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Preface

In 1995 the Standards of Care Committee of the British Thoracic Society set up a subcommittee to draw up a practical management strategy for suspected acute pulmonary embolism. Representation was sought from the Royal Colleges of Radiologists and of Pathology, and from the British Cardiac Society. In addition, two of the foremost international researchers in this field were approached. All agreed to contribute. None of the group had any financial or other interests of possible conflict. As far as possible all relevant literature was sought and evaluated, up until early 1997.

The principal aim of the group was to recommend a diagnostic and management strategy for suspected acute pulmonary embolism that could be used by junior medical staff with simplicity, practicality, and flexibility – in particular, in a user friendly format that could be adapted for junior doctors' handbooks. This is summarised in the Appendix on pp S16–S21. However, since much of the material in this document represents new approaches based on recent published research, little of which has filtered through to current clinical practice, it was recognised that a detailed review of the literature with graded recommendations and levels of evidence should be included. Because of the rapid developments taking place in diagnosis and treatment, it is likely that the advice will require updating within 2–3 years.

1 Introduction

A district general hospital with a catchment population of 200 000 may expect to diagnose 50 cases of pulmonary embolism annually.[1] Since some of these only become apparent at necropsy, the true incidence of pulmonary embolism is probably much higher at 1% of all admissions.[2] In this recent audit pulmonary embolism was not suspected clinically in 70% of patients in whom it was subsequently found to have been the major cause of death, although most of them had associated advanced other diseases. On the other hand, an earlier autopsy in patients previously diagnosed as having pulmonary embolism failed to confirm the diagnosis in 63% of cases.[3] Thus, pulmonary embolism (PE) is both underdiagnosed and overdiagnosed in clinical practice, which leads to one group of patients failing to receive treatment for a potentially life threatening problem and another receiving potentially life threatening treatment for a disease which is not present.

Although there is now a wealth of information that allows a rational approach to the management of suspected pulmonary embolism, ignorance is widespread and much of current practice is very unsatisfactory. There is an assumption that, because urgent anticoagulation is mandatory in major PE, minor episodes in otherwise fit people must not be missed and require similar urgent treatment. In a major teaching hospital clinicians commonly made dubious management decisions on the basis of inadequate imaging information.[4] In any case, most patients with suspected pulmonary embolism are not seen initially by well informed specialists but are referred to middle grade physicians by colleagues in emergency, general surgical, orthopaedic, and obstetric departments; such junior doctors are often unaware of the literature. Most published guidance does not translate well into actual clinical settings where (a) there are several clinical patterns of pulmonary embolism, (b) urgent action may be required, (c) there are usually other diagnoses that need to be considered, and (d) access to appropriate investigations can be a major problem.

The concept that a small PE in a patient with underlying severe pre-existing cardiopulmonary disease may require a different investigational approach from that in a previously fit person is not widely applied.[5] The perceived danger of failing to treat a patient with PE is more than matched by the consequences of overdiagnosing the condition. This inevitably leads to worry and further unnecessary treatment if chest symptoms recur, inappropriate withdrawal of oral contraceptives, mandatory anticoagulation during future pregnancies, and compromised insurance prospects.[6]

The problem of both underdiagnosis and overdiagnosis is in part due to over-reliance on the ability of ventilation/perfusion ($\dot{V}/\dot{Q}$) scanning to diagnosis or exclude PE. The prospective investigation of pulmonary embolism diagnosis (PIOPED) study,[7] designed primarily to assess the value of $\dot{V}/\dot{Q}$ scanning using pulmonary angiography as the definitive test, emphasised the poor predictive value of scans reported as "intermediate probability", a common occurrence in routine clinical practice.

The limitations of $\dot{V}/\dot{Q}$ scanning may be one reason why many clinicians are prepared to make management decisions without any specific imaging for PE. A recent American study found that in almost half of those with a discharge diagnosis of PE there was no imaging evidence to support the diagnosis.[1] Another study from Canada showed that in some clinical situations physicians did not anticoagulate patients with $\dot{V}/\dot{Q}$ suspicion of PE, with disastrous results.[5]

These guidelines seek to provide an approach to the diagnosis and treatment of PE in the UK that is both practical (see Appendix) and evidence-based, and are in line with consensus statements from North America.[8–10]

2 Predisposing factors

Table 1 summarises the recognised risk factors for venous thromboembolism, which includes both PE and deep vein thrombosis (DVT) because it is widely recognised that these are closely related. Over 70% of cases of fatal[11 12] or non-fatal[13] proven PE have proximal thrombus, even though this is usually clinically undetectable. It is assumed that failure to find DVT in the leg in the other 30% is due to the leg thrombus having already become dislodged, although this is unproven. Conversely, half of those with proximal DVT have concurrent PE.[14–19] Controversy remains as to whether isolated calf vein DVT carries a significant risk of subsequent PE; distal clot undergoes spontaneous lysis, but proximal propagation and PE have been reported to occur in those who are symptomatic[20] and after hip arthroplasty.[21]

In all studies of PE one or more predisposing factors are found in 80–90% of patients,[1 19 22–28] the most common being immobilisation for more than one week, a history of previous venous thromboembolism,[29] and recent surgery or fractures, particularly of the lower limb.[30] The presence of risk factors not only aids clinical diagnosis of venous thromboembolism[31] but also may guide decisions about repeat testing in borderline cases.[22] Moreover, the incidence of venous thromboembolism is particularly high when there are multiple risk factors.

The incidence of PE increases exponentially with age[1] so that in several studies age over 40 is included as an independent risk factor. This may reflect the higher frequency of medical illnesses and major operations with increasing age. The previous view that obesity may also be an independent risk factor has recently been confirmed.[32] Apart from long distance air travel, where lower limb immobility can lead to venous thromboembolism,[33 34] most immobile patients with PE have other risk factors.

In surgical series the risk of venous thromboembolism rises rapidly with age, length of general anaesthesia, site of surgery (especially abdominal and lower limb), and the presence of advanced cancer or previous thromboembolic disease.[18 35] Fatal PE occurs in less than one in 10 000 minor elective operations, but in up to 5% of high risk cases such as extensive surgery for advanced abdominal or pelvic malignancy, major orthopaedic lower limb surgery, or postoperative intensive care. There is increasing use of pharmacological and physical measures to reduce the risk of postoperative DVT in high risk patients, with substantial reduction in the incidence of fatal PE, but there are wide variations in practice[36] and even in highly motivated units protocols may be overlooked in patients who need emergency surgery.[37] In obstetrics there is a higher incidence of venous thromboembolism, particularly if operative delivery is used, and also in the early puerperium.[38 39]

In non-surgical patients there are three major risk factors:

- cardiorespiratory disorders, particularly myocardial infarction, congenital heart disease,[40] and chronic symptomatic illness such as congestive cardiac failure and irreversible airways disease;
- lower limb immobility due to stroke and other neurological diseases such as brain tumour and acute spinal injury;[41]
- malignancy, particularly of the uterus, pancreas, breast and stomach,[12] as well as advanced and metastatic cancer. The reported association between PE and occult malig-

