The efficiency of hybrid perfusion SPECT/CT imaging in the diagnostic strategy of pulmonary thromboembolism

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Abstract

Objective: Ventilation/perfusion single photon emission computed tomography (V/Q SPECT) is recommended as a reference radionuclide method in pulmonary thromboembolism (PTE) diagnosis. However, there is some logistic, economic, and infectious concern about the study's ventilation part. This study aimed to evaluate the effectiveness of hybrid perfusion SPECT with a low dose CT method in the diagnostic strategy of PTE. **Materials and Methods:** Two physicians reviewed 305 patients' data for this retrospective study. All patients had Q SPECT/CT data as initial imaging, and Ventilation SPECT was added to the selected patients' algorithm. The diagnostic performance and inter-observer agreement were determined for both Q SPECT and Q SPECT/CT methods. The final diagnosis was made by clinical decision with all tests and follow-up for at least 6-month. **Results:** The majority (92%) of our study group were correctly diagnosed with the Q SPECT/CT method with excellent inter-observer agreements (κ=0.914). The sensitivity, specificity, and accuracy of methods were as follows; 92.2%, 76.3%, and 80.3% for Q SPECT; 96.1%, 94.5%, and 98.8% for Q SPECT/CT (P<0.001). The ventilation scan was applied to 29% (n=88) of the study group. It is prominent in 21/88 patients whose Q SPECT/CT result was non-diagnostic or discordant with clinical probability. **Conclusion:** Q SPECT/CT recommended as the initial radionuclide imaging in PTE diagnosis, with high diagnostic accuracy and inter-observer agreement. Ventilation scans can be optimized according to Q SPECT/CT results avoiding unnecessary irradiation and other potential adverse effects, including infectious risk in the current pandemic context.

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Introduction

Finding an effective diagnostic strategy for pulmonary thromboembolism (PTE) is desirable and essential in improving patient outcomes. Although computed tomography pulmonary angiography (CTPA) offers high diagnostic values, it has certain limitations such as contraindications, indeterminate results, and radiation burden. Ventilation/Perfusion (V/Q) scintigraphy would be the alternative test in that situation because of its diagnostic performance and safety [1-4]. Besides, the implementation of tomographic single photon emission computed tomography (SPECT) and hybrid (with low dose CT) imaging technology and more effective ventilation agents increased the lung scans' diagnostic value significantly. Studies have confirmed that V/Q SPECT/CT has an excellent diagnostic value with a low rate of inconclusive results in detecting pulmonary embolism compared to CTPA [5-7]. However, practices with logistic, economic, and radiation safety are, therefore, of ongoing concern to find the most effective local test for diagnosing patients with suspected PTE. Some authors have investigated whether low dose CT can supplant the lung scan's ventilation component's need. However, there is not enough evidence that the ventilation component could be omitted since it has a unique functional capacity [8-13]. Besides, we still lack official recommendations of scientific societies regarding the hybrid method in clinical settings of PTE. Therefore, there is a clear need to evaluate the Q SPECT/CT method in the diagnostic algorithm of PTE.

At our institute, we have performed Q SPECT/CT as initial imaging for patients with suspected with PTE if there is not any contraindication for CT. Ventilation SPECT is added to the algorithm if the conclusion is non-diagnostic or discordant with pretest clinical probability (PCP). Our experience support that Q SPECT/CT can be an effective method for first-line imaging and reduce ventilation scan utilization in PTE diagnosis. The current study's most crucial goal was to assess the efficiency of Q SPECT/CT in PTE's diagnostic strategy. The diagnostic performances of both perfusion only methods (Q SPECT and Q SPECT/CT) were also evaluated comparatively.

Subjects, Material and Methods

We retrospectively reviewed all scintigraphy data of patients referred to our department for diagnosis PTE from 2015 to 2020. The clinical probability of PTE is assessed as low, intermediate, or high through revised Geneva criteria, age-adjusted D-dimer value, and the patient's medical history [14]. The scintigraphic method's preference was mainly the contraindications for CTA, including renal insufficiency and contrast agent allergy. Also, it can be just for the clinician's choice following the recommendations of current guidelines.

