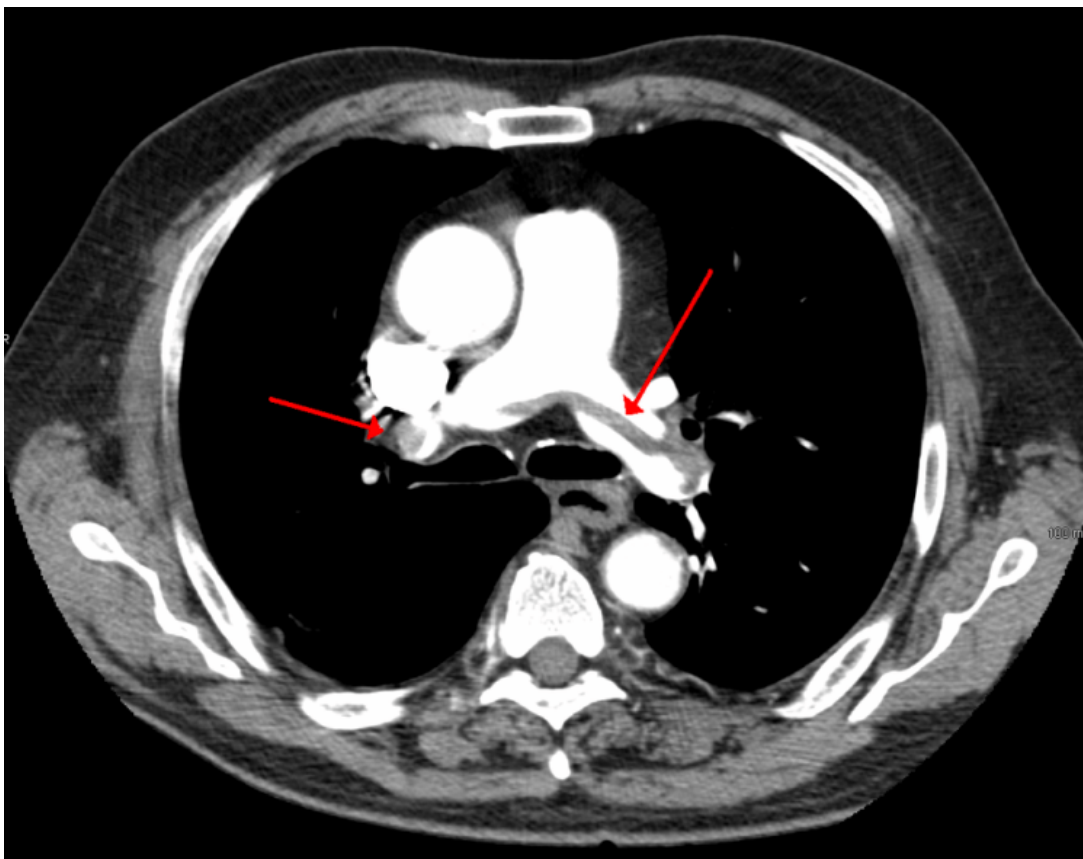


Pulmonary Embolism (PE) — Symptoms and Treatment

[See online here](#)

Pulmonary embolism (PE) is a potentially fatal clinical condition that occurs as a result of mechanical obstruction of the pulmonary artery or its branches by any material (such as thrombus, air, or fat) from anywhere in the body. Pulmonary embolism can be an acute condition, in which the signs and symptoms develop immediately after the event (i.e. the obstruction of the pulmonary vessels), or it can be chronic, in which the signs and symptoms develop progressively for years. In this article, we will review the definition, incidence, pathophysiology, risk factors, symptoms and signs, and prognosis of pulmonary embolism.



Definition of PE

Pulmonary embolism—mechanical obstruction of the

pulmonary vessels

Pulmonary embolism (PE) is a serious disease that is caused by obstruction of the pulmonary vessels mechanically by a thrombus, air, fat, or tumor elsewhere in the body, a process called embolization. PE can be classified as massive or submassive pulmonary embolism.

