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Pleural Effusion and Ventilation/Perfusion Scan Interpretation for Acute Pulmonary Embolus

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This study was conducted to determine if pleural effusion size affects ventilation/perfusion (V/Q) scan interpretation algorithms for acute pulmonary embolus (PE). **Methods:** Retrospective analysis identified 163 consecutive patients undergoing angiography for PE with radiographic evidence for pleural effusion. V/Q scanning was performed in 94 (58%) of cases and reported using original Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria. Effusions were classified as small, large and/or bilateral. Radiographic and scintigraphic results were correlated with regard to size and location of abnormalities. **Results:** Of the 163 patients, 57 (35%) had angiographically-proven PE, 77 (47%) had at least one large pleural effusion and 86 (53%) had a small effusion; 33 (43%) with large effusions and 24 (28%) with small effusions had emboli at angiography. Thirty-six of 119 patients (30%) with clear chest radiographs (a control group) had PE. Thus, large effusions were associated with a higher incidence of PE than those with small effusions or clear lungs ($p < 0.05$). Of those with V/Q scanning, 26 of 94 (28%) had a solitary large effusion, with 12 (46%) positive for emboli. V/Q-matched abnormalities limited to effusion size were found in 16 with a solitary large effusion and 10 with a solitary small effusion. In both groups, 50% were angiographically positive for emboli. Twenty-three (66%) of 35 with bilateral effusions had corresponding V/Q-matched defects at one ($n = 11$) or both ($n = 12$) lung bases, and 9 (39%) were positive for emboli. In total, 45% with a V/Q-matched defect of equivalent size to the effusion were angiographically positive for PE. **Conclusion:** Pulmonary emboli are associated with pleural effusions of all sizes. Matched V/Q defects corresponding to radiographically-evident pleural effusions are of intermediate probability for PE. Thus, revision of the traditional lung scan interpretive criteria based upon pleural effusion size is not warranted.

Key Words: pulmonary embolus; ventilation/perfusion scan; pleural effusion

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The association between pulmonary emboli (PE) and pleural effusions has long been known. In two large series, approximately 50% of those with proven pulmonary emboli had a pleural effusion (*1,2*). However, the role this radiographic finding plays in the interpretation scheme for the ventilation/perfusion (V/Q) scan is less well defined. Traditionally, any radiographic abnormality, including an effusion, that is comparable in size to matched perfusion and ventilation defects renders the region (and in most cases the V/Q scan) indeterminate for pulmonary embolism (*3*). Bedont and Datz (*4*), however, noted that only 2 of 53 (4%) patients with matched V/Q defects in the region of a pleural effusion had documented thromboembolic disease. They, therefore, concluded that such defects should be considered of low probability for PE. Recently, based upon reanalysis of Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) trial data, several authors have suggested that the size of the pleural effusion and its associated matched defect can influence the interpretation of the V/Q scan (*5*). In this new scheme, large effusions are associated with a low probability of PE and small effusions (defined as costophrenic angle blunting) are associated with an intermediate chance of embolism. A pleural effusion is not relevant if it does not cause an associated perfusion defect. Preliminary data from our recent study on chest radiograph findings and their effect on V/Q scan interpretation did not support this revision (*6*). This study was conducted to determine if pleural effusion size correlates with the presence of emboli, and to verify if effusion size alters V/Q scan interpretation.

METHODS

Patients

A retrospective search identified all consecutive patients undergoing pulmonary angiography for the indication of pulmonary embolism between January 1, 1990 and December 31, 1992 at our institution ($n = 622$). During this time period, 2,544 ventilation/perfusion scans were performed for detection of pulmonary emboli. In every case of pulmonary angiography, images were obtained of both lungs separately in the anteroposterior projection. When these views were initially negative, magnification views were obtained of the lung bases in the oblique projection. The results of angiography were used as the gold standard for the presence or absence of emboli.

All patients had either posteroanterior or anteroposterior chest radiographs within 24 hr of angiography. Based upon the written

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formal interpretation of these chest radiographs, 304 cases (49%) were noted to have either clear lungs (n = 119) or pleural effusion(s) (n = 185) as the sole radiographic abnormality. Of the 185 radiographs with reported pleural effusion, 22 cases (12%) were not included in the study. Eleven were excluded for technical reasons, most often for non-upright positioning of the chest radiograph. In 5 cases superimposed air-space disease was noted; and in 6 cases the radiograph could not be located. The remaining 163 upright, frontal radiographs were reinterpreted under blinded conditions by one investigator (SNG) to assess the amount of fluid present. Since it is well recognized that the size of a pleural effusion cannot be measured accurately on a chest radiograph, these radiographs were subdivided into only two groups: (a) effusions limited to costophrenic angle blunting (no higher than the 1 cm below the dome of the diaphragm) and (b) larger effusions. If the diaphragm was not seen secondary to pleural effusion, the radiograph was placed in the latter category. This method is similar to that used by the PIOPED investigators (*7*). In addition, the location of the effusion was noted as left, right or bilateral. For purposes of analysis, cases with both a small and a large effusion (i.e., bilateral) were classified as having large pleural effusions.

