Lung Perfusion Scans and Hemodynamics in Acute and Chronic Pulmonary Embolism

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To assess the relationship between pulmonary vascular obstruction and hemodynamic status in acute pulmonary embolism (APE) and in chronic thromboembolic pulmonary hypertension (CTEPH), perfusion lung scan and hemodynamic measurements were obtained in 31 consecutive patients with APE and in 45 with CTEPH. **Methods:** Lung scans were scored independently by two experienced observers who determined the percentage of vascular obstruction (PVOs). Mean pulmonary artery pressure (PAP) and total pulmonary resistance (TPR) were obtained during right heart catheterization. In patients with APE, measurements were recorded within a 1-hr interval before and 12 hours after thrombolysis. This yielded 62 paired PVOs values with concomitant PAP and TPR measurements. In patients with CTEPH, data were recorded within a 3-day interval. **Results:** Mean PVOs (%) values were similar in APE and CTEPH patients (59 ± 13 vs. 58 ± 15), whereas PAP and TPR were significantly higher in CTEPH patients (51 ± 17 mmHg and 23 ± 11 U/m^2, respectively) than in APE patients (23 ± 8 mmHg and 9 ± 5 U/m^2, respectively, $p < 0.001$). In APE patients, significant hyperbolic correlations were found linking PVOs with PAP and TPR ($r = 0.75$, $p < 0.01$ for PAP; $r = 0.71$, $p < 0.01$ for TPR). In CTEPH, there were no significant correlations between PVOs and PAP or TPR. For the same level of PVOs, patients with CTEPH had higher PAP and TPR values than patients with APE. **Conclusion:** In APE without prior cardiopulmonary disease, increases in PAP and TPR are correlated in a nonlinear fashion with the degree of pulmonary vascular obstruction as assessed by lung scanning. In CTEPH patients, the higher PAP and TPR values as compared to APE patients with comparable degrees of PVOs are consistent with previous reports that pulmonary hypertension in CTEPH is due not only to the obstruction of proximal pulmonary arteries but also to remodeling of small distal arteries in nonoccluded areas.

Key Words: pulmonary hypertension; thromboendarterectomy; pulmonary artery pressure; pulmonary embolism

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After an acute pulmonary embolism (APE), approximately 0.1% of patients fail to clear their thrombi. Persistent pulmonary thrombi can lead to severe chronic thromboembolic pulmonary hypertension (CTEPH) and terminal right ventricular failure (*1,2*). This condition may be correctable in selected patients by surgical pulmonary thromboendarterectomy (PTE) (*3*). In CTEPH, pulmonary hypertension is due not only to the mechanical effect of the proximal pulmonary arteries obstruction but also to remodeling of the small distal arteries in the "open" pulmonary vascular bed. Lung biopsy specimens from nonoccluded areas in patients with CTEPH have shown medial hypertrophy and intimal proliferation in the small distal arteries, which are the characteristic pathologic features of primary pulmonary hypertension (*4*). Distal artery remodeling is believed to be a major cause of worsening pulmonary hypertension in patients with longstanding disease and may also cause failure of thromboendarterectomy with residual pulmonary hypertension despite surgical reperfusion of the large vessels. In patients with longstanding disease, the ability to separate the primary, surgically accessible component of pulmonary hypertension from the secondary, small-vessel component would be of assistance in selecting patients for surgery, thereby improving both surgical and long-term outcomes (*5*). Thus, a tool for identifying patients with advanced small distal artery remodeling would be valuable. To evaluate the respective contributions of these two mechanisms of pulmonary hypertension, we analyzed the relationship between pulmonary vascular obstruction caused by thrombi and pulmonary hemodynamics in patients with CTEPH and in patients with APE, a condition in which pulmonary hypertension is due quasi-exclusively to mechanical obstruction of pulmonary vessels.

METHODS

Patients

CTEPH. Perfusion lung scans and hemodynamic parameters of 45 patients with CTEPH were analyzed. The diagnosis of CTEPH was based on three criteria (*2*):

1. Mean pulmonary artery pressure (PAP) above 25 mmHg at rest (under room air) and pulmonary artery wedge pressure below 12 mmHg during right heart catheterization.
2. Multiple perfusion defects on the perfusion lung scan.
3. Angiographic pattern of CTEPH (pouching, webs, stenosis, parietal irregularities, abrupt narrowing and vascular amputations denoting patchy distal perfusion defects) (*6*). The interval between the evaluation and the last acute PE exceeded 6 mo in all patients.

