Original Article

Ventilation/Perfusion SPECT lung scintigraphy and computed tomography pulmonary angiography in patients with clinical suspicion of pulmonary embolism

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A B S T R A C T

The aim was to compare ventilation/perfusion SPECT lung scintigraphy (V/Q-SPECT) and computed tomography pulmonary angiography (CTPA) in patients with suspicion of pulmonary embolism (PE).

Material and methods: This prospectively designed study included 53 patients with intermediate or high clinical probability of PE. A V/Q-SPECT and CTPA was performed on all patients. The V/Q-SPECT was interpreted according to the European Association of Nuclear Medicine and Molecular Imaging (EANMMI) guidelines. CTPA was reported as positive, negative or indeterminate.

Results: CTPA was positive in 22 cases, negative in 28, and indeterminate in 3. V/Q-SPECT was positive in 27 cases, negative in 24, and non-diagnostic in 2. In the 22 with positive CTPA, V/Q-SPECT was positive in 18, negative in 3, and non-diagnostic in 1. In the 28 with negative CTPA, V/Q-SPECT was positive in 8, negative in 19, and non-diagnostic in 1. In the 3 with indeterminate CTPA, V/Q-SPECT was positive in 1 and negative in 2. In the 2 non-diagnostic cases V/Q-SPECT, CTPA was positive in 1 and negative in one. In the 10 high clinical probabilities, CTPA and V/Q-SPECT were positive in 7, negative in 2, and in 1, CTPA was positive and V/Q-SPECT negative. In the 38 intermediate probability group, CTPA and V/Q-SPECT were positive in 11, negative in 17, with CTPA negative and V/Q-SPECT positive in 8, and in 2 CTPA was positive and V/Q-SPECT negative. The results show that V/Q-SPECT detected PE in 5 patients more than CTPA.

Conclusion: Our results show a 77% concordance of both techniques. Overall V/Q-SPECT detected PE in 18% more patients than CTPA in the intermediate group. Both techniques have a complementary role when a diagnosis cannot be made with one of them.

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Gammagrafía pulmonar SPECT de Ventilación/Perfusión y angiografía pulmonar computarizada en pacientes con sospecha clínica de tromboembolismo pulmonar

R E S U M E N

Objetivo: Comparar la gammagrafía pulmonar SPECT de ventilación/perfusión (SPECT-V/Q) y la angiografía pulmonar computarizada (CTPA) en pacientes con sospecha de tromboembolismo pulmonar (TEP).

Material y métodos: Estudio prospectivo en 53 pacientes con probabilidad intermedia y alta de TEP. A todos se les realizó SPECT-V/Q y CTPA. La SPECT-V/Q fue interpretada según la guía publicada por la European Association of Nuclear Medicine and Molecular Imaging (EANMMI). La CTPA fue reportada como positiva, negativa o indeterminada.

Resultados: La CTPA fue positiva en 22, negativa en 28 e indeterminada en 3. La SPECT-V/Q fue positiva en 27, negativa en 24 y no diagnóstica en 2. En 22 con CTPA positiva, la SPECT-V/Q fue positiva en 18, negativa en 3 y no diagnóstica en una. En 28 con CTPA negativa, la SPECT-V/Q fue positiva en 8, negativa en 19 y no diagnóstica en uno. En 3 con CTPA indeterminada, la SPECT-V/Q fue positiva en una y negativa en 2. En 2 con SPECT-V/Q no diagnóstica, la CTPA fue positiva en una y negativa en una. En 10 con probabilidad...

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Introduction

The thromboembolic disease is a clinical disorder caused by the sudden occlusion of the pulmonary arteries and it is the third most common cause of vascular disease behind ischemic heart disease and cerebrovascular disease. The estimated annual incidence is 100–200 per 100,000 inhabitants.\(^1\) Pulmonary embolism (PE) is a complication of deep vein thrombosis originating in lower limbs in more than 90% of the cases. PE is most frequent in admitted patients and in critical outpatients. Despite the progress made on prevention, diagnostic techniques and treatment, PE still remains frequently underdiagnosed with a lethal outcome. Unfortunately, clinical symptoms, signs and D-Dimer are unspecific.

