Methodology for ventilation/perfusion SPECT.

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Methodology for Ventilation/Perfusion SPECT

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Ventilation/perfusion single-photon emission computed tomography (V/Q SPECT) is the scintigraphic technique of choice for the diagnosis of pulmonary embolism and many other disorders that affect lung function. Data from recent ventilation studies show that the theoretic advantages of Technegas over radiolabeled liquid aerosols are not restricted to the presence of obstructive lung disease. Radiolabeled macroaggregated human albumin is the imaging agent of choice for perfusion scintigraphy. An optimal combination of nuclide activities and acquisition times for ventilation and perfusion, collimators, and imaging matrix yields an adequate V/Q SPECT study in approximately 20 minutes of imaging time. The recommended protocol based on the patient remaining in an unchanged position during the initial ventilation study and the perfusion study allows presentation of matching ventilation and perfusion slices in all projections as well as in rotating volume images based upon maximum intensity projections. Probabilistic interpretation of V/Q SPECT should be replaced by a holistic interpretation strategy on the basis of all relevant information about the patient and all ventilation/perfusion patterns. PE is diagnosed when there is more than one subsegment showing a V/Q mismatch representing an anatomic lung unit. Apart from pulmonary embolism, other pathologies should be identified and reported, for example, obstructive disease, heart failure, and pneumonia. Pitfalls exist both with respect to imaging technique and scan interpretation.
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Certain symptoms and signs are more commonly observed in pulmonary embolism (PE) than in other conditions. However, a diagnosis of PE cannot be established by clinical features alone. The diagnosis of PE must be confirmed or refuted with the use of a conclusive imaging test. Increasing evidence indicates that the optimal test for the detection of PE is ventilation/perfusion (V/Q) single-photon emission computed tomography (SPECT) interpreted along holistic principles. (Note: the ventilation/perfusion relationship, which, for consistency with other articles in this issue of the journal, is denoted "V/Q," has also recently been referred to in the European guidelines as "V/P." Both forms are in common use.) A methodology, including diagnostic algorithms and interpretation rules, has recently been proposed in the European guidelines for V/Q scintigraphy.[1] An important first step is the decision to undertake an imaging test. The guidelines suggest the use of a clinical prediction model for PE as suggested by Miniati et al[2] or Wells.[3] The model according to Miniati et al has the advantage that it does not depend on any laboratory test. An estimate of the likelihood of PE can be made at the patient's bedside with use of an electrocardiogram as the only additional test.

Resolution of PE in patients is variable. It has been reported that most patients continue to have unresolved PE 6 months after diagnosis.[4] Others have reported rapid resolution of a large PE within days or even hours of the onset of therapy.[5-7] Therefore, and to reduce the risks associated with untreated disease, it is recommended that imaging tests for PE diagnosis should be carried out as soon as possible, preferably within 24 hours of the onset of symptoms.[8]

In clinical practice, a test that is both fast and conclusive is essential. As the scintigraphic diagnosis of PE is determined by regions with absent perfusion but preserved ventilation, ie, mismatch, an efficient protocol should comprise V/Q studies in one session.

Basic Principles of PE Diagnosis

Each bronchopulmonary segment and subsegment is supplied by a single end-artery. The arteries supply a conical

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zone with apex towards the hilum and base along the pleural surface. Emboli, which are usually multiple, occlude the arteries causing lobar, segmental or subsegmental perfusion defects within still ventilated regions (Fig.1). During the process of resolution/breakdown of emboli, perfusion may be only partially restored, in which case the V/Q mismatch becomes less distinct. PE is often a recurring process that gives rise to multiple emboli in various stages of resolution. The objective of this work is to outline a state-of-the-art methodology for V/Q SPECT for diagnosis of PE and some other cardiopulmonary diseases.

Imaging Agents

Ventilation Agents

For scintigraphic ventilation studies the following agents have been used:

- inert gases ^{133}Xe and ^{81m}Kr;
- radiolabeled aerosols [^{99m}Tc]-DTPA; and
- ^{99m}Tc-labeled Technegas.

Gases

Historically, ^{133}Xe was the agent that was used for ventilation studies.[9,10] As it cannot be used for SPECT, it is not discussed further. ^{81m}Kr is a gas generated on-site from the parent rubidium (^{81}Ru).[11] It has the ideal gamma energy of 193 keV. The short half-life of 13 seconds implies that inhaled ^{81m}Kr disappears from the alveolar space by decay at a much faster rate than by exhalation. At normal respiratory rates, the regional alveolar ^{81m}Kr concentration will within minutes approach a level approximately proportional to regional ventilation.[12] As ^{81m}Kr is a gas, central airway deposition does not occur. To illustrate regional alveolar ventilation, SPECT acquisition is performed during continuous inhalation of ^{81m}Kr. Because ^{81m}Kr has greater gamma energy than ^{99m}Tc (140 keV), V/Q can be imaged simultaneously.[13-15] Radiation exposure from a ^{81m}Kr study is particularly low. The effective dose for 6000 MBq (reference amount) is only approximately 0.2 mSv. The ^{81m}Kr generator can be used only for one day because ^{81}Ru has a half-life of 4.6 hours. Limited access and high costs are further reasons why ^{81m}Kr is used sparingly. Gutte et al[15] reported that V/Q SPECT with ^{81m}Kr was uninterpretable in 8% of patients because of poor technical quality.

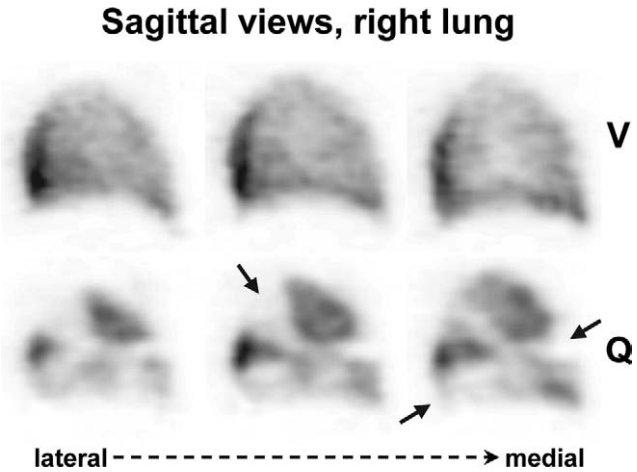

Figure 1 Patient with PE. Sagittal slices, right lung; ventilation with corresponding perfusion images. Multiple areas with absent perfusion (arrows) and preserved ventilation.

