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The quantitative ventilation/perfusion tomography for PE diagnosis and additional diagnostic outcomes

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Aim

To apply holistic interpretation criteria, including ancillary scintigraphic findings and tomography of ventilation/perfusion SPECT (V/PSPECT) with respect to PE and other lung diseases. Method: V/PSPECT is performed in clinical practice from 90-ties. However, the number of centres performing V/PSPECT has recently increased. In our clinic from 2003 until end of 2008, 8296 patients were examined with V/PSPECT. Result: Ventilation studies, essential for lung delineation greatly contributes to the recognition of peripheral perfusion defects typical for PE. Moreover, they explain perfusion defects of different nature such as heart failure, obstructive diseases and parenchymal changes as pneumonia. New standardised technique together with holistic interpretation reduced the rate of non-diagnostic reports to the level of 1 % [1]. Such results have been achieved in centres world over applying similar strategy [2-4]. Interpretation of ventilation /perfusion scintigraphy: Probabilistic contra holistic: Probabilistic interpretation based upon simplistic criteria were promoted through the PIOPED I study [5]. The terms used were high, intermediate, low and very low probability V/PSCAN, and indeterminate (non-diagnostic) examinations. Such or similar terminology is extremely rare in other clinical contexts. This language has not gained acceptance in other fields. The most likely reason is that in clinical practice this strategy is inherently impracticable. Probability can, according to Bayes' theorem, not be defined from a single test without taking into account prior probability. Furthermore, the PIOPED I criteria were formulated and applied on the basis of techniques, which are today obsolete. For example, regional ventilation was mapped from a posterior planar acquisition following the inhalation of ^{133}Xe . Additionally, an abnormal chest X-ray or ventilation scintigram implied that the scintigraphy was categorised as non-diagnostic, which is unwarranted as shown by more recent studies. In the PIOPED study, direct comparison of conventional PA and planar V/Pscint, using ^{133}Xe for ventilation, yielded poor results with agreement as low as 50%.

Interpretation of imaging tests like V/PSPECT and V/PPLANAR should be based upon

- basic criteria for reading the images
- knowledge and experience of the interpreter according to the principle of "Gestalt"
- pre-test probability in accordance with the principle of holistic interpretation

A holistic interpretation imply clinical information, laboratory test together with all observed signs and patterns in ventilation and perfusion scintigrams. Schemes for clinical probabilities may be of significant value.

Furthermore to be clinically useful interpretation of an imaging test is should be affirmative or negative with respect to PE (PE: yes or no) and should not be based on probability categories.

Freeman et al. argued that "the experts" successful interpretation of lung scans exceeds the best accuracy achievable by algorithms. The subjective of the whole is superior to any possible attempt to define its discrete parts" [6]. All areas with ventilation or perfusion defects are summed for estimation of total lung function. Within the holistic principle of image reading the following guidelines are applied for PE diagnosis.

No PE is reported at:

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

PE is reported if there is

- V/P mismatch of at least one segment or two subsegments that conforms to the pulmonary vascular anatomy.

Non-diagnostic for PE is reported if there are

- multiple V/P abnormalities not typical of specific diseases.

To meet requirements from our clinicians, the degree of PE is routinely quantified. In addition the total lung function reduction is validated.

Signs of obstructive or parenchymal lung disease and heart failure are included in reports.

Pulmonary embolism

In PE, a perfusion defect is due to an embolus blocking blood flow, while ventilation remains normal because there is no corresponding blockage in the airway. Perfusion defects due to blockage of a pulmonary artery should reflect the branching of pulmonary circulation and its classical segmental anatomy. A segmental defect is shaped as a wedge with its base on the pleura. On qV/PSPECT images it is rather simple to identify segmental and subsegmental patterns of perfusion defects even within the middle lobe or the lingula but ventilation study is crucial for validation in this area. Pulmonary circulation maps are very helpful facilitating interpretation of tomographic images.

Selection of therapeutic strategy

In order to select a therapeutic strategy the degree of PE obviously needs to be estimated. Very extensive PE may motivate thrombolysis, while PE with limited extension may be treated at home. Patients with lung perfusion defects up to 40 % and ventilation defects up to 20 % are treated at home [7]. Since 2004 until end of 2006 we found PE in 675 patients. 375 (56%) of them were treated at home with no thromboembolic mortality. Intermediate cases and patients with co-morbidity need in-hospital treatment.

Follow-up

Follow up is a frequently overlooked aspect of diagnostic strategies although it is essential both for clinical and scientific reasons. Follow up is needed, in order to:

1. assess the need for repeated thrombolytic therapy after each infusion of such drugs;
2. assess the need for prolonged oral anticoagulation beyond 6 months, in case of extensive remnants of PE;
3. allow differentiation between new and old PE at suspicion of recurring PE;
4. explain physical incapacity after PE in case of permanently deranged lung function;
5. evaluate and compare drugs and therapeutic strategies.