Table 1 Major risk factors for venous thromboembolism

Category	*Comments*
Surgery	• Major abdominal/pelvic surgery • Hip/knee surgery • Postoperative intensive care
Obstetrics	• Pregnancy/puerperium
Cardiorespiratory disease	• Acute myocardial infarction • Disabling disease
Lower limb problems	• Fracture • Varicose veins • Stroke/spinal cord injury
Malignant disease	• Abdominal/pelvic • Advanced/metastatic • Concurrent chemotherapy
Miscellaneous	• Increasing age • Previous proven PE/DVT • Immobility • Thrombotic disorders • Trauma

Lesser risk factors include prolonged air travel, oral oestrogens, central vein catheters.

nancy refers mainly to those with no risk factors and/or recurrent thromboembolism.[42–44]

The previous significant association with use of oral oestrogens appears to be less with current low dose formulations, whether used as oral contraception[45] or replacement therapy.[46] Although venous thromboembolism and PE are 2–4 times more common than in controls, PE is very uncommon in women on oestrogens. There is an increasing recognition of the importance of clotting disorders in venous thromboembolism, although it is unusual for these to present as unheralded PE, but investigations for thrombogenic disease at follow up should be considered in those without another apparent explanation.

Spontaneous clot in the upper limb is not only far less common, but also rarely leads to PE. PE may follow prolonged central venous catheterisation, although it is unusual for this to be fatal,[11 12] presumably because the iatrogenic clot is too small to cause major pulmonary vascular occlusion.

The frequent occurrence of serious underlying disease in patients with PE is underlined by the observations of the PIOPED group[47] that a quarter of those anticoagulated died within a year. Almost half of these died within two weeks and most of the rest without leaving hospital. Death due to recurrent embolism was exceptional. In this study, as in those with similar findings,[1] many were already inpatients before PE occurred. In such cases the prognosis of the underlying disease may be more serious than that of any complicating thromboembolism.

3 Clinical features

Several large studies[25–28] found that the most common clinical features of patients with proven acute PE are (in descending frequency from 70% to 10%): dyspnoea, tachypnoea, pleuritic pain, apprehension, tachycardia, cough, haemoptysis, leg pain, clinical DVT. However, those findings with high specificity have low sensitivity, and those with high sensitivity have low specificity. Thus the overall predictive value of any single feature in diagnosing or excluding PE is less than 80%.[48] Attempts have therefore been made to select combinations of features that allow PE to be diagnosed or excluded;[29 48 49] although useful, only a few patients can confidently be allocated to PE and non-PE groups, as was noted in the PIOPED study.[7] It is therefore often concluded that clinical features, even in combination, are of limited value in the clinical diagnosis of PE. Nevertheless, there are three considerations that suggest such reservations need to be reassessed.

(1) Although the presence of certain clinical features cannot be used to make a diagnosis of PE, their absence makes a diagnosis of PE very unlikely. Large studies have shown that dyspnoea plus tachypnoea (defined as respiratory rate >20/min) is absent in only 10% of patients, only 3% of patients have neither of these nor pleuritic pain; the reminder have either chest radiographic changes or a low Pa_{O_2}.[26 27 50 51] The absence of all these clinical features virtually excludes the diagnosis of PE.

(2) One of the main values of standard investigations is that they may help to eliminate other cardiac and respiratory diagnoses. Thus, conditions that may present with similar features to PE – including myocardial infarction, left heart failure, pericarditis, dissecting aneurysm, pneumothorax, pneumonia and lobar collapse – can often be detected by routine investigations such as electrocardiography, chest radiography, and lung function tests.

(3) Although the above studies assessed the clinical characteristics of all patients with PE, in practice there are subgroups with distinctive features. Table 2 collates the findings of several studies[23 26 27 51 52] which confirm that PE presents in one of three main ways:

- *Circulatory collapse* with hypotension and/or loss of consciousness; central chest tightness may occur. Signs are faintness on sitting up and jugular vein engorgement, and a diagnosis of massive PE is often obvious clinically if the physician is alert to this possibility. Suggestive electrocardiographic changes are common, whereas the chest radiograph is often unremarkable. Blood gas analysis shows marked hypoxia, often accompanied by hypocapnia due to hyperventilation. Because this group has the most extensive vascular occlusion, echocardiography usually shows characteristic features of acute right heart strain.
- *Pulmonary haemorrhage* with pleuritic pain and/or haemoptysis. In these patients chest radiographic changes are common, located to the site of pleuritic pain, whereas the electrocardiogram is often normal. This large group has the lowest severity as assessed by pulmonary angiography[53 54] which usually shows the emboli to be peripheral rather than central, so arterial gas tensions may be normal.[55] In otherwise healthy patients radiographic changes may clear rapidly, suggesting that the underlying pathology may be pulmonary haemorrhage without infarction.[53]
- *Isolated dyspnoea* defined as acute breathlessness in the absence of the other above symptoms; thrombus is more likely to be central and these patients are usually hypoxic. A pointer to the correct diagnosis is the sudden onset of unexplained dyspnoea in a patient with predisposing factors for venous thromboembolism.[54]

Most elderly patients with PE present with one of these patterns. The remainder may be diagnosed on the basis of an unexplained opacity on chest radiography, often accompanied by dyspnoea and/or clinical DVT.[56]

Table 2 also includes the important but little studied subgroup of patients with "poor reserve" (defined as chronic symptomatic cardiorespiratory disease). They can rapidly decompensate with a relatively small embolus; diagnosis is particularly difficult both for this reason and also because the clinical, ECG, and radiographic findings may mainly reflect the underlying disease. Recurrent thromboembolism is common and often fatal, yet clinicians often misinterpret lung scan reports,

Table 2 Main clinical presentations of pulmonary embolism

	Collapse, previously well	*Pulmonary haemorrhage*	*Isolated dyspnoea*	*Collapse, poor reserve*
Frequency	5%	60%	25%	10%
Pulmonary artery occlusion	Extensive	Small/moderate	Moderate/large	Small/moderate
Examination[1]	Acute right heart strain	May have localising signs	Tachypnoea	Unhelpful[2]
Chest radiograph[1]	Usually normal	Often suggestive	Usually normal	May be suggestive
ECG[1]	Often acute right heart strain	Normal	Non-specific changes	Unhelpful[2]
Arterial gas tensions	Markedly abnormal	May be normal	Usually abnormal	Unhelpful[2]

[1]May be very helpful in excluding other diagnoses.
[2]Because abnormalities are mainly due to underlying cardiorespiratory disease.

ignore the value of pulmonary angiography, and neglect anticoagulation.[5]

Two clinical settings deserve special mention because both are common and often poorly managed. The first is that of a young patient, often a women on oral contraception, who presents as an emergency with isolated pleuritic chest pain; the fear of missing PE leads to most such patients being admitted and given heparin until lung scanning can be performed. However, a large study[57] has shown that in such patients PE is very unlikely if there are no risk factors for thromboembolism and the patient is either (a) aged under 40 or (b) has a respiratory rate of <20/min plus a normal chest radiograph. Secondly, in the period immediately after upper abdominal surgery, when good quality chest radiographs may be hard to obtain, PE is often confused with segmental/lobar collapse or infection and there may be relative contraindications to anticoagulation. Because no recent publications have focused on this important group, this is not discussed further.