Aerosols

Ventilation scintigraphy is usually based upon inhalation of a radiolabeled aerosol. The aerosol particles may be liquid or solid and are suspended in air. The deposition of the particles depends on the aerodynamic properties of the particles, mainly their size. Large particles (>2 μm) are deposited mainly by impaction in large airways, from mouth to trachea. Particles <2μm reach small airways and even alveoli and are deposited by sedimentation and diffusion. Very fine particles (<1 μm) are mainly deposited in alveoli by diffusion. At first, the challenge for radio-aerosols was to make nebulized particles as small as possible. The need to use as small particles as possible has been demonstrated by Friedlander.[16] Aerosol deposition also depends upon flow pattern. Turbulent flow enhances particle deposition by impaction. This happens at bronchial branching and irregularities, for example, in patients with chronic obstructive pulmonary disease (COPD). This leads to "hot spots" ie, focal areas of intense radionuclide accumulation, in the central airways in ventilation images. Furthermore, high flow rates and forced breathing patterns contribute to this problem.

An important property of an aerosol is its mass median aerodynamic diameter (MMAD). The MMAD takes into account that the radioactivity carried by each liquid particle is proportional to its volume, which increases with the diameter raised to the power of 3. Fifty percent of the radioactivity resides in particles smaller than the MMAD and 50% in larger particles.[17] The MMAD should preferably be smaller than 1.2 μm.[18-21] It is not easy to define the aerodynamic properties of an aerosol. Hydrophilic particles may grow in size as the result of the humid environment of the airways. Particle aggregation is another problem. A basic recommendation is that the maximum droplet size inhaled by the patient should not exceed 2 μm. Due to the complexity of the physics behind aerosol deposition patterns, the performance of a nebulizer must be evaluated clinically.

Water-Soluble Agents. The principal water-soluble agent used for ventilation scintigraphy is diethylene-triaminepentaacetic acid labeled with technetium, [^{99m}Tc]-DTPA. Because it is a molecule of intermediate size (492 Da) and soluble in water, [^{99m}Tc]-DTPA diffuses through the alveolocapillary membrane to the blood. In a healthy nonsmoker, elimination of [^{99m}Tc]-DTPA occurs with a clearance half time of approximately 70 minutes. Increased clearance rate, leading to a shorter clearance half time, is observed where there is alveolar inflammation of any cause, such as alveolitis of allergic or toxic nature and even in smokers.[17,22,23] Clearance of [^{99m}Tc]-DTPA can for diagnostic purposes be measured using planar or tomographic scintigraphy.[24,25]

Solid Particle Agent. In many countries, Technegas (Cyclomedica Australia, Sydney, Australia) is the preferred agent for ventilation scintigraphy, mainly because of the extremely

small particle size, ie, about 0.005 to 0.2 μm.[26] ^{99m}Tc-labeled solid graphite particles are generated in a furnace at high temperature.[27,28] The particles are hydrophobic but tend to grow by aggregation and should therefore be administered within 10 minutes after generation.

Comparison of Ventilation Agents

Gases have the advantage that they are distributed according to regional ventilation without any local accumulation on airway walls. Ventilation scintigraphy using ^{81m}Kr is regarded by many as the gold standard for ventilation studies, although its regional concentration does not perfectly match ventilation in areas with extremely high or low alveolar ventilation in relation to volume.[12]

Ventilation studies with Technegas and with ^{81m}Kr give similar information.[29-33] This reflects the fact that Technegas particles are so small that the aerosol closely follows the gas flow down to the alveoli, where they are deposited by diffusion.[31,34] In comparison with liquid radio-aerosols, Technegas has significantly fewer problems of central airway deposition and peripheral "hotspot" formation in patients with obstructive lung disease. Recently, a group of patients routinely admitted for V/Q SPECT and a group of patients with known COPD were studied head to head with [^{99m}Tc]-DTPA and Technegas.[35] In both groups, overall unevenness of radiotracer deposition and degree of central deposition were more pronounced with [^{99m}Tc]-DTPA than with Technegas, particularly in the obstructive patients. In some cases, mismatched perfusion defects were only identified by the use of Technegas. This finding was attributable to the fact that general peripheral unevenness of [^{99m}Tc]-DTPA obscured mismatch, whereas a better peripheral penetration of Technegas highlighted the mismatch. Accordingly, PE might have been overlooked in COPD patients when [^{99m}Tc]-DTPA was used. In a few patients, [^{99m}Tc]-DTPA yielded images of very poor quality. It was concluded that Technegas is the superior imaging agent, particularly in patients with obstructive lung disease. A further advantage using Technegas is that a few breaths on the part of the patient are sufficient to deliver an adequate amount of activity to the lungs.

Perfusion Agents

[^{99m}Tc]-MAA

Technetium-labeled particles of macroaggregates of human albumin ([^{99m}Tc]-MAA) are almost universally used as the perfusion agent for lung scintigraphy. After intravenous injection, the particles of size 15 to 100 μm are lodged in the pulmonary capillaries and in the precapillary arterioles in proportion to perfusion. At least 60,000 particles are required to adequately image regional perfusion.[36] In clinical practice, approximately 400,000 particles are routinely injected. As there are approximately 300 million precapillary arterioles and many billions of pulmonary capillaries, a very small fraction of pulmonary vessels will be occluded. It is recommended that in patients with pulmonary hypertension the numbers of administered particles should be reduced in proportion to the severity of the condition. In infants and children, the number of particles is adjusted according to weight.[37] For the most uniform distribution, the [^{99m}Tc]-MAA suspension should be administered by slow intravenous injection, while the patient breathes at normal tidal breathing.

