Perfusion Lung Scintigraphy for the Diagnosis of Pulmonary Embolism: A Reappraisal and Review of the Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis Methods

Massimo Miniati, MD, PhD,* H. Dirk Sostman, MD,† Alexander Gottschalk, MD,‡ Simonetta Monti, MD, PhD,§ and Massimo Pistolesi, MD*

In this article, we review the evolution of scintigraphy for the diagnosis of acute pulmonary embolism (PE). We begin with perfusion (Q) scintigraphy, review the development of diagnostic systems that combine ventilation (V) scintigraphy and chest radiography with the Q scan, and describe in detail the Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISAPED) criteria for diagnostic categorization of the Q scan read in conjunction with the chest radiograph. Finally, we review the results obtained with the PISAPED criteria in clinical research studies. The PISAPED method for lung scan interpretation provides sensitivity and specificity for diagnosing acute PE that is comparable to V/Q scanning and to computed tomography angiography (CTA), with fewer nondiagnostic results than either V/Q or CTA. The criteria can be used effectively in a diagnostic management approach that incorporates the use of a clinical prediction rule. Clinical outcomes in patients in whom PE is excluded in this way are comparable to outcomes for patients in whom the diagnosis is excluded by CTA or conventional angiography.
Semin Nucl Med 38:450-461 © 2008 Elsevier Inc. All rights reserved.

The Evolution of Scintigraphy for the Diagnosis of Acute Pulmonary Embolism

Perfusion Scintigraphy: The Common Ancestor

In the beginning, there was the Q scan.[1-3] A normal Q scan has long been accepted to exclude pulmonary embolism (PE) for practical purposes (the morbidity and mortality of missed PE has been thought to be far less than that from continuing the diagnostic evaluation or with preemptive therapy).[4,5] It is the Q scan that is pivotal in excluding PE; as long as Q is normal, the V scan or chest radiograph (CXR) can be abnormal and the examination is still read as negative for PE. Excluding PE is an important decision, so it is generally felt that Q scans should be interpreted conservatively, and a "normal" diagnosis reserved for unequivocally normal Q studies. This is because it has been demonstrated experimentally that Q scintigraphy is not perfectly sensitive; in dogs, the sensitivity of the Q scan is approximately 80% for emboli that completely occlude pulmonary vessels, but only approximately 30% for partially occluding emboli.[6] A normal Q scan result stops the workup for PE and diverts attention to other possibilities. Although it is sensitive, Q scintigraphy has long been thought not to be specific for PE.[7] This is because all common pulmonary diseases, including neoplasms, infections, and obstructive airways disease, can produce decreased pulmonary blood flow to affected regions.[8] To overcome this perceived problem, Wagner et al[9] and DeNardo et al[10] suggested the technological solution of combined V/Q lung imaging.

*Department of Critical Care, Section of Respiratory Medicine, University of Florence, Florence, Italy.
†Office of the Dean, Weill Cornell Medical College and Methodist Hospital, Houston, TX.
‡Department of Radiology, Michigan State University, East Lansing, MI.
§CNR Institute of Clinical Physiology, Pisa, Italy.
Address reprint requests to H. Dirk Sostman, MD, Methodist Hospital, 6565 Fannin St, Houston, TX 77030. E-mail: Dsostman@tmhs.org

The Profusion of Diagnostic Approaches Using V/Q Scintigraphy

McNeil and coworkers[11] highlighted the findings of numerous investigators by pointing out that abnormalities in the Q scan that are matched by abnormal ventilation usually are not caused by pulmonary embolism, whereas mismatched abnormalities, coexisting with a normal CXR, have a high correspondence with angiographically demonstrated PE. Alderson and coworkers[12] later showed that the overall diagnostic accuracy for scintigraphic detection of pulmonary emboli was significantly improved when V studies were added to the Q scan and CXR. Extensive work by Biello and collaborators[13,14] further categorized Q defects matched by ventilation or radiographic abnormalities and provided grounds for reducing the number of "indeterminate" diagnoses. Further evaluation[15] confirmed that this diagnostic approach provided improved interobserver consistency and a 30% reduction in "indeterminate" readings compared with the results from an older system. By the early 1980s, it was accepted that a scintigraphic study demonstrating multiple large, wedge-shaped, pleural-based Q defects with normal V and CXR in the corresponding areas has an extremely high correspondence with PE, hence the term "high probability of PE."

However, the diagnostic criteria for patterns other than normal Q and classic "high probability of PE" continued to evolve. The need for this was emphasized by the results of the first Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study, which showed that the combination of pretest clinical assessment and V/Q scintigraphy could diagnose or exclude PE accurately but that such readings were possible in only 28% of patients.[16] Accordingly, with the best-available V/Q scintigraphic methods, most patients had diagnostic results that were insufficiently conclusive to guide definitive clinical management.

Further research was prompted by intriguing data that indicated some experienced individuals could achieve more accurate results by using their own subjective assessment than by using the corresponding reference criteria.[17,18] The PIOPED Nuclear Medicine Working Group revised the PIOPED criteria,[17] and a prospective trial[19] determined that, although they were more accurate than the original PIOPED criteria, the "gestalt" impression of experienced readers was still more accurate. Work by Stein and coworkers[20,21] helped in making the criteria for "high probability" easier to apply and more sensitive. A study by Worsley and coworkers[22] indicated that Q/CXR matches in the upper and middle lung zones have a low likelihood (11-12%) of being associated with PE in the same zone, whereas those in the lower zones have a greater likelihood (33%).

The focus of research was primarily aimed at reducing the number of "nondiagnostic" readings, defined as the sum of "low-probability" and "intermediate-probability" results.[23] The high proportion of nondiagnostic results was the principal reason for the decline in utilization of V/Q scans during the late 1990s and early 2000s. The research approach to this problem has been 2-fold. First, the validation of clinical prediction rules has added information to the diagnostic process and reduced the burden that previously was carried entirely by the scan. Second, further refinement of scan interpretation permitted many patients to be taken out of the "nondiagnostic" category; as mentioned, in PIOPED I, (32% outpatients), V/Q scans gave a definitive diagnosis in only 28% of patients.[16]

Gottschalk and coworkers[24] dramatically reduced the number of "nondiagnostic" readings by demonstrating that a large subset of "low-probability" scans that are categorized as "very low probability" can safely be used to exclude PE. A "very low probability" interpretation of the V/Q scan is as reliable as computed tomography angiography (CTA) in excluding PE when the clinical probability is low or moderate. In other studies, if the CXR was normal or nearly normal, a definitive reading of the V/Q scan was shown in 91%[25] of patients. However, without the very low probability interpretation, and considering a low probability interpretation as nondiagnostic, others found a definitive diagnosis by V/Q in patients with a normal CXR of only 22%[26] and 52%.[27] Retrospective analysis with recategorization of data from PIOPED II (75% outpatients) into "PE present," "PE absent," and "nondiagnostic" showed a definitive V/Q scan reading in 74% of patients, with moderate sensitivity and high specificity in the groups with such readings.[28] At the same time, a Canadian randomized clinical trial showed equivalent outcomes when comparing patients evaluated with a clinical prediction rule and either CTA or V/Q scintigraphy, although more patients with PE were detected by CTA.[29]

Back to Basics: PISAPED and Re-evaluation of the Q Scan

The Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISAPED) trial combined both approaches: incorporation of clinical prediction rules and revised scan interpretation criteria. The investigators suggested a new set of diagnostic criteria, intended to diagnose or exclude PE using the Q scan and CXR[30] with few nondiagnostic readings. In this study, researchers prospectively evaluated 890 consecutive patients with suspected PE. Before lung scanning, each patient was assigned a clinical probability of PE (very likely, possible, unlikely). Perfusion scans were independently classified as follows: (1) normal, (2) near-normal, (3) abnormal compatible with PE (PE+: single or multiple wedge-shaped Q defects), or (4) abnormal not compatible with PE (PE−: Q defects other than wedge-shaped). The diagnostic reference standard was pulmonary angiography. Clinical and scintigraphic follow-up was obtained in all patients with abnormal scans. Of 890 scans, 220 were classified as normal/or near-normal and 670 as abnormal. A definitive diagnosis was established in 563 (84%) patients with abnormal scans. Most patients were inpatients, and the overall prevalence of PE was 39%. Most patients with angiographically proven PE had PE+ scans (sensitivity: 92%). Conversely, most patients without emboli on angiography had PE− scans (specificity: 87%). A PE+ scan associated with a "very likely" or "possible" clinical presentation of PE had

positive predictive values of 99% or 92%, respectively. A PE scan paired with an "unlikely" clinical presentation had a negative predictive value of 97%. Clinical assessment combined with Q-scan evaluation established or excluded PE in the majority of patients with abnormal scans. This data suggested that accurate diagnosis of PE is possible by Q scanning alone, without V imaging. Combining Q scanning with clinical assessment helped to restrict the need for further diagnostic evaluation to a minority of patients with suspected PE.

