A Diagnostic Strategy Using Ventilation–Perfusion Studies in Patients Suspect for Pulmonary Embolism

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A diagnostic strategy for the assessment of pulmonary embolism was developed using results of scintigraphic examinations in over 100 patients, all of whom had angiographic assessment of their pulmonary vasculature and nearly 50% of whom had combined ventilation–perfusion studies. The highest-probability estimate of pulmonary embolism that could be made in the absence of a ventilation study was 80%. When a ventilation study was added, this probability increased to nearly 100% for patients with multiple large perfusion defects and normal ventilation. For smaller defects with normal ventilation, the probability of pulmonary embolism was only 50%. For perfusion defects corresponding to known radiographic abnormalities, the probability of pulmonary embolism was 25%.

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The diagnosis of acute pulmonary embolism has been plagued on the one extreme by the nonspecificity of clinical signs and symptoms and at the other extreme by the morbidity and high financial cost associated with pulmonary angiography (*1,2*). Perfusion lung scanning is intermediate in this spectrum in that its ability to detect patients with embolic disease is extremely high, 100% (*3*), but its specificity is lower, varying with the findings present on the concomitant chest radiograph and ventilation study (*4–10*). This investigation suggests a diagnostic strategy for the evaluation of patients suspect for pulmonary embolism once the results of perfusion or ventilation–perfusion studies are known.

METHODS

One hundred and five consecutive patients who had both pulmonary scintigraphy and angiography in the past 3 years were the subjects of this study. Seventy-seven percent of patients had angiograms within 24 hr of the lung scan, 87% within 48 hr, and 97% within 72 hr. The patients presented with a variety of symptoms, the most common being pleuritic chest pain or dyspnea.

Perfusion studies in all patients, and ventilation studies in 52 patients, were performed as previously described (*9*). In particular, ventilation studies were performed after the perfusion study, in the projection best displaying the defects. Twenty millicuries of ^{133}Xe dissolved in 600 ml of oxygen were used, so that a single-breath image of 100K counts was obtained in 10–15 sec.

Patients were categorized according to the presence (PE+) or absence (PE−) of pulmonary embolism when intraluminal filling defects or the trailing edge of a thrombus could be clearly defined. The locations of the thrombi were not correlated with the locations of perfusion abnormalities.

Defects on the perfusion study were categorized according to their number and then according to their relationship to the anatomic divisions of the lung. The proportions of patients with and without pulmonary embolism having a *single* perfusion defect, or one of the following patterns involving *multiple* defects, were determined: subsegmental defects

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only or both subsegmental and nonsegmental defects (designated SS); segmental defects only or segmental defects as well as smaller defects (designated S); and lung or lobar defects or lung or lobar defects as well as smaller defects (designated L). These proportions or conditional probabilities describing perfusion characteristics of patients with and without pulmonary embolism were designated $P(Q_i|PE+)$* and $P(Q_i|PE-)$*, where Q_i represents the above-described perfusion patterns. These probabilities were then used with Bayes' theorem to calculate the probability of pulmonary embolism in a patient once the results of the perfusion study were known (*11,12*). These probabilities were designated $P(PE+|Q_i)$.

Ventilation studies were categorized by the presence of normal or mildly reduced ventilation in a poorly perfused area (ventilation–perfusion mismatch) or by the absence of ventilation in a poorly perfused area (ventilation–perfusion match). Patients who had an area of poor perfusion and normal ventilation as well as another area of poor perfusion and poor ventilation on the same study were categorized as having both patterns. The incidence of these ventilation–perfusion patterns in each of the above three types of perfusion patterns was determined, and Bayes' theorem was used to calculate the probability of pulmonary embolism using the results from both the perfusion study and the ventilation study.

RESULTS

Pulmonary angiograms. The pulmonary angiograms of 41 of the 105 patients were initially interpreted as diagnostic of pulmonary embolism. One additional patient had a pulmonary angiogram which was only interpreted as abnormal retrospectively: this patient had a lung biopsy showing infarction. All 42 of these patients (40% of the total) were included in the category of patients believed to have pulmonary embolism. The pulmonary angiograms of the remaining 63 patients (60%) were not interpreted as showing pulmonary emboli.