Epidemiology of PE

Incidence of pulmonary embolism

A study of more than 42 million deaths in a period of 20 years has shown that only about 1.5% (600,000) of the cases were diagnosed with pulmonary embolism. About 200,000 deaths were assumed to be a result of PE. Although these are large numbers, they still underestimate the true incidence of pulmonary embolism because **more than half of the patients die undiagnosed**. More cases have been diagnosed over the past few years after the introduction of the CT pulmonary angiogram.

Classification of PE

Pulmonary embolism is classified into either massive pulmonary embolism or submassive pulmonary embolism.

Massive pulmonary embolism

Massive PE causes a severe lowering of blood pressure (hypotension). It should be suspected in patients with hypotension that is associated with jugular venous distention, if the latter is not fully explained by any other underlying disease, such as acute MI, pericardial tamponade, tension pneumothorax, or new arrhythmia. Criteria for diagnosis are as follows:

- Systolic BP < 90 mm Hg or a drop in systolic BP of ≥ 40 mm Hg from the patient's baseline blood pressure.
- Hypotension should persist for over 15 minutes.

The prognosis of massive pulmonary embolism is bad, and it usually results in right ventricular dysfunction and death.

Submassive pulmonary embolism

If acute PE doesn't meet the criteria for massive PE, it is considered submassive.

Pathophysiology of PE



Image: A deep vein thrombosis of the right leg. Note the swelling and redness.
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The process of **embolization is caused by thrombi** that have formed elsewhere in the body. Thrombi commonly originate from the **deep venous system of the lower extremities** via [deep vein thrombosis \(DVT\)](#). Therefore, assessment of the lower extremities' deep veins by duplex ultrasound is important to rule out DVT, especially in bedridden patients, who are at risk of blood stagnation and formation of thrombi. Although lower-limb DVT is the most common cause of pulmonary embolism, thrombi may also originate from the right side of the [heart](#), the upper extremities, and the pelvic or renal veins.

The most clinically recognized PE results from dislodged thrombi in the iliofemoral veins. About 60–80% of the iliac, femoral, and popliteal vein thrombi arise below the popliteal vein (calf vein thrombi), then propagate proximally, while the rest of the thrombi arise from the proximal veins themselves. Upper extremity venous thrombosis became a very common problem after the increased usage of central venous catheters and insertion of permanent pacemakers and internal cardiac defibrillators (ICDs).

The problem arises when these thrombi dislodge from their sites of formation and spread to the lungs through the right side of the heart, with subsequent lodging of the large thrombi at the **bifurcation of the main pulmonary arteries or their branches** causing **hemodynamic instability**.

Sometimes, an embolus may paradoxically pass through a congenital shunt between the right and left atrium (e.g., patent foramen ovale) into the arterial circulation, causing acute lower-limb ischemia. On occasion, smaller thrombi travel more distally into the smaller pulmonary branches, then initiate inflammatory reactions adjacent to the parietal pleura, causing pleuritic chest pain. About 10% of patients, especially those with underlying cardiopulmonary disease, are at risk of pulmonary infarction. Pulmonary emboli are usually quite numerous, and in the majority of cases, they lodge in the lower lobes of the [lungs](#).

Pathophysiological abnormalities in pulmonary embolism (PE)

- Obstruction of the pulmonary vessels and secretion of vasoactive agents from the platelets result in pulmonary vasoconstriction and increased pulmonary vascular resistance. This pathophysiological abnormality can cause an embolism-induced ventilation-perfusion mismatch at remote sites.
- Impairment of gas exchange caused by:
 1. An increase in the alveolar dead space, which occurs as a result of vascular obstruction by the emboli.
 2. Hypoventilation of alveoli relative to alveolar perfusion in the non-obstructed lung.
 3. Right-to-left shunting.
 4. Impairment of carbon monoxide transfer because of lost gas exchange surface.
- Reflex stimulation of irritant receptors in the lungs may result in alveolar hyperventilation.
- Increased resistance of the airway due to constriction of the airways distal to the lungs bronchi.
- Decreased pulmonary compliance as a result of:
 1. Loss of surfactant
 2. Lung edema
 3. Lung hemo

Right ventricular (RV) dysfunction

Pulmonary embolism usually causes RV dysfunction and progressive right-sided heart failure. This is due to increased pulmonary vascular resistance and right ventricular (RV) wall tension, resulting in further RV dilatation and dysfunction.