In only 28% of the patients in the PIOPED study investigated for PE was the diagnosis confirmed. The proportion is even lower in some recent studies[58,59] and in an earlier multicentre trial of thrombolysis only 8% of those recruited had a proven PE.[25] In almost all studies there is no information about the final diagnosis in the remainder or, indeed, whether this diagnosis was likely on entry. Some of the patients are likely to have had heart failure or pneumonia, but may have been unnecessarily investigated for PE because the clinician was afraid to miss this possibility. In the single exception an alternative diagnosis was made in 71% of those where PE was sought but excluded.[60] This confirmed the low threshold of clinicians for arranging investigations, which suggests that many of these might have been avoided by clearer clinical decision making. Although each individual symptom of PE has a wide differential diagnosis,[35] in a particular case there are usually very few alternative explanations.

One of the findings of the PIOPED study[7] was that the accuracy of interpretation of $\dot{V}/\dot{Q}$ scans could be increased by including clinical probability, the error rate for both high (13%) and low probability (16%) scans being reduced to 4% if clinical probability was concordant. When patients could be classified into high or low clinical probability groups this was usually correct, although less so in those with underlying cardiorespiratory disease or in intensive care units. However, 64% of patients could not be categorised as either, so that only 20% of patients were high (or low) probability both clinically and on the $\dot{V}/\dot{Q}$ scan.

The poor ability of clinicians to assign clinical probability in the above studies may have been partly due to lack of clearly specified criteria as to how such an assessment should be made. Rather than abandon the concept of clinical probability, it could prove useful to suggest clearer diagnostic guidelines. Such an approach proved successful in a recent study where senior respiratory physicians were given defined criteria for assessing patients with suspected PE; a confident clinical prediction of imaging findings was made in 77% of patients and confirmed in 91%.[61] These results are almost identical to those of a multicentre study of suspected DVT[31] using three clinical parameters: (a) findings on examination, (b) exclusion of another diagnosis, and (c) presence of identified risk factors. A similar approach for suspected PE is shown in the Appendix; however, this proposal has yet to be validated prospectively.

4 Investigations

The basic tests below should be performed in all patients both to support clinical suspicion of PE and, in particular, to exclude alternative diagnoses. More specific investigations are always required to confirm a diagnosis of PE.

Basic tests

CHEST RADIOGRAPHY

Although chest radiographic changes in PE are usually non-specific and appearances may be normal, chest radiography is extremely valuable in excluding other diagnoses such as heart failure, pneumonia, pneumothorax, or tumour. Common findings in PE include focal infiltrate, segmental collapse, raised diaphragm, and pleural effusion.[27 28 50 55] A wedge-shaped pleural based opacity, though well described, is rare; hypovascularity, described in larger emboli, is usually difficult to detect. A normal chest radiograph in an acutely breathless hypoxic patient increases the likelihood of PE.[51 62] In acutely ill patients it is often hard to obtain a good quality radiograph, which is also needed for accurate reporting of $\dot{V}/\dot{Q}$ scans.

ELECTROCARDIOGRAPHY (ECG)

ECG abnormalities in PE are common[27 63] but are usually non-specific changes in the ST segment and/or T wave. Features of acute right heart strain are common with massive emboli.[24] The ECG is also useful in excluding other diagnoses such as acute myocardial infarction and pericardial disease.

ARTERIAL BLOOD GAS TENSIONS

Pulmonary embolism is characterised by ventilation-perfusion mismatch and hyperventilation, usually accompanied by reduced Pa_{O_2} and normal or low Pa_{CO_2}.[64–66] The degree of hypoxia roughly correlates with the extent of the embolism as judged by $\dot{V}/\dot{Q}$ scanning and pulmonary artery pressure.[55] Normal Pa_{O_2} and Pa_{CO_2} values may be found,[67 68] particularly with smaller emboli. Such values do not exclude the need for further investigation. In acute massive PE cardiovascular collapse may cause a metabolic acidosis.

Lung imaging

VENTILATION/PERFUSION ($\dot{V}/\dot{Q}$) ISOTOPE SCANNING

This test, which has the advantage of being non-invasive, is widely available and most acute hospitals in the UK provide regular weekday access. However, less than a third of surveyed departments offer a seven day on-call service.[69]

Ventilation scans may be obtained with krypton-81 m (^{81m}Kr), technegas, Tc-DPTA aerosol, or xenon-133 (^{133}Xe). Over 80% of nuclear medicine departments have access to ^{81m}Kr or aerosols.[70] Xenon-133 is widely used but the ventilation images are of inferior quality for comparison with perfusion images. Perfusion scanning is performed by the intravenous injection of ^{99m}Tc-labelled macroaggregates of albumin or human albumin microspheres. Injection is carried out with the patient supine to reduce gravitational effects in the pulmonary circulation. After injection, scanning may be performed in the supine or erect posture using the same posture for ventilation and perfusion scans. A minimum of four views should be obtained: anterior, posterior, and right and left posterior oblique; lateral views may be added.

In pregnancy some departments choose to reduce the dose of ^{99m}Tc for perfusion studies and to avoid the use of ^{133}Xe for ventilation scans, but such precautions may not be necessary.[71] Nursing mothers should avoid breast feeding for the following 15 hours.

$\dot{V}/\dot{Q}$ scanning should normally be performed within 24 hours of clinical suspicion of pulmonary embolism, since some scans revert to normal quickly and half do so within a week.[72] Delay also increases the potential for misleading reports because of possible confusion

Table 3 Modified PIOPED criteria for interpretation of $\dot{V}/\dot{Q}$ scans

Probability	*Criteria*
High	• >1 large $\dot{V}/\dot{Q}$ mismatch • 1 large plus >1 moderate $\dot{V}/\dot{Q}$ mismatch • >3 moderate $\dot{V}/\dot{Q}$ mismatch
Intermediate (indeterminate)	• 1 large $\dot{V}/\dot{Q}$ mismatch • <4 moderate $\dot{V}/\dot{Q}$ mismatch • 1 matched $\dot{V}/\dot{Q}$ defect plus normal chest radiograph
Low	• 1 $\dot{V}/\dot{Q}$ mismatch plus normal chest radiograph • >1 matched $\dot{V}/\dot{Q}$ defects plus some normal $\dot{Q}$ plus normal chest radiograph • small $\dot{Q}$ defect(s) plus normal chest radiograph • non-segmental $\dot{Q}$ defects (e.g. small pleural effusion, cardiomegaly, enlarged mediastinal structures, raised hemidiaphragm)
Normal	• no $\dot{Q}$ defects present; $\dot{Q}$ exactly outlines the shape of the lungs on chest radiograph

caused by the development of pleural effusion and pulmonary opacities due to lung haemorrhage or infarction. Scans should be reported in conjunction with information on clinical features and a current good quality chest radiograph,[73] and direct communication between the reporter and the requesting clinician is likely to improve the value of the test. The report should both be factual and give an indication of the probability of pulmonary embolism using the modified PIOPED criteria (table 3).[74]

