SCINTIGRAPHIC STUDY OF PULMONARY BLOOD FLOW DISTRIBUTION IN CYSTIC FIBROSIS

A. Piepsz, P. Decostre, and D. Baran

Hopital Saint-Pierre, Brussels University, Brussels, Belgium

Considerable alterations of lung perfusion are evident in cystic fibrosis although no primary vascular involvement has been shown. Seventy-three children from the age of 6 weeks to 19 years have been investigated by means of perfusion scintigraphy with a scintillation camera. Special attention was paid to the actual clinical status (remission or acute phase) at the time of examination. In the remission phase, correlation was found between the perfusion abnormalities and the severity of the disease. In the acute phase, striking transient alterations develop; their prognostic value should be determined by further investigation.

Among the clinical manifestations of cystic fibrosis, pulmonary involvement represents its most critical problem. The early detection of pulmonary lesions and the evaluation of their extension are essential to establish adequate treatment. Earlier investigations have revealed considerable alterations of lung perfusion patterns. Perfusion defects were shown to follow ventilation abnormalities without primary involvement of the pulmonary vessels. The question arises whether the scintigraphic study of lung perfusion might be significant in cystic fibrosis. The present work shows that this technique represents a valuable test in the study of the distribution, the severity, and the evolution of the pulmonary lesions. In addition, it is a simple procedure, easily applicable to very young children who are not cooperative for functional tests.

MATERIALS AND METHODS

From 1969 to 1971, 115 scintigraphies were performed on 73 children, (38 boys and 35 girls) aged 6 weeks to 19 years. They all attend regularly our specialized clinic for cystic fibrosis. The diagnosis of their disease was established on the basis of the sweat test performed by the iontophoresis pilocarpine method (*1*). The periodic clinical examination and a recent chest x-ray made possible the estimation of the severity of the disease on the basis of the Shwachman score (*2*). Because of the age of most of our patients (60% are less than 6 years old), functional tests are available only in a small fraction of the older age group and are not considered in this work. All patients are on treatment including pancreatic enzymes, inhalation therapy, postural drainage (once or twice daily), mist-tent therapy, and prophylactic or therapeutic doses of antibiotics.

Lung perfusion scintigraphy was performed with the scintillation camera (Nuclear-Chicago Pho/Gamma III) using the parallel-hole or diverging collimator according to the size of the chest. Thirty-five scintigraphies were performed with ^{113m}In-macroaggregates* and, from June 1970, ^{99m}Tc-albumin microspheres* were used in the other 80 cases with two main advantages:

1. Homogenous size of labeled particles.
2. High efficiency of the scintillation camera crystal for the 140-keV gamma ray of ^{99m}Tc compared to the 393-keV gamma ray of ^{113m}In.

The radionuclide dose was established by taking into account the age of the patient and the geometric factors obtained from the literature (*3*). Although the upright position gives a more physiological partition of the particles in the lungs, the i.v. injection and the examination were performed in the recumbent position. This position enables more accurate positioning and better immobilization of the patient under the detector. The error due to movement of the child is reduced by using a vacuum-hardened

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For reprints contact: A. Piepsz, Dept. Pediatrics, Hopital Saint-Pierre, 322 rue Haute, 1000, Brussels, Belgium.

* In K4 and Tc K5—CEA—CEN—SORIN.

