

EANM guidelines for Ventilation/Perfusion Scintigraphy. Part 2. Algorithms and clinical considerations for diagnosis of pulmonary emboli with V/P_{SPECT} and CTPA

M. Bajc, B. Neilly, M. Miniati, C. Schuemichen, M. Meignan, B. Jonson

Abstract

As emphasized in Part 1 of these guidelines, the diagnosis of pulmonary embolism, PE, is done by Ventilation/Perfusion Scintigraphy, V/P_{SCAN}, or Multi Detector Computed Tomography of the pulmonary arteries, MDCT. To reduce costs, risks associated with false negative and false positive diagnoses and undue radiation exposure, pre-imaging assessment of clinical probability is recommended. Diagnostic accuracy is approximately equal for MDCT and planar V/P_{SCAN} and better for tomography, V/P_{SPECT}. V/P_{SPECT} is feasible in about 99% of patients, while MDCT is often contraindicated. As MDCT is more available both methods are essential for diagnosis of PE. V/P_{SPECT} gives an effective radiation dose of 1.2-2 mSv. For V/P_{SPECT}, the effective dose is about 35-40 % and the absorbed dose to the female breast 4 % of doses from MDCT performed with a dose saving protocol. V/P_{SPECT} is recommended as a first line procedure in patients with suspected PE. It is particularly favourable in young patients, particularly females, during pregnancy, for follow up and research.

Abbreviations

MDCT – Multi Detector Computed Tomography of the pulmonary arteries, MAA – Macro-aggregated human albumin, PA – Contrast enhanced Pulmonary Angiography, PE – Pulmonary Embolism, V/P_{PLANAR} – Ventilation and Perfusion Scan with planar imaging, V/P_{SCAN} – Ventilation and Perfusion Scan, V/P_{SPECT} – Ventilation and Perfusion single photon tomography.

Introduction and Background

The primary objective of the Task Group was to develop guidelines for the use of ventilation/perfusion scintigraphy for the diagnosis and follow up of PE. In the first part of Guidelines, principles, techniques and interpretation with focus on V/P_{SPECT} were presented with respect to diagnosis of PE and other diseases such as Chronic Obstructive Pulmonary Disease, left heart failure and pneumonia [1]. The objectives of this second part were to define the importance of clinical probability together with objective imaging tests and to analyze advantages and disadvantages of V/P_{SPECT} compared to MDCT.

Referral Criteria and Assessment of Clinical Probability

Diagnosis of PE

Knowledge of pre-disposing factors is a useful guide to the diagnosis but as many as 26 to 47% of first time cases of venous thromboembolism have no recognisable risk factor for this disease [2]. The electrocardiograph may provide pointers to the presence of right ventricular overload such as S1, Q3, T3, right bundle branch block, right axis deviation and, in longstanding cases, P-pulmonale. The chest radiograph may provide evidence of atelectasis, raised hemidiaphragm, cardiomegaly, pulmonary infarction and Westmark's sign (vascular rarefaction) [3]. However, while these are pointers, they are not diagnostic of PE [4]. The chest radiograph is useful for alternative diagnoses such as pneumothorax, pneumonia,

Chronic Obstructive Pulmonary Disease, lung cancer or pulmonary fibrosis. Patients with PE may have arterial hypoxaemia and hypocapnia [4-6]. However, these signs are non specific and are seen also in patients without PE.

Assessment of the clinical probability of pulmonary embolism

The results of broad prospective studies lend support to the concept that clinical probability assessment is an important step in the diagnosis of pulmonary embolism [4, 7-11]. When considered individually, symptoms, signs, or common laboratory tests have limited diagnostic power. Jointly, however, they may provide accurate assessment of the clinical probability of pulmonary embolism.

Assessment of the clinical probability can be accomplished empirically or by means of a prediction rule. The latter is preferable over empirical assessment, especially for less experienced clinicians. In recent years, structured prediction models for pulmonary embolism have been developed with the very purpose of improving and easing the diagnostic approach[12-17].

The Canadian model introduced by Wells at al. [16] is the most frequently used prediction rule for suspected pulmonary embolism (Table 1). It includes seven variables of which three refer to well-recognized risk factors for pulmonary embolism. The model heavily depends on the subjective judgement as to whether an alternative diagnosis is less likely than pulmonary embolism and, as such, it can hardly be standardized. The Wells’ model seems better suited to rule out rather than to rule in the diagnosis of pulmonary embolism [13], and its performance is likely to be better in clinical settings where the prevalence of the disease is expected to be low [18].

