Original Article

VALIDITY OF LUNG PERFUSION SPECT SCAN MATCHED WITH A CHEST RADIOGRAPH IN ACUTE PULMONARY EMBOLISM

Mehdi Raza, Mujahid Khalid Ali

Armed Forces Institute of Pathology Rawalpindi

ABSTRACT

Objective: To validate single photon emission computed tomography (SPECT) lung perfusion scan (LPS) matched with a recent chest radiograph against computed tomographic pulmonary angiography (CTPA) used as gold standard, for diagnosis of acute pulmonary embolism (PE).

Study Design: Validation study.

Place and Duration of Study: Nuclear Medical Centre, Armed Forces Institute of Pathology, Rawalpindi, Pakistan, from 31th May 2011 to 7th December 2012.

Patients and Methods: Thirty patients suspected of acute PE with Wells' score ≥ 2, representing intermediate and high PE probability were enrolled, through non-probability, consecutive sampling. LPS scans, acquired after intravenous injection of 175-200 MBq of Tc-99 m macro albumin aggregates, were matched with chest radiographs (instead of ventilation scans) and reported as positive or negative for acute PE. Outcomes were compared against CTPA results, and diagnostic measures were calculated.

Results: LPS scan (matched with chest radiograph) was found to have sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of 93.33%, each Cohen's Kappa coefficient (k) was 0.866.

Conclusion: Lung perfusion SPECT scan matched with a recent chest radiograph is a reliable investigation for the diagnosis of acute PE and can suffice as a stand-alone test to guide patient management.

Keywords: Computed tomography, Multidetector, Pulmonary embolism, Sensitivity and specificity, SPECT, Validity.

INTRODUCTION

Venous thromboembolism (VTE) is a fairly common pathology, which affects 5% of the population[1] and may manifest as deep vein thrombosis (DVT) or pulmonary embolism (PE). Estimated prevalence of acute PE in hospitalized patients, as calculated by Stein and Henry was 1% and around 15% of their patients were found to have PE on autopsy[2]. Prevalence of PE in South Asia is not well researched and limited studies conducted in Pakistan and India show a mixed trend[3,4]. As PE is a diagnostic challenge even in the developed world, it is rightly expected that the problem stays undetected or the diagnosis is frequently missed in the developing countries. Due to much research on various clinical, biochemical and imaging criteria for the diagnosis of acute PE, significant refinement in its diagnostic algorithm has been achieved. Ventilation/perfusion (V/Q) scanning, catheter pulmonary angiography (PA), digital subtraction angiography (DSA), computed tomographic pulmonary angiography (CTPA), magnetic resonance angiography (MRA), doppler ultrasonography (USG), serum D-dimer assays and clinical criteria, like Wells' scoring system [5] are some of the widely studied topics related to this subject.

Among the imaging modalities, V/Q scanning is non-invasive and much more economical compared to PA and CTPA and carries much less radiation burden for the patient. A recent study by Miles et al[6]. have reported the sensitivity and specificity values of V/Q scan employing single photon emission computed tomography (SPECT) for acute PE (against the respiratory physicians' reference diagnosis) as

Correspondence: Dr Mehdi Raza, Nuclear Medical Centre, AFIP Rawalpindi.
Email: mahdiraza@yahoo.com
Received: 11 Sep 2013; Accepted: 15 Nov 2013

83% and 98%, respectively. Another study published in 2008 by Bajc et al. has reported sensitivity and specificity values of 99% and 98%, respectively for the V/Q SPECT scan[7]. Helical CTPA, in comparison, on a systematic review, was found 90% sensitive and 95% specific for the diagnosis of acute PE[8], while MRA is still under evaluation and it has been reported that technically adequate images are difficult to obtain[9]. In the past, the major difficulty with V/Q scan – using the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria for PE was the indeterminate scan, which did not give a clear direction to the ordering clinician. PIOPED trial found a sensitivity of 98% and specificity of only 10% for V/Q scintigraphy, with an observed PE prevalence of 33%[10].

Recent research on V/Q scanning, has focused on enhancing lung scintigraphy with SPECT[11,12] and on combining lung perfusion scintigraphy with plain chest radiography (without a ventilation scan), in patients undergoing scintigraphic imaging[13]. Studies have also reassessed clinical criteria, like the Wells' scoring system to determine current relevance and diagnostic role in acute PE, in conjunction with LPS and V/Q scintigraphy[14]. Advances in CT technology, in the meanwhile, have made CTPA readily available and have led to its extensive use as a screening rather than a diagnostic test, despite higher cost, much higher radiation burden and chances of allergic reactions to contrast material[15]. Modern day clinicians' perceived preference for CTPA using helical or multi-detector computed tomography (MDCT) has been reported in literature[11,13,16] and has led to a fall in the frequency of positive CTPA examinations in the American and European hospitals from 25-30% in 1990s to 5-10% in the last decade[17,18]. In short, CTPA has emerged as a new gold standard in the diagnosis of acute PE, with reported sensitivity of 87-100%[19] and specificity of 94-100%, for 4-slice MDCT[20]. Better values have been documented with newer generation multidetector CT scanners.

