Ventilation-Perfusion Lung Scanning in the Evaluation of Pulmonary Hypertension

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The objective of this study was to define the sensitivity, specificity and accuracy of ventilation-perfusion (V/Q) lung scanning in distinguishing chronic thromboembolic pulmonary hypertension (PHT) from other nonembolic causes of PHT. **Methods:** The V/Q lung scans from 75 patients in whom a confirmed cause of PHT was established were retrospectively reviewed. Twenty-five patients (33%) had chronic thromboembolic PHT, whereas 35 patients (47%) and 15 patients (20%) suffered from primary PHT and secondary nonthromboembolic PHT, respectively. **Results:** A high-probability V/Q scan interpretation had a sensitivity of 96% and a specificity of 94% for detecting patients with thromboembolic PHT. The combination of high- and intermediate-probability V/Q scan interpretations had a sensitivity of 100% for detecting patients with thromboembolic PHT; however, the specificity decreased to 86%. Of the 35 patients with primary PHT, all but one patient had low-probability V/Q scan interpretations. **Conclusion:** In this series, a low-probability V/Q scan interpretation effectively excluded the diagnosis of chronic thromboembolic PHT. In patients with an intermediate- or high-probability V/Q scan interpretation, pulmonary angiography was required to confirm the diagnosis of chronic thromboembolic PHT and determine whether surgical intervention was indicated. The V/Q lung scan appears to be a highly sensitive test for chronic thromboembolism in the diagnostic evaluation of patients with PHT. However, its role needs to be defined further by application to a prospectively recruited cohort of patients with PHT.

Key Words: pulmonary embolism; radionuclide imaging; pulmonary hypertension; diagnosis; technetium-99m-macroaggregated albumin

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Pulmonary hypertension (PHT) can be defined as a sustained increase in the mean pulmonary artery pressure occurring at rest or during exercise. Chronic pulmonary thromboembolism is a serious and potentially surgically treatable cause of PHT (*1–4*). Between 0.5% and 4% of patients with acute pulmonary emboli will eventually have chronic thromboembolic PHT (*5,6*). Evaluation with pulmonary angiography is usually required to confirm the diagnosis and to determine whether surgical intervention is indicated (*7*). Although some authors have reported that pulmonary angiography can be performed safely in patients with severe PHT, others have documented a higher frequency of complications, including death (*8–11*). The availability of a safe noninvasive technique that could effectively select patients for pulmonary angiography would be beneficial. The purpose of this study was to determine the sensitivity, specificity and accuracy of ventilation-perfusion (V/Q) lung scanning in screening patients with suspected chronic thromboembolic PHT.

METHODS

Patients referred to the PHT service at the University of Pennsylvania who had undergone V/Q lung scanning as part of their diagnostic evaluation were included. The records and V/Q lung scans of 75 patients (mean age 40 yr, range 18–69 yr) with confirmed PHT (resting mean pulmonary arterial pressure greater than 30 mmHg) were retrospectively reviewed. Only those patients in whom a confirmed cause for PHT was found were included. Patients were classified as having either primary PHT, chronic thromboembolic PHT or secondary nonthromboembolic PHT, based on the final determination of the cause of their PHT. In addition to clinical presentation, history, physical examination and noninvasive testing of the causes of PHT were determined by the following means, autopsy (n = 13), pathologic examination of explanted lung (n = 6), open lung biopsy (n = 2), direct surgical visualization of thrombus (n = 14) and angiography (n = 35). In one patient, the diagnosis of chronic obstructive pulmonary disease was confirmed with pulmonary function tests; in addition, in two patients with scleroderma and in two patients with systemic lupus erythematosus, the diagnosis was confirmed by long-term clinical follow-up and serologic tests. All patients with chronic thromboembolic PHT were confirmed by pulmonary angiography or direct surgical visualization of a thrombus. Patients with nonthromboembolic secondary PHT represented a heterogeneous group of patients with various underlying causes for PHT, including congenital heart disease (n = 6), parenchymal lung disease (n = 3), scleroderma (n = 2), systemic lupus erythematosus (n = 2), pulmonary artery sarcoma (n = 1) and sarcoid lymphadenopathy (n = 1).

Ventilation studies were performed with 400 to 700 MBq of ^{133}Xe, using a 20% window centered over the 80-keV energy peak. A 100,000-count first-breath image, two consecutive 120-sec equilibrium images and serial 45-sec washout images were ob-

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TABLE 1
Ventilation-Perfusion Lung Scan Results in Three Groups of Patients with Confirmed Pulmonary Hypertension

	V/Q scan category			
	Very low/ normal (No. of patients)	Low (No. of patients)	Inter- mediate (No. of patients)	High (No. of patients)
Primary PHT (n = 35)	0	33	1	1
Chronic thromboembolic PHT (n = 25)	0	0	1	24
Nonthromboembolic secondary PHT (n = 15)	0	10	3	2

PHT = pulmonary hypertension; V/Q = ventilation-perfusion.

