# HEMODYNAMIC ALTERATIONS RELATED TO EXTENT OF LUNG SCAN PERFUSION DEFECT IN PULMONARY EMBOLISM

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Although pulmonary angiography remains the only specific diagnostic test for pulmonary embolism, the perfusion lung scan is probably the most useful tool for screening and following the course of this disease. The relationship between the magnitude of perfusion defects and the severity of hemodynamic impairment after pulmonary embolism has not been established in man. This study was undertaken to examine this relationship in patients free of cardiopulmonary disease; only in these patients can the perfusion defect and hemodynamic status be attributed with reasonable assurance to the embolic event.

## MATERIALS AND METHODS

This study includes 14 patients with acute pulmonary embolism confirmed by lung scans and selective pulmonary angiography. Underlying cardiac and pulmonary disease were excluded in the ten patients admitted for other disorders by history, physical examination, chest x-ray, and electrocardiogram. The four patients who were admitted because of pulmonary embolism had serial chest films and electrocardiograms. At discharge, all abnormal studies were shown to be normal with the exception of cardiac catheterization and systemic arterial $PO_2$ measurements, which were not repeated in all patients. Systemic $PO_2$ has already been shown to return to normal after pulmonary embolism only very slowly, if at all, in some patients in whom normal values were documented before embolism. Pulmonary function studies were performed in all patients in the recovery period and were judged to be normal. These included vital capacity, inspiratory capacity, expiratory reserve volume, residual volume, total lung capacity, airway resistance, and maximal voluntary

Received June 23, 1970; revision accepted Nov. 29, 1970.

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**TABLE 1. CLINICAL AND HEMODYNAMIC STATUS AND PERFUSION DEFECT BY LUNG SCAN IN 14 PATIENTS WITH PULMONARY EMBOLISM**

| | Name | Age | Diagnosis | $PO_2$ | $PA_m$ | $RA_m$ | CI | AVE | HtRt | BA | % perfusion defect |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | JS | 56 | Osteoarthritis, left hip, postarthroplasty | 55 | 16 | 5 | 3.27 | 5.0 | 92 | 83 | 13 |
| 2 | RM | 31 | Fractured right fibula | 54 | 28 | 5 | 3.40 | 3.6 | 100 | 103 | 39 |
| 3 | JA | 49 | Post ileofemoral endarterectomy | 46 | 30 | 5 | 3.20 | 4.9 | 110 | 101 | 45 |
| 4 | AZ | 69 | Vasculitis, unknown cause | 53 | 37 | 12 | 3.46 | 4.3 | 80 | 100 | 35 |
| 5 | LB | 50 | Pulmonary embolism | 69 | 32 | 8 | 2.55 | 4.7 | 63 | 99 | 45 |
| 6 | MK | 47 | Thrombophlebitis | 55 | 35 | 12 | 3.20 | 4.5 | 92 | 91 | 45 |
| 7 | SM | 45 | Pulmonary embolism | 66 | 18 | 4 | 2.70 | 3.9 | 112 | 95 | 62 |
| 8 | HT | 24 | Chronic venous insufficiency, lower extremities | 85 | 11 | 3 | 3.30 | 4.2 | 86 | 85 | 18 |
| 9 | DB | 37 | Pulmonary embolism | 79 | 15 | 3 | 6.00 | 3.2 | 85 | 90 | 20 |
| 10 | AS | 48 | Pulmonary embolism | 65 | 28 | 5 | 2.56 | 4.3 | 80 | 108 | 18 |
| 11 | CT | 52 | Retroperitoneal sarcoma | 53 | 38 | 14 | 2.40 | 7.0 | 104 | 79 | 54 |
| 12 | RP | 43 | Glioblastoma multiformans | 60 | 33 | 8 | 1.98 | 7.4 | 117 | 75 | 50 |
| 13 | GM | 48 | Regional enteritis | 50 | 32 | 9 | 1.52 | 7.1 | 135 | 75 | 60 |
| 14 | FS | 26 | Post arthrotomy, knee | 62 | 38 | 14 | 1.98 | 8.3 | 133 | 110 | 52 |
| Mean | | 44.6 | | 60.9 | 27.9 | 7.6 | 3.00 | 5.17 | 99 | 92 | 39.7 |
| Standard deviation | | ±12 | | ±11.1 | ± 9.2 | ±4.0 | ±1.1 | ±1.59 | ±21 | ±12 | ±16.4 |