Imaging Protocols

V/Q SPECT Acquisition

Administration of ventilation and perfusion agents should be performed with the patient in the supine position to minimize gravitational gradients. During inhalation of the ventilation agent, activity over the lungs should be monitored to ensure adequacy of pulmonary deposition.

To achieve adequate imaging quality, with low radiation exposure and in a short time, relationships between activities, acquisition times, collimators, and acquisition matrix size for SPECT imaging must be optimized. These issues were systematically analyzed by Palmer et al[24] in the context of a dual head gamma camera. Doses of 25 to 30 MBq for ventilation studies and 100-120 MBq for perfusion studies were found to be suitable. When a general purpose collimator was used, a 64 × 64 matrix was adequate. This allowed a total acquisition time of only 20 minutes. If a high-resolution collimator is preferred, a matrix of 128 × 128 should be used, requiring higher doses and/or longer acquisition time. Many consider that this suggestion is not advocated because it does not yield images of significantly higher quality, but this is an issue to be decided by each center.

Many centers are using much greater administered doses. We consider that the activities and acquisition protocol of Palmer et al should be used[24] because radiation exposure should be optimized to the lowest level possible if images of satisfactory quality can be produced. When these acquisition parameters are used, the total number of projections should be ~120, or 3° angular increments (~60 with each camera head on a dual head camera). For ventilation, each projection should be for ~10 seconds. For the perfusion study that follows immediately after the ventilation study, projections of ~5 seconds should suffice. During the examination it is important that the patient remains in the same supine position, carefully maintained between ventilaton and perfusion acquisitions. If ^{81m}Kr is used as the ventilation agent, both perfusion SPECT and ventilation SPECT can be obtained simultaneously within 13 minutes (ie, ~30 projections per head of 20 s each over 180°) with low-energy general-purpose collimators and acquired in a 128 × 128 matrix.[15]

V/Q SPECT Reconstruction and Display

Image reconstruction with the use of an iterative algorithm is recommended, for example, using Ordered-Subset Expectation Maximization with 8 subsets and 2 iterations.[24,38,39] Standard software can be used for this and also for image presentation in frontal, sagittal and transverse projections as well as for presentation of rotating 3-dimensional images. A further option is to calculate and display ventilation:perfusion quotient images, $V:Q_q$ (Fig. 2). It is based upon acquisitions in which the patient is examined without movement between ventilation and perfu-

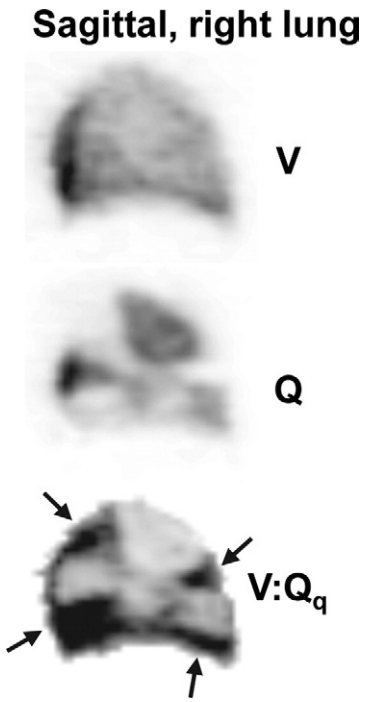

Figure 2 Patient with PE. Sagittal slice of right lung; ventilation, perfusion and V: $Q_{q(uotient)}$ image. Mismatches are nicely delineated in V:Q_q image that provides an improved visualization of PE extension (arrows).

sion imaging and with ventilation background being subtracted from the perfusion tomograms.[24,38] Hot spot removal is often an essential feature, particularly if [^{99m}Tc]-DTPA is used. Ventilation activity (counts) must normalized to perfusion activity, and then V:Q_q images can be calculated. V:Q_q images facilitate diagnosis and quantification of PE extension, particularly in complex cases.[7,38]

Display Options

An overview of ventilation and perfusion in coronal and sagittal slices is useful for quality control and fast orientation. For review of the study, it is important to present the images so that ventilation and perfusion are carefully aligned to each other (Fig. 3). This is greatly facilitated by the one session protocol with the patient unchanged in position. The option to triangulate between frontal (coronal), sagittal, and transverse slices is essential for identification of matching and nonmatching V/Q changes. Proper alignment is also a prerequisite for V:Q_q quotient images. These facilitate the interpretation and quantification of PE extension. However, quotient images are not crucial for high quality V/Q SPECT.

Volume images determined by maximum intensity projections are usually available with standard software. Such rotating images give a good overview of ventilation and perfusion changes. The evaluation of the segmental or nonsegmental character of the changes is thereby facilitated.

Protocols

One-Hour Assessment

V/Q scintigraphy should be performed according to a single day protocol for the following reasons: PE is an acute disease that should be diagnosed and treated without delay. Therefore, and to save time and resources, V/Q SPECT should be performed in one session. As shown, a complete study requires only 20 minutes for acquisition and, with optimal management, 1 hour from referral to report.[25,38,40] Perfusion assessment is fundamental to PE diagnosis. Therefore, the examination starts with a ventilation scan with as low an administered activity as possible that results in adequate image quality, or simultaneously with ^{81m}Kr V/Q SPECT.