Thus, it has become important for the imaging physicians to be knowledgeable about the subject and scientifically present the salient features of each imaging modality to the referring clinicians[21]. Awareness about the benefits of V/Q scintigraphy in the clinical fraternity may have remarkable financial implications for the patients and the health care system. It needs to be highlighted that marked reduction, in the radiation dose to the patient and chances of nephrotoxicity or an allergic reaction due to contrast material used for CTPA, is achievable[6,7,11]. Employing V/Q scanning in the diagnostic algorithm for acute PE, it may be possible to further decrease the radiation dose, employing perfusion-only lung scans[13,21]. The elimination of ventilation scan may reduce procedure time and costs[13,22]. CTPA, in this scenario, may be reserved for a select group of patients with high clinical suspicion but negative V/Q scan results and/or those with abnormal chest radiographs/pulmonary pathologies, in addition to acute PE.

In view of the foregoing, this study was designed to validate lung perfusion SPECT (LPS) scan matched with a recent chest radiograph against CTPA (used as gold standard), for the diagnosis of acute PE.

PATIENTS AND METHODS

This validation study was done in the nuclear medical centre (NMC), Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan from 31 May 2011 to 7 December 2012. Thirty indoor/outdoor patients, 24 males and 6 females (n = 30) amongst those referred for V/Q scintigraphy were recruited through non-probability, consecutive sampling. Sample size was calculated on the basis of sensitivity of 99% and specificity of 98% for the test[7]; with expected prevalence of 16%[5], desired precision of 10% and confidence level of 95%. Patients of any age/gender, who were diagnosed as acute PE, on CTPA, or suspected to have acute PE on the basis of Wells' score of ≥ 2[5] were included. Patients with a history of acute PE in the recent past, or any chronic lung pathology, detected on the basis of an abnormal chest radiograph or other tests/documents were excluded from the study. Ethical committee at AFIP, Rawalpindi granted its approval, prior to commencement of the study. Written, informed consent was obtained in each case.

Data Collection: For the study, CTPA done before or after the lung perfusion SPECT (LPS) scan, preferably within a period of 24 to 48 hours, was considered acceptable. LPS scintigraphy was done, employing the following apparatus / methodology: **Equipment:** Siemens e-cam® single head gamma camera system, employing e-soft ® software (Siemens Healthcare, Germany), fitted with a low energy all purpose (LEAP) parallel hole collimator, for acquisition and subsequent processing of acquired images.

Acquisition Protocol: Slow, direct intravenous injection of 175 to 200 MBq (5 mCi) of Tc-99m MAA, formulated using Maasol ® (GE Healthcare, Italy) was administered, over several moderately deep breath cycles. Number of particles injected was kept between 100,000 to 250,000. Pulmonary perfusion images were acquired immediately post-injection, using SPECT protocol. 128 x 128 matrix, with a 20% electronic window, centred at 140 keV, and a non-circular orbit were used (360° clock-wise acquisition was done in 64 steps). First view of 250,000 to 400,000 counts (depending on the dose administered and total imaging time) was followed by 63 views of the same time duration. In view of patient comfort, total imaging time was kept within 30 minutes[6].

Processing Protocol: Volume rendered image, along with axial, coronal and sagittal slices, reconstructed by filtered back projection – employing a third-order Butterworth filter and a cutoff frequency of 0.65 – were used for interpretation of tomographic lung perfusion images.

Scan Interpretation: Two experienced nuclear physicians independently interpreted and reported the scans as positive or negative for acute PE. A perfusion defect involving 50% or more of a bronchopulmonary segment was considered diagnostic for PE[6]. Recent, erect, plain chest radiograph – posteroanterior view, with good inspiratory effort, preferably not more than 24 hours old, reported by an experienced radiologist – was used instead of a ventilation scan, for comparison with the LPS scan and to determine if an observed defect was mismatched or otherwise. Any difference of opinion was resolved through mutual discussion.

CTPA: The study utilized images obtained using PE protocol, from two 64-multislice CT scanners, with 0.5 to 0.7 mm collimation, 0.3 to 0.5 second rotation time and 6.0 to 8.0 mm per rotation table speed. Two experienced consultants from Radiology and/or Cardiology reported on each examination, as positive or negative for acute PE. The diagnosis of pulmonary emboli on CTPA was made if a filling defect outlined by a thin rim of contrast was visualized within the lumen of a vessel[23].

