Pulmonary Embolism (PE) — Symptoms and Treatment

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Pulmonary embolism (PE) is a 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, you will be able to understand the definition, incidence, pathophysiology, risk factors, symptoms and signs and the prognosis of pulmonary embolism.

Definition of PE

Pulmonary embolism — mechanical obstruction of the
pulmonary vessels

Pulmonary embolism (PE) is a serious disease, which 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 into massive or submassive pulmonary embolism.

Epidemiology of PE

Incidence of pulmonary embolism

A study on 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. 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 since 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 angiography.

Classification of PE

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

Massive pulmonary embolism

Massive PE causes 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 of diagnosis are:

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

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

Submassive pulmonary embolism

If acute PE doesn’t meet the criteria of massive PE, then it’s considered as submassive.

Pathophysiology of PE
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 venous thrombosis (DVT). Therefore, assessment of the lower extremities’ deep veins by duplex is important to rule out DVT, especially in bedridden patients because they are at risk of blood stagnation and formation of thrombi. Although lower limbs 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**, insertion of permanent pacemakers and internal cardiac defibrillators (ICD).

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. 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 lodge in the lower lobes of the **lungs**.

Pathophysiological abnormalities in pulmonary
embolism (PE)

- Obstruction of the pulmonary vessels and secreting vasoactive agents from the platelets result in pulmonary vasoconstriction and increased pulmonary vascular resistance. This pathophysiological abnormality can cause an embol-induced ventilation-perfusion mismatching at remote sites.
- Impairment of gas exchange caused by:
  1. An increase in the alveolar dead space, which occurs as 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-side heart failure. This is due to increased pulmonary vascular resistance and the right ventricular (RV) wall tension, resulting in further RV dilatation and dysfunction.

Risk Factors of PE

The most common risk factor of pulmonary embolism is deep venous thrombosis (DVT), which accounts in 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 instrumentation within the last 3 months
- Malignancy
- Chronic heart disease
- Autoimmune diseases
- History of venous thromboembolism
- Risk factors in women include obesity (BMI ≥ 29 kg/m2), 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 so clinicians can’t depend on them to confirm or exclude PE. Occult pulmonary embolism is hardly diagnosed in 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 venous thrombosis (DVT) is the most common cause of PE, symptoms and signs of DVT have been found in more than 57 % of the 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 you in diagnosing the PE.

**Non-imaging diagnostic modalities**

**Laboratory tests**

<table>
<thead>
<tr>
<th>Routine lab tests (not specific)</th>
<th>1. Leukocytosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2. Increased erythrocyte sedimentation rate (ESR)</td>
</tr>
<tr>
<td></td>
<td>3. High serum LDH or AST with a normal serum bilirubin</td>
</tr>
</tbody>
</table>
**Arterial blood gas (ABG)**

Arterial blood gas (ABG) usually reveals:
1. **Hypoxemia**
2. **Hypocapnia**
3. **Respiratory alkalosis**

These typical ABG findings are not frequently seen, as:
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 PO$_2$ between 85–105 mmHg.

| Brain natriuretic peptide (BNP) | • Levels of BNP can be greater in patients with PE.
|                               | • It’s a insensitive test as it is not elevated in some patients with pulmonary embolism.
|                               | • It’s a non-specific test as it can be elevated by other causes.
|                               | • **Sensitivity and specificity of BNP is only 60%**.

**Troponin**

Troponin I and T can be elevated in 50% of the patients with large PE and usually resolve rapidly, within 40 hours, in patients with PE—in contrast to the longer duration in patients with myocardial infarction.

| D-Dimer | • 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 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:

- 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 non-invasive 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)**
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 a 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 non-ventilated areas in the lungs.

High-probability V/Q scan is defined as 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](https://example.com)

**Pulmonary angiography**

This invasive modality involves percutaneous catheterization of the pulmonary artery or one of its branches, usually via the femoral vein, and then injecting the 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**
Pulmonary angiography is now only reserved for two situations:

1. If diagnosis of PE is not successful using CT scan;
2. If patient might suffer catheter-used thrombolysis or embolectomy.