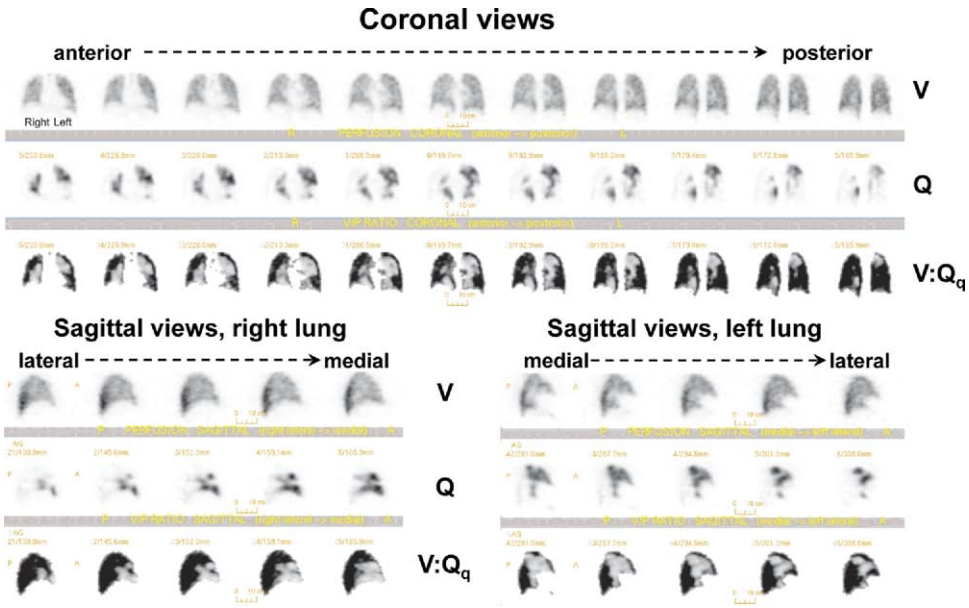

Figure 3 Overview image of ventilation, perfusion and V:Q_q in coronal and sagittal slices. Ventilation and perfusion are carefully aligned to each other.

SPECT Lung Scanning in Pregnancy

In the western world, venous thromboembolism is a leading cause of maternal death during pregnancy or postpartum.[41] Pregnant women represent a young and healthy population, in which the interpretation of lung perfusion scintigraphy is usually straightforward.[42] Although the radiation dose from V/Q SPECT is low, it is important to further minimize radiation exposure to the proliferating breast tissue. Therefore, many propose a perfusion-only SPECT being performed on day 1, using a dose of [^{99m}Tc]-MAA reduced to 50 MBq. In most cases, (90%-95%), the perfusion pattern is normal. Hence PE is reliably excluded. Where the perfusion pattern is abnormal, subcutaneous low molecular weight heparin can be given so that a ventilation study can be performed on day 2 to confirm mismatch.

The radiation dose to the female breast is much higher with X-ray multidetector computed tomography (MDCT) than with V/Q SPECT. Even when a dose-saving regime is used, Hurwitz et al[43] have noted that the dose to the breast from MDCT is about 25 times greater than from V/Q SPECT. Moreover, the sensitivity of MDCT has recently been shown to be very low, probably due to hemodynamic circumstances during pregnancy.[44-46] For the aforementioned reasons, we recommend that perfusion-only scintigraphy be considered during pregnancy.[47-49] Another situation in which perfusion-only SPECT is recommended is in emergencies with a strong suspicion of massive PE. As risks associated with perfusion SPECT are negligible, time can be saved when perfusion SPECT is readily available.

Reporting

Clinical Pretest Probability and D-Dimer

In accordance with Bayes' theorem, the population undergoing a test is of fundamental importance to its interpretation. For individual patients, the clinical pretest probability should be estimated.[50-55] This can be done empirically. In recent years, structured prediction models for PE have been developed.[2,3,56-60] The model of Wells et al is the most frequently used.[3] It depends on the subjective judgment of the medical officer as to whether an alternative diagnosis is less likely than PE and cannot be standardized.

A more precise prediction model is that of Miniati et al.[2] It rests on 16 variables, including older age, risk factors, preexisting cardiopulmonary diseases, relevant clinical symptoms and signs, and the electrocardiogram. The area under the receiver operating characteristic curve was 0.90 in the derivation sample (n = 1100), and 0.88 in the validation sample (n = 400). In contrast to other prediction models, this model includes variables that are negatively associated with PE. This gives the model a flexibility that may explain why it performs equally well both in predicting and ruling out PE. Easy-to-use software is available at http://www.ifc.cnr.it/pisamodel.

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.[61,62] However, the test features a low specificity (40%) because D-dimer may be raised in many conditions other than venous thromboembolism, such as acute myocardial infarction, stroke, inflammation, active cancer, and pregnancy. The specificity decreases with age and, in elderly patients, may reach only 10%.[61] Because of the low predictive value, a positive quantitative D-dimer test does not modify the pretest probability. A negative quantitative D-dimer test combined with a low clinical probability is associated with a low risk of thromboembolic disease.[61,62] At moderate to high pretest clinical probability, D-dimer has no added value.

V/Q Patterns

As discussed previously, the principal pattern for PE is absent perfusion in areas with preserved ventilation, ie, V/Q mismatch. Pulmonary arterial circulation can be affected by many disorders others than PE. In most diseases both V and Q are affected, leading to patterns referred to as V/Q match or when ventilation is more affected than perfusion, reversed V/Q mismatch.

For V/Q SPECT, we have previously proposed a new holistic principle for reporting that we believe is as important as the imaging technique itself. The clinician can only benefit from reports which clearly express the presence or absence of PE. This goal was not reached with the previous probabilistic reporting methods according to Prospective Investigation Of Pulmonary Embolism Diagnosis (PIOPED) or modified PIOPED.[50,63] Large V/Q SPECT trials have shown that interpretation of all patterns representing ventilation together with perfusion achieves this result.[15,39,40,64] Conclusive reports can be given in 97% to 99% of patients. It has been shown that more than 0.5 segment of V/Q mismatch is sufficient for the diagnosis of PE.[65]

The holistic interpretation of V/Q SPECT should be based upon:

- clinical pretest probability and
- criteria for interpreting V/Q patterns indicative for PE and other diseases.

Criteria for Acute PE

Our recommended criteria for interpreting V/Q SPECT with respect to acute PE are the following[47,49]:

No PE is reported if there is (are)

- normal perfusion pattern conforming to the anatomic boundaries of the lungs;
- matched or reversed mismatch V/Q defects of any size, shape or number in the absence of mismatch, and;
- mismatch that does not have a lobar, segmental or subsegmental pattern.

