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Chapter 2

Value of chest X-ray combined with perfusion scan versus ventilation/perfusion scan in acute pulmonary embolism

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Summary

Background: The main purpose of ventilation scanning, as adjunct to perfusion lung scintigraphy, in acute pulmonary embolism is to allow for the classification of segmental perfusion defects as mismatched, which is generally accepted as proof for the presence of pulmonary embolism. We examined whether this function of the ventilation scan could be replaced by the chest X-ray.

Methods: We analyzed retrospectively data of 389 consecutive patients with suspected pulmonary embolism and at least one segmental perfusion defect we classified the ventilation/perfusion (V/Q) scan and chest X-ray/perfusion (X/Q) scan as either mismatched (presence of at least one mismatched perfusion defect) or matched. Furthermore we analyzed whether this comparison was different in subgroups of patients with concomitant congestive heart failure or chronic obstructive pulmonary disease.

Results: Overall agreement between the X/Q and V/Q scan diagnostic category was found in 341 of 389 patients (88% ; 95% CI 84-92%). The positive predictive value for obtaining a mismatched V/Q scan result in case of a mismatched X/Q scan result was 86% (95% CI 81-90%). If the X/Q scan yielded only matched defects the V/Q scan resulted in the same classification in 90% (95% CI 85-95%). Analysis of the small subgroup of patients with chronic obstructive pulmonary disease showed that a mismatched X/Q scan was confirmed by V/Q scanning in 21 of 34 cases (62% ; 95% CI 45-78%).

Conclusion: This study shows that in the great majority of patients with clinically suspected acute pulmonary embolism combination of chest X-ray with perfusion scintigraphy reliably replaced ventilation/perfusion scintigraphy in defining (mis)matching of segmental perfusion defects. These results need confirmation before the chest X-ray can fully obviate the use of ventilation scintigraphy.

Introduction

Patients presenting with clinically suspected acute pulmonary embolism remain a diagnostic challenge. The annual incidence of suspected pulmonary embolism has been estimated to be approximately 2-3 per 1000 inhabitants (1,2). Clinical assessment remains the initial step in identifying patients with possible acute pulmonary embolism. However, objective diagnostic tests are necessary to establish or refute the diagnosis (3,4).

Lung perfusion scintigraphy is generally accepted as the appropriate first test in the diagnostic management of patients presenting with suspected pulmonary embolism. A normal perfusion scan, which may be found in up to 30% of patients, rules out clinically important pulmonary embolism. In those patients with at least one segmental perfusion scan defect, ventilation lung scintigraphy is indicated, since a mismatch (normal ventilation at the site of the perfusion defect) adequately predicts the presence of acute pulmonary embolism in approximately 90% of patients (5,6). Such mismatches, also called a high probability scan result, are present in approximately 20% of patients with suspected pulmonary embolism (7). The remaining 50% of patients with other ventilation/perfusion (V/Q) scan findings require further diagnostic tests, such as follow-up ultrasound of the lower extremities and/or pulmonary angiography.

Although ventilation scintigraphy is a valuable tool in the diagnostic management of pulmonary embolism it has several important disadvantages. These include the high cost of the tracer and the usually non-daily availability in most hospitals.

We determined whether the chest X-ray could replace ventilation lung scanning in defining a segmental perfusion defect to be matched or mismatched in patients with suspected pulmonary embolism. We therefore studied retrospectively a large series of consecutive patients and compared the classification by V/Q scintigraphy and chest X-ray/perfusion (X/Q) scintigraphy. In addition we analyzed whether this comparison was different in subgroups of patients with concomitant congestive heart failure or chronic obstructive pulmonary disease.

Patients and Methods

Patients

Consecutive patients with clinically suspected pulmonary embolism seen at the Sophia Hospital Zwolle, the Netherlands (in 1993 and 1994) or the Academic Medical Center, Amsterdam (April 1991 to March 1994) were eligible for the study. All underwent perfusion lung scanning within 24 hours of presentation. The present analysis was limited to those patients with at least one segmental perfusion defect and in whom the chest X-ray was made within 48 hours of the lung scintigraphy. Clinical characteristics and risk factors for pulmonary embolism were recorded in all patients.

Lung scintigraphy

Perfusion scans were obtained with ^{99m}Technetium macroaggregated albumin. Ventilation scans were performed using ^{81m}Krypton gas. After obtaining images in six directions the V/Q scan was classified as either mismatched (defined as one or more segmental perfusion defects with locally normal ventilation) or matched (no segmental mismatch present).

