VQ SPECT - As accurate as CTPA for the diagnosis of Pulmonary Embolism

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Abstract

Planar VQ imaging has been performed for more than 30 years but has recently been largely superseded by Computed Tomography Pulmonary Angiography (CTPA) as the technique of choice for many patients. The Nuclear Medicine department at County Durham and Darlington NHS Foundation Trust (CDDFT), still identifying a role for functional VQ imaging, investigated the introduction of a new single photon emission computed tomographic (SPECT) technique to aid in the diagnosis of PE.

Bespoke software was written to process and display the SPECT images for comparison with planar images during an initial assessment period. SPECT studies subsequently became the routine VQ technique in our Trust, becoming one of the first in the UK to do so. Initial audit of VQ SPECT results compared to CTPA investigations demonstrated good agreement, and assisted in clarifying the role of this new technique in the diagnosis process.

After the publication of reporting guidelines by the European Association of Nuclear Medicine (EANM)[1,2], a subsequent audit of VQ SPECT reporting demonstrated improved confidence when PE was absent and a definitive report was issued in 98% of cases, leaving just 2% of reports as equivocal or inconclusive.

VQ SPECT should be used as a primary imaging technique for the investigation of patients with suspected PE.

Introduction

Pulmonary embolism (PE) is a common condition with a high mortality rate for patients who are untreated[3]. Acute PE is caused by migration of thrombus to the pulmonary circulation and is the third most common cause of death after cardiovascular diseases and malignancies[4]. The treatments available including heparin, oral anticoagulants and thrombolytic agents have well-documented side effects, therefore it is imperative to make early diagnosis of PE and treat only when appropriate.

Planar VQ

Ventilation perfusion (VQ) scintigraphy has been widely used for 30 years as a first line investigation for the diagnosis of PE, as it is non-invasive, contributes a low radiation dose to the patient and has a high sensitivity for the detection of PE[5].

The patient is required to breathe in a radioactive gas or aerosol, which delineates the ventilated area of the lungs. The perfusion images are generated after the injection of radio-labelled macroaggregated albumin (MAA). These particles are 15–100ìm in size and cause microembolization of pulmonary capillaries, reflecting regional perfusion, although only a small fraction of the pulmonary vascular bed is obstructed. An embolus which is blocking blood flow will lead to a perfusion defect within the lung. There will be no corresponding blockage in the airway, so ventilation at this part of the lung will be normal, leading to a ventilation-perfusion mismatch. The blockage of the pulmonary artery reflects the branching of pulmonary circulation, leading to the characteristic pattern of wedge shaped segmental defects, with the base on the pleura.

The VQ planar technique widely used has been criticised for its relatively low specificity and a large number of non-diagnostic scans. The PIOPED study[6] and follow-up studies brought in the use of probability reporting (Normal; Very low, Low, Intermediate, High Probability), which can be confusing to the referring clinician. These studies were based on the then gold standard of pulmonary angiography, which is no longer considered as such. The method of ventilation imaging used for PIOPED studies was not standardised and often a single posterior projection alone was used to assess if a defect was matched. Planar VQ produced a large numbers of intermediate or indeterminate studies, a relatively high false positive rate and low specificity.

CTPA

More recently, Computed Tomography Pulmonary Angiography (CTPA) has been introduced for the diagnosis of PE. It has been demonstrated to have improved sensitivity and specificity compared to planar VQ imaging and has the advantage that the anatomy is well demonstrated and therefore other lung conditions can be identified even if PE is not present[7]. CTPA has been increasing in popularity in recent years and it has been suggested that VQ scans are no longer a useful investigation in comparison[8]. The British Thoracic Society (BTS) published guidelines[9] in 2003 which commented that "CTPA is now the recommended initial lung imaging modality for non-massive PE" and that "V/Q scan may be first line investigation if it's available on site, if the CXR is normal, if no concurrent lung disease, if standardised reporting criteria are used", i.e. PIOPED probability reporting.

At the time, the guidelines were probably correct in their assertion that "the PIOPED finding that PE can only be diagnosed or excluded reliably in a minority of patients by isotope lung scanning has been confirmed" but they go on to state that "continuing attempts to refine technology and to redefine interpretative criteria will not materially improve this". This latter statement, published eight years ago, has been demonstrably refuted with the introduction of VQ SPECT.

CTPA is not without its disadvantages. It is a technique that involves the administration of contrast and so is not suitable for patients with contrast allergies or poor renal function. CTPA is known to be very good for central emboli, but less sensitive for patients with peripheral emboli. CTPA may produce poor quality images, usually due to poor contrast enhancement or patient motion in up to 15% of patients.

