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ORIGINAL RESEARCH ARTICLE

The comparison of the diagnostic accuracy of lung perfusion scan between patients with and without chronic obstructive pulmonary disease

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ABSTRACT

Introduction: Diagnostic accuracy of lung perfusion scan (LPS) for detection of pulmonary thromboembolism (PTE) is not well defined in patients with chronic obstructive pulmonary disease (COPD). In the current study, we intended to compare the scan performance between patients with and without COPD.

Methods: Study comprised suspected PTE patients who had LPS in two group of patients with and without COPD. Scans were done employing SPECT imaging and interpreted using PISAPED positive/negative criteria considering chest CT comparison. The pulmonologist final decision on the presence or absence of PTE was collected at 3-month follow up visit. This clinical decision was made based on the response to anticoagulation or therapies directed to other diagnoses, and consideration of all imaging and examinations available including calf ultrasonography, echocardiography, CT angiography, and the 3-month delayed LPS. The accuracy of the LPSs between those with and without COPD was compared.

Results: Fifty-two patients without COPD and 49 patients with COPD were included. Out of all, 28 had PTE comprising 11 patients in COPD group (21.2%) and 17 in non-COPD (34.7%). In 3-month follow up, pulmonologist diagnosed 28 patients had PTE which exactly matched the initial report of LPS. The accuracy of the scan was 100% similarly in patients with and without COPD.

Conclusion: The results support the optimal diagnostic performance of LPS for PTE similarly in patients with and without COPD.

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INTRODUCTION

The diagnostic accuracy of lung perfusion scan (LPS) has been shown to be comparable to the performance of CT angiography for the diagnosis of pulmonary thromboembolism (PTE) [1]. In a previous study we documented that the scan accuracy was high at 88% for the detection of acute pulmonary emboli [2]. The previous failures of the diagnostic performance of the lung perfusion scan have been largely addressed by employing the up-to-date prospective investigative study of acute pulmonary embolism diagnosis (PISAPED) criteria and application of SPECT imaging which provided better comparability with the chest CT images [3]. Such application of CT scan is quite feasible in the in-patients setting where many patients have had a chest CT in their initial workups before PTE became a provisional differential diagnosis.

A possible flaw of the LPS could be the perfusion defects due to ventilation abnormalities in patients with COPD which do not correspond to a consolidation, atelectasis, mass, etc in chest CT. There are considerations that LPS is not advocated in patients with COPD due to high false positive results secondary to post-obstructive perfusion abnormalities. There is evidence that the LPS is not accurate in these patients [4]. In the current study, the accuracy of the LPS employing PISAPED criteria and SPECT imaging in patients with and without COPD is compared.

METHODS

Patients of a university hospital in the outpatient pulmonology clinic were included for whom exclusion of PTE was clinically needed and sent for LPS from 21 March 2023 to 22 June 2023. The LPS was done in an outpatients facility (Marian Institute of Nuclear Medicine, Tehran, Iran) employing multiple planar and SPECT settings by a Philips ADAC gamma camera after injection of 1.5-2.5 mCi of [^{99m}Tc]Tc-MAA. During the study period 260 patients had LPS out of which 106 patients including 53 patients with and 53 patients without COPD were recruited. COPD was confirmed based on the data collected from patient records of the patient and based on the pulmonary function tests. COPD was defined by the presence of a post-bronchodilator $FEV_1/FVC < 0.7$ without bronchodilator response [2]. The included patients were those with a definite diagnosis of COPD (i.e. suspicious COPD cases were not included). The patient selection process was registry based and when the target sample size (i.e. 53) reached the enrolment was stopped.

The interpretation of LPSs was done based on PISAPED criteria and a positive/negative approach. In brief, any peripheral moderate size or larger perfusion abnormality at the SPECT which was larger than the CT finding was considered PTE.

The patients were followed for 3 months. A complex clinical gold standard was set to discriminate patients with and without PTE. Above all, PTE was considered confirmed in patients with response to the anticoagulation and exclusion of alternative diagnosis, or response to therapies directed to diagnoses other than PTE. All the diagnostic measures were taken into account for final clinical diagnosis including D-dimer, calf color Doppler, ECG, saturation pressure of O_2 (SPO2), CT angiography, and follow up LPS at 3 months when available. Chronic thromboembolic pulmonary hypertension (CTEPH) was diagnosed based on the overall clinical assessment including follow up LPS and echocardiographic findings.