PE is reported if there is

- V/Q mismatch of at least 1 segment or 2 subsegments that conforms to the pulmonary vascular anatomy.

Nondiagnostic for PE is reported if there are

- Multiple V/Q abnormalities not typical of specific diseases.

The fundamental point is that for patients with clinical suspicion of emboli, PE is the principal cause of lobar, segmen-

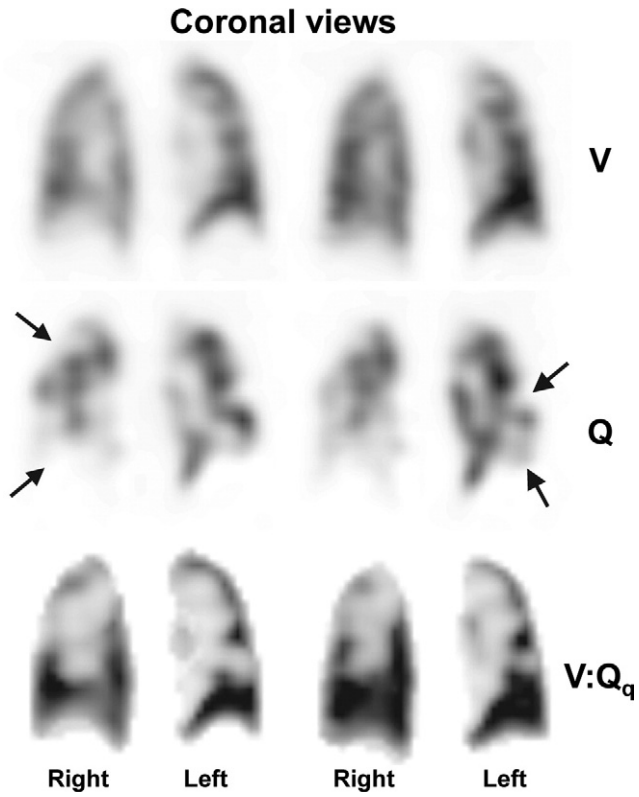

Figure 4 Patient with pulmonary hypertension caused by chronic PE. Coronal slices; Multiple segmental and subsegmental perfusion defects (arrows) in ventilated areas, well delineated on V:Q_q images. MDCT was normal.

tal, or subsegmental V/Q mismatch. Crucially, with PE, the hallmark is a mismatch that has its base along the pleura and conforms to known subsegmental and segmental vascular anatomy, a fundamental principle stressed in the PISAPED study.[51] Applying these principles of interpretation, recent V/Q SPECT studies amounting to more than 3000 cases report a negative predictive value of 97% to 99%, sensitivities of 96% to 99%, and specificities of 91% to 98% for PE diagnosis. Rates of nondiagnostic findings were 1% to 3%.[39,40,64,66] V/Q SPECT yields ventilation and perfusion images in exactly the same projections, facilitating recognition of mismatch. This is of particular importance in the middle lobe and lingula where mismatch may be overlooked if the lung is not accurately delineated by its ventilation images.[67]

An important step in the diagnostic procedure is to quantify the extent of embolism. V/Q SPECT is particularly suitable for this because of its greater sensitivity compared with alternative planar scintigraphy and MDCT.[15,64,68] As suggested by Olsson et al,[7] the number of segments and subsegments showing for PE typical mismatch are counted and expressed as a percentage of the total lung parenchyma. Furthermore, areas with ventilation abnormalities were recognized and this allowed the degree of total lung malfunction to be estimated. This may have treatment implications as this study showed that patients with up to 40% of the lungs affected by PE could be safely treated at home if ventilation abnormalities engaged not more that 20% of the lung. Since 2004, about 60% of patients with PE, numbering about 800, have been safely treated at home in the University Hospital of Lund.

Chronic Pulmonary Embolism

Chronic PE is a progressive disease that develops in about 1% to 5% after an acute episode of PE, even in treated patients.[69] It often has, however, an insidious onset. It leads to pulmonary hypertension, right heart failure, and arrhythmia, which are frequent causes of death.[70,71] The value of V/Q scintigraphy in this situation is well established.[72,73] This has recently been confirmed in a head-to-head comparison between MDCT and planar scintigraphy with pulmonary angiography as reference.[74] Among patients with pulmonary hypertension, scintigraphy had a sensitivity of 96% to 97% and specificity of 90%, whereas MDCT had a sensitivity of 51%. The conclusion was that V/Q scintigraphy "has a higher sensitivity than MDCT as well as very good specificity in detecting chronic pulmonary thromboembolic disease as a potentially curable cause of pulmonary hypertension." Scintigraphic features of chronic PE vary.

Figure 4 illustrates a case of multiple perfusion defects that are similar to acute PE. MDCT was normal. In some patients mismatch without clear segmental or subsegmental pattern is observed. Peripheral zones of the lung lack perfusion. The center of the lung is hyperperfused. The lung appears significantly smaller on perfusion images compared with ventilation and the V:Q_q images show mismatch along the lung periphery (Fig. 5).

In recent guidelines for the diagnosis and treatment of pulmonary hypertension it is stated that "ventilation/perfusion scan remains the screening method of choice for chronic pulmonary hypertension."[75] It was also noted that pulmonary veno-occlusive disease is a rare but important differential diagnosis.

