Imaging the patient with suspected pulmonary venous thromboembolism

Introduction

The clinical presentation and causes of pulmonary embolism vary, and the consequences may include dyspnoea, chest pain, cough, hypoxia, elevated right ventricular pressure, sustained hypotension or shock. Depending on the clinical presentation and disease severity, case fatality ranges from 1–60%, with overall mortality approaching 10% during the first 3 months after diagnosis (Agnelli and Becattini, 2010). Appropriate diagnostic tools are therefore essential. While other tests and clinical predictive scores are often used in the initial workup, this review focuses on imaging modalities.

Initial workup

In the patient presenting with suspected pulmonary embolism, the clinical probability of venous thromboembolic disease should be initially assessed, often aided with decision tools such as the modified Wells score (Wells et al, 2001). In patients who are haemodynamically unstable (with systolic blood pressure <90 mmHg or a drop in pressure of 40 mmHg), a rapid decision is required to determine whether they are sufficiently stable for an immediate computed tomography pulmonary angiogram to guide emergency management.

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In haemodynamically stable patients, consideration should be given to the modified Wells score. Patients with high clinical probability should proceed to imaging studies. In those with a low or intermediate score, a D-dimer test is indicated before further imaging procedures. D-dimers are cross-linked degradation products of fibrin, and their presence in plasma indicates fibrinolytic activity which in turn may be used as a proxy for an acute thromboembolic event (Hafter et al, 1985).

D-dimers may be measured by enzyme-linked immunosorbent assay (Roul et al, 1988) or by quantitative immunoturbidimetric assay (Wilson and Gard, 2003), of which the former is more sensitive. A study using a D-dimer threshold of 1.2 mg/litre has demonstrated 100% sensitivity and 100% negative predictive value for pulmonary embolism when negative in the low or moderate risk patient (Gupta et al, 2009). Even using a lower cut-off of 0.5 mg/litre, the negative predictive value of the combination of Wells score and D-dimer assay remains 94% (Soderberg et al, 2009). Use of such a diagnostic algorithm therefore prevents unnecessary imaging and radiation exposure for the patient (Ten Cate-Hoek and Prins, 2005).

Chest radiograph

The chest radiograph should be the first investigation in any patient presenting with a potential pulmonary embolism. It is useful in excluding other causes of hypoxia such as pneumonia or pneumothorax that may mimic the presentation of an acute pulmonary embolism.

A normal chest radiograph does not exclude pulmonary embolism: approximately 12% of chest radiographs in patients with confirmed pulmonary embolism are interpreted as normal. Features that may be present include Hampton's hump (a wedge-shaped infarct) (*Figure 1*) which, while of low sensitivity, has high specificity for the presence of an embolus (Worsley et al, 1993). The results of the chest radiograph are useful in directing further investigations and may aid the interpretation of ventilation/perfusion (V/Q) scans (*Figure 2*).

Pulmonary angiography

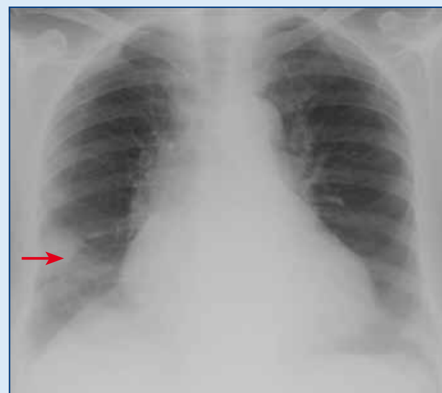
Conventional pulmonary angiography was traditionally seen as the gold standard for imaging pulmonary embolism. However, there is now very limited availability of this invasive and potentially dangerous procedure. In addition, inter-observer disagreements for sub-segmental clots occur in approximately one in three cases (Diffin et al, 1998).

Partly because of these observations, the 2003 British Thoracic Society guidelines for management of suspected acute pulmonary embolism recommended computed tomography pulmonary angiogram as the initial lung imaging modality. Direct angiography is now limited to a few centres with appropriate facilities and expertise for selective angiography and catheter fragmentation of large clots (British Thoracic Society, 2003).

Ventilation/perfusion scan

Perfusion lung scans have been used for the investigation of suspected pulmonary embolism since the 1960s. Ventilation scans were incorporated to improve accuracy by matching areas of normal ventilation with impaired perfusion (Wagner et al, 1968).

Figure 1. Presence of a Hampton's hump (arrow) on the chest radiograph of a patient presenting with suspected pulmonary embolism. Note the triangular pleurally-based area of increased density.



