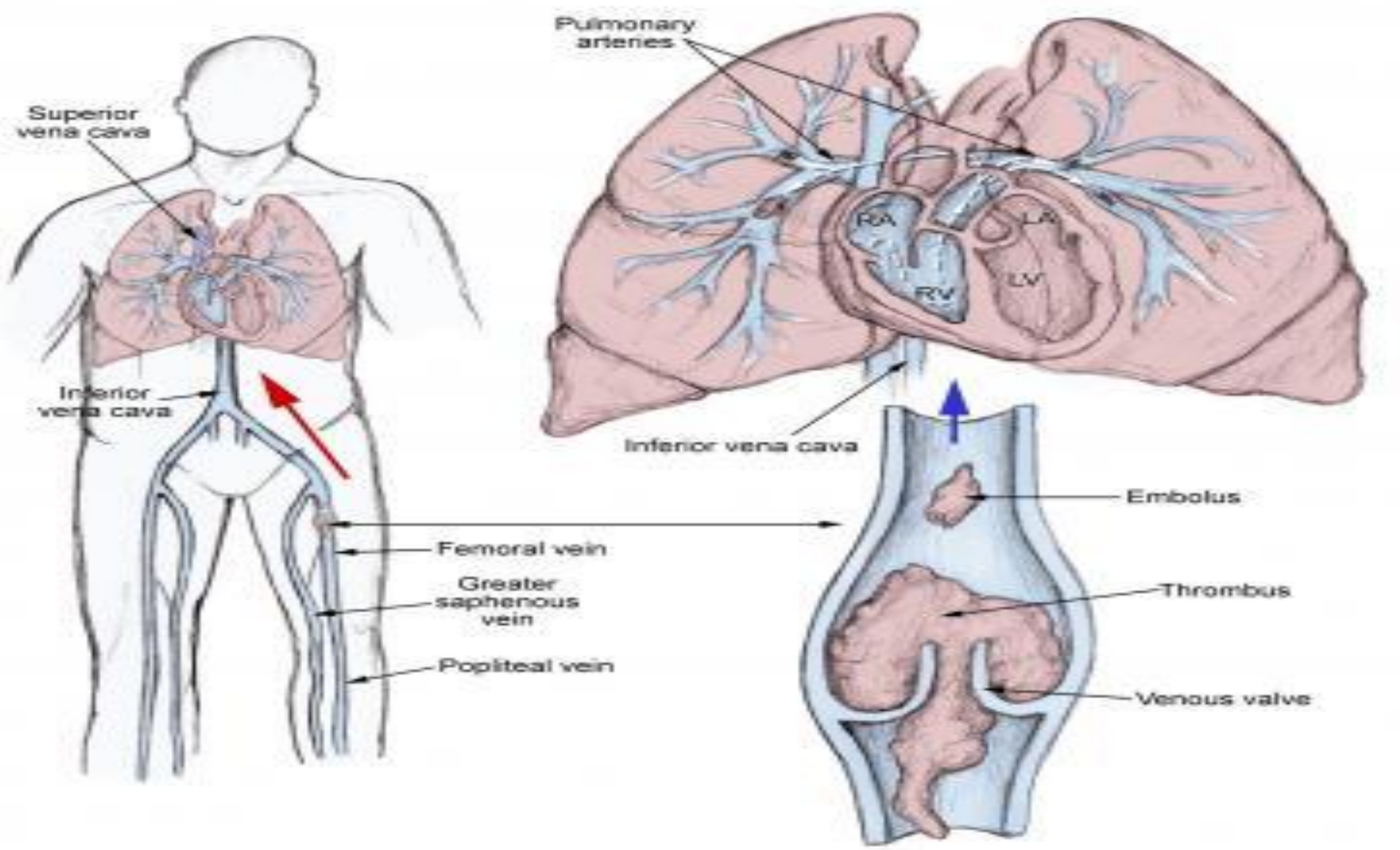
Other sources:

***a*-the pelvic veins** (pregnancy, pelvic infection, prostate disease, or recent pelvic surgery)

b-Emboli may also originate from **upper extremity thrombosis** associated with central venous catheters or intravascular cardiac devices

c-the renal veins

Pathogenesis



Thrombus often begins at a site where blood flow is turbulent, such as at a venous bifurcation, or behind a venous valve. When thrombus propagation exceeds the rate of thrombus organization and adherence to the endothelium, part or all of thrombus may break away and migrate via the venous system to the lungs

Classification

I. Thrombotic: The most common.

II. Non-thrombotic PE (NTPE)

- Embolization to the pulmonary circulation of different cell types (adipocytes, hematopoietic, amniotic or tumor), bacteria, fungi, foreign material or gas.

Etiology

Three primary influences predispose a patient to thrombus formation; these form the so-called ***Virchow triad***, which consists of the following:

a. Endothelial injury

b. Stasis or turbulence of blood flow

c. Blood hypercoagulability

Risk factors for venous thromboembolism

INHERITED RISK FACTORS:

.Factor V Leiden mutation

.Protein C deficiency

.Protein S deficiency

.Antithrombin deficiency

.Prothrombin gene mutation

.Anticardiolipin antibodies

.Lupus anticoagulant

Risk factors for venous thromboembolism

Major risk factors :

Surgery*

- Major abdominal/pelvic surgery
- Hip/knee replacement
- Postoperative intensive care

Obstetrics

- Late pregnancy
- Caesarian section
- Puerperium

Lower limb problems

- Fracture
- Varicose veins

Malignancy

- Abdominal/pelvic
- metastatic

Reduced mobility

- Hospitalization
- Institutional care

Miscellaneous

- Previous proven VTE

Risk factors for venous thromboembolism

Minor risk factors :

Cardiovascular

- Congenital heart disease
- Congestive cardiac failure
- Hypertension
- Superficial venous thrombosis
- Indwelling central vein catheter

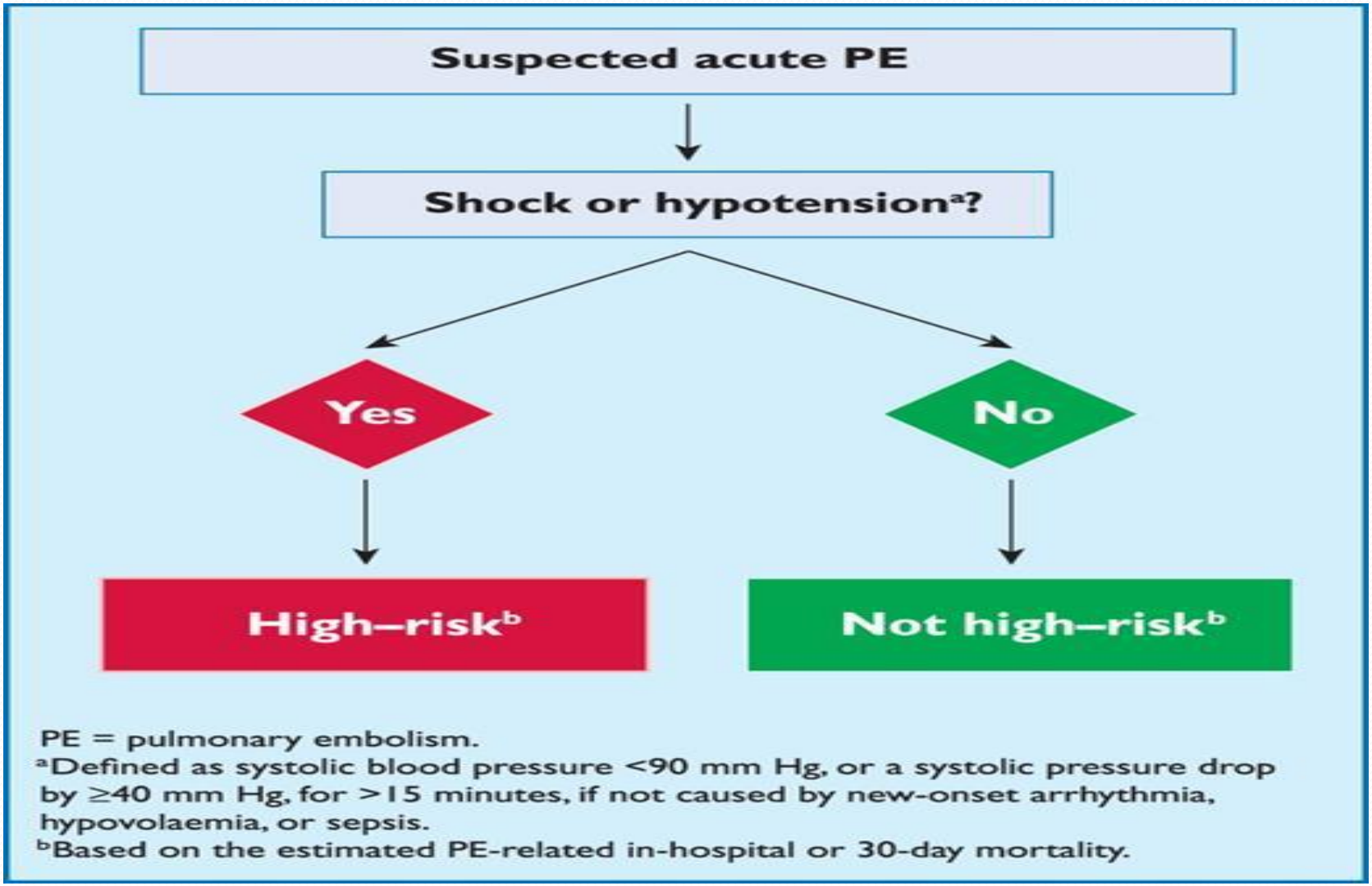
Estrogens

- Oral contraceptive
- Hormone replacement therapy

Miscellaneous

- COPD
- Occult malignancy
- Long distance sedentary travel
- Obesity

Clinical classification of pulmonary embolism severity



Diagnosis

Clinical presentation

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%

signs	PE confirmed
Tachypnea (respiratory rate >20/min)	96%
Crackles	58%
Accentuated second heart sound	53%
Tachycardia (heart rate >100/min)	44%
Fever (temperature >37.8°C	43%
Clinical signs and symptoms suggesting thrombophlebitis	32%
Lower extremity edema	24%
Cardiac murmur	23%
Cyanosis	19%

Differential Diagnosis for Acute Pulmonary Embolism

.Pneumonia

.Asthma or exacerbation of chronic obstructive lung disease

.Pleuritis

.Pericarditis/cardiac tamponed

.Pneumothorax

.Musculoskeletal pain

.Costochondritis

.Rib fracture

.Pulmonary edema/congestive heart failure

.Pulmonary hypertension

.Myocardial infarction

.Aortic dissection

Diagnosis

'**confirmed PE**' is defined as a probability of PE high enough to indicate the need for PE-specific treatment

'**excluded PE**' as a probability of PE low enough to justify withholding PE-specific treatment.

