Ventilation Perfusion Lung Scanning in the Evaluation of Right-to-Left Shunting

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From the Case Records of the Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

J Nucl Med 1992; 33:2036–2039

CASE PRESENTATIONS

Patient 1

A 57-yr-old white female was diagnosed with idiopathic pulmonary fibrosis and progressive deterioration in respiratory function in 1988. The patient first noted shortness of breath in approximately 1985. Her condition remained stable until approximately 1988, at which time she noticed significant dyspnea on exertion and easy fatigability. She was started on immunosuppressive therapy and bronchodilators as well as supplemental oxygen. At the time of her diagnosis, she was noted to have a PO_2 of 70 while breathing room air but exhibited exertional arterial oxygen desaturation.

At her current evaluation, the patient complained of severe dyspnea on exertion with palpitations and shortness of breath while walking just a few steps. She had a chronic cough and frequent episodes of pedal edema.

A blood gas obtained with the patient at rest and breathing supplemental oxygen via nasal canula at a flow rate of 6 liters per minute demonstrated a pH of 7.49, a PCO_2 of 41 torr, a PO_2 of 37 torr and an O_2 saturation of 72%. An additional blood gas was obtained with the patient breathing 100% oxygen to further evaluate the hypoxemia. This is most accurately performed by having the patient breathe 100% oxygen via a mouthpiece while wearing nose clips. The nitrogen concentration in the expired gas was measured and the arterial blood gas was not obtained until the expired nitrogen concentration was under 1%. The blood gas obtained with 100% oxygen demonstrated a pH of 7.43, a PCO_2 of 49 torr and a PO_2 of 211 torr. Arterial oxygen saturation was 99%. By the standard equation for calculating shunt fraction (*1*), the shunt fraction was calculated to be 23%, which is significantly higher than the normal physiologic shunt fraction of less than 7%.

Received May 13, 1992; revision accepted June 14, 1992.
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An echocardiogram was obtained to detect and define the location of the shunt. The M-mode study demonstrated a dilated right ventricle and small left ventricle, while the two-dimensional study demonstrated a markedly dilated right atrium and right ventricle with severe right ventricular dysfunction. There was abnormal septal motion consistent with right ventricular pressure overload; the left ventricular cavity was small with normal function. The Doppler study demonstrated mild tricuspid regurgitation. No evidence of intracardiac shunting was noted during a bubble contrast study. A chest radiograph did not demonstrate any vascular abnormalities (Fig. 1). A perfusion lung scan was obtained, which included images of the brain and kidneys (Fig. 2). Both organs demonstrated significant amounts of radioactivity, which suggested right-to-left shunting at a macrovascular level.

Because of the latter findings, the patient underwent cardiac catheterization. Pulmonary artery pressure was 93/37 with a mean of 57 mmHg and right ventricular pressure was 93/14 mmHg. The mean right atrial pressure was 14 mmHg. Aortic pressure was 100/70 with a mean of 82 mmHg and the left ventricular pressure was 100/8 mmHg. Systemic cardiac output was 2.9 liters per minute, as calculated by the estimated Fick method (*1*). Pulmonary

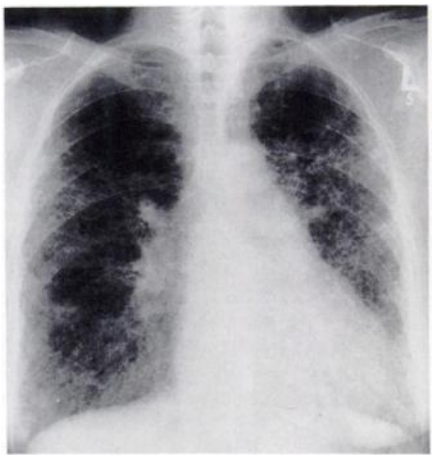

FIGURE 1. Chest x-ray. Posterior-anterior view demonstrates advanced diffuse interstitial lung disease with a peripheral predominance and suggestion of cystic changes. The heart is minimally enlarged.