In patients suspected of pulmonary embolism, a high probability V̇/Q̇ scan report correctly indicates pulmonary embolism in 86–92% of cases, and the accuracy in excluding PE is 86% for low probability scans and 96% for normal scans.[6 13 73 75 76] Agreement among scan readers is good for high probability and normal scans (>90% agreement) but is less good (70–75%) for indeterminate and low probability scans.[7] In large studies using single view ^{133}Xe ventilation images and conventional reporting criteria, many patients fell into the indeterminate category which is of no value in discriminating between PE and non-PE.[7 77] These patients require further imaging, not a management decision on clinical grounds. The use of newer ventilation scanning agents allowing multiple views should reduce the proportion of indeterminate scan reports.[78]

The interpretation of lung scans may be difficult or misleading in several situations and alternative imaging investigations are often more rewarding:

- previous pulmonary embolism unless a follow up scan has been performed;[7]
- left heart failure which can cause regional variations in pulmonary perfusion;
- chronic obstructive airways disease with local variations in ventilation and in which the vascular bed may be constricted due to local hypoxia or chronically damaged;[79 80]
- lung fibrosis where there are patchy unmatched defects in both ventilation and perfusion;[81]
- proximal lung cancer causing vascular occlusion leading to a marked perfusion defect with preserved ventilation.[82]

In the absence of these situations, the value of V̇/Q̇ scanning is unaffected by age.[56]

The principle behind V/Q scanning is that, in patients with PE, perfusion defects occur in parts of the lung with preserved ventilation. However, this is an oversimplification – for example, in some cases of PE matched ventilation defects can occur.[77] In theory the addition of ventilation imaging should improve the diagnostic usefulness of perfusion scanning, but the PIOPED study showed any such benefit to be marginal.[83] A recent large Italian study (PISA-PED)[61] used the same principle of performing both lung scanning and pulmonary angiography. Perfusion scanning alone was used, yet this gave a comparable diagnostic yield. This suggests that, in hospitals where ventilation scanning is unavailable either all the time or on certain days, perfusion imaging alone is acceptable. The simple PISA-PED reporting method, based on whether wedge-shaped perfusion defects are present, is likely to become an attractive alternative to the rather complex PIOPED criteria.

PULMONARY ANGIOGRAPHY

Although the technical facilities for pulmonary angiography are widely available, only 15% of British radiology departments offer a pulmonary angiography service and even in those departments only small numbers of procedures are performed. Although consensus statements suggest that at least one third of patients suspected of PE require angiography to clarify the diagnosis,[8] in the UK only one angiogram is performed for every 95 V̇/Q̇ scans.[84] This is probably because of (a) the reluctance of clinicians to consider this investigation, (b) difficulty in arranging it when indicated, and (c) lack of radiological experience. Acute hospitals with interventional radiologists should offer a regular service and be prepared to provide an emergency service.

Pulmonary angiography should be considered in patients suspected of PE (a) if cardiovascular collapse or hypotension is present, where it should be available urgently, and (b) where other investigations have failed to give a firm diagnosis. There are no absolute contraindications, although particular care should be exercised in patients with known sensitivity to contrast media, and in those with severe pulmonary hypertension, renal impairment, or following acute myocardial infarction. Otherwise, complications are no greater in the elderly.[56]

Full resuscitation facilities with continuous ECG, and pulse oximetry monitoring should be available; blood gas analysis and intravascular pressure monitoring are desirable. Although the femoral vein approach is commonly used, some prefer the internal jugular or subclavian approach because of the reduced risk of disturbing thrombi and the ability to maintain venous access for pressure monitoring and the administration of thrombolytic drugs where indicated. Good liaison between the radiologist and intensive care unit is recommended. Pigtail catheters of sufficient size (7 F) to enable high flow injections of non-ionic contrast media should be used; volume and flow will depend on facilities available. Superselective injections may be necessary; a main PA injection may be sufficient when prior echocardiography suggests the possibility of a large centrally placed clot and, where prior V̇/Q̇ scan is non-diagnostic, angiography can be confined to the more abnormal side.[84]

Using these techniques, minor complications have been reported in 2% and major or fatal complications in 0.5–1.3% of investigations,[85 88] mainly in those who are already severely ill. However, the introduction of low osmolar non-ionic contrast media has led to a reduction in complications, a recent report finding only one major (and non-fatal) complication in every 300 patients.[89]

Although pulmonary angiography is said to be the "gold standard", there may be difficulties in interpretation even with experienced radiologists. In the PIOPED study inter-observer disagreement occurred in 19%, varying from 2% for central to 34% for subsegmental abnormalities;[87] within-observer discrepancy occurred in 11%. A recent study[90] with consensus review in patients with non-diagnostic lung scans led to a change in initial diagnosis in 20%. Better agreement was found when digital subtraction was used, but this is not widely available.

SPIRAL COMPUTED TOMOGRAPHIC (CT) SCANNING

The latest range of CT scanners can record data with a continuously moving table and continuous radiation from the rotating arm so that most or all of the thorax can be scanned during a single breath hold with simultaneous intravenous contrast injection. Spiral (more accurately "helical" or "constant volume") CT scanning can detect intravascular clot from the pulmonary trunk to segmental arteries. The technique is faster and less complex than conventional pulmonary angiography.

Early studies suggest good sensitivity and specificity for central or segmental thrombus. Where available, rapid access to spiral CT scanning may make it the special investigation of choice in patients with major embolism and those in the "isolated dyspnoea" group. However, since not all of the lung periphery is included, and since emboli in subsegmental pulmonary arteries are not reliably visualised, it is less accurate than angiography in minor embolism. In a recent report of pulmonary angiography confined to patients with non-diagnostic $\dot{V}/\dot{Q}$ scans, 30% had abnormalities confined to the subsegmental level where spiral CT scanning is unreliable.[91] Further evaluation of the technique is required before confident statements can be made about its place in the diagnosis of PE.[59 92 93]

Leg imaging

As stated previously, the logic of leg vein imaging is that the majority of patients with PE have proximal clot even in the absence of clinical evidence of DVT, itself an indication for treatment even if there is no direct proof of embolism. Leg vein imaging is indicated in the assessment of PE (a) as a first line investigation in those with clinical DVT or in patients with chronic cardiorespiratory disease, and (b) following an indeterminate $\dot{V}/\dot{Q}$ scan. Tests should be performed within 24 hours.

Ascending contrast venography and ultrasound techniques are widely used to image clot in the veins of the lower limbs and pelvis. Both labelled fibrinogen tests[94] and impedance plethysmography[95] have limitations and are now used by only a few investigators.

Where $\dot{V}/\dot{Q}$ scanning is non-diagnostic, non-invasive leg imaging may confirm the presence of venous thromboembolism. If negative, possible strategies[8 96] include:

- using clinical probability of PE to decide on further action. Thus, if PE is thought to be unlikely it may be reasonable to withhold treatment, whereas if PE is probable further imaging should be considered;
- performing pulmonary angiography, especially in those with poor cardiorespiratory reserve;
- repeating the test at intervals, especially in those with multiple risk factors.