Patients in each effusion category were further subdivided according to the results of a ventilation/perfusion (V/Q) scan performed within 48 hr of angiography (n = 94; 58%). At our institution, all technically adequate V/Q scans are interpreted by a staff nuclear physician with results reported as normal, low, intermediate/indeterminate or high probability for pulmonary embolus using the original PIOPED study group criteria (*6*). Ventilation is assessed using ^{133}Xe rebreathing techniques, and perfusion is measured using ^{99m}Tc-labeled macroaggregated albumin with images acquired in multiple projections. All V/Q scan reports were reviewed to ensure adherence to the PIOPED classification based upon radiographic, ventilation and perfusion findings. In six cases (6%), V/Q scans were reviewed for objective findings (i.e., the site or size of a perfusion defect) because these were not clearly described in the report.

Radiographic and scintigraphic results were correlated with regard to size and location of abnormalities. Angiographic results demonstrated the presence or absence of pulmonary embolism in each case. Standard parametric methods of statistical analysis were used as appropriate to compare the groups.

RESULTS

Overall Study Population

Of the 163 patients with pleural effusions, 77 (47%) had at least one large pleural effusion and 86 (53%) had a small effusion. Of all patients with a pleural effusion, 57 (35%) had angiographically-proven evidence for pulmonary embolism anywhere in the lungs. Thirty-three (43%) of those with large effusions and 24 (28%) with small effusions had demonstrable emboli at angiography. Only 4 (3%) had an effusion that was larger than one third of the hemithorax, with only 1 (25%) positive for pulmonary embolism. By comparison, 36 of the 119 (30%) with clear chest radiographs had pulmonary embolism. Thus, a significantly greater percentage of those patients with a large pleural effusion had emboli than did those with either a small effusion ($p < 0.05$) or a normal chest radiograph ($p < 0.05$). No statistical difference was achieved between the small effusion and the clear chest radiograph groups. Similar differences were noted between the large and small effusion groups when patients with bilateral effusions were separated for analysis (Table 1).

TABLE 1
Percentage with Pulmonary Emboli by Effusion Type and Size

Type	N	Positive for PE	%
Solitary large	51	21	41
Solitary small	51	16	31
Bilateral large	26	12	46
Bilateral small	35	8	23
All effusions	163	57	35
Normal CXR	119	36	30

CXR = chest x-ray.

Specific Association of Pleural Effusions with Emboli

Thirty-three (58%) of the 57 patients with both pleural effusion(s) and pulmonary emboli had emboli shown angiographically to be limited to one lung; 12 (36%) had an effusion limited to the side of the embolus; 9 (27%) had an effusion on the opposite side only; and 12 (36%) had bilateral effusions. Of the 24 cases in which angiography identified bilateral pulmonary emboli, 9 (37%) had left-sided effusions, 7 (29%) had right-sided effusions and 8 (33%) had bilateral effusions. Chi-square analysis failed to demonstrate a difference in distribution of pleural effusion between this group and that with no angiographic evidence for pulmonary embolus ($p > 0.25$). Of the latter group (n = 106), 42 (39%) had left-sided effusions, 23 (22%) had right-sided effusions and 41 (38%) had bilateral effusions. Thus, the radiographic location of the pleural effusion could not predict the pattern or location of embolism with any degree of certainty.

Correlation with V/Q Scanning

Ninety-four of the 163 patients (58%) with pleural effusion had V/Q scans. Nine (10%) were interpreted as showing a high probability, 69 (73%) an intermediate probability and 16 (17%) a low probability for pulmonary embolus. Angiographic correlation revealed that among these patients 8 (89%) of high probability, 30 (44%) of intermediate probability and 0 (0%) of low probability V/Q scans had proven pulmonary emboli. Of all 94 patients, 26 (28%) had a large effusion on only one side and 12 (46%) of these were positive for emboli. Thirty-three (35%) had a small effusion on only one side and 13 (39%) of these were positive for PE. Of the 35 with bilateral effusions, 13 (37%) had pulmonary emboli. The percentage positive for pulmonary emboli in those who underwent V/Q scanning was only slightly higher than the total population, and this difference did not approach statistical significance ($p > 0.25$). Regardless, in this smaller sample, statistical significance was not achieved for the difference in the rate of emboli among those with large, small or bilateral effusions.