For analysis, SPSS v29 was used with p-values being significant at 5%. Cross tabulation and chi-square test were used, and receiver operating characteristics (ROC) curve analysis was performed. Logistic regression analysis was done to predict PTE in patients with and without PTE employing the clinical data (i.e. age, pulse rate, blood pressure, BMI, and SPO2).

RESULTS

Out of 106 recruited patients 5 died during the follow up period and finally 101 patients including 52 without and 49 with COPD were enrolled for the analysis. All five deceased patients had advanced malignancy (four in the COPD group and one in the non-COPD group) and none had a positive lung perfusion scan at baseline. Because the final diagnosis of PTE in this study was based on 3-month clinical follow-up, these patients were excluded from the diagnostic performance analysis. Health characteristics of the patients are presented in Table 1. Patients with COPD were older, and had higher pulse rate and lower SPO2 levels (p-value=0.027, 0.013, and 0.024, respectively).

Among 101 LPSs, 73 (72.3%) were reported negative and 28 (27.7%) positive for PTE. The PTE negative report rate was 78.8% (n=41) and 65.3% (n=32), respectively, in non-COPD and COPD participants. The difference was not statistically meaningful. At 3-month follow-up, the pulmonologist diagnosed pulmonary thromboembolism in 28 patients, which showed complete concordance with the initial lung perfusion scan interpretations, resulting in a diagnostic accuracy of 100%. Accordingly, sensitivity, specificity, positive predictive value, and negative predictive value were all 100%, with no false-positive or false-negative cases observed. Consistently, receiver operating characteristic curve analysis demonstrated optimal diagnostic

performance in both COPD and non-COPD subgroups, with an area under the curve (AUC) of 1.0 for each group. Five patients revealed to have CTEPH at 3 months, all of them were in non-COPD group.

In additional analysis using the collected data including age, BMI, pulse rate, and systolic blood pressure, and SPO2, only SPO2 was statistically different between patients with and without PTE (94.3±3.3vs. 96.5± 2.0; p-value = 0.003). In patients with COPD, the SPO2 of patients with PTE was significantly lower than that of COPD patients without PTE (93.6±3.4vs. 96.2±2.0; p-value= 0.002) but the values were similar between those with and without PTE in the non-COPD group (95.4±3.0 vs. 96.7±1.9; p-value= 0.184). Other variables were not different between PTE and non-PTE groups in the overall cohort or within COPD or non-COPD groups. The clinical variables (age, pulse rate, blood pressure, BMI, and SPO2) was capable to predict the presence of PTE in patients with and without COPD at 78% and 77% of cases, respectively.

Table 1. Health characteristics of participant with respect to the history of COPD. Age, pulse rate, and saturation pressure of O2 (SPO2) were statistically different between patients with and without COPD

	Non-COPD n=52	COPD n=49	Total N=101	Significance level
Age (years)	51.6 (15.5)	58.2 (13.8)	54.8 (15)	0.027
BMI (kg/m²)	24.9 (5.1)	25.2 (5.1)	25 (5.1)	0.742
Systolic Blood pressure (mm-Hg)	112.8 (11.8)	113 (15.6)	112.9 (13.7)	0.935
Pulse rate (beat/min)	72.3 (6.8)	76.5 (9.5)	74.3 (8.4)	0.013
SPO2 (%)	96.4 (2.2)	95.3 (2.8)	95.9 (2.6)	0.024

DISCUSSION

The lung perfusion scan with SPECT acquisition and comparison with chest CT in patients suspected of pulmonary thromboembolism demonstrated excellent diagnostic performance irrespective of the presence or absence of a history of COPD. Based on the final composite clinical diagnosis at 3-month follow-up, complete concordance was observed between initial lung perfusion scan findings and clinical outcomes, resulting in uniformly high diagnostic performance indices. While these findings support the clinical reliability of lung perfusion SPECT within an integrated diagnostic pathway, they should be interpreted in the context of the study's sample size and the use of a composite reference standard. In a previous report, we confirmed that the accuracy of LPS was high (i.e. 88%) for the diagnosis of PTE [2]. Interestingly, in contrast to routine clinical practice where false-positive or false-negative lung perfusion scan findings may occur, the present study demonstrated complete concordance between scan interpretations and final clinical diagnoses, with uniformly high diagnostic performance in patients with and without COPD.