For follow up, qV/PSPECT is the only suitable method for the following reasons:

- Detection of all emboli requires that the whole lung is examined with a sensitive method.
- The cumulative radiation dose is much lower than for CT, which is a central issue when the indication is relative.
- The functional impairment of lung units due to non-perfusion increases dead space and pulmonary vascular resistance. In severe cases it strains the right heart.
- To study efficacy of treatment in individual patients or in scientific materials, the same method should obviously be used for diagnosis and for follow up. This is a further strong argument in favor of qV/PSPECT as the primary diagnostic method for PE.

Sensitivity and specificity of V/PSPECT in diagnosis of PE

Although that the PIOPED study was performed with inferior technique and inflexible sub-optimal interpretation criteria, the results are still quoted as arguments against lung scintigraphy for the diagnosis of PE. In particular, PIOPED had a rate of non-diagnostic scintigraphies of 65%. A reduction in the number of non-diagnostic reports to 10% can be achieved even with planar lung V/P scintigraphy with adequate acquisition and a holistic interpretation strategy. With V/PSPECT, this number is further reduced to below 4%, as found in recent studies.

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The sensitivity of V/PSPECT was tested in a porcine model using latex emboli, labelled with ^{201}TI to enable precise localization of the emboli which were 2.2-3.7 mm in diameter and caused only sub-segmental defects. For the planar technique sensitivity and specificity were 67% and 80% and for V/PSPECT 93% and 94%, respectively. In a clinical study, 53 % more mismatch points were identified with qV/PSPECT compared to planar technique. Similar results have been found by others. SPECT eliminates superimposed structures, and clarifies segmental and subsegmental nature of perfusion defects caused by PE.

Additional diagnostic outcomes

Chronic obstructive pulmonary disease, COPD

A dominating finding in COPD is matched areas with defects in ventilation and perfusion. Ventilation defects are commonly more prominent than those of perfusion. Perfused but non-ventilated lung, i.e. reverse mismatch, is another common finding, explained by failure of blood flow diversion from hypoxic lung segments. A significant correlation between the degree of abnormalities on aerosol ventilation imaging and pulmonary function tests has been reported. PE is quite frequent in COPD and accounts for up to 10% of deaths in stable COPD patients. Using V/PSPECT, it is feasible to diagnose PE in patients with co-existing COPD.

Heart Failure

In patients with heart failure, redistribution of perfusion towards upper lung regions was described already in 1966 by Friedman and Braunwald 1966. As ventilation is usually not affected to the same grade as perfusion, mismatch is common, however, not of segmental character and should not be misinterpreted. Perfusion is more reduced than ventilation causing mismatch, however of non-segmental character.

In a recent study based on V/PSPECT in consecutive patients with suspected PE, redistribution of perfusion towards ventral lung regions was observed in 15 % of the cases, indicating left heart failure. The positive predictive value for heart failure was 88 % or higher [8].

Pneumonia

The most frequent finding is a matched defect. However, ventilation defects usually exceed perfusion defects causing reverse mismatch. Stripe sign is often present and refers to maintained perfusion along the pleural surface peripheral to a central matched defect, V/PSPECT facilitates the identification of stripe sign.

Pitfalls

As with any diagnostic test, it is vital that the clinician reporting the lung scan is aware of a number of sources of error. These include the following: Artefacts might be technical. Withdrawing blood into the syringe with ^{99m}Tc -MAA may cause aggregation of particles, creating hot spots in the images. Problems with planar imaging related to superposition of lung regions with normal perfusion which by shine through hide embolised regions, are eliminated by V/PSPECT.

In rare patients with emphysema, Technegas particles are trapped in bullae causing a pattern that may be mistaken for a mismatch. The pattern can in most cases be differentiated from the segmental pattern typical for PE. Non-segmental mismatch are observed in patients with tumor, mediastinal adenopathy, post-radiation therapy and heart failure. Importantly, total absence of perfusion in one lung without any other mismatch region is generally caused by pathology other than PE, such as a central tumor or abscess.

Conclusion

High quality V/PSPECT can be performed at low cost within one hour. Holistic interpretation gives superior results with respect to sensitivity, specificity and down to 1% of non-diagnostic findings. The V/PSPECT is the method of choice for quantification of PE extension total lung function and follow up. Furthermore, a close co-operation between clinicians, nuclear medicine and diagnostic radiology is essential to achieve optimal diagnosis and therapy of PE. No contraindication and low radiation exposure merit it as a first choice technique. With increasing number of tomographic gamma cameras V/PSPECT should be applied in each hospital applying the standard software offered together with modern systems.

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