After reviewing the database, patients with insufficient data or technically inadequate imaging and patients with the absence of clinical follow-up and final diagnosis were excluded from the study. Finally, 305 patient's data were eligible for this study.

Image acquisition and reconstruction

All images were acquired using a hybrid SPECT/CT dual-head gamma camera, Optima NM/CT 640 (GE Healthcare, Chicago, IL). Images were processed using a dedicated workstation equipped with a commercial software package (Xeleris version 4.0, GE Healthcare, Chicago, IL).

Lung perfusion scans were performed using technetium-99m albumin aggregated (^{99m}Tc-MAA) (Makro-Albumon®; Medi-Radiopharma Ltd., Hungary) at a dose of 150-200MBq and injected intravenously to the patient in a supine position. In 5-10 minutes, the SPECT images were acquired in a step-and-shoot sequence with a noncircular orbit with low-energy, high-resolution collimator. The 10% photo peak window was centered at 140 keV, and SPECT datasets were obtained with a 128×128 matrix, 30 projections per camera head over 180° with the time per projection was 10s.

Non-contrast low dose CT was performed immediately after SPECT under free-breathing with parameters as follows; 120kV tube voltage, 30mAs tube current, 500mm FOV, 512×512 matrices, 2.5mm slice thickness, 1s rotation time, and 1.25 pitch). The CT images were reconstructed us-ing an adaptive statistical iterative reconstruction algo-rithm (ASiRTM; GE Healthcare). Both SPECT and CT acquisi-tions were obtained with the same position of the patient's body.

A ventilation scan was acquired in 88/305 patients on the following day with a dose of 30-50MBq ^{99m}Tc labeled ultrafine solid graphite hydrophobic carbon nanoparticles (Technegas, Cyclomedica). Single photon emission computed tomography parameters for the ventilation scan were the same as the perfusion scan.

Image analysis and interpretation

Single photon emission computed tomography data processed using iterative reconstruction and dedicated lung application (Q.Lung, Xeleris version 4.0, GE Healthcare), which allowed the simultaneous review of SPECT, CT, and fused imaging data. For the quantification of perfusion images, the isocontour volume of interests was created on SPECT images applying a 40% threshold (Figure 1). Three-dimensional segmentation and computerized volumetry technique covering the whole lung volume was used for this purpose, as previously described in other studies [15-17].

Two nuclear medicine physicians (4 years and 20 years experienced) analyzed both Q SPECT and Q SPECT/CT methods independently for evaluating inter-observer agreement. Two reviewers made decisions in consensus as positive (PTE), negative (non-PTE), or non-diagnostic (ND) results for PTE. Pulmonary artery segments were assessed using