A subgroup analysis of the PIOPED data had also suggested that the V scan was not essential.[31] The results of this prospective study also were corroborated by a retrospective analysis in which one of the PISAPED investigators re-read 723 Q scans and CXR from the PIOPED I study. The sensitivity was 80% and the specificity 83%, using the PIOPED I angiographic result as the gold standard.[30]

Comparative Trial of PIOPED and PISAPED Criteria for Q Scintigraphy

We used the archived Prospective Investigation of Pulmonary Embolism Diagnosis II (PIOPED II) data and images to test the hypothesis that reading perfusion (Q) scans with chest radiographs (CXR) but without ventilation (V) scans, and categorizing the Q scan as "PE Present" or "PE Absent" can result in clinically useful sensitivity and specificity in a high proportion of patients in a new patient population.

Patients recruited into PIOPED II were eligible for the study if they had (1) computed tomographic angiography (CTA) and/or digital subtraction angiography (DSA) diagnosis, (2) interpretable Q scan and CXR and (3) prospectively recorded Wells'[32] score. Four readers re-read Q scans with CXR in eligible patients. Two readers used modified (for the absence of the V scan) PIOPED criteria and two readers used the PISAPED criteria. The CXR were read as "normal/near normal," "abnormal" or "nondiagnostic" and the Q scans were read as "PE Present," "PE Absent" or "Nondiagnostic." The primary analysis used a composite reference standard: (1) the PIOPED II DSA result, or (2) if there was no definitive DSA result, CTA results that were concordant with the Wells' score (ie, CTA positive and Wells' score >2, or CTA negative and Wells' score <6).

The prevalence of PE in the sample was 169 of 889 (19%). Using the modified PIOPED criteria, the sensitivity of a "PE Present" Q scan was 84.9% (95% confidence interval [CI], 80.1-88.8%), whereas the specificity of "PE Absent" was 92.7% (95% CI, 91.1-94.1%), excluding "nondiagnostic" results, which occurred in 20.6% (95% CI, 18.8-22.5%). Using the PISAPED criteria, the sensitivity of a "PE Present" Q scan was 80.4% (95% CI, 75.9-84.3%), and the specificity of "PE Absent" was 96.6% (95% CI, 95.5-97.4%); however, the proportion of patients with a "Nondiagnostic" scan was 0% (95% CI, 0.0-0.2%).

These results indicate that Q scintigraphy combined with chest radiography can provide diagnostic accuracy similar to that of CTA and V/Q. The additional benefits are lower cost and lower radiation dose. With modified PIOPED criteria, a

higher proportion of patients were nondiagnostic than the 6.2% rate found in PIOPED II using CTA, whereas with PISAPED criteria none were nondiagnostic.

# The PISAPED Criteria and Their Application in Reading Perfusion Scans

The value of the Q scanning approach compared with V/Q scanning stems from the flawed assumption that lung regions excluded from perfusion by emboli maintain a normal ventilation (V/Q mismatch). The V/Q mismatch criterion to diagnose PE is at variance with several studies[33-37] in which the authors showed that ventilation is shifted away from embolized lung regions.[38] The concept that dead space ventilation is not significantly increased in the course of PE[38] was widely held in respiratory pathophysiology before the V/Q scanning approach was developed as it was asserted by Julius H. Comroe, Jr, who, in 1966,[39] foresaw that: "[T]he decrease in wasted ventilation (ventilation to unperfused or poorly perfused lung) helps the patient but hinders the physician in diagnosis." This notion, besides explaining the low diagnostic sensitivity of V/Q scanning and of dead space ventilation technique, is in keeping with the observation from the PIOPED trial that about half of the patients with angiographically proven PE in the lower lung regions had atelectasis and/or parenchymal areas of increased opacity in the corresponding lung zones.[40] Such parenchymal abnormalities are likely to affect not only perfusion, but also ventilation scan images.[30]

Using the PISAPED Criteria

Perfusion lung scintigraphy is, by definition, an image of the regional distribution of pulmonary blood flow. Therefore, when examining a Q scan, one should ask the following questions: (1) is pulmonary blood flow distributed physiologically? (2) Is there any structural abnormality of the heart, mediastinum, pleura, diaphragms, or chest wall that alters the scintigraphic outline of the lungs? (3) Is there any perfusion defect within the lungs? (4) If so, is the perfusion defect due to embolic occlusion of the pulmonary vessels or is it due to a parenchymal disorder?

The Normal Scan

Under physiologic conditions, the blood flow to the lungs is preferentially distributed to the dependent and dorsal regions (Fig. 1). For many years, it has been thought that such preferential distribution is caused by the effect of gravity. Should it be so, there would be a vertical gradient of blood flow from the apex to base of the lung without any ventral-to-dorsal gradient. As shown in Figure 1, however, a ventral-to-dorsal gradient of blood flow is clearly discernible. On the basis of experiments performed during the last 10 years, it appears that the regional distribution of blood flow is primarily dictated by the anatomic configuration of the pulmonary arterial tree that is best described by fractal geometry.[41,42] According to PISAPED criteria, a Q scan is rated normal

A

B
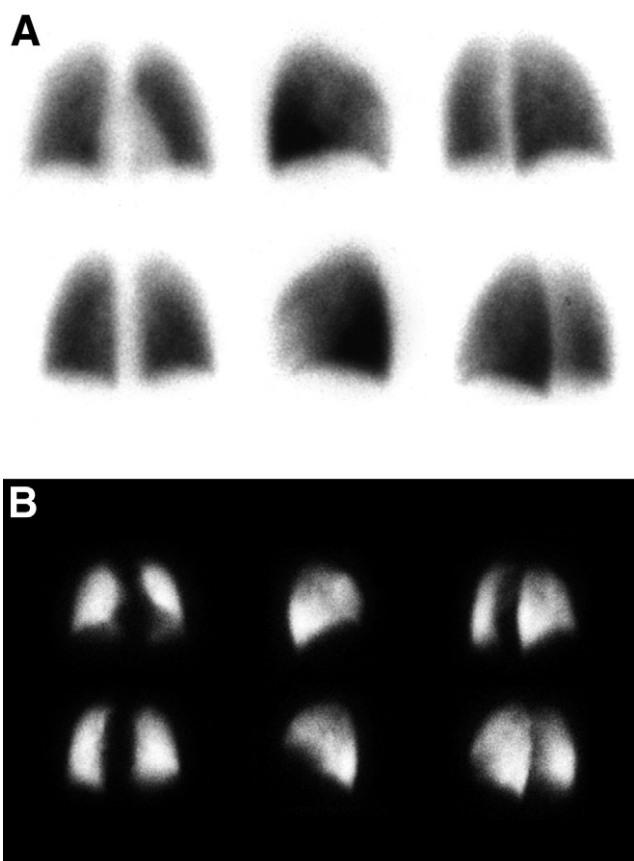
Figure 1 Normal perfusion scans (A) and (B). The pulmonary blood flow is predominantly distributed to basal and dorsal regions. The radiotracer was injected with the subject in the sitting position.

whenever the blood flow distribution, observed after the injection of the radiotracer with the patient in the sitting position, follows a physiological gradient and no abnormalities in the lung shape or true perfusion defects are observed.

Figure 2 Near-normal perfusion scan in a patients with dilated cardiomyopathy. The enlarged heart determines compression on lung parenchyma that is best seen in anterior, posterior, and left lateral views.

