ABSTRACT:
Acute pulmonary embolism (PE) is the obstruction of pulmonary artery or one of its branches by material that originated elsewhere in the body. Clinical features of acute PE are variable and nonspecific. Diagnostic testing is necessary to confirm a diagnosis of acute PE. Modified Wells criteria are applied to determine whether PE is unlikely or likely. Diagnosis of PE can be excluded in patients with clinically unlikely PE and D-dimer level < 500 ng/mL. A positive CT-pulmonary angiography (CTPA) or V/Q scan in patients classified as PE clinically likely confirms the diagnosis of PE. Anticoagulation is the mainstay of treatment and should be started at the earliest with subcutaneous low molecular weight heparin (LMWH) or intravenous unfractionated heparin (UFH). This is followed by warfarin which is overlapped with heparin for a minimum of five days. Anticoagulation is given for three months (in patients with reversible risk factors) to indefinitely. Thrombolysis may be given to patients of acute PE with persistent hypotension and no risk of increased bleeding. Inferior vena cava (IVC) filters are placed in patients where anticoagulation is contraindicated or there is recurrent PE despite adequate anticoagulation therapy. Embolectomy is considered in patients with severe persistent hypotension due to acute PE where thrombolysis is contraindicated or failed.

Introduction: Acute pulmonary embolism refers to acute obstruction of the pulmonary artery or one of its branches by material (e.g., thrombus, tumor, air, or fat) that originated elsewhere in the body. Most of the cases of PE are caused by blood clots that arise from the deep veins of the lower and upper extremities. Acute PE is associated with mortality rate of 30% without treatment which is reduced to 2-8 % with treatment. In a study of 42 million deaths over a period of 20 years, PE was found to be the cause of death in 1.5% patients [1]. However, true incidence and prevalence of PE is likely to be higher as more than half of all PEs are undiagnosed.

RISK FACTORS [2-5]:
Hereditary
1. Factor V Leiden and prothrombin gene mutations
2. Defects in Protein S, Protein C
3. Homocysteinemia
Acquired risk factors
1. Immobilization
2. Surgery within the last three months
3. Stroke
4. Paresis/paralysis
5. History of venous thromboembolism
6. Malignancy
7. Central venous instrumentation within the last three months
8. Chronic heart disease
9. Nephrotic syndrome
10. Women with obesity (BMI ≥ 29 kg/m2), heavy cigarette smoking, oral contraceptive and pregnancy.

Symptoms and signs [2-6]: Specific symptoms and signs are not helpful diagnostically because their frequency is similar among patients with and without PE. Common symptoms are dyspnoea (73%), pleuritic pain (44%), cough (34%), calf or thigh swelling/pain (41-44%), and wheezing (21%). The most common signs are tachypnoea (54%), tachycardia (24%), rales (18%), decreased breath sounds (17%), accentuated pulmonary component of
second heart sound (P2) (15 %), and jugular venous distension (14 %). Circulatory collapse is uncommon (8 %). Massive PE may be accompanied by acute right ventricular failure. Symptoms or signs of lower extremity deep venous thrombosis (oedema, erythema, tenderness, or a palpable cord in the calf or thigh) are present in around 47 % cases.

**DIAGNOSIS [7-9]:**

Clinical presentation of PE is variable and nonspecific. Thus, diagnostic testing (table 1) is necessary before confirming or excluding the diagnosis of PE.

**NONIMAGING DIAGNOSTIC MODALITIES:**

**Blood test:** Routine laboratory findings include leucocytosis, increased ESR, and elevated serum LDH or SGOT. These tests are not very useful in the diagnosis of PE.

**Arterial blood gas —** ABGs usually reveal hypoxemia, hypocapnia, and respiratory alkalosis but depending on the clinical situation ABG finding may vary also [10].

**D-dimer —** D-dimer is a degradation product of cross-linked fibrin. A level >500 ng/mL is considered abnormal. D-dimer assays have good sensitivity and negative predictive value, but poor specificity and positive predictive value. D-dimer levels are abnormal in 95 % of patients with PE. However, they are abnormal in only 50 percent of patients with subsegmental PE. Patients with normal D-dimer levels have a 95 percent likelihood of not having PE. D-dimer level <500 ng/mL is usually sufficient to exclude PE unless the pretest probability of PE is high. Abnormal D-dimer levels even without PE are common among hospitalized patients, especially those with malignancy or recent surgery [11].

**Brain natriuretic peptide —** Brain natriuretic peptide (BNP) levels are typically greater in patients with PE compared to patients without PE. However, many patients with PE do not have elevated BNP levels and also there are many alternative causes of an elevated BNP level [12].

**Troponin —** Serum troponin I and troponin T are elevated in 30 to 50 percent of patients with PE. However, Serum troponins are not useful for diagnosis of PE; but patients with elevated troponin level have increased risk of death [3, 8, 9].