Risk Factors of PE

The most common risk factor for pulmonary embolism is deep vein thrombosis (DVT), which accounts for about 50% of PE cases. The other risk factors account for the remaining 50% of the cases and include:

- Immobilization
- Surgery within the last 3 months
- Stroke
- Paresis
- Paralysis
- Central venous catheterization within the last 3 months
- Malignancy
- Chronic heart disease
- Autoimmune diseases
- History of venous thromboembolism
- Risk factors in women include obesity ($\text{BMI} \geq 29 \text{ kg/m}^2$), heavy cigarette smoking (> 25 cigarettes per day) and hypertension

Symptoms of PE

Signs of pulmonary embolism

Symptoms and signs of PE are not exclusive; they can occur in a patient without pulmonary embolism, and clinicians can't depend on them to confirm or exclude PE. Occult pulmonary embolism often remains undiagnosed in the presence of concomitant heart failure or [pneumonia](#). In such conditions, patients usually fail to respond to the standard medical treatment of the concomitant condition.

Most common symptoms of pulmonary embolism are:

1. [Dyspnea](#) at rest or with exertion, which starts suddenly, within seconds or minutes
2. Pleuritic pain
3. Cough
4. Orthopnea
5. Calf pain
6. Swelling of the calf or thigh
7. Wheezing

Most common signs of pulmonary embolism are:

1. Tachypnea
2. Tachycardia
3. Rales
4. Decreased breath sounds
5. Accentuated pulmonic component of the 2nd heart sound (P2)
6. Jugular venous distension

Massive pulmonary embolism can be associated with **RV dysfunction**, which manifests as:

1. An increased jugular venous pressure
2. Right-sided S3 [heart sound](#)
3. Parasternal heave

As deep vein thrombosis (DVT) is the most common cause of PE, symptoms, and signs of DVT have been found in more than 57% of cases of pulmonary embolism (PE). These include erythema, edema, tenderness, or a palpable cord in the calf or thigh.

Clinicians should realize that **PE is very frequently asymptomatic**, especially if it's submassive PE, which can manifest as oxygen desaturation without concomitant symptoms or signs suggestive of pulmonary embolism.

Investigations of PE

As symptoms and signs of pulmonary embolism are variable and not specific, additional diagnostic tests are important to help diagnose PE.

Non-imaging diagnostic modalities

Laboratory tests

Routine lab tests (not specific)	<ol style="list-style-type: none"> 1. Leukocytosis 2. Increased erythrocyte sedimentation rate (ESR) 3. High serum LDH or AST with a normal serum bilirubin level
Arterial blood gas (ABG)	<p>Arterial blood gas (ABG) usually reveals:</p> <ol style="list-style-type: none"> 1. Hypoxemia 2. Hypocapnia 3. Respiratory alkalosis <p>These typical ABG findings are not frequently seen, as:</p> <ol style="list-style-type: none"> 1. Massive PE with circulatory collapse and hypotension can cause hypercapnia with a combined respiratory acidosis and metabolic acidosis (high lactic acid). 2. Hypoxemia can be absent or minimal. 3. 18 % of patients have PO₂ between 85–105 mm Hg.
Brain natriuretic peptide (BNP)	<ul style="list-style-type: none"> • Levels of BNP can be elevated in patients with PE. • It's an insensitive test because it is not elevated in some patients with pulmonary embolism. • It's a nonspecific test because it can be elevated by other causes. • Sensitivity and specificity of BNP is only 60%.
Troponin	<p>Troponin I and T levels can be elevated in 50% of patients with large PE. Elevated troponin levels usually resolve rapidly, within 40 hours, in patients with PE—in contrast to the longer duration in patients with myocardial infarction.</p>
D-Dimer	<ul style="list-style-type: none"> • It's a product of the degradation of cross-linked fibrin. • It has good sensitivity and -ve predictive value and poor specificity and +ve predictive value (i.e. good negative test). • If quantitative assays are used, a level > 500 ng/mL is considered abnormal. • If D-Dimer level is < 500 ng/mL using quantitative ELISA or semi-quantitative latex agglutination → it excludes PE in patients with a low or moderate pretest probability of PE.