A

B
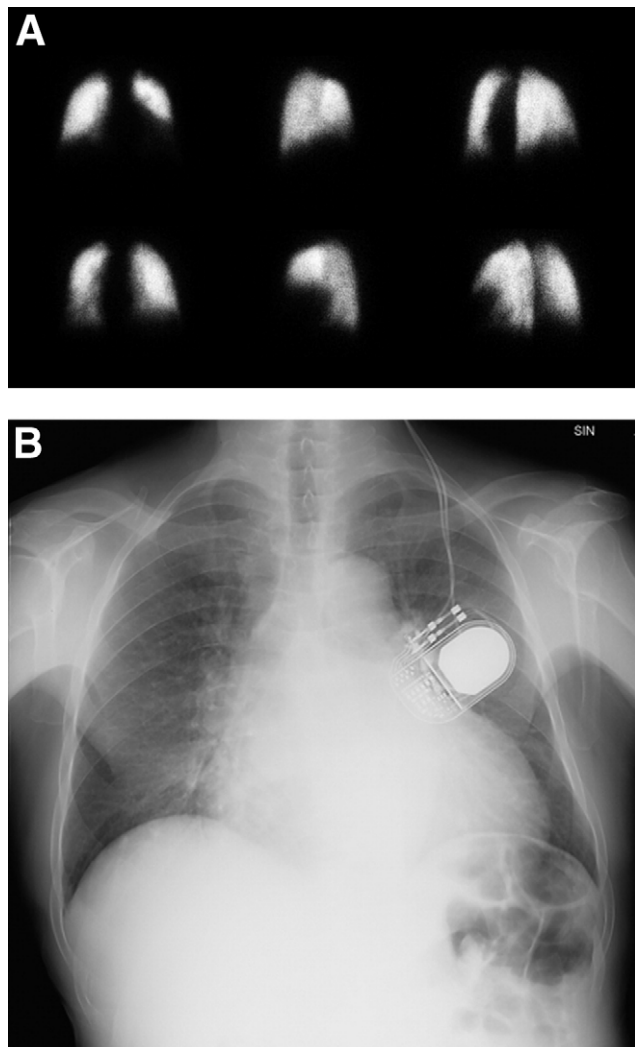
Figure 3 Near-normal perfusion scan in a patient with postischemic chronic left heart failure. (A) The pulmonary blood flow is distributed predominantly to upper and anterior regions; (B) CXR shows enlarged heart, dilated upper lobe vessels, and mild interstitial edema.

The Near-Normal Scan

A number of thoracic extrapulmonary abnormalities may affect the outline of the lung on Q scintigraphy. Such abnormalities are easily seen on the plain CXR, which is a necessary companion to the Q scan. The structural abnormalities that may alter the shape of the lungs include enlarged heart or hilar vessels, widened mediastinum, blunting of costophrenic angles, extensive thickening of the pleura, small pleural effusion (especially intrafissural), elevated diaphragm, or thoracic wall deformity (eg, severe kyphoscoliosis). Enlargement of the heart, which is frequent in clinical practice, creates an impression on the lung parenchyma that is best seen on the anterior, posterior, and left lateral views of lung scintigrams (Fig. 2). In patients with severe left heart valvular disease or long-standing left heart failure, the pulmonary blood flow is often distributed to the upper and anterior regions of the lungs (Fig. 3). Such redistribution is the consequence of an extensive remodeling of the pulmo-

Figure 4 Abnormal perfusion scan in a patient with acute pulmonary embolism. Multiple bilateral wedge-shaped defects are seen along with areas of overperfusion, featuring a wedge configuration.
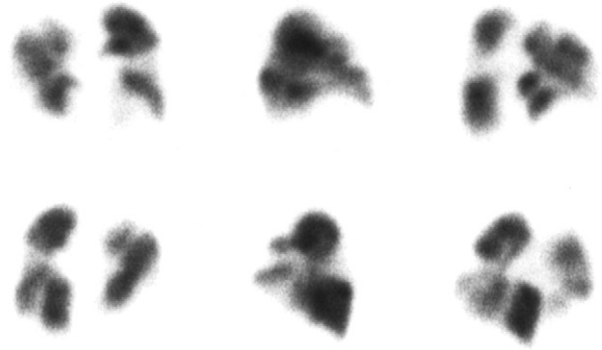
nary vessels in the dependent lung regions, characterized by medial hypertrophy, intimal proliferation and, ultimately, fibrotic occlusion of the lumen.[43,44] The reduction of the vascular cross-sectional area in the dependent lung zones causes a redistribution of blood flow that is linearly related to the elevation of pulmonary vascular resistance.[45] In a physiologic sense, any lung scan with a pathologic distribution of pulmonary blood flow, such that shown in Figure 3, should be rated abnormal. However, because there are no obvious perfusion defects, such a scintigraphic pattern is rated near-normal according to PISAPED criteria.

The Abnormal Scan

When perfusion defects are seen on the lung scan, the physician should make every effort to establish whether they are suggestive of PE or are associated with diseases of the lung parenchyma. Since the introduction of Q scintigraphy, it be-
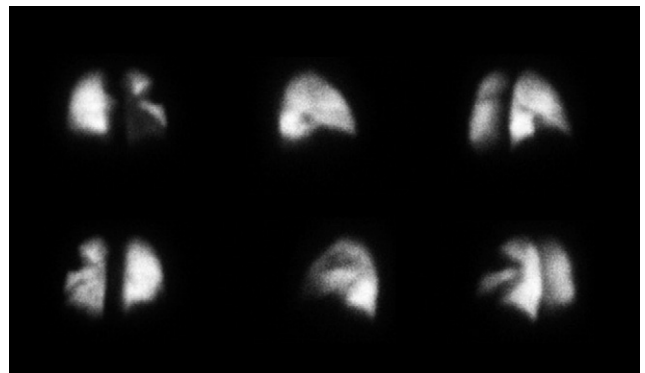

Figure 6 Abnormal perfusion scan in a patient with acute bilateral pulmonary embolism.

came evident that PE can be differentiated from other lung disorders by the presence of segmental or lobar perfusion defects.[46,47] At that time, the use of rectilinear scanners equipped with focusing collimators facilitated the identification of such abnormalities by virtue of the tomographic properties of the technique. With the use of gamma-cameras, the identification of segmental or lobar perfusion defects can be accomplished with the aid of multiple planar projections or by means of single-photon emission tomography. Since the perfusion defects in lung embolism are usually wedge-shaped, any lung scan showing one or more such defects is rated positive for PE according to PISAPED criteria. Accordingly, the shape of the perfusion defects is far more important than their number or size.

Examples of Q scans suggestive of PE are shown in Figures 4-8. In massive PE, such perfusion defects are often associated with multiple areas of overperfusion featuring a wedge configuration (Figs. 4-6). Such distinct areas of overflow—that were observed in some 80% of the patients with PE in the PISAPED study—are the expression of the redistribution of blood flow away from the embolized segments or lobes.

According to PISAPED criteria, any Q defect other than wedge-shaped should be regarded as negative for PE, whether or not there is a matching radiographic abnormal-

Figure 5 Abnormal perfusion scan in a patient with acute bilateral pulmonary embolism.

