The Utility of Hybrid SPECT/CT Lung Perfusion Scintigraphy in Pulmonary Embolism Diagnosis

Andrzej Mazurek Mirosław Dziuk Ewa Witkowska-Patena Stanisław Piszczek
Agnieszka Gizewska

Department of Nuclear Medicine, Military Institute of Medicine, Warsaw, Poland

Key Words

Single-photon emission computed tomography/
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Lung perfusion scintigraphy

Abstract

Background: Pulmonary embolism (PE) is diagnosed either by ventilation/perfusion (V/Q) scintigraphy or pulmonary CT angiography. One of the imaging methods used in nuclear medicine is hybrid SPECT/CT scintigraphy. **Objectives:** The aim of this study was to evaluate the utility of SPECT/CT(Q) scintigraphy in the diagnosis of PE and to compare SPECT/CT(Q) with planar(Q) and SPECT(Q) methods. **Methods:** The study group consisted of 109 consecutive patients suspected of having PE referred for performing lung scintigraphy. The inclusion criteria were: performance of perfusion planar, SPECT and SPECT/CT scans; availability of clinical data covering a 6-month follow-up period, and D-dimer level testing. The number of eligible patients was 84. PE was reported in patients with at least 1 segmental or 2 subsegmental perfusion defects without parenchymal abnormalities on CT scans. PE was excluded when there was a normal perfusion pattern or perfusion defects were caused by lung parenchymal abnormalities or were not arranged in accordance with

the pulmonary vasculature. **Results:** Twenty-six patients (31%) had a final diagnosis of PE. The sensitivity and specificity values of each method were as follows: planar(Q) 73 and 43%, SPECT(Q) 88 and 47% and SPECT/CT(Q) 100 and 83%. SPECT/CT(Q) yielded a significantly higher diagnostic accuracy than planar(Q) ($p < 0.001$) and SPECT(Q) ($p < 0.001$) scans. **Conclusions:** We conclude that hybrid SPECT/CT(Q) imaging has a high diagnostic efficacy in the diagnosis of PE. Lung perfusion scintigraphy performed with a hybrid SPECT/CT device has a significantly higher sensitivity and specificity than scanning performed with the planar or SPECT technique.

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Introduction

Pulmonary embolism (PE) is a frequent cause of death [1]. In autopsy studies in the population of Malmö in Sweden, PE was found in 18% of the deceased and was established to be the primary cause of death in 13% of the postmortem subjects [1]. The prevalence rate of PE is estimated at 95/100,000 individuals/year [2].

The diagnosis of PE is made on the basis of clinical presentation, D-dimer test results and imaging studies

such as multidetector CT (MDCT) and ventilation/perfusion (V/Q) scintigraphy. Radionuclide imaging has so far involved only planar and single-photon emission CT (SPECT) techniques. Although both modalities provide data on radioisotope distribution, they do not give any anatomical detail. Moreover, to confirm or rule out the diagnosis of PE, perfusion and ventilation studies are required [3].

The introduction of SPECT/CT allows correlation of the functional data from SPECT with the anatomical data from CT. However, there are only few studies concerning the utility of SPECT/CT in the diagnosis of PE, and we still lack official recommendations of scientific societies regarding this method. At our institute, we have performed both perfusion and ventilation SPECT/CT scanning for several years. According to previous publications and our experience, CT may potentially serve as a substitute for ventilation scintigraphy [4, 5]. Therefore, the main aim of this study was to evaluate the utility of SPECT/CT(Q) in the diagnosis of PE. The additional objectives were to compare the diagnostic performance of planar(Q), SPECT(Q) and SPECT/CT(Q) methods. In our study group, ventilation scintigraphy was only performed in 20% of the patients, so the results are not discussed due to their insufficient statistical power.

Materials and Methods

The study group consisted of 109 consecutive patients suspected of having PE. Patients were referred to the Department of Nuclear Medicine, Military Institute of Medicine, Warsaw, Poland, in 2010–2011 for lung scintigraphy. The study was approved by the Bioethics Commission of the Military Institute of Medicine (resolution No. 20/WIM/2012 of June 20, 2012) and all subjects signed a written informed consent form. All procedures performed in the studies involving human participants were in accordance with the ethics standards of the institutional and/or national research committee as well as with the 1964 Helsinki Declaration and its later amendments or comparable ethics standards.