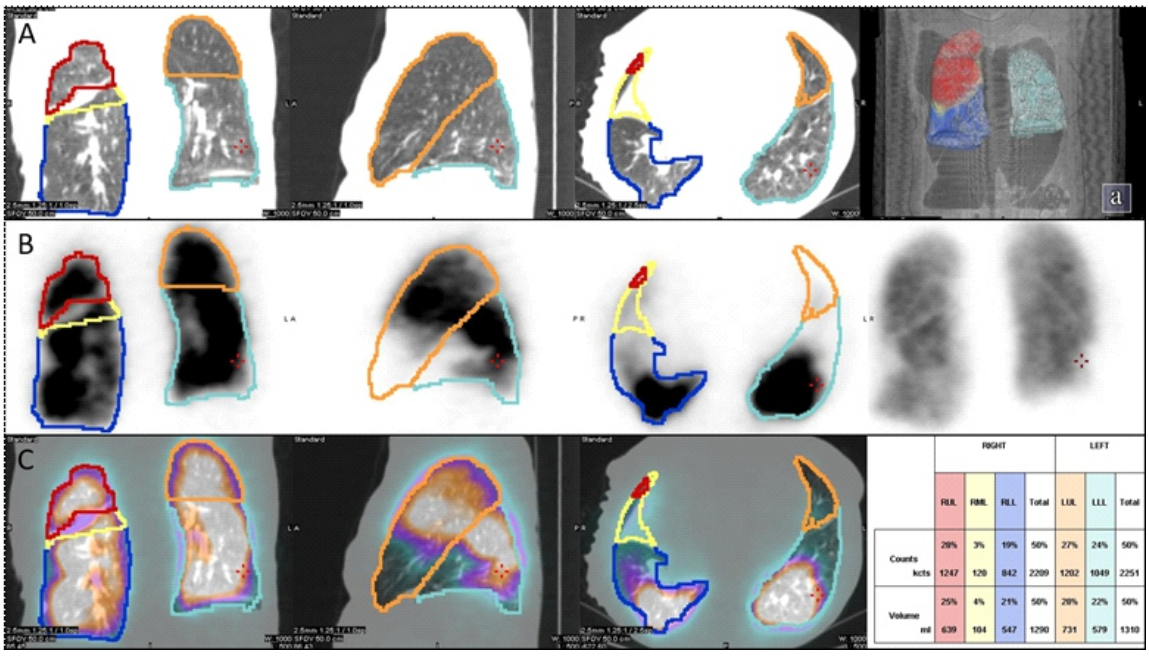

Figure 1. Coronal, sagittal, and transaxial slices of IdCT (line A), Q SPECT (line B), and Q SPECT/CT (line C) images in a patient with acute PE show multiple mismatched perfusion defects. ROIs for each lobe is semi automatically drawn in the sagittal CT images using the fissures as the anatomical reference. These ROI are also reflected in Q SPECT images and quantitate lobar perfusion, as seen right bottom (Q.Lung, Xeleris version 4.0, GE Healthcare).

Table 1. *The interpretation criteria for PE of Q SPECT, Q SPECT/CT and V/Q SPECT methods.*

Result	Q SPECT *	P SPECT/CT **	V/P SPECT ***
Positive	≥1 wedge-shaped perfusion defects	At least one segment or two subsegments peripheral wedge shaped defects (quantitatively reduced as <40% compared with normally perfused lung) without corresponding CT image abnormality	V/P mismatch of at least one segment or two subsegments that conforms to the pulmonary vascular anatomy (peripheral wedge shaped defects)
Non-diagnostic	All other findings	All other findings	Non-specific abnormalities
Negative	Near normal- normal perfusion or non-wedge shaped perfusion defects	Normal perfusion, nonperipheral-nonsegmental perfusion defects or defects corresponding to CT abnormalities.	Normal perfusion pattern, matched or reversed mismatch V/P defects of any size, shape, or number in the absence of mismatch; non-segmental mismatch perfusion defect.

*QSPECT, Perfusion SPECT; Q SPECT/CT, Perfusion SPECT/low dose CT; V/Q, Ventilation/Perfusion*PISA-PED criteria (ref); ** EANM, MSKCC criteria (ref); ***EANM criteria (ref)*

a standardized segmental lung reference chart. Perfusion only SPECT data were interpreted according to the PISA-PED criteria, which is commonly used in perfusion SPECT, however, suggested for planar imaging. The criteria for interpretation of Q SPECT/CT were defined using the perfusion threshold according to MSKCC criteria and according to the EANM guideline using the ldCT as the ventilation imaging [4, 8, 12]. Finally, the V/Q SPECT imaging was interpreted using standard V/Q criteria, which is well defined in the current guidelines [4, 18, 19]. All interpretative criteria Q SPECT, Q SPECT/CT, and V/Q SPECT imaging were tabulated in Table 1.

Final diagnosis

Clinical decision and follow-up data were used as a reference to estimate the diagnostic parameters of methods, similarly with previous studies in the literature [11, 20, 21]. The final PE diagnosis was made by the physician based on clinical symptoms, medical history, and the results of laboratory or other imaging tests (echocardiography, lower-extremity ultrasound, V SPECT/CT, CTPA). All patients with negative results have follow-up data of at least six months from hospital files or telephone interviews. If the patient did not have any PTE clinical signs within six months from the scintigraphy, PTE was ruled out. However, a patient with negative Q SPECT/CT presenting PE signs and received anticoagulant treatment on follow-up classified as falsely negative.