The first large multicentre prospective investigation of pulmonary embolism diagnosis (PIOPED) by V/Q scan (*Figure 2*) demonstrated good sensitivity (98%) but poor specificity (10%) for all abnormal scans. Following probability stratification, high pulmonary embolism probability scans were of low sensitivity at 41% with good specificity of 97%, and pulmonary embolism was also found in 12% of patients with low probability scans (PIOPED, 1990).

Further studies and attempts to improve the sensitivity and specificity of V/Q have had little overall impact and patients usually have to undergo further imaging studies when V/Q scans are reported as inconclusive. However, a normal chest radiograph together with a normal V/Q scan reliably excludes the presence of a pulmonary embolism (British Thoracic Society, 2003).

The technical issues with indeterminate V/Q scans and logistical difficulties in maintaining a 24-hour on-call service have gradually seen a decline in the use of V/Q scans. However, the V/Q scan remains an important investigation in the diagnostic work up of suspected pulmonary embolism, especially for patients with contraindications to a computed tomography pulmonary angiogram, such as poor renal function or allergies to iodine-based contrast. In addition, V/Q scans may often be better at picking up small vessel emboli from perfusion defects than a computed tomography pulmonary angiogram. Therefore, V/Q scans may be considered in patients who are clinically suspected of having chronic small vessel pulmonary emboli but with previous negative computed tomography pulmonary angiograms.

Computed tomography pulmonary angiography

Computed tomography pulmonary angiogram (*Figure 3*) has now overtaken both pulmonary angiography and V/Q scans as the investigation of choice.

Early studies using helical single slice computed tomography had demonstrated a pulmonary embolism pick-up sensitivity of between 53 and 100% and a specificity of 82–100% (Rathbun et al, 2000). Advances with the development of multidetector arrays have improved visualization of segmental and subsegmental pulmonary arteries and consequently improved both sensitivity and specificity of computed tomography pulmonary angiogram.

In a large multicentre trial – PIOPED II (Prospective Investigation of Pulmonary Embolism Diagnosis) – multi-detector computed tomography sensitivity was 83% with a specificity of 92%. The study also examined the specificity of computed tomography pulmonary angiogram combined with computed tomography venography of the pelvis and lower extremities and found improvement of sensitivity to 90% and specificity of 95%. It concluded that while the combination of computed tomography venography and computed tomography pulmonary angiogram did improve sensitivity, based on the risk benefits of increased radiation exposure, it would not be appropriate to undertake computed tomography venography routinely (Stein et al, 2006).

A negative result on computed tomography pulmonary angiogram is an excellent excluder of pulmonary embolism from other complex differentials. The prevalence of pulmonary embolism after negative computed tomography pulmonary angiogram was between 0.8% (Swensen et al, 2002) and 1.7% (Donato et al, 2003).

In addition to high specificity and sensitivity, incidental findings on computed tomography pulmonary angiogram may provide valuable information which, together with its easy accessibility out of hours, makes it invaluable as an essential diagnostic tool for haemodynamically unstable patients with suspected pulmonary embolism.

Figure 2. Ventilation/perfusion scan of the same patient as in Figure 1. Arrow demonstrates the right lower zone ventilation perfusion mismatch diagnostic of a pulmonary embolism, and corresponding to the Hampton's hump on the chest radiograph. There are multiple pulmonary emboli present bilaterally.

