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How do I manage a patient with suspected acute pulmonary embolism?

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Acute pulmonary embolism (PE) is characterised by obstruction of the pulmonary arterial tree by thrombi commonly originating from the leg or pelvic veins. Although deep vein thrombosis (DVT) and PE are manifestations of the same disease, mortality is higher in those who present with PE.[1] In 2005, it was estimated that 25,000 people in the UK die of preventable hospital-acquired venous thromboembolism (VTE) every year. Community studies have reported an annual incidence for VTE of 1.4–1.8 per 1,000 with a third presenting with PE. The incidence of VTE rises markedly with age; over the age of 75, the annual incidence reached 1 per 100 population.[2]

Ten per cent of acute PE are immediately fatal, with a further 5% mortality despite treatment. Perfusion defects resolve in 50% after one month of treatment, with complete resolution in two-thirds.[3] There is a two-year cumulative incidence of 3.8% for chronic thromboembolic pulmonary hypertension due to poor resolution and/or a pulmonary arteriopathy.[4] Six to 15% of patients have recurrent thrombosis after anticoagulation particularly in those with permanent risk factors.

Risk factors

The risk factors for development of VTE are venous stasis, vascular damage and hypercoaguability. Predisposing factors include reduced mobility, medical co-morbidities, surgery, active cancer, previous VTE, drugs, pregnancy, central lines, thrombophilias, obesity and varicose veins. In approximately 20% idiopathic PE may occur.

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Symptoms and signs

The symptoms include dyspnoea, pleuritic or retrosternal chest pain, cough, haemoptysis and syncope. Clinically the patient may be tachypnoeic, tachycardic, and hypoxic with an elevated jugular venous pressure, a gallop rhythm, a widely split second heart sound, a tricuspid regurgitation murmur and possible flow murmurs around the embolic obstructions. With pulmonary infarction there may be a pleural rub and pyrexia. In severe cases, the right ventricle fails to cope with the increase in afterload resulting in systemic hypotension and shock. Signs of a DVT increase the index of suspicion for PE.

Investigation of patients with suspected PE

The symptoms and signs in acute PE are neither sensitive nor specific and only a third of referred patients will have PE. Hence a pre-test assessment of clinical probability should be undertaken in all cases. Several clinical predictive models based on risk factors, symptoms and signs have been developed. The Wells prediction model for PE has been validated and is the most widely used.[5] As shown in Fig 1, PE can be excluded in patients who have a low clinical probability and a negative D-dimer without further investigations.

Investigations

Plasma D-dimer gives a measure of endogenous fibrinolysis. It has a good negative predictive value and is useful in excluding PE. It is not diagnostic as it has a low specificity and is elevated in a wide range of conditions including infection, trauma and cancer. It should not be measured in patients with a high clinical