The inclusion criteria were a perfusion scintigraphy performed using the three methods of planar scintigraphy, SPECT and SPECT/CT and the availability of observational data 6 months after the perfusion studies. A total of 84 out of 109 patients were included for further analysis. Patients for whom all three scintigraphy images (planar, SPECT and SPECT/CT) of the lungs could not be recorded due to increased dyspnea ($n = 8$) or absence of observational data 6 months after the examination ($n = 17$) were excluded from the study. There were no differences regarding dyspnea, Geneva scale score and age between the excluded patients and the study group.

Pulmonary perfusion assessment was performed using albumin macroaggregates labeled with radioactive technetium (^{99m}Tc -MAA Makro-Albumon[®]; Medi-Radiopharma Ltd., Hungary) in-

jected intravenously at a dose of 185 MBq (5 mCi) in the horizontal position. The imaging procedure was commenced immediately after administration of the radiotracer. Images were acquired with the SPECT/CT hybrid dual-head gamma camera Infinia VC Hawkeye 4 (GE Healthcare).

The planar scans were obtained in 8 projections: anterior, posterior, left lateral, right lateral, right anterior oblique, right posterior oblique, left anterior oblique and left posterior oblique. The planar scans were performed with a low-energy high-resolution collimator and acquired with a 128×128 matrix size (zoom 1.0). The time per projection was 200 s.

The SPECT scans were obtained with a low-energy high-resolution collimator with a 128×128 matrix size. The 10% photopeak window was centered at 140 keV. Sixty projections were collected at 6-degree increments over 360° (180° per camera head). The time per projection was 15 s. The iterative reconstruction parameters were as follows: reconstruction type: ordered-subset expectation maximization (OSEM); number of OSEM iterations: 2; maximal number of OSEM subsets: 10; prefilter type: Hann (cutoff frequency 0.9–0); 3D postfilter: Hann (cutoff frequency 0.9–10.0), and scatter correction: off.

The CT scan parameters were as follows: scan type: axial scanning; slice thickness: 5 mm; tube voltage: 140 kV; tube current: 2.5 mA; gantry rotation: 2.6/min; matrix: 512×512 pixels; average CDTI(vol): 3.47 mGy, and average DLP: 139 mGy cm. All planar, SPECT and CT acquisitions were obtained without modification of the patient's body position.

The collective effective dose received during SPECT/CT(Q) was 2.9 mSv: 0.9 mSv for CT and 2 mSv for the administered radiotracer [6, 7].

Analysis of Radionuclide Images

All the images, both the planar and the SPECT/CT ones, were interpreted with the use of Xeleris 1 and 2 Functional Imaging Workstations (GE Healthcare). Scintigrams were analyzed by 2 nuclear medicine specialists (with 5 and >30 years of experience).

Based on the overall assessment of the SPECT/CT results, the following scintigraphic criteria for the diagnosis of PE were adopted: at least 1 segmental or 2 subsegmental perfusion defects (wedge shaped, base directed at the pleura) without abnormalities in the lung parenchyma (as visualized on CT) (fig. 1a, b). The following scintigraphic criteria were established for excluding PE: normal perfusion pattern (fig. 2); perfusion defects that were not arranged in accordance with the pulmonary vasculature (fig. 3), and perfusion defects caused by abnormalities in the lung parenchyma (as visualized on CT) (fig. 1c, d).

Reference Test

To estimate the sensitivity and specificity of each imaging method, a composite reference standard was used. The final diagnosis of PE was made by side-by-side consensus based on all available data: clinical presentation (dyspnea, chest pain, hemoptysis, syncope, jugular vein distention and deep vein thrombosis symptoms), laboratory test results (arterial blood gas analysis, troponin and NT-proBNP levels), other imaging test results (chest X-ray, echocardiography and lower-extremity ultrasound) and follow-up data. PE was ruled out in patients who did not receive anticoagulant treatment and did not have clinical signs of PE within 6 months from the lung scintigraphy. The reference test used in this study was similar to the test used by other authors [8–10].