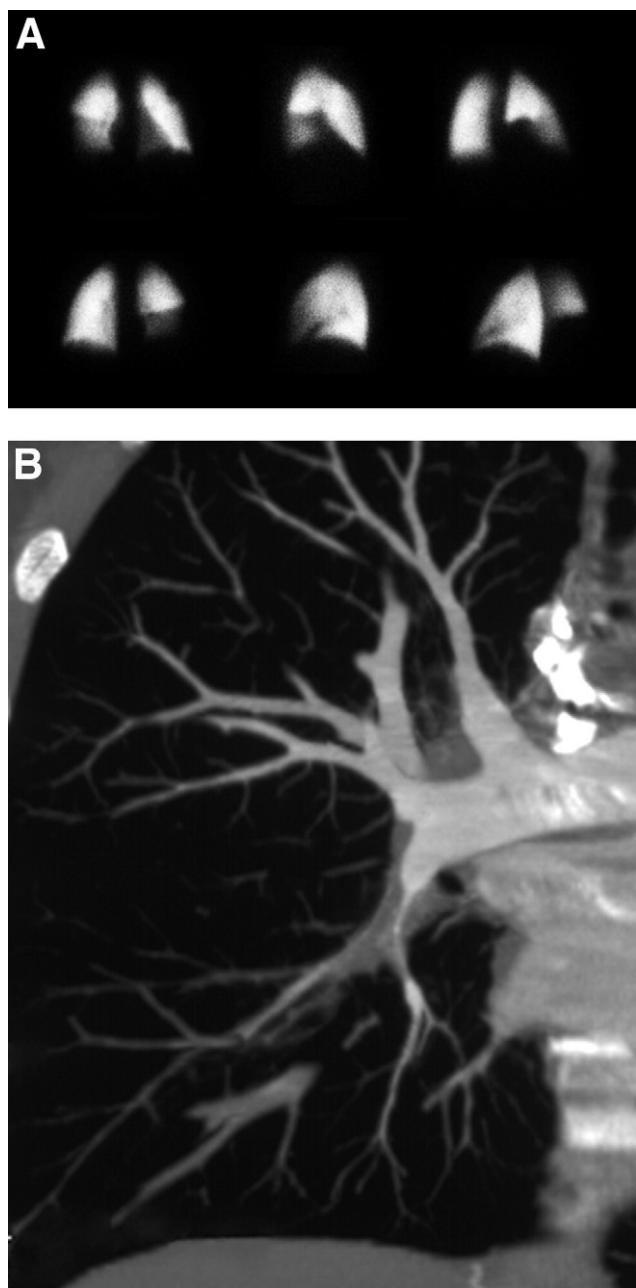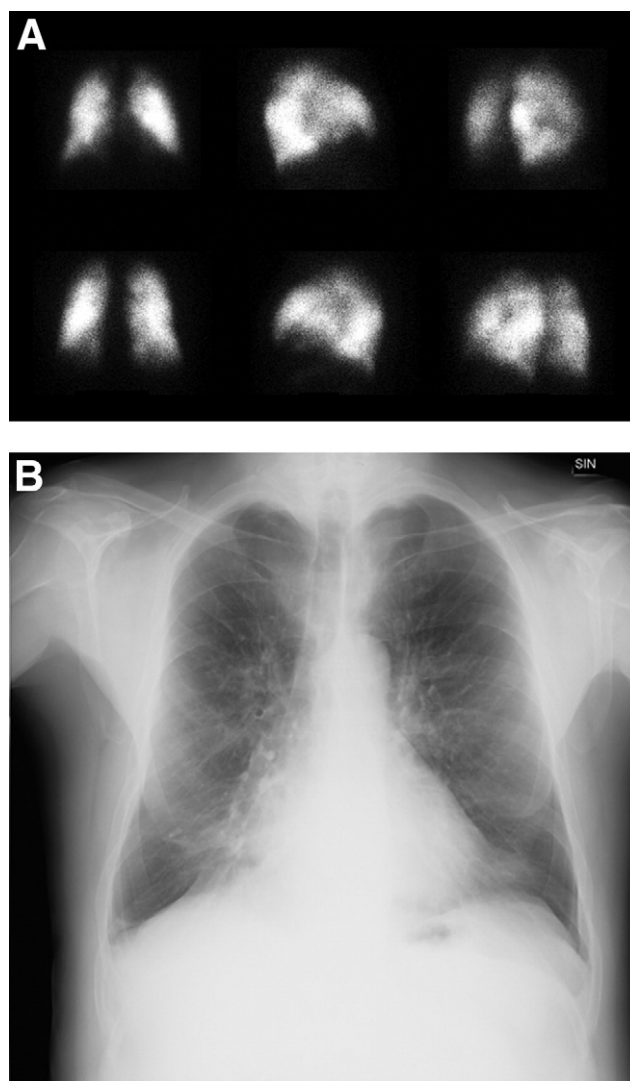**Figure 7** Abnormal perfusion scan in a patient with acute bilateral pulmonary embolism.

Figure 8 Abnormal perfusion scan in a patient with acute pulmonary embolism. Perfusion is absent in the right lower lobe. A small wedge-shaped perfusion defect is seen in the lingula (A). Coronal CTA image (B) shows vascular obstruction by embolism.

ity. Clinical conditions that are associated with perfusion abnormalities not caused by PE include pneumonia, lung cancer, alveolar edema, interstitial lung disease, and chronic obstructive lung disease (COPD). Epidemiological surveys in samples of the Italian general population indicate that the prevalence of COPD in subjects ages 50 years or older is approximately 30%.[48] Therefore, when one evaluates lung scans from elderly patients, COPD should be taken into account as a potential cause of the perfusion abnormalities. In this connection, the CXR may prove useful because it provides criteria for diagnosing moderate-

to-severe emphysema.[49] Perfusion lung scans from patients with COPD and no obvious emphysema are shown in Figures 9-11.

Examples of lung scans from patients with COPD and emphysema of varying degree of severity are given in Figures 12-16. In COPD, the Q scan may show a variety of abnormalities ranging from diffuse inhomogeneities to bilateral nonsegmental perfusion defects that are often symmetric in distribution. When emphysema is present, the outline of the lungs is poorly defined, especially along the upper regions. As emphysema becomes extensive, large unperfused areas are seen, which span from the apex to the base of the lung. In the most severe forms, only a small band of perfused lung tissue is left around the heart and over the diaphragms (Figs. 15 and 16). Such extensive perfusion abnormalities should not make the physician interpret the scan as nondiagnostic for PE for, if emboli were present, they would be distributed in those regions where the perfusion is still preserved. The

Figure 9 Abnormal perfusion scan in a patient with COPD. (A) Bilateral nonsegmental perfusion defects; (B) posteroanterior CXR shows increased bronchovascular markings but no signs of emphysema.
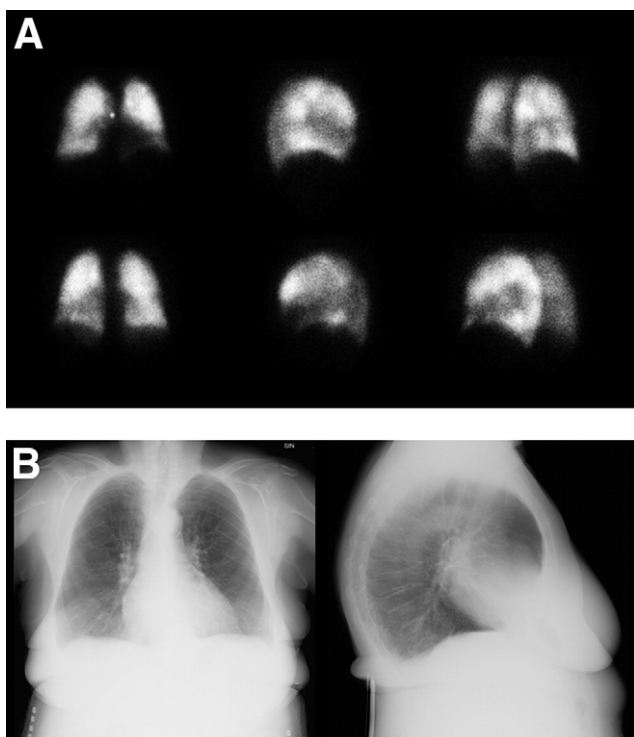
Figure 10 Abnormal perfusion scan in a patient with COPD. (A) Bilateral nonsegmental perfusion defects; (B) posteroanterior and lateral CXRs show no signs of emphysema.
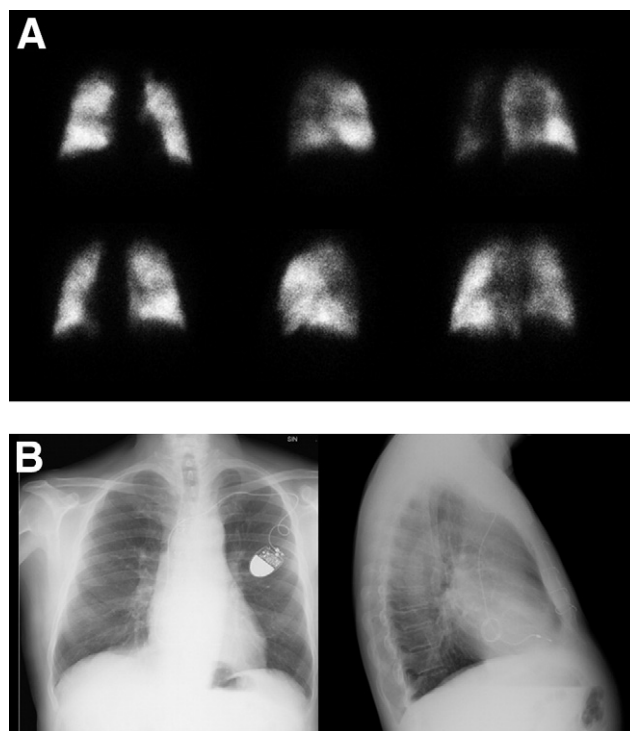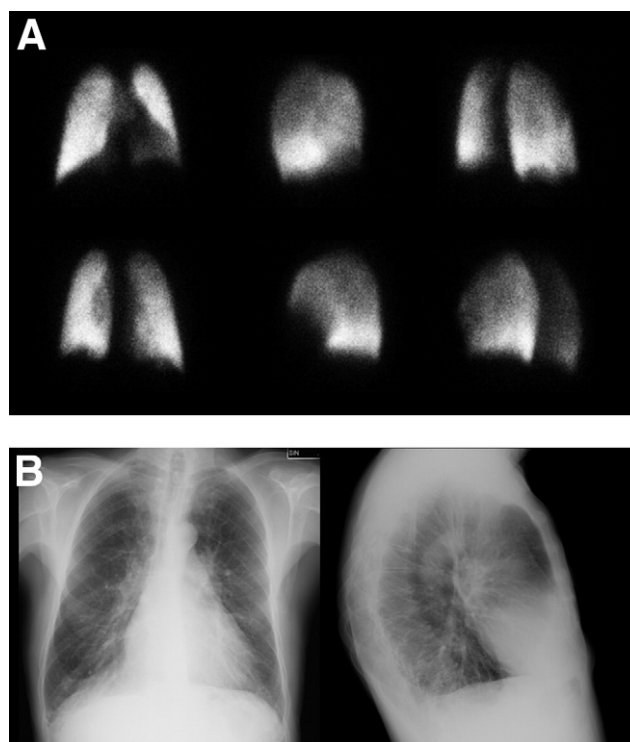