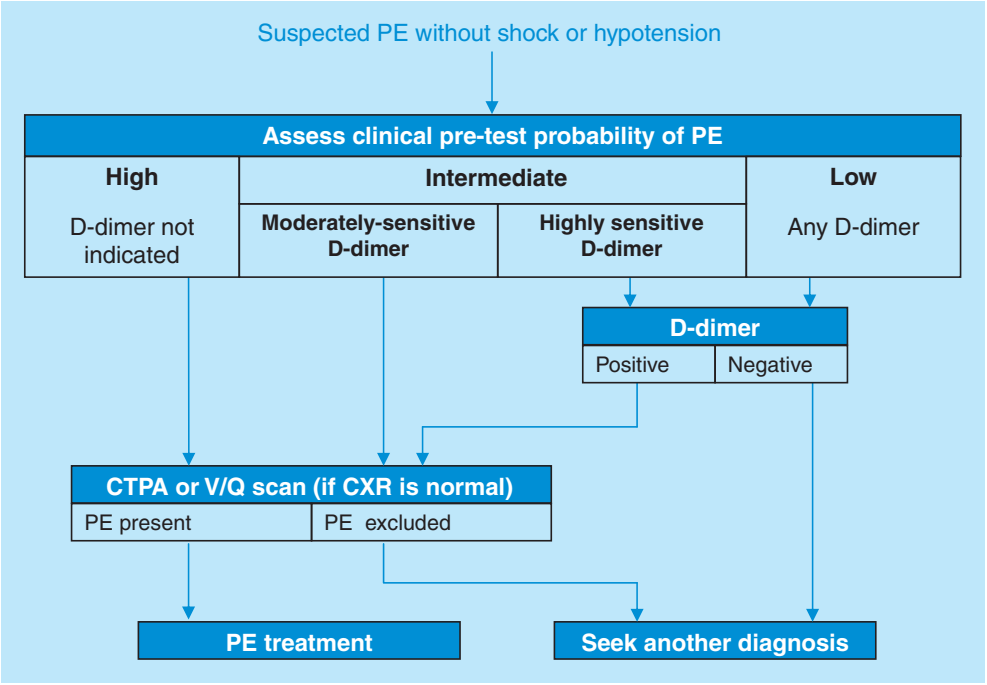

Fig 1. A survey of the conference delegates showed that most clinicians had access to both V/Q scintigraphy and computed tomography (CT) pulmonary angiography (CTPA). Here is a possible diagnostic algorithm for haemodynamically stable patients with a suspected pulmonary embolism (PE). Patients with an intermediate pre-test probability could follow the path of the low probability patients if a highly sensitive D-dimer test is used and local assessment shows this to be safe. Each hospital should develop a diagnostic strategy which will depend on local resources, expertise and the patient population. CXR =chest X-ray. Adapted with permission from BMJ Publishing Group Ltd.[10]

probability as it has a low negative predictive value in this population. Several assays are available each with different sensitivities, specificities and predictive values. The enzyme-linked immunosorbent assays are more sensitive and are useful in excluding PE in patients with a low or moderate clinical probability of PE (Fig 1).

A chest X-ray (CXR) may be normal or show atelactasis, a pleural effusion, hypovascularity (Westermark's sign) or wedge shaped peripheral infarcts (Hampton's hump). The electrocardiogram (ECG) may show non-specific signs of right ventricular strain such as inversion of T waves in leads V1-V4, a QR pattern in lead V1, S1Q3T3 pattern and incomplete or complete right bundle branch block.

Echocardiography shows signs of pulmonary hypertension, right ventricular overload or dysfunction in at least 25% of patients with PE. It rarely enables direct visualisation of PE but may reveal thrombus in the right heart chambers and excludes other diagnoses, such as cardiac tamponade or acute valvular dysfunction. It has an important role in prognostic stratification.

Ventilation-perfusion scintigraphy is a diagnostic test for PE in patients with normal CXRs.[6] It allows identification of hypoperfused segments with normal ventilation, so called mismatched defects. A normal test reliably excludes PE, however, patients with indeterminate results require further investigation.

Selective pulmonary angiography was the gold standard investigation showing direct evidence of a thrombus either as a filling defect or amputation of a pulmonary arterial branch. However, this invasive test has been increasingly replaced by computed tomography pulmonary angiography (CTPA). Multi-detector CTPA has improved the sensitivity and specificity of computed tomography in the diagnosis of PE. It allows adequate visualisation of the pulmonary arteries up to at least the segmental level and assessment of the secondary effects (Fig 2). CTPA has become the main thoracic imaging investigation for suspected PE. The disadvantages are contrast nephrotoxicity or allergies, and the radiation burden (2–6 mSv compared to 1.1 mSv for perfusion scintigraphy). In those with contraindications, leg ultrasonography may be performed to diagnose a DVT.

Risk stratification and prognosis

Risk stratification is paramount in managing patients with PE. The European Society of Cardiology has suggested that patients with PE can be stratified into three levels of risk as measured by in-hospital or 30-day mortality.[7] High-risk PE, previously known as massive PE, is characterised by cardiogenic shock or systemic hypotension (systolic blood pressure $<$90 mmHg or a fall in systolic blood pressure $\geqslant$40 mmHg, for $\geqslant$15 minutes which is not due to a new-onset arrhythmia, hypovolaemia or sepsis). This life-threatening situation carries an early mortality of more than 15%. In patients with suspected high-risk PE, echocardiography will show signs of pulmonary hypertension and right ventricular dysfunction, otherwise an alternative diagnosis must be sought.

Intermediate-risk PE is diagnosed in normotensive patients with evidence of right ventricular dysfunction and/or myocardial injury. Right ventricular dysfunction may be evident on echocardiography, CTPA, ECG or by an elevation in cardiac biomarkers. Brain natriuretic peptide (BNP) and its precursor, NT-proBNP, are released during myocardial stretch while cardiac troponins may be elevated during right ventricular infarction. New biomarkers for example heart-type fatty acid binding protein may have important roles in the future.