Table 1. Wells’ model	
Predictor	Score
Prior PE or venous thromboembolism	1.5
Heart rate >100 beats per minute	1.5
Recent surgery or immobilization	1.5
Signs of venous thromboembolism	3.0
Alternative diagnosis less likely than PE	3.0
Hemoptysis	1.0
Cancer	1.0

PE: pulmonary embolism.

Recently, a more precise prediction model [14] was introduced which rests on 16 variables including older age, risk factors, pre-existing cardiopulmonary diseases, relevant clinical symptoms and signs, and the interpretation of the electrocardiogram (Table 2). The area under the receiver operating characteristic curve was 0.90 in the derivation sample (N=1,100), and 0.88 in the validation sample (N=400). In contrast to other prediction rules, the model includes variables that are negatively associated with pulmonary embolism. This gives the model greater flexibility which may explain why it performs equally well in detecting and in

ruling out pulmonary embolism. Also, instead of using a point-scale score proportional to the regression coefficients, typical of other approaches [12, 16, 17], the probability of pulmonary embolism is estimated directly from the algebraic sum of the regression coefficients. This allows predicting the clinical probability as a continuous function. It estimates precisely likelihood ratios for PE. Its clinical value is explored in recent study [14] To facilitate the applicability of the model in clinical settings, easy-to-use software is available for online computation of the clinical probability on palm computers and mobile phones (<http://www.ifc.cnr.it/pisamodel>).

Predictor	Coefficient
Age 57-67 y	0.80
Age 68-74 y	0.87
Age 75-95 y	1.14
Male sex	0.60
Prior cardiovascular disease	-0.51
Prior pulmonary disease	-0.89
History of venous thromboembolism	0.64
Immobilization (> 3 days)	0.42
Sudden onset dyspnea	2.00
Orthopnea	-1.51
Chest pain	1.01
Hemoptysis	0.93
Fainting or syncope	0.66
Unilateral leg swelling suggestive of venous thromboembolism	0.80
Fever >38 °C	-1.47
Whezees	-1.20
Crackles	-0.61
ECG signs of acute cor pulmonale	1.96

ECG: electrocardiogram

Combining clinical probability with objective testing for pulmonary embolism

Assessing the clinical probability of PE helps clinicians choose the more appropriate objective test for diagnosing or excluding PE (Figure 1).

The measurement of D-Dimer - a breakdown product of cross-linked fibrin clot - is widely used in the investigative work up of patients with suspected venous thromboembolism [19]. Quantitative assay of D-Dimer, based on rapid ELISA method, has a high sensitivity (in the region of 95%) for venous thromboembolism [19]. Yet, the test features a low specificity (40%) because D-dimer may be raised in a number of conditions other than venous thromboembolism such as acute myocardial infarction, stroke, inflammation, active cancer, and pregnancy. The specificity falls with age and, in the elderly, may reach only 10% [19]. Accordingly, a negative quantitative D-dimer test has a high negative predictive value for venous thromboembolism. Results of outcome studies reveal that the risk of developing PE in patients with low clinical probability, who are untreated after a negative D-dimer test is < 1% at 3 months of the initial evaluation [18, 19]. On the other hand, due to the low predictive value, a positive quantitative D-dimer test does not modify the pretest (clinical) probability and is, therefore, clinically useless. Recent evidence, however, suggests that very high D-dimer levels are associated with a fourfold increase in the likelihood of PE [20]. It may be important in assessing the burden of thromboembolic disease [21] and may have prognostic significance [22, 23].

Clinical Algorithm for Investigation of Patients with Suspected PE

Stable patients

Based on the above, if the clinical likelihood of PE is low and the quantitative D-dimer is negative, a diagnosis of PE is unlikely and further investigations are not required (Figure 1). If the clinical likelihood of PE is low and the quantitative D-dimer is positive, further investigations for a range of diagnoses including PE may be required, particularly if the D-dimer level is markedly elevated. If the clinical probability is other than low, it seems more appropriate to skip D-dimer test and refer the patient directly to the appropriate imaging technique (Fig. 1). This may be V/P_{SCAN} or MDCT depending on the local availability, medical expertise, and patient's clinical condition. V/P_{SCAN} has virtually no contraindications and yields a substantially lower radiation burden than MDCT. The latter is more widely and readily available.