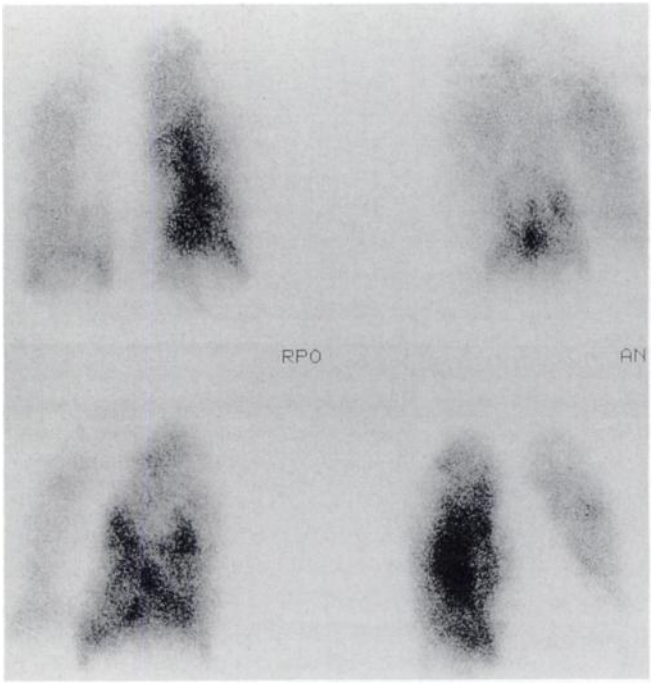

FIGURE 2. Perfusion scan of the lungs (posterior, LPO, RPO and anterior views) was obtained following the intravenous administration of ^{99m}Tc-MAA, which reveals significant reduced blood flow (via pulmonary artery) to the left lung. Both lungs demonstrate nonuniform perfusion suggesting diffuse parenchymal disease. Based on this pattern, chronic pulmonary embolism was considered as an unlikely underlying cause of pulmonary arterial hypertension in this patient.

blood flow was 3.0 liters per minute by the same method. Bidirectional shunting was documented with a left-to-right flow of 1.2 liters per minute and a right-to-left flow of 1.1 liters per minute. A transesophageal echocardiogram also was obtained, which demonstrated a small left ventricle with normal function, a dilated and hypokinetic right ventricle, mild tricuspid regurgitation and evidence of a right-to-left shunt through a patent foramen ovale. No atrial septal defect nor ventricular septal defect were visualized. All four pulmonary veins were visualized as draining into the left atrium.

Patient 2

A 53-yr-old white male was diagnosed in early 1989 as having primary pulmonary hypertension. For approximately 1 yr, he had experienced gradually progressive dyspnea on exertion. He was hospitalized after an episode of syncope and chest pain. When physical examination and ECG suggested pulmonary hypertension with right ventricular hypertrophy, he underwent cardiac catheterization and subsequent open lung biopsy. These studies confirmed the presence of significant pulmonary hypertension. The presence of plexogenic arteriopathy was noted on an open lung biopsy specimen and established the diagnosis as primary pulmonary hypertension (*2*). Since his diagnosis, he has been maintained on nifedpine and warfarin. When he developed signs of fluid retention secondary to right heart failure, he was begun on furosemide. His course has been one of progressive deterioration in his exercise tolerance, with intermittent episodes of chest pain and of syncope.

When admitted for reevaluation of his primary pulmonary hypertension approximately 2.5 yr after the initial diagnosis, he was found to be quite dyspneic even when breathing supplemental oxygen. His blood pressure was 130/80, pulse 90 and his respiratory rate 18. Examination of his chest by auscultation revealed a few crackles at both bases. The jugular venous pulse was noted to be up to the angle of the jaw when he was sitting upright. His apical impulse demonstrated a diffuse heave with a palpable right ventricular impulse; the pulmonic component of the second heart sound was palpable. The first heart sound was normal and there was a markedly increased pulmonic component on the second heart sound. There was also a very loud tricuspid regurgitation murmur and a right-sided S3 gallop. A chest x-ray demonstrated mild cardiomegaly with a prominent azygos vein and large main pulmonary arteries. Pulmonary function testing demonstrated a vital capacity of 3.1 liters (79% predicted), a residual volume of 2.12 liters (107% predicted), total lung capacity of 5.26 liters (88% of predicted) and an FRC of 2.55 liters (77% predicted). His forced vital capacity was 3.03 liters (76% predicted) and his FEV1 was 2.42 liters (77% predicted);