CLINICAL ASSESSMENT

- **Wells and Geneva Scoring Systems Used in Risk Assessment for the Diagnosis of Pulmonary Embolism (PE)*** Both scoring systems divide patients into groups with low, intermediate, and high clinical probability for diagnosis of PE

Table 57-3 **Wells and Geneva Scoring Systems Used in Risk Assessment for the Diagnosis of Pulmonary Embolism (PE)***

Wells Score	Points	Geneva Score	Points
Previous VTE	1.5	Previous VTE	2
Heart rate >100 beats/min	1.5	Heart rate >100 beats/min	1
Recent surgery or immobilization	1.5	Recent surgery	3
Clinical signs of DVT	3	Age (years)	
		60–79	1
		≥80	2
Alternative diagnosis less likely	3	$Paco_2$	
		<36 mm Hg	2
		36–38.9 mm Hg	1
Hemoptysis	1	Pao_2	
		<48.7 mm Hg	4
		48.7–59.9 mm Hg	3
		60–71.2 mm Hg	2
		71.3–82.4 mm Hg	1
Cancer	1	Atelectasis	1
		Elevated hemidiaphragm	1
Clinical Probability		***Clinical Probability***	
Low	0–1	Low	0–4
Intermediate	2–6	Intermediate	5–8
High	>6	High	≥9

LABORATORY TESTS

1-Arterial Blood Gas Analysis: hypoxemia

2-D-Dimer Assay :D-dimer is a plasmin-derived fibrin degradation product.

D-dimer testing has proven to be highly sensitive but not specific.

Blood D-dimer assay should only be considered following assessment of clinical probability.

D-dimer assay should not be performed in those with high clinical probability of PE.

A negative D-dimer test reliably excludes PE in patients with low or intermediate clinical probability; such patients do not require imaging for VTE.

3-B-Type Natriuretic Peptide Assay, Troponin Assay

Table 4 Principal markers useful for risk stratification in acute pulmonary embolism

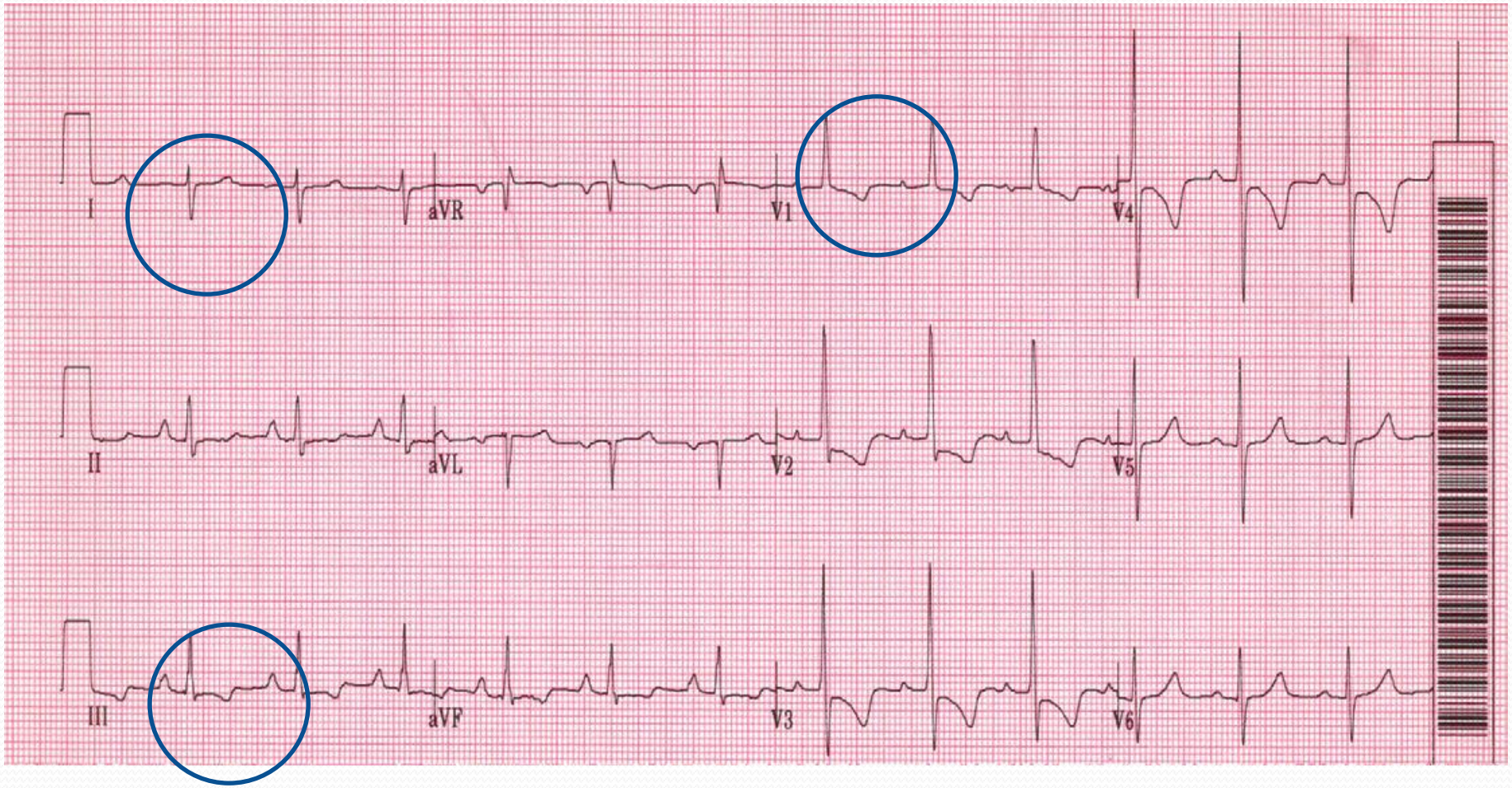
Clinical markers	Shock
	Hypotension[a]
Markers of RV dysfunction	RV dilatation, hypokinesis or pressure overload on echocardiography
	RV dilatation on spiral computed tomography
	BNP or NT-proBNP elevation
	Elevated right heart pressure at RHC
Markers of myocardial injury	Cardiac troponin T or I positive[b]

BNP = brain natriuretic peptide; NT-proBNP = N-terminal proBNP; RHC = right heart catheterization; RV = right ventricle.

[a]Defined as a systolic blood pressure <90 mmHg or a pressure drop of ≥40 mmHg for >15 min if not caused by new-onset arrhythmia, hypovolaemia or sepsis.

[b]Heart-type fatty acid binding protein (H-FABP) is an emerging marker in this category, but still requires confirmation.

