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Full Length Article

Accuracy of X-ray with perfusion scan in young patients with suspected pulmonary embolism

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ABSTRACT

Background: Computed tomography pulmonary angiogram (CTPA) has become the standard test in the diagnostic workup of patients with suspected pulmonary embolism (PE). However, young patients may have an increased risk of cancer with CTPA. Perfusion scanning combined with chest X-ray (X/Q) may offer an adequate alternative, but has never been prospectively validated. We directly compared this strategy with CTPA in patients aged ≤50 years with suspected PE.

Methods: Consecutive patients with a likely clinical probability or an abnormal D-dimer level underwent both CTPA and X/Q. Two trained and experienced nuclear physicians independently analyzed the X/Q-scans. The accuracy of X/Q according to the PISAPED criteria was calculated in terms of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Results: Seventy-six patients were included, with a PE rate of 33%. The inter-observer agreement for X/Q-scan reading was high ($\kappa = 0.89$). After consensus reading, 21 patients (28%) were categorized as 'PE present', 53 (70%) as 'PE absent', and two (2.6%) as 'non-diagnostic'. In 22%, there was a discrepancy between the X/Q-scan and CPTA for the diagnosis or exclusion of PE. The PPV and NPV were 71% and 83%, respectively.

Conclusion: In patients with a high risk of PE, a diagnostic strategy of chest X-ray and perfusion scanning using the PISAPED criteria seems less safe than CTPA. Additional studies should further investigate this diagnostic algorithm.

Introduction

A diagnostic algorithm based on clinical probability, D-dimer, and computed tomography pulmonary angiogram (CTPA) has been shown to be a safe and efficient strategy in the management of patients with suspected pulmonary embolism (PE) [1]. However, concerns have been raised regarding the risk of (breast) cancer following radiation exposure with CTPA [2,3].

Compared to CTPA, breast irradiation with ventilation/perfusion scintigraphy (V/Q-scan) is approximately 50-100 times lower [4–6]. Although V/Q-scan is an established diagnostic test, ventilation scintigraphy is expensive and not available in many hospitals. Also, the proportion of non-diagnostic scan results is around 50%, which limits its use in clinical practice.

Previously, several studies have evaluated whether ventilation lung scanning could be replaced by the chest X-ray in defining a segmental perfusion defect to be matched or mismatched in patients with suspected PE (X/Q-scan) [7–9]. Although the positive predictive value (PPV) of a high probability X/Q-scan was high (86%), the proportions of non-diagnostic test results were still considerable (ranging from 21% to 49%). The use of only perfusion scanning is also supported by the PISAPED group (Prospective Study of Acute Pulmonary Diagnosis) [10]. A retrospective validation of the PISAPED method [9], showed a sensitivity and specificity of 80% and 97%, respectively, compared to CTPA [9]. However, because of the retrospective design, the Q-scans were performed without following the PISAPED protocol. These studies assessed patients without stratification according to pre-test clinical

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probability. Moreover, young patients have less co-morbidity than elderly patients. Consequently, this may improve the diagnostic yield of an X/Q scan in this subgroup of patients [11,12].

The aim of this study was to prospectively investigate the sensitivity, specificity, PPV, negative predictive value (NPV) and the positive and negative likelihood ratio of the X/Q-scan according to the PISAPED criteria in comparison to CTPA in patients aged ≤ 50 years, with suspected PE.

Methods

Patients

The study was a prospective, multi-center cohort study of consecutive in- and outpatients younger than 51 years with suspected PE, who had either a likely clinical probability (according to Wells and/or Revised Geneva Score) [13,14] or an abnormal D-dimer test result [1]. The D-dimer test was considered normal when below 500 μg L^{-1}. Next to the CTPA, a chest X-ray and Q-scan were performed within 24 hours in all participants.

Patients were included in seven academic and non-academic medical centers in the Netherlands and Belgium. Participants were managed according to the outcome of the CTPA, and according to local hospital practice. Exclusion criteria were age < 18 years or > 50 years, pregnancy, use of therapeutic dose LMWH or unfractionated heparin for longer than 48 hours prior to eligibility assessment, thrombolytic therapy and inability to perform a perfusion scan within 24 hrs after CTPA. Demographic data and additional relevant information were collected on a Case Record Form. Institutional ethical review board of all participating centers approved the study protocol and written and oral informed consent was obtained from all included patients.

Although three months follow-up was not performed, we retrospectively evaluated whether PE occurred in patients with a discrepancy between the CTPA and the X/Q scan result.

