Diagnostic Imaging Pathways - Pulmonary Embolism (Haemodynamically Stable)

Population Covered By The Guidance

This pathway provides a diagnostic imaging algorithm for adult patients with suspected pulmonary embolism and who are haemodynamically stable.

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Quick User Guide

Move the mouse cursor over the PINK text boxes inside the flow chart to bring up a pop up box with salient points.
Clicking on the PINK text box will bring up the full text.
The relative radiation level of each imaging investigation is displayed in the pop up box.

SYMBOL	RRL	EFFECTIVE DOSE RANGE
	None	0
	Minimal	< 1 millisieverts
	Low	1-5 mSv
	Medium	5-10 mSv
	High	>10 mSv

Pathway Diagram

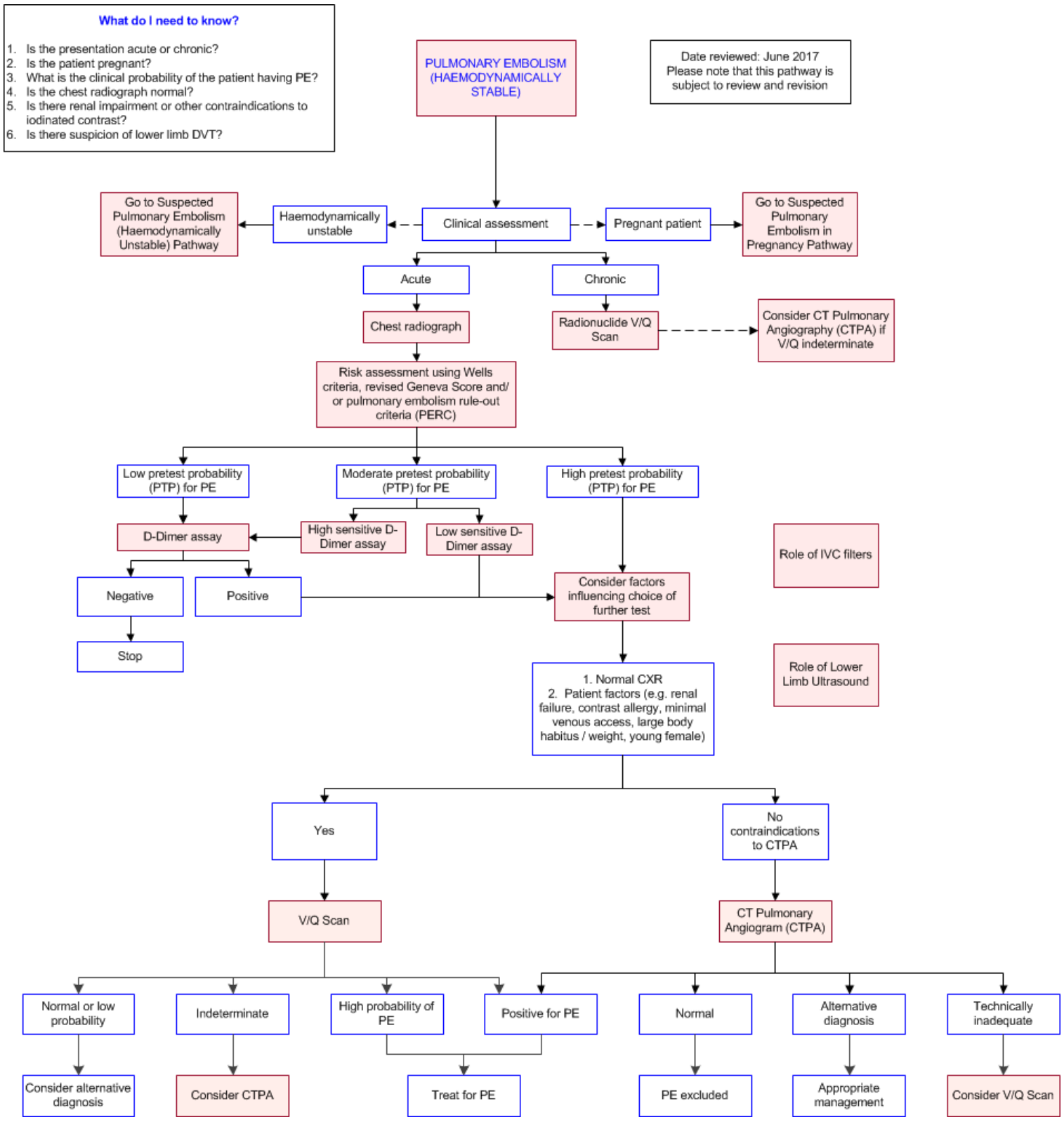


Image Gallery

Note: These images open in a new page

1 **Hampton's Hump**

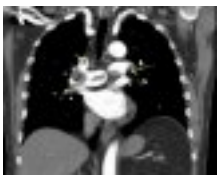
Image 1 (Plain Radiograph): There is a peripheral wedge shaped opacity representing pulmonary infarction and atelectasis secondary to a pulmonary embolus (arrow). This radiographic sign is referred to as Hampton's Hump.

2a

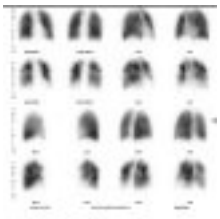
Bilateral Pulmonary Embolism

Image 2a and 2b (Computed Tomography): Axial and reconstructed images of bilateral pulmonary arterial emboli (arrows)

2b



3



Bilateral Pulmonary Embolism

Image 3 (Ventilation Perfusion Scan): The ventilation series demonstrates uniform distribution of tracer throughout both lung fields. The perfusion series demonstrates generalised reduced tracer uptake in the right lung with multiple segmental and subsegmental perfusion defects throughout both lung fields. These findings have a high probability for recent pulmonary embolism.

Teaching Points

- Prior to imaging, one must clinically calculate the probability of PE. This is based on the validated 'Wells Criteria'. Other criteria which have shown good pre-test probabilities are the Revised Geneva Score and Pulmonary Embolism Rule-out Criteria (PERC)
- Chest radiograph in suspected pulmonary embolism (PE) is to exclude other causes that may mimic PE and to guide further investigations
- Patients who are at low probability for PE should have a D-Dimer. A negative D-Dimer in a low probability case of suspected PE rules out the diagnosis and no further investigation is indicated
- Patients with moderate to high pre-test probability of PE should have further imaging
- The choice of imaging is reliant on a 'normal' chest radiograph and whether the patient has a history of a chronic underlying lung disease
- Patients with a normal chest radiograph and no history of lung disease should proceed to radionuclide scan