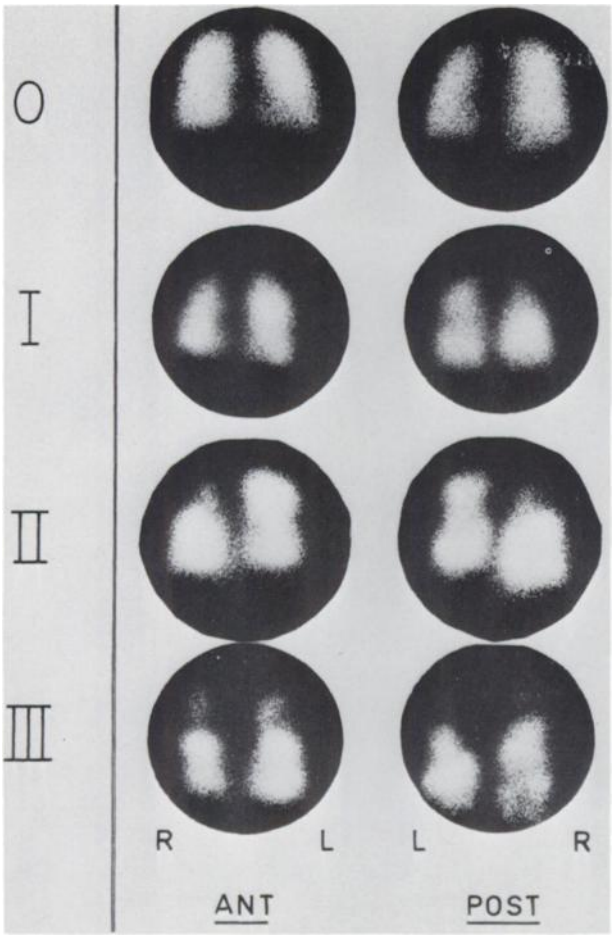

FIG. 1. Classification of pulmonary lesions on basis of scintigraphy.

cushion* in very young children. At least one anterior and one posterior view was obtained for each test. The separate counting of the two lungs was performed using the electronic separation of the Pho/Gamma III detector.

Lung scintigraphy was systematically performed in 69 patients in remission phase; 38 of them underwent a second investigation 6–18 months later. Four patients in acute phase all had a second investigation 1–5 weeks later when adequate treatment had induced remission.

Clinical evidence of pulmonary involvement was found in the majority of the 73 patients at the first investigation. In two children aged 9 years, only pancreatic insufficiency was evident at the time of the first lung scintigraphy. Ten patients died: eight from pulmonary failure, one from hepatic failure, and one from a car injury.

A scintigraphic index was defined as shown in Fig. 1:

Stage 0. No detectable lesions.
Stage 1. Minimal localized involvement of apex, hilum, or bases.
Stage 2. Advanced but localized lesions of apex, hilum, or bases.
Stage 3. Generalized diffuse involvement of one or two lungs.

The lesions were also classified on the basis of their localization. The disease stage according to our scintigraphic criteria was established independently by two investigators (Piepsz and Decostre) in order to minimize the scatter due to their personal estimate.

RESULTS

Among the 115 scintigraphies, 109 were identically classified by the two investigators (more than 95%); 66 of the 73 patients showed lesions from Stage 1 to 3 on their first scintigraphy. Twenty-four showed defects in multiple areas; the right apex was involved in 94% of the cases, the left apex in 60% (Table 1).

Distribution of the lesions according to the patient's age (first investigation—73 cases, Table 2).

TABLE 1. SPATIAL DISTRIBUTION OF LESIONS AMONG 65 POSITIVE SCINTIGRAPHIES IN PATIENTS WITH CYSTIC FIBROSIS

Location of the defects	No. of cases	%
Right upper area	61	94
Left upper area	39	60
Left middle area	35	54
Right middle area	29	45
Left lower area	17	26
Right lower area	15	23

TABLE 2. RELATION BETWEEN AGE AND SEVERITY OF THE LESIONS: FIRST SCINTIGRAPHY

Stage	Age	No. of cases	%	Total no. of cases
0	0–2	5	71	
	2–9	2	29	7
	9–19	0	0	
1	0–2	10	37	
	2–9	15	56	27
	9–19	2	7	
2	0–2	1	4	
	2–9	12	50	24
	9–19	11	46	
3	0–2	0	0	
	2–9	5	33	15
	9–10	10	67	

* Flexi-cast divided shape bag—Picker.