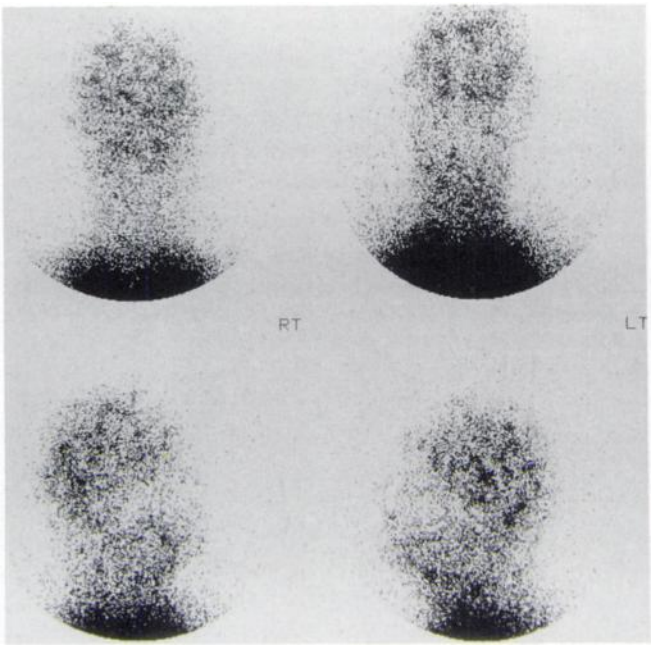

FIGURE 3. Anterior, posterior and both lateral view images of the head following the intravenous administration of ^{99m}Tc-MAA show evidence of particle trapping in the brain. This was interpreted to be consistent with right-to-left shunt. The mottled apppearance of uptake in the brain is probably due to the small number of particles that were trapped in the organ. In patients with suspected right-to-left shunting the number of administered particles is intentionally reduced to avoid any systemic side effects that may ensure following the trapping of MAA particles.

the FEV1-to-FVC ratio was 80%. His diffusing capacity was 16 ml/min/per torr (60% predicted). A blood gas obtained while he was breathing room air demonstrated a pH of 7.49, a PCO_2 of 24 torr and a PO_2 of 54 torr. A blood gas obtained on 100 percent oxygen using a mouthpiece and the nitrogen washout system described above demonstrated a pH of 7.46, a PCO_2 of 28 torr and a PO_2 of 388 torr. A perfusion lung scan demonstrated slight nonuniformity of perfusion to both lungs. There was, however, no significant radiotracer activity noted over the brain or kidneys. The scintigraphic findings were interpreted to represent low probability for pulmonary embolism and no evidence of right-to-left shunting.

An echocardiogram demonstrated a normal left ventricle cavity size with normal fractional shortening. The right ventricle was markedly dilated with paradoxical septal motion consistent with right ventricle pressure and volume overload. There was moderate-to-severe tricuspid regurgitation with no evidence of any right-to-left flow during administration of shaken saline for bubble contrast imaging. Cardiac catheterization demonstrated pulmonary hypertension with pulmonary artery pressure of 75/32 with a mean of 47 mmHg; right atrial pressure was 22 mmHg. There was no evidence of an atrial or ventricular septal defects, and the catheter could not be passed across the foramen ovale.

DISCUSSION

Right-to-left shunting of blood is a leading cause of arterial hypoxemia. In right-to-left shunting, venous blood reaches the systemic arterial circulation without passing through ventilated regions of the lung. Because a shunt is an extreme form of a ventilation perfusion mismatch in which the blood does not come in contact with ventilated alveoli, even with the administration of 100% oxygen, the lowered arterial PO_2 does not correct this. In this situation, although the end capillary PO_2 will be as high as that in the alveolar gas (in regions of the lung where ventilated alveoli are normally perfused), the PO_2 and O_2 content of the blood going through the shunt remains equivalent to that in venous blood. The mixture of these two differently oxgenated bloods results in a large fall in the measured PO_2 because the O_2 disociation curve is so flat in the upper range and the admixing of the shunted blood causes a profound fall in the resulting arterial PO_2. Measurement of the arterial PO_2 during 100% oxygen breathing makes it possible to detect even very small shunts.

Right-to-left shunting can occur both within and outside pulmonary circulation. Common causes of extrapulmonary right-to-left shunts include atrial or ventricular septal defects or a patent ductus arteriosus. Intrapulmonary shunts can occur in relatively large size vessels such as those caused by arteriovenous malformations or fistulas, or can occur at the microvascular level through either normal or abnormal pulmonary capillaries. When there is a completely unventilated but perfused area of lung, such as a consolidated pneumonia or an area of atelectasis, the blood flowing through these regions does not come in contact with ventilated alveoli and results in shunted blood flow even though the blood is flowing through normal pulmonary capillaries. On the other hand, in conditions that result in pulmonary hypertension, there may be an opening of abnormal vascular channels to decompress pulmonary circulation. These abnormal channels include "corner" capillaries which are not in close proximity with pulmonary alveoli. Flow through these vessels results in right-to-left shunt physiology.

In hypoxic patients who have been documented to have right-to-left shunt by obtaining an arterial blood gas while the patient is breathing 100% oxygen, it is very important to determine the site and mechanism of right-to-left shunting. If the shunting is at the level of the heart or the pulmonary artery, such as an atrial ventricular septal defect or a pulmonary arteriovenous malformation, it can probably be corrected surgically. On the other hand, if shunting occurs in pulmonary microcirculation, no specific surgical or arteriographic interventions can be employed to correct the condition.