APE. The data analyzed in this study were generated by a multicenter trial designed to compare the efficacy and safety of two different regimens of recombinant tissue-plasminogen activator in the treatment of massive acute pulmonary embolism. The design and results of this study have been reported elsewhere (*7*). Data were available for 31 patients with a negative history for cardiopulmonary disease and with angiographically proven APE. All patients had symptoms of APE within 5 days before the diagnosis of APE. In all patients, perfusion lung scans and hemodynamic measurements were obtained before and 12 hr after thrombolytic therapy. Data were pooled for the analysis (62 paired lung scans and 62 paired values for each hemodynamic parameter).

Assessment of Pulmonary Vascular Obstruction

Perfusion lung scans were performed after intravenous injection of 100 MBq (3–4 mCi) ^{99m}Tc-human albumin macroaggregates. Six or eight views were taken using a high-resolution, parallel-hole collimator; each perfusion scan was scored independently by two nuclear medicine physicians (MW and MAC) who were unaware of the hemodynamic status of the patients. The percentage of vascular obstruction (PVOs) was determined as described previously (*8*). Briefly, each lobe was assigned a weight based on the regional distribution of blood flow in the supine position: right

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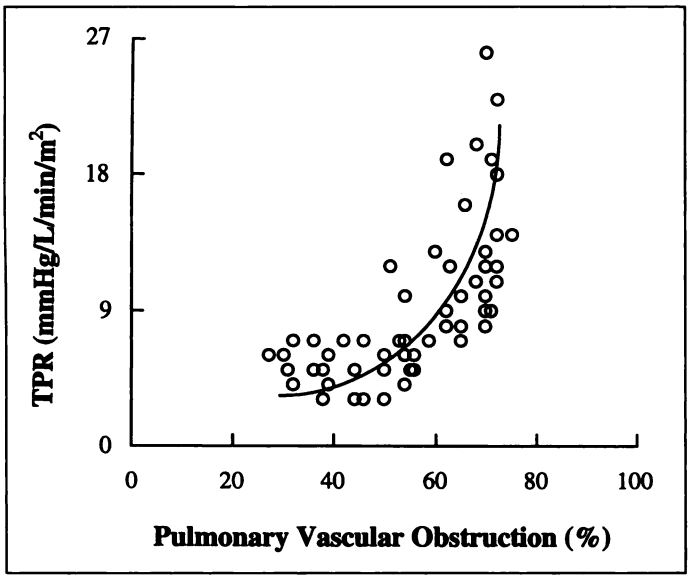

FIGURE 1. Relation between PVOs and TPR in APE. A strong hyperbolic correlation was found between PVOs and TPR ($y = 1578/(530 - 5.88x)$).

lower lobe, 25%; right middle lobe, 12%; right upper lobe, 18%; left lower lobe, 20%; left upper lobe, 25% (lingula 12%). Perfusion within each lobe was estimated from the anterior, posterior and oblique views. For each lobe, a semiquantitative score from 0 to 1 (0, 0.25, 0.5, 0.75 and 1) was estimated from the film density by comparison with an apparently normally perfused area. Each lobar perfusion score was then calculated by multiplying the weight by the perfusion score. The overall score was the sum of the six separate lobar scores. The PVOs was calculated as follows: PVOs (%) = (1 − total perfusion score) × 100. This score has been shown to be a reliable estimate of pulmonary vascular obstruction in a study that used the angiographic Miller index as the gold standard (*8*).

Hemodynamic Measurements

Right heart catheterization was performed using a balloon-tipped Swan-Ganz catheter. Mean pulmonary artery pressure was recorded. Cardiac output was measured by thermodilution, normalized for body surface area, and expressed as the cardiac index (CI).

