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The Diagnostic Accuracy of V/P Scintigraphy in Pulmonary Embolism and Superiority of V/P SPECT to V/P Planar Scintigraphy

Pulmoner Embolizmde V/P Sintigrafisinin Tanısal Doğruluğu ve V/P SPECT'in V/P Planar Sintigrafiye Üstünlüğü

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The Diagnostic Accuracy of V/P Scintigraphy in Pulmonary Embolism and Superiority of V/P SPECT to V/P Planar Scintigraphy

ABSTRACT

Objective: The aim of this retrospective study is to investigate the diagnostic accuracy of planar V/P scintigraphy and V/P single-photon emission computed tomography (SPECT) in patients who referred to our clinic for V/P scintigraphy with prediagnosis of pulmonary embolism (PE), as well as to investigate the contribution of V/P SPECT technique to planar V/P technique.

Material and Method: The records of 204 patients, who were preliminarily diagnosed with PE within 1 year, were retrospectively reviewed. In our investigation of the diagnostic accuracy of V/P scintigraphy in for PE, we excluded three patients who only underwent perfusion scintigraphy and 20 patients whose final diagnoses could not be confirmed. This left a total of 181 patients included in the statistical analysis. Furthermore, we evaluated the contribution of SPECT to planar imaging in 48 patients, for whom V/P Scintigraphy were reported as positive and whose final diagnoses confirmed PE.

Results: The sensitivity, specificity, negative predictive value, positive predictive value, and accuracy rate of V/P SPECT were calculated as 98%, 94.7%, 99.2%, 87.3%, and 95.6%, respectively. For planar scintigraphy, they were found to be 71.4%, 95.4%, 90%, 85.3%, and 88.9%, respectively. In SPECT, 13 (27.1%) patients who were not compatible with pulmonary embolism (PE) on planar imaging were found to have findings consistent with PE. In nine patients (18.8%), additional defects not observed on planar imaging were identified. Although the goodness of fit with the final diagnosis of both methods was statistically significant, SPECT (95.6%) performed better than planar (88.9%) imaging.

Conclusion: Consistent with previous studies, it was found that while both imaging methods were successful, SPECT demonstrated higher diagnostic accuracy than planar scintigraphy in diagnosing PE. Therefore, it can be hypothesized that V/P scintigraphy can be safely deemed the first-choice in the diagnosis of PE.

Keywords: Pulmonary Embolism, V-P Scintigraphy, SPECT.

ÖZET

Amaç: Bu çalışmada pulmoner embolizm (PE) tanısında, ventilasyon/perfüzyon (V/P) planar sintigrafinin ve tek foton emisyonlu bilgisayarlı tomografi (SPECT)'nin tanısal doğruluğunu ve SPECT'in planar görüntülemeye katkısını araştırmak amaçlandı.

Gereç ve Yöntem: 1 yıl boyunca Pulmoner Embolizm (PE) ön tanısı ile başvuran 204 hastanın kayıtları retrospektif olarak incelendi. Pulmoner embolizmde V/P sintigrafinin tanısal doğruluğu araştırılırken, sadece perfüzyon sintigrafisi yapılan 3 hasta ve son tanısına ulaşılamayan 20 hasta dışlandı ve toplam 181 hasta istatistiksel analiz çalışmasına dahil edildi. SPECT'in planar görüntülemeye katkısı, V/P SPECT' in PE ile uyumlu olarak raporlandığı ve son tanısı PE olan 48 hasta değerlendirilerek yapıldı.

Bulgular: 181 hasta göz önüne alındığında; V/P SPECT'in sensitivitesi %98 (48/49), özgüllüğü %94,7 (125/132), negatif öngörü değeri %99,2, pozitif öngörü değeri %87,3 ve doğruluk oranı %95,6 olarak hesaplandı. Planar sintigrafi için sırasıyla 71.4%, 95.4%, 90% (126/140), 85.3 % (35/41) ve 88.9% olarak hesaplandı. SPECT görüntüleme, planar V/P sintigrafi ile PE tanısı konulamayan 13 hastada (%27,1) PE ile uyumlu sonuçların raporlanmasını sağladı. V/P SPECT ile 9 hastada takip sintigrafisinde önemli olabilecek ek lezyonlar (%18,8) tespit edildi. Her iki yöntemin kesin tanı ile uyumunun istatistiksel olarak anlamlı olduğu gözlemlendi, ancak SPECT bulgularının kesin tanı ile uyumunun (%95.6) planar bulguların kesin tanı ile uyumundan (%88.9) daha iyi olduğu görüldü.