Figure 11 Abnormal perfusion scan in a patient with COPD. (A) Bilateral nonsegmental perfusion defects; (B) posteroanterior and lateral CXRs show no signs of emphysema.

scintigraphic diagnosis of PE in patients with COPD is undoubtedly difficult. However, when the PISAPED criteria are strictly applied, segmental defects can be identified in the context of diffuse perfusion inhomogeneities. An example of PE in COPD is shown in Figure 17. Perfusion defects associated with bilateral pneumonia and lung cancer are displayed in Figures 18 and 19.

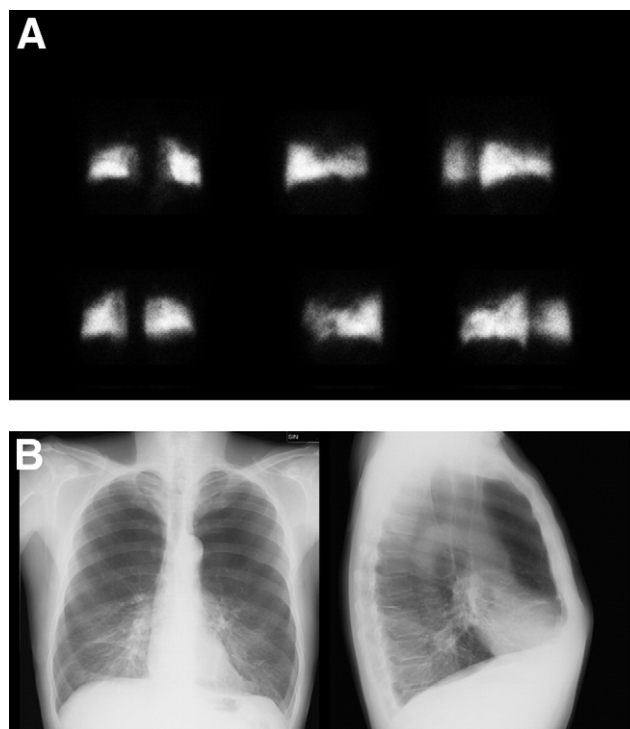## Combining Perfusion Scintigraphy With Pretest Probability of PE

The results of prospective studies support the concept that clinical probability assessment is a fundamental step in the diagnosis of PE. The strategy of combining Q scan interpretation with independent evaluation of clinical probability was tested in a management study including 390 patients with suspected PE.[50] The pretest probability of PE was rated according to a standardized clinical prediction model.[51] Pulmonary embolism was considered present in patients with abnormal scans suggestive of PE and a pretest probability >50%. Patients with normal or near-normal scans and those with abnormal scans not suggestive of PE with a pretest probability <10% were deemed not to have PE. All other patients were allocated to pulmonary angiography. All the patients were followed up for 1 year. PE was diagnosed noninvasively in 132 patients (34%) and excluded in 191 (49%). Pulmonary angiography was required in 67 of the 390 patients (17%). Therefore, the diagnostic yield of the noninvasive strategy was 83% (95%
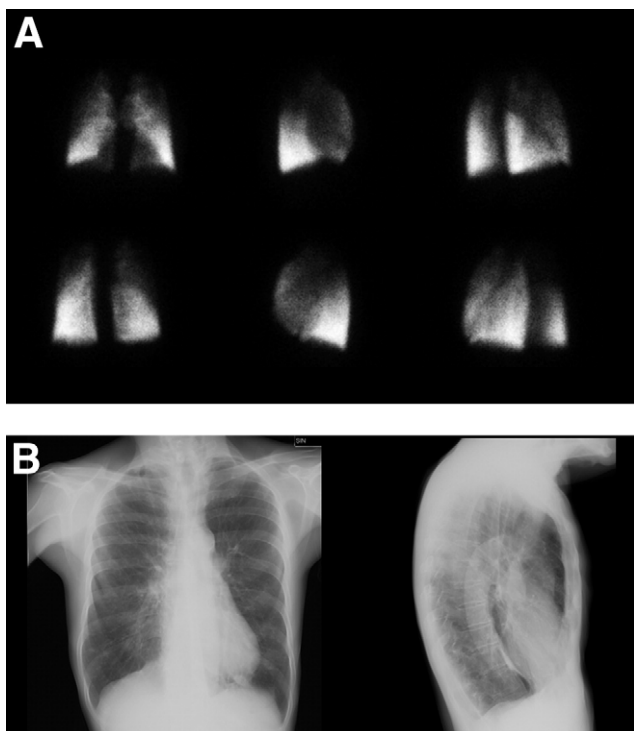