The chest X-ray (postero-anterior and lateral view in all patients) was interpreted by a radiologist unaware of the results of the V/Q scan and any abnormalities, such as pleural effusion, atelectase, tumor or parenchymal areas of increased density were recorded with reference to the anatomical location. Subsequently, the findings on perfusion scan were combined with the result of the chest X-ray (X/Q scan) and the same classification was used as described above for the interpretation of the V/Q scan. If a classification was not possible due to imprecise defect localization, the perfusion scan and/or chest X-ray were independently reread by one observer.

Overall agreement between the two assessments in the categories matched and mismatched, as well as the positive predictive value of the X/Q scan were calculated. The positive predictive value was defined as the proportion of all patients with mismatched X/Q scan findings, who had pulmonary embolism as defined by a mismatched V/Q scan. Values were calculated for the total study group, as well as separately for subgroups with known congestive heart failure or chronic obstructive pulmonary disease, using the New York Heart Association (NYHA) (8) and criteria of the European Respiratory Society (9), respectively. In addition, an analysis was performed restricting data only to patients in which the time between chest X-ray and V/Q scan was less than 24 hours.

Results

A total of 466 patients had at least one segmental defect on the perfusion scan. Seventy-four patients were excluded because the chest X-ray was not performed within 48 hours of lung scintigraphy. In two patients no ventilation scan was obtained and in one patient the chest X-ray was not available. Thus, data from 389 patients were analyzed. The clinical characteristics of these patients are shown in Table 1.

Table 1 Clinical characteristics of the 389 study patients with clinically suspected pulmonary embolism and at least one segmental perfusion defect

mean age, range	63	(19-93)
male/female	199/190	
known heart failure	48	(13%)
COPD[1]	67	(17%)
malignancy	112	(29%)
recent surgery[2]	83	(21%)
previous VTE[3]	49	(13%)
none of the above	173	(35%)

[1] COPD = chronic obstructive pulmonary disease

[2] within 3 months of presentation

[3] VTE = Venous Thromboembolism

Overall agreement for the diagnostic categories between the X/Q and V/Q scan was observed in 341 of 389 patients (88% ; 95% CI 84-92% , Table 2). In case the X/Q scan result indicated a mismatched defect (i.e. a high probability scan), the positive predictive value for obtaining a mismatched defect by V/Q scanning was 86% (95% CI 81-90%). If the X/Q scan revealed a matched defect, V/Q scanning resulted in the same classification in 90% (95% CI 85-95%) of the patients. Restricting data only to patients (81% of the total study cohort) in which the time between chest X-ray and

Table 2 Comparison of Ventilation/Perfusion scintigraphy with chest X-ray/Perfusion scintigraphy in defining matched or mismatched segmental perfusion defects in 389 patients.

		Ventilation/Perfusion scan		
		mismatch	match	total
Chest X-ray / Perfusion scan	mismatch	199	33	232
	match	15	142	157
	total	214	175	389

- overall agreement: 341/389 = 88% (95% CI 84% - 92%)
- positive predictive value: 199/232 = 86% (95% CI 81% - 90%)

Table 3 Ventilation/Perfusion scintigraphy versus chest X-ray/Perfusion scintigraphy in defining matched or mismatched segmental perfusion defects in the subgroup of 67 patients with concomitant chronic obstructive pulmonary disease.

		Ventilation/Perfusion scan		
		mismatch	match	total
Chest X-ray / Perfusion scan	mismatch	21	13	34
	match	1	32	33
		22	45	67

- overall agreement: 53/67 = 79% (95% CI 67% - 88%)
- positive predictive value: 21/34 = 62% (95% CI 45% - 78%)

lung scanning was less than 24 hours, showed a similar overall agreement and positive predictive value (data not shown).

Concurrent chronic obstructive pulmonary disease was present in 67 of the 389 patients with suspected pulmonary embolism and at least one segmental perfusion defect. Analysis of the diagnostic value of the chest X-ray in this subgroup showed that in 13 of 34 mismatched X/Q scans the V/Q scan revealed matched defects which results in a decrease in positive predictive value from 86% to 62% (95% CI 45-78% , $p < 0.05$) ; Table 3). Excluding patients with chronic obstructive pulmonary disease from the overall study cohort resulted in a small increase of positive predictive value from 86% to 90% (since patients with chronic obstructive pulmonary disease constituted only 15% of mismatched X/Q scans). In 36 patients with congestive heart failure, comparison of X/Q and V/Q scan yielded similar results as in the overall study group (positive predictive value 94% , 95% CI 70-100%).