Statistical analysis

Statistical analyses were carried out using SPSS Statistics for Windows, Version 23.0 (IBM Corporation, Armonk, NY, United States). Whether numerical (continuous) data is normally distributed was evaluated using histograms, probability plots, and the analytical method (Kolmogorov-Smirnov test). The age was not normally distributed; it was presented using the median and interquartile range (IQR). A non-parametric test, the Mann-Whitney U test, was used to compare groups in terms of age. The Chi-square test was used to compare groups between two or more independent groups. Diagnostic performance was assessed by sensitivity, specificity, positive and negative predictive values, and accuracy. The inter-observer agreement between the two nuclear medicine physicians in determining the positive, negative, and non-diagnostic were investigated using the Kappa test (κ). A P-value of less than 0.05 was considered to show a statistically significant.

Results

Seventy-six patients (24.9%) were finally diagnosed with PTE; patient characteristics (age, gender, PCP, and CPD) for PTE and non-PTE groups are summarized in Table 2.

The demographic and clinical characteristics of patients were similar for each group except for PCP. More patients with intermediate/high pretest probability in the PTE group, while significantly more patients with low pretest probability in the non-PTE group (P=0.001).

Two nuclear medicine physicians analyzed each method independently for evaluating inter-observer agreement; however, decisions were made by two reviewers in consensus. The inter-observer agreements for both Q SPECT and Q SPECT/CT were excellent; kappa values were 0.864 and 0.914, respectively (P=0.001 and P<0.001).

According to the final diagnosis, the distribution of all results and diagnostic parameters for both Q SPECT and Q SPECT/CT were tabulated in Table 3. The sensitivity, specificity, and accuracy were significantly higher with the hybrid imaging method than perfusion only SPECT (P< 0.001).

Non-diagnostic Results

There were 51 patients (17%) with non-diagnostic (ND) re-

Table 2. *Patient characteristics of the PE and non-PE group*

		PE n (%)	Non-PE n (%)	P-value	Total n (%)
Patient size		76 (24.9 %)	229 (75.1 %)		305
Age median (IQR)		68 (15)	69 (14)	0,652*	68 (15)
Gender	Female	40 (52.6 %)	130 (56.8 %)	0,529	170 (55.7 %)
	Male	36 (47.4 %)	99 (43.2 %)		135 (44.3 %)
PCP	Low	10 (13.2 %)	155 (67.7 %)	0.001	165 (54.1 %)
	Intermediate	43 (56.6 %)	57 (24.9 %)		100 (32.8 %)
	High	23 (30.3 %)	17 (7.4 %)		40 (13.1 %)
CPD		31 (40.8 %)	80 (34.9 %)	0.358	111 (36.4 %)

PE, pulmonary embolism; IQR, interquartile range; PCP, Pretest Clinical Probability; CPD, Cardiopulmonary Disease
**Mean Rank of groups was 149.1 vs. 154.3, and the difference was not statistically significant (Mann-Whitney U=8402.5, P=0.652).*

Table 3. *The distribution of results (n) and the diagnostic parameters (%) of the methods.*

Method	TP	TN	FP	FN	ND	Sensitivity	Specificity	Accuracy
Q SPECT	59	145	45	5	51	92.2 %	76.3 %	80.3 %
Q SPECT/CT	73	208	12	3	9	98.6 %	94.5 %	94.9 %

QSPECT, Perfusion SPECT; Q SPECT/CT, Perfusion SPECT/low dose CT; TP, true positive; TN, true negative; FP, false positive; ND, non-diagnostic results.

sults for the Q SPECT method, and these patients were mostly with low PCP (82.4%). The prevalence of CPD was significantly high (49% vs. 33.9%, P=0.040). The ratio of male to female was significantly low (0.457 vs. 0.881, P=0.042) in that group when compared to the rest of the study population. However, the median age of patients with ND results was similar to the rest of the study group (Mean Ranks were 152.7 vs. 153.1, Mann-Whitney U=8402.5, P=0.967). Among these 51 patients, only nine patients had ND results with Q SPECT/CT. As a result, the non-diagnostic rate (NDR) was significantly low for Q SPECT/CT than Q SPECT (3% vs. 17%, P< 0.001).

Interpretation of low dose CT

A total of 83 patients (27%) had additional CT findings including bronchopulmonary infection (n=28), pleural/pericardial effusion (n=22), atelectasis (n=17), parenchymal nodules (n=13), mediastinal lymphadenopathy or mass (n=8) and others (n=5), some patients had more than one findings. The majority of these patients (70/83) were in the non-PTE group, and its proportion was significantly higher when compared with the PTE group (30.6% vs. 17.1%, P= 0.022).