Electrocardiography (ECG)

[ECG](#) changes can be observed in a person without PE, which limits the role of ECG in PE diagnosis. The characteristic ECG abnormalities that are commonly present in massive PE and cor pulmonale are as follows:

- S1Q3T3 pattern
- Right ventricular strain → T-wave inversion in chest leads may indicate severe RV dysfunction
- New, incomplete, right bundle branch block

Some ECG changes may indicate poor prognosis, such as:

1. Atrial arrhythmias
2. Right bundle branch block
3. Inferior Q waves
4. Precordial T-wave inversion and ST-segment changes

Non-invasive imaging modalities

Chest CT with contrast (CT pulmonary angiography)

Chest CT with contrast is an important noninvasive imaging modality used to diagnose PE. It is now considered to be the **gold standard in PE investigation** and has largely replaced the invasive modalities. Chest CT also provides very good images of both ventricles of the heart. RV enlargement may indicate a greater risk of death within the following 30 days as compared to a patient with PE without RV enlargement.

Ventilation/perfusion scan (V/Q scan)

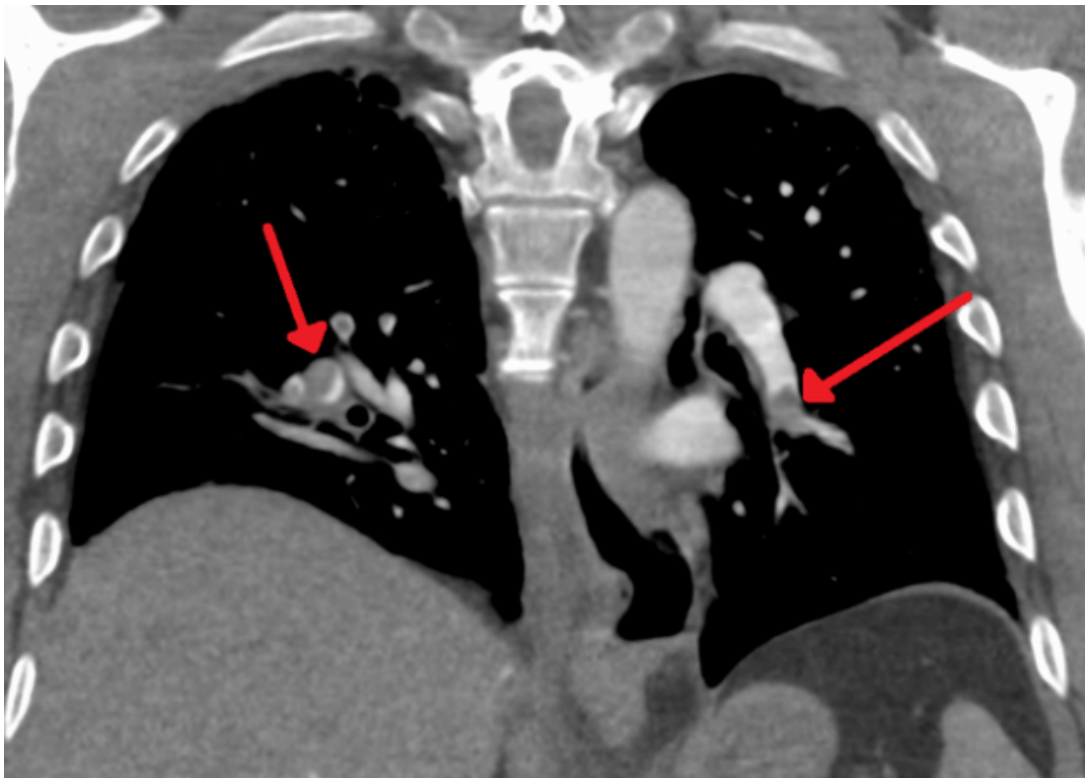


Image: Segmental and subsegmental pulmonary emboli on both sides, by James Heilman, MD. License: [CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/)

A lung scan is considered the **second-line diagnostic modality** for patients with pulmonary embolism who can't tolerate IV contrast due to risk of contrast-induced nephropathy. The diagnosis involves intravenous administration of albumin labeled with gamma-emitting radionuclides, which then get trapped in the pulmonary capillary bed.

- **Perfusion scan:** Perfusion defect indicates decreased or absent pulmonary blood flow.
- **Ventilation scan:** Abnormal ventilation indicates nonventilated areas in the lungs.

High-probability V/Q scan is defined as the presence of two or more segmental perfusion defects with normal ventilation.

Echocardiography

Echocardiographic findings suggestive of pulmonary embolism are observed in only **30-40% of patients**, especially those with massive PE, and include:

- Increased right ventricular (RV) size
- Decreased RV function
- Tricuspid regurgitation
- RV thrombus
- **McConnell's sign:** Regional wall motion abnormalities, which spare the apex of the RV

Venous ultrasonography

Normal veins are compressible when gentle pressure is applied via the ultrasound transducer. **Loss of normal compressibility of the vein due to the effects of the acute thrombus** is considered the primary criterion for diagnosis of DVT. The diagnosis of DVT can be confirmed largely by visualization of the homogeneous thrombus. Presence

of DVT suggests diagnosis of pulmonary embolism, and the patient should receive PE treatment.

Chest radiography

Radiographic changes in patients with pulmonary embolism are not specific and can also be observed in someone without PE. These include:

- Atelectasis or pulmonary parenchymal abnormality
- Pleural effusion
- Cardiomegaly