In addition the radiation dose from CTPA may be four to ten times larger than for a VQ scan, and contributes a very large dose to sensitive breast tissue - of the order of ten to twenty times the dose a patient would receive from a mammogram. For CTPA, the breast is not even the organ of interest and this large dose to sensitive tissue is of concern, especially in young women. This could lead to a lifetime attributable cancer risk of 1 in 143 (for a 20 year old woman) or 1 in 284 (for a 40 year old woman)[10].

In pregnancy, the fetus receives a very low dose from CTPA in the early stages, but in late pregnancy, when the fetus is positioned directly underneath the diaphragm, it may actually be within the primary x-ray beam and receive a much higher radiation dose than it would receive from VQ imaging. In pregnancy, it can also be difficult to time the administration of contrast, essential for a good quality diagnostic image, thought to be due to the increased plasma volume and increased cardiac output.

SPECT VQ

Two-dimensional planar images of the 3D structure of the lungs results in poor visibility of individual lung segments and shine through of radiation where segments overlap. Single Photon Emission Computed Tomography (SPECT) is a common technique in nuclear medicine and involves the acquisition of multiple projections over 360 degrees so that the 3 dimensional distribution of activity may be reconstructed. SPECT imaging has already replaced planar imaging for all nuclear medicine procedures for the brain (e.g. cerebral perfusion imaging and Datscan) and for myocardial perfusion imaging, due to the higher sensitivity and accuracy possible with the technique.

Several published studies have demonstrated this improvement of SPECT compared with planar imaging. One pivotal study[11] involved 16 pigs injected with latex emboli, which were labelled with radioactive ^{201}Tl so their exact position could be identified on planar imaging. Ventilation and perfusion images were then performed using both the planar and SPECT techniques and randomised images were reported by two experienced clinicians. The results indicated 53% more perfusion-ventilation mismatch was detected in the SPECT images compared to planar. For planar imaging, the sensitivity was 67% and specificity 80%. For the SPECT images, sensitivity was increased to 93% and specificity to 94 %. Other studies have compared planar and VQ SPECT to CTPA and have demonstrated similar improvements in accuracy[12], Table 1.

	Planar VQ	SPECT VQ	CTPA
Sensitivity	76 %	97 %	86 %
Specificity	85 %	91 %	98 %
Accuracy	81 %	94 %	93 %

Table 1

The nuclear medicine department at County Durham and Darlington NHS Foundation Trust (CDDFT) investigated the use of SPECT rather than planar acquisitions for the diagnosis of PE. SPECT techniques allow an organ to be visualised in three dimensions giving axial, coronal and sagittal views of all lung segments.

Method

Patients who were referred for assessment of PE had both planar and tomographic (SPECT) images acquired of lung perfusion and ventilation in order to evaluate the technique. The patient was positioned supine on the imaging couch and was required to breathe in the radioactive gas or aerosol to delineate the ventilated area of the lungs. Anterior, posterior and left and right posterior oblique static planar images were acquired. Tomographic projections were then acquired, 64 projections in total over 360 degrees around the patient. The patient was then given an injection of ^{99m}Tc.labelled MAA and tomographic images were acquired followed by the four planar projections, similar to those acquired for the ventilation images.

Planar images were displayed with each ventilation projection, viewed side by side with the corresponding perfusion image, to assess for perfusion defects which were not matched by ventilation defects, which would indicate the presence of PE.

Ventilation and perfusion images were then reconstructed using iterative reconstruction and post reconstruction filtering to produce the best quality coronal, sagittal and axial slices through the lungs. These slices were then displayed with matching ventilation and perfusion slices side by side for assessment of the presence of PE.

Results

Examples of the VQ planar and SPECT images acquired during this initial investigation phase are shown in figures 1-3*(overleaf)*. Normal ventilation and perfusion planar images and the corresponding SPECT images are demonstrated in Figure 1. One patient had a high probability planar lung scan and the mismatched perfusion defects were very clearly demonstrated in the corresponding SPECT study, Figure 2.

The planar lung scan shown in Figure 3 (top left) was assessed by two experienced reporters to have a low probability of PE, as there was largely matching perfusion and ventilation images. However the SPECT study for this same patient Figure 3 (top right, bottom left and right) demonstrated a large mismatched perfusion defect in the right lung anteriorly, and also a smaller defect in the upper left lung. These defects were not well visualised in the planar images due to the activity in the overlying segments reducing the contrast of the area of absent perfusion. The diagnosis of PE would have been missed in this patient had SPECT images not been performed. Consequently the SPECT acquisition became the routine lung imaging technique.