CTPA

CTPA was the reference standard in this study. All CTPAs were assessed by the radiologist on-call. Standard contrast enhanced CTPAs were performed using a multi-detector row CT-scanner according to state-of-the-art protocols for the diagnosis and evaluation of PE [15]. Patients were scanned during a single breath-hold, in caudocranial direction, from the upper level of the diaphragm to a level slightly above the aortic arch (pitch of 1, 120 kV, 150-200 mAs). One hundred milliliters of contrast was administered intravenously. An imaging delay of 20 seconds was used and overlapping images were reconstructed every 3 mm. PE was confirmed by the presence of a constant intraluminal defect in sub-segmental or more proximal branches of a pulmonary artery.

Perfusion Scintigraphy

Six-view perfusion lung scintigraphy (anterior, posterior, both posterior oblique and both anterior oblique images) was performed within 24 hours of referral following the guidelines of the Society of Nuclear Medicine (SNM 2004) [16]. Images were obtained immediately after the administration of 148-155 MBq of technetium-99 m macroaggregated albumin particles (MAA) after several deep breaths. According to the PISAPED protocol, care was taken to inject the radioactive bolus with the patient positioned in a sitting position in order to preserve the effect of gravity on the regional distribution of pulmonary blood flow [10]. The effective radiation dose varied per MBq dose, ranging from 0.55 – 1.1 mSv.

Chest Radiographs (X)

In examining the chest radiographs, the PISAPED readers considered the size and shape of the heart and hilar arteries, position of the diaphragm, presence or absence of pulmonary parenchymal abnormalities (consolidation, atelectasis, edema), and pleural effusion. Chest radiographs were rated as abnormal if one or more of the following were present: enlargement of the heart or hilar vessels; elevated (hemi-) diaphragm; pleural effusion (including intrafissural liquid); increased lung density (focal or diffuse); pulmonary edema; consolidation suggestive of infarction; emphysema; or fibrothorax.

X/Q-scan

The X/Q- scans were centrally adjudicated according to the PISAPED criteria [10] (Table 1) and compared with the CTPA. For our analysis we used the results of the chest X-ray combined with Q-scan (X/Q-scan). All images at time of the diagnosis were stored on CD-Rom or comparable storage. Two trained and experienced nuclear physicians, who were blinded of clinical information or the CTPA result, analyzed all X/Q-scans, independently. In case of disagreement, a consensus reading was carried out with a third reviewer. In case of abnormalities on the perfusion scan, the findings were combined with the result of the chest radiograph (X/Q-scan). The results of the X/Q scans were stored and interpreted later.

The readers interpreted the Q-scans according to PISAPED criteria (Table 1). Abnormal perfusion scans were classified as 'PE present' when single or multiple wedge-shaped perfusion defects were present, irrespective of abnormalities on the chest X-ray, aiming to reduce the number of non-diagnostic scans. PE was considered as 'PE absent' in case of either no perfusion defects of any kind or perfusion defects which are smaller or equal in size and shape to chest radiograph abnormalities. Also, if the perfusion defects were not wedge-shaped regardless matching chest radiograph abnormalities, X/Q-scan was considered as 'PE absent'. Wedge-shaped areas of overperfusion are usually not seen. In all other cases the X/Q-scan was considered non-diagnostic. These patients would, theoretically, require additional testing (Table 1, criteria adapted from Miniati et al. [10]).

Statistical Analysis

We assumed that the prevalence of PE among patients < 50 years with a 'likely' clinical probability and/or an abnormal D-dimer was approximately 30% [1]. We needed to enrol 200 patients with suspected

Table 1
PISAPED Scintigraphic Criteria (Prospective Study of Acute Pulmonary Diagnosis) [10].

PE present	
Abnormal: PE	One or more wedge-shaped perfusion defects, with or without matching chest X-ray abnormalities. Wedge-shaped areas of overperfusion usually coexist.
PE absent	
Normal:	No perfusion defects of any kind
Near normal:	Perfusion defects smaller or equal in size and shape to the following chest X-ray abnormalities: - cardiomegaly - enlarged aorta, hila and mediastinum - elevated diaphragm blunting of the costophrenic angle - pleural thickening - intrafissural collection of liquid
Abnormal: no PE	Perfusion defects not wedge-shaped with or without matching chest X-ray abnormalities. Wedge-shaped areas of overperfusion are usually not seen
Non-diagnostic	
Cannot classify as PE + or PE-	