TABLE 2
The Sensitivity, Specificity and Accuracy of High- and Intermediate- or High-Probability Ventilation-Perfusion Lung Scan Interpretations for the Detection of Chronic Thromboembolic Pulmonary Hypertension Among 75 Patients with Pulmonary Hypertension

V/Q scan category	Sensitivity	Specificity	Accuracy
High	96%	94%	95%
High or intermediate	100%	86%	91%

V/Q = ventilation-perfusion.

tained in the posterior projection. Perfusion scans were obtained with 100 to 150 MBq of ^{99m}Tc-labeled macroaggregated albumin (^{99m}Tc-MAA), using a 20% window centered over the 140-keV energy peak. Patients were injected intravenously over 5 to 10 respiratory cycles in a supine position with 90,000 to 150,000 particles of ^{99m}Tc-MAA. No untoward effects related to the injection of this drug were noted. Images were obtained for 500,000 to 750,000 counts in at least six views. The V/Q lung scans were independently interpreted by two physicians using modified PIOPED criteria (*12*). For cases in which disagreement occurred, the V/Q lung scan probability classification was determined by consensus between the two readers. No information regarding the patient's underlying diagnosis or other studies was provided, with the exception of a chest radiograph used to interpret the V/Q lung scans. Sensitivity, specificity and accuracy were calculated according to standardized methods for proportions (*13*).

RESULTS

In 25 patients, chronic thromboembolism was determined to be the underlying cause of PHT (10 women and 15 men, mean age 41.8 yr). Primary PHT was diagnosed in 35 patients (26 women and 9 men, mean age 38.2 yr). A third group of 15 patients (12 women and 3 men, mean age 42.3 yr) had nonthromboembolic secondary PHT. Reader agreement occurred in 95% (71 of 75) of the studies. Only 7% (5 of 75) of patients had V/Q lung scans that were interpreted as intermediate probability for pulmonary embolism.

Table 1 demonstrates the results of V/Q scan interpretations for each of the three groups. In patients with chronic thromboembolic PHT, 96% (24 of 25) had V/Q lung scans that were interpreted as representing a high probability of pulmonary embolism. In the remaining patient from this group, the V/Q lung scan was interpreted as representing an intermediate probability of pulmonary embolism. For patients with primary PHT, all but two patients (33 of 35) had V/Q lung scans interpreted as representing a low probability of pulmonary embolism. The remaining two patients had intermediate- and high-probability V/Q lung scan interpretation. The one patient with primary PHT and a high-probability V/Q lung scan interpretation had extensive vasculature pruning on pulmonary angiography, which resulted in multiple regions of V/Q mismatch. For patients with secondary nonthromboembolic PHT, 67% (10 of 15), 20% (3 of 15) and 13% (2 of 15) had V/Q lung scans interpreted as representing low, intermediate and high probability of pulmonary embolism, respectively. The two patients with high-probability V/Q lung scan interpretations had obstruction of the pulmonary vasculature related to sarcoid lymphadenopathy and a primary pulmonary artery sarcoma.

In this series, none of the patients with PHT had normal or very low-probability V/Q lung scan interpretations. A high-probability V/Q lung scan interpretation had a sensitivity of 96% and a specificity of 94% for detecting patients with chronic thromboembolic PHT. The combination of high- and intermediate-probability V/Q lung scan interpretations had a sensitivity of 100% and a specificity of 86% for detecting chronic thromboembolic PE (Table 2).

DISCUSSION

Chronic thromboembolic PHT is a relatively uncommon and frequently misdiagnosed cause of PHT (*6,14,15*). However, the importance of the diagnosis cannot be overemphasized because chronic thromboembolic PHT can be cured surgically. Unfortunately, the clinical features, laboratory investigations and other noninvasive investigations are often unreliable in distinguishing chronic thromboembolic PHT from primary and nonthromboembolic secondary PHT (*14–16*). Although pulmonary angiography can often distinguish thromboembolic PHT from primary and nonthromboembolic secondary PHT, the procedure is not without risk (*9,10*). In addition, the angiographic findings that are suggestive of chronic thromboembolism can occur in other conditions, and therefore, correlation with history, physical examination and laboratory investigations plus CT or angioscopy may be required prior to surgical intervention (*7,17,18*). Both V/Q lung scanning and pulmonary angiography have been shown to underestimate the severity of chronic thromboembolic material within the pulmonary vasculature, as determined during thromboendarterectomy (*7,19,20*). However, despite its limitations, the V/Q lung scan remains a safe noninvasive test to determine

which patients warrant further evaluation with pulmonary angiography.