Low dose CT findings changed the diagnosis in 26% (n= 80) of the patients. That change was related to other pleural-parenchymal pathologies (n=35) or due to CT based attenuation correction and detection of postural and anatomic variations (n=45) (Figure 2). Their Q SPECT results were as follows; 42 non-diagnostic (ND), 33 false-positive (FP), and three false-negative (FN). Pulmonary thromboembolism was correctly excluded in 63/80 patients and confirmed in 14/80 patients. Among these 80 patients, only three patients interpreted as false negative with Q SPECT/CT. Those three patients had non-diagnostic Q SPECT results and some parenchymal changes in ldCT that could be matched with perfusion defects. However, PTE was confirmed with a normal ventilation scan in all of them.

Interpretation of Ventilation SPECT

The V SPECT imaging was selectively used (29%, n=88) in our study group, and the indication was not the same for all these patients. Therefore, the diagnostic parameters of V/Q SPECT/CT were not presented in this study. Ventilation indications were non-diagnostic results with Q SPECT/CT (n=9), discordance between images and clinical probability (n=27), inter-observer variability (n=14), or just for practi-

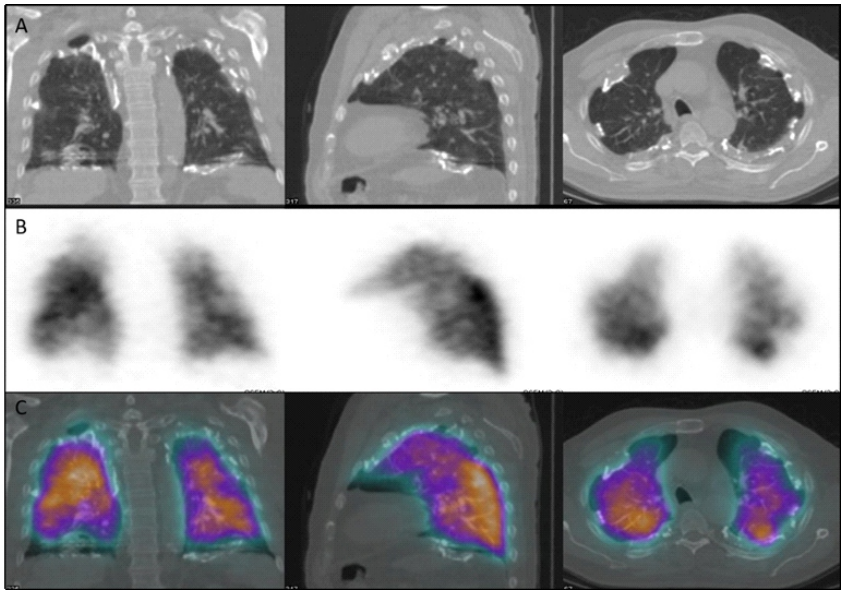

Figure 2. In a case with asbestosis, CT scan (line A- coronal, sagittal, and transaxial slice) helps identify calcified pleural plaques as the cause of perfusion defects on Q SPECT imaging (line B). The fused SPECT/CT images (line C) show the perfusion defect corresponding to calcified pleural plaques, not parenchymal. Pulmonary thromboembolism was correctly excluded with Q SPECT/CT in this case, which is interpreted as non-diagnostic with Q SPECT.