These approaches were derived from studies[22 58] using impedance plethysmography which is far inferior to the latest ultrasound techniques at imaging calf DVT.

ASCENDING CONTRAST VENOGRAPHY (ACV)

Venography is widely performed but moderately invasive. It involves the injection of iodinated contrast agent into a foot vein. Minor complications are less common since the widespread introduction of low osmolar contrast media. Relative contraindications include contrast sensitivity (increased risk of anaphylaxis) and pregnancy (small radiation risk). Technical failures preclude an adequate examination in up to 20% of cases.[97 98]

Although venography is considered to be the "gold standard" and is accurate in detecting proximal DVT, a recent screening study in orthopaedic patients showed that half the distal DVTs were missed[20] and false positives may also occur.[99]

ULTRASOUND TECHNIQUES

A number of different techniques are in use and there are a number of major developments. Compression ultrasound can be performed on basic real-time equipment and shows a high degree of accuracy in the femoropopliteal segment.[100] It is enhanced by the addition of colour Doppler imaging which allows the iliac and calf veins to be successfully examined in most cases.[101] Failure to identify thrombosis of the calf veins rarely has serious sequelae,[102] and the procedure can be readily repeated if there is persisting clinical concern. Where available, colour Doppler imaging is now the investigation of choice in the detection of suspected DVT of the lower limb.[103 104] However, although accurate at detecting proximal DVT, it is less reliable in screening for asymptomatic distal DVT.

Other tests

ECHOCARDIOGRAPHY

In patients with major central PE echocardiography can establish the diagnosis as well as exclude other diseases.

A number of changes on four chamber two-dimensional echocardiography have been described in PE, including right ventricular dilatation and hypokinesis, pulmonary artery enlargement, tricuspid regurgitation (from which pulmonary artery pressure can be derived), abnormal septal movement, and lack

of inferior vena cava collapse during inspiration.[105 106] In addition, conditions such as myocardial infarction, aortic dissection, and pericardial tamponade which may mimic PE can easily be distinguished by echocardiography.[107]

As expected, changes only occur when there has been significant obstruction to the pulmonary circulation. Diagnostic abnormalities are typically found in patients with PE who have systemic hypotension. In those with normal blood pressure right ventricular hypokinesis is only likely if the perfusion defect is more than 30%, and even then a third of investigations are normal.[108] Changes are more frequent in patients with extensive vascular obstruction than in the pulmonary infarction syndrome. Moreover, interpretation is difficult in patients with underlying congestive cardiac failure or advanced chronic obstructive airways disease, and distinction from right ventricular infarction and cardiomyopathy can be difficult. Accuracy can be increased by using the transoesophageal route which is much more likely to show clot in either the right heart or main pulmonary arteries,[109] an ominous finding.[110] This technique may also be normal with smaller emboli and is only readily available in a few centres.

PLASMA D-DIMER

Since venous thromboembolism leads to activation of fibrin degradation, there has been considerable interest in developing blood assays based on this as a way of avoiding other investigations. The most promising of these has been D-dimer, a breakdown product of cross-linked fibrin. Values are rarely in the normal range in those with active venous thromboembolism, but are commonly raised in other hospitalised patients. D-dimer assays can therefore be used to exclude, but not to confirm, venous thromboembolism, and could reduce the number of investigations in patients with suspected PE.[111]

The rapid latex test is not as accurate as ELISA assays and requires refinement and further studies.[112 113]

5 Treatment

General supportive measures

Analgesia should be given to patients with severe pleuritic pain, but opiates should be avoided in patients with incipient cardiovascular collapse as they are vasodilators. Hypoxaemia should be treated with high percentage inspired oxygen. In hypotensive patients colloid should be administered whilst monitoring central venous pressure.[114 115] Right atrial pressure should be allowed to remain high (15–20 mm Hg) to ensure maximal right heart filling. Diuretics and vasodilators are not indicated.

Anticoagulation

Anticoagulation remains the mainstay of treatment of PE and has been shown to reduce the incidence of fatal recurrent embolism.[116] Detailed recommendations on anticoagulation have been published.[9]

Unless contraindicated, heparin should be started where there is a high or intermediate clinical suspicion pending the results of investigations. A loading dose of 5000–10 000 units should be given followed by 400–600 units/kg daily as a continuous infusion. The dose should be titrated against measurement of activated partial thromboplastin time (APTT) which should be maintained at 1.5–2.5 times the control values. APTT should be measured 4–6 hours after starting treatment to ensure adequate anticoagulation and exclude overtreatment, repeated 6–10 hours after every change of dose and subsequently at least daily. Compared with a standard regimen, one corrected for the patient's weight causes fewer fluctuations in APTT and achieves a therapeutic level more quickly with a shorter warfarin overlap.[117] An unexpectedly poor response to heparin may suggest pre-existing thrombophilia.

Heparin should be continued until adequate maintenance anticoagulation with warfarin is achieved. A five day course appears to be as effective as a 7–10 day course;[118 119] if continued beyond five days the platelet count must be monitored because of the risk of heparin-induced thrombocytopenia with thrombosis.[120] Warfarin may be started as soon as the diagnosis is confirmed.

Low molecular weight heparin (LMWH) has been shown to be as effective as standard heparin in the treatment of proximal DVT.[121–123] It has the advantages of predictable rapid anticoagulation, a simple subcutaneous dosing regimen, and no need for laboratory monitoring. Recent reports have indicated that LMWH may be as effective as standard unfractionated heparin in non-life threatening pulmonary embolism[124] and preliminary results from other studies are promising.

Heparin may be discontinued if the international normalised ratio (INR) is in the therapeutic range of 2.0–3.0. The INR can be measured whilst the patient is on heparin provided the APTT is not greater than 2.5 times the control value; otherwise protamine must be added to the sample to neutralise heparin. Detailed warfarin schedules are published in the British National Formulary and in many hospital handbooks.

In pregnancy warfarin is contraindicated because, unlike fractionated and unfractionated heparin, it crosses the placenta and is associated with fetal abnormality, particularly in the first trimester. The prophylaxis and treatment of venous thromboembolism in obstetric practice requires specialist advice.[38 71 125]

Where there are temporary risk factors for venous thromboembolism, such as after surgery, recurrence during and after treatment is unusual. Most studies on the duration of anticoagulation suggest that treatment for six weeks to three months is adequate for venous thromboembolism if there is no persisting underlying risk factor or thrombotic disorder such as antithrombin III deficiency or factor V Leiden.[126–129]

Recurrent embolism in the absence of a recurrent or new risk factor should be treated with long term anticoagulation. Lifelong treatment may be required after the first episode of embolism in patients with a thrombophilic condition[9 130] and such patients should be referred to a haematologist.