When performing the V/Q lung scan in patients with PHT, it is important to avoid any adverse hemodynamic effects by reducing the number of ^{99m}Tc-MAA particles that are injected. Previous studies demonstrate that fewer than 60,000 particles cause an inhomogeneous distribution of activity within the pulmonary vasculature (*21*). In this study, between 90,000 and 150,000 particles were administered, and no untoward effects were observed. Other evidence to support the safety of perfusion lung scanning was obtained from the National Institutes of Health primary PHT registry, which included 187 patients in whom perfusion lung scanning was safely performed (*22*).

The authors previously reported on eight patients with chronic thromboembolic PHT who all had high-probability V/Q lung scan interpretations (*23*). In the current series, 24 of 25 patients with chronic thromboembolic PHT had at least two large (greater than 75% of a segment) regions of V/Q mismatch. In this series, more than one half of the patients with chronic thromboembolic PHT underwent surgical thromboendarterectomy. These findings were concordant with those found by other investigators (*16*). Although a single case report suggested that diffuse symmetric thrombi may have a normal lung scan appearance, this finding was not reproduced by other investigators (*20*). Thus, a normal perfusion lung scan in patients with chronic thromboembolic PHT would be rare.

In the current series, a low-probability V/Q lung scan interpretation effectively excluded the diagnosis of chronic thromboembolism as a cause of PHT. Most patients with primary PHT and nonthromboembolic secondary PHT had low-probability V/Q lung scan interpretations, which demonstrated diffuse inhomogeneous distribution of ^{99m}Tc-MAA within both lungs. Only 7% of patients with PHT had intermediate-probability V/Q lung scan interpretations, which was substantially lower than has been reported in patients suspected of having acute pulmonary embolism (*24*).

Other modalities that are currently under investigation for the evaluation of chronic thromboembolism include CT, intravascular ultrasonography, pulmonary angioscopy, transesophageal echocardiography and MRI (*17,18,25–29*). However, none of these newer modalities has demonstrated clear advantages over the combination of V/Q lung scanning and pulmonary angiography.

In conclusion, the V/Q lung scan provides a safe and highly sensitive screening test to evaluate patients with PHT. In patients with a low-probability V/Q lung scan interpretation, the diagnosis of chronic thromboembolic PHT was effectively excluded, and pulmonary angiography was not required. In patients with intermediate- or high-probability V/Q lung scan interpretations, angiography was justified to confirm the diagnosis and determine surgical accessibility. Further studies addressing the application of V/Q lung scanning in a prospectively recruited cohort of patients with PHT are warranted.

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Condensed from
15 Years Ago:

Resolution Rates of Pulmonary Embolism Assessed by Serial Positron Imaging with Inhaled Oxygen-15-Labeled Carbon Dioxide

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Embolic obstruction of pulmonary blood flow results in delayed regional clearance of inhaled $^{15}CO_2$. Focally retained $^{15}CO_2$ appears as zones of increased ^{15}O activity on serial positron scintigrams, which show the locations of occluded pulmonary segments. Inhalation of $^{15}CO_2$, with serial imaging by a multicrystal positron camera, was used to locate and assess the magnitude of occluded pulmonary segments in eight patients with arteriographically documented pulmonary emboli. Imaging with $^{15}CO_2$ inhalation was repeated after 1 wk of i.v. heparin therapy to evaluate the ability of this technique to determine resolution rates of pulmonary emboli during anticoagulant therapy. In all patients, zones of increased $^{15}CO_2$ activity corresponded with sites of emboli identified arteriographically. After 1 wk of continuous heparin therapy, zones of focally retained $^{15}CO_2$ were totally resolved in three patients, diminished in four and unchanged in one. The regional pulmonary clearance rate of $^{15}CO_2$ was delayed over embolized pulmonary segments in all patients (mean clearance half-time = 42.2 sec ± 11.2 s.e.m.) and improved after heparin therapy (13.9 ± 3.9 sec; $p < 0.05$). Serial $^{15}CO_2$ inhalation imaging is a rapid noninvasive radionuclide technique for detection of pulmonary emboli. It can be repeated at frequent intervals to assess the resolution of emboli during anticoagulant therapy.

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