Data Analysis: Statistical analysis was done using 2 x 2 contingency table. Calculations were done manually and through Microsoft Excel ® (Microsoft Corporation, USA) and InStat ® (GraphPad Software Incorporated, USA). Frequency/percentage were computed for gender and mean and standard deviation (SD) for age. Sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) were computed for LSP scan taking CTPA as gold standard and Cohen's kappa coefficient (κ) was calculated to determine the extent of agreement between both tests.

RESULTS

A total of 30 patients were enrolled in the study. Twenty four (80%) of these subjects were males, with a mean age ± standard deviation (SD) of 37.96 ± 15.56 years (age range = 20 to 76 years). 6 (20%) of the subjects were females, with a mean age ± SD of 42.33 ± 8.96 years (age range = 33 to 56 years). The patients underwent CTPA and lung perfusion SPECT scintigraphy, with the order of the tests determined by convenience. No remarkable untoward effect during or after the tests was reported. Figures 1 and 2 show CTPA, plain chest radiographs and LPS scans from two patients included in the study. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 93.3% each (Table). Co-efficient of Cohen's Kappa is 0.866.

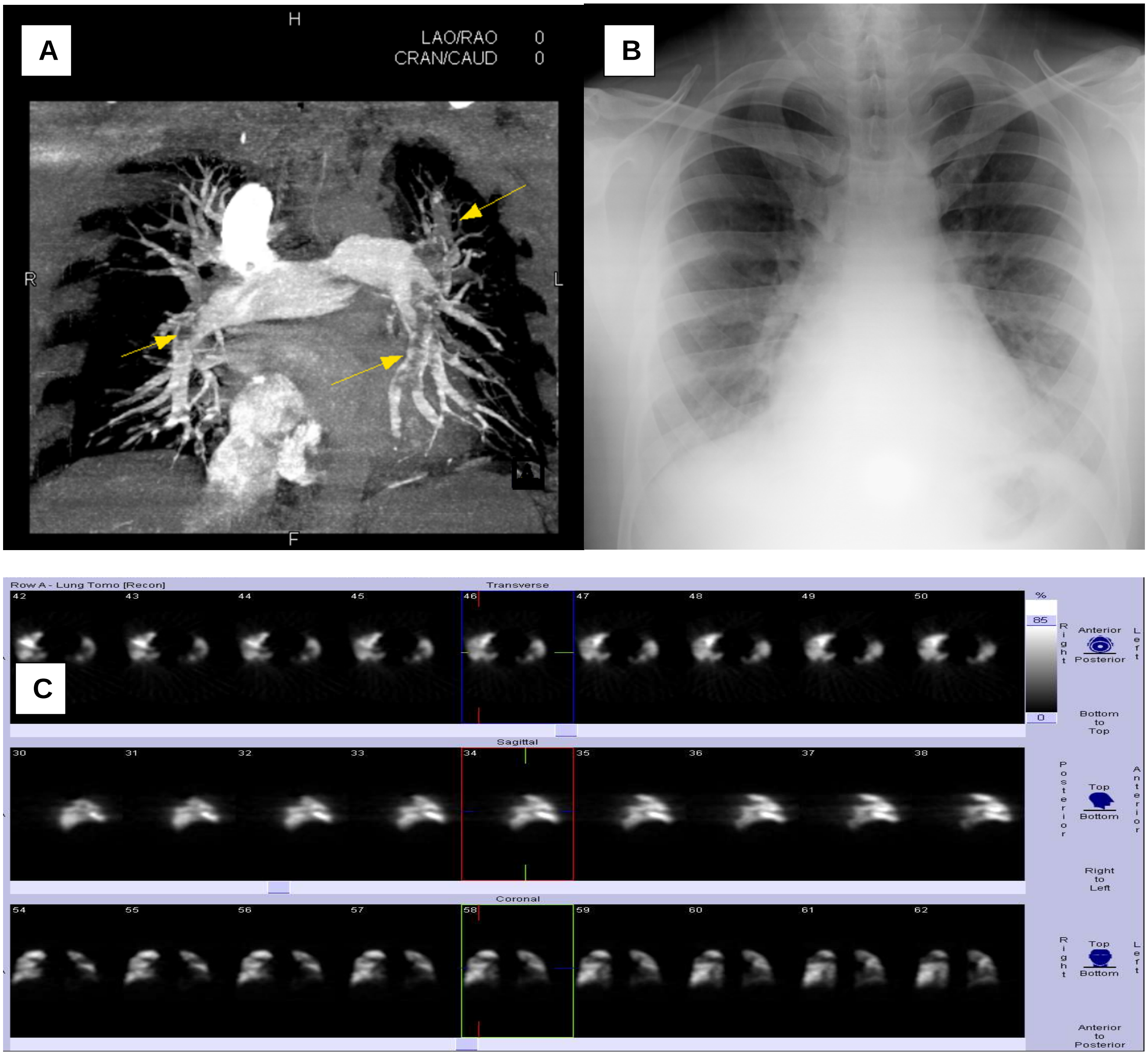

Figure-1: A 28 year old male patient, with bilateral acute pulmonary embolism. (A) CTPA – Coronal reconstruction in aortopulmonary window. Arrows show multiple filling defects in the pulmonary vasculature, bilaterally (CRAN / CAUD–cranial / caudal, F–foot, H–head, LAO / RAO–left anterior oblique / right anterior oblique, L–left, R–right). (B) Plain chest radiograph shows mild cardiomegaly. (C) LPS scan – Transverse, sagittal and coronal reconstructed slices show multiple wedge-shaped perfusion defects in both lung fields.

DISCUSSION

This study sought to address the clinicians' perceived preference for CTPA in comparison to

V/Q scintigraphy in suspected cases of acute PE, despite the presence of multicentre studies about similar sensitivity and specificity values of both tests. Another fact in view was the occasional sub-optimal ventilation scan and other limitations of V/Q scintigraphy, seen more often in patients with dyspnoea and/or chronic obstructive airway disease[24], who are unable to demonstrate a good inspiratory effort.