Sonuç: Önceki çalışmalarla benzer şekilde, V/P sintigrafide her iki görüntüleme yöntemi de başarılı olmasına rağmen, SPECT'in planar görüntülemeye önemli ölçüde katkıda bulunduğu ve SPECT'in PE tanısında yüksek hassasiyet, özgüllük ve doğruluk sağladığı bulundu.

Anahtar Sözcükler: Pulmoner Emboli, V/P Planar Sintigrafi, SPECT.

Introduction

Pulmonary embolism (PE) is a prevalent obstructive vascular disease with an annual incidence of approximately 39–115 per 100,000. Due to the high mortality rate in untreated cases, immediate diagnosis and treatment are crucial (1,2,3). Thus, it is essential to rapidly and accurately diagnose PE to plan treatment successfully. Lung ventilation/perfusion (V/P) scintigraphy is a non-invasive, fast diagnostic procedure with low radiation exposure, making it one of the preferred methods for diagnosing PE. This process is based on identifying areas with impaired pulmonary blood supply but preserved alveolar ventilation (mismatch defects) (4).

Combined V/P scintigraphy enhances the diagnostic specificity of PE and can provide further information on alternate diagnoses such as pneumonia, chronic obstructive pulmonary disease (COPD), and heart failure. In selected cases such as pregnant patients and suspected instances of massive embolism, it is possible to use only perfusion scintigraphy (5). Moreover, studies have indicated that both V/P planar imaging, and V/P single-photon emission computed tomography (SPECT) are highly effective for diagnosing chronic thromboembolic pulmonary hypertension (CTEPH). Additionally, perfusion SPECT in conjunction with low-dose computed tomography (CT) is a reliable alternative method for those patients for whom ventilation imaging is unsuitable (6). During the COVID-19 pandemic, using only perfusion scintigraphy without ventilation is more suitable as ventilation scintigraphy might escalate the risk of infection spread through aerosol leakage. Lung X-ray imaging or SPECT/CT is preferable to evaluate lung parenchyma in cases where ventilation scintigraphy may not be performed (7,8).

SPECT is a scanning method utilized in nuclear medicine. Images are acquired by rotating the gamma camera 360 degrees around the patient, producing three-dimensional data. The preparation of the patient, along with the injection and inhalation of radiopharmaceuticals, mirrors the procedures used in planar imaging. SPECT is a readily applicable technique aimed at enhancing diagnostic accuracy in planar V/P without necessitating an additional radiopharmaceutical injection. Studies affirm its superior positive and negative predictive value, as well as its objectivity in assessing PE (9). Occasionally, SPECT may be fused with low-dose CT to perform the hybrid imaging technique, SPECT/CT (10).

The objective of this retrospective study was to evaluate the diagnostic accuracy of planar V/P scintigraphy and V/P SPECT in patients referred to out clinic for V/P scintigraphy with suspected PE. Additionally, we aimed to analyze the added diagnostic value provided by the V/P SPECT technique compared to the planar V/P technique.

Material and Method

This retrospective study received approval from the Education Planning and Coordination Committee of Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital (No: 2014/360, Date: 11.09.2014), and the need for informed consent was thus waived.

Two hundred and four patients suspected of having PE, who were referred to our clinic for V/P scintigraphy over 1 year (2014-2015), were considered for the current study. A retrospective review of their records was conducted. Three patients who underwent only perfusion scintigraphy and another 20 patients for whom final diagnostic information was unavailable, were excluded from the study. Consequently, a total of 181 patients were included in the statistical evaluation.

V/P Scintigraphy: Perfusion imaging was carried out following the intravenous injection of 100–120 MBq Technetium-99m macroaggregated albumin (99mTc-MAA) while the patient was under the camera in a supine position. The average particle number applied was between 300,000–500,000 in patients with normal Pulmonary Artery Pressure (PAP). However, in 23 patients with increased PAP, the particle number was halved. Ventilation Scintigraphy utilized Technegas, with ultrafine aerosol prepared using specialized heating devices (Cyclomedia tecnegasplus, Australia). The system's ventilation set was used for inhaling a radiotracer, established by positioning double 550 MBq technetium in carbon graphite. V/P imaging was completed using general-purpose low-energy parallel hole collimators. Imaging was conducted after 3–5 cycles of respiration, without delay.