During decades ventilation/perfusion (V/Q) planar scintigraphy was, after chest X-ray, the functional imaging technique of choice in the approach of PE diagnosis. The contribution of V/Q planar scintigraphy was evaluated in depth and extensively after the PIOPED study.\(^3\) Since that milestone study, further clinical evaluations were carried out to optimize the use of the technique by updating the reporting criteria of V/Q planar lung scintigraphy.\(^4\)–\(^7\) The acceptance and recognized contribution of the technique for the diagnosis of PE led to its generalized use in the clinical setting. However, the limitations due to the considerable number of non-diagnostic studies categorized as low and intermediate probability of PE were also evident.\(^5\)

In this context, the introduction of the spiral CT, providing in most of the cases a dual report in terms of Yes/No PE, replaced the V/Q planar lung scintigraphy for the diagnosis of PE. As a result spiral CT was thereafter included as the first imaging option in the protocols of most of the hospitals, despite the radiation dose involved.\(^8\)–\(^1\) In general, V/Q was kept only for patients in whom spiral CT was not technically feasible or was contraindicated because of iodide contrast allergy, renal failure or any lack of patient collaboration whatever the cause was.\(^1\)

The recent studies demonstrating the relevant contribution of the SPECT technique to the V/Q scintigraphy are a major breakthrough in the PE diagnostic imaging approach.\(^1\)–\(^1\) The results reported, revealed a high reduction of the so-called, until then, low and intermediate probability scans. Therefore, V/Q SPECT, allowed a much more confident dual report when compared to V/Q planar scintigraphy,\(^1\) and as a result of this new framework the terminology used, in terms of probabilities, has changed to the positive/negative report terminology included in the current guidelines.\(^1\) However, despite the higher sensitivity of V/Q SPECT over V/Q planar scintigraphy for PE diagnosis, and in the context of the known limitations of spiral CT, the scarce number of studies comparing the current X-ray technique, multidetector computed tomography pulmonary angiography (CTPA) and V/Q SPECT stands out.\(^1\)–\(^2\)

On these bases there is a need to assess the contribution of the current available imaging techniques, V/Q SPECT and CTPA in the PE diagnosis. Therefore, we carried out the present prospective study to compare both techniques with the aim of optimizing its use in the clinical setting.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients (n=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33–96</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>23</td>
</tr>
<tr>
<td>Female</td>
<td>30</td>
</tr>
<tr>
<td>Inpatient/outpatient</td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td>46</td>
</tr>
<tr>
<td>Outpatient</td>
<td>7</td>
</tr>
<tr>
<td>Symptoms and signs</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>40</td>
</tr>
<tr>
<td>Chest pain</td>
<td>9</td>
</tr>
<tr>
<td>Syncope</td>
<td>3</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>1</td>
</tr>
<tr>
<td>Prior PE</td>
<td>7</td>
</tr>
<tr>
<td>Prior VTE</td>
<td>5</td>
</tr>
<tr>
<td>Malignancy</td>
<td>4</td>
</tr>
<tr>
<td>Post-OP</td>
<td>4</td>
</tr>
<tr>
<td>Antithrombin deficiency</td>
<td>2</td>
</tr>
</tbody>
</table>

PE: Pulmonary embolism; VTE: Venous Thromboembolism; Post-op: Post-operative.
high-resolution collimators (ECAM Siemens, Chicago, IL, USA). Ventilation SPECT was carried out after inhalation of $^{99m}$Tc-Technegas (Technegas; Cyclomedica, Lucas Height, Australia) over 3–5 respiratory cycles. Technegas was produced by the evaporation of 703 MBq $^{99m}$Tc placed in a graphite crucible at high temperature in a pure argon atmosphere. This system allows the accumulation of 30 MBq of activity in the lungs. All patients remained in supine position throughout the examination. Ventilation SPECT was acquired in an orbit of 360° (180° per detector), on a $128 \times 128$ matrix and 128 projections at 20 s each. Immediately after the ventilation SPECT and with the patient in supine position 150 MBq of $^{99m}$Tc-MAA were administered by slow intravenous injection, under inspiration. A perfusion SPECT was also acquired with the same parameters, a $128 \times 128$ matrix and 128 projections, but 10 s each.