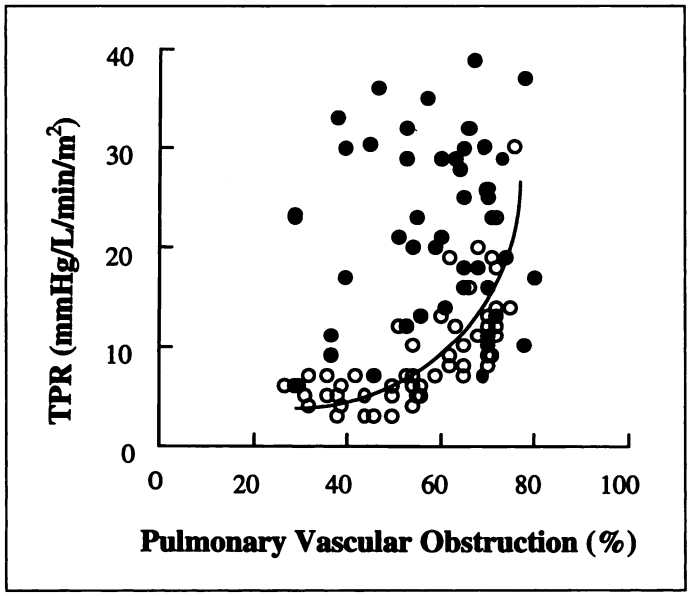

FIGURE 2. Relation between PVOs and TPR in APE (○) and chronic thromboembolic pulmonary hypertension (●). For a given degree of obstruction, patients with CTEPH had higher TPR values than patients with APE.

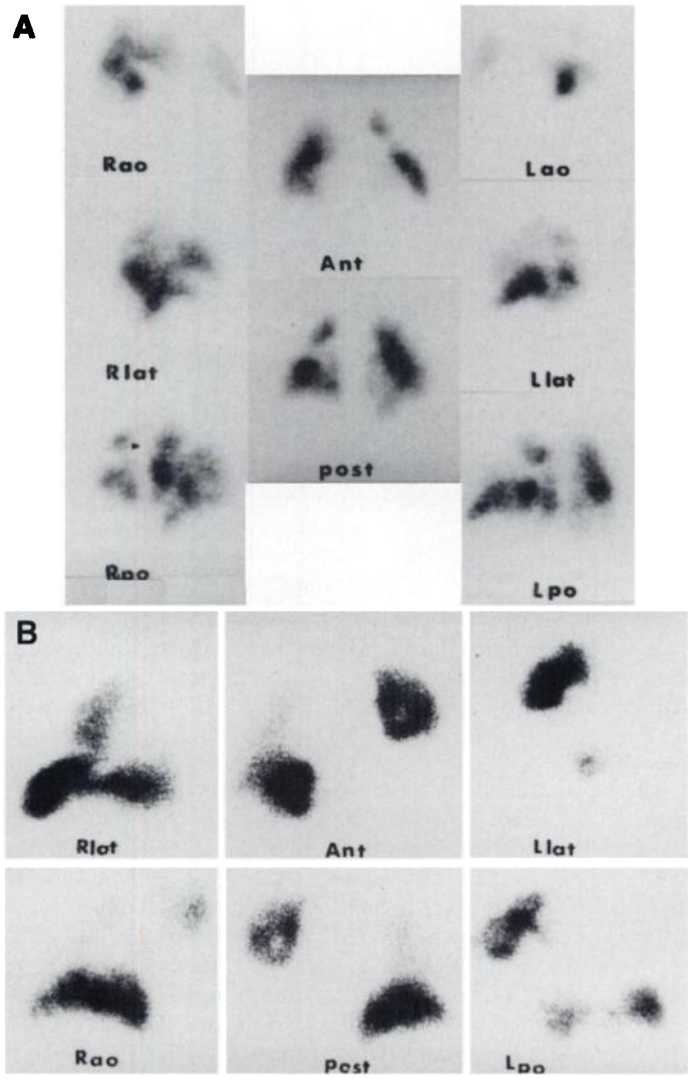

FIGURE 3. Lung perfusion scans of a patient with (A) CTEPH and (B) APE.

Total pulmonary vascular resistance (TPR) was calculated as PAP/CI (mmHg)/(liter/min/m²). In patients with APE, measurements were made within a 1-hr interval before or after lung scanning; in patients with CTEPH, this interval did not exceed 3 days.

TABLE 1
Pulmonary Vascular Obstruction and Hemodynamics in Acute and Chronic PE

No. of patients	APE (n = 62)	p	CTEPH (n = 45)
PVOs (%)	58 ± 15	NS	59 ± 13
(range)	(27.25–75)		(28.75–80)
PAP (mmHg)	23 ± 8	<0.005	51 ± 17
(range)	(10–38)		(20–99)
TPR (mmHg/liter(min/m²)	9 ± 5	<0.005	23 ± 11
(range)	(3–26)		(6–48)

Values are expressed as means ± s.d. (range).