Invasive imaging modalities

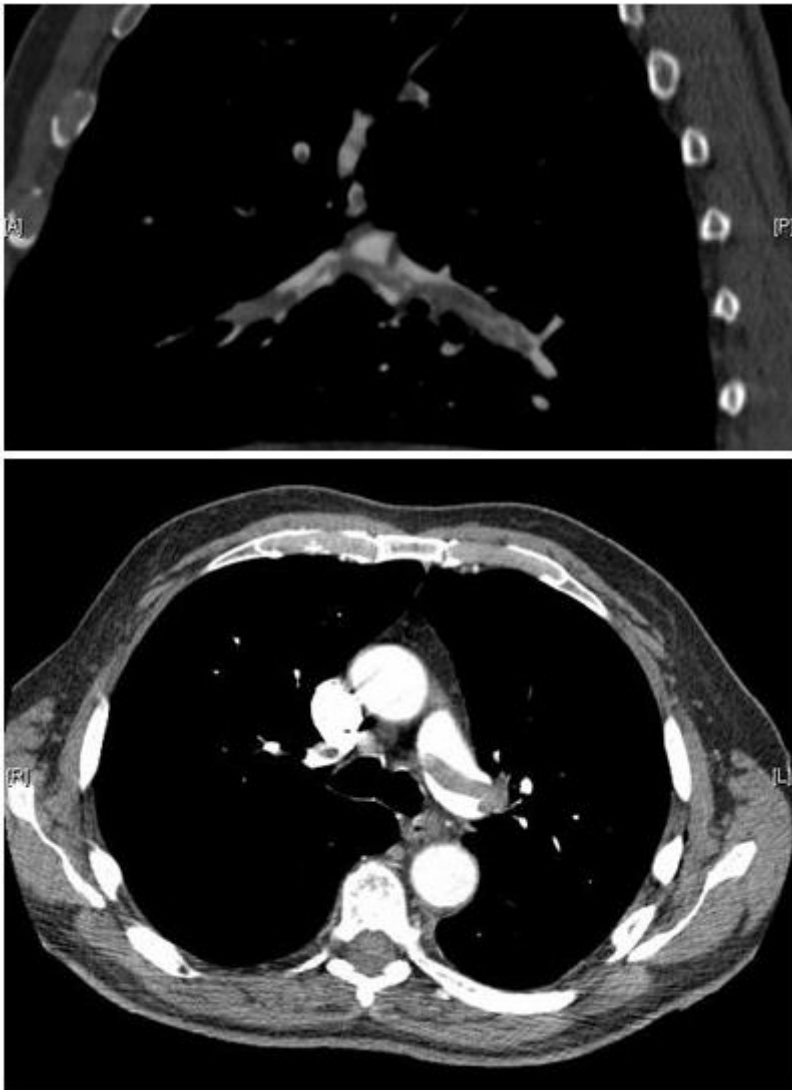


Image: CT pulmonary angiography images confirming the presence of a saddle embolus and substantial thrombus burden in the lobar branches of both main pulmonary arteries, by Aung Myat and Arif Ahsan. License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

Pulmonary angiography

This invasive modality involves percutaneous catheterization of the pulmonary artery or one of its branches, usually via the femoral vein, and then injection of contrast dye to delineate the pulmonary vasculature. Although it is considered the definitive diagnostic modality of pulmonary embolism, it has been replaced largely by **spiral CT chest with**

contrast. Pulmonary angiography is now reserved for only two situations:

1. If the diagnosis of PE is not successful using CT scan
2. If the patient might undergo catheter-directed thrombolysis or embolectomy

Diagnosis of PE

There are scoring methods that are useful in estimating the patient's likelihood of DVT and pulmonary embolism (PE):

• The score is zero or less → Low clinical likelihood of DVT • 1 to 2 → Moderate likelihood • 3 or greater → High likelihood	
Clinical variable	Score
Active cancer	1
Paralysis, paresis, or recent cast	1
Bedridden for > 3 days; major surgery < 12 weeks	1
Tenderness along with distribution of deep veins	1
Entire leg swelling	1
Unilateral calf swelling > 3 cm	1
Pitting edema	1