The V/Q SPECT was reconstructed using iterative method OSEM (8 subsets and 2 iterations). The images of ventilation and perfusion were reoriented and aligned so that both could be compared properly. The reconstructed tomographic images were presented in axial, sagittal and coronal planes.

Computed tomography pulmonary angiography (CTPA)

CTPA examination of the chest was done using a 32-detector row scanner (Lightspeed, Pro 32, GE Healthcare, USA) using a bolus tracking method after intravenous injection of 75 mL contrast medium at a flow rate of 4 mL/s (Optiray 300, Mallinckrodt Spain S.L.). Images were acquired with the patient in supine position maintaining a deep breath. The scan extended from the diaphragm of the lung to the apices on a $512 \times 512$ matrix. Scan parameters were 100 kV, 180 mAs, tube rotation time 0.5 s pitch 0.969 and table speed of 38.75 mm per rotation. We used a standard reconstruction; axial slices were displayed in 1.25 mm thick sections with an interval of 0.625 mm. Images were presented using soft tissue and lung windows.

Image analysis

The images were evaluated by two experienced physicians on V/Q lung scintigraphy. According to the EANM guidelines, studies were interpreted as positive if there was V/Q mismatch in at least one segment or two subsegments, as negative if the perfusion was normal or there was a maximum of one sub-segmental mismatch, and as non-diagnostic if the V/Q abnormalities did not allow a positive or negative diagnosis. The perfusion defects were analyzed in terms of location (upper lobe, middle lobe, basal lobe) and size (segmental and sub-segmental). V/Q SPECT was reported using a template of the tomographic representation of the lung segments. Discrepancies were resolved by consensus.

Images of the CTPA were interpreted by a vascular radiologist as positive, negative or indeterminate. Positive studies were defined as showing definite PE (occlusive or no occlusive). Negative studies showed normal enhancement of pulmonary vasculature. Indeterminate CTPAs were attributed to patient or technical factors.

The results of the V/Q SPECT and CTPA were compared. Final diagnosis was established by 6 months clinical follow-up. The general criteria to decide treatment were based on a positive V/Q and/or CTPA. However, in cases when the probability of PE was high (for example, a positive Doppler US, cardio-pulmonary compromise, etc.) anti-coagulant therapy was also started even if both studies were negative. For the purpose of the study, the V/Q SPECT and the CTPA comparison, this does not seem very relevant; in fact, if only one of the 2 techniques, CTPA or V/Q SPECT, was routinely applied the challenge would be the same and the therapy decision independent most probably of the imaging results.

Results

Out of the 53 patients, CTPA was positive in 22, negative in 28 and indeterminate in 3; V/Q SPECT was positive in 27, negative in 24 and non-diagnostic in 2. Of the 22 patients with positive CTPA, V/Q SPECT was positive in 18, negative in 3 and non-diagnostic in 1 patient. Of the 28 patients with negative CTPA, V/Q SPECT was positive in 8 (Fig. 1), negative in 19 and non-diagnostic in 1 patient. Of the 3 indeterminate CTPA, V/Q SPECT was positive in 1 and negative in 2 patients. Of the 2 non-diagnostic V/Q SPECT, CTPA was positive in 1 and negative in the other one (Table 2). In total in the 53 patients included in the study V/Q SPECT detected PE in 5 more patients than CTPA.

If we focus on the 48 patients who had positive or negative reports, and we exclude the non-diagnostic or indeterminate results, we found that in 37 patients of the 48 (77%) both

![Fig. 1. Image of 66-y-old man with chest pain, Wells score 3 and D-Dimer 5472 ng/ml. (A) shows negative CTPA. (B) shows V/Q SPECT perfusion defects in the left lung (posterior segment upper lobe, basal lower lobe and lingula), in the right lung (posterior segment upper lobe, basal lower lobe and middle lobe). (C) shows normal ventilation of the perfusion defects. P-SPECT: Perfusion SPECT; V-SPECT: Ventilation SPECT; L: Left; R: Right.](image-url)
examinations agreed. Of them, 18 (37%) were positive and 19 (40%) negative. In the other 11 patients (23%) both techniques were discordant. In 8 of them, V/Q SPECT was positive and CTPA negative (Fig. 2) and in 3 V/Q SPECT was negative and CTPA positive (Table 3).