Thrombolysis

Despite the fact that heparin only reduces the incidence of recurrent PE, it is often the only form of treatment given for massive pulmonary embolism. Several controlled trials have concluded that pulmonary emboli clear more rapidly with thrombolytic therapy than with heparin alone, and thrombolysis appears to be as successful as embolectomy in patients with massive PE.[131] In the early trials of streptokinase and urokinase, mortality was not significantly altered but did show a trend towards reduction in the group treated with thrombolysis.[132–134] This trend might have reached statistical significance if more severely ill patients had been included. The major factor limiting the use of thrombolytic agents is the poor risk:benefit ratio.[135] Thrombolysis is therefore indicated primarily in patients who are haemodynamically unstable, particularly in the presence of systemic hypotension.[10] There is controversy regarding its use in those with echocardiographic evidence of right ventricular dysfunction.[10 136]

The regimen currently recommended for streptokinase is a loading dose of 250 000 IU

over 20–30 minutes followed by 100 000 IU/hour intravenously for up to 24 hours. It is not yet established whether a single dose of 1.5 million units, as used for myocardial infarction, is as effective.[135] Hydrocortisone should be given with streptokinase to reduce the incidence of allergic reactions, and its use on one occasion precludes its use in subsequent episodes because it is highly antigenic with development of neutralising antibodies; neither of these problems occurs with urokinase.

Recombinant tissue plasminogen activator (rtPA) has been investigated as an alternative to streptokinase and found to be equally effective with a lower risk of hypotension and systemic symptoms such as fever and chills. It accelerates the normalisation of pulmonary artery pressure and pulmonary perfusion much more rapidly than heparin alone in haemodynamically stable patients with PE.[136] Recent research found no difference between a bolus dose of 0.6 mg/kg over 15 minutes (maximum dose 50 mg) and 100 mg over two hours in terms of bleeding complications, adverse clinical events, or imaging studies.[137] In all cases heparin was given after rtPA in a dose of 1280 IU/hour as a continuous infusion as soon as the APTT was less than twice the upper limit of normal.

Thrombolytic therapy is equally effective via a peripheral vein or pulmonary artery catheter. It should be used with caution in the early postoperative period, depending upon the type of surgery undertaken. Although mainly indicated in patients with acute massive embolism, it appears to be effective for up to 14 days.[138]

RISK OF BLEEDING

Haemorrhage is the major complication of either anticoagulation or thrombolysis. High risk patients include those who have undergone surgery, obstetric delivery, or invasive vascular studies within the preceding seven days, and those with a history of peptic ulcer disease, gastrointestinal or urinary tract bleeding, disorders predisposing to bleeding, or a platelet count of less than 150×10^9/l . Major bleeding with heparin occurs in 10% of this group compared with 1% in low risk patients.[139]

Absolute contraindications to heparin or thrombolysis are recent haemorrhage, stroke (thrombolysis higher risk than heparin), and current gastrointestinal haemorrhage. Relative contraindications include peptic ulcer disease, surgery within the preceding seven days, and prolonged cardiorespiratory resuscitation. The risk of bleeding in patients on warfarin is closely related to the INR.[140]

In obstetrics current evidence suggests that thrombolysis is appropriate treatment for massive PE during pregnancy, but not within six hours of delivery nor in the early post-partum period because of the high risk of bleeding complications.[39 71]

Surgical procedures

Pulmonary embolectomy is rarely indicated. It should be considered in a patient with massive PE who fails to respond to thrombolytic therapy over the first hour[141] or in whom thrombolytic therapy is contraindicated. One group has had considerable success with transvenous catheter suction embolectomy, avoiding the need for such major surgery.[142]

Inferior vena caval (IVC) filters are underused in the UK. Although less effective than thrombolysis in protecting against PE in patients with persisting venous thrombosis in the acute situation,[143] they should be considered for patients at high risk of further emboli in whom anticoagulation is contraindicated, and in those with recurrent embolism despite adequate anticoagulation.[144 145] Filter selection and insertion should only be undertaken by an experienced interventional radiologist.

Is treatment mandatory?

Early pathological[146] and clinical[116] studies suggested that the mortality of untreated patients with PE was 25–35%, figures which are still quoted as representative[29] and information which causes many clinicians to use anticoagulation even when proof of venous thromboembolism is lacking.[4] However, in these early studies most patients had moderate to severe embolism since the diagnosis of PE had to rely on clinical assessment and basic investigations alone. Current evidence suggests that untreated patients with either proven or probable smaller emboli have a much lower recurrence rate. In a series of almost 8000 hip replacement patients in which there were 83 postoperative deaths due to sudden PE, 308 who survived postoperative PE were not anticoagulated with only 10 recurrences, none of which was fatal.[147] A review of the PIOPED pulmonary angiograms found that 20 patients were not anticoagulated because smaller PE had been overlooked; there were only two recurrences, one of which was fatal.[148] In 627 patients with suspected PE who had indeterminate $\dot{V}/\dot{Q}$ scans and no proximal DVT, a situation in which it can be estimated that 60–70 probably did have PE, anticoagulation was withheld and subsequent PE was rare.[58]

Considering the well recognised but often overlooked risks of oral anticoagulation, it is possible that the benefit:risk ratio of this treatment in PE is less than previously assumed. It may be that patients with suspected or even proven minor embolism and no evidence of residual DVT do not necessarily require treatment, particularly if risk factors are only temporary. Such an approach may become an acceptable alternative in selected patients. Since pulmonary emboli confined to the subsegmental level are not detectable by echocardiography, are often missed by spiral CT scanning, and commonly cause difficulties in interpretation of pulmonary angiography, it is important to discover whether treatment is necessary in such cases.

6 Recommendations

Management recommendations are set out in table 4 and are graded as shown; this includes levels of evidence.[149 150]

In addition, the following statements, which fall short of recommendations, summarise other important clinical aspects.

- Clinicians need to be more careful in diagnosing PE, which is both overdiagnosed and underdiagnosed in clinical practice.
- Clinicians should be aware of the importance of risk factors; predisposing factors are found in 80–90% of patients, the commonest being immobilisation for more than one week, a history of previous venous thromboembolism, recent surgery, and lower limb fractures or surgery.
- Young women whose only risk factor is oral contraception who present with isolated pleuritic chest pain are very unlikely to have PE if they have a respiratory rate of <20/min plus a normal chest radiograph.
- It is important to recognise the subgroup of patients with chronic symptomatic cardiorespiratory disease who decompensate with a relatively small PE.
- In patients with suspected major central PE, transthoracic echocardiography can establish the diagnosis and exclude other important diseases.
- Spiral CT scanning has good sensitivity and specificity for detection of thrombus to the level of segmental arteries. Further evaluation of the technique is required before confident statements can be made about its place in the diagnosis of PE.
- In PE following surgery with no persisting risk factors anticoagulation for 4–6 weeks is sufficient.
- Thrombolytic agents may be given via a peripheral vein or pulmonary artery catheter.