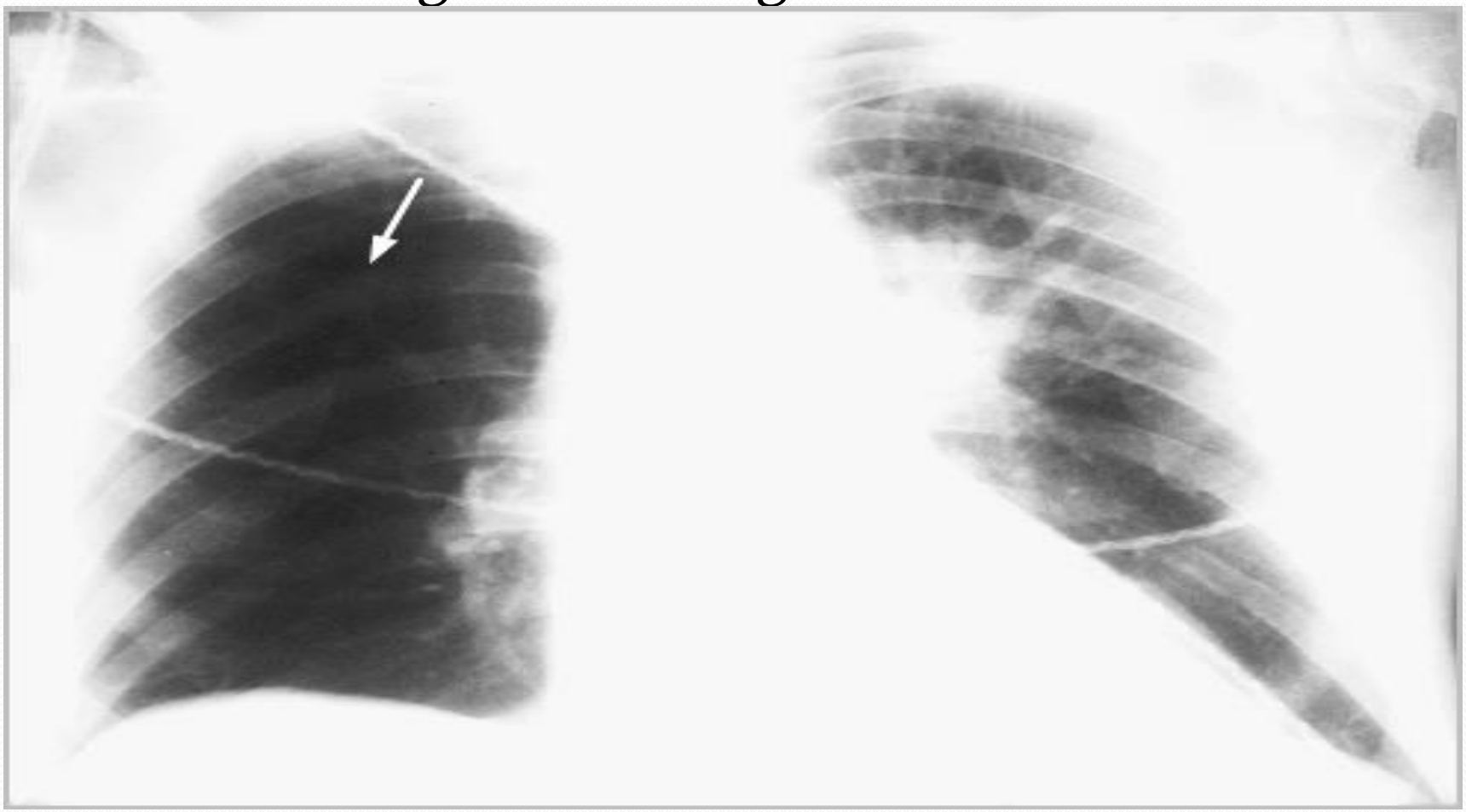
Electrocardiogram



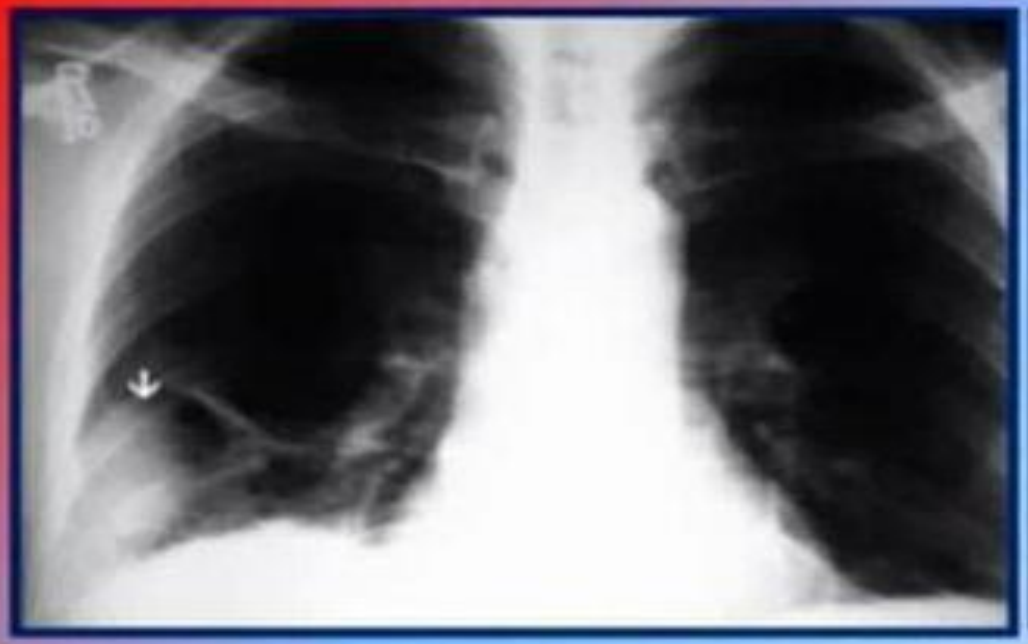
Chest Radiographs

Classic abnormalities include:

Westermark's Sign - focal oligemia

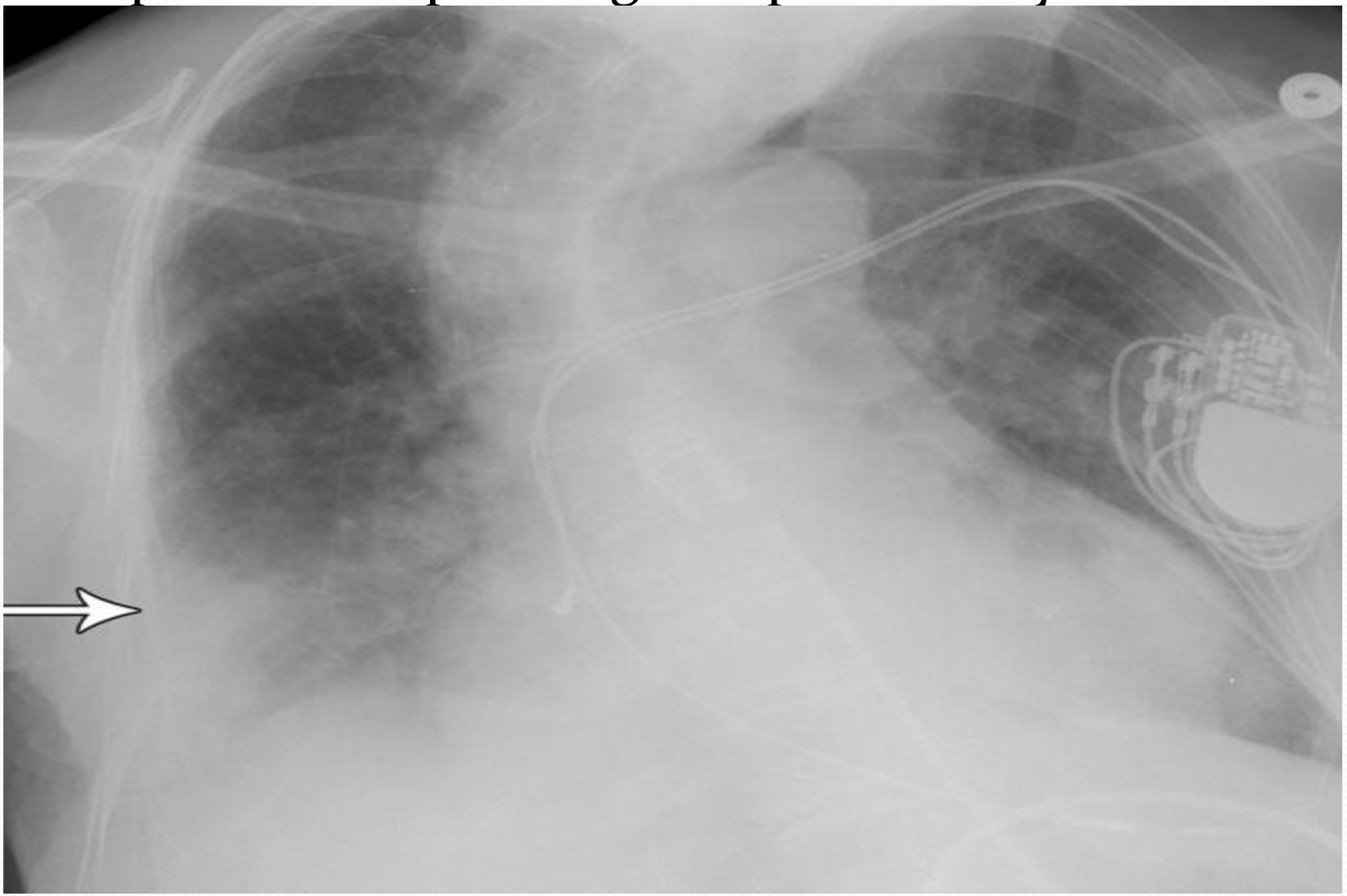


Hampton's Hump - wedge shaped density

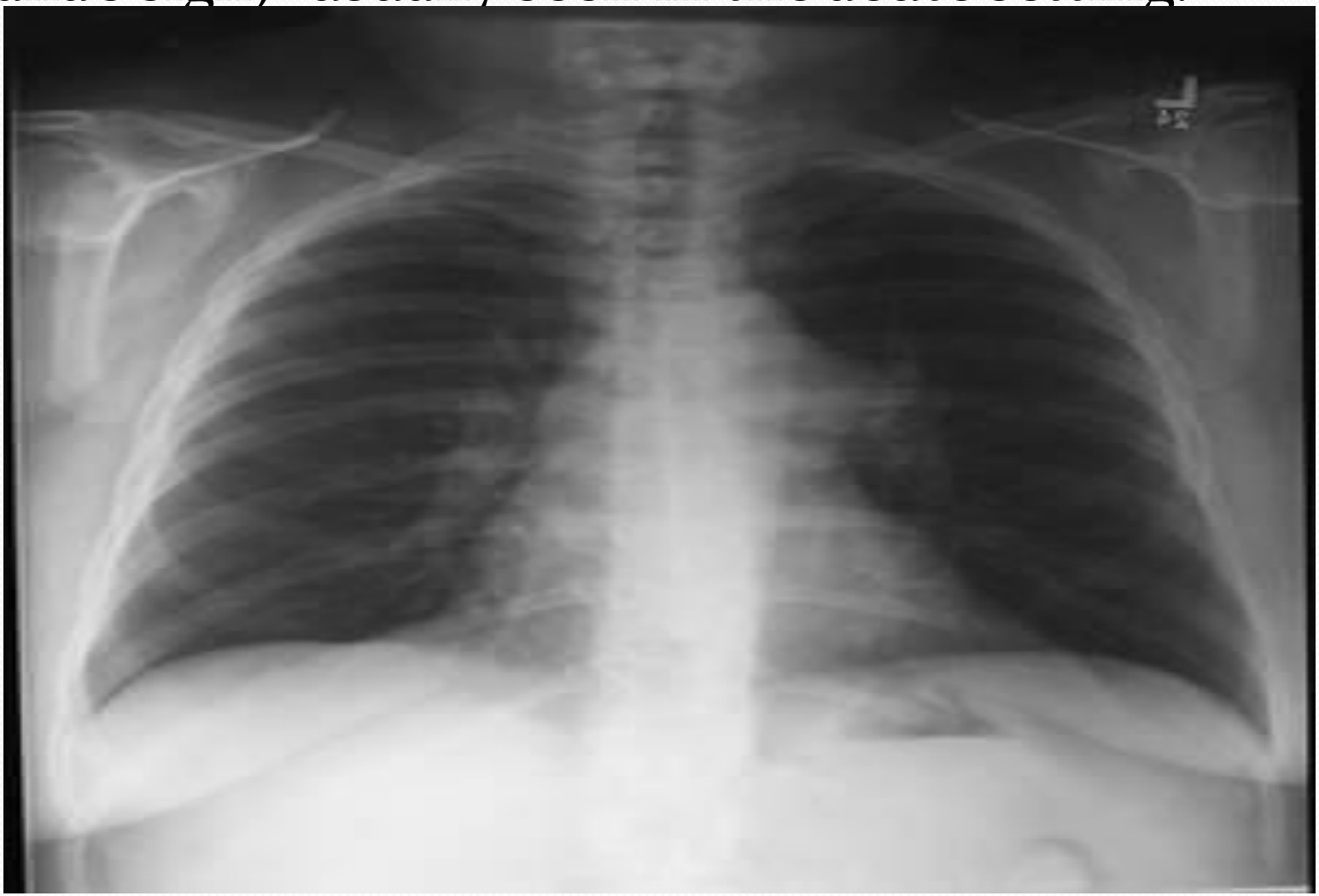


a, b. **Hampton hump sign.** a. Chest X-ray of a patient with pulmonary embolism showing a peripherally located, wedge-shaped homogenous opacity consistent with the infarct area *(arrow)*. b. *Hump of a camel.*