- Patients with an abnormal chest radiograph or history of lung disease should proceed to CTPA

Pulmonary Embolism (Haemodynamically Stable)

- Pulmonary embolism refers to obstruction of the pulmonary artery or one of its branches by material (e.g. thrombus, tumour, air, or fat) that originated elsewhere in the body 1
- It is important to determine the onset of presentation as initial imaging can differ. A chronic history, markedly elevated systolic pulmonary arterial pressures, RV and bronchial artery hypertrophy, thrombus calcification, webs and a mosaic perfusion pattern should raise suspicion of chronic

rather than acute PE [2, 3]

- The role of a chest radiograph in suspected Pulmonary Embolism (PE) is to exclude other causes that may mimic PE and to guide further investigations
- Prior to imaging, one must clinically calculate the probability of PE. This is based on the validated 'Wells Criteria'
    - Clinical signs and symptoms of Deep Vein Thrombosis (DVT)
    - PE as or more likely than an alternative diagnosis
    - Previous history of DVT
    - Active cancer
    - Recent immobilisation
    - Tachycardia
    - Haemoptysis
- Patients who are at low probability for PE should have a D-Dimer. A negative D-Dimer in a low probability case of suspected PE rules out the diagnosis and no further investigation is indicated [4]
- Patients with moderate to high pre-test probability of PE should have further imaging
- The choice of imaging is reliant on a 'Normal' chest radiograph and whether the patient has a history of a chronic underlying lung disease
    - Patients with a normal chest radiograph and no history of lung disease should proceed to radionuclide scan
    - Patients with an abnormal chest radiograph or history of lung disease should proceed to CTPA

Chest Radiograph

- Mainly useful for excluding conditions that can mimic pulmonary embolism [5]
- Features [6]
    - Approximately 12% of patients with angiographically proven PE have a normal CXR
    - The most common CXR findings with PE are atelectasis and parenchymal opacities in the affected lung zone
    - Oligaemia was the only CXR finding that occurred significantly more frequently in patients with PE compared to those without.
    - Positive predictive value of a normal CXR - 18%
    - Negative predictive value of a normal CXR - 74%
- The other main use of a CXR is to assist in determining whether a VQ or a CTPA is the most appropriate next investigation [7]
    - Patients with an abnormal CXR are more likely to have a non-diagnostic VQ scan than those with a normal CXR [8]
    - CT Pulmonary Angiography should therefore be used ahead of VQ in these patients [8]