V/P imaging was performed using general-

purpose low-energy parallel hole collimators and double-headed gamma detector cameras (Siemens E-cam, Germany). The planar imaging utilized a 256 × 256 matrix with a 360-degree rotation angle, taking eight views from four projections: anterior-posterior, right anterior oblique-left posterior oblique, right lateral-left lateral, right posterior oblique-left anterior oblique. Each projection captured 500,000 counts. The SPECT study was conducted with a 64 × 64 matrix and a 360-degree rotation angle in 32 steps (one step every 10s in ventilation scintigraphy and one step every 5s in perfusion scintigraphy). Images were reconstructed using the back-projection technique. A 'Butterworth filter' was employed for filtering the images, which were then evaluated after processing in workstations (Xeleris-GE).

In patients who underwent the 1-day protocol, ventilation scintigraphy was performed first, followed by perfusion scintigraphy without changing the patient's position. For the 2-day protocol, perfusion scintigraphy was carried out on the first day, and ventilation scintigraphy was performed on the following day. There are no specific selection criteria for either the 1-day or 2-day protocols. The 1-day protocol requires a longer scanning time, so it was preferred when the patient's general condition was stable. For both protocols, planar imaging was conducted first, followed by SPECT imaging.

V/P Planar and V/P SPECT images were assessed as either positive or negative for the presence of PE, and non-diagnostic, in line with the main criteria recommended by the European Association of Nuclear Medicine (EANM) guidelines. The report was based on findings from the V/P SPECT (5).

Images exhibiting at least one segmentary or two subsegmentary mismatch defects on V/P scintigraphy were classified as being consistent with PE. A normal perfusion pattern, matched or reverse mismatch defects of any number and size, and mismatch defects that failed to align with the lobar-segmentary or subsegmentary pattern were documented as incompatible with PE. A variety of V/P anomalies that were not specific to any disease were reported as non-diagnostic or suspicious findings.

Therefore, like previous studies, we based our final diagnosis on clinical and laboratory findings, imaging results, treatment, and follow-up re-evaluation. Follow-ups were conducted 6–12 months post-diagnosis, using findings procured from the hospital database (clinical, laboratory, control V/P scintigraphy, and CT pulmonary angiography).

Statistical Analysis

The data gathered from V/P planar scintigraphy and SPECT findings were statistically analyzed for the detection of PE. The "Cochran's Q test" was used to determine if there was a correspondence between the diagnoses, while the significance of the distribution of the methods according to the categories of presence or absence of embolism was tested with the "pairwise comparisons" approach, and the final diagnosis. The compatibility of SPECT and planar methods with the final diagnosis was analyzed using the "chi-square" goodness of fit test. *p-values <0.01* were considered significant. The sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy of both planar scintigraphy and SPECT were calculated. The contribution of SPECT to planar imaging was analyzed for the true positive patients (n = 48), these patients had positive V/P scintigraphy results and were diagnosed with PE.

Results

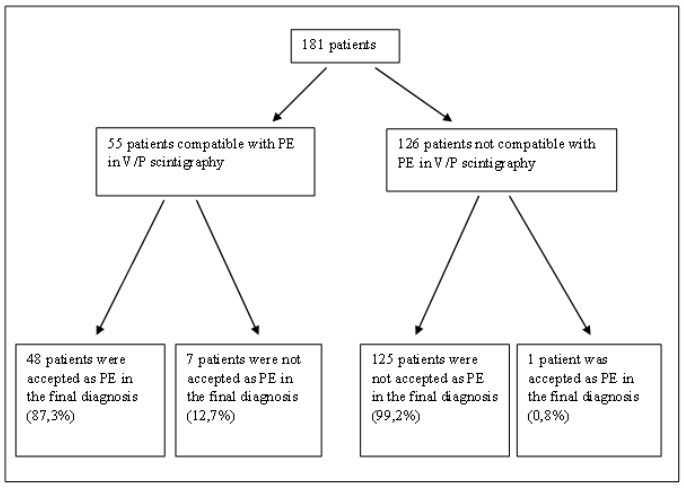
In the study, 181 patients were included, of which 130 were women and 51 were men, with a mean age of 60 ± 15.2 (age range: 19–88). The patients' reasons for seeking out a clinician, in order of frequency, were chest-back pain, shortness of breath, and more infrequently, a cough, palpitations, presyncope, and occasionally, a combination of these symptoms. The risk factors for PE in patients are shown in Table I. Analyses were conducted with the 181 patients for whom final diagnosis information was available (Figure l).