There are evidences in the literature that the diagnostic accuracy of LPS may be diminished in patients with COPD due to the perfusion defects reciprocal to the parenchymal and ventilation abnormalities [5]. It is known that 30% of patients with COPD, present with perfusion abnormalities [6]. In the current LPS reporting system (i.e. PISAPED criteria), comparison of the trans-axial perfusion images acquired by SPECT and the anatomic image acquired by chest CT is intended to reduce misinterpretation related to such abnormalities [7]. On this basis, the present study was designed to evaluate whether these methodological advances could mitigate potential diagnostic limitations, and our findings suggest comparable diagnostic performance of LPS in patients with and without COPD within the applied clinical framework, rather than implying absolute equivalence under all conditions.

The higher accuracy in the current study may in part be attributable to the systematic availability of chest CT for comparison, which enhanced the SPECT image interpretations. High accuracy of LPS has been previously well documented mainly when the ventilation study accompanies perfusion scan. In a study on 2328 patients, 99% of patients with PTE had positive perfusion/ ventilation scans [8]. In a recent meta-analysis including 1171 patients, the presence of PTE in patients with normal LPS was 0.3% [9]. Differences between prior studies, including our previous publication [2], and the present work—particularly with respect to study design, reference standards, and imaging protocols—should be taken into account when comparing results. The improved concordance observed compared with our earlier report [2] may also reflect increased interpreter experience. This finding contrasts with the relatively low contemporary utilization of lung perfusion scintigraphy compared with CT pulmonary

angiography in many healthcare systems [10, 11]. Accordingly, these findings should be interpreted with appropriate caution, particularly in light of the relatively limited sample size. The continued lower global utilization of LPS compared with CT angiography likely reflects differences in availability, institutional expertise, and clinical practice patterns, rather than diagnostic performance alone.

SPO2 was lower in patients with COPD and was further reduced in those with concomitant PTE compared with COPD patients without PTE. In contrast, SPO2 levels did not differ significantly between patients with and without PTE in the non-COPD group. This finding further supports the concept that the compensatory increase in ventilation observed in acute PTE may mitigate the development of significant hypoxemia [12]. Oxygen saturation tends to decrease primarily in patients with underlying ventilatory lung disease, such as COPD, where increased dead space ventilation amplifies hypoxemia in the presence of PTE [13].

Logistic regression and ROC curve analyses demonstrated comparable predictive performance of clinical variables for detecting PTE in patients with and without COPD. This is noteworthy given that baseline characteristics such as age, pulse rate, and oxygen saturation differed between the two groups; nevertheless, the discriminatory capacity of these clinical parameters for PTE remained similar. However, this observation should be validated in larger, independent cohorts.

The present study has several limitations that should be acknowledged. First, studies on pulmonary thromboembolism inherently lack a universally accepted, non-invasive gold standard. Conventional pulmonary angiography is invasive and not routinely feasible, and neither lung perfusion scintigraphy nor CT pulmonary angiography alone can be considered a definitive reference standard in all clinical scenarios. Accordingly, consistent with many prior investigations, we relied on a composite clinical reference standard integrating longitudinal clinical assessment, response to therapy, and available imaging findings to determine the final diagnosis of PTE [14]. This approach, while pragmatic and reflective of real-world practice, introduces the possibility of incorporation bias and may have contributed to an overestimation of diagnostic performance. Second, follow-up data were unavailable for five patients who died during the study period, four of whom had COPD. Lastly, although several clinical variables were analyzed, other potentially relevant clinical and laboratory indices were not included and therefore could not be assessed. In addition, the absence of ventilation imaging and hybrid SPECT/CT acquisition represents a methodological limitation. Although complete concordance was observed within the applied diagnostic framework in our cohort, the inclusion of these modalities may increase diagnostic confidence in different clinical environments or practice settings with alternative imaging workflows and therefore warrants further evaluation in future studies.

CONCLUSION

Lung perfusion scintigraphy performed with SPECT acquisition and interpreted in conjunction with comparative chest CT demonstrated high diagnostic performance for the detection of PTE in this cohort. Within the limitations of the present study, the diagnostic performance of LPS appeared comparable in patients with and without COPD.

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