Fig. 1. **a, c** Lung SPECT/CT(Q) images. **b, d** Low-dose CT images; pulmonary window; coronal slices. **a, b** PE present: wedge-shaped perfusion defects (yellow arrows) without parenchymal abnormalities. **c, d** PE absent: lobar perfusion defect in the right lung caused by emphysema (yellow stars); pulmonary fibrosis is also revealed in the remaining parenchyma.

Fig. 2. **a** Lung SPECT/CT(Q) image. **b** Low-dose CT image; pulmonary window; coronal slice. PE absent: normal perfusion pattern (**a**) without lung parenchymal abnormalities (**b**).

Fig. 3. Lung SPECT/CT(Q) images. **a** Axial slice. **b** Sagittal slice. PE absent: the perfusion defect of the right lung (yellow arrows) is not arranged according to the pulmonary vasculature territory. There is a pleural effusion in the right lung (yellow stars).

Table 1. Comparison of patients with and those without PE

	PE+ (n = 26)	PE- (n = 58)	P
Age, years	68±14.3	69±13.2	0.646
PE probability ¹			0.015
Low	1 (4)	17 (29)	
Moderate	23 (88)	39 (67)	
High	2 (8)	2 (4)	
D-dimer level, µg/dl	2.00±2.9	2.58±7.0	0.118
Sex			0.376
Female	13 (50)	35 (60)	
Male	13 (50)	23 (40)	
PE probability ¹ women (n = 48)			0.249
Low	1 (8)	10 (29)	
Moderate	11 (84)	24 (68)	
High	1 (8)	1 (3)	
PE probability ¹ men (n = 36)			0.048
Low	0 (0)	7 (31)	
Moderate	12 (93)	15 (65)	
High	1 (7)	1 (4)	

Values are means ± SD or n (%). ¹ Low, moderate or high clinical probability of PE in accordance with the Geneva score.

Statistical Analysis

Diagnostic performance was assessed by sensitivity, specificity, positive and negative predictive values and accuracy. Ninety-five-percent confidence intervals were calculated. p values of <0.05 were considered significant. As a normality test, the Kolmogorov-Smirnov test was used. Patient characteristics were compared between the PE and non-PE groups using Fisher's exact test. The Mann-Whitney U test was used to compare D-dimer levels (non-normal distribution). In order to compare the effectiveness of the diagnostic imaging methods, a χ^2 test was used. The calculations were performed using the STATISTICA 10 suite (StatSoft, Poland).

Results

Study Group Description

The study group included 84 patients (48 female, 36 male). PE was confirmed in 31% (n = 26) and ruled out in 69% of the patients (n = 58) based on the reference test. For most patients included in the study group, i.e. 73.8% (n = 62), a moderate clinical probability of PE was established in accordance with the Geneva score [11] (table 1).

A high clinical probability was established for 4 patients (4.8%) and a low clinical probability for 18 patients (21.4%). Twenty-six patients (31%) in the study group had COPD. Heart failure in the study group was observed

in 46.4% of the cases (n = 39). All the patients (n = 84) underwent pulmonary perfusion scanning by planar, SPECT and SPECT/CT imaging.

Assessment of Diagnostic Efficacy Parameters

The accuracy of the diagnosis of PE based on pulmonary perfusion images acquired by the planar, SPECT and SPECT/CT methods was evaluated by comparison with the reference test (table 2). The planar(Q) scans had a sensitivity of 73% and a specificity of 43%. The SPECT(Q) scans had a sensitivity of 88% and a specificity of 47%. When CT was added [SPECT/CT(Q)], the sensitivity was 100% and the specificity increased to 83%.

A total of 33 false-positive and 7 false-negative results were obtained based on planar(Q) images. Based on SPECT(Q) images, 31 false-positive and 3 false-negative results were obtained. After combining SPECT and CT [SPECT/CT(Q)], the number of false-positive results was reduced to 10 (from 31) and that of false-negative results to 0 (from 3) (table 3).

To check if the specific imaging methods were statistically different in terms of their accuracy of PE assessment, a series of χ^2 tests was performed (table 4). The analyses showed that statistically the SPECT(Q) and planar(Q) methods are less effective in predicting PE than the SPECT/CT(Q) method. There were no statistically significant differences in the accuracy of PE assessment between the SPECT(Q) and the planar(Q) method.