Findings suggestive of PE were detected in 43 patients via planar scintigraphy and in 59 patients via SPECT, whereas 158 patients were not accepted as having PE based on planar scintigraphy (with no defects, single sub-segmentary defects, or match/reverse mismatch defects), and 142 patients were excluded in the case of SPECT.

In 181 patients, SPECT imaging identified positive scintigraphic findings compatible with PE in 13

patients (27.1%) that were not detected by planar V/P scintigraphy alone. Furthermore, V/P SPECT allowed for clearer differentiation between suspicious defects in 8 patients (16.7%), and it revealed additional defects in 9 patients (18.8%) (Figure II).

Figure I. Final Diagnosis of the Patients According to the Results Obtained by Evaluating V/P Scintigraphy, PE: pulmonary embolism, V/P: ventilation/perfusion



According to the results from the Chi-square goodness of fit test, the correspondence between SPECT and the final diagnoses was 95.6% [(125 + 48) / 181], a significantly notable finding (χ2: 145.032; *p<0.01*). Similarly, the agreement between planar imaging and the final diagnoses was 88.9% [(126 + 35) / 181], and this result was also significant (χ2: 91.237; *p <0.01*). Although both methods' goodness of fit with the final diagnosis was statistically evident, the SPECT findings' concurrence with the final diagnosis (95.6%) was substantially higher than the final diagnosis concurrence with planar findings (88.9%) (*p=0.001*; Table I)

Table I. The Frequencies of Patients' Risk Factors for PE

Risk Factor	Incidence (n:181)
Deep vein thrombosis	12 (6.6%)
Previous pulmonary embolism	6 (3.3%)
Malignancy	39 (21.5%)
Chemotherapy/Radiotherapy	19 (10.5%)
Obesity	77 (42.5%)
Recent operation/immobilization	4 (2.2%)

Post-treatment control V/P scintigraphy was administered to 8 out of 48 patients being treated for embolism, and pulmonary CT angiography was administered to 4 patients. Of the 8 who underwent post-treatment V/P scintigraphy, 5 showed complete disappearance of the defects that were observed at the time of diagnosis, while in 2 patients, some defects regressed and others disappeared. There were new defects observed in 1 patient. Among the patients who underwent post-treatment CT angiography, no significant thrombus was observed in 3 patients, yet findings suggestive of a thrombus were still detected in 1 patient.

Table II. Comparison of V/P Planar and SPECT Results with Final Diagnosis

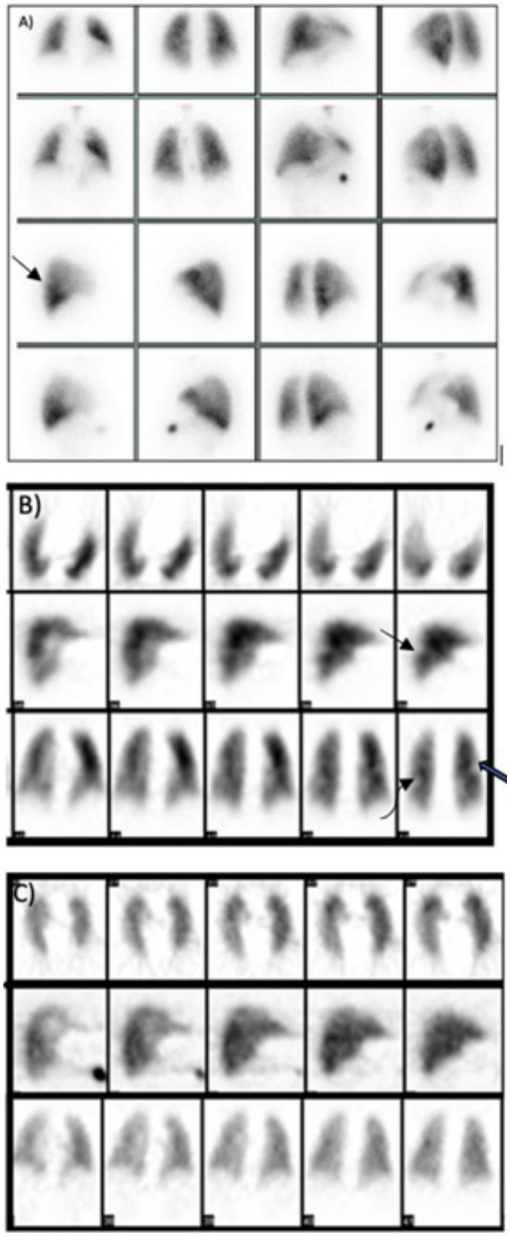
		Final Diagnosis (n:181)		
		Accepted as PE	Not accepted as PE	*p value*
Planar	With PE	35 (71.4%)	6 (4.5%)	*<0.01*
	Not with PE	14 (28.6%)	126 (95.5%)	
SPECT	With PE	48 (97.9%)	7 (5.3%)	*<0.01*
	Not with PE	1 (2.1%)	125 (94.7%)	

