

The diagnostic accuracy of prospective investigative study of acute pulmonary embolism diagnosis criteria for the detection of acute pulmonary thromboembolism in acutely ill patients

ABSTRACT

The practical diagnostic performance of Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISAPED) criteria for the detection of acute pulmonary thromboembolism (APTE) in hospitalized patients is not yet well determined. This is the report of the initial results of our recently implemented protocol to employ PISAPED. One hundred and forty-seven pulmonary perfusion scans with 1–3 mCi ^{99m}Tc -MAA of patients of a single pulmonologist were included. Patients with suspicious perfusion defects underwent single-photon emission computed tomography. Interpretations were done by consensus of two nuclear medicine specialists. Comparisons were done with chest X-ray or chest computed tomography when available. The interpreters had access to the clinical records. The scans were reported based on the PISAPED criteria as negative or positive for APTE or indeterminate. Patients were followed up for 6.2 ± 5.3 months when the final diagnosis confirming or excluding APTE was achieved. Patients aged 55.9 (17.2) years; 78 (53.1%) of them were female and 64 (43.8%) had high Wells' score. The scans were positive, negative, and indeterminate in 17 (11.6%), 126 (85.7%), and 4 (2.7%) patients, respectively. In 6 out of 147 patients, follow-up was not completed and the final diagnosis was not achieved. APTE was finally diagnosed in 21 (14.3%) patients; 12 (57.1%) of them had positive scans. APTE was excluded in 116 (78.9%) patients; 112 (96.5%) of them had negative scans. The accuracy of the test for the diagnosis of APTE was 87.9%. Lung metastasis was the most frequent reason among false-negative cases. The lung perfusion scan using PISAPED criteria could be used with good accuracy in inpatient settings.

Keywords: Diagnostic accuracy, perfusion lung scan, Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis criteria, pulmonary thromboembolism

INTRODUCTION

The application of lung perfusion scan for the detection of acute pulmonary thromboembolism (APTE) has been overwhelmed in our clinical practice for years by pulmonary computed tomography (CT) angiography corresponding with its reportedly high accuracy. Five years ago, when the lung perfusion scans were reported according to the probability-based criteria of Modified Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED),^[1] we had seldom lung perfusion scan requests peaking to 1 or 2 per week. The lack of radioaerosol or Technegas ventilation scans hindered further the use of nuclear medicine scintigraphy for the detection of APTE in Iran where the

ventilation scan with ^{81}Kr is available in few centers once a week. The results of PIOPED I and II studies highlighted the

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flaws of perfusion scan for the diagnosis of APTE.^[2,3] On the other hand, the high sensitivity for CT angiography leads to a significant clinical burden mainly secondary to the diagnosis of subsegmental pulmonary artery thromboembolism.^[4] The benefit of the treatment of these subsegmental PTEs is not well documented. Furthermore, the high radiation to the breast of the youngsters and the complications of the radiocontrast substrates were considered as significant drawbacks.^[5] Meanwhile, the widespread use of single-photon emission computed tomography (SPECT) imaging in different scintigraphy protocols was employed for pulmonary perfusion scans in certain studies.^[6,7] The use of SPECT imaging for pulmonary perfusion scan is still not a guideline-supported advice, but in our practice, we found its superior application over usual planar imaging.^[8] We discussed the reasons for the low referral with the local pulmonologists. Seemingly, high rates of intermediate and low probability for PTE reports were the main obstacle. In line with other investigators, including the practice in the Montefiore Medical Center, we changed our reporting system from probability-based PLOPED criteria into definite reporting based on the Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISAPED) criteria.^[9] Furthermore, SPECT imaging was used in abnormal scans with suspicious wedge-shaped perfusion defects. The performance of the scan was seemingly convincing and there was an increase in the clinical requests for pulmonary perfusion scan. After 5 years of clinical practice, the ratio of requests for CT angiography and perfusion scans dramatically changed and at the time of this publication CT angiography and lung perfusion scan have an equal share of the requests for the evaluation of APTE (i.e., about 600 requests per year). In the current study, we assess the results of the lung perfusion scans that were reported using PISAPED criteria done 3 years ago to document the diagnostic accuracy of the method.