Discussion

The main purpose of ventilation scanning in the diagnostic work-up of patients with suspected acute pulmonary embolism is to allow for the classification of segmental perfusion defects as mismatched, which is generally accepted as proof for the presence of pulmonary embolism (3-6). However, its high cost and non-daily availability in many hospitals hamper the application of ventilation scanning. In this study in 389 consecutive patients with suspected pulmonary embolism we showed that the combination of perfusion scanning and chest X-ray can reliably replace the V/Q scan in defining segmental perfusion defects as mismatched, i.e. as a high-probability scan for the presence of pulmonary embolism (positive predictive value 86% ; 95% CI 81-90% Table 2). This appears applicable to the wide variety of patients presenting with suspected pulmonary embolism, with the possible exception of those with known chronic obstructive pulmonary disease in whom the classification by X/Q scanning is less reliable then V/Q scanning (positive predictive value 62% , Table 3).

Our findings are in agreement with a small previous study by Stein and colleagues (10). They compared the diagnostic accuracy of V/Q scanning and X/Q scanning in 98 randomly selected patients with suspected pulmonary embolism in whom the gold standard, pulmonary angiography, was performed. The positive predictive value of a

segmental mismatched V/Q or X/Q test result were both high and fully comparable (94% and 93% respectively), indicating a similar clinical utility. Miniati et al. showed that a diagnosis of pulmonary embolism could be made accurately purely relying on the presence of a single or multiple wedge-shaped perfusion defects, while the result of both the ventilation scan and chest X-ray were unknown to the investigator interpreting the perfusion scan (11). Although this is an interesting concept, confirmation by other groups have to be awaited. Furthermore, since the chest X-ray will be available in nearly all cases, the clinician will likely compare the perfusion defects with the chest X-ray.

Several issues regarding the design of our study should be addressed. To avoid selection in this retrospective analysis we included the complete data set of consecutive patients seen during the study period in the two teaching hospitals. Only 17% of the initial cohort had to be excluded, mainly because the chest X-ray was performed more than 48 hours before the combined V/Q scan was obtained. The clinical characteristics of these patients were similar to those included in the analysis. We minimized bias in the interpretation of the X/Q and V/Q scans using a priori defined criteria for mismatched defects. We purposely compared X/Q with V/Q scanning and not with pulmonary angiography since a segmental mismatched V/Q scan defect is generally accepted to indicate the presence of pulmonary embolism and justifies anticoagulant treatment (5). Consequently, we cannot relate the X/Q and V/Q findings to the gold standard, pulmonary angiography, and therefore cannot determine the accuracy of either test in predicting the presence of pulmonary embolism in our study cohort. However, discrepancies between X/Q and V/Q scan findings were present in only 12% of the total study cohort, thus pulmonary angiography would not likely have influenced our conclusion that X/Q scan and V/Q scan perform equally in predicting prescence or absence of pulmonary embolism. We, therefore, believe that our findings are valid.

What are the potential clinical implications of our study results? The consequences of a diagnostic management strategy based on the X/Q scan instead of the V/Q scan can be addressed by focussing on the clinical outcome of the small number of patients with discrepancy in test results. In our study the 15 patients (4% of all study subjects) in whom the X/Q scan resulted in matched defects, whereas the V/Q scan classified them as mismatched, are of limited concern because further diagnostic work-up (i.e. pulmonary angiography) is recommended in cases with matched scan defects which

will lead to a definitive diagnosis. The 33 patients (8% of all study subjects) diagnosed by X/Q scan to have pulmonary embolism, while the V/Q scan indicated matched defects, may raise more concern since they would have been treated with anticoagulants if the X/Q scan was used to diagnose pulmonary embolism. The use of the X/Q scan to diagnose pulmonary embolism cannot be advocated in patients with chronic obstructive pulmonary disease, because of the low correlation of a mismatched X/Q scan with a mismatched V/Q scan (Table 3). Furthermore, it should be realized that approximately a quarter of patients with matched V/Q scans still have pulmonary embolism revealed by pulmonary angiography (5). Thus, when treatment decisions are based on the X/Q scan instead of the V/Q findings, excluding patients with chronic obstructive pulmonary disease, this would result in an increase of unnecessary treatment in at most 4% of all patients, which, in the setting of the diagnosis of pulmonary embolism is acceptable in our opinion. This approach would be feasible in many hospitals and would be cost-effective. The addition of other non-invasive diagnostic tests to this approach, such as D-dimer testing (12-14) and clinical assessment (13) may further improve the diagnostic accuracy.

In conclusion, this study shows that the combination of chest X-ray with perfusion scintigraphy can reliably replace ventilation/perfusion scintigraphy in defining (mis)matching of segmental perfusion defects in patients with clinically suspected acute pulmonary embolism. Concomitant chronic obstructive pulmonary disease appears to be a pitfall in defining a high-probability X/Q scan. Although a diagnostic strategy without ventilation scintigraphy is attractive, prospective (multi-center) studies must confirm our study results before this strategy can be advocated in general practice.

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