Figure 12 Abnormal perfusion scan in a patient with COPD and mild emphysema. (A) Perfusion is reduced in upper lung regions where the outline of the lungs is poorly defined; (B) posteroanterior and lateral CXRs show reduced vascularity and hyperlucency in upper lung lobes.
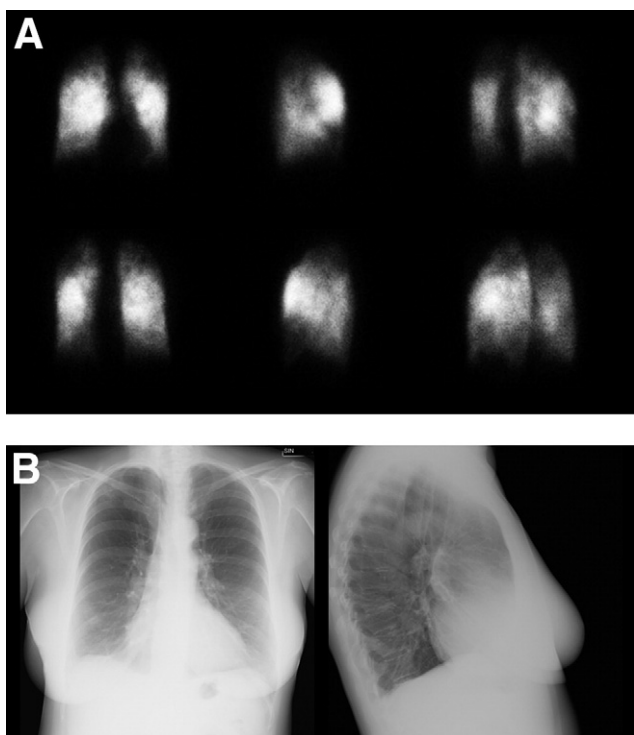
Figure 13 Abnormal perfusion scan in a patient with COPD and moderate emphysema. (A) The scintigraphic outline of the lungs is ill-defined with non segmental bilateral perfusion defects predominantly in upper lung regions; (B) posteroanterior and lateral CXRs show clear signs of emphysema predominantly in upper lung lobes.
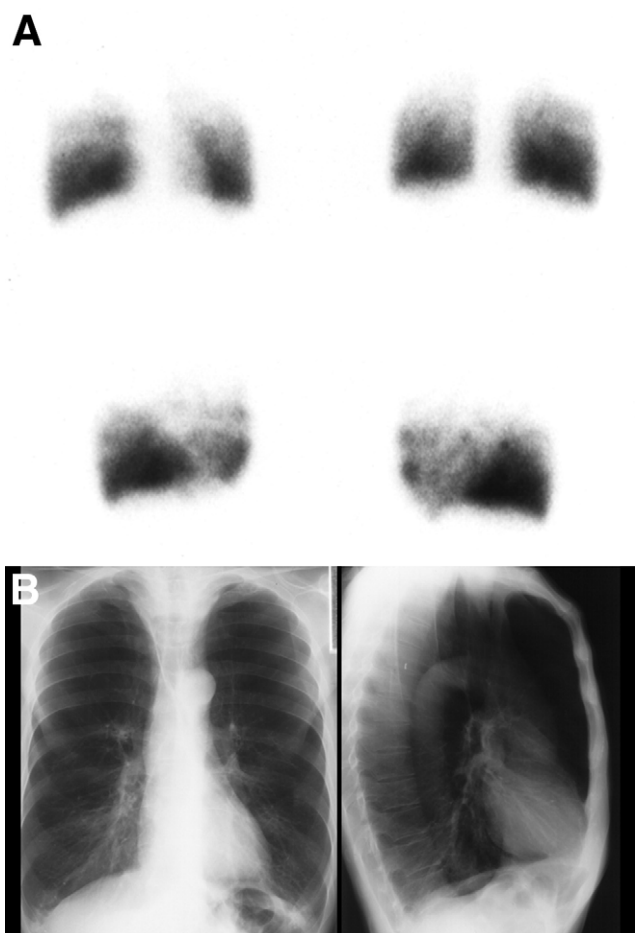

Figure 14 Abnormal perfusion scan in a patient with COPD and severe emphysema. (A) Large, symmetric nonsegmental perfusion defects extend from apical to basal and anterior lung regions; (B) posteroanterior and lateral CXR show large areas of emphysematous tissue destruction.

Figure 15 Abnormal perfusion scan in a patient with COPD and very severe bullous emphysema. (A) The scintigraphic outline of the lungs is not discernible, and the perfusion is preserved only in the parenchyma around the heart and over the diaphragms; (B) posteroanterior and lateral CXRs show extensive bullous emphysema.

CI, 79-86%). The patients in whom PE was excluded had a 1-year thromboembolic risk of 0.4% (95% CI, 0-2.8%). Combining Q scintigraphy with independent assessment of the clinical probability of PE may prove particularly useful in women of childbearing age who may be at risk of breast cancer when exposed to the substantial radiation burden associated with extensive use of CTA.

Perfusion Scintigraphy in the Follow-Up of PE

The rationale of following over time patients with an established diagnosis of PE is 2-fold: (1) to assess the restoration of pulmonary perfusion, and (2) to identify patients with persistent large perfusion defects who may be at risk of developing chronic thromboembolic pulmonary hypertension. Perfusion scintigraphy offers a number of advantages over CTA for this purpose. It is less expensive, entails a substantially lower radiation burden, and provides an overall view of the regional distribution of pulmonary blood flow, thereby permitting the identification of very small perfusion abnormalities. In a recent study, including 320 patients with angiographically confirmed PE, Q scans were obtained at diagnosis, and at 1 week, 1 month, and 1 year of inclusion.[52] The median extent of scintigraphically detectable pulmonary vascular occlusion at diagnosis was 43% (range, 5-82%). Most of the patients who survived a full year after PE showed near-complete restoration of pulmonary perfusion along with considerable improvement in arterial oxygenation. Only

Figure 16 Abnormal perfusion scan in a patient with COPD and very severe panlobular emphysema. (A) The perfusion abnormalities are similar to those of Figure 15; (B) posteroanterior and lateral CXRs show extensive emphysema.

4 (1%) of the 320 patients with PE at presentation developed chronic thromboembolic pulmonary hypertension. All these patients featured persistent large perfusion defects in sequential scintigrams. Therefore, monitoring the resolution of PE by lung scanning is a practical and relatively inexpensive means to identify patients with persistent perfusion abnormalities who may be at risk of chronic thromboembolic pulmonary hypertension.

Role of CXR

The CXR is considered by most investigators not to be an accurate means of diagnosing PE.[53] Most patients with PE have abnormal CXR, but the CXR changes are generally considered nonspecific. Common findings include consolidation, various manifestations of atelectasis, pleural effusion (usually small), and diaphragmatic elevation. Less common findings include nodules, focal oligemia, proximal pulmonary artery enlargement and acute heart failure. Some diagnostic signs (particularly focal oligemia or changes in proximal pulmonary artery size) can be subtle and difficult to interpret unless high quality comparison films are available.

However, the CXR is an essential component in the evaluation of a patient clinically suspected of having PE. The CXR is needed to establish or exclude clinical mimics of PE such as pneumonia, rib fracture or pneumothorax. It is also essential for adequate evaluation of the lung scintigram, particularly when the V scan is omitted. One should obtain a high quality PA and lateral examination at the same time as the lung scan. Portable AP films are a poor substitute, and if a portable film must be used, the patient's position should be accurately recorded so that account may be made for layering of pleural fluid. Chest radiographs more than a few hours old are also suboptimal.