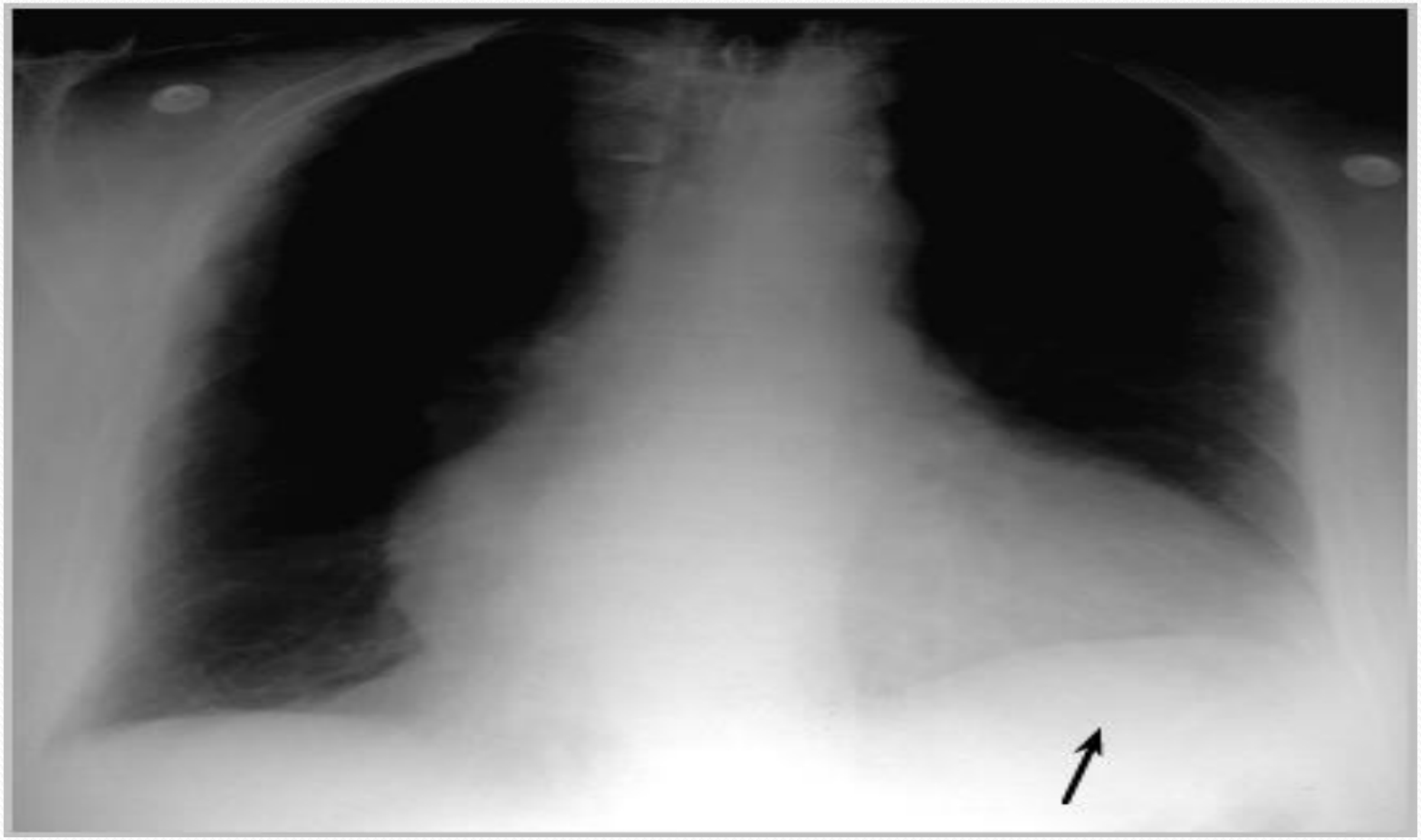
Hampton's Hump - wedge shaped density



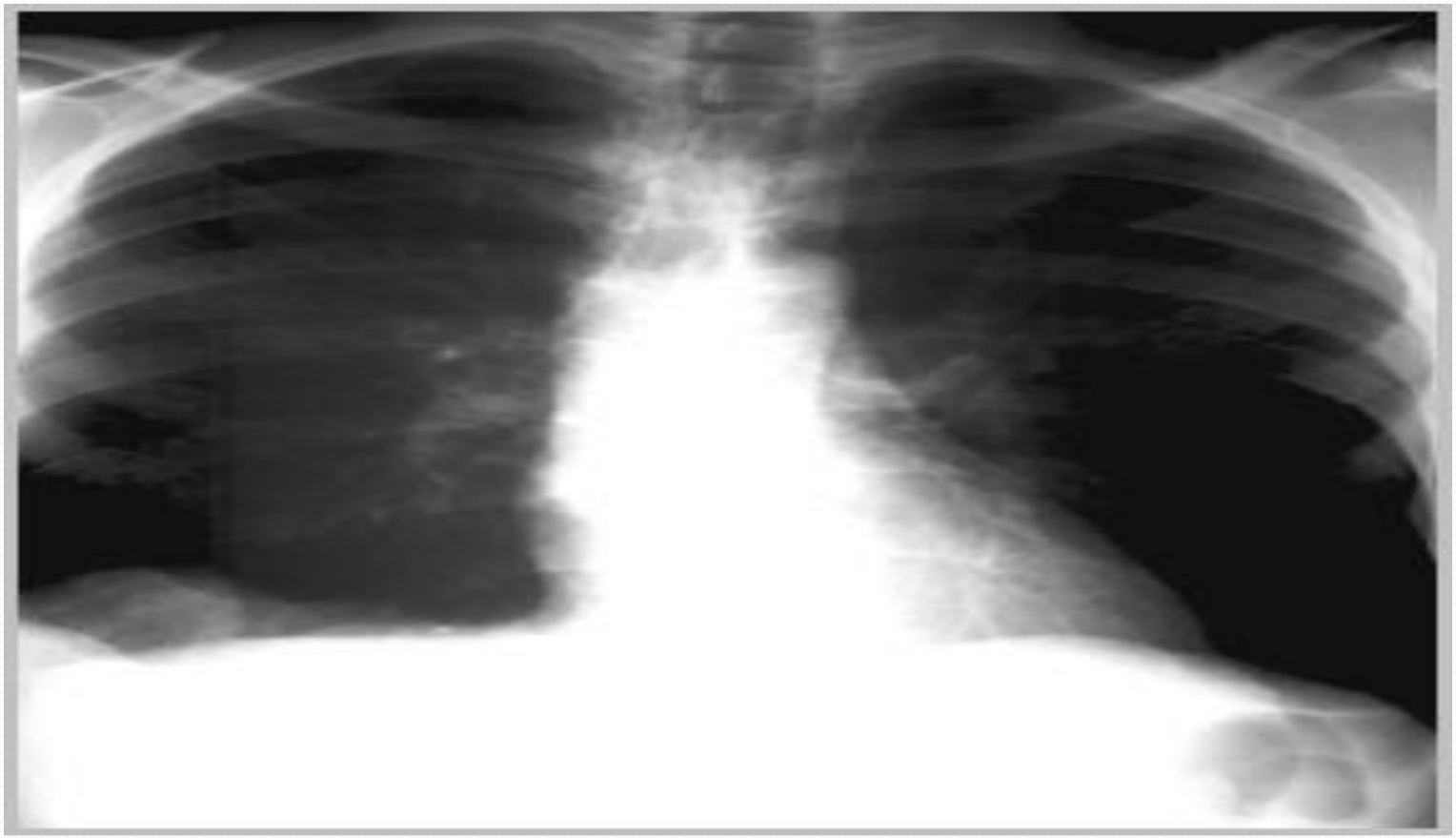
Enlarged Right Descending Pulmonary Artery (Palla's sign) usually seen in the acute setting.



A diaphragm may be elevated, reflect in volume loss in the affected lung.