APE = acute pulmonary embolism; CTEPH = chronic thromboembolic pulmonary hypertension; PVOs = pulmonary vascular obstruction score assessed by perfusion lung scanning; PAP = mean pulmonary artery pressure; TPR = total pulmonary resistance.

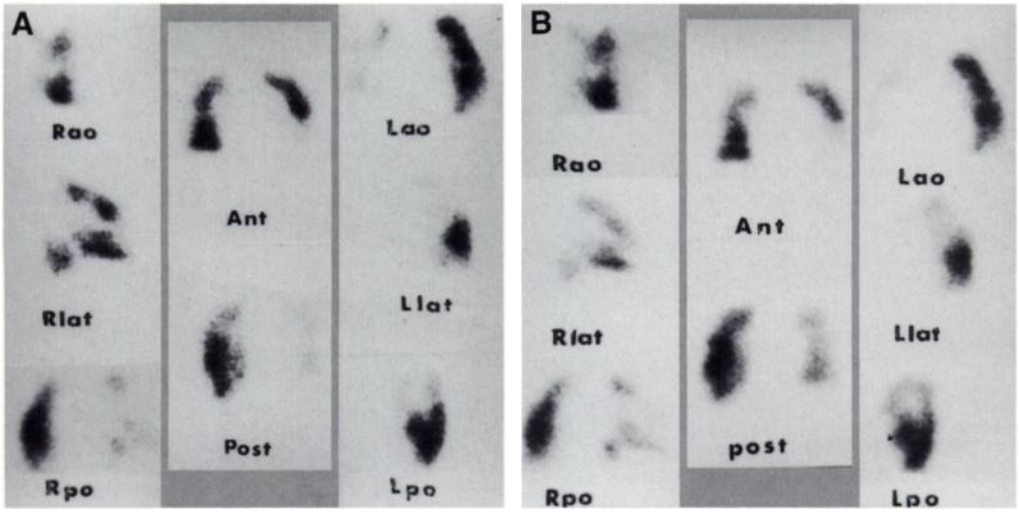

FIGURE 4. Lung perfusion scans of a characteristic patient with (A) CTEPH who exhibited dramatic hemodynamic worsening over a 6-mo period without changes in lung perfusion scans (B).

Statistical Analysis

All data are reported as mean values ±1 s.d. Between-group comparisons were done using Student's t-test. Nonlinear regression analysis was performed using Kaleidagraph software. Spearman's test was used to analyze regressions. The level of statistical significance was set at $p < 0.05$.

RESULTS

The hemodynamic characteristics of both groups of patients are listed in Table 1. Mean PVOs values were not statistically different between the two groups. PAP and TPR were significantly higher in the CTEPH group than in the APE group. In patients with APE, significant hyperbolic correlations were observed between PVOs and PAP ($r = 0.75$, $p < 0.001$) and between PVOs and TPR ($r = 0.71$, $p < 0.001$) (Fig. 1). In patients with CTEPH, there were no significant correlations between PVOs and PAP or TPR. At a given PVOs, the ranges of PAP and TPR values were fairly broad in CTEPH patients (Fig. 2).

Typical examples of patients with CTEPH and APE are shown in Figure 3.

DISCUSSION

This study demonstrated that pulmonary hypertension was more severe in CTEPH than in APE for a given degree of vascular obstruction. Vascular obstruction, measured as a percentage (PVOs), was assessed using lung scanning rather than pulmonary angiography. The perfusion lung scan scoring system used in our study provides results that are in close agreement with angiographic estimates of vascular obstruction (*8*). Functional obstruction is better evaluated by lung scanning than angiography. Lung scanning analyzes spontaneous flow distribution, whereas angiography (selective injection pressure) evaluates anatomical obstruction. In our study, we found that correlations linking PVOs with PAP and TPR were hyperbolic in APE patients. This is in agreement with results of previous experimental and human studies (*9,10*). The nonlinearity of the relationship can be explained by the fact that the pulmonary vascular bed is a capacious and highly expansible system (*11*). When PVOs was less than 50%, PAP and TPR did not exceed 20 mmHg and 8 mmHg/liter/min/m^2, respectively. Even in patients with the highest PVOs values (above 70%), PAP did not exceed 40 mmHg, which appears to be the highest pressure that a normal human right ventricle can maintain under acute conditions (*12*). By contrast, in CTEPH, neither PAP nor TPR was correlated to PVOs. This is in keeping with a previous study of pulmonary obstruction assessed by lung scanning or angiography in 25 patients with CTEPH (*13*). Our most interesting finding was that for a comparable level of PVOs patients with CTEPH, they had higher PAP and TPR values than patients with APE. This result is consistent with previous reports that, contrary to APE, pulmonary hypertension in CTEPH is not due only to mechanical obstruction of proximal arteries but also to lesions of small arteries (*4*). The latter lesions cannot be detected by perfusion lung scanning (*14*). They are probably due to the high pressure and flow regimen to which the open vascular bed is exposed (*4*). This mechanism could explain vascular steals that occur after thromboendarterectomy in desobstructed areas from previously nonoccluded areas (*15*) (i.e., new postoperative hypoperfusions in areas previously preoperatively normally perfused). It could also contribute to explain hemodynamic worsening in some patients with unchanged lung scans (Fig. 4). We have no explanation for the scattered distribution of the relationships linking PVOs with PAP and TPR in CTEPH. However, we suspect disease duration in each individual, which cannot be analyzed since most patients do not report a history of APE, plays a role.