Perfusion studies. Of the 105 perfusion studies, 104 were abnormal. Only 16 of the abnormal studies had a single perfusion defect and only three of these were in patients with pulmonary embolism (Table 1). Thirty-nine of the 42 patients (93%) with pulmonary embolism and 49 of the 63 (78%) without pulmonary embolism had multiple perfusion defects.

In patients with multiple perfusion defects, 52% of patients with pulmonary embolism had perfusion defects involving at least lung or lobar areas; only 8% of patients without pulmonary embolism had similar findings (Table 2). Segmental defects occurred with about equal frequency (22–33%) in both groups. Subsegmental defects only were rarely seen in patients with pulmonary embolism but were common in patients without pulmonary embolism (48% of these patients). Application of Bayes' theorem to these data shows that the highest-probability estimate for the presence of pulmonary embolism obtainable from perfusion data alone, $P(PE+|Q_i)$, is 81% (Table 2).

Sixteen of the 105 patients (15%) had perfusion studies whose defect(s) matched radiographic abnormalities (consolidation, effusions, atelectasis) in location and extent. Four of these 16 patients (25%) had pulmonary embolism with associated radiographic findings of consolidation (two patients), atelectasis and consolidation (one patient), and atelectasis and bilateral effusions (one patient). Twelve of these 16 patients did not have pulmonary embolism. The diagnosis most often responsible for the presenting complaint in these 12 patients was pneumonia (five patients). Other diagnoses respon-

TABLE 1. CORRELATION OF NUMBER OF DEFECTS ON PERFUSION STUDY WITH PE+ AND PE−

Perfusion pattern	PE+	PE−
No defects	0	1
Single defect:		
Lung	1	2
Lobar	2	2
Segmental	0	3
Subsegmental or nonsegmental	0	6
Many defects	39	49
Total	42	63

TABLE 2. PROBABILITY OF VARIOUS PERFUSION PATTERNS WITH MULTIPLE DEFECTS IN PE+ AND PE−, AND THE ASSOCIATED PROBABILITY OF PE+

Perfusion pattern Q_i*	$P(Q_i\|PE+)$	$P(Q_i\|PE-)$	$P(PE+\|Q_i)$
L	.52	.08	.81
S	.33	.22	.50
SS	.07	.48	.09

* See Methods for explanation of notation.

* $P(Q_i|PE+)$ is read as the probability of perfusion pattern Q_i in the presence of PE+ and is a measure of the sensitivity of the pattern Q_i in detecting patients with disease. $P(Q_i|PE-)$ is read as the probability of perfusion pattern Q_i in patients without pulmonary embolism. Thus, $1 - P(Q_i|PE-)$ is the specificity of the perfusion pattern in identifying patients without pulmonary embolism.

sible for the radiographic abnormalities and scintigraphic patterns were renal failure with pleural effusions, systemic lupus erythematosis, trauma, hypoalbuminemia (all with unilateral or bilateral pleural effusions) and granulomatous disease with an effusion and consolidation.

Ventilation studies. Ventilation studies were performed in 52 of the 104 patients with abnormal lung scans (Table 3). Ventilation studies were not performed in the remaining 52 because (A) an abnormality on chest radiograph matched the perfusion abnormality in location and extent (16 patients), (B) the defects were too small to resolve with ^{133}Xe (28 patients), or (C) there was poor patient cooperation (eight patients). All 32 patients with pulmonary embolism in this group had at least one area with a ventilation–perfusion mismatch; 30 had studies showing only ventilation–perfusion mismatches and two had studies with mixed patterns.

Among the 20 patients without pulmonary embolism, 12 had ventilation–perfusion matches only. Three of the 20 patients had studies with both patterns and five had studies showing ventilation–perfusion mismatches only. The discharge diagnoses of the five patients showing ventilation–perfusion mismatches and no angiographic evidence of pulmonary emboli were pneumonia (three patients), dog-worm infestation (one patient), and no identifiable cause (one patient).

TABLE 3. CORRELATION OF VENTILATION–PERFUSION PATTERNS WITH PRESENCE AND ABSENCE OF PULMONARY EMBOLISM

	PE+	PE−
Ventilation–perfusion mismatch only*	30	5
Ventilation–perfusion match only†	0	12
Both patterns	2	3

* Ventilation normal, perfusion abnormal.
† Ventilation and perfusion both abnormal.