Clinical Prediction Rules for Pre-test Probability of Pulmonary Embolism

- Clinical prediction rules are now well accepted as key components in the diagnostic approach to pulmonary embolism. The post-test probability of PE depends not only on the accuracy of the test but also on the pre-test probability as determined by these prediction rules as noted in the Table below [9, 10]

Item	Clinical decision rule points

	Original version	Simplified version
A. Wells criteria [11-13]		
Previous PE or DVT	1.5	1
Heart rate ? 100 beats/min	1.5	1
Surgery or immobilization within the past 4 weeks	1.5	1
Haemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Clinical probability		
Three-level score		
? Low	0-1	Not applicable
? Intermediate	2-6	Not applicable
? High	?7	Not applicable
Two-level score		
? PE unlikely	0-4	0-1
? PE likely	?5	?2
B. Revised Geneva score [11, 14, 15]		
Previous PE or DVT	3	1
Heart rate		
? 75-94 beats/min	3	1
? ?95 beats/min	5	2
Surgery or fracture within the past month	2	1
Haemoptysis	2	1
Active cancer	2	1
Unilateral lower limb pain	3	1
Pain on lower limb deep venous palpation and unilateral oedema	4	1
Age ?65 years	1	1
Clinical probability		
Three-level score		
? Low	0-3	0-1
? Intermediate	4-10	2-1
? High	?11	?5
Two-level score		
? PE unlikely	0-5	0-2
? PE likely	?6	?3

C. Pulmonary embolism rule-out criteria (PERC) 11, 16, 17	
Age ?50 years	1
Pulse rate ? 100 beats/min	1
SaO2 (pulse oximetry) < 95% on room air	1
History of haemoptysis	1
Current exogenous oestrogen use	1
Prior history of venous thromboembolism	1
Recent surgery or trauma in the previous 4 weeks	1
Unilateral leg swelling (on inspection)	1
PERC score	
? 0	Negative ('PERC ruled out')
? 1	Positive ('PERC rule inclusive') – further diagnosis is required

- The simplified Geneva score (with a similar accuracy as the Geneva one) identifies a high or low PE probability, especially in combination with D-dimers , with a prognosis value as well 18
- The Wells and simplified Wells scores identify the high or low probability, being improved by the level of D-dimers, having similar results with the Geneva score 18
- When comparing the Wells criteria, Geneva score, revised Geneva score and Charlottes rule, available clinical prediction rules (CPR) for assessing clinical probability of pulmonary embolism (PE) show similar accuracy 19
- Whether Wells criteria, Geneva score or their revised versions were used, the proportion of patients with PE is around 10% in the low probability category, 30% in the moderate probability category and 65% in the high clinical probability category 9, 10
- The existing scores are, however, not equivalent and the choice among various prediction rules and classification schemes (three- versus two-level) must be guided by local prevalence of PE, type of patients considered (outpatients or inpatients) and type of D-dimer assay applied 19
- Another report has suggested that when comparing diagnostic and prognostic accuracy, the Geneva and the Pulmonary Embolism Severity Index (PESI) scores remain the most valuable instruments of diagnosis and prediction of clinical prognostic outcomes, respectively 18
- PESI predicts the short-term death and adverse outcome events in patients with acute pulmonary embolism. The simplified version has similar accuracy and is easier to use 9, 20
- A recent systematic review and meta-analysis found 12 qualifying studies evaluating the PERC rule and ultimately determined that the pooled sensitivity to rule out pulmonary embolism is 97.2%, which the authors concluded to be a low, but acceptable sensitivity to rule out PE without further testing. The pooled negative LR was 0.17. The overall proportion of missed PEs was 0.32% (44 of 13,855 total cases) 16
- Therefore, it is advised that clinicians not obtain D-Dimer measurements or imaging studies in