Of the 94 patients, 58 (62%) had a matched V/Q defect corresponding to the radiographic size of at least one pleural effusion. Sixteen (62%) of those with a solitary large pleural effusion and 10 (30%) with a solitary small pleural effusion had only one V/Q-matched defect limited to the size of the effusion. In both the large and small effusion groups, 50% (8 and 5 cases, respectively) were angiographically positive for emboli. Twenty-three (66%) of 35 patients with bilateral effusions had only corresponding V/Q-matched defects at one (11 patients) or both (12 patients) lung bases. Nine (39%) of these were positive for emboli. In total, 22 of 49 (45%) with a V/Q-matched defect associated with a pleural effusion as the only radiographic abnormality were positive for pulmonary embolism. For all groups, 6 of 9 (67%) with the matched defect and a second segmental unmatched defect, and 10 of 18 (53%) with a

TABLE 2
Association of V/Q Findings, Pleural Effusions and Angiographically-Proven Pulmonary Emboli (n = 94)

Findings	No.	%	Pulmonary embolus		
			Positive	Negative	% Positive
Large solitary effusion	26	28	12	14	46
Solitary matched V/Q defect	16	62	8	8	50
Matched and other V/Q defect(s)	4	15	3	1	75
Unmatched V/Q defect on same side	1	4	0	1	0
Unmatched V/Q defect on opposite side	2	8	1	1	50
Bilateral unmatched V/Q defects	0	0	0	0	0
No moderate or large perfusion defects	3	12	0	3	0
Small solitary effusion	33	35	13	20	39
Solitary matched V/Q defect	10	30	5	5	50
Matched and other V/Q defect(s)	5	15	3	2	60
Unmatched V/Q defect on same side	2	6	1	1	50
Unmatched V/Q defect on opposite side	6	18	4	2	67
Bilateral unmatched V/Q defects	1	3	0	1	0
No moderate or large perfusion defects	9	27	0	9	0
Bilateral effusions	35	37	13	22	37
Unilateral matched V/Q defect	11	31	4	7	36
Bilateral matched V/Q defects	12	34	5	7	45
Unmatched V/Q defects	6	17	4	2	67
No moderate or large perfusion defects	6	17	0	6	0

solitary, unmatched segmental defect had pulmonary emboli at angiography. None of the 18 patients with normal perfusion studies had pulmonary emboli. Further breakdown of this analysis is provided in Table 2.

DISCUSSION

This study demonstrates that larger pleural effusions are associated with at least an equal incidence of pulmonary embolism than those with smaller effusions. The comparison group of patients with unremarkable chest radiographs had a rate of embolism similar to that of the small effusion group. Although pulmonary emboli were found in a substantial fraction of those with pleural effusion who underwent pulmonary angiography (36%), this study is based on a select population in which clinical suspicion for embolism was high, based upon other objective clinical findings. Hence, this study should not be interpreted as supporting a diagnostic evaluation for pulmonary embolism when pleural effusion is the only objective finding.

In the recent PIOPED trial, the sensitivity and specificity for a pleural effusion associated with pulmonary emboli were 34% and 70%, respectively (*8*). In our study, the pleural effusion did not occur on the same side as the pulmonary emboli in one-third of the cases. It is therefore likely that the finding of embolism in the presence of effusion is often unrelated to a common pathophysiology. Although pulmonary emboli and infarcts have been shown to cause pleural effusions, they may not be the primary cause of this finding in most patients undergoing V/Q scanning.

Several previous reports have shown that pleural effusions associated with emboli are usually, but not always, unilateral and small (*1,2*). However, in this study, bilateral effusions were present in 25% of patients who were positive for pulmonary emboli and the larger effusion group was associated with a greater incidence of thromboembolic disease than those with a small pleural effusion. Differences in experimental design and terminology such as "costophrenic angle blunting" (which is both imprecise and not standardized) may limit the ability to compare individual studies. It is also well known that effusion volume correlates poorly with the apparent effusion size on the frontal chest radiograph (*9*). Despite this multitude of conflicting reports, it remains clear that pulmonary emboli can be seen with all types of effusions. From the diagnostic perspective, the cause and size of the pleural effusion is a secondary consideration. Of greater importance is that the pleural effusion, by altering both ventilation and perfusion scans, can interfere with scintigraphic diagnosis of pulmonary embolism. Thus, emphasis should be placed on creating a reproducible and accurate interpretive scheme for V/Q defects seen in the presence of effusion.

In this study, the presence of a pleural effusion was not invariably associated with V/Q scan abnormalities. A V/Q-matched defect corresponding to the effusion was seen only 61% of the time. These defects can be caused by loculated fluid, compressive atelectasis or emboli. It is not surprising that no emboli were seen on angiography in many (55%) of these patients. In 19%, usually in the small pleural effusion category, no perfusion defect was noted in the region of the effusion. In these cases, it is likely that the effusion was free flowing and layered posteriorly during the recumbent perfusion scan. As a result, no perfusion defect was detected and the study was interpreted as low probability for embolism.