TABLE 4. PROBABILITY OF PULMONARY EMBOLISM IN PATIENTS WITH MULTIPLE PERFUSION DEFECTS AND ASSOCIATED VENTILATION–PERFUSION MISMATCHES

Perfusion pattern*	Probability of PE+ $[P(PE+\|Q_i)]$
L	0.94
S	1.00
SS	0.50

* See Methods for explanation of notation.

Adding a ventilation study to the perfusion study considerably increased the reliability with which pulmonary embolism could be diagnosed (Table 4). In patients with multiple defects involving at least a lung or a lobe, a ventilation–perfusion mismatch raised the probability of pulmonary embolism slightly, from 0.81 to 0.94. For patients with smaller defects, on the other hand, the increase was greater: from 0.5 to 1.0 for multiple defects involving at least a segment, and from 0.09 to 0.50 for multiple subsegmental defects. Thus, the reliability with which pulmonary embolism could be diagnosed approached 100% for patients with multiple large defects and an associated ventilation–perfusion mismatch.

DISCUSSION

Several studies have described the number and size of perfusion defects in patients with pulmonary embolism, and a few studies have provided similar information in patients without pulmonary embolism. The introduction of ventilation–perfusion examinations 5 years ago resulted in similar tabulations using data from these combined studies (*5–7*). However, the limited angiographic proof of the diagnosis in these investigations precluded development of a reliable diagnostic strategy for suspected pulmonary embolism.

Development of such a diagnostic strategy for pulmonary embolism must consider the differences in sensitivity and specificity of scintigraphic and angiographic procedures. Perfusion studies alone are highly sensitive for detection of disease and, when combined with ventilation studies, may be highly specific as well. Angiography, on the other hand, is more specific but at the same time less sensiitve. Although opacification of an intraluminal filling defect or the trailing edge of a thrombus is diagnostic of pulmonary embolism, failure to observe these findings does not necessarily rule out embolic disease, because of the difficulty in opacifying small peripheral emboli or because of the rapid resolution of larger emboli present earlier (*13–16*).

This investigation attempted to define a diagnostic strategy using results of scintigraphic examinations in over 100 patients, all of whom had angiographic assessment of their pulmonary vasculature and nearly 50% of whom had combined ventilation–perfusion studies. The trends suggested by the data point out the major role that combined ventilation–perfusion studies have in the diagnosis of pulmonary emboli and in the selection of patients either most or least in need of angiography for definition of their disease.

There are several situations in which angiography is not essential for the diagnosis of pulmonary embolism. At one extreme are patients in whom pul-

monary embolism is very likely. These patients have multiple large (segmental or greater) defects and normal ventilation. At the other extreme are patients in whom pulmonary embolism is very unlikely (probability near zero) either because they have a normal perfusion study or because they have multiple perfusion defects associated with abnormal ventilation. In our series, patients with a solitary segmental or subsegmental defect would also be included in this category. However, in the urokinase study, a larger percentage of patients would probably have had solitary perfusion defects since 7% had angiograms which showed an embolus in or just proximal to a single segmental artery (*17*). The decision to perform angiograms in patients with solitary segmental defects should be based in large part on nonscintigraphic data.

The need for angiography in patients who have multiple defects, lobar and smaller in size, but who do not have an associated ventilation study is likely to vary because the probability of embolic disease in this group is over 80%. Thus the decision to perform angiography should be dictated by other associated historical or physical findings, by the probability of a false-negative or technically inadequate pulmonary angiogram, and by the relative risks and benefits of anticoagulation therapy.

There are several situations in which the diagnosis of pulmonary embolism from scintigraphic and radiographic data is under 50% and in these patients angiography is needed to define the etiology of the abnormal perfusion or ventilation–perfusion patterns. Angiography is therefore recommended when:

1. a single defect involves a lobe or lung;
2. there are multiple segmental or segmental and subsegmental defects and no ventilation study;
3. multiple subsegmental defects are associated with normal ventilation;
4. the perfusion defect(s) match radiographic abnormalities;
5. there are multiple perfusion defects, some of which have normal ventilation and some of which have diminished ventilation.

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