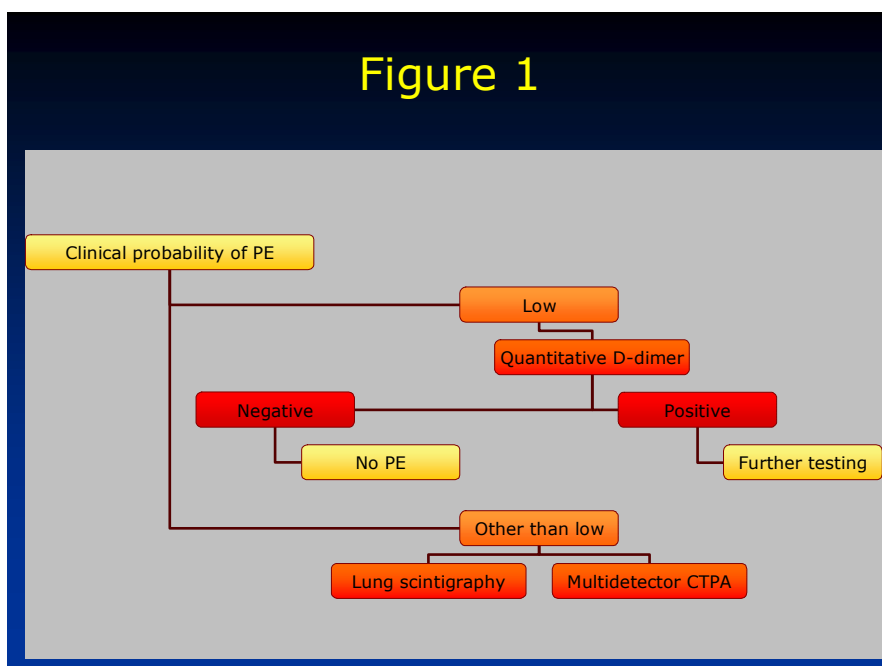


Fig. 1. Algorithm for referral of patients with suspected acute PE for imaging test

Massive PE

If the patient presents with severe hypotension or cardiogenic shock (Figure 2), transthoracic echocardiography may stand as the first-line imaging technique. It allows detection of right heart dilatation and hypokinesis [24]. In rare circumstances, it may visualize emboli within the right heart cavities or main pulmonary artery [25]. Perfusion lung scintigraphy is an alternative option as it may quickly show multiple segmental or lobar perfusion defects that are typical of acute pulmonary embolism [8]. If an acute dissection of the thoracic aorta is suspected because of chest pain, MDCT may offer the opportunity of this differential diagnosis. Given the need for haste in diagnosis and treatment of such patients, the diagnostic strategy employed at a particular institution must be adapted to the specific clinical situation and to the local circumstances.

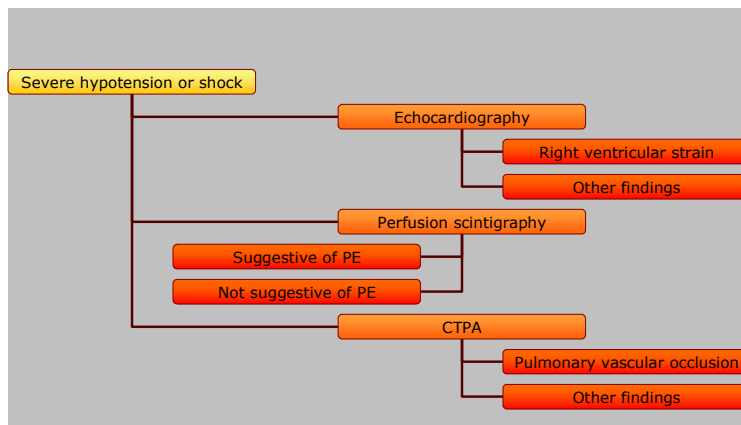


Fig. 2. Algorithm for referral of patients with suspected acute PE for imaging test

When the initial exam suggests massive PE further action must be adapted to the clinical situation. Thrombolytic therapy might be given. If not already performed, a perfusion scan should be performed as soon as possible as a basis for further follow up.