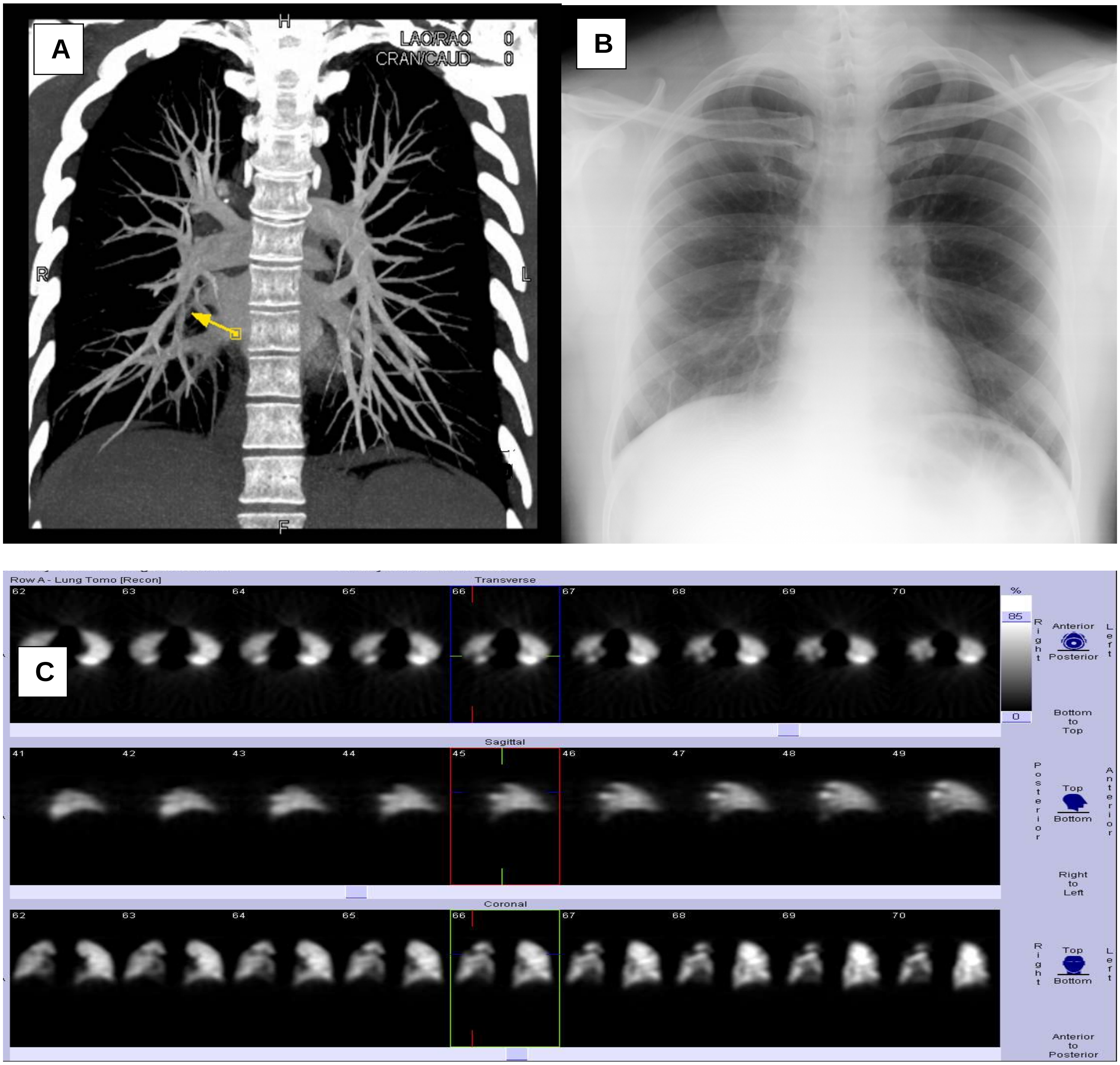

Figure-2: A 37 year old male patient, with bilateral acute pulmonary embolism. (A) CTPA – coronal reconstruction. Arrow shows a lumenal area of inhomogenous contrast density, with a filling defect at the junction of lobar / segmental pulmonary arteries on the right side (CRAN / CAUD–cranial / caudal, F–foot, H–head, LAO / RAO–left anterior oblique / right anterior oblique, L–left, R–right). (B) Plain chest radiograph is normal. (C) LPS scan – Transverse, sagittal and coronal reconstructed slices show multiple perfusion defects with areas of hyperperfusion, bilaterally, most marked in the right lung. Location of the largest defect corresponds to CTPA findings.

This study, hence, did not resort to ventilation scan by design and utilised a recent, plain chest radiograph instead, for comparison with the lung perfusion scan. This meant relatively hassle free, supine imaging sessions, with no surrounding ventilation scan gadgetry. It also translated into decreased radiation exposure, cost and imaging time for majority of patients imaged. To the knowledge of the authors, no other recent study has compared lung perfusion SPECT scintigraphy matched with a plain chest radiograph against CTPA performed by the modern (64-slice) multidetector CT scanners.

Prospective investigative study of acute pulmonary embolism diagnosis (PISAPED) investigators used a similar approach of dropping the ventilation scan, in the diagnosis of pulmonary embolism, with addition of objective clinical evaluation and probability assessment criteria and a recent chest radiograph for interpretation of perfusion scans. They analysed prospective and retrospective data, published in many studies, to conclude – in a review article – that the perfusion scan could be read independently, with the chest radiograph used to obtain ancillary information, which may help differentiate PE and other pathologies leading to an abnormal perfusion scan. They acknowledged that the ventilation scan may be helpful in some cases and left it to future studies to clarify how a chest radiograph could be objectively incorporated into the scheme[25].

