



Lung scintigraphy for pulmonary embolism diagnosis during the COVID-19 pandemic: does the benefit-risk ratio really justify omitting the ventilation study?

Pierre-Yves Le Roux¹ · Grégoire Le Gal² · Pierre-Yves Salaun¹

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Dear Sir,

The COVID-19 pandemic is challenging nuclear medicine facilities around the world. One important complication associated with COVID-19 disease is coagulopathy, with an increased risk of venous thromboembolism [1]. Lung ventilation/perfusion (V/Q) scintigraphy is a well-established test for pulmonary embolism (PE) diagnosis. Lung scintigraphy has been validated in several large multicenter management outcome studies [2], in which the V/Q scan was interpreted based on the recognition of the well-known perfusion mismatched defect, i.e., a perfusion defect with normal ventilation.

With the recent COVID-19 outbreak, it has been repeatedly proposed in the nuclear medicine community to omit the ventilation scintigraphy and to only perform a perfusion planar scan or a perfusion SPECT/CT, in patients with suspected acute PE [3–6]. The rationale for this approach is to minimize potential exposure to aerosolized secretions of others in the nuclear medicine department. Rightly, the inhalation procedure increases the potential risk of contamination by the expired air and the aerosol secretion, especially if the patient coughs. For these reasons, adequate personal protective equipment is required for healthcare workers.

On the other hand, not performing a ventilation scan is associated with a high risk of false positive result. In a retrospective analysis of 393 patients with suspected PE assessed

by V/Q SPECT, 42 out of 283 (15%) patients with a negative V/Q SPECT would have been wrongly diagnosed with PE and would have been unduly exposed to anticoagulant therapy by substituting the ventilation SPECT by a low-dose CT [7]. Similarly, in a series of 81 patients from Gutte et al., specificity decreased from 100 with V/Q SPECT/CT to 51% with a Q SPECT/CT approach, with 20 patients unduly diagnosed with PE by omitting the ventilation [8]. In another study including 93 patients, 12 out of 69 (17%) negative V/Q SPECT were falsely positive using a P SPECT/CT approach without ventilation [9]. Accordingly, Q SPECT/CT is not an accurate diagnostic test for PE diagnosis as a positive result has an unacceptably high likelihood to be a false positive result.

What are the implications of a false positive diagnostic test in a patient with suspected acute PE? First, anticoagulant therapy is associated with a risk of bleeding. Second, current clinical guidelines suggest indefinite anticoagulation in most of the patients with PE, including patients with a first unprovoked PE [2]. Third, once a diagnostic test has been reported as positive for PE, even if the clinical probability is low and the other tests are negative, the benefit of the doubt makes it difficult for the referring physician not to treat the patient with anticoagulant therapy, an efficient treatment to prevent potentially fatal recurrence. Fourth, once a patient has been treated with anticoagulant therapy for several days or weeks, it is impossible to assert in retrospect whether he actually had a PE or not. Accordingly, nuclear medicine physicians should keep in mind that a false positive lung scintigraphy will mean lifelong anticoagulant therapy and its risks for many patients. In women, other implications of PE diagnosis include daily heparin injections during any subsequent pregnancy and a definitive contraindication to any hormone therapy including the birth control pill.

In a recent editorial, Lu et al. proposed to only perform Q SPECT/CT [3] and to diagnose PE with an even lower diagnostic cut-off ($\geq 50\%$ of a segment) than the threshold commonly used with V/Q SPECT (≥ 1 segment or 2 subsegments

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✉ Pierre-Yves Le Roux
pierre-yves.leroux@chu-brest.fr

¹ Service de médecine nucléaire, CHRU de Brest, EA3878 (GETBO), Université de Brest, CHRU Morvan, Médecine nucléaire, 2 avenue Foch, 29609 Brest Cedex, France

² Department of Medicine, Ottawa Hospital Research Institute, University of Ottawa, Ottawa, Canada

mismatched defects [10, 11]). We believe that this approach exposes the patients to an unacceptably high risk to unduly receive anticoagulant therapy. Zuckier et al. proposed a different approach with a diagnostic algorithm to limit imaging to appropriate patients and minimize performance of ventilation studies [4]. If the perfusion scan does not show segmental defects, the scan is deemed negative for PE. If the perfusion scan demonstrates segmental defects, the scan should be interpreted as indeterminate and the patient referred for alternate testing. We agree with this statement as discussed above. However, a high proportion of COVID-19 patients with respiratory symptoms are unlikely to have a strictly normal perfusion scan. Furthermore, given that most of the COVID-19 patients referred for a lung scan are those with a contraindication to CT pulmonary angiography, the alternative test is likely to be a repeated lung scintigraphy with a ventilation study. Accordingly, especially if there is no shortage of supply of personal protection equipment, we believe that the benefit of omitting the ventilation as the first-line approach should be balanced against the risk of increasing transfers of patients through the healthcare facilities and the number of contact between individuals.

While the risk of contamination due to the inhalation procedure exists and must be taken into account, it can be considerably reduced by appropriate personal equipment. In non-COVID-19 patients, we believe that the benefit-risk ratio definitely does not justify omitting the ventilation, especially in regions with low disease prevalence. In COVID-19 patients, as long as there is no shortage of personal protective equipment for healthcare workers (FFP2 masks, eye protection, gloves, gown), we would also recommend to perform both perfusion and ventilation studies. In any event, reaching diagnostic certainty in every patient with suspected PE should remain the priority, and this implies performing a ventilation scan to confidently conclude to PE diagnosis.

In summary, if a lung scan is required in a patient with suspected PE, we would recommend performing both ventilation and perfusion scintigraphy, with appropriate aerosol precautions for technologists. If for any reason a perfusion SPECT/CT is performed and is positive for PE, the referral physician should be advised of the risk of false positive result.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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