TABLE 3. RELATION BETWEEN AGE AND SEVERITY OF THE LESIONS: SECOND SCINTIGRAPHY

Stage	Age	No. of cases	%	Total no. of cases
0	0–2	2	67	
	2–9	1	33	3
	9–19	0	0	
1	0–2	5	25	
	2–9	13	65	20
	9–19	2	10	
2	0–2	2	20	
	2–9	4	40	10
	9–19	4	40	
3	0–2	0	0	
	2–9	2	22	9
	9–19	7	78	

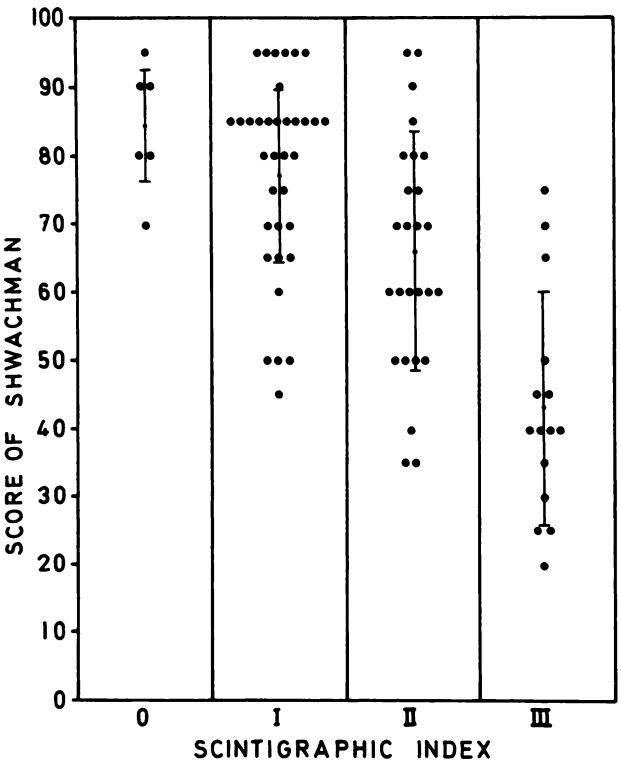

FIG. 2. Correlation between scintigraphic index and Shwachman score. For each scintigraphic index, Shwachman score is represented as mean ± s.d.

TABLE 4. EVOLUTION OF THE LESIONS FROM FIRST TO SECOND SCINTIGRAPHY (42 CASES)

Evolution	No. of cases	%
Improvement with change of stage	3	7
No change of stage	34	81
Aggravation with change of stage	5	12

Among the seven patients with no detectable defect (Stage 0), 71% were less than 2 years old.

Among the 27 patients classified as Stage 1, 37% were between 0 and 2 years of age, 56% between 2 and 9 years, only 7% were more than 9 years old.

Twenty-four patients were classified as Stage 2: only 4% were between 0 and 2 years of age, 50% between 2 and 9 years, and 46% were older than 9 years.

Among the 15 patients presenting as Stage 3, none were less than 2 years old, 33% were between 2 and 9 years old, and 67% older than 9 years.

Second investigation (42 cases). The percentages were very similar when a second investigation was performed (Table 3).

Correlation between clinical status and scintigraphy. Among the 115 scintigraphies a Shwachman score could be established in 82 occasions at the time the scintigraphy was performed. Figure 2 shows the evident correlation between the scintigraphic index and the Shwachman score.

Among the eight patients who died from respiratory failure, six had a Stage 3 on scintigraphy. A Stage 2 was noted in the two other cases, one year before death. No more recent scintigraphy was available in these patients.

Evolution of the perfusion defects from first to second scintigraphy (Table 4). Among the 42 cases studied, three dramatically improved with change of stage (7%). In each case, the first investigation was performed during an acute phase.

Five showed striking aggravation of the perfusion pattern (12%). In none of these cases had defects seen on the first examination disappeared or been replaced by others.

Thirty-four scintigraphies showed no change of stage (81% of the cases).

Distribution of the activity between the two lungs. Among the 42 patients in whom two scintigraphies were available, distribution of activity between the two lungs could only be accurately measured by separate counting rates in 29 cases (Table 5). Twenty-five of them were in remission at the time of both examinations and no significant difference ($<5\%$) was found. Four were in acute phase at the first investigation and differences from 6 to 26% were observed.