Abbreviations in title line, from left to right, include systemic arterial partial pressure of oxygen ($PO_2$), pulmonary arterial mean pressure ($PA_m$), right atrial mean pressure ($RA_m$), cardiac index (CI), arteriovenous oxygen extractions (AVE), heart rate (HtRt) and brachial arterial pressure (BA).

ventilation. Only those patients with intravascular filling defects or unequivocal cutoffs on angiography were admitted to the study (*1,2*). Angiography and hemodynamic studies were generally performed within 24 hr, and all within 36 hr of the embolic event. All patients had lung scans performed within 4 hr of the hemodynamic determinations. The 14 patients were males, ranging in age from 24 to 69 years, with a mean age of 45. The underlying diagnoses are shown in Table 1.

Hemodynamic measurements were made during a steady state. Paired cardiac output determinations were done by the Fick method. Pressure measurements were generally made before angiography or after return of right ventricular pressure to preinjection levels. Van Slyke determinations of systemic arterial oxygen capacity were used. Oxygen saturations of arterial and mixed venous samples were measured by spectrophotometry.

Four-view lung scans (anterior, posterior, right, and left laterals) were obtained using a dual 5-in. Ohio Nuclear detector scanner. Iodine-131 or $^{99m}$Tc-macroaggregated human serum albumin (Cambridge Nuclear) was administered through a peripheral vein after dosage was normalized for body weight. The pulmonary photoscans were evaluated with 6-ft films (anteroposterior and lateral) obtained in the supine position on the scan table. After overlaying the scans upon the chest films, the projected 100% normal perfusion area was traced on all views and quantified by planimetry. The sum of the planed areas was equated to 100% normal perfusion area. The areas of each complete defect (absent radioactivity) were also determined by planimetry on all views and totaled. Areas of decreased radioactivity were then determined by planimetry and multiplied by the decrease in optical density from the maximal density; this value was added to the totaled area of the complete defects. The cumulative defect determined in this manner was then expressed as a percent of the total projected normal perfusion.

## RESULTS

The results are summarized in Table 1. The hemodynamic data are also plotted in Fig. 1. The extent of embolic obstruction by pulmonary photoscanning ranged from 13 to 62%, the average defect being 39.7%. A perfusion deficit equal to or greater than 50% was present in five patients.

A depression of arterial oxygen tension ($PO_2$ less than 90 mmHg) was noted in all 14 patients, the mean value being 61 mmHg (Fig. 1A). Although depressions of $PO_2$ were present with photoscan defects as small as 13% of total pulmonary perfusion, a significant relationship was not observed between the two. There was a direct relationship between the magnitude of perfusion defect and elevation of pulmonary artery pressure (Fig. 2). Elevations in pulmonary arterial mean pressure ($PA_m$) above 20 mmHg were observed in ten patients (Fig.