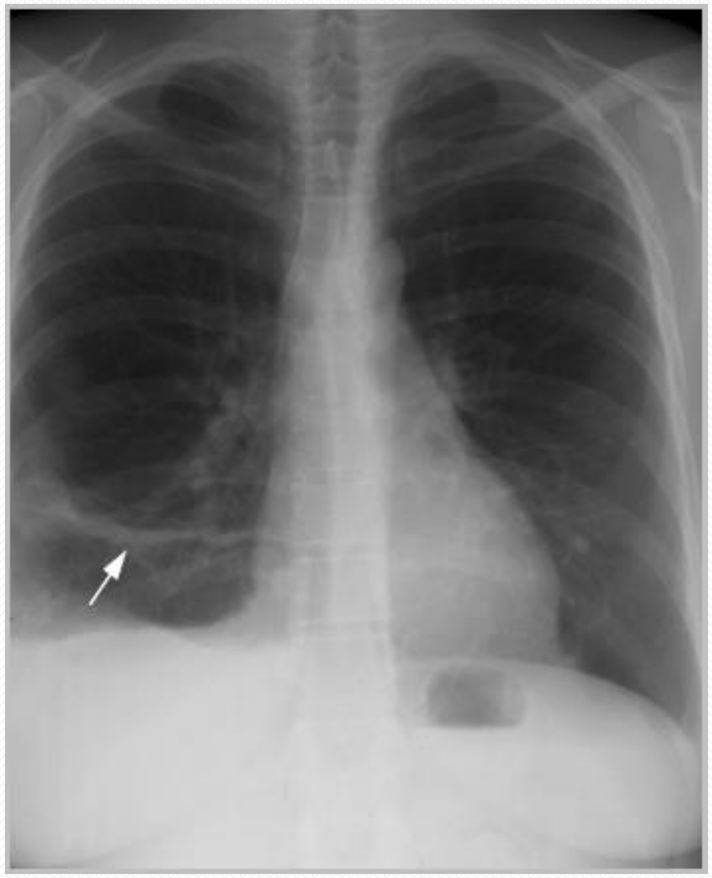


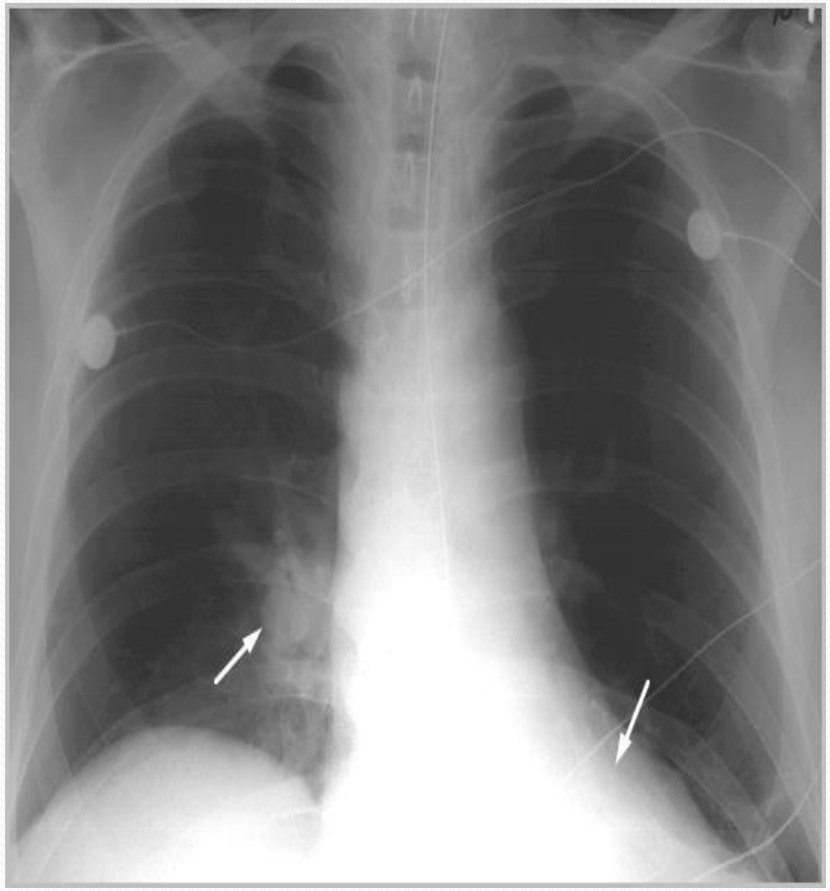
Pleural Effusion 48%



Atelectasis 68%

Atelectasis and parenchymal densities are quite common. Most of these densities are caused by pulmonary hemorrhage and edema





Venous Compression Ultrasonography

Ultrasound imaging frequently is used when the initial tests for PE are non diagnostic.

A positive ultrasound test result confirms the need for anticoagulation and obviates the need for further diagnostic studies.

Echocardiogram

Transthoracic and trans esophageal echocardiography have limited use in the diagnosis of PE. The sensitivity and specificity of these tests are inadequate for diagnosis, because the offending emboli are rarely proximal enough to be visualized. A more important role of echocardiography in the evaluation of patients with PE is that of risk stratification.

Right ventricular dysfunction develops in association with an acute PE. Worsening right ventricular function relates directly to the degree the pulmonary vascular bed is affected by the thrombus and, therefore, the size of the embolic event. Some investigators have suggested that more aggressive therapy, such as thrombolysis, is indicated in patients with right ventricular dysfunction emboli

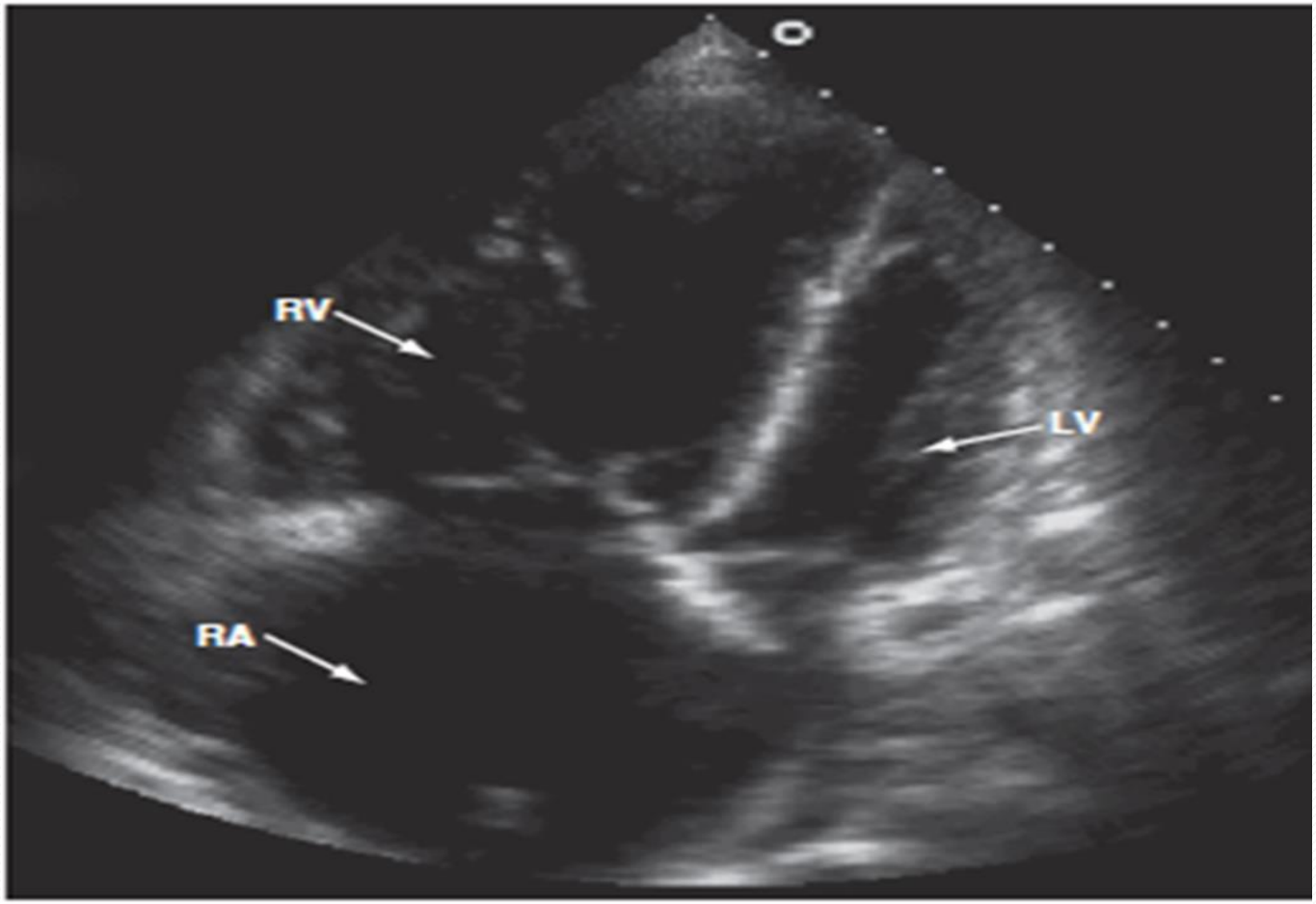
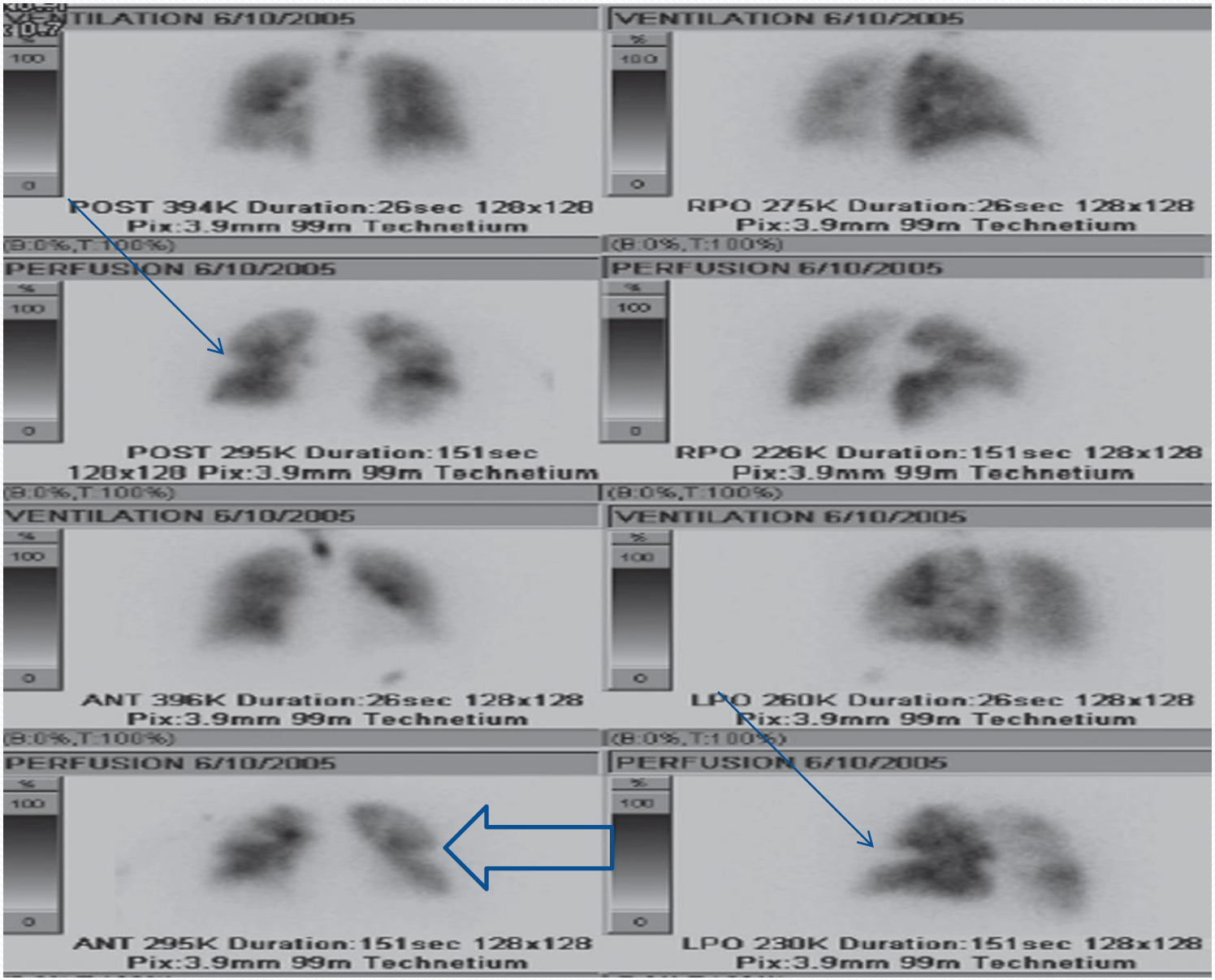


Figure 57-4 Echocardiogram of a patient with markedly dilated right ventricle (RV) and right atrium (RA) secondary to pulmonary thromboembolic disease. The interventricular septum is bowing into and compressing the left ventricle (LV).

Ventilation-Perfusion Lung Scan



Ventilation-Perfusion Lung Scan

For many years, the ventilation-perfusion lung scan was considered the imaging study of choice to evaluate for PE.