patients with a low pre-test probability of PE and who meet all PERC criteria 21

D-Dimer Assay

- D-Dimer is formed as a result of plasmin generated degradation of thrombin and is therefore a marker of the presence of thrombus
- There are various qualitative and quantitative assays available for D-dimer, but in general they have a high sensitivity and negative predictive value for the presence of thrombus 22, 23
- Of the various assays, the quantitative enzyme linked immunosorbent assay (ELISA) has the best negative likelihood ratio and is significantly superior to non-ELISA assays for excluding the presence of pulmonary embolism (sensitivity >90%, specificity 40%) 9, 24, 25
- A negative quantitative ELISA D-dimer result is as diagnostically useful for excluding PE as a normal helical CT lung scan. (9, 24) In such patients, the 3-month risk of thromboembolism is only 0.14% (95% confidence interval, 0.05 to 0.41) if no anti-coagulation is given 26
- A negative D-dimer result in a highly sensitive assay (e.g. ELISA) safely excludes PE in patients with a low or moderate clinical probability 24, 25 while a moderately sensitive assay excludes PE only in patients with a low clinical probability 9
- When using the dichotomous clinical prediction rule(which classifies patients as PE unlikely and PE likely), a negative D-dimer result is able to exclude PE safely in PE-unlikely patients either by a highly sensitive or moderately sensitive assay 9
- When PE is suspected, a normal D-Dimer avoids further investigation in about 50% of outpatients and 20% of inpatients 27

Factors Influencing Choice of Further Tests

- A radionuclide scan emits a lower radiation dose compared to a standard dose(120KvP) CT pulmonary angiogram (CTPA) and is therefore preferred in younger patients
- Radionuclide scans should also be performed in those with contraindications to CT with contrast including patients with iodinated contrast allergy and with severe renal impairment. For more details, please see section on Contrast Media and Contrast Induced Nephrotoxicity
- Radionuclide scans are frequently non-diagnostic in those with abnormalities on chest radiography or with known chronic lung disease and CTPA should be considered in these patients
- Availability of new generation MDCTs with dose reduction technologies can also influence the choice of investigation as these have been shown to cause far less radiation exposure compared to traditional CTPAs 28
- Patient's body habitus, inability to co-operate with CT examination may hinder performing CTPA in these patients and radionuclide VQ scan may need to be used

Inferior Vena Cava (IVC) Filters

- Routine use of IVC filters is not recommended 2
- Should be considered in patients with 22, 29
    - Absolute or relative contraindication to anticoagulation
    - Complication of anticoagulation
    - Failure of anticoagulation
    - Recurrent PE despite adequate therapy
    - Inability to achieve / maintain adequate anticoagulation

- Propagation / progression of DVT during therapeutic anticoagulation
- Massive PE with residual DVT in a patient at risk for further PE
- Free-floating iliofemoral or IVC thrombus
- Severe cardiopulmonary disease and DVT (eg, cor pulmonale with pulmonary hypertension)

Bilateral Lower Limb Doppler Ultrasound

- The role of Doppler ultrasound in the evaluation of patients with suspected PE is controversial
- Approximately 10% of patients with a PE will have an abnormal ultrasound and a further 2% will have evidence of DVT on serial scans 30
- May be useful if the pre-test probability is discordant with the result of the VQ scan or CTPA 30
- Advantages:
  - Widely available
  - Non-invasive
- Limitations:
  - Low sensitivity for patients with PE

Radionuclide Lung Scan

- Lung perfusion images are taken after the intravenous injection of technetium-99m macroaggregated albumin. A PE characteristically appears as a pleural based segmental perfusion defect 3
- Any perfusion defects are compared to ventilation images and any regions of mismatch are considered suspect for PE 3
- Ventilation perfusion scans, compared to CTPA, are associated with lower radiation exposure but the extreme difference between the effective doses as existed previously has been reduced drastically with the new generation MDCT helical scanners that use low dose (using tube currents of 80kVp or 100kVp) 28, 31-34
- A perfusion scan alone (without the ventilation scan) can lead to significant reductions in cost and radiation exposure. A normal perfusion scan excludes PE with a negative predictive value close to 100% 16, 35-37
- A Ventilation-Perfusion scan has the following diagnostic features 4, 38
  - A high-probability scan usually indicates PE but only a minority of patients with PE have a high probability scan
  - A low-probability scan combined with a low pre-test probability of PE makes a PE very unlikely
  - An intermediate-probability scan is not usually helpful in establishing a diagnosis. Patients with an intermediate-probability scan (or low-probability scan with a high pre-test probability) should be reviewed and considered for further testing with a CTPA if there is persisting clinical suspicion for PE
- Limitations
  - Frequent non-diagnostic results, particularly for patients with an abnormal chest radiograph or a significant history of chronic obstructive lung disease 8
- Advantages
  - Lower radiation exposure compared to standard dose CT Pulmonary Angiography
  - Widely available
  - A normal scan useful for excluding PE in the majority of patients 38