Table 4 Management recommendations, with grades

	Management strategy	*Grade*
1	Patients presenting with a combination of unexplained acute dyspnoea, hypoxia and normal chest radiograph should be investigated for PE	B
2	Respiratory rate should be recorded in all patients with suspected PE	B
3	Chest radiography, ECG and arterial gas measurements should be performed in all patients with suspected PE	B
4	In the absence of all three of tachypnoea (>20/min), pleuritic pain and arterial hypoxaemia, a diagnosis of PE can be excluded	B
5	Occult malignancy need only be considered in patients (a) presenting with PE and no apparent risk factors or (b) with recurrent PE	B
6	Lung scanning should be performed within 24 hours of clinical suspicion of PE	B
7	Ventilation should be assessed by technetium-labelled aerosol (or ^{81m}Kr) rather than ^{133}Xe	B
8	Requests for lung scans should be accompanied by an estimate of clinical probability of PE	B
9	Lung scans should be reported in conjunction with a current chest radiograph and give an indication of probability according to PIOPED or PISA-PED criteria	B
10	Patients with indeterminate lung scans require further imaging rather than management based on clinical features	C
11	Pulmonary angiography should be considered in patients with suspected PE when other investigations fail to confirm the diagnosis	C
12	Leg vein imaging should be performed as a first line investigation for suspected PE in patients with previous PE, clinical DVT, or chronic cardiorespiratory disease	B
13	Where a laboratory offers a reliable D-dimer test, normal levels exclude PE	B
14	Thrombolytic therapy is indicated in patients who are haemodynamically unstable, particularly if systemic hypotension is present	B
15	Heparin should be started on the basis of high or intermediate clinical suspicion before the diagnosis of PE is clarified	C
16	Heparin should be continued until maintenance anticoagulation with warfarin is achieved	B
17	Patients with spontaneous PE and no persistent underlying risk factor should be anticoagulated with warfarin for a maximum of three months	B
18	Pulmonary embolectomy should only be considered in a patient with massive PE if thrombolysis either is contraindicated or leads to no clinical improvement within one hour	C
19	IVC filter should be used in patients (a) at high risk of further emboli in whom anticoagulation is contraindicated or (b) with recurrent PE despite adequate anticoagulation	B

Grades of recommendations: A = requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendaton; B = requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation; C = requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities; indicates absence of directly applicable studies of good quality.

- LMWH, as used in the treatment of DVT, will probably replace unfractionated heparin in PE.
- In many cases the prognosis of the underlying disease is potentially more serious than that of complicating PE and should receive equal consideration in management.
- Failure to anticoagulate patients with minor PE and no persistent risk factors carries a low incidence of recurrence. The benefit:risk ratio of treating such patients is less than previously assumed and a decision not to treat may be appropriate in selected patients.

Each acute hospital needs to ensure that:

- the advice in the Appendix is discussed and modified to fit local facilities and expertise;
- a strategy is developed for arranging urgent investigations in patients with life threatening PE;
- in less seriously ill patients, where there is a high or intermediate probability of PE, appropriate imaging can be arranged within 24 hours;
- there is a clearly defined system for arranging pulmonary angiography when indicated, including as an emergency;
- thrombolytic therapy can be instituted urgently if required;
- junior medical staff have ready access to the Appendix;
- there is at least one physician with a particular interest in pulmonary embolism, so that expert clinical advice can be sought when necessary.

Nationally, the following changes should be considered:

- standardisation of lung $\dot{V}/\dot{Q}$ scanning, both in methodology and in reporting;
- acceptance of the wider availability of pulmonary angiography, with appropriate teaching of training grades in interventional radiology;
- in the light of rapid advances in diagnosis and treatment, the advice in this document is regularly updated and revised.

Appendix: Summary Charts for Handbooks for Junior Doctors

In the light of the considerations in the previous sections, the following charts have been designed for inclusion in hospital handbooks, offering practical advice to junior doctors on:

- how to assess the likelihood of pulmonary embolism, and what to do next (Chart 1);
- how to investigate and manage a patient with suspected pulmonary embolism, using a flow diagram with explanatory notes designed to cover most clinical scenarios; this section can be adapted to suit local facilities and requirements (Chart 2 + Notes);
- details of drug treatment (Chart 3);
- a discharge check list (Chart 4).

For this approach to work in practice, it is important for individual hospitals to ensure that, when required:

- appropriate investigations – for example, pulmonary angiography – can be readily arranged even if not available on site;
- a strategy is in place for rapid investigation of patients with suspected major pulmonary embolism;
- specialist advice can be obtained readily from at least one nominated physician.

Chart 1 *Initial Assessment and Action*

STEP 1 – Assess probability of pulmonary embolism

Clinical patterns of PE include:

(a) sudden collapse with raised jugular venous pressure (*faintness and/or hypotension*)

(b) pulmonary haemorrhage syndrome (*pleuritic pain and/or haemoptysis*)

(c) isolated dyspnoea (*i.e. no cough/sputum/chest pain)*

- PE is easily missed
  - (a) in severe cardiorespiratory disease
  - (b) in elderly patients
  - (c) if only symptom is breathlessness ("isolated dyspnoea")
- most are breathless and/or tachypnoeic (rate > 20/min)
- PE is rare if age < 40 with no risk factors
- oestrogens are only a *minor* risk factor

If PE is suspected, ask the following questions:

1. Are other diagnoses *unlikely*?

- on clinical grounds
- after basic investigations:
  - white cell count
  - chest radiography
  - ECG
  - spirometry or peak flow
  - blood analysis

If *YES*, score +1

2. Is a major risk factor *present*?

- recent immobilisation or major surgery
- recent lower limb trauma and/or surgery
- clinical deep vein thrombosis
- previous *proven* DVT or PE
- pregnancy or post-partum
- major medical illness