Imaging Studies in PE

As clarified in Part 1 [1], the diagnosis PE relies upon imaging tests notably V/P_{SCAN} and MDCT. These techniques are discussed below with focus on the following:

- A. Diagnostic value with respect to accuracy of PE diagnosis
- B. Clinical feasibility with respect to contraindications and availability
- C. Radiation exposure
- D. Suitability for follow up and research
- E. Overall diagnostic strategies for good clinical practise

Comparison of V/P_{SPECT} and MDCT

Diagnostic accuracy

MDCT is often recommended as the imaging test of first choice for PE diagnosis [26]. The evidence base for the use of MDCT as the principal imaging tool for PE diagnosis is not as robust as was generally thought. There is an emerging evidence base showing improved

diagnostic accuracy for PE using V/P_{SPECT}. The following is a discussion of the merits of V/P_{SPECT} versus MDCT in PE diagnosis.

In many clinical studies, including recent ones, comparisons between V/P_{SCAN} and MDCT have been based upon obsolete scintigraphic techniques and interpretation criteria [7, 10]. In particular, PIOPED I had a non-diagnostic outcome of 65% using scintigraphy. It has been shown that a reduction in the number of non-diagnostic reports to 10% can be achieved even with V/P_{PLANAR} with adequate acquisition [27] and a holistic interpretation strategy [28]. With V/P_{SPECT} and non-probabilistic interpretation, this number is further reduced to below 3% [29-33].

The lack of a satisfactory gold standard for PE diagnosis poses difficulties for the assessment of sensitivity, specificity and accuracy of all diagnostic methods for PE. The best available benchmark is an adequate follow up of the patients for recurrence of PE or alternative diagnoses. The most rigorous study of MDCT in PE diagnosis is the PIOPED II study using 4-16 slice MDCT [10]. This study showed a sensitivity for PE of 83 % excluding non-diagnostic studies. This led to the observation that “The false negative rate of 17 % for MDCT indicates the need for additional information to rule out PE” [34]. If non-diagnostic studies were included the overall sensitivity fell to 78%. In the PIOPED II study the positive predictive value for a PE within a lobar pulmonary artery was 97 % but fell to 68 and 25 % in segmental and subsegmental pulmonary vessels, respectively.

After a negative single slice CT, PE occurred in 1.4 % of patients in a metaanalysis of 4637 patients [35]. After a negative PA study this was 1.6% [36] and after a negative MDCT 1.5 % (n=318). After a negative V/P_{SCAN}, occurrence of PE during follow up was 0.4 % in all together 1877 patients % % [37-39,

29]. Freeman stated that the results from the PIOPED II study “do not clearly support the superiority of CT angiography over ventilation/perfusion scanning for the diagnosis of PE” [40]. Notably, this conclusion was based upon V/P_{PLANAR} and probabilistic interpretation. A direct comparison between V/P_{SPECT} and 4-slice MDCT showed a higher sensitivity by V/P_{SPECT} [33]. In a recent retrospective study Bajc et al, showed that V/P_{SPECT} had higher sensitivity, and specificity and less non-diagnostic findings than 16-slice CT [29]. Further prospective comparisons between up to date V/P_{SPECT} and MDCT are needed. In reading of V/P_{SPECT}, low inter-observer variability has been shown by a kappa value of 0.92 [30].

In Part 1 of these guidelines additional diagnoses, which are found at V/P_{SPECT}, includes chronic obstructive pulmonary disease, left heart failure and pneumonia [29] According to everyday practise also MDCT provides a lot of diagnostic information apart from PE, like aortic aneurysm, tumor, pleural effusion and pneumonia.

Feasibility

PIOPED II illustrates well the limited clinical utility of MDCT. In 50 % of eligible cases, MDCT could not be performed because of kidney failure, critical illness, recent myocardial infarction, ventilator support and allergy to the contrast agent. Furthermore, 6 % of performed MDCT studies were of insufficient quality for conclusive interpretation. In about 1 % complications like allergy, contrast extravasation and increased creatinine level were observed.

By contrast, V/P_{SPECT} has no contraindications and was performed in 99 % of patients referred in the study of Bajc et al. [29]. Complications do not occur, and the rate of technically suboptimal studies is close to zero. It is possible to accommodate patients who are

mechanically ventilated by connecting a nebulizer to the inspiratory ventilator line. In rare cases, when V/P_{SPECT} cannot be performed, V/P_{PLANAR} remains an alternative.