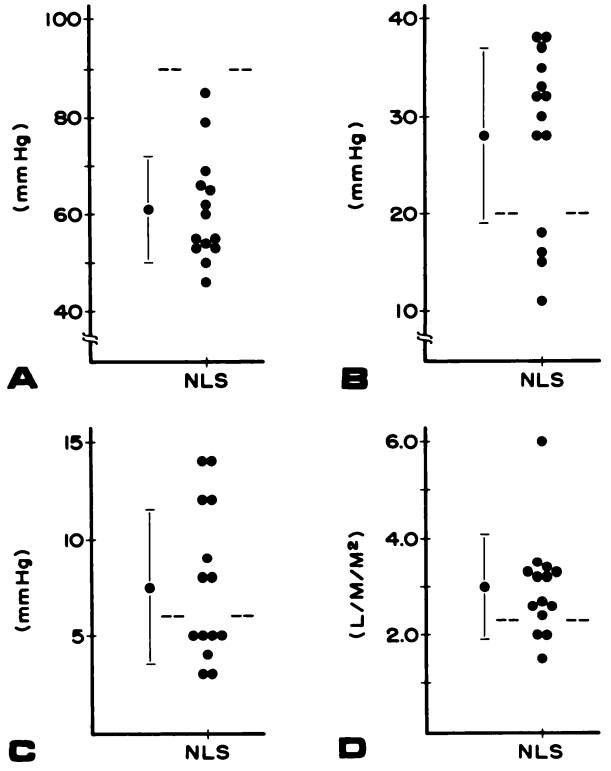


**FIG. 1.** Values for systemic arterial $PO_2$ (A), pulmonary artery mean pressure (B), and right atrial mean pressure (C) are shown in mmHg, while those for cardiac index are expressed in liters/min/meter$^2$ (D). The mean value and 1 s.d. are indicated.

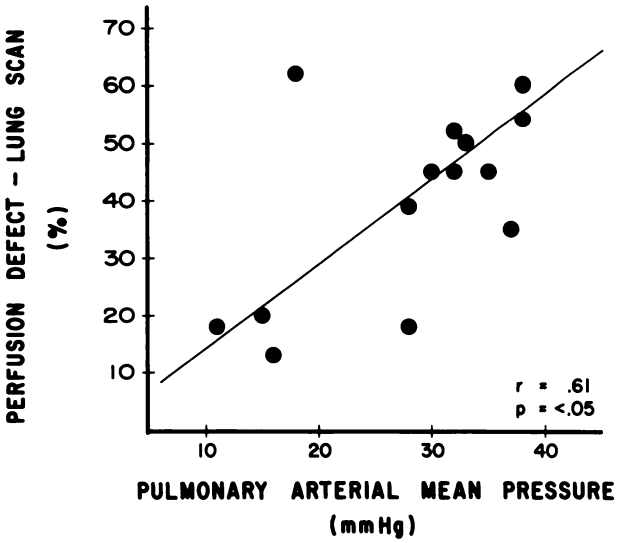


**FIG. 2.** Relationship between perfusion defect by pulmonary photoscan expressed in percent (vertical axis) and pulmonary arterial mean pressure in mmHg (horizontal axis) is shown.

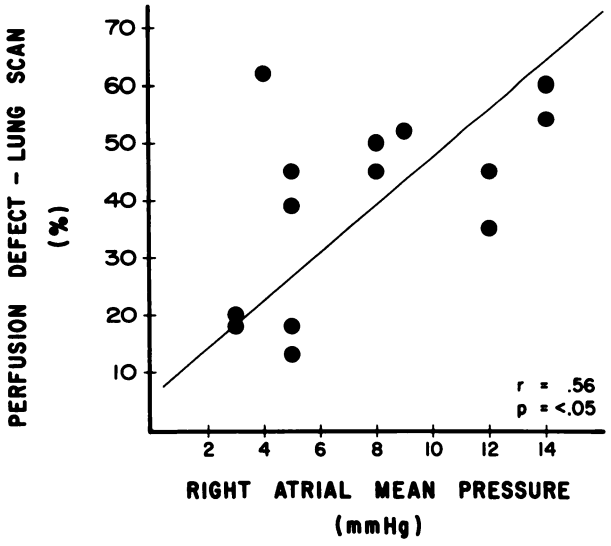


**FIG. 3.** Relationship between perfusion defect by pulmonary photoscan (%) and right atrial mean pressure (mmHg) is shown.

1B), all of whom had estimated photoscan defects of at least 25–30% of total pulmonary perfusion. There was a significant relationship between the elevation in right atrial mean pressure ($RA_m$) and degree of perfusion defect (Fig. 3). The $RA_m$ was elevated (greater than 5 mmHg) in one-half of the patients studied (Fig. 1C). Although all patients in whom the $RA_m$ was elevated had scan perfusion defects in excess of 30%, one patient had a normal $RA_m$ with a perfusion defect of 62%. An inverse relationship between the magnitude of perfusion defect and cardiac index (CI) (Fig. 4), as well as stroke volume (Fig. 5) was noted. The cardiac index was depressed below the lower limit of normal (2.3 liters/min/meters$^2$) in only three patients, the mean value being 3.0 liters (Fig. 1D). Depressions of CI below lower limits of normal were only observed when the perfusion defect was equal to or greater than 50% of total pulmonary perfusion. Seven patients had heart rates of 100 beats/min or more, with a maximum rate of 135/min. As shown in Fig. 6, the heart rate rose as the degree of perfusion defect increased.