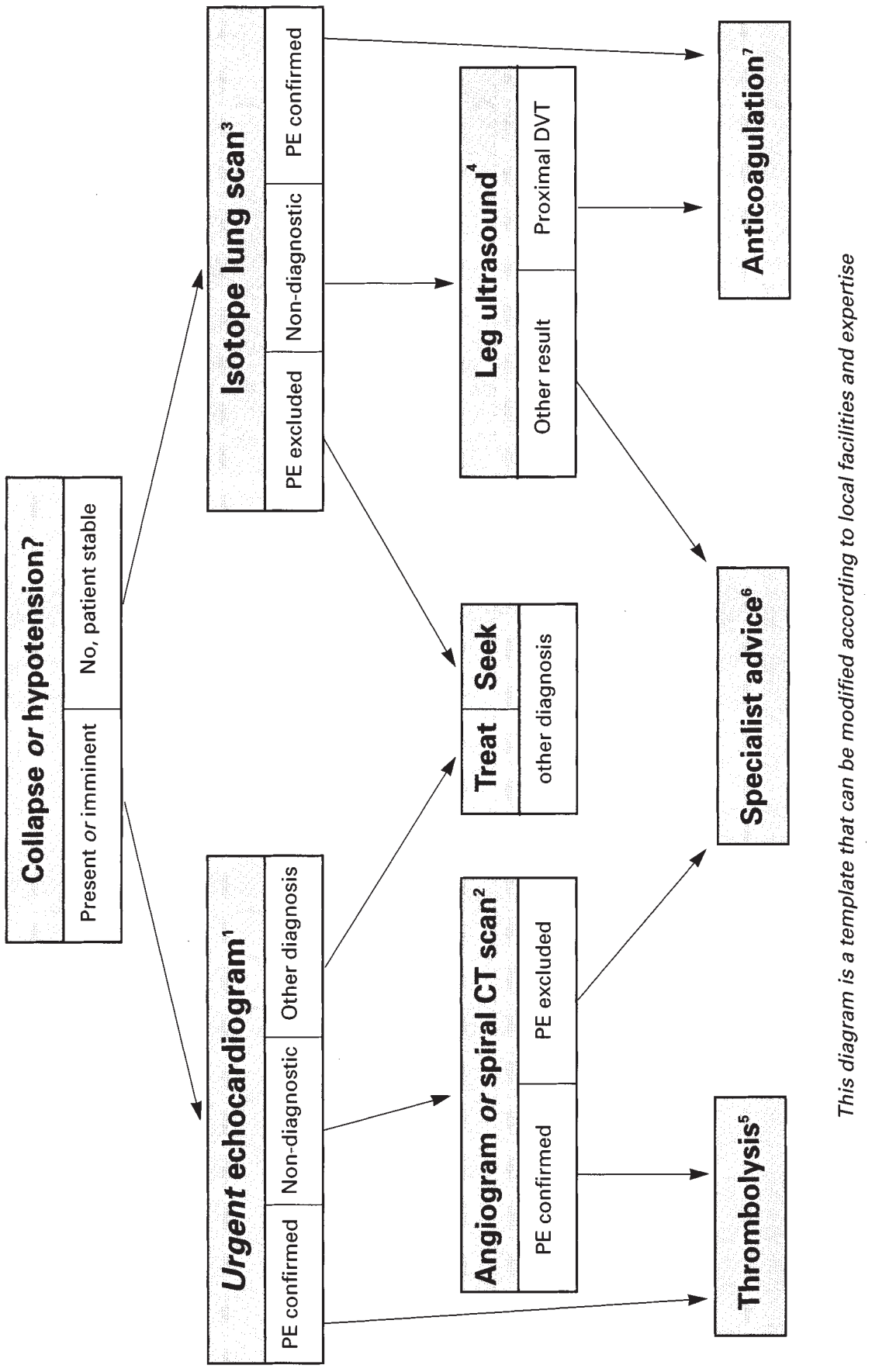
If *YES*, score +1

STEP 2 – Take action according to score

Action / Score / Probability	2 High	1 Intermediate	0 Low
Heparinise?	Yes[a]	Yes[a]	Wait
Tests for PE?	Urgent[b]	Early[b]	Consider
Another diagnosis?	Consider	Seek	Seek

[a] Unless contraindicated.
[b] See Chart 2.

Chart 2 ***Investigations and Action***



This diagram is a template that can be modified according to local facilities and expertise

NOTES

1
- contact senior staff urgently (a) because of severity of illness, (b) to expedite investigations;
- if massive PE obvious clinically (a) start heparin, (b) arrange angiography *or* spiral CT immediately;
- "other diagnosis" mimicking massive PE includes aortic dissection, pericardial tamponade, acute myocardial infarction;
- "non-diagnostic", start heparin (unless active GI bleeding, cerebral haemorrhage).

2
- whichever can be arranged quicker, as far as possible within one hour;
- perfusion (without ventilation) lung scan is an alternative urgent investigation;
- spiral CT scanning may miss a small PE, but this rarely causes cardiovascular collapse.

3
- start heparin unless (a) contraindicated *or* (b) low clinical probability;
- preferably request leg imaging at the same time; it can be cancelled if lung scan is diagnostic;
- consider leg imaging instead (a) if previous proven PE, (b) in pregnancy or (c) poor cardiorespiratory reserve;
- "PE excluded" by lung scan *either* if normal, *or* if low probability *plus* low clinical probability;
- "PE confirmed" if lung scan high probability *plus* high clinical probability.

4
- compression ultrasound, preferably with colour Doppler imaging;
- "other" includes (i) calf vein DVT, (ii) poorly visualised veins, (iii) normal study. Specialist will advise either:
  (a) treat as possible PE, especially if either (i) or (ii) in those with poor cardiorespiratory reserve;
  (b) that PE has been excluded, especially if (iii) and low clinical probability;
  (c) further imaging *either* pulmonary angiography *or* repeat ultrasound at 3–7 days.

5
- surgical or catheter embolectomy is an alternative, especially if medical treatment is contraindicated;
- thrombolysis is followed by anticoagulation.

6
- advice from a senior chest physician or cardiologist should be sought if:
  (a) there is undue delay in arranging investigations;
  (b) diagnostic uncertainty remains after both lung scanning and leg imaging;
  (c) PE has been excluded but the correct diagnosis remains elusive.

7
- IVC filter should be considered if anticoagulation is contraindicated;
- for anticoagulation with heparin + warfarin, see Treatment section.

Pulmonary angiography, where readily available, may be chosen as the initial imaging modality

Close co-operation with imaging departments is essential

Chart 3 *Drug Treatment*

Intravenous thrombolysis		
	Initial treatment	Further treatment
rtPA	100 mg in 2 hours	
Streptokinase*	250 000 units in 20 minutes	100 000 units/hour for 24 hours
Urokinase	4400 IU/kg in 10 minutes	4400 IU/kg/hour for 12 hours
Before treatment, stop heparin; after treatment, use maintenance dose as below		
*Plus hydrocortisone to prevent further circulatory instability		

Intravenous heparin		
	Initial dose	Maintenance dose
Standard	5000–10 000 IU	1300 IU/hour
Weight-adjusted	80 IU/kg	18 IU/kg/hour
Adjust infusion rate until APTT = 1.5–2.5 × control (45–75 seconds).		
APTT monitoring	After initial bolus	4–6 hours later
	After any dose change	6–10 hours later
	APTT in therapeutic range	Daily
Discontinue heparin 5 days after starting warfarin if INR at least 2.0.		

Warfarin	
Initial doses	5–10 mg daily for 2 days
Subsequent treatment	1–10 mg daily
Adjust dose to INR = 2–3 × control, initially measured every 1–2 days	

Chart 4 *Discharge Check List*

1 The international normalised ratio (INR) is between 2.0 and 3.0.

2 The general practitioner

- is aware the patient is on anticoagulant, *and*
- has been informed of the proposed duration of treatment, *and*
- has a discharge summary stating diagnosis as *either* PE suspected *or* PE confirmed.

3 The patient

- is aware of side effects of anticoagulants and interactions with other drugs, *and*
- has written information on warfarin therapy, *and*
- has an appointment for anticoagulant supervision.

4 Follow up review at 6–12 weeks has been arranged. At that time, if

- first episode *and* temporary risk factors, anticoagulation may be discontinued
- idiopathic *or* recurrent episode, consider (a) thrombophilic disorder (b) occult cancer

5 Specialist advice has been sought for female patients on oral contraception.

Abbreviations

APTT	activated partial thromboplastin time
CT	computed tomography with contrast
DVT	deep vein thrombosis
ECG	electrocardiogram
GI	gastrointestinal
INR	international normalised ratio
IU	international units
IVC	inferior vena cava
PE	pulmonary embolism
rtPa	recombinant tissue plasminogen activator

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