METHODS

The study population consists of 147 consecutive patients of a single pulmonologist (MA) hospitalized from March 2014 who had been sent for lung perfusion scan to the department of nuclear medicine of our teaching university hospital. The pulmonologist was piloting the already implemented protocol in the hospital to substitute PISAPED for PLOPED criteria. Patients were injected with 1–3 mCi ^{99m}Tc-MAA (Pars Isotope, Tehran, Iran) containing 250,000–750,000 particles. The injection and imaging were done in a supine position and imaging was done by either ADAC Forte (ADAC Laboratories, Milpitas, CA, USA) or AnyScan (Mediso, Budapest, Hungary) dual-head gamma cameras. The abnormal planar images with suspicious or indeterminate perfusion defects underwent

SPECT imaging. The matrix size of 128 × 128, projection time of 12 s, and 60 stops were employed. The report was done by two nuclear physicians (MA and SF). They accessed the medical files, clinical risk factors, and chest CT or chest X-ray of the patients. The scan was reported as one of the following three categories: (1) normal or negative for APTE, (2) positive for or in favor of APTE, and (3) suggesting certain further procedures including ventilation scan or chest CT or stating that the scan is nondiagnostic. Any single moderate- or large-size wedge-shaped peripheral perfusion defect larger than the findings of chest X-ray or CT scan was considered an evidence of APTE irrespective of the location or multiplicity of the defects. The clinical data of the patients were collected. The presence of S₁Q₃T₃, ST-T changes in precordial leads and right bundle branch block were considered as electrocardiograph findings in favor of PTE.^[10] The presence of right ventricular (RV) enlargement and highly pulmonary pressure were considered signs in favor of PTE in echocardiography.^[11] Wells' score was also calculated; the scores ≥4 were considered highly probable for PTE.^[12] Inherited and acquired risk factors for PTE were also collected, and the number of risk factors was calculated.^[13,14] Patients were followed up, and the final diagnosis about the presence or absence of APTE was made retrospectively by the pulmonologist; she had access to all data including clinical probability, results of the laboratory data, and imaging including scan and CT angiography and the follow-up of the patients. The exact process she employed for the final diagnosis is rather undefinable; however, it can be underscored that improvement of the patients with anticoagulation in the line of positive imaging on one hand and recurrence hence confirmation of the PTE in the follow-up period on the other hand were the main decision anchors and lead points. Furthermore, many of patients who had discordant results of pulmonary perfusion scan with the clinical probability for APTE had CT angiography imaging. When the CT angiography was positive, the scan was considered false negative. In our hospital, this approach is now included in the protocol for the assessment of suspected patients for APTE.^[15] Patients without either recurrence during the follow-up or anticoagulation were considered negative for APTE.

RESULTS

Patients (male: 68, 46.6%) aged 55.9 ± 17.2 were followed up for 6.2 ± 5.3 months (1–48 months). The follow-up was not completed in six patients. Of all, 21 (14.3%) patients were diagnosed to have PTE. The clinical characteristics and findings of patients with respect to their final diagnosis are presented in Table 1. The scans were positive, negative,

and indeterminate in 17 (11.6%), 126 (85.7%), and 4 (2.7%) patients, respectively. The accuracy of the test for the diagnosis of PTE was 87.9%. The diagnostic performance of the perfusion scan is presented in Table 2. The frequency of highly probable cases for PTE according to the Wells' criteria correlated with the final diagnosis [85.7% vs. 35.3% in patients positive and negative for PTE, respectively; Table 1]. The results of echocardiography, as we defined a predictor for PTE, were inversely correlated with the occurrence of PTE [25% in patients positive vs. 45.6% in patients negative for PTE; Table 1]. Four patients out of nine with false-negative results were highly probable for APTE: three of them had multiple lung metastases and a patient had a previous history of PTE. Among other patients with false-negative results, a patient had sleep apnea with acute respiratory distress; a patient had a history of lichen planus with acute dyspnea; and a female patient was receiving oral contraceptive pills with dyspnea. A report was technically wrong in which a positive scan with indicative findings had erroneously been reported negative for APTE.