DISCUSSION

Until now, few scintigraphic studies of lung perfusion have been performed in cystic fibrosis. Comparison of ventilation and perfusion (*4,5*) showed a good correlation in the topography as in the extent of the defects. More recently, Samanek, et al (*6*) reviewed 30 perfusion scintigraphies performed

in 21 patients. These authors did not distinguish acute attacks from remission phases at the time of the investigation. This might explain the absence of significant correlation between the clinical picture and the perfusion pattern. By repeated scans performed in eight patients, they concluded that the technique was useful in the evaluation of dynamic alterations in cystic fibrosis.

Our study, as well as the above mentioned work, shows the preferential involvement of the right apex (94% of the cases). This topography can be compared to the high frequency of pneumonia in the same area in young children with cystic fibrosis. It should be emphasized that, although the x-ray opacity has disappeared after adequate treatment, the obstruction is still present with significant alterations of the perfusion pattern. It suggests that special care should be given to the drainage of that region.

The pathological studies of cystic fibrosis (7) did not show any primary lesion of the pulmonary vessels. In reality, bronchial obstruction and consequent disturbances of gas exchange induce perfusion abnormalities. Considering the secondary development of perfusion defects, two questions had to be answered before applying lung perfusion scintigraphy in the followup of the disease.

TABLE 5. DISTRIBUTION OF RADIOACTIVITY BETWEEN THE TWO LUNGS IN 29 CASES (ONLY THE RIGHT PERCENTAGE IS NOTED)

Scan I	Scan II
Remission phase (25 cases)*	
52	52
55	56
60	60
52	57
47	46
51	52
48	50
60	55
55	55
53	54
31	32
65	65
58	58
54	52
55	51
52	49
46	45
50	55
55	55
50	50
52	56
56	53
51	53
57	54
58	57
Acute phase (4 cases)†	
60	60
58	48
50	24
34	40

* Interval: 6–18 months.
† Interval: 1–5 weeks.

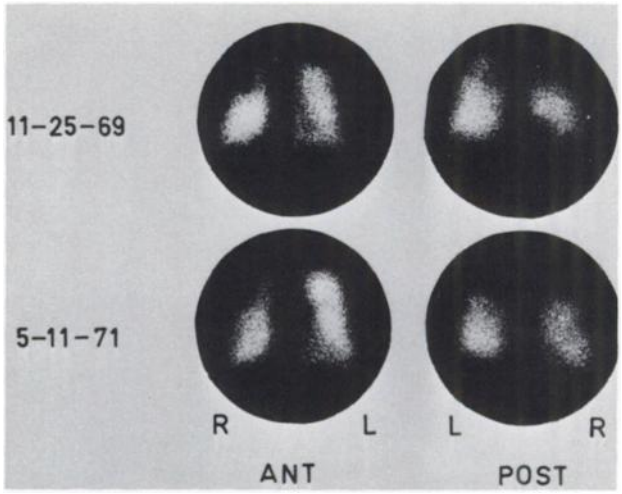

FIG. 3. Two scintigraphic studies at 18-month interval showing no significant variation in size or location of lesions.

How do the perfusion defects correlate with the severity of the disease?

First, in most of our patients, neither clinical nor scintigraphic changes were noticed between the two studies. Nearly the same age distribution was found in the initial 72 patients and in the controls 6–18 months later.

Second, a Stage 0 or 1 was noted on the first scintigraphy in two children aged 9 years, who only evidenced clinical signs of pancreatic involvement. Slight respiratory disturbances appeared during the following year in both cases. Three children less than 2 years old had early pulmonary alterations with a dramatic evolution. This correlated well with Stage 2 perfusion defects.

Third, a good correlation exists between the scintigraphic index and the Shwachman score (Fig. 2).

It appears from these data that the scintigraphic pattern actually reflects the severity of the disease.