Discussion

Radionuclide diagnostics of PE presents the following two difficulties: (1) detection of perfusion defects and (2) determination of the etiology of perfusion defects (embolic vs. nonembolic). The following assumptions have been made in this study: the SPECT method helps to detect pulmonary perfusion defects, and the anatomical parameters obtained from low-dose CT scans allow differentiating perfusion defects (embolic vs. nonembolic) (fig. 1–3).

Based on the analysis (table 2), the diagnostic efficacy of the imaging methods of planar(Q), SPECT(Q) and SPECT/CT(Q) in PE diagnosis was established compared with the reference test. Planar(Q) scans detect PE with 73% sensitivity and 43% specificity. SPECT(Q) scans allow diagnosing PE with a sensitivity and specificity of 88 and 47%, respectively. If SPECT is combined with CT [SPECT/CT(Q)], the sensitivity increases to 100% and the specificity to 83%. SPECT(Q) and planar(Q) scans are

Table 2. Summary of the diagnostic efficacy of the imaging methods in PE diagnostics

Imaging method	Sensitivity	Specificity	Accuracy	PPV	NPV
Planar(Q)	73 (55–87)	43 (35–49)	52 (41–61)	36 (28–43)	78 (64–89)
SPECT(Q)	88 (72–97)	47 (39–50)	59 (49–65)	43 (35–47)	90 (76–97)
SPECT/CT(Q)	100 (86–100)	83 (77–83)	88 (80–88)	72 (62–72)	100 (93–100)

Values are percentages (95% confidence intervals). PPV = Positive predictive value; NPV = negative predictive value.

Table 3. False-positive and false-negative results of the specific imaging methods

Results	Imaging methods		
	Planar(Q)	SPECT(Q)	SPECT/CT(Q)
False positive	33	31	10
False negative	7	3	0

Table 4. Statistical comparison of the imaging methods in terms of the accuracy of PE assessment

Imaging methods	χ^2 (1)	p
Planar(Q) vs. SPECT(Q)	0.87	0.351
SPECT/CT(Q) vs. SPECT(Q)	17.74	<0.001
SPECT/CT(Q) vs. planar(Q)	25.63	<0.001

characterized by a relatively high sensitivity for detecting PE (SPECT > planar), but also by a low specificity. For this reason, it is recommended that perfusion scans should be performed in combination with ventilation scans instead of performing only perfusion scans [3]. The aim of ventilation scans is to increase the specificity of the perfusion scans, that is, to exclude nonembolic perfusion defects.

An interesting fact was noted from the combination of SPECT and CT: the sensitivity was 100% and the specificity 83%. Compared with SPECT(Q), the sensitivity increased slightly (from 88 to 100%) and the specificity increased nearly twice as much (from 47 to 83%). In comparison with the data from the literature, the sensitivity and specificity of the SPECT/CT(Q) scans were similar to those achieved by the authors using the SPECT(V/Q) method [12–15].

A series of χ^2 tests was performed to check if the respective PE imaging methods (planar, SPECT and SPECT/CT) differed in their accuracy of PE assessment (table 4). Three conclusions were reached based on these analyses: (1) hybrid SPECT/CT(Q) imaging has a high diagnostic efficacy in the diagnosis of PE; (2) the SPECT(Q) and planar(Q) methods are statistically less effective in PE prediction than the SPECT/CT(Q) method, and (3) no statistically significant differences were determined in the accuracy of PE assessment between the SPECT(Q) and planar(Q) methods.

The first conclusion may be of significant practical importance. As already mentioned above, the sensitivity and specificity of SPECT/CT perfusion scanning (without ventilation) were similar to those achieved by the authors using the SPECT(V/Q) method [12–15]. Thus far, scientific societies [3, 16] have suggested that both perfusion and ventilation scans be performed in PE diagnostics, because assessments based only on perfusion scans have been giving false-positive results in numerous cases.

