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Evaluation of Individual Criteria for Low Probability Interpretation of Ventilation-Perfusion Lung Scans

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The purpose of this investigation was to identify characteristics or combinations of characteristics of the ventilation-perfusion (V/Q) scan in patients with suspected acute pulmonary embolism (PE) that can be used for a "very low probability" interpretation (<10% positive predictive value). **Methods:** Data were culled from individual lungs of 532 patients in the randomized arm of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study and 205 patients in the referred arm. All patients had a <20% consensus probability estimate of PE based on V/Q scan results, and all underwent pulmonary angiography. **Results:** Nonsegmental perfusion abnormalities, perfusion defects smaller than opacities on the chest radiograph, a combination of these types of perfusion abnormalities, and matched V/Q abnormalities in two or three zones of a single lung had a positive predictive value < 10%. These criteria can therefore be used for a very low probability interpretation. A matched V/Q defect in only one zone of the lung had a positive predictive value greater than 10% and is not a criterion for very low probability classification but can be considered a criterion for low probability. Perfusion defects associated with small pleural effusions (obliteration of the costophrenic angle) had a positive predictive value of 25%–33%, depending on the group studied, and are a criterion for intermediate probability. **Conclusion:** Criteria appropriate for very low probability (<10% positive predictive value) interpretation of V/Q scans in patients with suspected acute PE have been identified.

Key Words: pulmonary embolism; thromboembolism; ventilation-perfusion lung scans

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The criteria for the interpretation of low probability ventilation/perfusion (V/Q) lung scans in patients with suspected acute pulmonary embolism (PE) used in the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study (*1*) have been modified since the conclusion of PIOPED (*2*) (Table 1). The Nuclear Medicine Working Group of PIOPED (*2*) recommended that the following modifications be made for low probability interpretations:

1. A single moderate mismatched perfusion defect should be categorized as intermediate rather than as low probability.
2. Multiple and relatively extensive matched ventilation/perfusion abnormalities are appropriate for low probability, provided that the chest radiograph is clear.
3. Single matched defects may be better and categorized as intermediate probability, although this cannot be definitely validated statistically.

These revised PIOPED criteria were recently tested and found to be more accurate than the original PIOPED criteria (*3*).

The modifications of the PIOPED criteria for low probability were made on the assumption that patients with low probability interpretations of V/Q scans should have a positive predictive value of PE < 20% (*2*). The PIOPED Nuclear Medicine Working Group indicated that, "further analysis which includes combined patterns may define other subgroups of patients who have a V/Q match and a higher frequency of PE."

In the present study, we evaluated individual characteristics and combinations of characteristics of the low probability V/Q lung scan to identify criteria that can be used for a very low probability interpretation (<10% positive predictive value). This classification is more useful than a low probability interpretation, which, has a positive predictive value of 20% or higher (*4*).

MATERIALS AND METHODS

Patients

Data from the PIOPED study were evaluated from patients with suspected acute PE in whom the diagnosis was made or excluded by pulmonary angiography (*1*). We evaluated data from two arms of the PIOPED study: (a) those patients with suspected PE who were randomized for obligatory pulmonary angiography provided their V/Q lung scans were abnormal and (b) those with a suspicion of PE who were referred for angiography only at the request of their physicians. We defined the first group as the "randomized group." The randomized group plus patients referred for angiography were defined as the "combined group." Only the randomized group was included in the original PIOPED report (*1*). The methods for obtaining V/Q scans and pulmonary angiograms have been previously described (*1*).

To expand the useful database, we evaluated individual lungs rather than individual patients. Lungs were excluded if they showed any mismatched perfusion defects or pleural effusions larger than obliteration of the costophrenic angle. Pulmonary angiograms were obtained in each lung evaluated to determine the presence or absence of acute PE in that lung. In PIOPED, lung zone was defined as the upper, middle or lower third of the lung divided in the cranial-caudal direction without regard to lung volume (*5*).

Very low probability for PE was defined as a positive predictive value of less than 10% among patients in both the randomized and combined groups. A criterion for a low probability V/Q scan was a positive predictive value of 10%–19% for PE in one or both groups. Intermediate probability for PE was defined as a positive predictive value of 20%–79% in either group.

TABLE 1
Revised PIOPED Criteria for Low Probability V/Q Lung Scans*

Nonsegmental perfusion defects (e.g., very small pleural effusion causing obliteration of the costophrenic angle, cardiomegaly, enlarged aorta, hila and mediastinum, and elevated diaphragm).
Any perfusion defect substantially smaller than associated abnormality on the chest radiograph.
Matched ventilation/perfusion abnormalities, provided that the chest radiograph is clear.
Small segmental perfusion defects (<25% of a segment) with normal findings on the chest radiograph.

*Criteria based on recommendations of the PIOPED Nuclear Medicine Working Group after retrospective evaluation of the PIOPED data (*1,2*).

Intergroup Comparisons

We analyzed the lungs of patients from the randomized and combined groups who had a consensus probability estimate of PE of ≤20% ("consensus low probability" scans). The V/Q scans of patients in this group were evaluated by two members of the PIOPED Nuclear Medicine Working Group (*1,5*) who were responsible for providing the final V/Q computerized description subsequently entered into the PIOPED database (*5*). By assessing the intuitive percent probability of PE as ≤20%, they indicated their belief that the V/Q scan suggested low probability for PE. There were 513 patients in the randomized group with consensus low probability scans; there were 718 patients in the combined group with consensus low probability scans.

We performed subgroup analyses on the lungs of patients with consensus low probability V/Q scans who were stratified according to the presence or absence of prior cardiopulmonary disease. Information about prior cardiopulmonary disease was available for 513 patients in the randomized group with consensus low probability V/Q scans and in 718 patients in the combined group with such V/Q scans. Previous experience among patients with high probability assessment of the V/Q scan showed that different diagnostic criteria can be applied to each stratified group (*6*).

Abnormalities Assessed on V/Q Scans

V/Q scan abnormalities assessed alone or in combination include:

1. Small pleural effusion causing obliteration of the costophrenic angle, in which the perfusion defect is less than or equal to the radiographic defect.
2. Nonsegmental perfusion defects where perfusion defect is less than or equal to the radiographic defect. These include: enlarged mediastinum, enlarged heart, enlarged hilum and an elevated diaphragm.
3. Parenchymal defect on the chest radiograph where the perfusion defect is less than the radiographic abnormality. These include: opacity, linear opacity, atelectasis, pleural abnormality, radiolucencies and diffuse lung disease.
4. Matched V/Q abnormalities where the chest radiograph is clear and the perfusion defect is less than or equal ventilation to the defect.

The PIOPED database allowed separate examination of each of three zones (upper, middle, lower) of each lung shown on the V/Q scan (*5*). A matched V/Q abnormality in the presence of a clear chest radiograph may have been present in a single zone or more than one zone. Similarly, a parenchymal abnormality with a perfusion defect smaller than the radiographic defect may have been observed in one to three zones.

One criterion used as an indicator of low probability for acute PE is small (<25% of a segment) mismatched V/Q defects (*7,8*) or such small perfusion defects in the presence of a normal chest radiograph (*1,2*). We were unable to test the PIOPED data for the positive predictive value of this abnormality on the V/Q lung scan

TABLE 2
Positive Predictive Value of Criteria Used for Low Probability Assessment of V/Q Scans in Lungs of Randomized Group Patients

	PE/Total (%)	95% Confidence interval
One perfusion defect		
Type of costophrenic angle effusion (CAE)	3/12 (25)*	5–57
Nonsegmental abnormality (nonseg. abnor.)	4/72 (6)	2–14
Perfusion defect < radiograph		
1 zone	1/13 (8)	0–36
2 or 3 zones	1/11 (9)	0–41
All zones	2/24 (8)	1–27
Matched V/Q (radiograph normal)		
1 zone	4/24 (17)	5–37
2 or 3 zones	1/19 (5)	0–26
All zones	5/43 (12)	4–25
Two types of perfusion defects†		
CAE and nonseg. abnor.	1/9 (11)	0–48
CAE and matched V/Q (radiograph normal)	0/5 (0)	0–52
Nonseg. abnor. and perfusion defect < radiograph	2/26 (8)	1–25
Nonseg. abnor. and matched V/Q (radiograph normal)	4/25 (16)	5–36

*$p < 0.05$ CAE versus nonseg. abnor.

†Combinations of two perfusion defects were excluded from the table if the combination was observed in only three or fewer lungs.

CAE = pleural effusion with obliteration of the costophrenic angle with the perfusion defect ≤ radiograph abnormality; nonseg. abnor. = nonsegmental perfusion abnormality, including enlargement of the hilum, mediastinum or heart, elevated diaphragm with the perfusion defect ≤ radiograph abnormality; perfusion defect < radiograph = parenchymal abnormality on the chest radiograph with the perfusion defect < radiographic abnormality; matched V/Q (radiograph normal) = matched ventilation-perfusion defect with normal chest radiograph and perfusion defect ≤ ventilation defect.

because the PIOPED data did not identify the lung in which small perfusion defects were observed, and we analyzed individual lungs, not individual patients.

Statistical Analysis

Chi square was used to compare the frequency of PE with various single abnormalities or combinations of abnormalities of the V/Q scan among lungs of patients in each group and subgroup. The 95% confidence intervals were calculated on the basis of the exact binomial distribution.

RESULTS

Lungs with a Single Type of Perfusion Defect

In the randomized group, PE was observed in 3 of 12 (25%), lungs in which a small pleural effusion causing obliteration of the costophrenic angle was the only type of perfusion abnormality (Table 2). Such pleural effusions had higher positive predictive values for PE than nonsegmental perfusion abnormalities (4 of 72, 6%, $p < 0.05$). Comparisons with other single types of abnormalities or combina-

TABLE 3
Positive Predictive Value of Criteria Used for Low Probability Assessment in Lungs of Patients in Combined Group

	PE/Total (%)	95% Confidence interval
One type of perfusion defect		
CAE	4/14 (29)*	8–58
(Nonseg. abnor.)	8/103 (8)	3–15
Perfusion defect < radiograph		
1 zone	2/24 (8)	1–27
2 or 3 zones	1/16 (6)	0–30
All zones	3/48 (8)	2–20
Matched V/Q (radiograph normal)		
1 zone	4/34 (12)	3–27
2 or 3 zones	1/30 (3)	0–17
All zones	5/64 (8)	3–17
Two types of perfusion defects†		
CAE and nonseg. abnor.	1/10 (10)	0–45
CAE and matched V/Q (radiograph normal)	1/8 (13)	0–53
Nonseg. abnor. and perfusion defect < radiograph	3/34 (9)	2–24
Nonseg. abnor. and matched V/Q (radiograph normal)	4/29 (14)	4–12

*CAE vs. nonseg. radiograph abnor., $p < 0.02$; CAE vs. perfusion defect < radiograph, all zones, $p < 0.05$; CAE vs. matched V/Q two or three zones, $p < 0.02$, all zones, $p < 0.05$.

†Combinations of two perfusion defects were excluded from the table if the combination was observed in only four or fewer lungs.

CAE = pleural effusion with obliteration of the costophrenic angle with the perfusion defect ≤ radiograph abnormality; nonseg. abnor. = nonsegmental perfusion abnormality, including enlargement of the hilum, mediastinum or heart, elevated diaphragm with the perfusion defect ≤ radiograph abnormality; perfusion defect < radiograph = parenchymal abnormality on the chest radiograph with the perfusion defect < radiographic abnormality; matched V/Q (radiograph normal) = matched ventilation-perfusion defect with normal chest radiograph and perfusion defect ≤ ventilation defect.

TABLE 4
Positive Predictive Value of Low Probability Criteria in Patients with and without Previous Cardiopulmonary Disease*

	No prior CPD PE/Total (%)	Prior CPD PE/Total (%)
One type of perfusion defect		
CAE	2/6 (33)	2/8 (25)
Nonseg. abnor.	1/44 (2)	7/56 (13)
Perfusion defect < radiograph	2/17 (12)	1/23 (4)
Matched V/Q (radiograph normal)	4/22 (18)†	1/40 (3)
Two types of perfusion defects‡		
Nonseg. abnor. and perfusion defect < radiograph	1/8 (13)	2/25 (8)
Nonseg. abnor. and matched V/Q (radiograph normal)	1/8 (13)	2/19 (11)

*Some patients had no information regarding CPD or no CPD. Therefore, the totals in this table do not equal the values in Table 3.
†$p < 0.05$ no CPD vs. CPD.
‡Combinations of two perfusion defects were excluded from the table if the combination was observed in only four or fewer lungs.
CAE = pleural effusion with obliteration of the costophrenic angle with the perfusion defect ≤ radiograph abnormality; nonseg. abnor. = nonsegmental perfusion abnormality including enlargement of the hilum, mediastinum or heart, elevated diaphragm with the perfusion defect ≤ radiograph abnormality; perfusion defect < radiograph = parenchymal abnormality on the chest radiograph with the perfusion defect < radiographic abnormality; matched V/Q (radiograph normal) = matched ventilation-perfusion defect with normal chest radiograph and perfusion defect ≤ ventilation defect.

tions of abnormalities showed no statistically significant differences (Table 2).

In the combined group, lungs with a pleural effusion that caused obliteration of the costophrenic angle had a positive predictive value of 4 of 14 (29%), which was higher than any other single type of perfusion abnormality ($p < 0.05$ to $p < 0.02$) (Table 3).

Nonsegmental perfusion abnormalities, when occurring alone, had a positive predictive value of 4 of 72 (6%) in the randomized group and 8 of 103 (8%) in the combined group (Tables 2, 3).

Perfusion defects smaller than associated parenchymal abnormalities on the chest radiograph, when occurring as the only type of perfusion defect, had a positive predictive value of 8% in both the randomized and referred groups (Tables 2, 3).

Matched V/Q abnormalities, in the presence of a normal chest radiograph, when occurring as the only type of perfusion defect, had a positive predictive value of 5 of 43 (12%) in the randomized group and 5 of 64 (8%) in the combined group (Tables 2, 3).

Lungs with Two Types of Perfusion Defects

A pleural effusion with blunting of the costophrenic angle along with a nonsegmental perfusion defect had a positive predictive value of 11% in the randomized group and 10% in the combined group (Tables 2, 3).

A nonsegmental perfusion defect in combination with a perfusion defect smaller than the chest radiographic abnormality radiograph had a positive predictive value of 8% in the randomized group and 9% in the combined group (Tables 2, 3).

A nonsegmental perfusion defect and a matched ventilation/perfusion defect had a positive predictive value of 16% in the randomized group and 14% in the combined group (Tables 2, 3). Other combinations of two types of perfusion defects had too few patients for analysis (Tables 2, 3). Data were insufficient to analyze three or four types of perfusion defects in combination.

Perfusion Defect in Single or Multiple Lung Zones

For perfusion defects smaller than the chest radiographic abnormality, the positive predictive value in the randomized and combined groups was comparable if the perfusion defect was in one, two or three zones of a single lung (Tables 2, 3).

On the other hand, in both the randomized and combined groups, a matched perfusion defect as the defect in one zone of a single lung was not associated with a statistically significant higher positive predictive value for PE than matched perfusion defects in two or three zones in a single lung. In the randomized group, the positive predictive value for PE with matched perfusion defects in one zone was 4 of 24 (17%), 1 of 13 (8%) in two zones and 0 of 6 (0%) in three zones. In the combined group, the positive predictive value for PE with matched perfusion defects in one zone was 4 of 34 (12%), 1 of 20 (5%) in two zones and 0 of 10 (0%) in three zones.

Stratification According to Previous Cardiopulmonary Disease

In the randomized group, there were no statistically significant differences in frequency of PE with various single perfusion defects or combinations of perfusion defects between patients with prior cardiopulmonary disease and those with no previous disease. In the combined group, however, a matched V/Q defect in the presence of a normal chest radiograph had a higher positive predictive value for PE in patients with no prior cardiopulmonary disease compared to patients with previous disease: 4 of 22 (18%) versus 1 of 40 (3%) ($p < 0.05$) (Table 4). The frequency of PE in patients with a perfusion defect smaller than the opacity on the chest radiograph tended to be higher in patients with no prior cardiopulmonary disease, but the difference was not statistically significant.

TABLE 5
Categorization of Criteria for Low Probability V/Q Scans Based on Individual Positive Predictive Values

Criteria for very low probability V/Q scan (PPV < 10%)
Nonsegmental abnormality
Perfusion defect < radiograph
Matched V/Q (radiograph normal) in two or three zones of a single lung
Nonsegmental abnormality and perfusion defect < radiograph
Criteria for low probability V/Q scan (PPV 10%–19%)
Matched V/Q (radiograph normal) in one zone of a single lung
Costophrenic angle effusion and nonsegmental abnormality
Costophrenic angle effusion and matched V/Q (radiograph normal)
Nonsegmental abnormality and matched V/Q (radiograph normal)
Criteria for intermediate V/Q scan (PPV 20%–79%)
Costophrenic angle effusion

PPV = positive predictive value.
Definitions as in Tables 2–4.

DISCUSSION

Perfusion defects smaller than the associated radiographic abnormality have been one of the criteria used in interpreting V/Q scans as low probability of acute PE (*1,7,9*). A matched V/Q defect in the presence of a normal chest radiograph has also been a criterion used to assess low probability (*1,7–11*). Small perfusion defects (<25% segment) were also included among the criteria for low probability assessment (*1,7,9*) but were not assessed in the present investigation because the lungs in which such small perfusion defects occur were not identified in the PIOPED database.

Based on the original PIOPED criteria outlined earlier, 14% of patients in the PIOPED study with V/Q scans interpreted as low probability had PE (*1*). These criteria included nonsegmental perfusion defects less than or equal to radiographic abnormality, perfusion defects less than or equal to ventilation defects with normal chest radiograph, perfusion defects less than radiographic defects, more than three small perfusion defects with a normal chest radiograph or a single moderate size mismatched perfusion defect with a normal chest radiograph (*1*). Some physicians believe that the percentage of patients with PE who have a low probability V/Q scan (14% using original PIOPED criteria) is too high to adequately exclude PE (*4*). Therefore, patients with low probability V/Q scans require further diagnostic studies (*4,12,13*).

Gottschalk et al. (*2*) undertook a retrospective revision of the PIOPED criteria using the PIOPED database. They found that a single moderate size mismatched perfusion defect was not suitable for inclusion in the criteria for low probability. They also found PE was present in 6 of 23 (28%) patients with a single matched V/Q defect, whereas PE was present in 9 of 66 (14%) patients with multiple matched V/Q defects. Of patients with nonsegmental perfusion defects, 0 of 29 (0%) had PE. For those patients with a perfusion defect substantially smaller than the chest radiographic abnormality, 1 of 12 (8%) lung zones with this pattern indicated PE.

The data presented here are designed to refine further the low probability V/Q criteria suggested by Gottschalk et al. (*2*). Our aim was to define criteria for a very low probability interpretation, which would have a 10% positive predictive value for PE. We evaluated the arm of the PIOPED study that included patients referred for pulmonary angiography as well as patients randomized for pulmonary angiography.

Nonsegmental perfusion abnormalities associated with enlargement of the hila, mediastinum, heart or elevated diaphragm had <10% positive predictive value for of PE and may therefore be used as the criteria for a very low probability for PE (Table 5). Perfusion defects smaller than the associated radiographic abnormality also positive predictive values <10% and are suited for inclusion in the criteria for very low probability. These two types of perfusion defects in combination also satisfy the very low probability criterion.

A matched perfusion defect in two or three zones in a single lung may be used as inclusion criteria for very low probability (0%–8% positive predictive values) (Table 5). A matched perfusion defect in only one zone (12% positive predictive value) is suited for inclusion in low probability criteria but not very low probability. Contrary to impressions based on limited data used to develop the revised PIOPED criteria (*2*), a single matched perfusion defect should not be interpreted as intermediate probability for PE.

Criteria appropriate for a low probability interpretation (10%–20% positive predictive for PE) but not very low probability interpretation (<10% positive predictive value) are, nonsegmental perfusion abnormalities in combination with a matched V/Q defect, perfusion defect associated with a small pleural effusion in combination with a nonsegmental perfusion abnormality, and perfusion defect associated with a small pleural effusion in combination with a matched V/Q defect (Table 5).

A criterion previously used for low probability, a perfusion defect associated with a small pleural effusion, had a positive predictive value greater than 19%. This criterion appears to be more appropriate for intermediate probability (Table 5).

Stratification of patients according to the presence or absence of prior cardiopulmonary disease suggests that some criteria suited for the general population as "very low probability" (positive predictive value <10%) might only be "low probability" (positive predictive value 10%–19%) in patients without previous cardiopulmonary disease.

CONCLUSION

This analysis of PIOPED data identified V/Q scan criteria appropriate for very low probability interpretation (<10% positive predictive value) in patients with suspected acute PE. The data are limited, and statistically significant differences were not shown between positive predictive values of V/Q criteria categorized as very low probability and those categorized as low probability.

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