Recently, CTA has replaced the ventilation-perfusion lung scan as the predominant diagnostic test. However, the ventilation-perfusion scan maintains an important place in the evaluation of patients for thromboembolic disease who have contraindications to CTA such as renal insufficiency or contrast allergy.

Computed Tomography Angiography

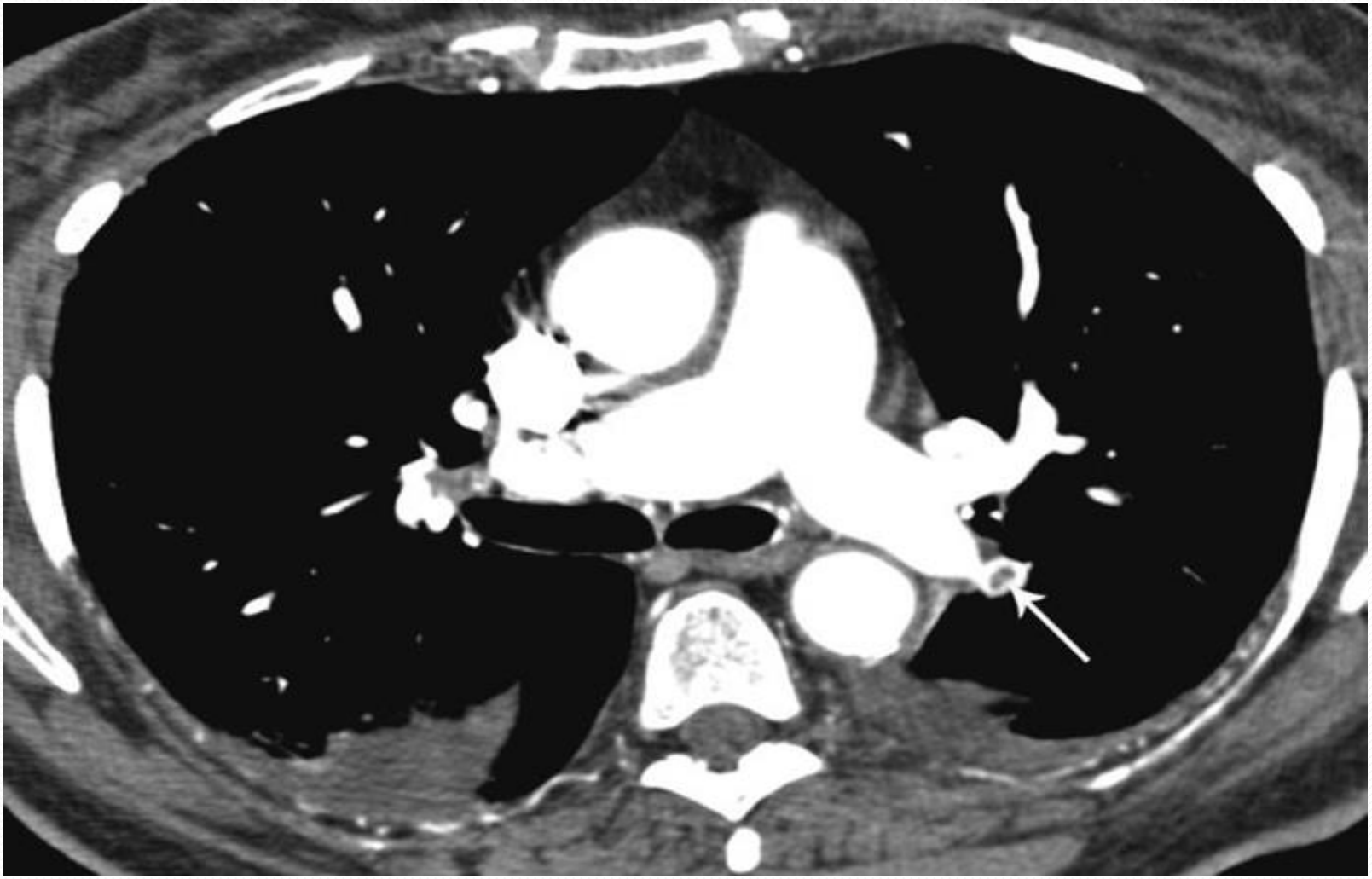
CT pulmonary angiography (i.e., CTA) has become a favored study for the evaluation of PE.

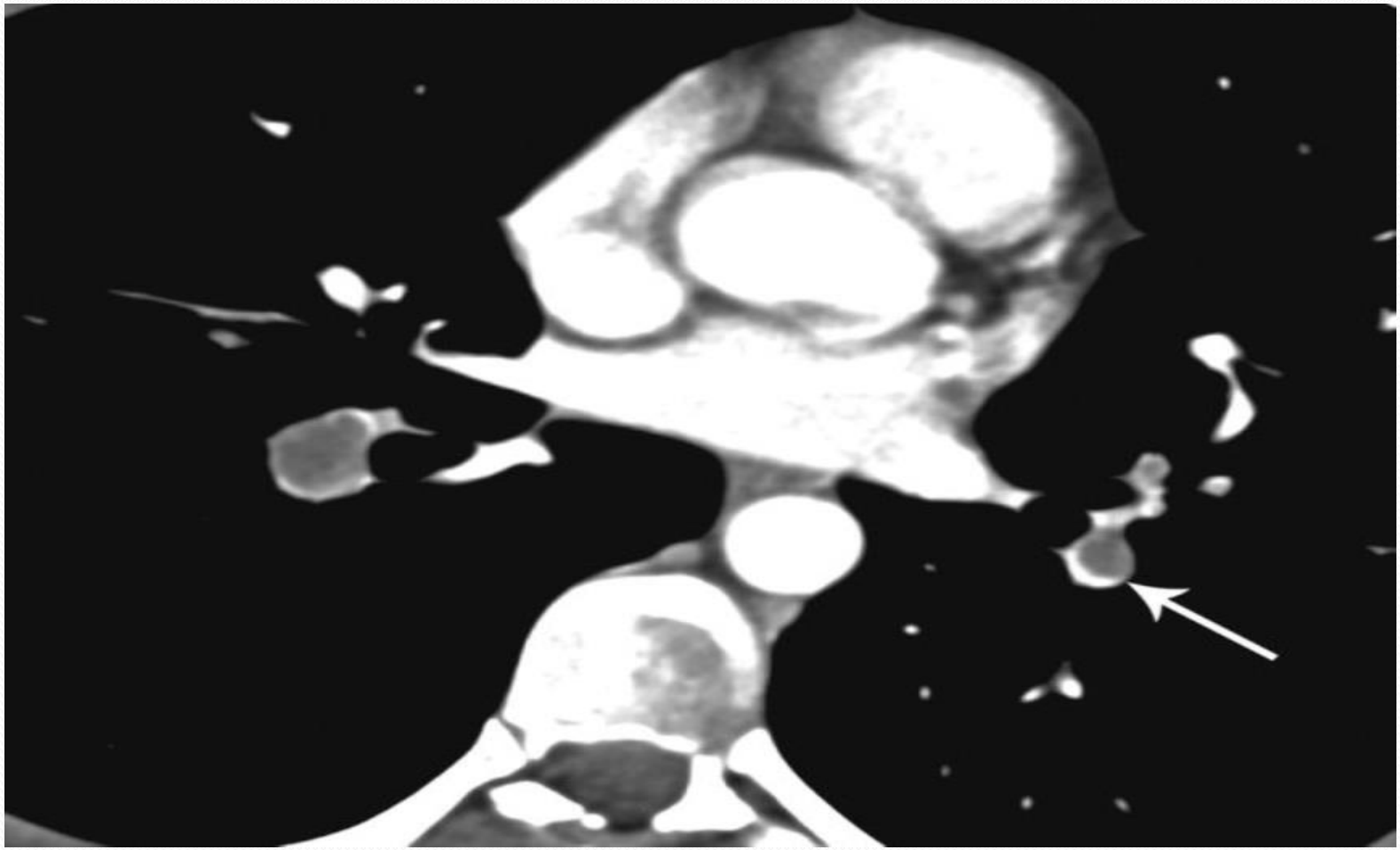
CTA provides several potential advantages over other imaging modalities in the diagnosis of PE, including:

(1) direct visualization of the embolus

(2) the ability to assess for other potential causes for the patient's complaints such as pneumonia

(3) imaging algorithms that scan through the pelvis and lower extremities, as well as the chest, allowing simultaneous evaluation for PE and for DVT