Other researchers, in the recent and not so recent past, have similarly studied the importance of a chest radiograph in the diagnosis of acute PE. Most employed planar V/Q scintigraphy for the purpose. Gottschalk et al., using PIOPED II data, proposed that normal lung perfusion, with low probability clinical assessment could rule out PE. They emphasized that in 89% of such patients, a categorical ‘PE present or absent’ diagnosis could be given, if the chest radiograph was normal or near normal[26].

Most review articles have recognised algorithms using both CTPA and V/Q SPECT scintigraphy as safe for diagnosis and management of acute PE. Anderson and Barnes identified multidetector CTPA as more sensitive but with significant radiation exposure and V/Q scintigraphy as having a fraction of radiation risk. Scintigraphy, in their opinion, could be preferred in certain patients[27]. Other researchers even explored the idea of fusion of CTPA and V/Q scintigraphic images through automatic registration software to complement the information provided by either test[28].

In the results from this study, the kappa coefficient (κ) of 0.866 represents excellent agreement[29] between the results of LPS scintigraphy (matched with a chest radiograph) and CTPA, in the diagnosis of acute PE. Sensitivity and specificity values of 93.33%, each, are comparable to evidence from other published studies[6,13,30]. PPV and NPV of 93.33%, each, also support the utility of this approach and are similar to values documented by other researchers for LPS scintigraphy matched with a ventilation scan[6]. A very recent study has calculated the NPV of V/Q SPECT scintigraphy at 97%[31]. The observations are generally similar to a randomised, controlled trial, designed as a non-inferiority study, to analyse if CTPA was reliable and safe compared to planar V/Q scintigraphy. The trial found CTPA more sensitive and preferred by clinicians. Multislice CT was used in 499 out of 694 CTPA studies, while only planar V/Q scintigraphy was used for comparison[32].

Out of 30 patients included in this study, 14 were found negative for acute PE on lung perfusion SPECT scan, while 16 were found positive for acute PE. Similar results were seen on CTPA analysis, with 2 discordant results vis-à-vis the LPS findings. Prevalence of PE in the patients included in the study was 50%.