Are the scintigraphic defects permanent as far as their topography and size are concerned?

It is now generally accepted that in bronchial asthma striking perfusion alterations are transient (*8*). In order to be useful for the evaluation of cystic fibrosis, lung perfusion defects should not have that transient character. This is the reason why a control was performed in the same patients at a one-year interval. The comparison of the two examinations revealed the constancy of the lesions in the majority of the cases (Fig. 3). The partition of the activity between the two lungs remained remarkably constant: in 95%, the difference in the partition did

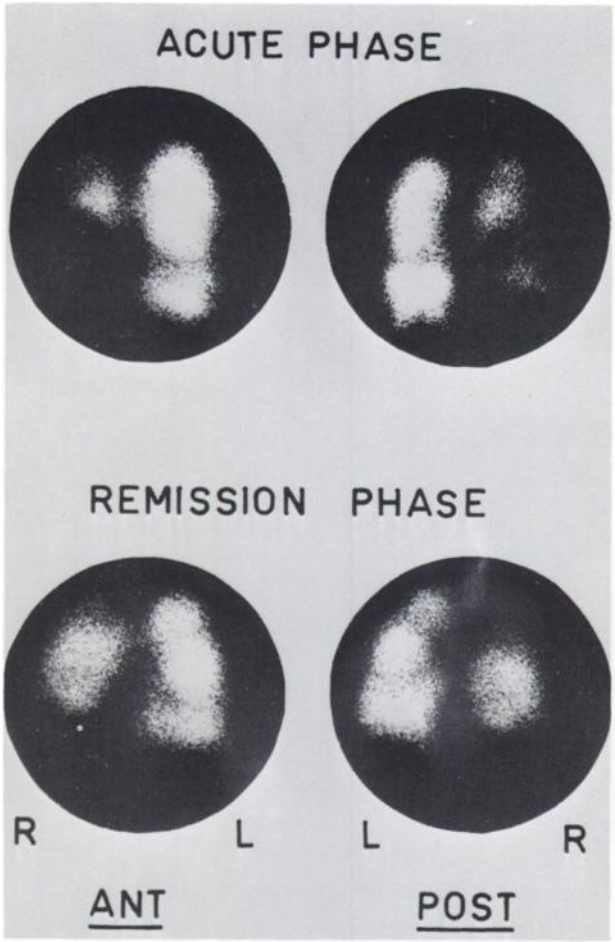

FIG. 4. Two scintigraphic studies at 1-month interval. First study performed during acute phase; on second study obtained during remission phase, there is striking improvement in lesions.

not exceed 5% in spite of the difficulty of accurate repositioning of the patient at a one-year interval. Although the perfusion alterations only represent a reflex response to the ventilation disturbances, they appear to be remarkably stable. The medical treatment seems to have no effect on already organized lesions but may slow down the evolution of the disease.

On the contrary, patients in acute phase with respiratory distress showed the transient scintigraphic defects usually observed in bronchial asthma. In these cases, the scintigraphic pattern improved considerably after remission (Fig. 4) and in three of them a change of stage was noted with a dramatic change in the right-to-left partition of the tracer.

The existence of striking perfusion defects during an acute phase of the disease has no prognostic value and has to be controlled when remission occurs. However, in one of the four patients admitted with respiratory distress, the scintigraphic image revealed a Stage 1. In that case, in spite of the severe clinical picture, improvement rapidly occurred. Similar studies in the future should define whether perfusion scintigraphy can be of value for an early prognostic evaluation. When pictures before the acute phase are available, it is possible in the acute phase to determine the obstruction level by detecting new perfusion disturbances and to undertake a selective postural drainage on an objective basis.

Lung scintigraphy is an adequate test for the evaluation of the pulmonary involvement in cystic fibrosis if the clinical status is kept in mind for each examination. In remission phases it shows the evolution of the lesions with time and in our hands represents a good criterion of the severity of the disease and its prognosis. During acute phases it defines the newly involved areas and should lead to a more eclectically therapeutic attitude.

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