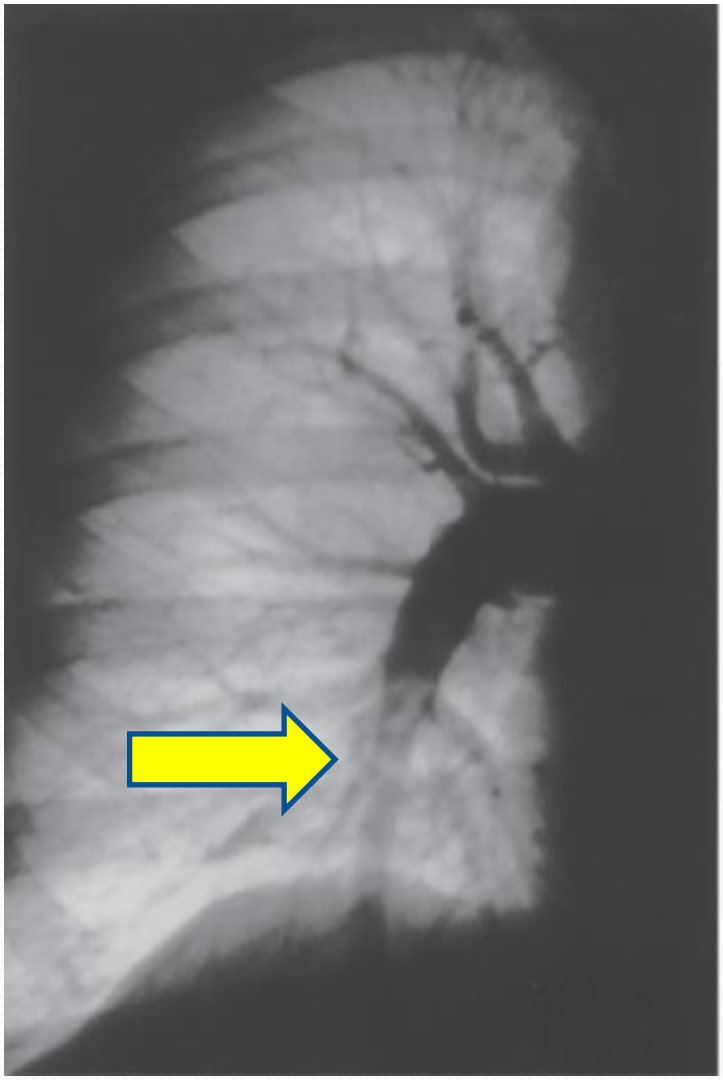


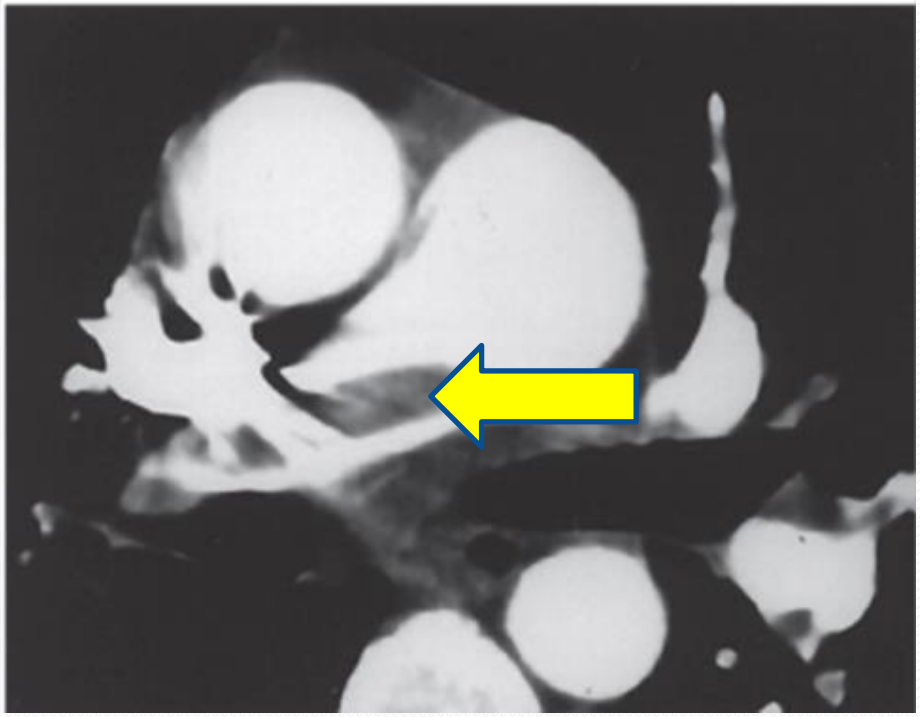


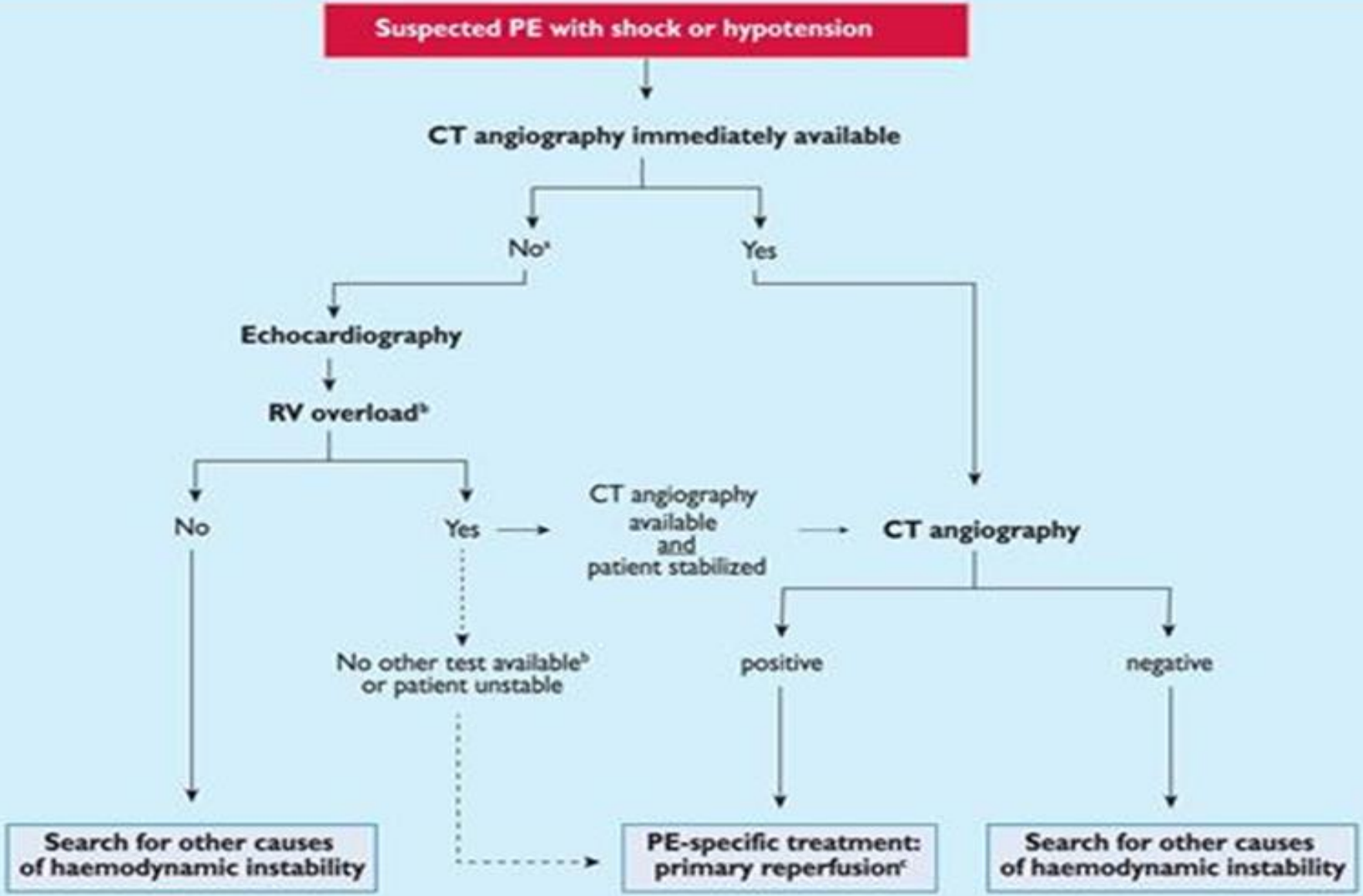
8-Pulmonary angiography

The diagnosis of acute PE is based on direct evidence of a thrombus in two projections, either as a filling defect or as amputation of a pulmonary arterial branch. Thrombi as small as 1–2 mm within the sub-segmental arteries can be visualized

Pulmonary angiography





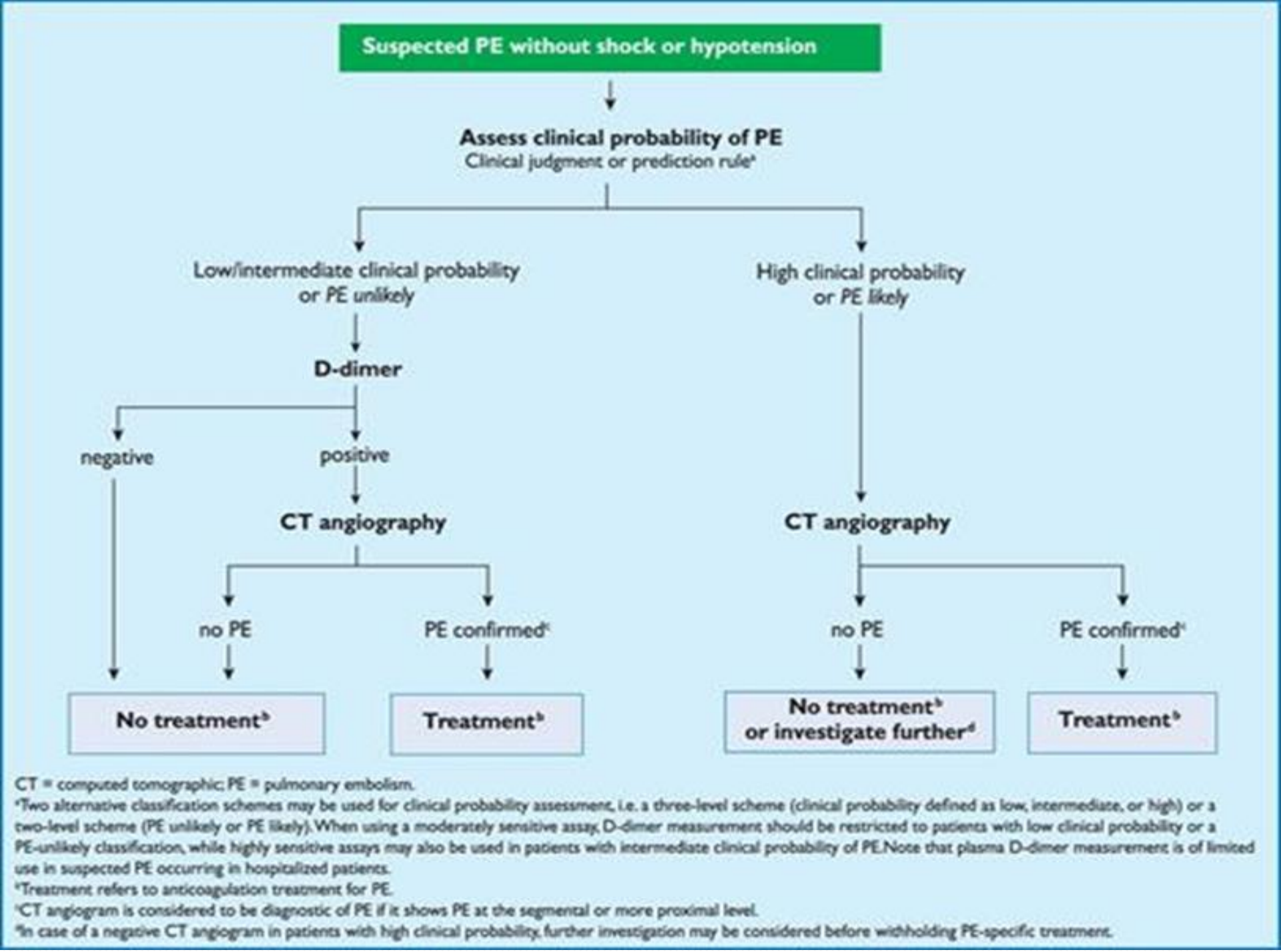


CT = computed tomographic; PE = pulmonary embolism; RV = right ventricular.

[a]Includes the cases in which the patient's condition is so critical that it only allows bedside diagnostic tests.