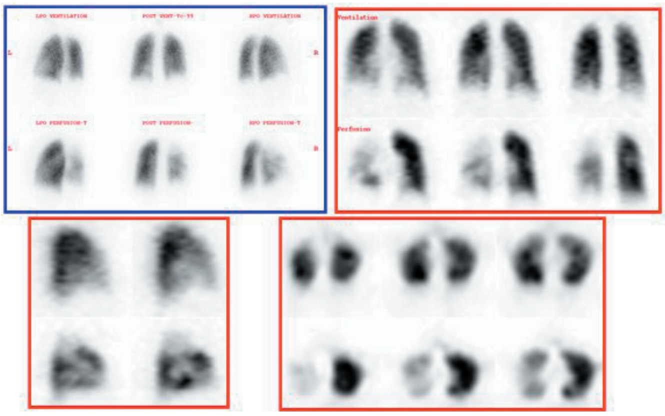

Figure 1: *Normal planar lung scan (top left), demonstrating matching posterior and left/right posterior oblique images. Normal SPECT lung scan acquired on the same patient on the same day, matching coronal (top right), sagittal (bottom left) and axial (bottom right) images.*

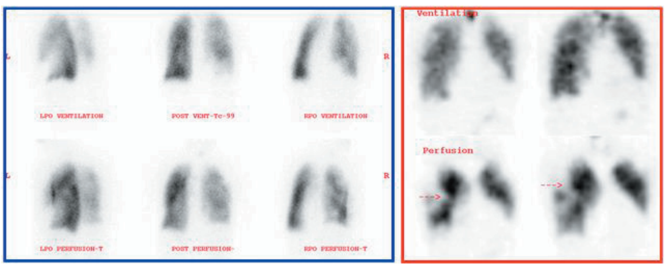

Figure 2: *Planar lung scan (top left), demonstrating mismatched posterior defects in the right lung, with normal ventilation images. This study has a high probability of PE. SPECT lung scan, for the same patient on the same day. The mismatched perfusion in the right lung is very clearly demonstrated in multiple slices on all of the coronal (top right), sagittal (bottom left) and axial (bottom right) projections. Appearances are consistent with PE.*

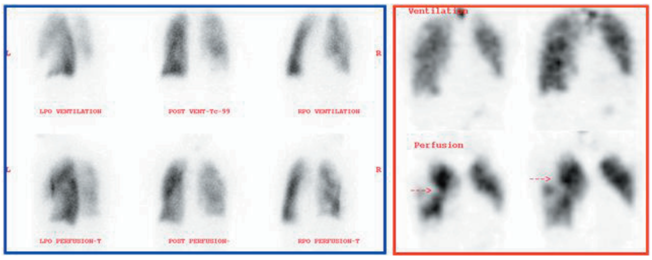

Figure 3: *The images on the left are the matched ventilation (top) and perfusion (bottom) images for the patient's planar lung study. No definite mismatched perfusion defects are identified therefore there is a low probability of pulmonary embolism. The images on the right are selected coronal slices from the SPECT study on the same patient demonstrating a large wedge-shaped perfusion defect indicated by the arrows in the perfusion slices (bottom) which are not matched on the ventilation images (top). This appearance would be consistent with pulmonary embolism.*

Audit of clinical results

VQ SPECT scanning has now been performed at the University Hospital of North Durham since 2007, and was introduced to Darlington Memorial Hospital in 2011. In total, more than 740 patients have been scanned, 96% of whom have tolerated the SPECT technique. Pregnant patients undergo perfusion-only studies to reduce the radiation dose to the fetus.

During 2008 and 2009, the majority of patients who were referred for VQ imaging were women (73%). Half of all patients under 50 years of age, in whom the high radiation dose to breast tissue from undergoing CTPA would be of most concern. This age and sex referral pattern was again demonstrated during a repeat audit period of 2009 and 2010.

The European Association of Nuclear Medicine guidelines[1,2] recommend using a more definitive reporting style than probability reporting, as used for other types of imaging studies, including CTPA. Extensive experience of reporting VQ SPECT studies have led to the recognition of perfusion/ventilation patterns indicative of diseases other than PE.

Perfusion may therefore be categorised as:

- No evidence of PE : Perfusion matching anatomical boundary of lung
- Consistent with PE : Mismatched perfusion segmental or sub-segmental defects
- Chronic Obstructive Pulmonary Disease (COPD) : Focally increased ventilation, especially centrally
- Ventilation defect more extensive that perfusion defect : Parenchymal lung disease, e.g. pneumonia
- Left heart failure : Perfusion distributed anteriorly and superiorly

To attempt to assess how VQ SPECT contributes to patient management, and might fit into the clinical pathway, the reports for all patients who had VQ SPECT and CTPA within five days of one another were retrieved.