Contrast dye studies traditionally have been used to detect large right-to-left shunts. Either during cardiac catheterization (for septal defects) or during pulmonary angiography (for arteriovenous malformations), contrast is injected and the immediate appearance of the contrast in the systemic circulation is considered as evidence of shunting. Unfortunately, these studies are invasive, requiring passage of a catheter into and through the right side of the heart, and carry risks, particularly in patients with pulmonary hypertension. In addition, the injection of relatively large volumes of contrast in these patients is considered somewhat dangerous and may cause significant complications. In order to determine who may benefit from these invasive procedures, we advocate the use of a perfusion lung scan along with images acquired over other organs as a first-order screening test to distinguish between the two major types of right-to-left shunts.

Recently, the use of noninvasive techniques, such as transthoracic echocardiography and transesophageal echocardiography, for the diagnosis of right-to-left shunt lesions has been advocated. There are, however, many patients in whom adequate imaging with transthoracic echocardiography is not feasible. The sensitivity of this technique for detecting small septal defects is not adequate, even with imaging while administering a shaken saline solution as "bubble" contrast. Transesophageal echocardiography appears to be able to diagnose septal defect with adequate sensitivity. However, this method should be considered a semi-invasive procedure and does requires sedation in order to perform the procedure and obtain optimal images. Echocardiography techniques have no role in the evaluation of pulmonary arteriovenous shunts.

Magnetic resonance imaging (MRI) also has been increasingly advocated as a means of imaging structural

cardiac and vascular lesions that result in right-to-left shunting. Although quite expensive, MRI can easily detect larger septal defects and pulmonary arteriovenous malformations, but the sensitivity of this technique for smaller lesions, such as a patent foramen ovale, remains to be established.

Measurements of arterial blood gases while the patient is breathing 100% oxygen is quite sensitive for the detection of a right-to-left shunt. However, this technique cannot determine the exact anatomic location of the shunt.

Because of the shortcomings enumerated above, radionuclide perfusion scanning plays a major role in the initial evaluation of patients suspected of having right-to-left shunts. In a normal lung, essentially all of the macroaggregated albumin (MAA) particles administered intravenously for a perfusion scan will be trapped within the pulmonary capillary bed (*3*). This is true even when capillaries not in proximity to ventilated alveoli are perfused. Thus, the capillaries in an area with pneumonia, an area of atelectasis, or the abnormal "corner" capillaries associated with shunting in pulmonary hypertension, will effectively trap MAA particles. Thus, if the right-to-left shunt occurs on a microvascular level, all of the radiopharmaceutical will be cleared within the lung and imaging of the brain or kidneys will not demonstrate significant amounts of radiotracer activity.

On the other hand, if the right-to-left shunt is outside the pulmonary capillary level, then the radiolabeled particles will pass through the shunt and enter the systemic circulation (*4–7*). In these instances, scanning over organs with high systemic blood flow, such as the brain or the kidneys, will demonstrate uptake of the radiopharmaceutical in these organs. While methodologies have been developed to use radiopharmaceuticals for the quantification of right-to-left shunts (*5,8,9*), particularly in the setting of congenital cardiac defects, these methods are neither as accurate nor as easy to perform and reproduce as quantification of right-to-left shunts with arterial blood gases obtained while patients are breathing 100% oxygen. Physicians have relied upon this radionuclide technique to distinguish microvascular from larger right-to-left shunts, because the latter may have specific therapeutic options.

Thus, in a patient with a right-to-left shunt, if a perfusion lung scan is performed and evidence of systemic circulation of radiopharmaceutical is demonstrated, then further investigation and use of invasive diagnostic techniques are warranted. In Patient 1, scanning the brain and kidneys after a perfusion lung scan demonstrated such evidence. Further investigation with both transesophageal echocardiography and cardiac catheterization demonstrated an intra-atrial shunt through a patent foramen ovale. In such a patient, the possibility of closing the opening via a percutaneous catheter technique or even a surgical procedure needs to be considered. In Patient 2, despite evidence of a sizable right-to-left shunt demonstrated on the arterial blood gas obtained with 100% oxygen, scanning other organs after the perfusion lung scan did not demonstrate any systemic uptake of the radiopharmaceutical. This would indicate that no additional work-up for a right-to-left shunt is warranted. The studies performed on this patient were obtained for other reasons and only serve to confirm the absence of a detectable (macrovascular) shunt lesion, as indicated by the lung scan.

Our approach to a patient with hypoxemia is relatively simple. First, obtain an arterial blood gas with the patient breathing 100% oxygen to determine whether hypoxemia is due to shunting or another ventilation perfusion mismatch. If evidence for a shunt is documented, a ventilation perfusion lung scan is obtained, after which the brain and kidneys are scanned. If these organ images demonstrate radiopharmaceutical uptake, then further investigation is undertaken to determine the site of the right-to-left shunt. If no systemic uptake is demonstrated, then the right-to-left shunt is assumed to be at the microvascular level and no further work-up is indicated since no specific therapies are available for such shunts.

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