Collateral superficial non-varicose veins	1
Alternative diagnosis at least as likely as DVT	-2
High clinical likelihood of PE if point score exceeds 4	
Major criteria	Score
Signs and symptoms of DVT	3.0
Alternative diagnosis less likely than PE	3.0
Heart rate > 100/min	1.5
Immobilization > 3 days; surgery within 4 weeks	1.5
Prior PE or DVT	1.5
Hemoptysis	1.0
Cancer	1.0

Treatment of PE

Resuscitation

If pulmonary embolism is suspected in any patient, the clinician should focus first on stabilizing the patient, which requires:

Respiratory support

The patient should receive **high-flow oxygen** (about 60-100%) if hypoxemia is present. Severe hypoxemia and respiratory failure may require intubation and mechanical ventilation.

Hemodynamic support

Hemodynamic support should be provided to a patient with massive PE and hypotension with systolic blood pressure < 90 mm Hg or a drop in systolic BP greater than or equal to 40 mm Hg from baseline. Hemodynamic support involves:

1. **IV fluid** administration, which is considered the first line of treatment.
2. If the patient's hemodynamic state is not improved with fluids, then IV vasopressor

therapy, such as norepinephrine, dopamine, dobutamine, or epinephrine, should be considered.

Empirical anticoagulant

If the physician suspects a pulmonary embolism, empirical anticoagulation using **subcutaneous low-molecular-weight heparin** is indicated, provided there is no excess risk for bleeding.