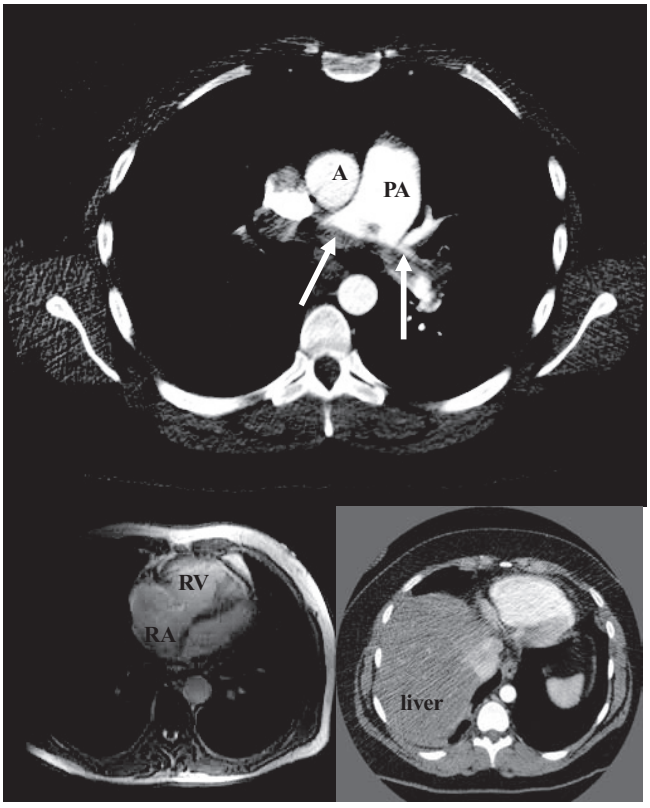

Fig 2 . Computed tomography (CT) pulmonary angiography (CTPA) showing a saddle embolus extending into the right and left pulmonary arteries (white arrows). The secondary effects of PE are also shown including dilatation of the main pulmonary artery (PA) compared to the aorta (A), a dilated right atrium (RA) and right ventricle (RV), and evidence of tricuspid regurgitation.

Low-risk PE is diagnosed in haemodynamically stable patients with no evidence of right ventricular dysfunction or myocardial injury and the risk of early mortality is less than 1%. This has important implications as these patients may be considered for early discharge if they do not have additional co-morbidities.

Treatment

Patients with intermediate to low-risk PE are treated with a rapidly acting anticoagulant (unfractionated heparin, low molecular weight heparin or fondaparinux), followed by oral vitamin K antagonists, commonly warfarin. Parenteral anticoagulants should be stopped when the international normalised ratio lies between 2.0 to 3.0 for at least two consecutive days. Intravenous unfractionated heparin should be considered for initial treatment in patients with high-risk PE, a high risk of bleeding, or severe renal impairment. The duration of anticoagulation depends on the presence of permanent risk factors, previous VTE, bleeding risks and patient preference. Patients with their first PE should be treated with at least three to six months of anticoagulation and evaluated for their risk-benefit ratio of long-term anticoagulation.

Who should receive thrombolysis?

Thrombolysis accelerates clot lysis resulting in greater haemodynamic benefits compared to heparin-treated patients in the first few days. However, after one week, there is no difference in the degree of vascular obstruction or RV dysfunction between thrombolysis and heparin-treated patients. Patients with high-risk PE are the only patients who are considered for early thromolysis. This improves survival[8] but pooled data has shown a 13% cumulative rate of major bleeding and a 1.8% rate of intracranial/fatal haemorrhage. A randomised controlled trial of early thrombolysis in intermediate-risk patients is underway. Uncontrolled data suggest that thrombolysis may be an alternative to surgery in patients with PE and right heart thrombus.[9]

Alternatives to thrombolysis

High-risk patients with PE who have failed thrombolysis or in whom thrombolysis is contraindicated may be considered for surgical embolectomy or percutaneous catheter embolectomy. Studies with inferior vena cava (IVC) filters have not shown survival benefits and there are late complications in particular recurrent DVT and post-thrombotic syndrome. IVC filters may be used when there are absolute contraindications to anticoagulation and a high risk of VTE recurrence.

Summary

Acute PE is a cardiovascular emergency and early risk stratification is important in the management of these patients. Pre-test clinical prediction models together with D-dimer assays help select those who require imaging. Each hospital should develop a strategy for investigating patients with suspected PE depending on local expertise, resources and the patient population.

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