Ventilation scans and low-dose CT scans have one feature in common: both methods help to improve the specificity of the perfusion examination. However, recording ventilation scans is a time-consuming procedure and may be technically difficult in some patients. This is important, because patients suspected of having PE are usually elderly people. Dyspnea, fear of examination (the procedure involves breathing into a tube while not breathing through the nose) and cognitive disorders may effectively hamper the procedure. Another disadvantage of ventilation scans is the risk of false-positive results in patients with frequently observed pulmonary emphysema. Emphysematous bullae are revealed as nonperfusion foci in scintigrams. The radiotracer used in ventilation scans may penetrate into emphysematous bullae (air space). The resulting picture indicates perfusion defects (of non-embolic etiology) with maintained ventilation – very difficult to distinguish from true embolic perfusion defects

without access to anatomical data. CT scans performed using SPECT/CT hybrid gamma cameras have none of these disadvantages. Low-dose CT in hybrid SPECT/CT lung imaging could show other (nonembolic) pathologies – such as pneumothorax, pneumonia, lung tumor or lymphadenopathy – responsible for a patient's symptoms. The above-mentioned conditions would not be visible on X-ray or V/Q planar and SPECT scans.

Radioisotope imaging of suspected PE utilizes planar, SPECT and SPECT/CT acquisition techniques. The recommendations of the European Society of Cardiology (ESC) do not advocate performing lung scintigraphy for the diagnosis of PE because of the high percentage of intermediate results [16]. These recommendations, however, are based on studies having evaluated planar imaging (the oldest imaging technique). The recommendations are also based on the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria for the diagnosis of PE [17]. The PIOPED criteria determine the probability of pulmonary emboli (as high, intermediate or low or 'normal scan') following lung scintigraphy. Yet, application of the PIOPED criteria in clinical practice led to an unacceptably high percentage of 'intermediate probability' results, which were considered nondiagnostic.

The 2009 guidelines of the European Association of Nuclear Medicine (EANM), based on SPECT, an acquisition method much more advanced than planar imaging, does not recommend the PIOPED criteria for the diagnosis of PE [3]. According to the EANM recommendations, PE can be diagnosed when lung scintigraphy shows at least 1 segmental or 2 subsegmental perfusion defects with a normal ventilation pattern (V/Q mismatch).

The latest technological advancement in the scintigraphic diagnosis of PE is the hybrid SPECT/CT gamma camera, acquiring coregistered SPECT and CT images. Such a device and the EANM criteria were used in this study. However, we still lack recommendations regarding the SPECT/CT technique. In the studied population, we did not find inconclusive scintigraphic results.

In the literature, only a few studies have been published that describe the usefulness of the hybrid SPECT/low-dose CT technology in PE diagnostics. Gutte et al. [9] performed pulmonary V/Q scintigraphy by SPECT + low-dose CT and MDCT with the use of intravenous contrast media in 81 patients suspected of having PE. The sensitivity and specificity of SPECT(V/Q) were 97 and 88%, respectively. SPECT(V/Q) combined with CT helped to increase the specificity (up to 100%), while the sensitivity remained unchanged (97%). The authors eval-

uated the diagnostic efficacy of the SPECT(Q) (without ventilation) + low-dose CT method: the sensitivity was 93%, but the specificity was only 51%. Note that 17% of the SPECT(Q) (without ventilation) + low-dose CT scans had no diagnostic value. Additionally, the diagnostic efficacy of MDCT with contrast media was evaluated: the sensitivity was 68% and the specificity was 100%.

In this study, the sensitivity and specificity of SPECT(Q) (without ventilation) were 100 and 83%, respectively, and no nondiagnostic results were observed. Therefore, what is the reason for the different diagnostic efficacy found in the two studies? It seems that the difference arises from the classification of perfusion defects (embolic vs. non-embolic). According to the diagnostic criteria of Gutte et al. [9], all perfusion defects were considered embolic defects if ventilation was maintained.

Unfortunately, they provided no explanation as to how the SPECT(Q) (without ventilation) + low-dose CT scintigrams were interpreted (were all perfusion defects considered embolic defects?). It is unclear whether the shape of the perfusion defects or their position with respect to the pulmonary blood vessels was taken into account and how pulmonary interstitial lesions at abnormal perfusion sites were evaluated. The authors indicated 6 patients with false-positive SPECT(V/Q) results due to perfusion defects caused by interlobar fissures, pulmonary parenchyma consolidations and atelectasis, pleural effusion and emphysema. Except for emphysema, the morphological lesions lead to matched perfusion and ventilation defects (i.e. nonembolic defects), and thus it is unclear how the authors obtained false-positive results.