Among the 2 cases showing discordant LPS scan results (when compared with CTPA), one case with a CTPA report positive for PE (a small thrombus in a lobar pulmonary artery), was found negative on LPS scintigraphy, perhaps due to initiation of thrombolytic therapy prior to LPS scan (which was delayed due to gamma camera non-availability). The other case had a CTPA report negative for PE but was found positive for PE, on LPS scintigraphy. In this instance, both studies were performed within hours of each other and no thrombolytic therapy was administered. This case, however, was referred with a differential diagnosis of idiopathic pulmonary hypertension and transthoracic echocardiographic findings showed mild right atrioventricular dilatation and pressure overload. This could be a case of chronic thromboembolic pulmonary hypertension, wherein sensitivity of CTPA has been reported to be as low as 51%[33].

The issue of radiation exposure and cost involved in CTPA was adequately analysed by a study, which employed 8 and 16-slice CT scanners and mentioned a radiation exposure per examination of 1.6 to 8.3 mSv, with an increase of 5.7 mSv with venography; vis-à-vis a radiation dose of 1.2 to 2.0 mSv for a V/Q scan. A perfusion only scan gave a dose of 0.8 mSv, while a plain chest radiograph (two views) added another 0.07 mSv. The price of contrast enhanced spiral CT was nearly twice the V/Q scan, US $ 1739 versus US $ 917, respectively[34]. It is pertinent here to highlight the average normal background radiation exposure to general population, which is 2.4 mSv per year, i.e., more than the radiation dose from a V/Q scan[35].

Additionally, already published research has amply demonstrated that the radiation exposure for multislice CT is higher compared to single slice CT scanners, by upto 36%[36]. A 64-slice CTPA examination gives a mean radiation exposure of 19.9 + 1.38 mSv[18], which is 25 times the exposure from a lung perfusion scan. These factors enhancing the lifetime risk of induced cancer, and nephrotoxicity and contrast associated allergic reactions have encouraged continuing research in CTPA and V/Q scintigraphic techniques. Use of SPECT/CT, PET/CT, newer ventilation agents and Tc-99m labelled anti-D-dimer monoclonal antibodies for imaging[37] are some of the promising options, being explored by researchers on the subject.

Table: Comparison of outcomes of single photon emission computed tomography (SPECT) lung perfusion scan (LPS) against computed tomographic pulmonary angiography (CTPA).

LPS scan	CTPA	
	Positive	Negative
Positive	14	1
Negative	1	14

CONCLUSION

Lung perfusion SPECT scan matched with a recent chest radiograph is a reliable investigation for the diagnosis of acute PE and can suffice as a stand-alone test to guide patient management.

Recommendations: The results of this study highlight lung perfusion SPECT scintigraphy (matched with a recent chest radiograph) as a valuable, stand-alone test in the diagnosis of acute PE. These findings warrant a large multi-centre trial to generate broad-based evidence, to facilitate changes in professional guidelines on the subject and to increase awareness about the benefits of this approach.

Strength/Limitations: Strength of this study lies in the validation of lung perfusion SPECT scintigraphy against CTPA employing 64-slice CT scanners, using a prospective study design, with the use of a recent, plain chest radiograph instead of a ventilation scan, for the purpose. This methodology is extremely cost effective, requires one scintigraphic appointment and involves the lowest radiation exposure among all comparable imaging options for the diagnosis of acute PE. Another remarkable feature of the study is its South Asian setting, with hardly any similar studies from this part of the world, published internationally.

Regarding the limitations of the study, some patients whose CTPA was done before LPS scan, and was found positive for acute PE, received thrombolytic therapy forthwith; according to the policy of prompt administration of standard treatment, after confirmation of diagnosis. LPS scan in such cases was performed later.

Use of a single head gamma camera for SPECT scan was another constraint, as it can lead to uncomfortable imaging times for the old, or often dyspnoeic PE patients, limiting cooperation and compromising scan quality. Use of multi-head cameras in such cases may improve scan quality, by decreasing imaging time and increasing patient comfort. Further decrease in radiopharmaceutical dose may also be possible.

Acknowledgements

The authors wish to acknowledge the help of Dr Abdul Hameed Siddiqui, Dr Tahir Iqbal and Prof Dr Sohail Aziz, consultant cardiologists from the Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi, in data collection and patient referral. Gratitude is also due to Dr Tariq Mahmood Mirza and Dr Umer-i-Farooq, consultant nuclear physicians from Nuclear Medical Centre, Armed Forces Institute of Pathology, Rawalpindi, for help in data analysis and interpretation. Finally, the contribution of Prof Dr Hashim Ali Kazmi, erstwhile Head of Pathology Departments at Dow/Sindh/Baqai Medical Colleges, Karachi and Associate Prof Dr Zehra Naz, Head of Biochemistry Department, Islamic International Medical College (Riphah International University), Rawalpindi – who helped in analysing the manuscript critically and gave valuable suggestions – is also gratefully acknowledged.