Availability

MDCT is available in nearly all medical centres and community hospitals. Service is often available around the clock seven days a week. V/P_{SPECT} is available in much fewer hospitals and seldom on a 24 hours basis. Obviously the choice between MDCT and scintigraphy is often based upon the difference in availability. In hospitals with nuclear medicine facilities the routine may vary in dependence upon when scintigraphy is available.

Radiation dose

Image quality can be enhanced allowing higher radiation doses both when using X-ray techniques and isotope studies. Obviously, any clinical routine should be based upon procedures offering as low as possible radiation dose but with image quality that is proven appropriate with respect to a particular diagnosis.

V/P_{SPECT}

Radiation doses for V/P_{SPECT} are rather exactly estimated according to the International Commission for Radiation Protection (ICRP). A systematic analysis of imaging protocols for V/P_{SPECT} showed that 25-30 MBq $^{99\text{m}}\text{Tc}$ -aerosol for ventilation and 100-120 MBq $^{99\text{m}}\text{Tc}$ -MAA for perfusion in combination with proper collimation and time for imaging rendered optimal V/P_{SPECT} images for PE diagnosis[41]. The protocol has documented efficacy for diagnosis of PE and also for left heart failure [29, 42]. Using these activities the effective radiation dose from V/P_{SPECT} is 1.2-2 mSv (Table 1 in Part 1)[1]. The absorbed dose to the female breast is estimated to 0.8 mGy [43, 44]. During the first trimester the data of Hurwitz applied to the recommended dose for perfusion study (50 MBq) gives a fetal absorbed dose of 0.1-0.2 mGy [45].

MDCT

At centres with identical multi-slice-scanners, the estimation of absorbed doses may vary with a factor of 7 depending on CT-protocols and other variables [46]. In general, MDCT results in higher direct radiation and scatter doses than single slice CT [47-49]. This may change with the introduction of radiation saving protocols, vide infra. In the literature, estimations of radiation dose from MDCT vary within wide limits. According to ICRP publication 102 [50], the average effective dose for 4-16-detector MDCT is 5.4 mSv. Notably, this information was based on computed rather than measured dose data. Hurwitz et al. reported for current adult PE protocol with 64-detector MDCT a measured effective dose of 19.9 ± 1.38 mSv [51]. These authors point out that real measured doses are about 50 % higher than those computed. The absorbed dose to the breasts was 35-42 mGy. Absorbed radiation dose to the breast for a single slice CT was 20-50 mGy and 30-50 % greater with a 4-slice CT [52]. In a very recent study Hurwitz et al. [53] studied radiation dose saving regimes. Phantoms of women were exposed to MDCT protocols with automatic current modulation, lower tube voltage and bismuth shields over the chest. For the medium sized woman with automatic current modulation, the breast dose was at 140 kVp 62 mGy, and 33mGy when bismuth shields were added. At 120 kVp the dose was 44 mGy without shields and 20 mGy with shields. Some limitations of the study were discussed. No phantom with significant subcutaneous fat was studied. The authors were not able to directly assess the effect of increased noise for the diagnosis of PE. Dose saving protocols are promising.

The fetal radiation dose from a 16 slice MDCT was recently analyzed by Hurwitz [45]. During the first trimester the absorbed fetal dose was estimated to 0.24-0.66 mGy and significantly higher later during gestation.

Recent studies show that MDCT is often technically suboptimal during pregnancy. The rate of non-diagnostic MDCT exams was 27.5% during pregnancy, versus 7.5% in non-pregnant women [54]. In 10 out of 16 pregnant women, contrast opacification within pulmonary arteries was borderline or insufficient for diagnosis [55]. A reason for poor diagnostic outcome of MDCT in pregnancy is probably increased cardiac output and plasma volume.

V/P_{SPECT} and MDCT. Based upon data from ICRP reports, the effective dose for V/P_{SPECT} with the recommended protocol is about 35-40 % of the dose from MDCT [43,44,50]. The dose to the female breast for V/P_{SPECT} is only 4 % of the dose from MDCT with full dose saving means according to Hurwitz [53]. This may have particular importance in pregnant women with proliferating breast tissue [56]. During the first trimester of pregnancy the fetal dose of MDCT is greater than or equivalent to that of V/P_{SCAN}[45]. The advantage of V/P_{SPECT} increases after the 1st trimester.