**Electrocardiography —** There is limited diagnostic usefulness of ECG in PE. S1Q3T3 pattern, right ventricular strain, new incomplete right bundle branch block are uncommon findings during acute PE. However, they are common among patients with massive acute PE and cor pulmonale. Atrial arrhythmias, right bundle branch block, T-wave inversion and ST-segment changes are associated with a poor prognosis [14].

**NONINVASIVE IMAGING MODALITIES**

**Chest radiography —** Radiographic abnormalities including focal oligemia (Westermark’s sign), peripheral wedged shaped density (Hampton’s hump), or an enlarged right descending pulmonary artery (Palla’s sign) are some of the finding of acute PE, though chest x-ray may be normal in many cases of acute PE [15].

**Echocardiography —** Only 30 to 40 percent of patients with PE have echocardiographic abnormalities suggestive of acute PE: (a) increased right ventricular (RV) size, (b) decreased RV function, and (c) tricuspid regurgitation. Additional echocardiographic findings suggestive of PE include: (d) RV thrombus and (e) regional wall motion abnormalities that spare the right ventricular apex [16].

**Ultrasound —** Duplex ultrasound (combination of Doppler venous flow and real time B-mode imaging) of lower extremity venous ultrasound is performed during the diagnostic evaluation of PE. Venous thrombosis detected by ultrasound is treated similar to confirmed PE [17].

**V/Q scan —** The perfusion scan defect indicate absent or decreased blood flow due to PE. A high probability scan for PE is defined as having two or more segmental perfusion defects in the presence of normal ventilation. Diagnosis of PE is very unlikely in patients with normal scans [18].

**Spiral CT —** CT pulmonary angiography (CT PA) is being used increasingly as a diagnostic modality for patients with suspected PE. CT-PA may also detect alternative pulmonary abnormalities that may explain the patient’s clinical presentation. Clinicians should consider the pretest probability of PE when deciding whether to use CT-PA. There is a low risk of PE following a negative CT-PA.A positive CT-PA in a patient with intermediate or high probability of disease confirms PE. Role of CT venography of lower extremity in evaluation of PE is limited [19].

**MRI —** The use of magnetic resonance angiography (MRA) for the diagnosis of PE is limited at present by respiratory and cardiac motion artifact. However it is reported to be at least as sensitive and specific as duplex ultrasonography in detecting venous thrombosis [20].

**Invasive Diagnostic modalities**

**Angiography —** Pulmonary angiography is the "gold standard" in the diagnosis of acute PE. A filling defect or abrupt cutoff of a small vessel is indicative of PE. Pulmonary angiography is generally safe and well tolerated in the absence of haemodynamic instability. Using 64-MDCT and above scanners in future visualization of PE will improve further [21].

**DIAGNOSTIC APPROACH**

**Institutions with facilities for CT Pulmonary Angiography (CTPA)**

When PE is suspected, the modified Wells criteria should be applied to determine if PE is unlikely (score <4) or likely (score >4). The modified Wells Criteria include the following parameters: (a) Clinical symptoms of DVT (3 points), (b) other diagnoses less likely than PE (3 points), (c) heart rate >100 (1.5 points), (d) immobilization ≥ 3 days or surgery in previous four weeks (1.5 points), (e) previous DVT/PE (1.5 points), (f) haemoptysis (1 point), (g) malignancy (1 point). Patients classified as PE unlikely should
undergo quantitative D-dimer testing. If the D-dimer level is <500 ng/mL, the diagnosis of PE can be excluded. Patients classified as PE likely and patients classified as PE unlikely who have a D-dimer level >500 ng/mL should undergo CT-PA. A positive CT-PA confirms the diagnosis of PE, and a negative CT-PA excludes the diagnosis of PE. A pulmonary angiogram is able to diagnose PE, but either modality can help to determine whether treatment should be instituted or can be withheld. A reasonable alternative approach for patients with a low or intermediate clinical probability of PE is to obtain a D-dimer. A negative D-Dimer excludes PE.

**Institutions without facilities for CT pulmonary angiography (CTPA)**

The Modified Wells criteria are initially applied to determine whether the clinical probability of PE is unlikely (score <4) or likely (score >4). A ventilation-perfusion (V/Q) scan is then performed. The following combinations of outcomes will be possible: (a) normal V/Q scan with any clinical probability excludes PE, (b) low probability V/Q scan with low clinical probability excludes PE, (c) high probability V/Q scan with high clinical probability confirms PE. Any other combination of V/Q scan result plus clinical probability should prompt either a pulmonary angiogram or serial lower extremity venous ultrasound examinations. Only the pulmonary angiogram can definitively diagnose PE.

**Treatment**

The clinical severity of PE can be highly variable, ranging from asymptomatic to severe hypoxemia, right ventricular failure, shock, and death. As a result, therapy (table 2) varies from patient to patient and requires considerable clinical judgment.