It has long been thought that the CXR provides information that is complementary and important to the interpretation of the Q scan.[47] This is of particular note with the PISAPED criteria. When using the PISAPED criteria, in examining the CXR, the reader must consider the following items: size and shape of the heart and hilar arteries, position of the diaphragm, presence or absence of pulmonary parenchymal abnormalities (consolidation, atelectasis, oligemia, edema), and pleural effusion. On evaluating the hilar arteries, attention is paid to the presence of abrupt vascular amputation that gives the hilum a "plump" appearance.[51] Pulmonary consolidations are considered suggestive of infarction if they have a semicircular or half-spindle shape and are arranged peripherally along the pleural surface.[51] Oligemia is considered to be present if, in a given lung region, the pulmonary vasculature is greatly diminished with or without concomitant hyperlucency of the lung parenchyma.[51] Chest radiographs are rated as abnormal if one or more of the following are present: enlargement of the heart or hilar vessels; elevated
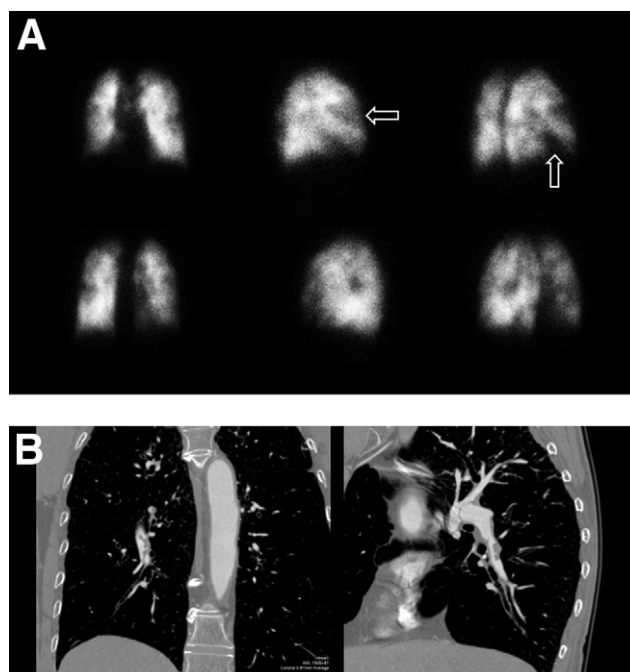
Figure 17 Acute pulmonary embolism in a patient with COPD. (A) wedge-shaped perfusion defects are seen in the right lung (arrows); (B) coronal and sagittal CTA images show multiple arterial filling defects.
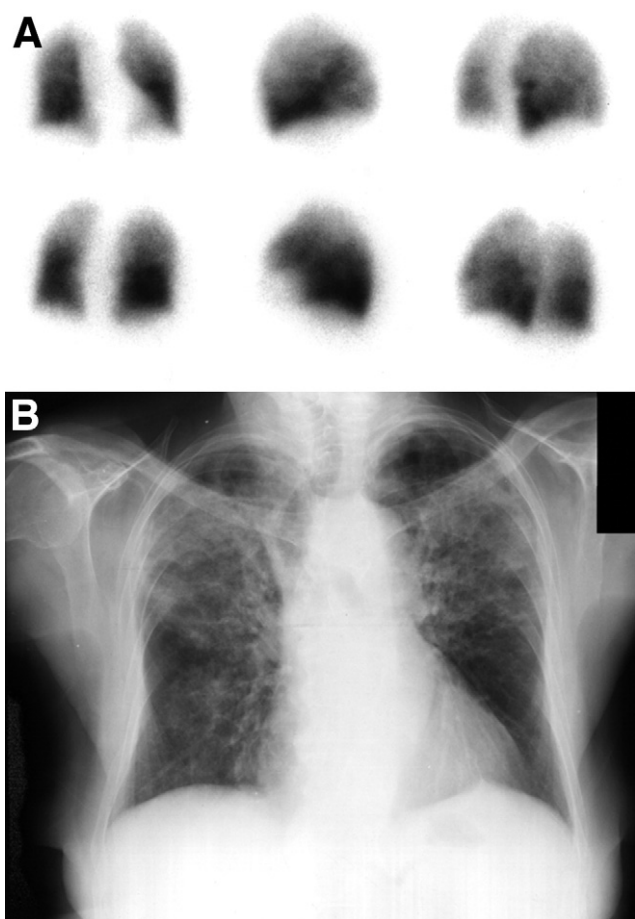
Figure 18 Bilateral pneumonia. (A) Nonsegmental perfusion defects are seen in the upper lung lobes; (B) posteroanterior CXR shows bilateral opacities in the upper lobes.

diaphragm (unilateral or bilateral); pleural effusion (including intrafissural liquid); increased lung density (focal or diffuse); pulmonary edema; oligemia with or without pleonexia in the contralateral lung; consolidation suggestive of infarction; emphysema; fibrothorax.

These observations, instead of being used simply to consider the CXR as abnormal, can be used to increase or reduce the clinical likelihood of PE.[51] Furthermore it has to be stressed that in the PISAPED reading of the Q scan the CXR is not used as a surrogate of the ventilation scan. In fact, the shape of the Q scan defects (wedge shaped or not) that determines the scintigraphic diagnosis is judged irrespective of the radiographic findings in the corresponding lung regions. This prevents the possible increase in nondiagnostic results that could derive from interpreting perfusion defects and radiographic increased density as matching defects (eg, in the modified PIOPED criteria).[27]

Conclusion

It might appear that pulmonary scintigraphy for acute PE has traversed a circular path, arriving after 40 years of research back at its point of origin with a recommendation for using Q scans and CXR for diagnostic evaluation. This would be su-

perficially correct, but would miss more important perspectives.

First, it should be acknowledged that, in some individual cases, V scans may be helpful in arriving at a diagnosis; in such cases, they can be obtained after the Q scan and CXR are performed. Second, the task of imaging is now more focused because of important developments in clinical evaluation (the validation of clinical prediction rules) and laboratory testing (D-dimer measurement) have enabled more accurate assessment of pretest probability, and the information content of the diagnostic process thus has been enhanced. Third, the basis and correlates of disease on the Q scan are now better understood as a result of decades of clinical research. Accordingly, the apparently naïve simplicity we now observe is actually the simplicity of sophistication, due to elimination of superfluous elements. Finally, the cost and patient safety perspectives have been firmly entrenched in the diagnostic and patient management value calculus.

Further work will be needed to confirm and extend the results obtained to date with the PISAPED criteria. It remains to be proven that these criteria can be taught to, and employed by, new observers who do not have years of experience correlating clinical, imaging and diagnostic outcome data. We do not yet understand how influential the findings on the CXR may be in using the Q scan with this system in such settings, nor how the CXR findings can be incorporated systematically and objectively. We need
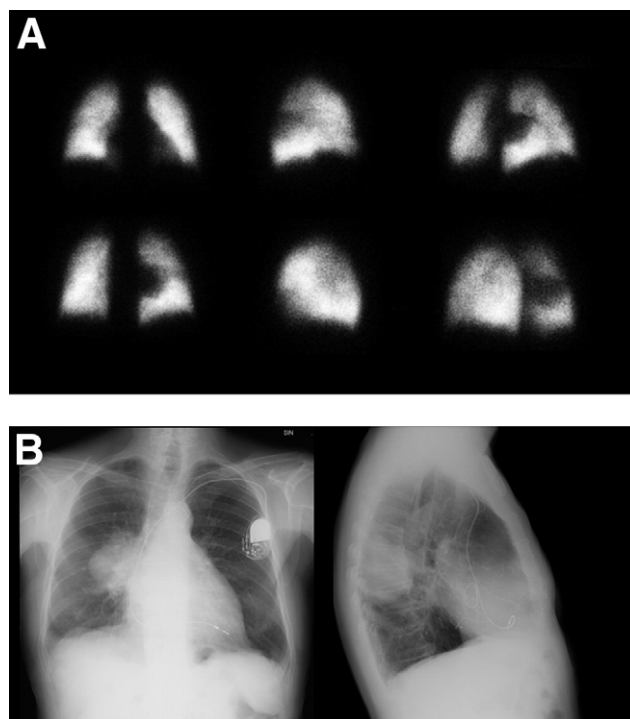
Figure 19 Lung cancer in a patient with no history of COPD. (A) a single nonsegmental perfusion defect is seen in the posterior regions of the right lung; (B) posteroanterior and lateral CXRs show a rounded sharply defined opacity in the costo-vertebral region of the right lung.

to document that patient outcomes are satisfactory in a large number of patients with a wide spectrum of disease when managed according to the diagnostic results of this method, but with multiple new readers. Finally, it is possible that some hybrid of the modified PIOPED and PISAPED classification systems might further improve on the results thus far obtained with each of them individually, and this should be investigated.

