

# Clinical and Anatomic Outcomes after Embolotherapy of Pulmonary Arteriovenous Malformations



Jeffrey S. Pollak, MD, Sanjay Saluja, MD, Ashraf Thabet, MD,<sup>1</sup> Katharine J. Henderson, MS, Neil Denbow, MD, and Robert I. White Jr, MD

**PURPOSE:** To assess long-term clinical and imaging results of technically successful pulmonary arteriovenous malformation (AVM) embolization.

**MATERIALS AND METHODS:** One hundred fifty-five patients with pulmonary AVMs underwent embolization during a period of 3 years. Recommended follow-up included clinical assessment, helical computed tomography, and physiologic evaluation within 1 year and then every 5 years.

**RESULTS:** Hereditary hemorrhagic telangiectasia was present in 148 patients (95%). Four hundred fifteen pulmonary AVMs were occluded during 205 procedures. Clinical follow-up was available in all patients over 3–7 years and imaging follow-up was available in 144 patients (393 lesions) over 1–7 years (mean, 2.9 y). Problems related to pulmonary AVMs occurred in 35 patients (23%) at 42 time points: 22 patients with 23 symptomatic events and 17 patients with 19 asymptomatic events. Symptoms resulted from growth of nonembolized pulmonary AVMs ( $n = 19$ ), residual embolized pulmonary AVMs ( $n = 5$ ), or both ( $n = 2$ ). Symptoms consisted of respiratory manifestations ( $n = 13$ ), cerebral ischemia ( $n = 4$ ), brain abscess ( $n = 5$ ), hemoptysis ( $n = 3$ ), and seizure ( $n = 1$ ). Imaging showed pulmonary AVM involution in 97% of embolized lesions and 11 residual lesions (2.8%) in 10 patients (6.9%). These were caused by recanalization ( $n = 7$ ), presence of an accessory feeding artery ( $n = 1$ ), pulmonary collateral vessels ( $n = 1$ ), and bronchial collateral vessels ( $n = 2$ ). CT detected 10 of the 11 residual lesions. Imaging detected 97 previously small pulmonary AVMs that had enlarged to a significant size in 28 patients (18%), 15 of whom were symptomatic and 13 of whom were asymptomatic.

**CONCLUSIONS:** Clinical and anatomic evaluation after pulmonary AVM embolization is important to detect persistent or reperfused lesions and enlarging lesions, with the latter more common. Patients with persistent, reperfused, or enlarging lesions often have symptoms, but a significant minority of patients are asymptomatic. More frequent assessment may improve detection before the onset of symptoms.

J Vasc Interv Radiol 2006; 17:35–45

**Abbreviations:** AVM = arteriovenous malformation, HHT = hereditary hemorrhagic telangiectasia

PULMONARY arteriovenous malformations (AVMs) are abnormal vessels in which there is a direct connection

from the pulmonary arterial circulation to the pulmonary venous circulation with no intervening capillary bed

(1). Approximately 85% of pulmonary AVMs are simple, in which one or more arteries arising within a single pulmonary segment supply the malformation (2). Complex lesions have arterial feeder vessels from more than one pulmonary segment and account for 5%–10% of cases. As many as 5% of lesions are diffuse, in which there is disseminated involvement of multiple segments or lobes with numerous, variably sized lesions. Typically, an aneurysmal sac will exist at the arteriovenous connection, commonly a

From the Section of Vascular and Interventional Radiology, Department of Radiology, Yale University School of Medicine, PO Box 208042, 333 Cedar Street, New Haven, Connecticut 06520-8042. Received June 9, 2005; accepted October 3. From the SIR 2005 Annual Meeting. **Address correspondence** to J.S.P.; E-mail: jeffrey.pollak@yale.edu

Josephine Lawrence Hopkins Foundation, and Yale-New Haven Hospital General Clinical Research Unit Grant NIH M01-RR-00125. None of the authors have identified a conflict of interest.

<sup>1</sup> Current address: Department of Radiology, Massachusetts General Hospital, Boston, MA.

© SIR, 2006

R.I.W. and K.J.H. are supported in part by grants from the March of Dimes (grant HHT-FY04-677), the

DOI: 101097/01.RVI.0000191410.13974.B6

single one for simple lesions with one or two feeder vessels and more likely a plexiform, septate, or multichanneled one for lesions with multiple feeder vessels.