This study was supported by the Armed Forces Institute of Pathology, Rawalpindi, Pakistan, through a grant from its own resources. The authors declare that they have no conflict of interest.

Excerpts from the data in this paper were presented as a poster in the 11th Annual General Meeting of the Asian Regional Cooperative Council for Nuclear Medicine (ARCCNM), held at Seoul, Korea from 24 – 26 October 2012 and published in the conference abstracts book.

REFERENCES

1. Freeman LM, Blaufox MD. Letter from the editors. Semin Nucl Med. 2008; 38(6):403.
2. Stein PD, Henry JW. Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy. Chest 1995; 108(4):978-81.
3. Mirza MW, Ashraf S, Fawad A. Role of routine use of thromboprophylaxis in patients undergoing major surgery. Pakistan J Med Res 2005; 44(1):4-11.
4. Bagaria V, Modi N, Panghate A, Vaidya S. Incidence and risk factors for development of venous thromboembolism in Indian patients undergoing major orthopaedic surgery: results of a prospective study. Postgrad Med J 2006; 82(964):136-9.
5. Wells PS, Anderson DR, Rodger M, Stiell I, Dreyer JF, Barnes D, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: Management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and D-dimer. Ann Intern Med 2001; 135(2):98-107.
6. Miles S, Rogers KM, Thomas P, Soans B, Attia J, Abel C, et al. A comparison of single-photon emission CT lung scintigraphy and CT pulmonary angiography for the diagnosis of pulmonary embolism. Chest 2009; 136(6):1546-53.
7. Bajc M, Olsson B, Palmer J, Jonson B. Ventilation ⁄ perfusion SPECT for diagnostics of pulmonary embolism in clinical practice. J Intern Med 2008; 264(4):379–87.
8. Segal JB, Eng J, Tamariz LJ, Bass EB. Review of the evidence on diagnosis of deep vein thrombosis and pulmonary embolism. Ann Fam Med 2007; 5:63-73.
9. Stein PD, Chenevert TL, Fowler SE, Goodman LR, Gottschalk A, Hales CA, et al for the PIOPED III (Prospective Investigation of Pulmonary Embolism Diagnosis III) Investigators. Gadolinium-enhanced magnetic resonance angiography for pulmonary embolism: A multicenter prospective study (PIOPED III). Ann Intern Med 2010; 152(7):434-43.
10. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). The PIOPED Investigators. JAMA 1990; 263(20):2753-9.
11. Roach PJ, Bailey DL, Harris BE. Enhancing lung scintigraphy with single-photon emission computed tomography [abstract]. Semin Nucl Med 2008; 38(6):441-9.
12. Stein PD, Freeman LM, Sostman HD, Goodman LR, Woodard PK, Naidich DP, et al. SPECT in acute pulmonary embolism. J Nucl Med 2009; 50(12):1999–2007.
13. Sostman HD, Miniati M, Gottschalk A, Matta F, Stein PD, Pistolesi M et al. Sensitivity and specificity of perfusion scintigraphy combined with chest radiography for acute pulmonary embolism in PIOPED II. J Nucl Med 2008; 49(11):1741-8.
14. Yap KSK, Kalff V, TurlakowA, Kelly MJ. A prospective reassessment of the utility of the Wells score in identifying pulmonary embolism. Med J Aust 2007; 187(6):333-6.
15. Costantino MM, Randall G, Gosselin M, Brandt M, Spinning K, Vegas CD et al. CT angiography in the evaluation of acute pulmonary embolus. Am J Roentgenol 2008; 191(2):471-4.
16. Jha S, Ho A, Bhargavan M, Owen JB, Sunshine JH. Imaging evaluation for suspected pulmonary embolism: what do emergency physicians and radiologists say? Am J Roentgenol 2010; 194(1):W38-W48.
17. Woo JKH, Chiu RYW, Thakur Y, Mayo JR. Risk-benefit analysis of pulmonary CT angiography in patients with suspected pulmonary embolus. Am J Roentgenol. 2012; 198(6):1332–9.
18. Mamlouk MD, vanSonnenberg E, Gosalia R, Drachman D, Gridley D, Zamora JG, et al. Pulmonary embolism at CT angiography: implications for appropriateness, cost, and radiation exposure in 2003 patients. Radiology 2010; 256(2):625-32.
19. Subramaniam RM, Blair D, Gilbert K, Sleigh J, Karalus N. Computed tomography pulmonary angiogram diagnosis of pulmonary embolism. Australas Radiol 2006; 50(3):193-200.