Acknowledgment

References

1. Moser KM, Harsanyi P, Rius-Garriga G, et al: Assessment of pulmonary photoscanning and angiography in experimental pulmonary embolism. Circulation 39:663-674, 1969
2. Gilday DL, Poulose KP, DeLand FH: Accuracy of detection of pulmonary embolism by lung scanning correlated with pulmonary angiography. Radiology 115:137-143, 1972
3. Tow DE, Simon AL: A comparative analysis of pulmonary perfusion scans with pulmonary angiograms. Am Heart J 92:700-706, 1976
4. Kipper MS, Moser KM, Kortman KE, et al: Long-term follow-up in patients with suspected pulmonary embolism and a normal lung scan. Chest 82:411-415, 1982
5. Hull RD, Raskob GE, Coates G, et al: Clinical validity of a normal perfusion lung scan in patients with suspected pulmonary embolism. Chest 97:23-26, 1990
6. Alderson PO, Doppman JL, Diamond SS, et al: Ventilation-perfusion lung imaging and selective pulmonary angiography in dogs with experimental pulmonary embolism. J Nucl Med 19:164-171, 1978
7. Tetalman MR, Hoffer PB, Heck LL, et al: Perfusion lung scan in normal volunteers. Radiology 106:593-594, 1973
8. Secker-Walker RH, Siegel BA: The use of nuclear medicine in the diagnosis of lung disease. Radiol Clin North Am 11:215-241, 1973
9. Wagner HN Jr., Lopez-Majano V, Langan JK, et al: Radioactive xenon in the differential diagnosis of pulmonary embolism. Radiology 91:1168-1174, 1968
10. DeNardo GL, Goodwin DA, Ravasini R, et al: The ventilatory lung scan in the diagnosis of pulmonary embolism. N Engl J Med 282:1334-1336, 1970
11. McNeil BJ, Holman L, Adelstein J: The scintigraphic definition of pulmonary embolism. JAMA 227:753-756, 1974
12. Alderson PO, Rujanavech N, Secker-Walker RH, et al: The role of 133-xenon ventilation studies in the scintigraphic detection of pulmonary embolism. Radiology 120:633-640, 1976
13. Alderson PO, Biello DR, Sachariah KG, et al: Scintigraphic detection of pulmonary embolism in patients with obstructive pulmonary disease. Radiology 138:661-666, 1981
14. Biello DR, Mattar AG, McKnight RC, et al: Ventilation-perfusion studies in suspected pulmonary embolism. AJR 133:1033-1037, 1979
15. Carter WD, Brady TM, Keyes JW, et al: Relative accuracy of two diagnostic schemes for detection of pulmonary embolism by ventilation-perfusion scintigraphy. Radiology 145:447-451, 1982
16. The PIOPED Investigators: Value of the ventilation/perfusion scan in acute pulmonary embolism. JAMA 263:2753-2759, 1990
17. Gottschalk A, Sostman HD, Juni JE, et al: Ventilation-perfusion scintigraphy in the PIOPED study. Evaluation of the scintigraphic criteria and interpretations. J Nucl Med 34:1119-1126, 1993
18. Sullivan DC, Coleman RE, Mills SR, et al: Lung scan interpretation: Effect of different observers and different criteria. Radiology 149:803-807, 1983
19. Sostman HD, Coleman RE, Newman GE, et al: Experience with revised PIOPED criteria for V-Q scans in a clinically selected population. Radiology 193:103-107, 1994
20. Stein PD, Gottschalk A, Henry JW, et al: Stratification of patients according to prior cardiopulmonary disease and probability assessment based on the number of mismatched segmental equivalent perfusion defects. Chest 104:1461-1467, 1993
21. Stein PD, Henry JW, Gottschalk A: Mismatched vascular defects. Chest 104:1468-1472, 1993
22. Worsley DF, Kim CK, Alavi A, et al: Detailed analysis of patients with matched ventilation-perfusion defects and chest radiographic opacities. J Nucl Med 34:1851-1853, 1993
23. Hull RD, Hirsch J, Carter CJ, et al: Pulmonary angiography, ventilation lung scanning and venography for clinically suspected pulmonary embolism with abnormal perfusion lung scan. Ann Intern Med 98:891-899, 1983
24. Gottschalk A, Stein PD, Sostman HD, et al: Very low probability interpretation of ventilation-perfusion lung scans in combination with low probability clinical assessment reliably excludes pulmonary embolism: Data from PIOPED II. J Nucl Med 48:1411-1415, 2007
25. Forbes KP, Reid JH, Murchison JT: Do preliminary chest X-ray findings define the optimum role of pulmonary scintigraphy in suspected pulmonary embolism? Clin Radiol 56:397-400, 2001
26. Goldberg SN, Palmer EL, Scott JA, et al: Pulmonary embolism: prediction of the usefulness of initial ventilation–perfusion scanning with chest radiographic findings. Radiology 193:801-805, 1994
27. Stein PD, Alavi A, Gottschalk A, et al: Usefulness of non-invasive diagnostic tools for diagnosis of acute pulmonary embolism in patients with a normal chest radiograph. Am J Cardiol 67:1117-1120, 1991
28. Sostman HD, Stein PD, Gottschalk A, et al: Sensitivity and specificity of ventilation–perfusion scintigraphy for acute pulmonary embolism in PIOPED II. Radiology 246:941-946, 2008
29. Anderson DR, Kahn SR, Rodger MA, et al: Computerized tomographic pulmonary angiography versus ventilation-perfusion lung scanning in patients with suspected pulmonary embolism: a randomized controlled trial. J Am Med Assoc 298:2743-2753, 2007
30. Miniati M, Pistolesi M, Marini C, et al: Value of perfusion lung scan in the diagnosis of pulmonary embolism: Results of the Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISA-PED). Am J Respir Crit Care Med 154:1387-1393, 1996
31. Stein PD, Terrin ML, Gottschalk A, et al: Value of ventilation/perfusion scans compared to perfusion scans alone in acute pulmonary embolism. Am J Cardiol 69:1239-1241, 1992
32. Wells PS, Anderson DR, Rodger MA, et al: Excluding pulmonary embolism at the bedside without diagnostic imaging: Management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and D-dimer. Ann Intern Med 135:98-107, 2001
33. Allgood RJ, Wolfe WG, Ebert PA, et al: Effects of carbon dioxide on bronchoconstriction after pulmonary artery occlusion. Am J Physiol 214:772-775, 1968
34. Austin JMH, Sagel SS: Alterations of airway caliber after pulmonary embolization in the dog. Invest Radiol 7:135-139, 1972
35. Levy SE, Simmons DH: Redistribution of alveolar ventilation following pulmonary thromboembolism in the dog. J Appl Physiol 36:60-68, 1974
36. Dantzker DR, Wagner PD, Tornabene VW, et al: Gas exchange after pulmonary thromboembolization in dogs. Circ Res 42:92-103, 1978
37. Santolicandro A, Prediletto R, Fornai E, et al: Mechanisms of hypoxemia and hypocapnia in pulmonary embolism. Am J Respir Crit Care Med 152:336-347, 1995
38. Giuntini C: Ventilation/perfusion scan and dead space in pulmonary embolism: Are they useful for the diagnosis? Q J Nucl Med 45:281-286, 2001
39. Comroe JH Jr: The main function of the pulmonary circulation. Circulation 33:146-158, 1966
40. Worsley DF, Alavi A, Aronchick JM, et al: Chest radiographic findings in patients with acute pulmonary embolism: Observations from the PIOPED study. Radiology 189:133-136, 1993
41. Glenny RW, Lamm WJE, Albert RK, et al: Gravity is a minor determinant of pulmonary blood flow distribution. J Appl Physiol 71:620-629, 1991

42. Glenny RW: Blood flow distribution in the lung. Chest 114:8S-16S, 1998

43. Parker F, Weiss S: The nature and significance of the structural changes in the lungs in mitral stenosis. Am J Pathol 12:573-598, 1936

44. Smith RC, Burchell HB, Edwards JE: Pathology of the pulmonary vascular tree. IV. Structural changes in the pulmonary vessels in chronic left ventricular failure. Circulation 10:801-808, 1954

45. Giuntini C, Pistolesi M, Miniati M: Pulmonary venous hypertension—mechanisms and consequences, in Wagenvoort CA, Denolin H (eds): Pulmonary Circulation. Advances and Controversies. Amsterdam, Elsevier Science Publisher, 1989, pp 131-147

46. Gilday DL, James AE Jr: Lung scan patterns in pulmonary embolism versus those in congestive heart failure and emphysema. Am J Roentgenol Radium Ther Nucl Med 115:739-750, 1972

47. Moses DC, Silver TM, Bookstein JJ: The complementary roles of chest radiography, lung scanning, and selective pulmonary angiography in the diagnosis of pulmonary embolism. Circulation 49:179-188, 1974

48. Viegi G, Matteelli G, Angino A, et al: The proportional Venn diagram of obstructive lung disease in the Italian general population. Chest 126: 1093-1101, 2004

49. Miniati M, Monti S, Stolk J, et al: Value of chest radiography in phenotyping chronic obstructive pulmonary disease. Eur Respir J 31:509-515, 2008

50. Miniati M, Monti S, Bauleo C, et al: A diagnostic strategy for pulmonary embolism based on standardised pretest probability and perfusion lung scanning: a management study. Eur J Nucl Med Mol Imaging 30: 1450-1456, 2003

51. Miniati M, Monti S, Bottai M: A structured clinical model for predicting the probability of pulmonary embolism. Am J Med 114:173-9, 2003

52. Miniati M, Monti S, Bottai M, et al: Survival and restoration of pulmonary perfusion in a long-term follow-up of patients after acute pulmonary embolism. Medicine (Baltimore) 85:253-262, 2006

53. Greenspan RH, Ravin CE, Polansky SM, et al: Accuracy of the chest radiograph in diagnosis of pulmonary embolism. Invest Radiol 17:539-543, 1982.