Gutte et al. [9] did not recommend performing SPECT(Q) + low-dose CT (without ventilation) scanning in PE diagnostics due to its low specificity. This study has provided conclusions to the contrary. Gutte et al. [9] pointed out the greater specificity of SPECT(V/Q) combined with CT (increasing from 88 to 100%). In this study, the specificity of SPECT(Q) (without ventilation) combined with CT was also observed to have increased, but by much more (from 47 to 83%) than what was reported by Gutte et al. [9].

The utility of perfusion SPECT/CT in the diagnosis of PE was evaluated by Palmowski et al. [18]. SPECT(V/Q) scanning (reference test) and low-dose CT were performed in 93 patients with suspected PE. According to the SPECT/CT(Q) scans, PE was diagnosed when scintigraphy yielded perfusion defects and lung CT was normal. However, the authors did not provide precise information on the diagnostic criteria they applied. The sensitivity and specificity of SPECT/CT(Q) reached 95.8 and

82.6%, respectively, and thus are similar to the values reported in the present study.

An attempt to determine whether combining CT and SPECT(Q) can replace ventilation scans was undertaken by Gradinscak et al. [5]. Their study included 30 patients suspected of having PE who underwent SPECT(V/Q) and CT-MDCT examinations (in contrast to this study, which involved performing low-dose CT). Perfusion defects with no pulmonary parenchymal lesions were considered embolic defects. The SPECT(V/Q) images revealed 96 embolic defects, of which 87% were also considered embolic defects based on the MDCT results. False-negative defects based on MDCT images were observed for atelectatic foci (less extensive compared with perfusion defects, according to the authors), and false-positive defects were observed in 2 patients with bronchial asthma (due to the presence of air trapping, according to the authors). Gradinscak et al. [5] concluded that SPECT(Q) + MDCT scanning can be considered an alternative method if ventilation scanning cannot be performed. However, false-positive results should be expected. The authors encountered some difficulties (also encountered in this study) in interpreting perfusion defects combined with pulmonary parenchymal lesions if the latter were much less extensive. Thus, can pulmonary parenchymal lesions be considered the cause of abnormal perfusion (PE excluded), or is abnormal perfusion only accompanied by interstitial lesions (PE confirmed)?

Viau et al. [4] performed SPECT(V/Q) and CT in a group of 75 patients with suspected PE. The EANM guidelines for PE diagnosis were applied. The sensitivity and specificity of SPECT(V/Q) were 88 and 93%, while for SPECT/CT(Q), they were 100 and 82%, respectively (p value not significant). The results suggest SPECT/CT(Q) may be successfully performed instead of SPECT(V/Q) provided that the data are confirmed in a larger group of patients. Notably, the sensitivity and specificity of SPECT/CT(Q) in the study by Viau et al. [4] and in our study were similar.

Lu et al. [19] compared the accuracy of planar(V/Q) and SPECT/CT(Q) scintigraphy in the evaluation of suspected PE. The study group consisted of 106 cancer patients with a Wells score of 4.4 ± 2.5 (range: 1–8.5). The planar scans were evaluated based on the PIOPED II and the Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISA-PED) criteria. Any wedge-shaped perfusion defect (>70% from the normal perfusion pattern) occupying $\geq 50\%$ of the lung segment seen on SPECT/CT(Q) images was considered to show PE. The reference test was also clinical consensus. SPECT/

CT(Q) had a higher accuracy than planar(V/Q) imaging. The sensitivity and specificity of SPECT/CT(Q) for PE were 91 and 94%, respectively. Our study yielded similar results: SPECT/CT(Q) had a higher accuracy than planar(Q) scanning, and the sensitivity and specificity of SPECT/CT(Q) were 100 and 83%, respectively. Yet, it is worth mentioning that the diagnostic criteria used in the two studies as well as the study population's characteristics varied. Moreover, the EANM diagnostic criteria for PE [3] are the accepted standard in Europe, while the criteria of Lu et al. [19] are not commonly used.