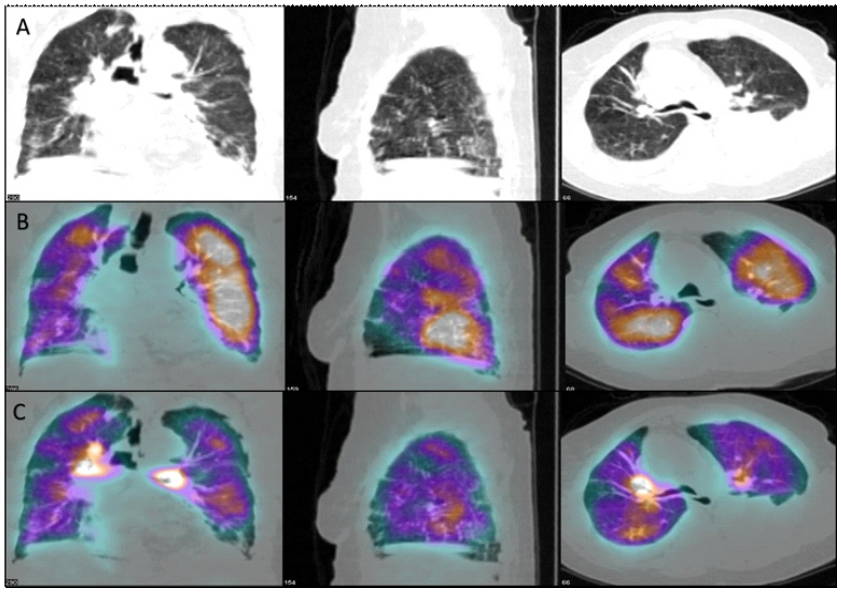

Figure 3. Coronal, sagittal, and transaxial slices of ldCT (line A), Q SPECT/CT (line B), and V SPECT (line C) images in a patient with chronic obstructive pulmonary disease. LdCT shows some non-specific parenchymal abnormalities which not corresponded to perfusion defects. Therefore the patient has non-diagnostic results with Q SPECT/CT. However, ventilation defects are thoroughly matched with perfusion abnormality, and PTE was excluded in this patient.

tioner's choice (n=38).

When added V SPECT to Q SPECT data, the diagnosis was changed in 43 patients; PTE was excluded in 27 patients and confirmed in 16 patients with V/Q SPECT. However, the result was already adjusted correctly in 25/43 patients with Q SPECT/CT hybrid images. Hence, V SPECT on determination was prominent in the remaining 18 patients (6 %); they were non-diagnostic or false positive with Q SPECT/CT (Figure 3).

According to the final diagnosis, there were only two patients with FP and one patient with FN results with V/Q SPECT. Pulmonary thromboembolism was correctly excluded from Q SPECT/CT in one of the FP patients who had bullous emphysema.

Discussion

The PTE prevalence was 24.9 % in the present cohort, consisting of patients predominantly with intermediate or low pretest probability. The majority (92%, n=281) of our patients had a correct diagnosis with the Q SPECT/CT method. Among other (8%, n=24) patients, 21 were correctly diagnosed when adding V SPECT to the algorithm. Hence a ventilation scan was prominent in these 21 patients (7%). Our re-

sults suggested that a ventilation scan could be optimized according to Q SPECT/CT imaging results in diagnosis PTE to avoid excessive irradiation and other potential adverse effects, including infectious risk in this pandemic context. Perfusion only evaluation of PTE has already been proposed in the PISA-PED study, based on planar perfusion scintigraphy [22]. However, a planar perfusion scan has not been recommended due to its low specificity yet. The sensitivity and the specificities were 92.2% and 76.3% for the perfusion only method (Q SPECT) in the current study. Mazurek et al. (2015) reported that the Q SPECT scan allowed diagnosing PTE with a sensitivity of 88% and a negative predictive value (NPV) of 90% [11]. However, the specificity was only 47% in their study group. When comparing their results, Q SPECT's diagnostic values in our study were higher, especially for specificity. The difference may be attributed to the diagnosis criteria difference as they did not report any ND results with Q SPECT. Some patients with ND results could be classified as positive, falsely in that study. Indeed, the FP results for Q SPECT was reported 37 % (31/84) in their patient population, while it was 15% (45/305) in our study. Simanek et al. (2016) also concluded that Q SPECT, combined with X-ray, is very efficient for excluding PTE [21]. They reported a very high exclusion rate for Q SPECT as 70%; however, this rate was 48% in our study. That may differ due to their limitation about the reference method (V/Q SPECT/CT), which was not used in all patients, and the predictive values were not assessed. Our reference was the final diagnosis. The NPV was very high (96.7%) with Q SPECT.