CONCLUSION

Since pulmonary hypertension in APE is primarily due to the mechanical effects of clots in the pulmonary vascular bed, the relationship between hemodynamic variables and PVOs may help to assess the respective roles of chronic thrombi and hypertensive lesions in CTEPH (Fig. 2). When variables (i.e., PVOs and TPR) in a patient with CTEPH are similar to those seen in APE, pulmonary hypertension can be assumed to be primarily due to the mechanical effect of chronic thrombi. Inversely, variables that move up from the curve indicate advanced hypertensive lesions of distal arteries, which may lead to failure of thromboendarterectomy. The usefulness of this screening method in selecting CTEPH patients for thromboendarterectomy requires further investigation in a larger group of patients.

ACKNOWLEDGMENT

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FIRST IMPRESSIONS

Thoracic Uptake of Technetium-99m-MDP

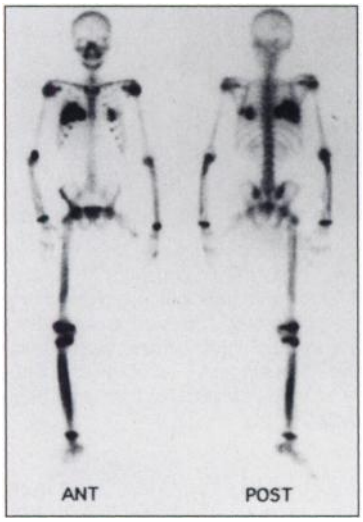

Figure 1.

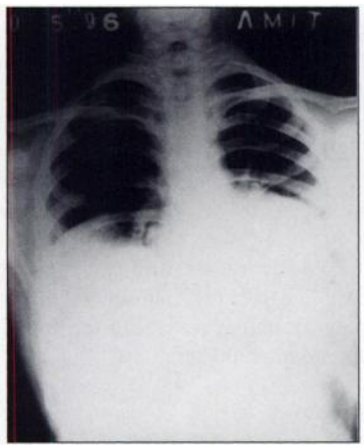

Figure 2.

PURPOSE

A 14-yr-old boy who complained of cough with fever of 1-mo duration was referred for a bone scan. Several years earlier, he had had a mid-thigh amputation for fibrosarcoma of the left tibia mid shaft. A ^{99m}Tc-MDP whole-body scan showed diffusely increased tracer uptake in the right lower limb bones due to weight bearing. The large irregular area of increased tracer uptake in the right mid chest and the smaller irregular area of increased tracer uptake in the left mid chest were reported as pulmonary metastases from the previously diagnosed fibrosarcoma (Fig. 1). A chest radiograph showed large, homogenous opacity in the left paracardiac region and another small homogenous opacity in the right mid-zone region (Fig. 2). A CT scan of the chest showed large calcified masses in the lateral segment of the right middle lobe, in the lingular segment of the left lobe which extended into left retrocrural space and a small satellite nodule in the superior segment of the right lower lobe. Subsequent surgery confirmed that the intrathoracic lesions were recurrent fibroscarcoma.

TRACER

Technetium-99m-MDP, 15 mCi (185 MBq)

ROUTE OF ADMINISTRATION

Intravenous injection

TIME AFTER INJECTION

Three hours (anterior and posterior projections)

INSTRUMENTATION

Siemens Diamcam SPECT gamma camera fitted with a LEAP collimator

CONTRIBUTORS

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