DISCUSSION

The diagnostic accuracy of lung perfusion scan based on the PISAPED reporting system, without the use of ventilation scan, in the setting of our inpatient suspected PTE cases was about 88%. False-negative results are concerning, and about half of the false-negative reports occurred in patients clinically probable for PTE. We employed PISAPED criteria without ventilation scan which has been superior over the

Table 1: Health characteristics, Wells' score, echography, and electrocardiogram findings of patients with and without pulmonary thromboembolism

	Positive	Negative	Total	Significance
Age (years)	57.5 (18.2)	55.1 (17.1)	55.9 (17.2)	0.575
Follow-up (months)	5.6 (1.2)	6.3 (5.7)	6.2 (5.3)	0.576
Female	14 (66.6)	60 (50)	78 (53.1)	0.110
History of risk factors	12 (57.1)	69 (57.5)	83 (56.5)	0.506
Tachycardia	9 (47.4)	29 (26.4)	42 (31.3)	0.070
High well's score	18 (85.7)	42 (35.3)	64 (43.8)	0.001
Abnormal ECG	6 (37.5)	17 (19.8)	23 (21.7)	0.159
Abnormal echocardiography	4 (25)	36 (45.6)	40 (40.4)	0.048

Data are mean (SD), frequency (%), or median (minimum-maximum). The final diagnosis for 6 patients was not determined. ECG: Electrocardiograph; SD: Standard deviation

Table 2: Diagnostic performance of the perfusion scan

Perfusion scan	Clinical gold standard (APTE)						Accuracy (%)
	Positive	Negative	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	
Positive	12	4	57	93	75	93	88
Negative	9	112					
Indeterminate	0	4					

APTE: Acute pulmonary thromboembolism; PPV: Positive predictive value; NPV: Negative predictive value

old PIOPED and modified PIOPED criteria.^[16] The evidences, opposing the essential theory to detect PTE based on the mismatch perfusion and ventilation, indicate degrees of matched perfusion and ventilation defects occur in PTE patients during the course of disease.^[17]

The radiation dose from the lung perfusion scan with the injection of 1–3 mCi ^{99m}Tc-MAA is below 2 mSv, which is far below the radiation from the chest CT and chest angiographies (personal communication, unpublished data). Many dose reduction protocols for CT angiography are not actually employed in practice. Furthermore, the radiation to the chest and breast of young female patients and its cancer-added risk are concerning. Addition of SPECT imaging does not add into the injected dose, and by obviation of the need for ventilation scan would keep the radiation optimally low. The dose employed in pregnant women is even reduced with a lower number of used particles with preserving the quality of the scan to be diagnostic.^[18] Hence, future studies may focus on the dose reduction in general population assessing the quality of the scan and its diagnostic accuracy.

In the setting of inpatients who have a high prevalence of diabetes and history of frequent use of radiologic contrast agents, lung perfusion scan provides with the advantage that imposes no further burden on the renal system. The lung perfusion scan is quite affordable comparable to the fee for CT angiography in our practice. Disadvantages are among the unavailability during the night hours and the failure to diagnose conditions other than PTE. Albeit, in our setting, most of the patients have had a chest CT which could be used for both evaluation of other pathologies and for comparison with SPECT images.

The subsegmental PTE cannot be detected in the lung perfusion scan using the PISAPED criteria. In PISAPED criteria, at least one moderate-to-large size perfusion defect should be detected which comprises more than 25% of any segment.^[19] Subsegmental occlusions which would result in defects less extended than this cutoff could not be evaluated. This might be a source of the error and the reason for false-negative results. Nevertheless, the clinical importance of subsegmental PTEs is controversial.^[20] Three of false-negative patients were cancer patients. We may consider this fact in the way that

perfusion defects and lung metastases were undifferentiable for the nuclear physician reviewing SPECT and chest CT images. The prevalence of chronic obstructive pulmonary disease (COPD) in inpatient subjects suspected of APTE is high. Nevertheless, just one of false-negative results occurred in an asthmatic patient, whereas many chest X-ray and CT images were abnormal. We do not believe that abnormal chest findings in COPD patients obviate the use of perfusion scan for the diagnosis of PTE.

The clinical probabilities and the Wells' criteria score correlated very strongly with the final diagnosis. The absence of such correlation for the echocardiographic findings could possibly be rooted in the wrong selection we did among the echocardiographic findings for PTE. RV dysfunction and RV shape (i.e., D sign) are possibly more important than the presence of RV dilation and pulmonary hypertension.^[21] Because the clinical risk factors were reviewed interpreting the scan, pretest clinical probability could introduce bias in interpretation of images. However, if the objective is to evaluate the overall scan value, one may add clinical/laboratory data into the test.

CONCLUSION

The accuracy of perfusion-only lung scan was reasonably high using PISAPED criteria in our practice. Considering the cost, low radiation burden, and absence of nephrotoxicity, the lung perfusion scan could be used effectively in inpatient settings.

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Conflicts of interest

There are no conflicts of interest.

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