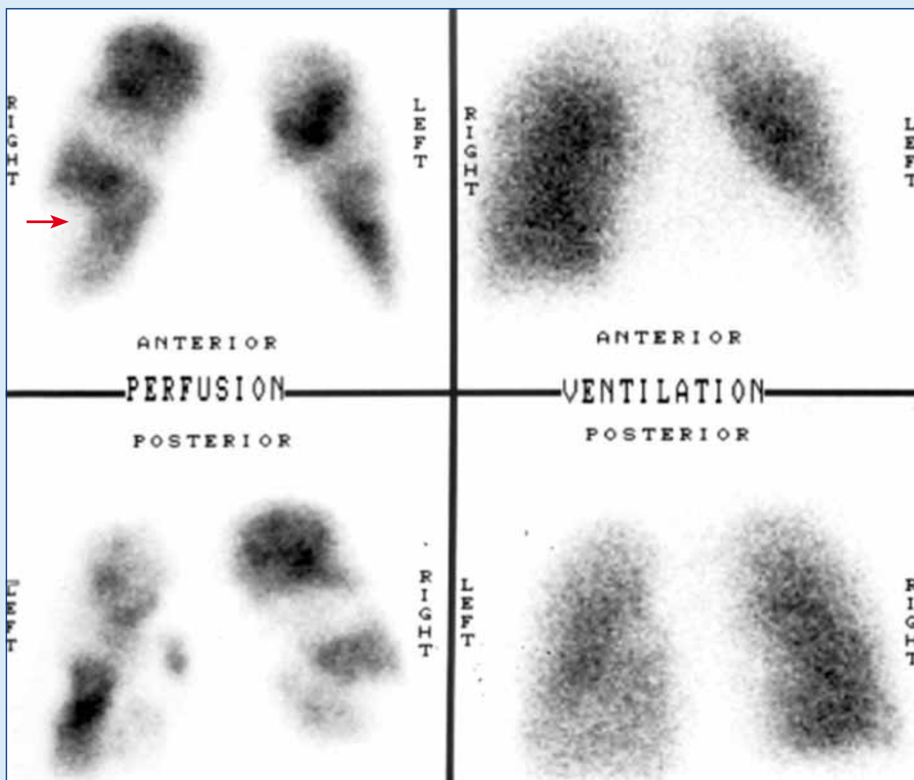
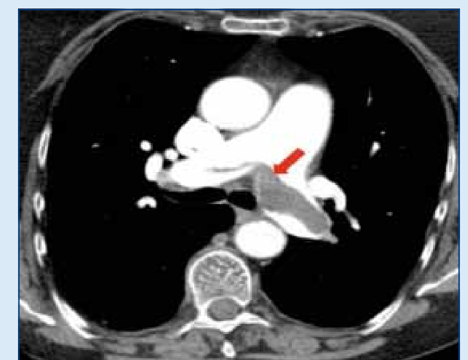


Figure 3. An axial image of a computed tomography pulmonary angiography scan demonstrating a large filling defect (arrow) caused by a thrombus in the left pulmonary artery extending across the bifurcation.



Ventilation/perfusion single photon emission computed tomography

A V/Q single photon emission computed tomography scan works with the same principle as a V/Q scan, but acquires images from multiple directions and generates a three-dimensional image by using computed tomography. The resultant image can then be manipulated and displayed in different configurations, providing a better depiction of subsegmental or even segmental ventilation perfusion defects. The improved resolution of the images significantly reduces indeterminate results as compared to standard V/Q planar scans and thus improves specificity of test results (Leblanc and Paul, 2010).

While V/Q single photon emission computed tomography has been recommended by the European Association of Nuclear Medicine as the preferred nuclear imaging modality for suspected pulmonary embolism (Bajc et al, 2009), the widespread adoption of V/Q single photon emission computed tomography as the preliminary imaging for pulmonary embolism is still limited because of logistical difficulties similar to those occurring with V/Q planar scans.

Ultrasound

Some patients may not tolerate a computed tomography pulmonary angiogram procedure for a variety of reasons. For these cases transthoracic ultrasound and transthoracic echocardiography may be used, together with other clinical signs and laboratory results, to establish a diagnosis of a proximal pulmonary embolism.

A review and meta-analysis using transthoracic ultrasound for pulmonary embolism by experienced practitioners reported a sensitivity and specificity of 80% and 93% respectively (Reissig and Kroegel, 2003). In these patients, typical pulmonary sonographic findings include multiple hypoechoic, wedge-shaped lesions well demarcated from the surrounding lung parenchyma, often with the absence of flow signal on Doppler ultrasound (Reissig and Kroegel, 2003). Two-dimensional echocardiogram and Doppler echocardiogram are likely to show right heart strain and right ventricular hypokinesia as well as a decreased acceleration time in the pulmonary artery outflow – with the decrease in acceleration time correlating to the severity of the perfusion defect (Kjaergaard et al, 2008). By using myocardial performance index ratio of the right to left ventricle, with a cut-off value of >1.2, Doppler echocardiograms identify pulmonary embolisms with a sensitivity of 82% and specificity of 83% (Hsiao et al, 2006).

Magnetic resonance imaging angiogram

A magnetic resonance pulmonary angiogram may offer an alternative diagnostic imaging method for patients with suspected pulmonary embolism when a computed tomography angiogram or pulmonary angiogram is contraindicated. A small scale study of gadolinium-enhanced magnetic resonance angiogram initially demonstrated high specificity and sensitivity for the diagnosis of pulmonary embolism (Meaney et al, 1997) and a large scale multicentre prospective study of the suitability of magnetic resonance angiogram for pulmonary embolism (with parallel methods to the PIOPED II computed tomography pulmonary angiogram study) took place between 2006 and 2008 (Stein et al, 2008). This study reported a sensitivity of 78% and specificity of 98% for technically adequate magnetic resonance angiogram images (Stein et al, 2010). As with computed tomography pulmonary angiogram, the addition of venography increases the sensitivity (92%).