VQ SPECT and CTPA are complementary techniques with VQ SPECT demonstrating a slightly higher published sensitivity, and CTPA has higher published specificity (Table 1))[12]. Neither technique is the gold standard and the true diagnosis of patients in this study was unknown.

A total of 50 patients had VQ SPECT & CTPA scans performed within five days of one another. The majority of these were in the period immediately after changing to VQ SPECT when the reporters were relatively inexperienced and a number of VQ reports stated that although there was no good evidence of PE, it could not be excluded and CTPA was recommended to exclude PE. More recently a number of VQ SPECT scans have been requested after "sub-optimal quality" CTPA examinations.

Several patients had VQ SPECT and CTPA studies in which the reports disagreed. Ten patients had a VQ SPECT study which was reported as "No evidence of PE". One patient out of these ten cases had a PE demonstrated on CTPA which was not demonstrated or suspected on the VQ SPECT images. This embolus was only just detectable and sub-segmental emboli are thought to be often missed with CTPA, which has an overall sensitivity of around 85%, less than that quoted for VQ SPECT [13]. However, advocates of CTPA over VQ imaging insist that small sub-segmental emboli are common and of doubtful clinical significance[14]. It is not known if this patient's PE is acute thrombus or chronic condition, but the patient was treated with anticoagulants presumably because of the possibility of further PEs. The treatment of this patient does suggest that these small emboli were considered to be clinically significant.

Five patients were thought to have PE on the VQ SPECT images but no PE was found with CTPA. Two of these patients had documented PE in the past and unresolved previous PE is a known cause of a false positive VQ scan. It is possible that the patients had residual perfusion defects from emboli that were no longer present. Three patients had no evidence of PE on CTPA, although sub-optimal quality images were noted on one report. This patient had a solitary, sub-segmental perfusion defect on VQ SPECT, which was clear-cut and wedge-shaped. The EANM guidelines[1,2] recommend that a defect should be segmental, rather than sub-segmental, for an image to be deemed consistent with PE. However there is some evidence that smaller defects may also be significant[15] although there is limited data on the appropriate management of such patients. This patient may well have had a small PE not visible on a sub-optimal quality CTPA investigation. No additional information is available about these patients to indicate if it is most likely the result was a false positive on the VQ scan or falsely negative on the CTPA. VQ SPECT is the technique with the highest published sensitivity and the safety of withholding anticoagulant therapy in such a patient has not yet been evaluated in peer-reviewed publications.

Discussion

VQ SPECT has demonstrated excellent sensitivity and specificity for the detection of PE in numerous publications. A recent study[16] followed up 1785 patients who had a VQ SPECT scan for at least six months to ascertain the final clinical diagnosis. Of these 1785 patients, 1159 (65%) patients had a VQ SPECT scan demonstrating no PE. The final diagnosis for 1153 patients was the patients did not have PE. Six patients were found to have PE (0.5% of the total with a negative VQ SPECT scan).

A positive VQ SPECT scan was recorded for 607 (34%) of the total, consistent with PE. The final diagnosis in 601 patients was PE, and 6 patients were not thought to have PE (0.9% of the total number of patients with a positive scan). Just 19 patients had non-diagnostic VQ SPECT scans; 1% of the total number of scans in the study. One of these 19 patients had a final diagnosis of PE.

At CDDFT, continued refinement of the technique has demonstrated current image quality as excellent or good in 92% of patients (using a ventilation agent of radioactive carbon particle pseudo gas). Image quality is often good or better even in very elderly patients, without normal chest x-rays. Poor quality ventilation studies were seen in just 2% of patients.

Repeated audits of image reporting and comparison to CTPA reports where available has demonstrated good agreement. Increasing reporter confidence when PE was absent and the recent publication of EANM guidelines for Lung imaging[1,2] has enabled a definitive result for 98% of patients referred for VQ SPECT imaging at CDDFT. Just 2% of patients had an indeterminate report.

The BTS guidelines[9] opinion of VQ scanning is obsolete with respect to the modern VQ SPECT scan. PE can now be diagnosed or excluded reliably in the vast majority of patients by isotope lung scanning. Good quality imaging can be acquired even in elderly patients without normal chest x-rays, studies may be used to identify other (limited) pathology and recent local audits confirm there are just 2% indeterminate or equivocal results.

Conclusion

Within the constraints of a single camera department working with tight demands for patient waiting times, the nuclear medicine department has researched, implemented and audited a superior technique of VQ imaging to improve the sensitivity and accuracy of the investigation of PE. County Durham and Darlington Foundation NHS Trust was one of the first in the UK, and the first in the northern region, to routinely utilise this new technology.

VQ SPECT imaging provides a definitive result in approximately 98% of patients and should a primary imaging technique for the investigation of patients with suspected PE.

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