Most pulmonary AVMs are congenital, with approximately 70% of patients having hereditary hemorrhagic telangiectasia (HHT); however, with intensive screening for telangiectases, epistaxis, and family history of these manifestations, the incidence is probably 80%–90% or higher (3–9). The remaining congenital pulmonary AVMs are idiopathic lesions not associated with any condition. Approximately 10% of pulmonary AVMs are acquired fistulas, most commonly in the setting of cirrhosis (ie, hepatopulmonary syndrome), in which the treatment undertaken is generally of the underlying pathologic process (10). Symptoms are present in more than 70% of patients with congenital pulmonary AVMs and are caused by right-to-left shunting and/or hemorrhage. Although hypoxemic symptoms such as dyspnea and fatigue predominate, they tend to be relatively well-tolerated; however, more than 50% of patients can develop the more serious and occasionally life-threatening complications of paradoxical embolization and rupture. It is the prevention of these events that represents the more critical need for treatment. Most identifiable paradoxical emboli involve the central nervous system and result in stroke, transient ischemic attack, or brain abscess.

Since the first description of pulmonary AVM embolization by Porstmann in 1977 (11), many series have been reported (3,5,8,11–16). Technical success rates are high at 88%–100%, and patients who have been successfully treated with embolization show improved oxygenation and a reduced shunt. However, few studies have reported long-term follow-up (9), and the primary methods of follow-up are typically clinical evaluation, arterial oxygen tension measurement, and shunt fraction studies. In this study, we evaluated our long-term results of technically successful pulmonary AVM embolization with anatomic imaging follow-up, principally with unenhanced helical chest computed tomography (CT), as well as clinical follow-up.

## MATERIALS AND METHODS

### Patients

Previously unreported patients were enrolled in this prospective study over a 3-year period from July 1, 1996, to June 30, 1999. Approval from our institutional review board (Human Investigation Committee) was obtained. Patients underwent evaluation for manifestations of pulmonary AVM and HHT. This consisted of a thorough history and physical examination, baseline pulse oximetry for oxygen saturation, often an arterial blood gas analysis for oxygen tension, and an imaging evaluation. Imaging evaluation included chest radiography and/or CT. These two studies were often performed at other institutions, given the referral nature of our practice. During the time of this study, a diagnosis of HHT was made if the patient had any two of the following: recurrent spontaneous epistaxis, multiple telangiectases, visceral involvement with vascular malformations, and an autosomal-dominant inheritance pattern (17). A consensus article from 2000 (18) stipulates a definitive diagnosis if three of these clinical criteria are present and a possible or suspected diagnosis if two are present.

### Embolization Technique

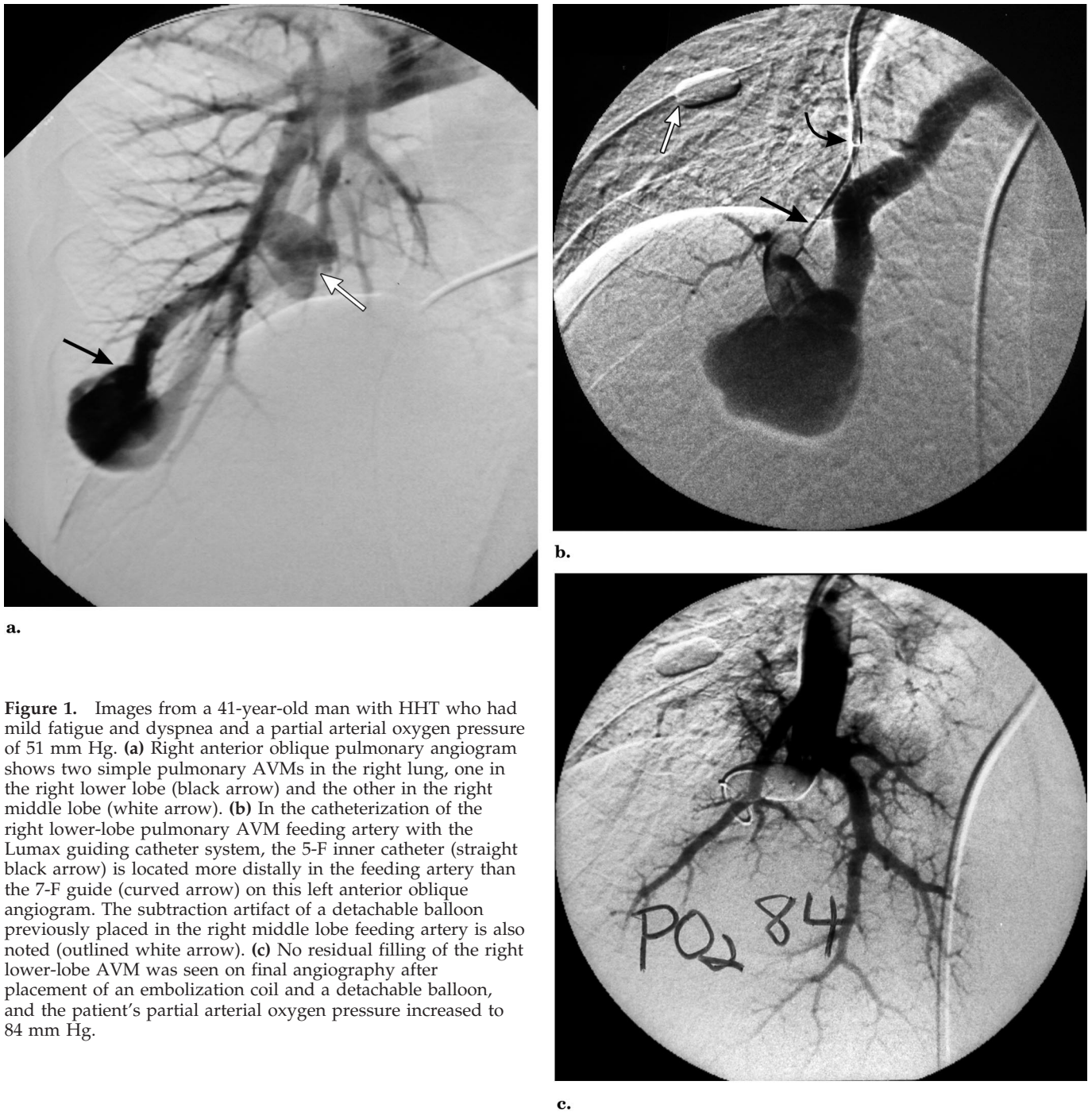
Diagnostic pulmonary angiography was performed from a transfemoral vein approach according to standard catheterization techniques to place a pigtail catheter sequentially in the main pulmonary artery to each lung. The goal was to identify all malformations with feeding arteries 3 mm or greater in diameter that would require occlusion. This diameter represents a significant size for permitting bland paradoxical embolization and stroke (19–21).