- High sensitivity, specificity and accuracy in chronic pulmonary embolism and is the first choice of investigation in chronic thromboembolic pulmonary hypertension 39, 40

CT Pulmonary Angiography (CTPA)

- Multidetector computed tomography pulmonary angiography (CTPA) is now the primary imaging modality for evaluating acute PE 7, 41, 42
- Demonstrates a pulmonary embolism by showing a filling defect within contrast filled pulmonary arteries
- New generation MDCT (64 slice helical scanners) with low tube currents (80kVp, 100kVp and 120kVp) with / without dose modulations have been shown to not affect image quality of the angiography studies and at the same time have reduced effective radiation doses by 40% to 60% compared to the older scanners (140kVp). 31-33, 43 Also of note is the increase in contrast enhancement with low voltage scans and reduced amount of contrast medium needed for the study 28
- These MDCTs are increasingly available and should be the first choice of modality in acute PE as long as no contraindications for contrast material exists
- The radiation exposure is of particular importance to young females with breast tissue that has a higher turnover rate, who are therefore most susceptible to radiation-induced carcinogenesis. The absorbed dose to the breast tissue by CTPA was estimated between 10-30 mGy, which was 30-40 times greater compared to a perfusion scan but recent studies with newer MDCT scanners have been shown to deliver much lower organ doses to breast skin and breast parenchyma 31, 44
- A single-centre study to compare breast radiation dose in women undergoing CTPA protocol found decreasing the default peak kV resulted in an 88% and 79% reduction in monitoring scan breast dose for pregnant and non-pregnant patients, respectively 44
- Studies using bismuth breast shields have shown radiation dose reductions of 34-57% to the breast, without significant decrease in image quality or diagnostic accuracy 45-47
- The role of CTPA in the diagnostic algorithm for PE is dependent to some degree on the type of scanner available
    - Older scanners are limited by relatively long scan times and the associated respiratory motion artefact 3
    - Multi-slice CTPA has a number of advantages over older scanners that make it the central imaging modality for the investigation of PE at many centres
    - High acquisition speed meaning larger volumes can be covered more quickly 48
    - Better detection of sub-segmental emboli 7, 49-53
    - Better interobserver agreement rates 7, 49
- The Prospective Investigation of Pulmonary Embolism Diagnosis II (PIOPED II) trial reported a sensitivity of 83% and specificity of 96% using mainly 4-row multi-detector CT(MDCT) without consistent use of bolus tracking contrast administration. Discordant CTPA and pre-test clinical risk stratification required further investigation. The negative predictive value of high risk patients with a negative CTPA was only 60% and the positive predictive value of patients at low risk with a positive CTPA was 58%. Relatively high rates (6%) of studies were non-diagnostic 54
- A systematic review of 49 studies with 13,162 patients found that increased RV/LV diameter ratio measured on transverse CT images conferred the strongest risk for PE related mortality compared to other CT parameters 55
- A recent randomised study by Righini et al, compared one group who were assessed with D-Dimer followed by multislice CTPA, to another group had D-Dimer followed by lower limb venous ultrasonography and CTPA for exclusion of pulmonary embolism. Their primary outcome was the proportion of venous thromboembolic events in the 3-month follow-up period in each group in patients who were left untreated on the basis of the exclusion of pulmonary embolism by the

diagnostic strategy. They found no difference in the 3 month thromboembolic risk between the groups (0.3% for each group respectively). Based on this evidence, pulmonary embolism can effectively be excluded with a negative CTPA in patients who have a low or moderate pre-test probability 56

- CT is also able to provide information on alternative diagnoses that may mimic PE and has high sensitivity, specificity and accuracy in chronic PE. 42, 57, 58 CTPA findings may also correlate with surgical outcomes in these cases 39, 40
- Limitations
    - Radiation exposure if standard protocol if being implemented.
    - Risk of contrast allergy and renal impairment.
    - Subject to interpretive pitfalls such as respiratory motion artefact, streak artefact and problems related to patient body habitus 59

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Date of literature search: July 2017

References are graded from Level I to V according to the Oxford Centre for Evidence-Based Medicine, Levels of Evidence. Download the document

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