In the 27 positive V/Q SPECT, 67 perfusion defects were detected. Of the 67 perfusion defects 29 were segmental and 38 subsegmental. Of the 29 segmental defects 15 were located in the upper lobe, 3 in the middle lobe and 11 in the lower lobe. Of the 38 subsegmental defects, 29 were located in the upper lobe and 9 in the lower lobe.

According to the clinical probability, of the 10 high clinical probability patients, CTPA and V/Q SPECT were positive in 7, negative in 2, and in 1 CTPA was positive and V/Q SPECT negative. Of the 38 intermediate clinical probability patients, CTPA and V/Q SPECT were positive in 11, negative in 17, CTPA negative and V/Q SPECT positive in 8 and in 2 CTPA was positive and V/Q SPECT negative; therefore V/Q SPECT detected PE in 5 patients more than CTPA: In the intermediate clinical probability group V/Q SPECT detected 6 more than CTPA, while in the high probability CTPA detected one more than V/Q SPECT. Therefore in the intermediate clinical probability group V/Q SPECT detected PE in 18% more patients than CTPA.

With regard to the non-diagnostic V/Q SPECT (2) or indeterminate CTPA (3) (Table 2), all of them were included in the intermediate clinical probability of PE; in one patient of the 2 with non-diagnostic V/Q SPECT, the CTPA was positive and negative in the other one. On the other hand in the 3 patients with indeterminate CTPA, the V/Q SPECT was positive in 1 and negative in 2 patients.

The clinical outcome was evaluated by the clinicians, either the specialist or the general practitioner. At the 6 months follow up the 32 positive V/Q SPECT and/or CTPA patients progressed well with remission of the symptomatology and without anticoagulation complications. On the other hand, in the 19 patients with negative CTPA and V/Q SPECT the following pathology was found: cardiac and/or vascular pathology in 8, lung pathology in 7 and infectious pathology in 4. In the 2 patients with indeterminate CTPA and negative V/Q SPECT the pathology found was cardiac failure in one and unknown pathology in the other one.

**Discussion**

The interest of the results of our study lies on the fact that they express the direct comparison between the two more relevant imaging techniques, V/Q SPECT and CTPA, in the diagnosis of PE in the clinical setting. The impact of these techniques has been already assessed separately before and the published evidence is enormous.3,24-26

The widespread availability of CTPA along with its superiority over the planar V/Q lung scintigraphy has been included in most hospitals and in many guidelines as the first imaging modality in previous diagnostic algorithms of PE.12

The SPECT technology improves the detection of perfusion defects and avoids the overlapping of pulmonary segments providing tomographic images comparable to CTPA. In this context the addition of SPECT to planar V/Q led to a re-evaluation of this situation. Several studies have demonstrated that V/Q SPECT reduces the number of non-diagnostic studies of planar V/Q and facilitates a dual report, positive or negative.13,17,27 In fact, comparing the V/Q planar and V/Q SPECT, we have reported that V/Q SPECT allowed a better definition of the perfusion defects and reduced the non-diagnostic reports of planar V/Q from 62% to 4.9% for the SPECT.10 In this framework and for optimization of the techniques new studies are required to evaluate its performance in the clinical practice.15

With regard to the aim of our study it is noteworthy that both techniques, V/Q SPECT and CTPA were concordant in 77% of the cases (37/48), that is, provided the same information either confirming or excluding PE. These results are in accordance with those published by Mahdavi et al. who reported 80% of concordance between two techniques when positive or negative results were included, unlike Miles et al. who reported a 95% agreement between CTPA and V/Q SPECT perhaps due to the different clinical features of the population studied.20,21

Both techniques were discordant in the other 23% (11/48). Obviously, the discordant group is the most interesting for the purpose of the study and deserves further analysis. Actually, 8 patients had negative CTPA and positive V/Q SPECT. In these patients, segmental perfusion defects were detected in 2 patients, segmental and sub-segmental defects in 2, and sub-segmental defects in 4. All the 8 patients received anticoagulant therapy without developing complications over the next 6 months. A possible explanation for the negative CTPA results could be the sub-segmental size of the defects which is a well-recognized limitation of this technique.15