## DISCUSSION

Pulmonary photoscanning has become the most useful method for screening patients in whom the diagnosis of pulmonary thromboembolic disease is suspected. Its minimally invasive nature and safety have also permitted repeated evaluations in the same patient, a characteristic which sharply distinguishes this tool from angiography. The severity of the hemodynamic derangements in this study was found to be related to the magnitude of the perfusion deficits as estimated by photoscanning.

A correlation between lung scan and certain hemodynamic parameters after pulmonary embolism may depend upon the reliability of the lung scan in portraying the mechanical load imposed on the right ventricle by embolic obstruction. Experimental studies report both false negative and false positive diagnoses of pulmonary embolism using perfusion lung scanning. Large emboli in major pulmonary arterial branches usually produce the greatest degree of mechanical obstruction. It also is more likely to be incomplete, however, so that a defect in capillary perfusion may not be present on lung scan (*3*). Small peripheral defects in flow on the other hand, may be outside of the resolving capability of the technique. This may explain in part the occasional disparity between lung-scan and hemodynamic status in individual patients.

False positive evidence of emboli may occur since a number of processes other than pulmonary embolism may be responsible for perfusion defects (*4,5*). This variable is minimized in patients free of cardiac and pulmonary disease. Atelectasis may occur, however, even in patients previously free of cardiopulmonary disease and produce perfusion abnormalities, particularly when local hypoventilation is present due to chest splinting for pleuritic pain. Pulmonary angiography demonstrated that perfusion defects were associated with pulmonary embolism in all cases in this study. Localization of emboli by angiography corresponded to lung-scan perfusion defects in most instances, but not in all. A failure of

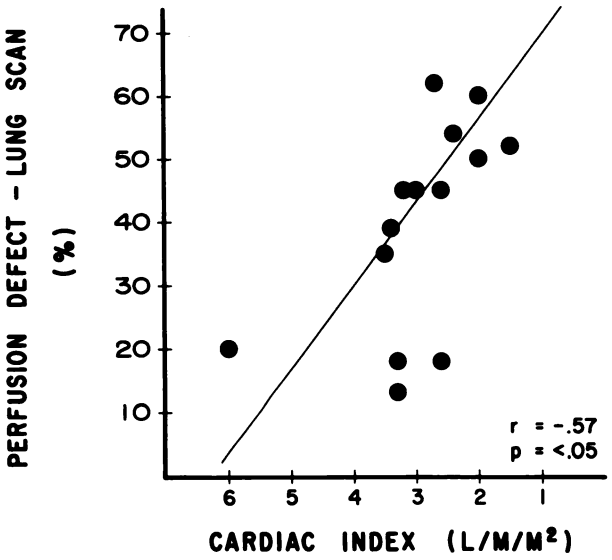


**FIG. 4.** Relationship between cardiac index, expressed in liters/min/meter$^2$ on horizontal axis and perfusion defect by pulmonary photoscan (%) is shown.

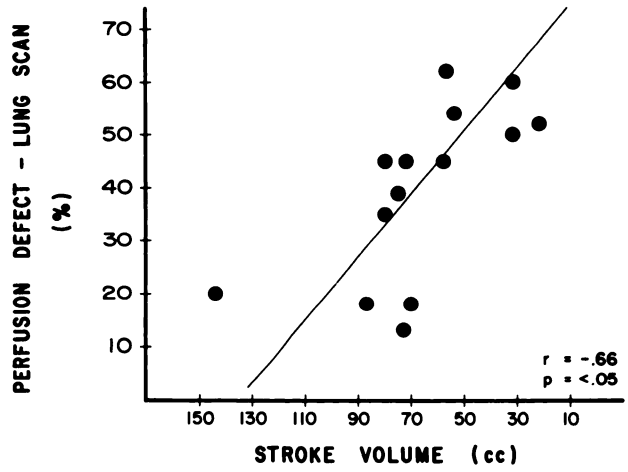


**FIG. 5.** Inverse relationship between stroke volume, expressed in cubic centimeters on horizontal axis and perfusion defect by pulmonary photoscan (%) is indicated.