**Resuscitation**

When a patient presents with suspected PE, the initial focus is on stabilizing the patient. Supplemental oxygen should be administered if hypoxemia exists. Severe hypoxemia or respiratory failure should prompt consideration of intubation and mechanical ventilation.
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ventilation. Hemodynamic support should be instituted promptly when a patient presents with PE and hypotension. If the patient's hypotension does not resolve with intravenous fluids, intravenous vasopressor therapy should promptly follow [22].

Anticoagulation — Anticoagulation prevents further clot formation, but does not lyse existing thromboemboli or decrease thrombus size. Anticoagulation be initiated immediately (once it is deemed safe) when there is a high clinical suspicion of pulmonary embolism and continued during the diagnostic evaluation. For haemodynamically stable patients with PE, initial treatment with subcutaneous low molecular weight heparin (SC LMWH) is preferred. Inj enoxaparin is given in the dose of 1 mg/kg body weight every 12 hourly. For patients with PE who have persistent hypotension, an increased risk of bleeding, or in whom thrombolysis may be performed, IV unfractionated heparin is preferred over an alternative anticoagulant. It is given as bolus 80 units/kg followed by infusion at 18 units per hour. It is titrated every 4 to 6 hours to achieve target aPTT (INR of 2.0 to 3.5). Fondaparinux is a synthetic highly sulfated pentasaccharide which catalyses factor Xa inactivation by antithrombin without inhibiting thrombin. It is given subcutaneously in a dose of 5 (<50 kg) or 7.5 (> 50 kg) mg [23].

Long-term therapy — After initial therapy with heparin (LMWH or UFH) or fondaparinux, long-term therapy is completed with a vitamin K antagonist, such as warfarin. Warfarin therapy can be initiated at the same time or after heparin or fondaparinux. The warfarin dose is adjusted to achieve an INR of 2.5 (range 2.0 to 3.0). Warfarin should be overlapped with heparin for a minimum of five days.

Duration — For patients with a first episode of PE due to a temporary risk factor (e.g., surgery, immobilization, trauma), warfarin therapy for three months is preferred. For patients with a first episode of unprovoked PE, warfarin therapy for at least three months is recommended. The potential benefits and risks of indefinite anticoagulant therapy should be assessed after the three months of anticoagulant therapy. For patients who do not have an increased risk of bleeding, or patients with two or more episodes of PE, indefinite warfarin therapy is recommended.

Thrombolysis — Thrombolytic therapy for pulmonary embolism accelerates clot lysis and has short-term physiologic benefits, but has not shown to improve mortality. For patients with confirmed PE who are persistently hypotensive and do not have an increased risk of bleeding, thrombolytic therapy should be followed by anticoagulation. Common thrombolytic regimen include (a) recombinant tissue type plasminogen activator (tPA)-100 mg IV over 2 hours, (b) Streptokinase (SK) 2,50,000 Units IV over 30 minutes, then 1,00,000 units/ hour for 24 hours, and (c) Urokinase 4400 units over 10 minutes, then 2200 units /kg for 12 hours. When there are contraindications to thrombolysis, catheter or surgical embolectomy may be warranted if the necessary resources and expertise are available [24].

IVC Filter — Inferior vena caval (IVC) filters provide a screen in the inferior vena cava, allowing blood to pass through while preventing large emboli from traveling from the pelvis or lower extremities to the lungs.

Indications — (a) recurrent PE despite adequate anticoagulant therapy, (b) absolute contraindication to anticoagulation (e.g. active bleeding), (c) complication of anticoagulation (e.g. severe bleeding), (d) haemodynamic or respiratory compromise that is severe enough that another PE may be lethal [25].

Embolectomy — Embolectomy can be performed using catheters or surgically. It should be considered when a patient's presentation is severe enough to warrant thrombolysis (e.g. persistent hypotension due to PE), but this approach either fails or is contraindicated [26].

Catheter embolectomy — Intrapulmonary arterial techniques (e.g. rheolytic embolectomy, rotational embolectomy) have been utilized to reduce the embolic burden in patients with PE. Catheter technique is most effective compared to alternative treatment modalities.

Rheolytic embolectomy — Using a rheolytic embolectomy catheter embolism is accomplished by injecting pressurized saline through the catheter's distal tip, which macerates the emboli. The saline and fragments of clot are then sucked back into an exhaust lumen of the catheter for disposal.

Rotational embolectomy — Rotational catheter fragmentation of emboli has been performed using conventional cardiac catheters which do not require venotomy at the insertion site.

Surgical embolectomy — Surgical embolectomy is done for systemic hypotension due to PE in a patient in whom thrombolysis is contraindicated. It is done in tertiary care centres with experienced surgeons and with facility for cardiopulmonary bypass.

Conclusion: Acute pulmonary embolism is a common and often a fatal disease. Although considerable effort is directed towards the development of newer diagnostic techniques and therapeutic agents, a considerable impact on mortality related to the disease would arise from an understanding of the subtle clinical presumption of the disease and the appropriate application of the existing diagnostic technique. Further reduction in mortality may be achieved by systemic approach in the therapy with early intervention, patient risk stratification, selection of therapy and determination of treatment duration.

REFERENCES:


