Modified PIOPED Criteria Used in Clinical Practice

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To assess the use of modified PIOPED scintigraphic criteria for lung scan (V/Q) interpretation to detect pulmonary embolism (PE), we prospectively applied these criteria in suspected PE patients referred for V/Q from 9/1/92 to 2/7/94. PIOPED criteria were modified by placing a moderate segmental perfusion mismatch in the intermediate instead of low probability of PE category and using the "stripe sign." Methods: Patients were studied by six-view V/Q imaging using 74 MBq (2 mCi) 99mTc-MAA followed by 148-370 MBq (4-10 mCi) 99mTc-DTPA aerosol, contrast pulmonary selective angiography and Doppler sonography with leg compression as needed. Patients underwent follow-up (mean 13.9 mo) to detect subsequent thromboembolic events. In this study group, 1000 patients were studied by V/Q followed by angiography in 133 patients. Results: The distribution of V/Q-assigned PE probabilities was: high probability 5.7%, intermediate 17.4%, low 41.4% and normal 35.5%. Group A patients (133) underwent angiography, which resulted in the determination of a 27.1% PE prevalence. Group B patients (867) did not have angiograms; the clinical prevalence of PE was 7.5%. In the total study population, the positive predictive value of a high probability V/Q study for PE (10.1% prevalence) was 98.2%, intermediate probability V/Q study for PE was 24.1% and a low probability study for PE was only 0.5%. Conclusion: Modified PIOPED V/Q interpretation criteria afford better angioproven PE discrimination between intermediate (31.8% PE prevalence) and low (5.5% PE prevalence) probability V/Q results than reported for PIOPED intermediate (32.6% PE prevalence) and low (16.3% PE prevalence) probability V/Q interpretation criteria.

Key Words: ventilation-perfusion imaging; PIOPED criteria; technetium-99m-MAA; technetium-99m-DTPA aerosol; pulmonary angiography

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he incidence of venous thrombosis and pulmonary embolism (PE) has remained constant for 30 yr (1). Although death from PE for in-patients is declining, PE continues to

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be underdiagnosed (2,3). The clinical suspicion of PE is essential to its diagnosis, which is based initially on the physician's clinical assessment of the patient for signs and/or symptoms of venous thrombosis and PE supplemented, as needed, by studies such as a chest radiograph, EKG and arterial blood gases. Unfortunately, neither the chest radiograph, EKG or arterial blood gases provide the physician with sufficient information to make or exclude the diagnosis of PE. The chest radiograph serves to exclude disease entities that mimic PE, but findings such as oligemia (Westermark's sign), vascular redistribution or pleural-based areas of increased opacity (Hampton's hump) do not have sufficient sensitivity or specificity to obviate further evaluation (4). Following careful clinical evaluation and assessment of the presence of any predisposing factors to PE (5), the clinician determines the most likely diagnosis and, if PE is suspected, initiates further PE evaluation through such imaging studies as radionuclide ventilation-perfusion (V/Q) scintigraphy and/or pulmonary angiography (6,7).

V/Q scintigraphy has played a major role in the evaluation of patients with suspected PE for more than two decades, depicting the sequelae of PE as a V/Q mismatch (8,9). Such a mismatch, especially when solitary, is nonspecific, and various interpretive schemes or algorithms have been advanced (10-13) to improve the sensitivity and specificity of V/Q scintigraphy in the detection of pulmonary embolism. These schemes rely on the natural history of pulmonary thromboembolism, in which clot fragmentation in the right heart induces multivessel segmental embolization of the pulmonary vasculature with preservation of segmental ventilation (14). Although this approach has its limitations because of interpretive underestimation of segmental size and nonrecognition of some segmental defects (15, 16), such schemes have demonstrable clinical utility. Retrospective analysis of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) scintigraphic criteria for V/Q scan interpretation demonstrated that the original prospective criteria should be modified by categorizing a single moderate perfusion defect as intermediate rather than low probability and extensive matched V/Q defects with clear chest radiograph as low rather than in-

TABLE 1

Assignment of V/Q Probability of Pulmonary Embolism

Rules: Always begin with Probability = Normal. Continue to the next question until you are instructed to STOP. Once a given Probability (PROB) has been assigned, it may only increase, never decrease. For one defect to be "much larger than" another, it should be ≥ twice as large. A >25% segmental defect exhibiting the "stripe sign" within that segment is ignored.

Begin with Perfusion Scan Probability = Normal.

1. Are there any Q defects?

No → PROB = NORMAL. STOP.

Yes \rightarrow PROB = LOW. Continue to question 2.

2. Are there any Q defects >25% of a segment?

No \rightarrow PROB = LOW. STOP.

Yes → Continue to question 3?

3. Are there any chest radiograph abnormalities overlapping Q defects (>25% of segment)?

 $No \rightarrow PROB = LOW$. Continue to question 5.

Yes → Continue to question 4.

4. Are all Q defects >25% of a segment matched by much larger chest radiograph defects?

No → PROB = INTERMEDIATE. Continue to question 5.

Yes → PROB = LOW. STOP.

5. Are there any Q defects >25% of a segment not matched by chest radiograph abnormality?

No \rightarrow STOP.

Yes → Continue to question 6.

Perform Ventilation Scan

6. Are ALL >25% of a segment Q defects matched by V defects despite normal chest radiograph?

No → Continue to question 7.

Yes → PROB ≥ LOW. Continue to question 9?

7. Are there ≥2 large Q defects "much larger than" corresponding V or chest radiograph defects?

Answer no if V and chest radiograph are normal in defect regions or only one large defect is present.

No → PROB = INTERMEDIATE. Continue to question 8.

Yes → PROB = HIGH. STOP.

8. Are there >2 segmental equivalent Q defects with normal V and normal chest radiograph?

 $No \rightarrow PROB = INTERMEDIATE.$ STOP.

Yes → PROB = HIGH. STOP.

9. Do matched V and Q defects cover >50% of the combined lung fields?

No \rightarrow PROB = LOW. **STOP.**

Yes → PROB = INTERMEDIATE. STOP.

determinate probability (17). A subsection of this analysis also confirmed the validity of the "stripe sign" (18) as an indication that a segmental perfusion defect showing the sign was not likely due to PE (19).

To determine if the new knowledge gleaned from retrospective analysis of the PIOPED study would improve the clinical utility of V/Q scintigraphy in our clinical practice, we conducted the following prospective study.

METHODS

From 9/1/92 to 2/7/94, we prospectively applied modified PIOPED criteria to our scintigraphic interpretation of V/Q studies performed on 1000 patients (593 women, 407 men) with suspected PE who were referred to the radiology department. An additional seven patients with a lung or hilar mass and ten patients who underwent pulmonary angiography without prior V/Q scintigraphy were excluded from further analysis. The medical records of these 1000 patients were reviewed to determine the presence or absence of PE. During this time interval, the hospital's primary and secondary discharge diagnoses of more than 34,000 in-patients revealed 101 patients with PE. The diagnosis of PE was felt to be established by: (a) detection of PE by pulmonary angiography or (b) the presence of venous thrombosis, an abnormal lung perfusion study and clinical assessment and confirmation of PE by the attending pulmonologist.

Scintigraphic Techniques

Perfusion studies were performed with 74 MBq (2 mCi) ^{99m}Tc-MAA. A standard six-view (no LAO or RAO) study was obtained with 500,000 ct/view using a parallel-hole, low-energy, all-purpose collimator on a gamma camera. If the perfusion was abnormal, a ventilation study was then performed in the standard fashion with ^{99m}Tc-pentetate (DTPA) using an Aerovent (MediNuclear, Baldwin Park, CA) aerosol delivery system that provided 148–370 MBq (4–10 mCi) of aerosol to the patient to achieve at least three to four times the count rate achieved during the perfusion images. Ventilation images (500,000 cts/view) were obtained in the same projections as the abnormal perfusion images. In 402 patients, ventilation images were not obtained because the perfusion images were normal, ventilation images were not possible or ventilation images were not indicated (e.g., matched perfusion defect with chest radiograph abnormality).

Chest radiographs, portable AP or standard PA and lateral, were obtained on all patients within 24 hr of the V/Q scan and all V/Q studies were interpreted together with the chest radiograph.

Scintigraphic Interpretation

The V/Q studies were classified into four categories: normal, low, intermediate or high probability using the algorithm shown in Table 1. This algorithm, the patient's current chest x-ray and an anatomical lung segment reference chart (20) were used by each observer to determine the probability assignment of each V/Q

study. Seven patients unable to perform a satisfactory ventilation study but who had at least one moderate or large segmental perfusion defect were designated as having intermediate probability of PE. V/Q studies were interpreted by multiple observers (17 total), but 782 studies were read by four experienced observers. The formal V/Q interpretation issued by a staff physician at the time of the V/Q procedure was used in this analysis.

Pulmonary Angiography

Six experienced angiographers performed pulmonary angiography by the transfemoral approach using selective and subselective arterial contrast injections in multiple projections as needed to adequately assess the perfusion defects shown on the V/Q study. Bilateral pulmonary angiography was performed in almost all patients, unless PE was readily apparent in the first lung studied, as suggested by the V/Q report, at which point the angiogram study was terminated. The presence of a vascular cut-off or intraluminal filling defect confirmed the diagnosis of PE. The formal angiogram report issued at the time of the procedure was used in this analysis.

Compression Doppler Sonography

Compression doppler sonography of the calf, popliteal fossa and thigh was performed in the usual manner. The presence of venous thrombosis was confirmed by the lack of compressibility of the vein or direct visualization of intraluminal thrombus.

Patient Follow-up

The hospital inpatient and outpatient records were reviewed retrospectively from 9/1/92 to 9/30/94 through a computerized search for a primary or secondary diagnosis of venous thrombosis or PE. Patients diagnosed as having venous thrombosis or PE at discharge or during a visit to the clinic were cross-referenced with our prospective study patient population to determine the frequency of the development or recurrence of these diagnoses in our study group.

RESULTS

The distribution of V/Q assigned PE probabilities in our 1000 patients using modified PIOPED V/Q interpretation criteria was: 5.7% for high, 17.4% for intermediate, 41.4% for low and 35.5% for normal, respectively. Pulmonary angiography was performed in 133 patients (Group A) but not in the remaining 867 patients (Group B). Angiography was performed more frequently (52.3%) in patients with an intermediate probability V/Q study but only infrequently (8.9%) in patients with high or low probability studies. The diagnosis of PE was made in 101 patients: 36 by angiography and 65 by a combination of lung scan, sonography and clinical assessment.

Group A patients (PE prevalence of 27.1%) had a V/Q distribution of 6 for high probability, 91 for intermediate probability and 36 for low probability studies as compared to the PIOPED distribution (Table 2). In the 42 patients with high or low probability studies, the V/Q result was discordant with their pretest clinical assessment and angiography was ordered. Angiography confirmed PE in 5 of 6 high probability, 29 of 91 intermediate studies and 2 of 36 low probability studies as compared to the PIOPED study (Table 3).

TABLE 2
V/Q Scan Category Distribution: Current Versus PIOPED
Study

Scan category (Probability)	Current study* (%)	PIOPED study [†] (%)
High	6 (4.5)	117 (15.5)
Intermediate	91 (68.4)	331 (43.8)
Low	36 (27.1)	250 (33.1)
Normal/Almost normal	0 (0)	57 (6.6)

^{*}Results from 133 patients.

Modified PIOPED V/Q interpretation criteria provide better angio-proven PE discrimination between intermediate (31.8% PE prevalence) and low probability (5.5% PE prevalence) V/Q results than reported for PIOPED intermediate (32.6% PE prevalence) and low (16.3% PE prevalence) probability V/Q interpretive criteria (p < 0.001). This better discrimination is accomplished in part by recategorizing 14 V/Q scans demonstrating a single moderate V/Q mismatch from the low probability (under PIOPED) to the intermediate probability category (17). Six of these 14 patients (42.9%) had angio-proven PE (Fig. 1). Similarly, five patients with a solitary segmental or multisegmental mismatch exhibiting the stripe sign were recategorized from intermediate (under PIOPED) to low probability; none of these patients had angio-proven PE.

Group B patients did not have angiograms but had a V/Q distribution of 51 high (5.8%), 83 intermediate (9.6%), 378 low (43.6%) and 355 normal (40.9%) probability studies. Sixty-five of these patients were diagnosed as having PE (PE prevalence 7.5%) based on a high probability lung scan and concordant clinical assessment in 51 and an intermediate probability scan with positive sonogram for venous thrombosis and concordant clinical assessment in 14.

In the total study population (PE prevalence 10.1%), the positive predictive value (PPV) of a high probability V/Q study for PE was 98.2%, 24.1% for an intermediate probability V/Q study, 0.5% for a low probability study.

Compression doppler sonography was performed in 195 patients: 25 patients with high probability, 65 patients with intermediate probability, 84 patients with low probability and 21 patients with normal V/Q scans. Venous thrombosis was present in 45 patients (17 with high probability, 18 with intermediate probability, 8 with low probability and 2 with

TABLE 3Comparison of Angiographic Findings with V/Q Scan Category

Scan category (Probability)	PE present (%) Current study	PE present (%) PIOPED study
Intermediate	29 (31.8)	105 (32.6)
Low	2 (5.5)	39 (16.3)

[†]Results from 775 patients.

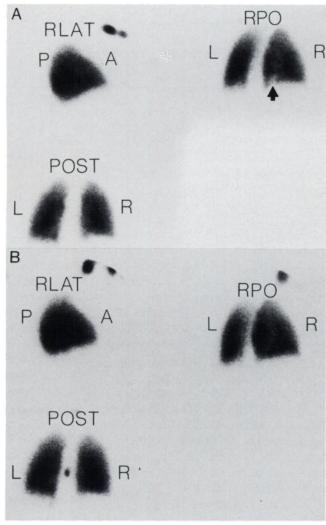


FIGURE 1. (A) Selected perfusion images demonstrate a moderate right posterior basal perfusion defect (arrows). (B) Selected ventilation images demonstrate mismatched ventilation to this segment

normal V/Q scans). In the latter 6 mo of our study, patients with an intermediate probability V/Q study, a positive doppler study for venous thrombosis and concordant clinical assessment for PE underwent angiography less frequently for confirmation of PE since the angiographic results would not affect the referring physician's decisions on therapeutic regimen.

Nine patients (0.9%) were found to have thromboembolic events during the mean follow-up period of 13.9 mo. Six patients had venous thrombosis only, two patients had venous thrombosis and PE and one had PE. All three patients with PE, however, had had PE diagnosed initially during the prospective study and were felt to have recurrences (one presumed treatment failure).

DISCUSSION

This prospective study demonstrates that modified PIOPED interpretation criteria applied to perfusion and

then to aerosol ventilation V/Q images perform better in the clinical arena than PIOPED criteria. The interpretation criteria algorithm (Table 1) used in this study does not differ in content from the modified PIOPED criteria proposed initially by one of the authors (JEJ) in 1991 (13) but is presented in a dichotomous question and answer format to facilitate its use by the staff physicians in our practice with limited V/Q scan interpretation experience. The V/Q scan distribution for this total study population is significantly different from that reported in the PIOPED study but is similar to that reported from other non-university settings where the majority of patients referred for V/Q studies are not in-patients at the time of referral (21).

Unlike the PIOPED study, the patients in our Groups A and B represent considerable selection bias as the patients in Group A presented difficult diagnostic and therapeutic decisions for their referring physicians necessitating angiography for clarification of their clinical status. All 42 patients in Group A with high or low probability V/Q studies demonstrated major discordance between their referring physician's pretest clinical assessment of the likelihood of PE and the reported V/Q probability.

In this population, the high probability and normal scan results seen in 412 patients were concordant with the final clinical diagnosis in all but one patient. This patient's study (Fig. 2) was read as high probability of PE incorrectly, since clearly, on review, this V/Q study has only a low or, at most, an intermediate probability of PE. Similarly, one of the two patients with a low probability study, subsequently confirmed to have PE by angiography, was interpreted incorrectly (Fig. 3). As exemplified by these two interpretive errors, despite supposed adherence to a defined diagnostic algorithm, it is well recognized that erroneous interpretations occur if proper attention to detail is not maintained (22).

We believe that the lung scan should be reviewed by the angiographer prior to performing pulmonary angiography and that the lung with the most suspicious defects should be catheterized first. This approach shortens the angiography procedure time significantly in many patients and reduces the contrast load in compromised patients. The precise segmental location of the perfusion defects seen on the lung scan must be considered by the angiographer when interpreting the angiogram. In 3 of our 36 positive angiograms, the preliminary impression of "negative angiogram" was reversed when PE was subsequently identified after direct comparison to the pre-angiogram lung scan.

We believe that our V/Q technique has advantages over that used in the original PIOPED study (12). Performing the perfusion prior to the ventilation study permits the ventilation study to be tailored for optimal positioning to determine the presence or absence of V/Q mismatches. Also, direct overlay of the ventilation image on the perfusion image allows detection of previously unrecognized perfusion defects, especially in the posterior basal, lingular and anterior segments. Such perfusion defects may not be well demonstrated on xenon images acquired prior to per-

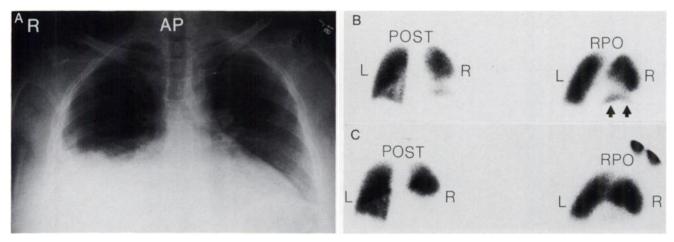


FIGURE 2. (A) AP chest radiograph demonstrates right lower lobe opacification. (B) Selected planar images demonstrate matched perfusion defect with stripe sign (arrows). (C) Selected ventilation images demonstrate that ventilation is much worse than perfusion.

fusion imaging. The better quality of our postperfusion ventilation studies achieved with our sequential approach enables the reader to ascertain that subtle 0.5–1.0 segmental mismatch(es) are indeed present in certain patients.

We do not believe that our 13.3% angiography rate sig-

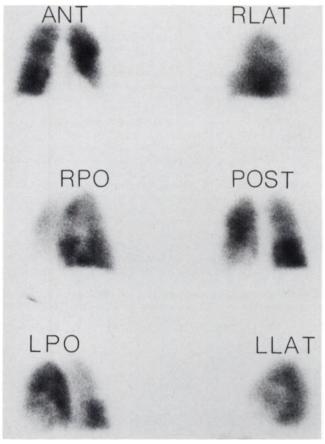


FIGURE 3. A perfusion-only study in which the decreased perfusion to the entire right upper lobe and right superior segment was not acknowledged. A ventilation study should have been performed but was not because of this oversight and subsequent angiography demonstrated a nonocclusive thrombus in the right main pulmonary artery.

nificantly underestimates the true prevalence of PE in this patient population, as suggested by the lower PE prevalence in Group B versus Group A. Retrospective review of 272 consecutive patients at this institution studied prior to 9/1/92 using aerosol ventilation initially and then a perfusion V/Q scan demonstrated almost identical results for determining PE prevalence (10%), despite a 19.5% angiography rate. In addition, our total study group demonstrated only a 0.9% venous thrombosis or PE event rate during our follow-up period. It is unlikely that a significant number of patients with untreated, undiagnosed thromboembolic disease would have such a low incidence of recurrence if left untreated. Our follow-up event rate is slightly lower than that reported by others and may possibly reflect a lack of complete knowledge of our study population since some patients with subsequent venous thrombosis and/or PE recurrence may have sought treatment elsewhere during the follow-up period (23,24). It more likely reflects, however, the lower overall prevalence of venous thrombosis and PE in our patient population as compared to a university hospital setting.

CONCLUSION

In this prospective study, we have demonstrated that a perfusion test followed by a ventilation V/Q study using modified PIOPED interpretation criteria better discriminates between the intermediate and low probability scan categories than PIOPED interpretation criteria. This result was achieved through an interpretation criteria algorithm, despite a variety of readers with variable V/Q interpretation experience. We recommend the diagnostic approach shown in Figure 4 to our referring physicians. This approach is similar to the diagnostic strategy suggested recently by Stein et al. (25) but emphasizes compression sonography in preference to impedance plethysmography because of sonography's greater sensitivity and predictive value (24).

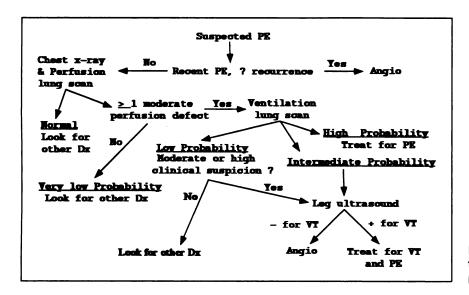


FIGURE 4. Diagnostic scheme for the evaluation of patients with suspected pulmonary embolism.

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