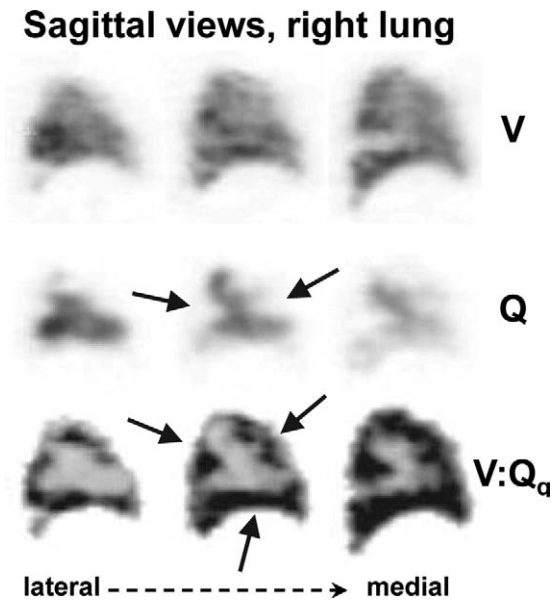

Figure 5 Patient with pulmonary hypertension caused by chronic PE. Sagittal slices; peripheral zones of the lung lack perfusion (arrows). The center of the lung is hyperperfused. The lung appears significantly smaller on perfusion images compared with ventilation. V:Q_q images shows mismatch along the lung periphery (arrows).

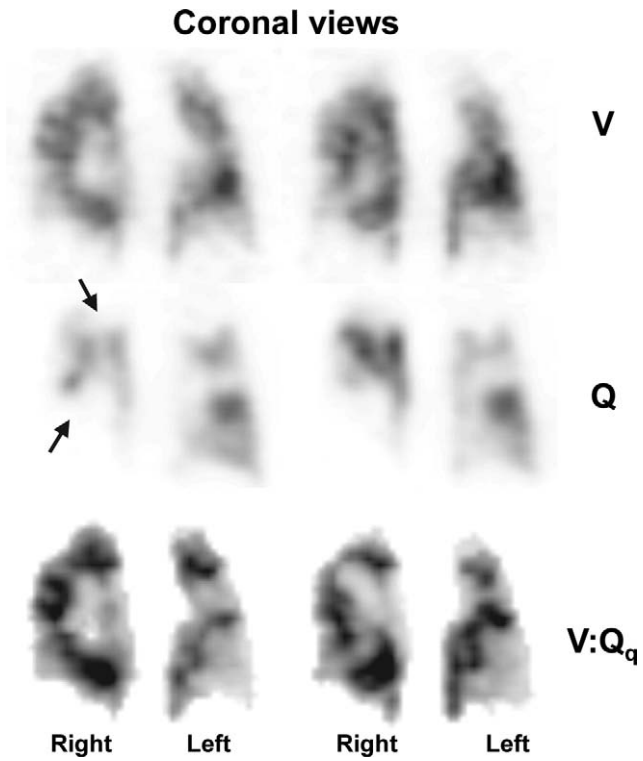

Figure 6 Patient with COPD and chronic PE. Coronal slices; ventilation is very uneven in the whole lung. In addition, multiple perfusion defects are seen in ventilated areas. Mismatch is highlighted in V:Q_q images.

Other Diagnostic Outcomes

For alternative diagnoses to PE, the total pattern of V/Q distribution is crucial.

Chronic Obstructive Pulmonary Disease

A common alternative or additional diagnosis is COPD. The hallmark is a general unevenness of ventilation. Focal deposition may be observed in central or peripheral airways even when Technegas is used. A very important fact is that COPD patients are at high risk of PE. The rate of PE in patients hospitalized for acute exacerbations of COPD may be as high as 25%.[76] PE accounts for up to 10% of deaths in stable COPD patients.[77] The degree of unevenness of aerosol distribution correlated with lung function tests.[78] With V/Q SPECT, PE can be diagnosed even in the presence of COPD.[47,49,64] Significantly, because there are no contraindications to V/Q SPECT, even very sick and breathless patients can be studied. Figure 6 shows coronal slices in a patient with COPD and chronic PE. Ventilation is very uneven in the whole lung. In addition, multiple perfusion defects are seen in ventilated areas. Mismatch is highlighted in V:Q_q images.

Pneumonia

Among patients investigated with V/Q SPECT for suspected PE, pneumonia is common.[64] A typical finding is a ventilation defect in a region usually with better preserved perfusion, known as reverse mismatch (Fig. 7).[79,80] V/Q SPECT allows diagnosis of PE and pneumonia when combined in a patient with COPD (Fig. 8). One of the typical patterns, which strongly support the diagnosis of pneumonia, is the "stripe sign." It refers to maintained perfusion along the pleural surface, peripheral to a central matched defect. A good example is shown in Figure 9B.[81,82]

Left Heart Failure

Left heart failure is a further diagnosis that is frequently observed among patients suspected of having PE. The typical pattern is antigravitational redistribution of perfusion.[83,84] In consecutive patients with suspected PE, V/Q SPECT showed redistribution of perfusion towards ventral lung regions in 15% of the cases indicating left heart failure.[85] The positive predictive value for heart failure was at least 88%. As ventilation is usually less redistributed than perfusion, V/Q mismatch may be observed in dorsal regions. Figure 9A shows a V/Q mismatch with a nonsegmental pattern which should not be misinterpreted as PE. The follow-up scan 10 days later (Fig. 9B) showed normalization of gravitational distribution of V/Q. However, the patient had developed a clearly delineated pattern of pneumonia in the upper right lobe.

Comments

Advocates for MDCT stress that this method has the advantage over V/Q SPECT in that it allows alternative diagnoses. It is also true, however, that V/Q SPECT provides evidence about alternative diagnoses. In a V/Q SPECT study comprising 1785 patients, an alternative diagnosis was reported in 39% of patients without PE, whereas among patients with PE an additional pathology was reported in 22%.[64] In fact, a properly performed V/Q SPECT that is interpreted by all patterns of ventilation and perfusion very frequently allows diagnoses of other pulmonary