Our findings are not in accord with the observation of the PIOPED study group—that 11% of solitary V/Q-matched defects associated with a large effusion and 25% associated with costophrenic angle blunting were associated with pulmonary embolism (*7*). Based upon these results, several authors have independently recommended reclassifying matched defects associated with large effusions as low probability for embolism and those associated with small pleural effusions as intermediate probability (*5*). In our study, 50% of matched V/Q defects corresponding to a solitary pleural effusion were positive for pulmonary embolism, regardless of effusion size. Further, 45% of cases with a matched V/Q defect associated with pleural effusions as the only radiographic abnormality were positive for pulmonary emboli. Our findings support the traditional approach of classifying matched defects associated with a pleural effusion as intermediate probability for pulmonary embolism, as originally postulated by the PIOPED investigators, and as had been standard in earlier interpretive schemes (*3*).

The discrepancy in results between this study and PIOPED may lie in the small number of cases with solitary matched defects associated with pleural effusions in the PIOPED trial. In

the PIOPED trial, only 27 cases of V/Q-matched defects associated with pleural effusion as the sole radiographic and scintigraphic abnormalities were identified. Data from patients where bilateral effusions were seen on the chest radiograph and where perfusion defects were visualized away from the costophrenic angles when effusions were present are not discussed per se in the reports of the PIOPED investigators. Given these limitations, the PIOPED investigators initially warned that their findings concerning the modification of traditional interpretive schemes based upon effusion size required verification (*7*). Our slightly larger series does not confirm the initial findings.

A distinction must be drawn between the nature of the PIOPED study and our own. The current study is retrospective in nature and incurs all of the biases such studies entail. However, although the PIOPED trial was prospective in design, significant institutional variation in patient recruitment (33–70%) and obtaining of angiograms (64–92%) was reported (*10*). Thus, during the PIOPED study time frame, less than 50% of those eligible for enrollment actually underwent pulmonary angiography. While 39% of those in the PIOPED study had intermediate probability lung scans, those who refused or were ineligible for the study had intermediate probability scans in 22% of cases. This difference was significant ($p < 0.01$), and suggests some bias in the PIOPED trial as well.

In the present series, 45% of those with a solitary V/Q-matched defect accompanied by a pleural effusion had evidence for embolism. This represents a significantly greater percentage of thromboembolic disease than reported by Bedont and Datz (*4*). Yet, in their series, less than one-third of patients underwent pulmonary angiography, with diagnosis based in a majority of cases upon thoracentesis results or other clinical findings. Brown et al. (*11*), however, has strongly questioned the value of thoracentesis in the diagnosis of pulmonary embolism. Biello et al. (*3*) and Worsley et al. (*12*) have reported, in two large studies, that matched V/Q defects that correspond in size to all types of radiographic abnormalities are associated with a 26% chance of pulmonary embolism. Perhaps our higher incidence is due to selection bias, limiting the population to only those with effusions, different techniques of pulmonary angiography or sample size.

CONCLUSION

Pulmonary emboli are associated with pleural effusions of all sizes. Matched V/Q defects corresponding to radiographically evident pleural effusions are of intermediate probability for PE. Our data suggest that revision of the PIOPED criteria based upon pleural effusion size is not warranted.

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Small Perfusion Defects in Suspected Pulmonary Embolism

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The purpose of this investigation was to assess the diagnostic value of 1 to 3 versus >3 small subsegmental defects on perfusion lung scans of patients with suspected acute pulmonary embolism (PE). **Methods:** Data from the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) were evaluated from patients with suspected acute PE. Angiograms, follow-up data and outcome classifications were used to determine PE status. The perfusion scan of included patients showed only small subsegmental defects (<25% of a segment) in the presence of a regionally normal chest radiograph. Findings on the ventilation scan were irrelevant. **Results:** The positive predictive value for PE of perfusion lung scans with 1–3 small subsegmental defects was 1% to 3%, depending on the group analyzed. The positive predictive value for PE of perfusion lung scans with >3 small subsegmental defects was 11% to 17% depending on the group analyzed. **Conclusion:** Perfusion lung scans with 1–3 small subsegmental defects satisfy the criterion for a very low probability (<10% positive predictive value) for PE and perfusion lung scans with >3 small subsegmental defects satisfy the criteria for a low probability (<20% positive predictive value) for PE.

Key Words: pulmonary embolism; ventilation/perfusion lung scan; thromboembolic disease

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Criteria for a low-probability interpretation of ventilation/perfusion (V/Q) lung scans in the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) included small segmental perfusion defects (<25% of a segment) with a normal regional chest radiograph (*1*). If the only scintigraphic

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