[b]Apart from the diagnosis of RV dysfunction, bedside transthoracic echocardiography may, in some cases, directly confirm PE by visualizing mobile thrombi in the right heart chambers. Ancillary bedside imaging tests include transoesophageal echocardiography, which may detect emboli in the pulmonary artery and its main branches, and bilateral compression venous ultrasonography, which may confirm deep vein thrombosis and thus be of help in emergency management decisions.

[c]Thrombolysis; alternatively, surgical embolectomy or catheter-directed treatment (Section 5).



CT = computed tomographic; PE = pulmonary embolism.

[a]Two alternative classification schemes may be used for clinical probability assessment, i.e. a three-level scheme (clinical probability defined as low, intermediate, or high) or a two-level scheme (PE unlikely or PE likely). When using a moderately sensitive assay, D-dimer measurement should be restricted to patients with low clinical probability or a PE-unlikely classification, while highly sensitive assays may also be used in patients with intermediate clinical probability of PE. Note that plasma D-dimer measurement is of limited use in suspected PE occurring in hospitalized patients.

[b]Treatment refers to anticoagulation treatment for PE.

[c]CT angiogram is considered to be diagnostic of PE if it shows PE at the segmental or more proximal level.

[d]In case of a negative CT angiogram in patients with high clinical probability, further investigation may be considered before withholding PE-specific treatment.

Treatment

Indication for hospitalization :

1-Older patients who may have less cardiopulmonary reserve, or significant coexisting illnesses

2-Those who may not be able to follow instructions or have adequate follow-up.

3-Hypoxemia, hypotension, hemodynamic instability

1-Heparin

The major anticoagulant effect of heparin is to reduce thrombus propagation and prevent embolic recurrence. Choices include either intravenous unfractionated heparin (UFH) or subcutaneous LMWH preparation.

Unfractionated heparin (UFH) should be considered (a) as a first dose bolus, (b) in massive PE, or (c) where rapid reversal of effect may be needed.

Dosing regimen

.using an initial intravenous bolus of 80 units of heparin per kilogram followed by a continuous infusion initiated at 18 U/kg/h.

.The heparin drip is adjusted based on monitoring of the aPTT, drawn 6 hours after the initial bolus dose, then 6 hours after each dose adjustment, with a target aPTT ratio of 1.5 to 2.5.

.Protamine Sulphate

2-LMWH

LMWH preparations have displaced unfractionated heparin as the anticoagulant of choice in uncomplicated venous thromboembolism including PE

Advantages of LMWH compared with UFH include

(1) longer half-life and ease of use

(2) ability to consistently achieve early therapeutic anticoagulation

(3) no need to monitor anticoagulant effects

(4) reduced incidence of major bleeding complications.

Enoxaparin: 1 mg/kg every 12h

3-FACTOR XA INHIBITORS

Fondaparinux:

a. Subcutaneous administration

b. Also has been demonstrated to be efficacious in the treatment of VTE.

c. Has a relatively long half-life (17 hours) and can be administered once daily

Rivaroxaban:

Their excellent bioavailability, rapid onset, predictable effect, and ease of use will greatly facilitate outpatient therapy.

.Close monitoring of coagulation levels, as is required with the vitamin K antagonists, is unnecessary, and the risk of over- or under anticoagulation is negligible.

.One potential complicating factor regarding the use of the Xa inhibitors is the lack of a specific antidote for rapid reversal of anticoagulation.

4-Thrombolytic therapy

.Thrombolytic drugs cause direct lysis of thrombi by increasing plasmin production through plasminogen activation.

.Thrombolysis is the first line treatment for massive PE

.Streptokinase, alteplase (rt-PA), and urokinase

5-Adjuvants therapy

Oxygen

Antibiotics

Rest in bed

6-PULMONARY EMBOLECTOMY

Consider surgical embolectomy:

.Patients with persistent hypotension, shock, or cardiac arrest

.Who either failed thrombolysis or have a contraindication to thrombolytic management.

LONG-TERM MANAGEMENT

WARFARIN

.Vitamin K antagonist, is generally used for long-term treatment of venous thromboembolism because of its proven efficacy.

.Warfarin inhibits activation of coagulation factors II, VII, IX, and X as well as proteins C and S.

.Warfarin has a narrow therapeutic index and patients are generally monitored closely by measuring the prothrombin time corrected to the reagent being used (the INR). To maximize efficacy while minimizing side effects, an INR range between 2 and 3 is recommended for most patients

LONG-TERM MANAGEMENT

NOVEL AGENTS:

Novel agents are new oral anticoagulant, have been used successfully for long-term management of patients with venous thromboembolism. As noted previously, rivaroxaban used for the initial and long-term treatment of PE with or without DVT.

Table 57-4 Recommendations for Duration of Anticoagulation in Patients Diagnosed With Venous Thromboembolism (VTE)

Indication for Anticoagulation	Duration of Therapy
First VTE with reversible or transient risk factor	Minimum of 3 months
First episode of idiopathic VTE	Minimum of 6-12 months; consider use for indefinite period
VTE associated with malignancy	LMWH for the first 3-6 months; then indefinitely or until the malignancy resolves
First episode of VTE associated with hypercoagulable state	12 months; suggest indefinitely
Two or more documented episodes of VTE	Indefinite

LMWH, low-molecular-weight heparin.

PROPHYLAXIS

Most hospitalized patients are at risk of venous thromboembolism and should receive some form of prophylaxis unless its use is contraindicated.

Prophylaxis may not be necessary in rare instances, as in the case of a young (less than 40 years), ambulatory patient who is admitted for a short (less than 48–72 hours), hospital stay without a history of prior venous thromboembolism history.

PROPHYLAXIS

Prophylactic anticoagulation is safe and effective with an absolute reduction in the incidence of venous thromboembolism in the range of 40% to 60%.

PROPHYLAXIS

Categories of drugs have been used successfully:

A- unfractionated heparin, LMWH (enoxaparin, dalteparin),

B-factor Xa inhibitors (fondaparinux, rivaroxaban)

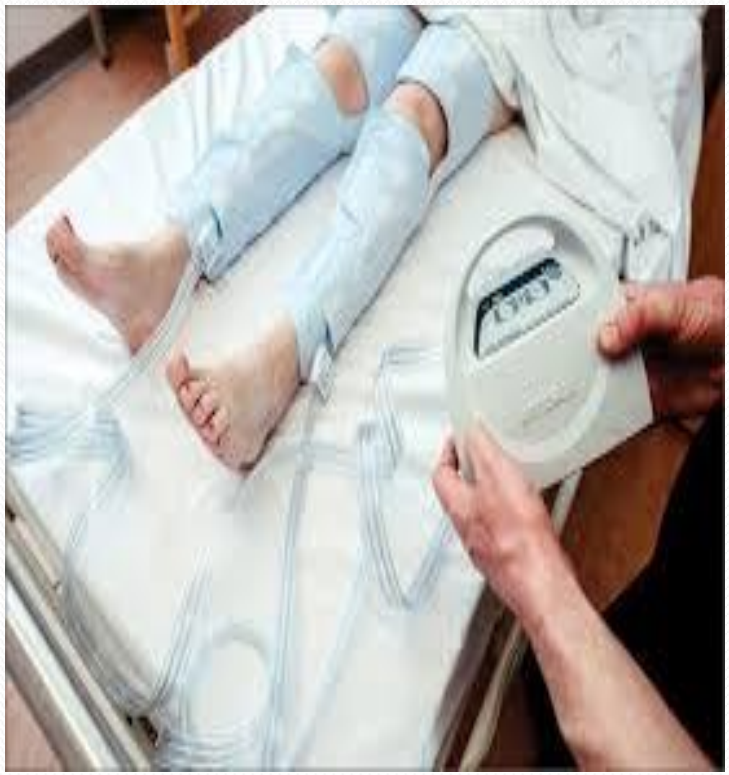
c- the vitamin K antagonist warfarin., prophylactic dosing of warfarin is subtherapeutic but sufficient to decrease the likelihood of thrombus formation.

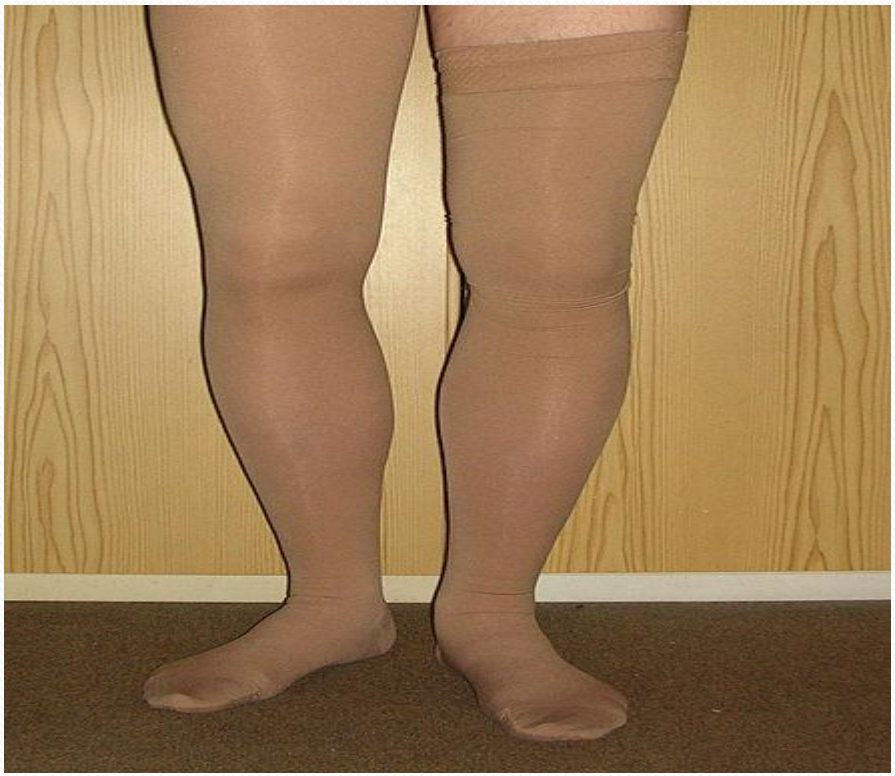
PROPHYLAXIS

Prevention of venous thromboembolism may also be achieved using mechanical devices.

These devices fall into two categories, graduated compression stockings and intermittent pneumatic compression stockings

the use of pneumatic compression has been shown in selected patients to be as effective as subcutaneous unfractionated heparin in preventing thrombosis. Mechanical methods of prophylaxis are especially useful in patients at bleeding risk.





Thank You