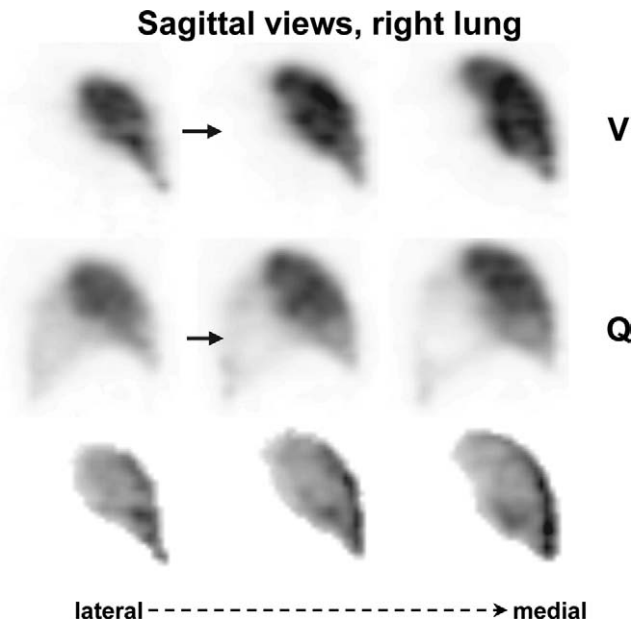

Figure 7 Patient with suspected pneumonia in the right lung, seen on chest X-ray. Sagittal slices; Absent ventilation posterior in the right lung. Perfusion is less affected.

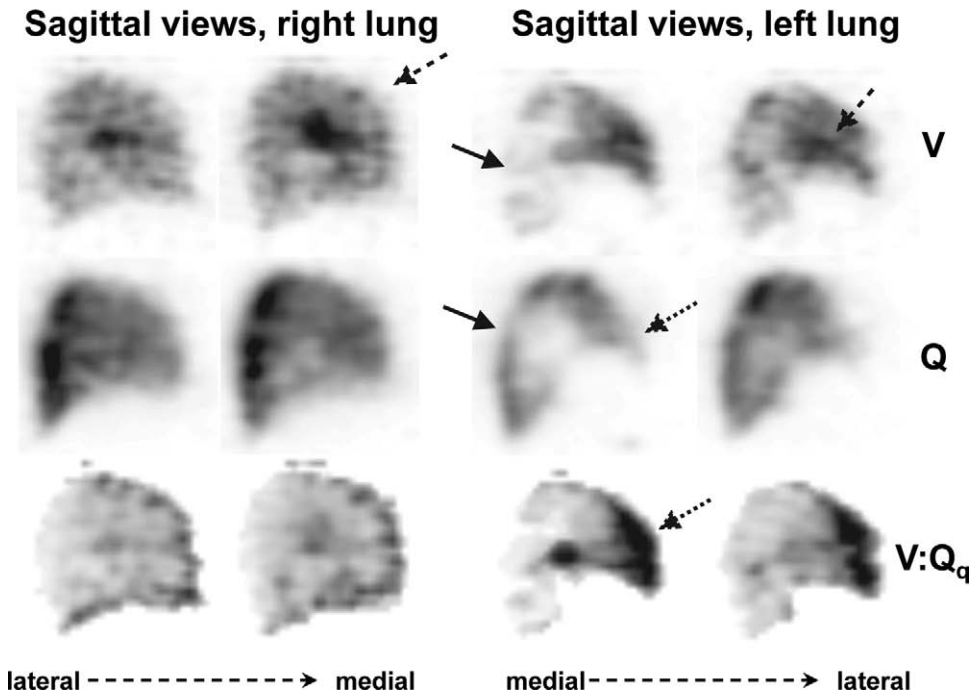

Figure 8 Patient with COPD, complicated with pneumonia and PE. Sagittal slices: in the right lung, there is uneven ventilation with central deposition of Technegas (interrupted arrows). In the left lung, ventilation is absent posteriorly with relative preservation of perfusion and the "stripe sign" (drawn arrows), which is a typical finding for pneumonia. In the left lung there is absent perfusion anteriorly whereas ventilation is preserved (mismatch). This is characteristic of PE and is well demonstrated on the V:Q_q images (dotted arrows).

disease, with or without PE, and may provided a comprehensive understanding of the patient's symptoms. This added value of V/Q SPECT appears at least as high as for MDCT. Further studies are needed to demonstrate the clinical impact of alternative diagnoses obtained by both methods.

Pitfalls for V/Q SPECT

As with any diagnostic test, it is vital that the medical staff members reporting the V/Q scan are aware of many sources of error related to technical factors or interpretation.

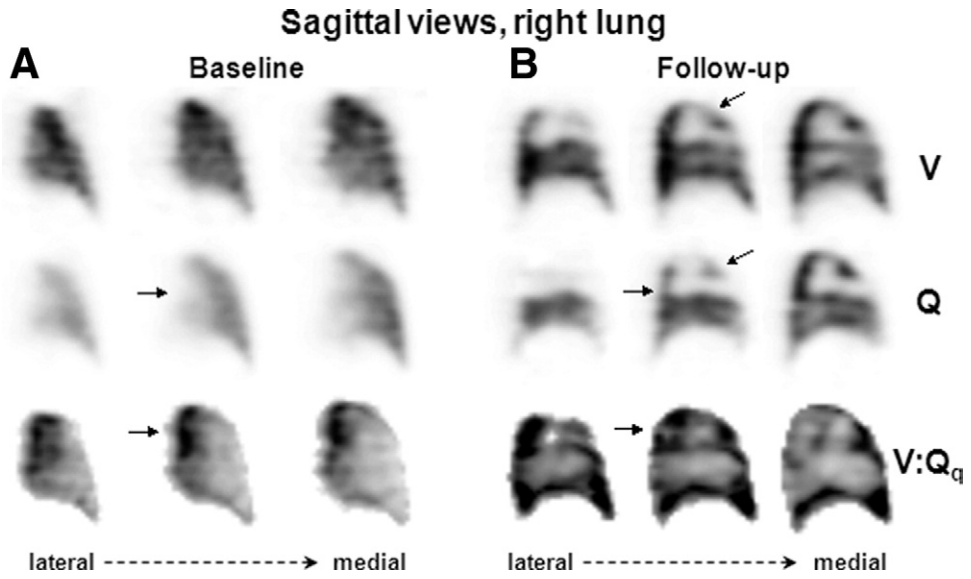

Figure 9 (A) Patient with left heart failure in the initial acute stage. Sagittal slices: antigravitational distribution of ventilation and more so of perfusion, causing nonsegmental V:Q mismatch in dorsal regions (arrows). (B) The same patient, follow-up after 10 days of treatment for left heart failure. Normalization of gravitational distribution of V/Q. However, the patient had developed a clearly delineated pattern of pneumonia in the upper right lobe (arrow), absent V/Q with "stripe sign."