Despite good sensitivity and specificity, the study was significantly limited by a high technical inadequacy rate of 25% among magnetic resonance angiogram scans and 52% for combined magnetic resonance angiogram and magnetic resonance venogram, and therefore cannot be at present recommended for routine use.

Dual energy computed tomography pulmonary angiography

In recent years, the development of dual-energy computed tomography has enabled the use of two tube voltages from a dual source computed tomography. This has allowed simultaneous imaging of the pulmonary arterial vasculature as per computed tomography pulmonary angiogram together with the distribution of the contrast medium in the lung parenchyma. The lung parenchyma perfusion can subsequently be colour coded and fused with the computed tomography pulmonary angiogram to produce a comprehensive image where both tissue perfusion and pulmonary vessel patency can be visualized. Initial small scale studies have suggested excellent accuracy with sensitivity and specificity of 100% and 100% for acute pulmonary emboli (Thieme et al, 2010).

Imaging in the pregnant patient

In pregnancy, the concern about radiation exposure is overcome by the hazard of missing a potentially fatal diagnosis or exposing the mother and fetus to unnecessary anticoagulant treatment. Current studies indicate that computed tomography pulmonary angiogram exposes the fetus to similar or lower doses of radiation as V/Q scans (Bourjeily et al, 2010). Currently, there are no definitive guidelines for pulmonary embolism imaging in pregnancy.

In many centres, V/Q scans (with half dose perfusion or perfusion-only scans) are still preferred to computed tomography pulmonary angiogram because of the lower radiation exposure to the breasts. Furthermore, studies have demonstrated V/Q scans to be diagnostically more reliable in pregnancy since during computed tomography pulmonary angiogram there may be transient interruption of contrast material by unopacified blood from the inferior vena cava resulting in a much higher percentage of non-diagnostic scans (Ridge et al, 2009). In addition, the higher proportion of normal V/Q scans in pregnancy than in the non-pregnant population would probably increase the negative predictive value of normal or near normal scans (Bourjeily et al, 2010). Performing a perfusion-only scan allows increased access to the investigation as there are significantly fewer logistical requirements than for a full V/Q scan. However, the accuracy of these scans depends on the experience of the local radiologists.

As such, the decision to use a computed tomography pulmonary angiogram or a V/Q scan in imaging for suspected pulmonary embolism in pregnancy strongly depends on the facilities and available expertise in each individual hospital.

Conclusions

A patient presenting with a suspected pulmonary embolism should always be initially investigated with a basic chest radiograph to risk stratify and exclude other associated pathology.

Pulmonary angiography is no longer routinely performed in view of its invasive nature and associated risks. Computed tomography pulmonary angiogram currently remains the standard diagnostic test in most centres for patients presenting with a possible pulmonary embolism. It is also safe for use in pregnancy.

V/Q scans are increasingly going out of routine practice except in pregnancy where a half dose perfusion scan may be preferred to computed tomography pulmonary angiogram, or in patients who have an allergy to contrast medium.

Ultrasound remains useful in aiding the diagnosis of a pulmonary embolism, especially in patients too unstable to be transferred. However, it is rarely diagnostic on its own and is highly dependent on the operator's skill level.

While magnetic resonance angiogram may provide similar information to computed tomography pulmonary angiogram, the high level of technically inadequate scans effectively limits its use to specific centres with good technical experience and only on patients with contraindications to computed tomography pulmonary angiogram and inadequate results from other imaging.

Technical advances in nuclear medicine, molecular imaging and equipment are further improving both sensitivity and specificity of imaging. Newer scans such as dual energy computed tomography pulmonary angiogram may soon overtake computed tomography pulmonary angiogram as the diagnostic test of choice for patients with suspected pulmonary embolism. **BJHM**

Conflict of interest: none.

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KEY POINTS

- A chest X-ray should be the first imaging modality in haemodynamically stable patients presenting with suspected pulmonary embolism.
- A negative D-dimer together with a low clinical probability on clinical scoring algorithms excludes the need for further imaging.
- Computed tomography pulmonary angiogram remains the imaging modality of choice for patients with suspected pulmonary emboli. It is safe to use in pregnancy.
- Ventilation/perfusion scans may be used for imaging patients in whom a computed tomography scan with contrast is contraindicated.