Follow up

Follow up of PE using imaging is essential to:

- assess the effect of therapy
- differentiate between new and old PE at suspicion of PE recurrence
- explain physical incapacity after PE

In symptomatic patients treated for PE, the outcome varies, from total resolution of thrombi within days, to permanent vascular occlusion. In spite of this, most patients are treated with heparin/warfarin for six months. Some patients have a tendency to recurrent episodes of PE. Without initial and follow up images, it is often impossible to differentiate between old and new PE. In patients with low degree of resolution and, particularly in those with recurrent emboli, life long therapy is indicated. In this group of patients the physical capacity is often reduced. Follow up imaging may explain symptoms caused by unresolved PE [59] or by other diseases e.g. Chronic Obstructive Pulmonary Disease or heart failure.

Patients treated with thrombolysis for massive PE suffer risks for bleeding, but also dangers related to unresolved PE. Immediate control gives objective information about the need for repeated thrombolysis.

Symptomatic patients with small emboli are diagnosed with sensitive methods, particularly V/P_{SPECT}. The natural history and the value of treatment in this group of patients are rather unknown. Follow up is indicated to individualise therapy, as further discussed under Research.

Requirements on a method used for follow up are:

- Applicability in all patients
- Low radiation dose
- High sensitivity to allow estimation of resolution of even small emboli and occurrence of new ones

Recommendation

V/P_{SPECT} is ideally suited for use in the follow up of PE because small and large emboli are recognized so that regression or progression of thrombotic disease can be studied in detail. Furthermore, the low radiation exposure allows repeated studies. It can be applied in all

patients. Obviously, using the same method for diagnosis and for follow up has great advantages.

Suitability for research

Knowledge about the natural history of PE is limited. There is a need to study alternative strategies for PE therapy, with respect to therapy duration and choice of drugs in different categories of patients. It is likely that shorter and less dangerous treatment programs might be preferable in selected patients. The low incidence of symptomatic PE at follow up after negative imaging tests might be explained by that most emboli are non-occlusive and cause no harm. The lung is an efficient filter for emboli, which may be a common and natural phenomenon. It has in most people a high capacity to resolve thrombi fast, regardless of initial PE extension. This was shown by a 44 % decrease of perfusion defects after only five days of low molecular heparin treatment, which in itself has no thrombolytic effect [58]. Very short treatment, or even non-treatment, might be a favourable strategy in selected patients. The demands on an imaging technique for research of PE and its treatment are in principle the same as for clinical follow up. However, in research, the motivation to use non-traumatic procedures associated with lowest possible risks is on ethical reasons even stronger.

Recommendation

V/P_{SPECT} is recommended for research about the natural course and treatment of PE.

Diagnostic algorithms

PE, when suspected, must be confirmed or refuted to avoid risks of both over and under treatment. This requires imaging tests. Only optimal techniques are recommended. These are MDCT and V/P_{SPECT} with holistic interpretation.

The imaging modality used will depend on availability. While MDCT is more readily available it is contraindicated in substantial numbers of patients as shown in the PIOPED II study [10]. At present, V/P_{SPECT} is rarely available over 24 hours 7 days a week. Accordingly, these two methods should be available at least in tertiary hospital centres because both are crucial for adequate diagnostic algorithms of PE. In each centre, the diagnostic algorithm applied for diagnosis of PE must be based upon local circumstances, first and foremost upon the availability of V/P_{SPECT} and MDCT.

- MDCT is in general much more available than V/P_{SPECT}
- V/P_{SPECT} carries no risk associated with contrast injection
- V/P_{SPECT} give much lower radiation burden
- V/P_{SPECT} yields lower rate of non-diagnostic reports
- V/P_{SPECT} has higher sensitivity at similar specificity
- V/P_{SPECT} allows better estimation of PE extension based upon functional impact of PE

It follows that, when available, V/P_{SPECT} offers considerable advantages over other imaging techniques for the diagnosis of PE. These advantages include its high sensitivity and specificity for PE diagnosis, its lower and predictable radiation burden, and its suitability for follow up of patients with PE and for research into the natural history of PE. On the basis of recent methodological development of V/P_{SPECT} and documentation of its performance it is recommended that this method is spread and made more generally available. Under ideal circumstances either V/P_{PLANAR} or V/P_{SPECT} can be performed and interpreted within one hour

after referral [41, 59], It is acknowledged that MDCT is widely and readily available and that it will take some time for V/P_{SPECT} to reach parity with MDCT. Accordingly, diagnostic algorithms should be based upon V/P_{SPECT} and MDCT. From centres with no availability for V/P_{SPECT}, patients may be referred for V/P_{SPECT} studies elsewhere, when indicated.