Although these promising results and perfect interobserver agreement (kappa value=0.864, P=0.001) of imaging, positive predictive value (PPV) was relatively low (56.7%), and the NDR was 17% for Q SPECT in the current study. The ND results or intermediate probability are well-known concern with perfusion only methods in PTE diagnosis [20, 23, 24]. Therefore, combination V/Q SPECT with a binary reporting approach has been recommended to strengthen and simplify the PTE diagnosis [4, 18, 19]. However, following developments in hybrid imaging systems and dedicated software for processing, it has been debated whether perfusion imaging in conjunction with ldCT is sufficient for PE diagnosis. A ventilation scan is a time-consuming, expensive procedure and may be technically challenging in some patients. The latter issue is of great interest, particularly for patients with clinical instability, massive dyspnea, incompliance, or reduced consciousness, as patients suspected of having PE are usually older people. This context has attracted more attention recently due to the infectious risk in the COVID-19 pandemic [25, 26]. Coagulation disorders are common in patients with all SARS infection. These patients are also associated with a significant risk of renal failure; hence scintigraphic methods become the choice for diagnosing PE [25, 27].

In agreement with previous studies, our study supported that Q SPECT/CT had a satisfying clinical outcome with a minimal NDR in PTE diagnosis [8, 11]. The sensitivity and specificity of Q SPECT/CT were 96.1% and 94.5%, respectively, with a low NDR (3%). When added ldCT findings to Q SPECT imaging, false-positive results were reduced to 4% from 15%. The ND results were reduced to 3% from 17%. This observation agrees with a previous study by Kumar et al. (2015) in which the NDR for Q SPECT/CT was only 4.9% in their study cohort, which composed of 182 patients with indeterminate planar V/Q scan [12]. Mazurek et al. (2015) reported that the sensitivity and specificity were the highest at 100% and 83% for the Q SPECT/CT method when they compared planar, SPECT, and hybrid methods [11]. In line with that study, Lu et al. (2014) also reported high sensitivity (91%) and the specificity value (94%), similar to us [8]. However, their study population was highly selec ted (e.g., patients with cancer). Palmowski et al. (2014) reported that the sensitivity and specificity values reached 95.8% and 82.6%; however, they combined Q SPECT data with multidetector CT (MDCT) if ventilation scanning cannot be performed [9].

The other studies dealing with assessing the usefulness of hybrid imaging focused on improving V/Q SPECT's diagnostic efficacy when combined with CT [28-30]. Ling et al. (2012) revealed that V/Q SPECT combined with CT offered a diagnosis other than PTE in 27% of the examined patients [30]. Le Roux et al. (2015) referred to alternative diagnoses for 24% of 393 patients in their retrospective analyses [10]. In line with previous studies, we observed the alternative diagnosis in 26% (n=80) of the patients when added ldCT findings to the Q SPECT. The diagnosis was correctly changed in the majority of them (25%, n=77). Nevertheless, alternative diagnoses can probably be dependent on the composition of patients in a group. Indeed, Simanek et al. (2016) reported that low dose CT scans showed an alternative diagnosis to PTE in 11% of examined patients without breast cancer. The value raised to 33% in breast cancer patients for their cohort [21].

On the other hand, our findings contrast with a few previous studies [10, 20]. Gutte et al. (2009) reported the sensitivity of Q SPECT/ldCT (without ventilation) in PTE diagnosis was 93%, with low specificity (51%) and 17% NDR [20]. Though it was pointed out that the greater specificity as 100% for V/Q SPECT combined with CT in that study, they did not recommend Q SPECT/CT as an initial PTE method due to low specificity and high NDR. High FP rates were also reported as 15% and 17.3% in other studies [9, 10]. It was stated that using ldCT as a substitution to V/Q SPECT is associated with a high risk of over-diagnosis [10]. However, methods were compared with V/Q SPECT as the gold standard in those studies; hence, there were limitations about the reference method.