Diagnosis of PE

There are score methods useful in estimating the patient’s likelihood of DVT and pulmonary embolism (PE):

<table>
<thead>
<tr>
<th>Clinical variable</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer</td>
<td>1</td>
</tr>
<tr>
<td>Paralysis, paresis, or recent cast</td>
<td>1</td>
</tr>
<tr>
<td>Bedridden for &gt; 3 days; major surgery &lt; 12 weeks</td>
<td>1</td>
</tr>
<tr>
<td>Tenderness along distribution of deep veins</td>
<td>1</td>
</tr>
<tr>
<td>Entire leg swelling</td>
<td>1</td>
</tr>
<tr>
<td>Unilateral calf swelling &gt; 3 cm</td>
<td>1</td>
</tr>
<tr>
<td>Pitting edema</td>
<td>1</td>
</tr>
<tr>
<td>Collateral superficial non-varicose veins</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis at least as likely as DVT</td>
<td>-2</td>
</tr>
</tbody>
</table>

High clinical likelihood of PE if point score exceeds 4

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs and symptoms of DVT</td>
<td>3.0</td>
</tr>
<tr>
<td>Alternative diagnosis less likely than PE</td>
<td>3.0</td>
</tr>
<tr>
<td>Heart rate &gt; 100/min</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization &gt; 3 days; surgery within 4 weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Prior PE or DVT</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Treatment of PE

Resuscitation

If pulmonary embolism is suspected in any patient, clinicians 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 mmHg or a drop in the systolic BP more than or equal to 40 mmHg from the patient’s 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 should be considered, such as norepinephrine, dopamine, dobutamine or epinephrine.

**Empirical anticoagulant**

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

**Post-resuscitation**

**Anti-coagulation therapy**

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

If further evaluation of the patient confirms the presence of PE, then anti-coagulant treatment should be initiated or continued, if it has already been empirically started. Clinicians can easily use subcutaneous, low-molecular-weight heparin (LMWH) without PTT monitoring, or unfractionated heparin (UH) with target PTT of 50–70. LMWH should be administered for at least 5 days as a bridge, during which oral warfarin is given concomitantly. Stop the LMWH when the patient’s INR target is reached (2-3).

**Duration of oral anti-coagulation:**

- A patient with persistent risk factors or history of previous PE should be given an oral anti-coagulant for life, to avoid further events.
- Patients with reversible and identifiable risk factors should be given an oral anti-coagulant for 3 months only.
- Anti-coagulation 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 survival benefit in massive pulmonary embolism. It’s indicated in:

1. Hemodynamically unstable patients with massive PE;
2. 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:

1. There are contraindications to anti-coagulation;
2. Anti-coagulation failed;
3. The patient developed complications due to administered anti-coagulation.

**Embolectomy**

Embolectomy is the removal of the emboli. 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 where the thrombolytic therapy failed or contraindicated.
**PE Prognosis**

Patients who have a history of PE carry a high risk for repeated episodes in the future, especially if there are associated persistent risk factors. The highest risk of recurrence is in the first 6 to 12 months after the previous event, and about one-third of the patients will suffer from new episode 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, and persistent pulmonary hypertension (PHTN) may exist in about 5% of the patients for about two years. A few patients may progress into overt RV failure and develop signs and symptoms of Right-side heart failure.

**Review Questions**

The correct answers can be found below the references.

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

   A. ...CT pulmonary angiography.
   B. ...echocardiography.
   C. ...elevated D-Dimer test.
   D. ...chest x-ray.

2. **A 60-year-old male patient presented with confirmed pulmonary embolism; the risk factors were identified and reversible. The duration of anti-coagulation for this patient to prevent further similar events is...**

   A. ...anti-coagulation for life.
   B. ...anti-coagulation for 6 months.
   C. ...anti-coagulation for 3 months.
   D. ...anti-coagulation for 12 months.

3. **This most common risk factor for pulmonary embolism, whose diagnosis would confirm diagnosis of PE, is...**

   A. ...deep venous thrombosis (DVT).
   B. ...continuous immobilization.
   C. ...recent surgery within the last 3 months.
   D. ...history of malignancy.

**References**


PARK B et al: Recent trends in clinical outcomes and resource utilization for pulmonary


Correct answers: 1A, 2C, 3A

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