The knowledge on V/P_{SPECT} is available. As there are only few centres using this technique and particularly its holistic interpretation there is a need for systematic teaching and training. This is a responsibility of the discipline Nuclear Medicine.

According to good clinical practice V/P_{SPECT} should be widely implemented and followed by clinical audits.

In the algorithm illustrated in Figure 3, the entry point is based on clinical probability of PE, as illustrated in Fig. 2.

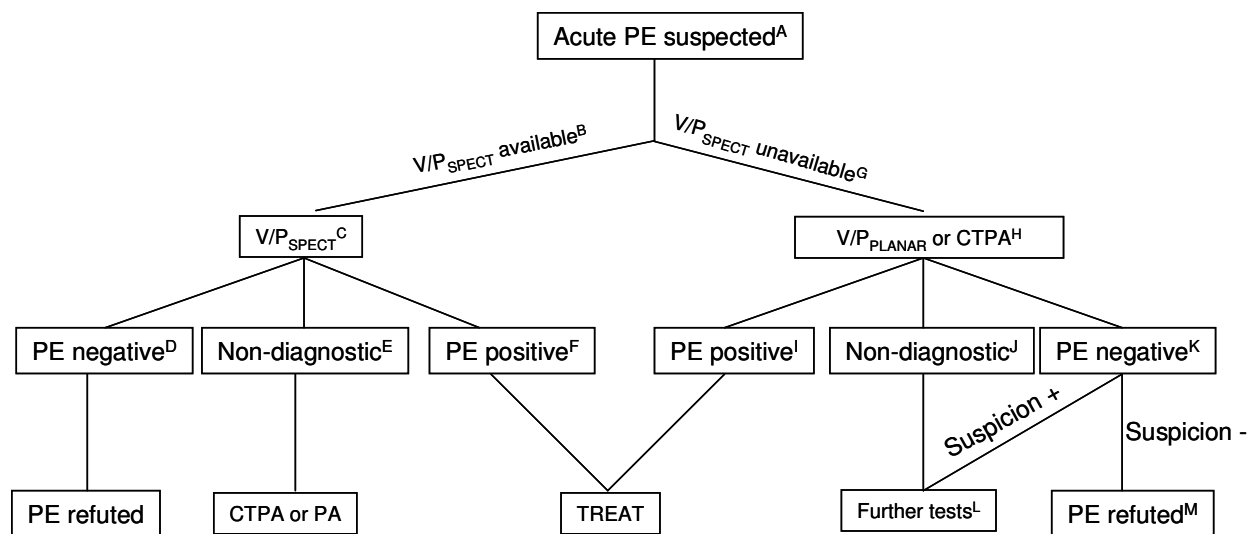


Figure 3

- A) Clinical suspicion derived from symptoms and signs in accordance with Entry Criteria.
- B) V/P_{SPECT} is procedure of choice. If V/P_{SPECT} is not immediately available, consider treatment (low molecular heparin) depending on clinical circumstances.
- C) V/P_{SPECT} is interpreted according to the holistic principle in which clinical pretest probability is a part.
- D) A normal V/P_{SPECT} is observed in the majority of cases and excludes PE to nearly 100 %.
- E) Few cases are non-diagnostic. Further diagnostic procedures are recommended as MDCT or in special cases PA.
- F) V/P_{SPECT} is the most sensitive method. Positive findings should lead to treatment in nearly all cases. Research is urgently needed about treatment of very low grade of mismatch indicating PE.
- G) V/P_{PLANAR} , holistically interpreted, or MDCT is recommended when V/P_{SPECT} is not available within acceptable delay.
- H) V/P_{PLANAR} is preferred on the basis of better negative predictive value, no contraindications and much lower radiation exposure.
- I) A positive V/P_{PLANAR} or MDCT indicates treatment in most cases. At low pretest probability, a positive MDCT without direct visualization of the embolus indicates further diagnostic procedures.
- J) At non-diagnostic V/P_{PLANAR} or MDCT, further tests are indicated.
- K) At negative MDCT, further tests should be performed in patients with remaining clinical suspicion of PE.
- L) V/P_{SPECT} is the preferred further test. If not possible, MDCT should be followed by V/P_{PLANAR} or vice versa. PA remains an alternative after non diagnostic findings.
- M) Normal V/P_{PLANAR} excludes PE adequately. At pathological V/P_{PLANAR} but negative for PE, or at negative MDCT, PE is refuted in patients with discontinued clinical suspicion.

