Computer analysis of ventilation-perfusion scans for detection and assessment of lung disease

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ABSTRACT A previously reported computer analysis has been used to provide numerical ventilation-perfusion lung scan data, for comparison with tests of airways function and results of arterial blood gas analysis in 11 patients with pulmonary embolism, 18 with asthma, and 37 with chronic obstructive lung disease. In pulmonary embolism an index of underperfusion showed high sensitivity, and an index of ventilation-perfusion mismatching correlated well with severity (hypoxaemia). In asthma an index of underventilation was sensitive and correlated well with severity of airways obstruction. In chronic obstructive lung disease the same index was sensitive but correlated poorly with severity. This was attributed to heterogeneity of the lung disease (airways obstruction plus emphysema) in chronic obstructive lung disease. Ventilation-perfusion mismatching was frequently present in airways disease, and was often of great severity in chronic obstructive lung disease. Discrimination between pulmonary embolism and either type of airways disease was possible by using a combination of underfusion and underventilation indices. The technique offers the prospect of increasing the information derived from lung scans and of automating the reporting of scans.

We have recently reported a technique of computer analysis of ventilation-perfusion lung scans, which is fully automated and provides numerical data on the distribution of ventilation and perfusion, their matching, and the extent of departure of any of these quantities from a normal range.[1]

To explore the possible usefulness of the technique, both in diagnosis and in assessing severity, we have compared scan data with relevant indices of physiological function of the lung in groups of patients carefully selected to represent uncomplicated pulmonary embolism, asthma, and chronic obstructive lung disease with a wide range of severity.

Methods

SELECTION OF PATIENTS
Pulmonary embolism
Patients were selected retrospectively from a large group whose diagnosis at discharge had included pulmonary embolism. This diagnosis would, of course, have been influenced by lung scan appear-

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ances. Selection for the present study, however, ignored the lung scan and was based on the following criteria:

(a) A firm clinical diagnosis of acute minor pulmonary embolism. The diagnosis was based on: the sudden onset of dyspnoea with or without cough, haemoptysis, or pleuritic chest pain where the dyspnoea could not be accounted for by any other mechanism on clinical examination and chest radiograph; no known pre-existing cardiovascular or respiratory disease; a predisposing factor to the development of thromboembolic disease; the presence on examination of tachypnoea and tachycardia; hypoxaemia(or an abnormally high alveolar-arterial gradient for oxygen tension). *(b) A ventilation-perfusion lung scan* taken within seven days of the acute event and within 24 hours of arterial blood gas analysis.

Eleven patients fulfilled these criteria. There were seven men and four women, mean age 58·2 (SD 17·7) years.

ASTHMA
The diagnosis of asthma was based on a history of intermittent cough, dyspnoea, and wheezing with little or no sputum. Earlier tests of airways function had shown airflow obstruction that was reversible

(>20%) either by bronchodilator or by oral steroids. Eighteen patients were studied; there were 10 men and eight women, mean age 42·2 (SD 16·5) years. Airways tests and a ventilation-perfusion lung scan were performed within five days of each other in all patients. In 13 the interval was less than 24 hours; in the other five airways function was stable during the study period.

CHRONIC OBSTRUCTIVE LUNG DISEASE
Subjects were selected who had a firm diagnosis of stable chronic obstructive lung disease based on: the Medical Research Council criteria[2] for chronic bronchitis; evidence of airways obstruction from lung function testing (reduction of FEV_1 both absolutely and as a fraction of forced vital capacity); airways obstruction showing less than 20% reversibility with inhaled bronchodilator; no evidence of an acute exacerbation of chronic obstructive lung disease; no eosinophilia; no radiological evidence of any disease process other than emphysema affecting the lungs or pleura.

All tests (lung function, blood gas analysis, and lung scan) were carried out within two weeks of each other.

On the basis of these criteria, 37 patients were included in the study, mean age 65·1 (SD 11·4) years. All but one were or had been smokers, with a mean exposure of 50 (29) pack years; there were 32 men and five women. In all but four cases there was other evidence to support the diagnosis of irreversibility. In 15 there was radiological or postmortem evidence of emphysema. In a further 10 there had been no bronchodilatation in response to high dose corticosteroid treatment, and in seven cases follow up of at least a year with serial spirometric tests showed decline or no significant change.