angiography to validate the presence of pulmonary embolism proximal to a lung-scan perfusion defect did not exclude embolism as an etiologic factor. There is adequate experimental evidence that emboli may produce perfusion defects detectable by scan without displaying evidence of emboli angiographically (*3*). It is possible that some perfusion defects due to atelectasis, not detectable on plain chest x-ray, cannot be excluded, but the influence on the correlation of hemodynamic status and extent of perfusion abnormality would still be small since inconsistencies between scan defect and angiographic evidence of embolism were infrequent.

The value of multiple-view scanning was reaffirmed by this study, since both the incidence of lung-scan abnormalities and the magnitude of the perfusion defect would both have been substantially less if multiple views, including laterals, had not been obtained (*6*). While the use of multiple views carries with it the risk of overestimating the perfusion defect by reading the same defect in each view, an individual expression of the percent defect in each view followed by an averaging of the defects in all views reduces this source of error.

Systemic arterial hypoxemia was the most frequent manifestation of pulmonary vascular obstruction. It was observed in all patients in this study, including those with photoscan defects as small as 13%. The induction of pulmonary arteriovenous shunting was generally considered to be the mechanism by which pulmonary emboli produced systemic hypoxemia. Recently, a diffusion defect and diminished ventilation-perfusion ratios have been recognized as other factors responsible for hypoxemia in about one third of the patients (*7,8*). It would appear from this observation that embolization detectable by pulmonary photoscanning virtually does not occur without producing a measurable decline in systemic arterial oxygen tension. As demonstrated by four of the 14 patients in this study, hypoxemia may be the only manifestation of a cardiopulmonary disturbance after pulmonary embolism. Furthermore, when hypoxemia did occur as an isolated finding, the photoscan defect was usually less than 20% although in one patient hypoxemia alone was present with a photoscan defect of 62%.

Pulmonary hypertension ($PA_m$ greater than 20 mmHg) was present in 10 of 14 patients studied. It appears that once the photoscan defect exceeds 30%, pulmonary hypertension is likely to develop, despite the observations in man after unilateral balloon occlusion of the pulmonary artery (*9*) or after pneumonectomy that pulmonary hypertension occurs only after mechanical occlusion or removal of more than 50% of the pulmonary vasculature. However, the pulmonary photoscan, which is ultimately a manifestation of capillary perfusion, is not sensitive to generalized vasoconstriction. Therefore the overall mechanical consequences of an embolic event, which include both thromboembolic obstruction and constriction of the pulmonary vascular bed, may not be fully appreciated by pulmonary photoscanning. A predictable relationship, however, generally exists between the photoscan defect and the level of pulmonary hypertension in patients free of antecedent cardiopulmonary disease. Previous studies have suggested that pulmonary arterial pressures between 30 and 40 mmHg very likely represent the maximum pressure response of the previously normal right ventricle (*10,11*). In the present study, eight patients had a $PA_m$ in this range; seven of these had perfusion defects equal to or greater than 45%, sug-

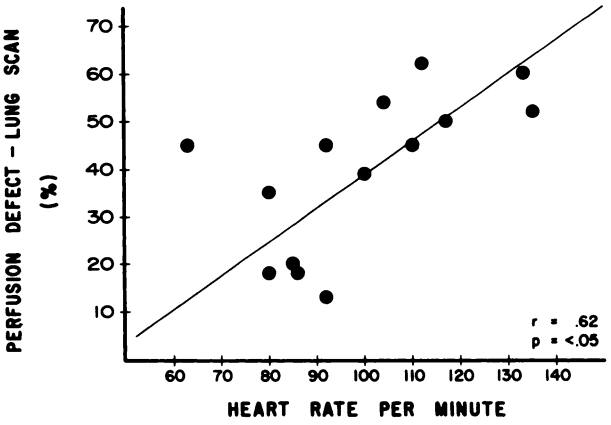


**FIG. 6.** Heart rate (horizontal axis) is shown relative to perfusion defect by pulmonary photoscan (%).

gesting that the underlying right ventricle may very well be approaching its maximum mechanical capability when the lung scan defect exceeds this level.