Post-resuscitation

Anti-coagulation therapy

If the further evaluation of the patient **excludes** the presence of PE, then empirical anticoagulation should be discontinued, and an alternate diagnosis should be considered.

If the further evaluation of the patient **confirms** the presence of PE, then anticoagulant treatment should be initiated or continued, if it has already been empirically started.

Clinicians can easily use subcutaneous low-molecular-weight heparin (LMWH) without partial thromboplastin time (PTT) monitoring, or unfractionated heparin (UH) with target PTT of 50–70 seconds. LMWH should be administered for at least 5 days as a bridge, during which oral warfarin is given concomitantly. Stop the LMWH when the international normalized ratio (INR) target is reached (2–3).

Duration of oral anticoagulation:

- A patient with persistent risk factors or a history of previous PE should be given an oral anticoagulant for life to avoid further events.
- Patients with reversible and identifiable risk factors should be given an oral anticoagulant for 3 months only.
- Anticoagulation for a period of 6 months is recommended if the condition is idiopathic or the risk factors are weak.

Fibrinolytic therapy

Thrombolytic therapy, such as streptokinase, will remove the pulmonary emboli rapidly and provide a survival benefit in massive pulmonary embolism. It's indicated in:

- Hemodynamically unstable patients with massive PE
- Hemodynamically stable patients with adverse outcomes, such as RV dysfunction

Inferior vena cava (IVC) filters

IVC filters provide a guard barrier in the inferior vena cava preventing the large emboli from passing to the lungs. Placement of IVC filters is generally indicated if:

- There are contraindications to anticoagulation
- Anticoagulation failed
- The patient developed complications due to administered anticoagulation

Embolectomy

Embolectomy is the **removal of the embolus**. This can be accomplished surgically or by using a catheter directed to the involved pulmonary branch. Embolectomy is indicated when the patient has massive PE with hemodynamic instability, and thrombolytic therapy has failed or is contraindicated.

Prognosis of PE

Patients who have a history of **PE carry a high risk for repeated episodes** in the future, especially if there are associated with persistent risk factors. The highest risk of recurrence is in the first 6 to 12 months after the previous event. About one-third of patients will suffer from new episodes of PE if risk factors are persistent. The risk of recurrence is low in patients with reversible or temporary risk factors.

The mortality rate is highest in patients with echocardiographic findings of RV dysfunction or cardiogenic shock. Most people with RV dysfunction will attain normal RV function within 3 weeks. Pulmonary hypertension (PHTN) may persist in about 5% of the patients for about 2 years. A few patients may progress into overt RV failure and develop signs and symptoms of right-sided heart failure.

Review Questions

The correct answers can be found below the references.

1. A 59-year-old male patient, who smokes and is hypertensive, recently had a total hip replacement. At 3 days post-operative, the patient started to complain of unexplained acute shortness of breath, tachypnea, and drowsiness. His blood pressure was 90/60 mm Hg and his heart rate was 120 beats/minute. ECG showed right-axis deviation with ST-segment depression and T-wave inversion in V1-V3. The patient is suspected to have a massive pulmonary embolism. Which of the following is the gold standard diagnostic test to confirm the diagnosis of pulmonary embolism?

- A. CT pulmonary angiography
- B. Echocardiography
- C. Elevated D-Dimer test
- D. Chest X-ray

2. A 60-year-old man presented with confirmed pulmonary embolism; the risk factors were identified and reversible. Which of the following is the recommended duration of anticoagulation for this patient to prevent further similar events?

- A. Lifelong
- B. 6 months
- C. 3 months
- D. 12 months

3. The diagnosis of which common risk factor confirms the diagnosis of pulmonary embolism?

- A. Deep vein thrombosis (DVT)
- B. Continuous immobilization
- C. Recent surgery within the last 3 months
- D. History of malignancy

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Correct answers: 1A, 2C, 3A

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Notes