**Table 3**

<table>
<thead>
<tr>
<th>Technique</th>
<th>V/Q SPECT (+)</th>
<th>V/Q SPECT (-)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTPA (+)</td>
<td>18</td>
<td>3</td>
<td>21</td>
</tr>
<tr>
<td>CTPA (-)</td>
<td>8</td>
<td>19</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>22</td>
<td>48</td>
</tr>
</tbody>
</table>

CTPA: Computed tomography pulmonary angiography.
Similar results have been published by Mahdavi et al. who reported 5 patients with negative CTPA and positive V/Q SPECT. In contrast, Miles et al. reported only 1 patient with negative CTPA and positive V/Q SPECT results, which is not surprising given the high concordance, 95% reported. In the remaining 3 patients out of the discordant 11 patients showed in Table 3, the CTPA was positive and V/Q SPECT negative. In all these patients CTPA showed filling defects in the segmental arterial branches. All patients received anti-coagulant therapy and good clinical response was obtained after 6 months follow up, indicating that the 3 CTPA examinations were true positive and the V/Q SPECT was false negative. However, in a similar clinical situation, the patients with positive CTPA and negative V/Q SPECT reported by Miles et al. were not treated with anti-coagulant and after 3 month follow up no thromboembolic events developed. Such different behavior may be explained by the different features of the perfusion defects found in each of the study populations; for instance the perfusion defects of our patients were segmental in the CTPA, unlike those found in the Miles population which could be considered, according to some authors, as clinically no relevant.

On the other hand, the number of non-conclusive results was similar for both techniques, 2 non-diagnostic for the V/Q SPECT and 3 indeterminate for the CTPA. The most common cause of the non-diagnostic studies was the presence of underlying parenchymal disease. However, after reviewing the 3 CTPA it was found that in 2 the contrast injection was technically deficient and in 1 was artifacted by the respiratory movements. According to some authors indeterminate CTPA examinations would account for up to 10% of the scans while in 27% the limitation would be due to patient movement or obesity. Remarkably, when the same authors compare V/Q planar, V/Q SPECT and CTPA, they report non-diagnostic or indeterminate scans in 25% of V/Q planar, 0% in V/Q SPECT and 9% in CTPA.

From the clinical practice perspective the role of each of the techniques when the other was non-conclusive is outstanding and deserves also to be highlighted, even when the prevalence of cases in this situation is low. Therefore, our study shows that a non-diagnostic result of one of the techniques can be solved by the other, something which confirms the complementarity of the techniques.

With regard to the influence that the time interval between CTPA and V/Q SPECT could have on the results, it is interesting to highlight that out of the 17 patients within the 2- and 3-day-interval, the 12 with positive V/Q and/or CTPA were anti-coagulated and did well without complications after 6 months follow up. On the other hand, it could be argued that in those patients in whom anti-coagulation was started immediately after the first positive imaging study, it could interfere the comparison between the two techniques. However, this is unlikely since according to previous published work the complete endogenous lysis of the pulmonary clots would take between 2 and 3 days and a week depending on its size.

At the 6 months follow up the 31 positive V/Q SPECT and/or CTPA patients progressed well with remission of the symptomatology and without anti-coagulation complications. On the other hand in the 22 patients with negative CTPA and/or V/Q SPECT who were not anti-coagulated, a final diagnosis was established: cardiac and/or vascular pathology in 10, lung pathology in 8 and infectious pathology in 4.

Our study may suffer from some limitations and the main one is the lack of an objective gold standard technique something which is not uncommon in this kind of studies when the techniques being assessed are normally used as the gold standard in the daily clinical practice. However, this limitation is very relative as applies to both techniques. Also, it can be expected that co-morbidity might make difficult an adequate V/Q SPECT acquisition, something which is especially relevant when it applies to the ventilation scan. In fact this was the case for 3 patients who had to be excluded from the study.

Conclusion
Our results show high concordance of both techniques, 77%, but when the V/Q SPECT and CTPA were discordant, the performance of V/Q SPECT was superior. In addition V/Q SPECT is associated with low radiation dose and few contraindications and therefore is highly recommended for the diagnosis of pulmonary embolism. Both techniques have a complementary role when diagnosis cannot be reached by one of them.

Conflict of interest
The authors declare no conflict of interest.

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