Elevations of $RA_m$ occurred less frequently than either of the two abnormalities noted above, and greater perfusion abnormalities, usually in excess of 35%, were required before the $RA_m$ exceeded the normal level of 5 mmHg. Still greater perfusion defects, usually 50% or greater, were required before CI was depressed. As the perfusion defect increased, cardiac index and stroke volume decreased while heart rate increased. Since filling pressure ($RA_m$) also increased with larger perfusion defects, it is likely that the decline in stroke volume was not a function of increased rate alone. It is, perhaps, more reasonable to suggest that declines in CI were mediated by impairment of stroke volume as the perfusion defect increased and that efforts to compensate by increases in heart rate fell short of maintaining cardiac output.

## SUMMARY

The severity of the hemodynamic abnormality after pulmonary embolism can be related directly to the magnitude of the perfusion defect by pulmonary photoscans in patients free of underlying cardiopulmonary disease. Photoscan defects ranged from 13 to 62%. Systemic hypoxemia was present in all patients. Elevations of pulmonary artery pressure were present in ten patients (71%), all of whom had defects in excess of 25%. Right atrial mean pressure was elevated in half the population, all of whom had defects in excess of 30%. Cardiac index was depressed in only three patients, all of whom had defects of 50% or more, and the depression appeared to be mediated by a progressive impairment in stroke volume as the perfusion defect increased. Each of these hemodynamic parameters became progressively more abnormal as the perfusion defect increased. These relationships permit hemodynamic inferences to be made after pulmonary embolism in patients free of underlying cardiopulmonary disease on the basis of a minimally invasive technique.

## ACKNOWLEDGMENTS

This study was supported by the Veterans Administration Pilot Study of Pulmonary Embolism under the direction of Mark Wolcott, Director of Surgical Research, Veterans Administration. We are also grateful for the valuable assistance of Miss Susan Wielinski as well as Robert G. Simpson, Paul F. Godin, Curtis E. Wrenn, Wilfred Farland, and John S. Belko.

## REFERENCES

1. SASAHARA AA, STEIN M, SIMON M, et al: Pulmonary angiography in the diagnosis of thromboembolic disease. *New Eng J Med* 270: 1075–1081, 1964

2. STEIN PD, O'CONNOR JF, DALEN JE, et al: Angiographic diagnosis of acute pulmonary embolism: evaluation of criteria. *Amer Heart J* 73: 730–741, 1967

3. MOSER KM, HARSANYI P, RIUS-GARRIGA G, et al: Assessment of pulmonary photoscanning and angiography in experimental pulmonary embolism. *Circulation* 39: 663–674, 1969

4. HAYNIE TP, HENDRICK CK, SCHREIBER MH: Diagnosis of pulmonary embolism and infarction by photoscanning. *J Nucl Med* 6: 613–631, 1965

5. QUINN JL, HEAD LR: Radioisotope photoscanning in pulmonary disease. *J Nucl Med* 7: 1–22, 1966

6. SASAHARA AA, BELKO JS, SIMPSON RG: Blended scintiscans of lungs with a dual detector system. *Radiology* 88: 363–365, 1967

7. SASAHARA AA, SIDD JJ, TREMBLAY G, et al: Cardiopulmonary consequences of acute pulmonary embolic disease. *Progr Cardiovasc Dis* 9: 259–274, 1966

8. SASAHARA AA, CANNILLA JE, MORSE RL, et al: Clinical and physiologic studies in pulmonary thromboembolism. *Amer J Cardiol* 20: 10–20, 1967

9. BRANDFONBRENER M, TURINO GM, HIMMELSTEIN A, et al: Effects of occlusion of one pulmonary artery on pulmonary circulation in man. *Fed Proc* 17: 19, 1958

10. MCINTYRE KM, SASAHARA AA: Determinants of the hemodynamic response to pulmonary embolism. *Clin Res* 17(2): 254, 1969

11. DALEN JE, BANAS JS, BROOKS HL, et al: Resolution rate of acute pulmonary embolism in man. *New Eng J Med* 280: 1194–1198, 1969