PE: pulmonary embolism, With PE: compatible with PE, Not with PE: not compatible with PE

During the follow-up, conducted 6–12 months post-treatment, clinical examination, imaging, and laboratory tests (CT angiography, V/P scintigraphy, D-dimer) indicated that symptoms had disappeared in 38 patients. Complaints were reduced in 6 patients, continued in 1 patient, and 3 patients died due to malignant-metastatic disease.

At the time of diagnosis, Pulmonary CT angiography was performed on 4 out of 7 patients who were considered to be deemed positive for PE in V/P SPECT (considered as false positive) but were not ultimately diagnosed with PE. In the Pulmonary CT angiography, the distal branches could not be evaluated in 3 patients, and the study was reported as suboptimal for 1 patient. In the follow-up examination, it was observed that the complaints of 5 patients persisted, while the complaints of 2 patients ceased. In 1 patient (considered a false negative), whose V/P scintigraphy was reported to be negative for PE, the final diagnosis indicated the presence of PE due to compelling clinical suspicion, taking into account the patient's age, symptoms, and existing malignancy. The treatment for PE was initiated and it was observed that the patient's complaints disappeared during follow-up.

Figure II. A 68-year-old female patient, followed up for breast cancer, presented to the chest diseases outpatient clinic with complaints of shortness of breath that started 1 day ago.
A) On the V/P planar images (The lines from top to bottom are as follows: sections of coronal perfusion, coronal ventilation, sagittal perfusion, sagittal ventilation), a subsegmental defect in the superior segment of the right lower lobe was observed, although unclearly (arrow). B) In the SPECT perfusion scan, perfusion defects were observed in the superior (arrow) and posterobasal segments (curved arrow) of the right lower lobe, as well as in the superior segment of the left lower lobe (thick arrow). C) In SPECT ventilation scan, ventilation was preserved in areas with perfusion defects (mismatch defects). These mismatch defects were reported as consistent with pulmonary embolism (PE). In the follow-up visit of the patient at 6 months after the initiation of treatment, it was found that her symptoms (the symptoms that lead to suspicion of pulmonary embolism) had disappeared.



Considering the patients for whom we could access the final diagnosis (n = 181); the sensitivity of V/P SPECT was calculated to be 98% (48/49), the specificity 94.7% (125/132), the NPV 99.2%, the PPV 87.3%, and the accuracy was 95.6%.

The sensitivity for planar scintigraphy was found to be 71.4% (35/49), specificity 95.4% (126/132), NPV 90% (126/140), PPV 85.3% (35/41), and accuracy 88.9%.

Discussion

Acute PE is a severe clinical presentation with a high mortality rate in untreated cases (1). Whereas the mortality rate for PE is approximately 25–30% without treatment, it can be reduced to 2–8% with proper and timely treatment. Pulmonary ventilation/perfusion (V/P) scintigraphy is frequently employed in diagnosing PE because of its non-invasive nature, ease of use, affordability, low radiation dosage, and high sensitivity (2).

This study demonstrated that V/P SPECT is highly reliable for the diagnosis of pulmonary embolism (PE), even without the inclusion of low-dose CT, providing evidence that V/P SPECT offers comparable diagnostic performance to SPECT/CT in detecting PE. Our findings highlight the utility of V/P SPECT as an effective and non-invasive imaging modality for PE diagnosis, aligning with previous studies that support its high sensitivity and specificity.

In a study published by Bajc et al. in 2008, 2328 patients who underwent V/P SPECT due to suspected PE were evaluated holistically. This approach, like our study, concluded that V/P SPECT had both a high negative and PPV (11).