20. Russo V, Piva T, Lovato L, Fattori R, Gavelli G. Multidetector CT: a new gold standard in the diagnosis of pulmonary embolism? State of the art and diagnostic algorithms [abstract]. Radiol Med 2005; 109(1-2):49-61;quiz 62-3.
21. Freeman LM. Don't bury the V/Q scan: It's as good as multidetector CT angiograms with a lot less radiation exposure. J Nucl Med 2008; 49(1):5-8.
22. Goco GFL, Ote ELP, Ortiz AO, Torres MT, Vizcarra RP, Nolido RAB, et al. Evaluation of SPECT lung perfusion scintigraphy in patients with suspected pulmonary embolism. World J Nucl Med 2009; 8(3):148-53.
23. Callaway M, Wilde P. Acquired heart disease II: non-invasive imaging. In: Sutton D, editor. A textbook of radiology and imaging, 7th ed. Edinburgh: Churchill Livingstone, Elsevier Science Ltd 2003:342-3.
24. Leblanc M, Paul N. V/Q SPECT and computed tomographic pulmonary angiography [abstract]. Semin Nucl Med 2010; 40(6):426-41.
25. Miniati M, Sostman HD, Gottschalk A, Monti S, Pistolesi M. Perfusion lung scintigraphy for the diagnosis of pulmonary embolism: A reappraisal and review of the prospective investigative study of acute pulmonary embolism diagnosis methods. Semin Nucl Med 2008; 38(6):450-61.
26. Gottschalk A, Stein PD, Sostman HD, Matta F, Beemath A. Very low probability interpretation of V/Q lung scans in combination with low probability objective clinical assessment reliably excludes pulmonary embolism: Data from PIOPED II. J Nucl Med 2007; 48(9):1411–5.
27. Anderson DR, Barnes DC. Computerized tomographic pulmonary angiography versus ventilation perfusion lung scanning for the diagnosis of pulmonary embolism. Curr Opin Pulm Med 2009; 15(5):425-9.
28. Harris B, Bailey D, Roach P, Bailey E, King G. Fusion imaging of computed tomographic pulmonary angiography and SPECT ventilation/perfusion scintigraphy: initial experience and potential benefit. Eur J Nucl Med Mol Imaging. 2007; 34(1):135-42.
29. Viera AJ, Garrett JM. Understanding Interobserver Agreement: The Kappa Statistic. Fam Med 2005; 37(5):360-3.
30. Gutte H, Mortensen J, Jensen CV, von der Recke P, Petersen CL, Kristoffersen US, et al. Comparison of V/Q SPECT and planar V/Q lung scintigraphy in diagnosing acute pulmonary embolism. Nucl Med Commun. 2010; 31(1):82-6.
31. Ling IT, Naqvi HA, Siew TK, Loh NK, Ryan GF. SPECT ventilation perfusion scanning with the addition of low-dose CT for the investigation of suspected pulmonary embolism. Intern Med J 2012; 42(11),1257–61.
32. Anderson DR, Kahn SR, Rodger MA, Kovacs MJ, Morris T, Hirsch A, et al. Computed tomographic pulmonary angiography vs ventilation-perfusion lung scanning in patients with suspected pulmonary embolism: A randomized controlled trial. JAMA 2007; 298(23):2743-53.
33. Tunariu N, Gibbs SJR, Win Z, Gin-Sing W, Graham A, Gishen P, et al. Ventilation-perfusion scintigraphy is more sensitive than multidetector CTPA in detecting chronic thromboembolic pulmonary disease as a treatable cause of pulmonary hypertension. J Nucl Med 2007; 48(5):680-4.
34. Stein PD, Woodard PK, Weg JG, Wakefield TW, Tapson VF, Sostman HD, et al. Diagnostic pathways in acute pulmonary embolism: recommendations of the PIOPED II investigators. Radiology 2007; 242(1):15–21.
35. Kuiper JW, Geleijns J, Matheijssen NA, Teeuwisse W, Pattynama PM. Radiation exposure of multi-row detector spiral computed tomography of the pulmonary arteries: comparison with digital subtraction pulmonary angiography. Eur Radiol. 2003;13(7):1496–1500.
36. Moro L, Bolsi A, Baldi M, Bertoli G, Fantinato D. Single-slice and multi-slice computerized tomography: dosimetric comparison with diagnostic reference dose levels [abstract]. Radiol Med 2001; 102:262–5.
37. Morris TA, Gerometta M, Yusen RD. Detection of pulmonary emboli with 99mTc-labeled anti–D-dimer (DI-80B3) Fab fragments (ThromboView). Am J Respir Crit Care Med 2011; 184(6): 708-14.

....