COMPUTER ANALYSIS OF THE
VENTILATION-PERFUSION LUNG SCAN
Details of the method for performing the ventilation-perfusion lung scan and the computer analysis of the posterior views have been published.[1] The computer analysis was confined to the posterior scan views and derived numerical values from these views, which were presented graphically. In the graphs the vertical length of each lung was normalised to 50 units. The horizontally summed counts in each of the 50 units were plotted against normalised lung length, and were themselves expressed as a percentage of the total counts for both lungs Thus low activity in one area implies high activity elsewhere since the total is always 100%.

The form of the graph is shown in figure 1. Normalised lung length from apex to base forms the vertical axis, and normalised activity in left and right lungs is plotted either side of this axis, superimposed on the subject's age and sex matched normal range for each lung. The program also analysed departure from normal limits, giving a separate numerical score to areas above and below these limits. Thus for a perfusion scan all areas where perfusion exceeded the upper limit of normal were summed to make the overperfusion score, and all areas below the lower limit of normal were summed to make the underperfusion score. The ventilation scan was treated similarly to yield over- and under-ventilation scores. These scores have the dimensions of activity (expressed as a percentage of the total for both lungs, scaled up ×50 for computational convenience) multiplied by fractional lung length. Finally a third graph was produced showing the difference between individual ventilation and perfusion values at each point down each lung. Deviations from the normal range for this V-Q graph (fig 1E) were also analysed and expressed as high and low V-Q scores. Separate
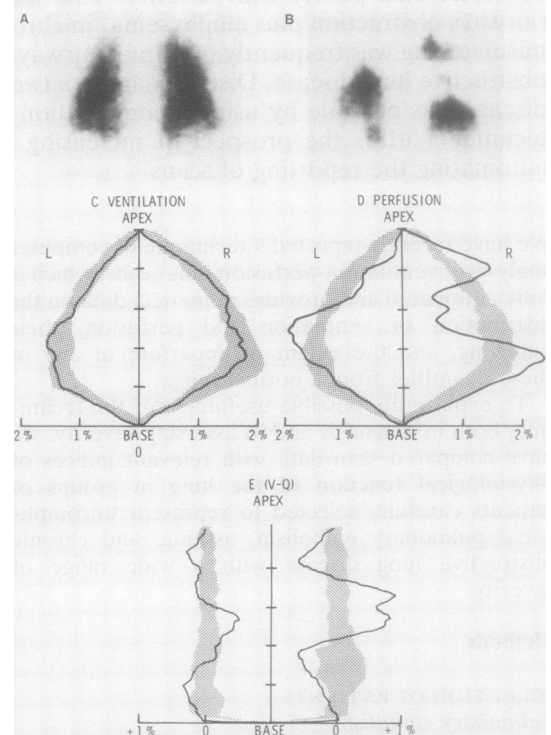

Fig 1 *Posterior ventilation (A) and perfusion (B) images in acute, uncomplicated minor pulmonary embolism. Scan analysis presented graphically for ventilation (C), perfusion (D), and ventilation minus perfusion (E). In C, D, and E the data are presented as a solid line with lung length on the vertical axis and counts, expressed as percentages of total counts, on the horizontal axis. The shaded area shows the age and sex matched normal range (mean and 2 SD).*

normal limits (95% probability of normality) were constructed for all these scores using probability distributions for the normal and abnormal patient groups.

In asthma and chronic obstructive lung disease, obstruction of airflow will reduce ventilation locally, so that the underventilation score is of principal interest. In vascular disease, on the other hand, the underperfusion score might be expected to be the main indicator. To detect the mismatching of ventilation and perfusion in all groups, low V-Q scores were examined since these represent relative underventilation, which causes hypoxaemia.

AIRWAYS TESTS AND BLOOD GAS ANALYSIS
Values of forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and peak expiratory flow rate (PEFR), corrected to BTPS, were obtained via a heated Fleisch No 3 pneumotachograph (Hewlett-Packard Vertek Series VR5600). Predicted values were determined from Cotes.[3]

All patients with chronic obstructive lung disease and pulmonary embolism had arterial blood drawn for measurement of oxygen tension (PO_2), carbon dioxide tension (PCO_2), and pH. The sample was taken with the subject breathing room air and analysed in a Corning 165 or 168 blood gas analyser. To allow for hyperventilation and hypoventilation, with abnormal PCO_2, the difference between the oxygen tension of alveolar air and arterial blood (alveolar-arterial oxygen gradient), was preferred to PO_2. It was calculated from the PO_2 and PCO_2 on the basis of a simplified form of the alveolar gas equation[4] and on the assumption of a respiratory quotient of 0·8.

Informed consent was obtained from all subjects undergoing non-diagnostic lung scans, and the project had the approval of the Hospital Ethical Committee.

Results

PULMONARY EMBOLISM
In all 11 cases one or more defects in perfusion were visible on the lung scan, without corresponding defects in ventilation (figs 1A and B). The ventilation scan analysis (fig 1C) was normal in all cases. The perfusion scan analysis (fig 1D) showed several features. Firstly, the major perfusion defects pro-
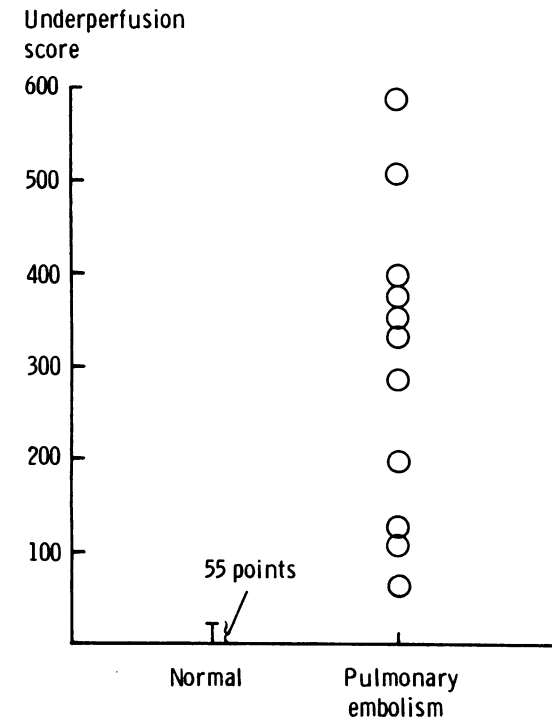
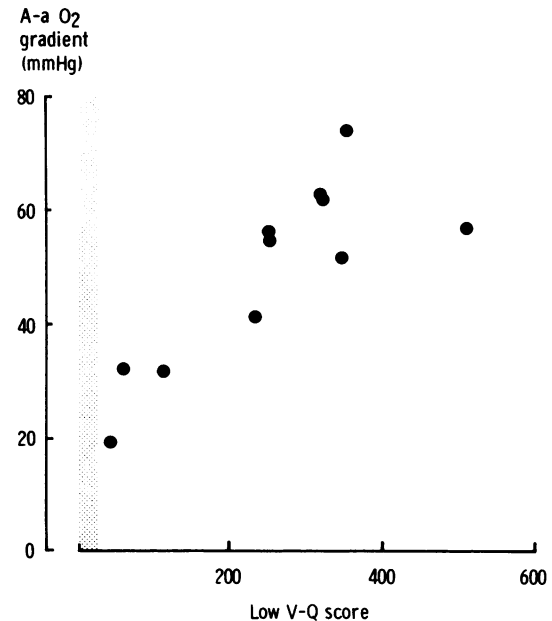Fig 2 *Underperfusion scores for 11 patients with pulmonary embolism and 55 normal subjects.*

Fig 3 *Severity of hypoxaemia (expressed as alveolar-arterial oxygen gradient—see under "Methods") plotted against extent of ventilation-perfusion mismatching (low V-Q score) for 11 cases of acute pulmonary embolism. Correlation coefficient (r) = 0.81, p < 0.01. The shaded area indicates the normal range for low V-Q score. Conversion: SI to traditional units: Alveolar-arterial oxygen (A-a O_2) gradient: 1 kPa = 7.5 mm Hg.*

duced areas where the graph fell below the normal range. Secondly, unaffected areas of the lung showed high perfusion counts. Finally, because each point on the graph is the sum of a horizontal row, a small perfusion defect adjacent to an area with normal or high counts may be missed. The left base in fig 1 is an example of this. Some small defects were missed in this way in scans with many small defects and in scans where there were large defects. This occurred only where there were three or more defects.

When the perfusion scores were examined, the embolised area of the lung produced underperfusion scores outside the normal range in all patients (fig 2). The analysis also shows abnormal overperfusion scores in unaffected areas in all cases. This is a real effect, since cardiac output is maintained or even increased in minor pulmonary embolism.[5] Since all ventilation scores were normal, each patient showed appreciable ventilation-perfusion mismatch. The low V-Q score showed a correlation with the alveolar-arterial oxygen gradient (fig 3).

ASTHMA

The scans of the seven asthmatic patients who were in remission at the time of study, with normal results in airways tests, were normal on visual inspection.
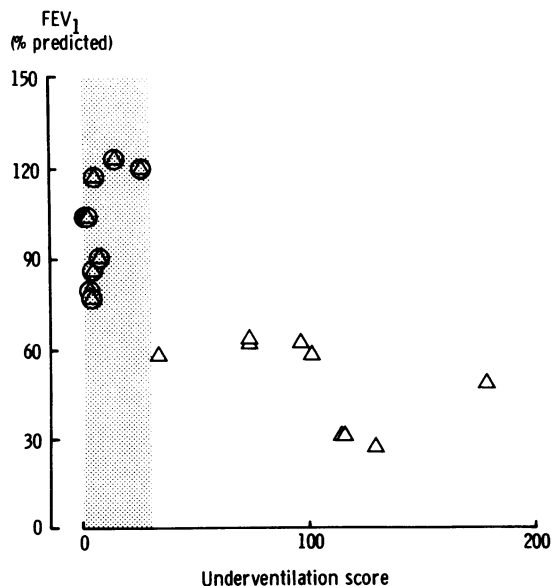

Fig 4 *Severity of airways obstruction (FEV₁ as percentage of predicted FEV₁) plotted against underventilation score for 18 patients with asthma. The shaded area indicates the normal range for underventilation score. Ringed points represent patients with normal airways function.*

Abnormalities were visible in the scans of all the other subjects. In 10 of the 11, ventilation defects with corresponding but less severe defects in perfusion were present; this type of lesion was commonly multiple. In the 11th patient, who had bilateral defects of this kind, there was also a small perfusion defect unaccompanied by any abnormality of ventilation.

Scan analysis showed that in five of these 11 patients there was a generalised relative reduction in ventilation in both lower zones, with a corresponding relative increase higher up. Perfusion was similarly redistributed. This shift was not always detectable by simple inspection of the scans.

Figure 4 shows a plot of the underventilation score against a test of airways obstruction (FEV₁ expressed as a percentage of its predicted value) for the 18 asthmatic patients. A strong inverse correlation exists ($r = -0.85$, $p < 0.001$). A similar correlation obtains if FEV₁/FVC ratio is plotted against underventilation score ($r = -0.84$, $p < -0.001$). Figure 4 also shows that in this small group scan analysis is sensitive in detecting abnormal airways function.

Perfusion scans were normal in the asthmatic patients who were in remission, but underperfusion scores occurred in nine of the other 11. Again, for the whole group there was a significant negative correlation between results of airways tests and underperfusion score ($r = -0.63$, $p < 0.01$ for both FEV₁% and FEV₁/FVC). Seven of the 11 patients with active asthma showed mild mismatching, with low V-Q scores in the range 30–135; these values overlap those of the three mildest cases of pulmonary embolism, shown in figure 3. For the whole asthma group the low V-Q score showed significant negative correlation with FEV₁% ($r = -0.73$, $p < 0.001$) and with FEV₁/FVC ratio ($r = -0.81$, $p < 0.001$).

Chronic obstructive lung disease

Figure 5 shows an example of a scan and its analysis in a patient with chronic obstructive lung disease. The scan shows multiple defects of ventilation and perfusion, which occur in the same regions of the lungs and are usually described as matched. This general pattern was typical of all the patients studied.

Analysis of the ventilation scan showed underventilation scores outside the normal range in all 37 patients. These correlated poorly with FEV₁ as a percentage of predicted FEV₁ (fig 6A; $r = -0.18$, NS), and with FEV₁/FVC ratio, ($r = -0.12$, NS). The range of severity of underventilation scores was

much greater than that seen in asthma (compare fig 6A and fig 4).

Abnormal underperfusion scores, arising in one or more areas of the lungs, occurred in 34 of the patients. In six of these the underperfusion score was caused in part by a region where underperfusion was unaccompanied by underventilation. In other areas of these six scans, and throughout the scans of 27 other patients, underventilation scores were always present in the region of the underperfusion score. In the remaining patient there was an under-perfusion score just above the normal limit arising from a single region of the left lung and an area of underventilation, without underperfusion, in the right lung. Low V-Q scores, implying mismatching with relative underventilation, occurred in 24 patients. Fig 6B shows a plot of the alveolar-arterial oxygen gradient versus low V-Q score for all 37 patients. There is a much wider range of scores than in asthma, and the scores correlate poorly with alveolar-arterial oxygen gradient (r = 0.27, NS). Nine patients with high gradients showed normal scores.

Fig 5 *Ventilation and perfusion images and analyses in a patient with chronic obstructive lung disease. Details as in figure 1.*

Discussion

The purpose of this study was to challenge a method of numerical lung scan analysis with scans from patients with abnormal lungs to establish whether
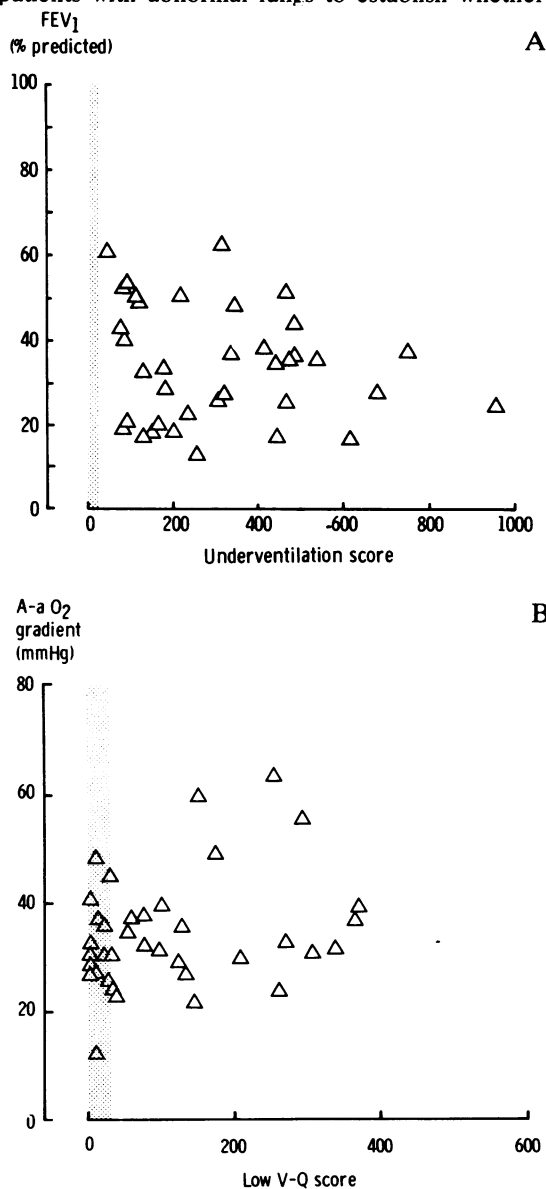

Fig 6 *A—Severity of airways obstruction (FEV$_1$ as percentage of predicted FEV$_1$) plotted against underventilation score for 37 patients with chronic obstructive lung disease. Details as in figure 4 but different scale for abscissa. B—Severity of hypoxaemia plotted against extent of mismatching in 37 patients with chronic obstructive lung disease. Details as in figure 3.*
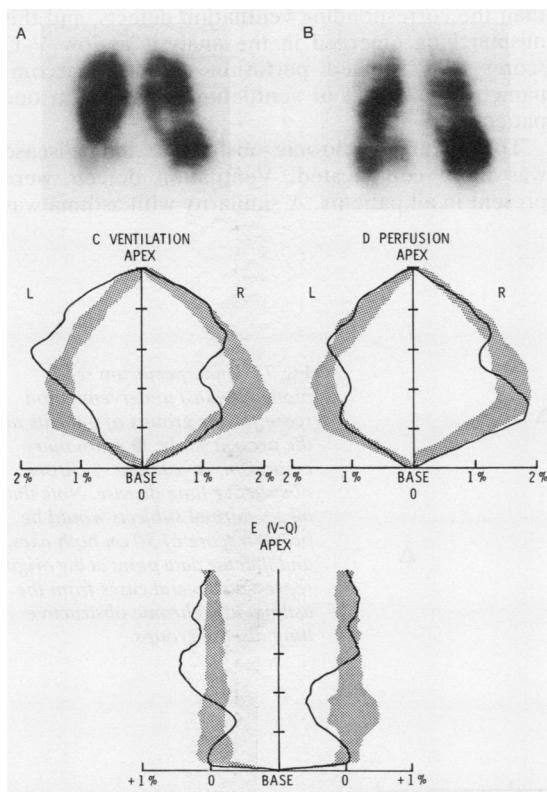
abnormalities can be detected, whether the numerical results correlate with severity of disease, and whether different diseases had specific patterns of abnormality.

We selected only patients with unequivocal diagnoses in whom clinical and physiological data relevant at the time of the lung scan were available; this latter criterion severely restricted numbers, particularly in the case of pulmonary embolism. In all groups visual inspection of the scans revealed patterns typical of previously published descriptions.

The criticism can be made of our cases of pulmonary embolism that, because they were selected retrospectively, the scan appearances were themselves a factor in establishing the diagnosis originally. This is probably true but it does not invalidate the present use of such cases to test the underperfusion score as a test of detection and the V-Q score as a test of severity of ventilation-perfusion disturbance.

Asthma was taken as a source of ventilation defects, and the underventilation score was examined both as a test of detection and, when correlated with lung function, as an indicator of severity. In chronic obstructive lung disease we looked at both ventilation and perfusion analyses.

In the patients with acute pulmonary embolism, the scans all showed the typical appearance of perfusion defects unaccompanied by ventilation defects.[6-9] Analysis of the perfusion scan detected underperfusion in all cases (fig 2). Small perfusion defects occurring in the presence of larger defects were not always detected. This is because the presence of a large perfusion defect in one area of the lung led to augmentation of counts elsewhere, including those in the region of other defects. Since cardiac output is not depressed in minor pulmonary embolism,[5] this effect is physiologically appropriate.

Hypoxaemia in pulmonary embolism, whether due to shunting or to ventilation-perfusion mismatching, should correlate best with a low V-Q score (relative underventilation). Figure 3 shows that this was the case in our series and, since hypoxaemia correlates well with severity in minor pulmonary embolism,[5] the low V-Q score appears to be a useful indicator of severity.

In asthma, areas of underventilation are present in all patients with disturbances of airways tests. As figure 4 shows, the underventilation score correlates well with the severity of airways obstruction. Most ventilation defects were accompanied by a local reduction in perfusion, so that underperfusion score also correlated with airways obstruction. These perfusion defects were, however, usually less noticeable than the corresponding ventilation defects, and this mismatching emerged in the analysis as low V-Q scores. An isolated perfusion defect, unaccompanied by a defect of ventilation, occurred in one patient.

The picture in chronic obstructive lung disease was more complicated. Ventilation defects were present in all patients. A similarity with asthma was
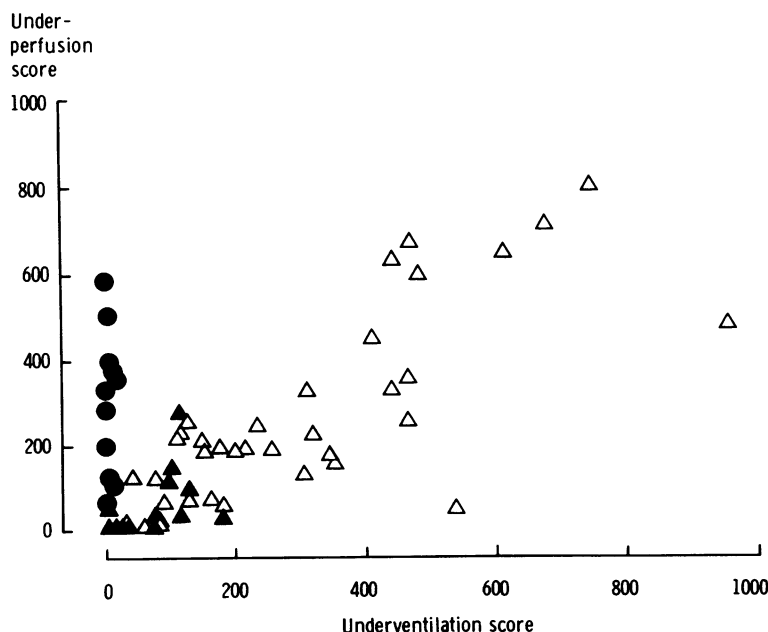

Fig 7 *Underperfusion score plotted against underventilation score for the groups of patients in the present study. ● pulmonary embolism; ▲ asthma; △ chronic obstructive lung disease. Note that all 55 normal subjects would lie below a score of 30 on both axes, and that the data point at the origin represents several cases from the asthma and chronic obstructive lung disease groups.*

that perfusion defects were present in the same region of the lung as the ventilation defects and were usually less severe. In contrast with asthma, the range of underventilation scores was wide, and there was a lack of correlation between underventilation score and severity of airways obstruction (fig 6A). A possible reason for this might be the existence of more than one pathological form of chronic obstructive lung disease. All our patients had chronic bronchitis and, since all but one were smokers, a considerable proportion are likely also to have had emphysema. This possibility is supported by the demonstration of emphysema in four of the patients in this group who have since had necropsies and in a further five patients who have undergone computed tomography of the thorax.

These considerations also apply to the perfusion scan results, which showed abnormal underperfusion scores in most patients, uncorrelated with indices of airways obstruction. In both asthma and chronic obstructive lung disease such areas of underperfusion might arise as a compensatory response to underventilation through the mechanism of hypoxic pulmonary vasoconstriction. In emphysema, however, patchy obliteration of the peripheral vascular bed occurs in addition.

Conventional descriptions of the lung scan in chronic obstructive lung disease emphasise a pattern of coexisting ventilation and perfusion defects.[9 10] The present analysis shows that matching is incomplete in these areas (fig 6B); 24 (65%) of our patients had low V-Q scores. The mixed pathological features, the fact that the scans show the distributions rather than absolute levels of ventilation and blood flow, and the non-linearity of the oxygen dissociation curve of haemoglobin are the likely explanations of the poor correlation between low V-Q and alveolar-arterial oxygen gradient in figure 6B.

In summary, there is high sensitivity of appropriate scan indices in both pulmonary embolism and asthma, and good correlation between appropriate scan indices and physiological indices of severity. In chronic obstructive lung disease, probably because of dual pathological processes in the lung, correlations with airways tests are much less impressive— though overall sensitivity, based on underventilation score, is still high.

In the present series of patients, those with pulmonary embolism could be separated from both normal subjects and those with airways disease by examination of underperfusion and underventilation scores (fig 7). As mentioned earlier, our cases of pulmonary embolism were uncomplicated. It will be of interest to test whether this discriminatory ability is maintained in more complicated cases of pulmonary embolism—for example, those with pleural effusion, pulmonary infarction, cardiac failure, and pre-existing lung disease. It will also be of interest to make a formal comparison between scan analysis and conventional visual assessment in the diagnosis and assessment of pulmonary embolism and airways disease.

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