Types of Evidence and Grading

The definition of types of evidence and the grading of recommendations used in the guidelines follow that of the Agency for Healthcare Research and Quality (formerly Agency for Health Care Policy and Research, AHCPR), as set out below:

Type of evidence

Level	Type of evidence
1a	Evidence obtained from meta-analysis of randomised controlled trials
1b	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomisation
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies
IV	Expert opinion

Based on AHCPR, 1992

Grading of recommendations

Grade	Evidence level	Description
A	1a, 1b	Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation
B	IIa, IIb, III	Requires availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation
C	IV	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality

Based on AHCPR, 1994

Recommendations	Level	Grade
Clinical Assessment of Suspected PE		
Clinical probability should be used to select patients for imaging studies in suspected PE	Ib	A
Patients with a low clinical probability of PE and a normal quantitative D-dimer, further imaging tests for PE are not normally required	IIa	B
Patients requiring imaging tests for suspected PE, should undergo these investigations within 24 hours of referral	III	C
In patients with suspected massive pulmonary embolism, diagnosis should be established with haste allowing appropriate treatment to commence. In these circumstances echocardiography, MDCT or V/P _{SCAN} imaging may assist with diagnosis depending on availability.	III	C
Ventilation Scans		
A ventilation study should be done to support the perfusion scan in all cases of suspected PE, except during the first trimester of pregnancy.	Ib	A
^{81m} Kr is the radioactive gas of choice, when available, being a true gas and allowing simultaneous acquisition with the perfusion images.	III	C
Radiolabelled aerosols with documented particle size and distribution pattern are recommended on the basis of their widespread availability.	III	C
^{99m} Tc-Technegas is the agent of choice in the presence of obstructive lung disease.	III	C
^{99m} Tc-DTPA aerosol is the agent of choice when ^{99m} Tc-Technegas is not available.	III	C
Perfusion Scans		
^{99m} Tc-MAA is the agent recommended for perfusion scintigraphy.	IIa	B
The minimum number of particles is 60 000 but ideally the number should be about 400 000.	III	C
In infants/children and in patients with known pulmonary hypertension the number of particles should be reduced.	III	C
The vial should be gently shaken before injection and blood withdrawal into the syringe before injection should be avoided.	III	C
Injection should be performed under normal tidal breathing in the supine posture.	III	C
Imaging Protocols		
For PE imaging a one-day V/P study should be performed, starting with ventilation, followed by perfusion, aiming for an activity ratio of 1:4	IIb	B
V/P _{SPECT} is preferred to V/P _{PLANAR} when using V/P _{SCAN} for PE diagnosis	IIb	B
When using planar imaging, a minimum of 6 views is recommended.	IIb	B
In pregnancy, particularly during the first trimester, a 2 day protocol starting with a perfusion-only scan followed if necessary by a second day ventilation study	IV	C

DTPA – Diethylene Triamine Pentaacetic Acid

Recommendations	Level	Grade
Interpretation and Reporting of V/P Scans		
Probabilistic criteria such as that used in the PIOPED studies are flawed and should not be used for the interpretation of V/P _{SCAN}	1b	A
No PE should be reported if the perfusion scan is normal as defined by the anatomic boundaries of the lungs.	1a	A
No PE should be reported if perfusion defects are matched or reverse mismatched	IIb	B
No PE should be reported if perfusion defects do not conform to vascular anatomy, i.e pulmonary, lobar, segmental or sub-segmental in pattern	IIb	B
PE should be reported if there is at least one segmental or two sub-segmental perfusion defects.	IIb	B
The lung scan report should include mention of all relevant findings particularly when this may have a bearing on further patient management.	III	B
V/P _{SPECT} is ideally suited for use in the follow up of PE because small and large emboli can be assessed for regression or progression.	IV	C
V/P _{SPECT} is a useful tool for research about the natural course and treatment of PE.	IV	C

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