Gutte et al. conducted a prospective study in 2010, comparing V/P planar and SPECT/CT imaging with 41 patients. The study reported that the sensitivity of V/P planar scintigraphy was 64%, with a specificity of 72%. Sensitivity for V/P SPECT/CT amounted to 100%, and specificity was 87%. Furthermore, V/P SPECT/CT demonstrated superior diagnostic accuracy, sensitivity, and specificity compared to Multidetector CT (MDCT) (12). The likelihood of a PE event following a negative MDCT of the pulmonary arteries is 1.5%, whereas the possibility of PE in follow-up after a negative V/P SPECT is at 0.4%

(13). Generally, MDCT is seen as a more efficient method for detecting larger and medium-sized emboli, while V/P SPECT might be more beneficial for lower-risk situations and smaller emboli (9). Although untreated subsegmental thrombi might not cause severe clinical issues, they can recur and give rise to chronic PE and pulmonary hypertension (14). Some studies suggest that a new generation of MDCT angiography, offering better spatial and temporal resolution, may be more sensitive than previous iterations in detecting subsegmental thrombi (14). Approximately 10–30% of patients cannot undergo CT angiography due to kidney diseases or contrast allergy. Moreover, V/P SPECT and V/P SPECT/CT expose patients to lower radiation doses in comparison to CT pulmonary angiography (14). According to the National Institute for Health and Care Excellence (NICE) guidelines, V/P scintigraphy was used as the first-choice in patients with a contrast allergy, renal insufficiency, and high radiation risk (15). For cases involving contrast allergy, pregnancy, and renal insufficiency – which are also mentioned in current guidelines – this imaging modality should be considered as the first-choice method.

In a retrospective study conducted by Gutte et al. and published in 2009, V/P SPECT/CT and MDCT were compared (9). Based on this study's results, Gutte et al. proposed that V/P SPECT, when combined with low-dose CT, could offer excellent diagnostic performance and thus be the first method of choice in the diagnosis of PE.

In our study, the sensitivity and specificity of V/P SPECT, even without low-dose CT, were as high as those reported in the SPECT/CT results of Gutte et al.'s study (9). The differences observed between the studies might be attributed to variations in study designs, the technical methods of scintigraphy used, and observer experiences.

In the 2019 EANM guidelines, V/P SPECT was considered the first-choice method for PE diagnosis, if available/applicable (10). An important advantage of V/P SPECT over planar imaging is the reduction of non-diagnostic/indeterminate results. In the study by Leblanc et al., 18 (3%) out of 584 patients, Bajc et al. reported 19 (1%) out of 2328 patients, and Lemb et al. reported 5 (0.5%) out of 991 patients as non-diagnostic when using V/P SPECT (10,16,17). A study conducted by Reinartz et al. in 2004 compared the V/P planar, SPECT imaging, and multi-spiral CT methods. They found that SPECT had the highest sensitivity, whereas CT had the highest specificity. The numbers of accurate diagnoses in the study population (n=83) were 67, 78, and 77 for the V/P planar, V/P SPECT, and CT methods, respectively. The study concluded that SPECT could replace the planar method (18). We found that SPECT is highly reliable for PE diagnosis, despite the absence of the CT component. However, the CT component would provide significant additional information regarding parenchymal pathologies, particularly in situations where ventilation scintigraphy is not preferred, like during the COVID-19 pandemic. A systematic review of perfusion-ventilation scans in COVID-19 patients concluded that SPECT/CT and perfusion scintigraphy combination could aid in mitigating diagnostic challenges associated with COVID-19 (19). The increased incidence of thromboembolic events and suspected pulmonary embolism during the COVID-19 pandemic has highlighted the valuable contribution of Perfusion SPECT-CT in the investigation of PE (20).

Our study has several limitations. First, this study is a retrospective study conducted at a single center. Another limitation is that not all patients could undergo pulmonary angiography, the gold standard test in diagnosing PE, due to its invasive nature and unfeasibility at times. Furthermore, not all patients received V/P scans during follow-up to assess treatment efficacy.

Conclusion

Both V/P planar scintigraphy and SPECT imaging were effective in diagnosing PE. However, SPECT provided greater diagnostic value than planar scintigraphy. Due to its low radiation exposure, suitability for use in pregnant women, low rate of non-diagnostic results, and high diagnostic performance, V/P scintigraphy combined with SPECT imaging should be an indispensable part of clinical practice.

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