Technical Factors

- Incorrect handling of the [^{99m}Tc]–MAA preparation may cause aggregation of particles, creating hot spots in the images. Reasons may be inadequate shaking of the vial with the MAA suspension or preinjection withdrawing of blood into the syringe.
- When DTPA aerosols are used, ventilation images in obstructive airway disease may be confounded by central and peripheral airway deposition. However, this is much less of a problem when Technegas is used.[35]
- In rare instances, in emphysema patients Technegas can become trapped in bullae and lead to mismatch.[66] The pattern is however, not of a segmental or subsegmental character and should not be mistaken for PE.
- Patient movement between ventilation and perfusion scanning will cause artifacts in the V/Q_q quotient images. The particular nonsegmental character distinguishes this pattern from PE (Fig. 10).

Interpretation

Several diseases and conditions lead to mismatch. Proper recognition of mismatch patterns characteristic for different diseases is essential to avoid pitfalls in interpretation.

- In nonacute PE that is partly resolved, mismatched perfusion defects that have lost their clear segmental character may be seen with or without signs of acute PE and lead to false negative diagnosis and inadequate treatment;
- Mismatched defects are observed in, for example, lung cancer, mediastinal lymphadenopathy, postradiation pneumonitis, vasculitis, and heart failure. In general, such mismatches have a nonsegmental character. It is very important to take all patient information into account to minimize the risks of misdiagnosis of diseases other than PE;
- Some emboli do not lead to mismatch because, like a saddle embolus, they do not cause vascular occlusion.[86] Nevertheless, a normal perfusion scan excludes PE according to wide experience. Accordingly, missed major nonocclusive emboli do not lead to clinical consequences like sudden death. The reason for this is probably that such emboli are accompanied by small occluding emboli, which are detected with V/Q SPECT, so that PE is diagnosed and treated. Small emboli should not be overlooked or disregarded;
- Unilateral whole lung mismatch without any mismatch in the other lung is usually not due to PE.[87,88] In such cases, a CT is recommended to reveal much more likely pathologies, such as tumor and other mediastinal processes or extremely rarely congenital pulmonary vascular abnormalities or aortic aneurysm;
- When V/Q abnormalities not typical for any particular disease are observed, the patient should be referred to MDCT to avoid both under and overdiagnosis of PE.

Conclusions

In our opinion, V/Q SPECT is the best method for the diagnosis of PE because it has highest diagnostic accuracy, very few nondiagnostic reports and no contraindications or complications.

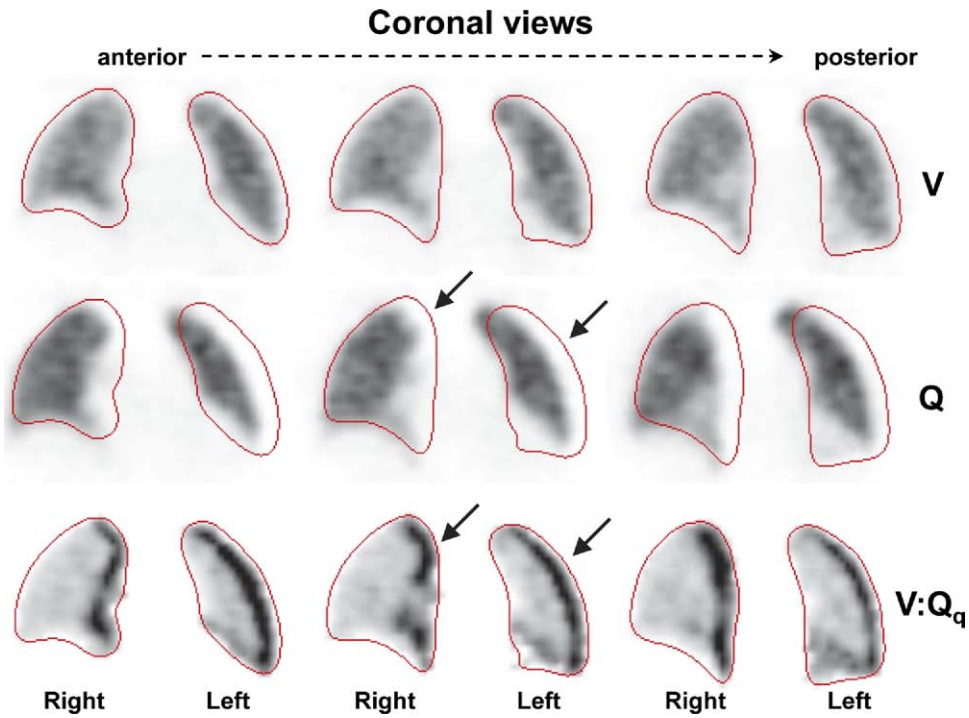

Figure 10 Coronal slices: the V:Q_q image displays nonsegmental "mismatch" along the left border of both lungs. This pattern is typical for nonalignment due to patient movement between V/Q imaging. Lung delineation from V:Q_q images are overlaid on ventilation and perfusion images for quality control.

Furthermore, radiation doses are very low. This is particularly important for women in the reproductive period and during pregnancy.

To take full advantage of the V/Q SPECT potential, it is crucial to apply an optimal protocol for a single session imaging of both ventilation and perfusion using low radionuclide activities. Furthermore, full use should be made of all display options, which are available with modern camera and computer systems. Most important of all is the holistic interpretation, giving a clear report with respect to PE, its extent as well as other diagnoses based on V/Q patterns typical for various diseases.

The above-mentioned advantages of V/Q SPECT for studying PE imply that it should be recognized as the only suitable technique both for follow up in patients with PE as well as for research regarding its treatment and pathophysiology.

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