The other studies dealing with an assessment of the usefulness of SPECT/CT were focused on the improvement of the diagnostic efficacy of SPECT(V/Q) when combined with CT rather than on the replacement of ventilation scanning with CT-based examinations. Herald et al. [20] performed SPECT(V/Q) + low-dose CT scanning in 48 patients suspected of having PE. PE was diagnosed in 16 patients and excluded in 32 patients. The SPECT(V/Q) images revealed PE in 15 of the 16 patients (94%) – a truly positive result. In 6 patients (of the 32 patients without PE), the diagnosis of PE based on SPECT(V/Q) results was considered false positive. In 3 of those 6 patients (50%), combining CT and SPECT helped to exclude PE. The authors concluded that combining CT and SPECT(V/Q) adds to the diagnostic efficacy by reducing the number of false-positive results by 50%. Similar conclusions were drawn in this study: with SPECT combined with CT (only perfusion, without ventilation scanning), the number of false-positive results was reduced by 32%. In the study by Herald et al. [20], surprisingly, despite the performance of both perfusion and ventilation scanning, perfusion defects due to interlobar fissures were misinterpreted as embolic defects. A similar diagnostic strategy [focusing on improving the diagnostic efficacy of SPECT(V/Q) combined with CT] was adopted by Ling et al. [10]. SPECT(V/Q) combined with CT offered the possibility of a diagnosis other than PE in 27% of the examined patients.

Some limitations of this study have to be kept in mind. The only acceptable reference test in the scintigraphic diagnosis of PE is clinical consensus. There are two gold standard imaging modalities for diagnosing PE: conventional angiography and CT angiography. In our study group, neither of the above-mentioned tests was performed. Conventional angiography is not frequently used, because of its invasive character and associated morbidity [16]. CT angiography is not an accurate reference test for PE, as it shows the presence of emboli only to the level of segmental or subsegmental arteries [21].

Lung perfusion scintigraphy, on the other hand, visualizes the pulmonary vasculature up to the capillary vessel level, since the albumin macroaggregates injected into the bloodstream are only 15–100 µm in diameter. CT angiography could therefore have a lower sensitivity than the evaluated test (lung perfusion scintigraphy).

Moreover, pulmonary angiography and CT angiography require the administration of iodinated contrast agents. Scintigraphy, on the other hand, is a contrast-free procedure which can be safely used in patients with allergic reactions to iodinated radiological contrast media and those with renal failure. Such patients composed the majority of the evaluated group.

The authors are aware that one of the limitations to our work is the study group, which mainly consisted of elderly patients with a moderate PE probability. We believe such patients' characteristics were the result of the PE diagnostic algorithm used at our institute. According to the ESC guidelines [16], the first-line imaging method for high-PE-probability patients is CT angiography (MDCT). Additionally, MDCT – in contrast to scintigraphy – is easily available on a 24 basis. A similar limitation (institutional preference for MDCT) was faced by Lu et al. [19], who studied a group of patients with a Wells score of 4.4 ± 2.5 . In the study by Gutte et al. [9], the patients with PE (PE+) and without PE (PE–) had Wells scores of 3.1 ± 2.4 and 2.2 ± 1.8 , respectively. The majority of patients assessed in the two studies were patients with a moderate PE risk.

In our study, D-dimer levels did not differ significantly between the groups of patients with and those without PE ($p = 0.118$). This may be due to the older age of the patients, as the specificity of D-dimer testing declines with age [22]. In comparison with the PE– patients, those with PE were more often characterized to be at high or moderate risk according to the Geneva score. Likewise, low-risk patients were less abundant in this group ($p =$

0.015), which confirms the utility of the Geneva score in determining the pretest probability of PE.

Also, a significant number of patients were excluded from the study. We were unable to perform all three imaging examinations (planar, SPECT and SPECT/CT) in 8 patients; the time required for scanning (20–30 min) occurred to be exceedingly long for those patients with marked dyspnea. Another 17 patients were excluded because no 6-month follow-up data were available.

Finally, the literature search yielded only a few publications concerning the utility of the perfusion SPECT/CT method in PE diagnosis. The poor performance of planar scanning may be due to a lack of comparative analysis with ventilation scanning.

Conclusions

Lung perfusion scintigraphy combined with CT performed by hybrid SPECT/CT gamma cameras has a high diagnostic efficacy in the diagnosis of PE. We also found that lung perfusion scintigraphy performed with a hybrid SPECT/CT device has a significantly higher accuracy than scintigraphy performed by the planar or SPECT technique.

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Conflicts of Interest

The authors declare that there are no conflicts of interests.

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