The inter-observer agreement was perfect (κ value= 0.914, P=0.001), and specificity Q SPECT/CT was generally higher in the current study than all the mentioned studies. This difference might be due to appropriate diagnostic criteria, advanced imaging equipment, and dedicated software to pulmonary perfusion imaging. Unfortunately, there are no definitive Q SPECT/CT interpretation criteria for PE. We combined the quantitative threshold method to the standard binary interpretation approach recommended in the current guidelines. Therefore, we could precisely define perfusion defects using dedicated lung SPECT software (Q.Lung), which provides a quantitative evaluation of perfusion and the defects defined as a reduced activity using a 40% threshold [16, 17]. The quantitative approach to perfusion defects was previously suggested by Lu et al. (2014)

from MSKCC and supported by Kumar et al. (2015); however, quantification was defined visually in that criteria [8, 12]. PE is indicated by at least one wedge-shaped peripheral defect estimated as ≥50% of a pulmonary segment and visually reduced by <70% compared with normally perfused lung. Derlin et al. (2018) used software-based quantification with SPECT/CT using thresholds 40% to 60% in chronic thromboembolic pulmonary hypertension (CTEPH) patients [17]. They concluded that quantitative analysis of perfusion defects using SPECT images is feasible, provides a direct measure of disease severity, and correlates well with established clinical parameters.

The two major concerns with hybrid imaging methods are excessive radiation dose and overdiagnosis. The administered dose of ^{99m}Tc MAA is usually 100-200MBq yielding an effective dose of 2-2.2mSv for Q SPECT. Low-dose CT adds only 0.5-1mSv, comparing favorably with the 11mSv of pulmonary MDCT angiography and 15mSv of CTPA. If ventilation SPECT is needed, the effective radiation dose of 0.5-0.8mSv for 30-50MBq ^{99m}Tc-Technegas is also added. As a result, the effective dose for V/P SPECT with ldCT is about 35%-40% of the dose from MDCT [3, 31, 32]. We use Q SPECT/CT as an initial method for the patients suspected of PTE, avoiding unnecessary radiation doses from ventilation SPECT in most patients.

Another concern with Q SPECT/CT is over-diagnosis; however, there were only 12 patients (4%) with FP results in our study. Pulmonary thromboembolism was correctly excluded when added ventilation SPECT in 11 of these 12 patients. This finding confirms that the diagnostic strategy we recommended for the diagnosis of PTE is based on applying a ventilation scan in selected patients according to the Q SPECT/CT results. A ventilation scan would also be helpful for accurate diagnosis in some cases. Patients with asthma exacerbations, radiation pneumonitis, vasculitis, and vasoconstrictive responses to hypoxia (the Euler-Liljestrand mechanism) can show perfusion defects without parenchymal abnormalities [33]. They all may cause a false-positive diagnosis of PTE on Q SPECT/CT. Another important fact is that COPD patients are at high risk of PTE. Severely obstructive airway diseases may be the main reason for a perfusion defect, and that can be interpreted falsely as a PTE in Q SPECT/CT [23, 34, 35]. Indeed, all patients with FP and ND results with Q SPECT/CT had co-morbidities associated with hypoxia, including cardiovascular disease, pulmonary hypertension, or neurological disease in our study group.

Despite providing additional information on a clinical topic of significant interest, our study has several limitations that should be acknowledged. Firstly, the retrospective observational nature of the study carries an inherent risk of selection bias. However, it was a relatively large sample size; most patients had a low pretest probability for PTE and contraindications to CTPA. Therefore some of the observations reported would need further exploration in patients with high PCP. Another limitation of our study is the lack of a more substantial gold standard as CTPA due to our ethical standard. We used a clinical follow-up, including all available clinical information, other imaging studies, and patient outcome, as the reference for PTE diagnosis. There might have been a verification bias; we could not be sure whether these patients had a PTE precisely as they received anticoagulant therapy.

Finally, non-contrast-enhanced and low dose CT images, which consisted of a 4-row CT scanner, were interpreted by nuclear medicine physicians, not by a radiologist. Hence, a technical and diagnosing limitation might be considered in our study.

In conclusion, according to our results, Q SPECT/CT pulmonary imaging could be recommended as the initial diagnostic imaging method in patients with suspected PTE, with high diagnostic accuracy and interobserver agreement. Due to the advantages of hybrid perfusion-low dose CT in differential diagnosis to PTE, ventilation SPECT can be optimized for essential patients. Thus, we avoided unnecessary irradiation and other potential adverse effects, including infectious risk in the current pandemic context.

Ethical Approval

All procedures performed in studies involving human participants followed the institutional and national research committee's ethical standards and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was waived at the approval of the IRB for this retrospective study.

The manuscript has not been published before and is not under consideration for publication anywhere else, and all co-authors have approved it.

The authors declare that they have no conflict of interests

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