Initially, the embolization procedure was usually performed on a different day with use of the contralateral femoral vein, although children and pregnant women underwent a limited diagnostic angiography procedure and embolotherapy on the same day. Over time, the diagnostic and therapeutic procedures were more often performed on the same day, especially if there were only one or two pulmonary AVMs of significant size.

During the procedure, patients re-

ceived prophylactic antibiotic coverage with 1 g of intravenous cefazolin (Kefzol; Eli Lilly and Company, Indianapolis, IN) and prophylactic anticoagulation with 3,000–5,000 U of intravenous heparin, and strict attention was paid to avoiding the introduction of any intravascular air bubbles or thrombi, which could paradoxically embolize. Over the course of the study, a coaxial guiding catheter system was developed for the embolization procedure. These Lumax catheters (Cook, Bloomington, IN) consist of an outer 7-F multipurpose guiding catheter and an inner 5-F catheter with a short distal angle. The outer catheter provides support across the heart and large vessels as well as some selective capability, whereas the inner catheter provides finer selective maneuvers. Additionally, the guiding catheter permits exchange for a variety of differently shaped 5-F inner catheters. When the feeding artery to a pulmonary AVM is engaged with the inner catheter, the outer catheter can generally be advanced into it as well (Fig 1a,1b). The distal aspect of the feeding artery, beyond any significant normal lung branches yet proximal to the aneurysmal sac between the artery and vein, was then occluded with a detachable silicone balloon (Target Therapeutics/Boston Scientific, Fremont, CA) placed through the guiding catheter, embolization coils placed through the inner 5-F catheter, or a combination of the two agents (Fig 1c). After the availability of 0.035-inch and 0.038-inch soft platinum Tornado embolization coils (Cook), and then Nester coils (Cook), these were the preferred agents. Although 14 cm long when stretched out, Nester coils permit tight internal packing to yield a high degree of cross-sectional occlusion over a relatively short distance. To enhance stability of the first coil, its initial few centimeters could be placed in a small, distal normal side branch (ie, “anchored”) with the remainder of the coil released in the feeding artery. Microcoils (0.018 inch) were used if the feeding artery could be catheterized only with a microcatheter system or if the artery was extremely short, necessitating intraaneurysmal occlusion through a microcatheter (22).

After embolization of the feeding artery or arteries, segmental and lobar angiography was performed to assess



**Figure 1.** Images from a 41-year-old man with HHT who had mild fatigue and dyspnea and a partial arterial oxygen pressure of 51 mm Hg. **(a)** Right anterior oblique pulmonary angiogram shows two simple pulmonary AVMs in the right lung, one in the right lower lobe (black arrow) and the other in the right middle lobe (white arrow). **(b)** In the catheterization of the right lower-lobe pulmonary AVM feeding artery with the Lumax guiding catheter system, the 5-F inner catheter (straight black arrow) is located more distally in the feeding artery than the 7-F guide (curved arrow) on this left anterior oblique angiogram. The subtraction artifact of a detachable balloon previously placed in the right middle lobe feeding artery is also noted (outlined white arrow). **(c)** No residual filling of the right right lower-lobe AVM was seen on final angiography after placement of an embolization coil and a detachable balloon, and the patient's partial arterial oxygen pressure increased to 84 mm Hg.

for adequate occlusion and any accessory feeding vessels that might also require embolization. Patients were generally hospitalized overnight.

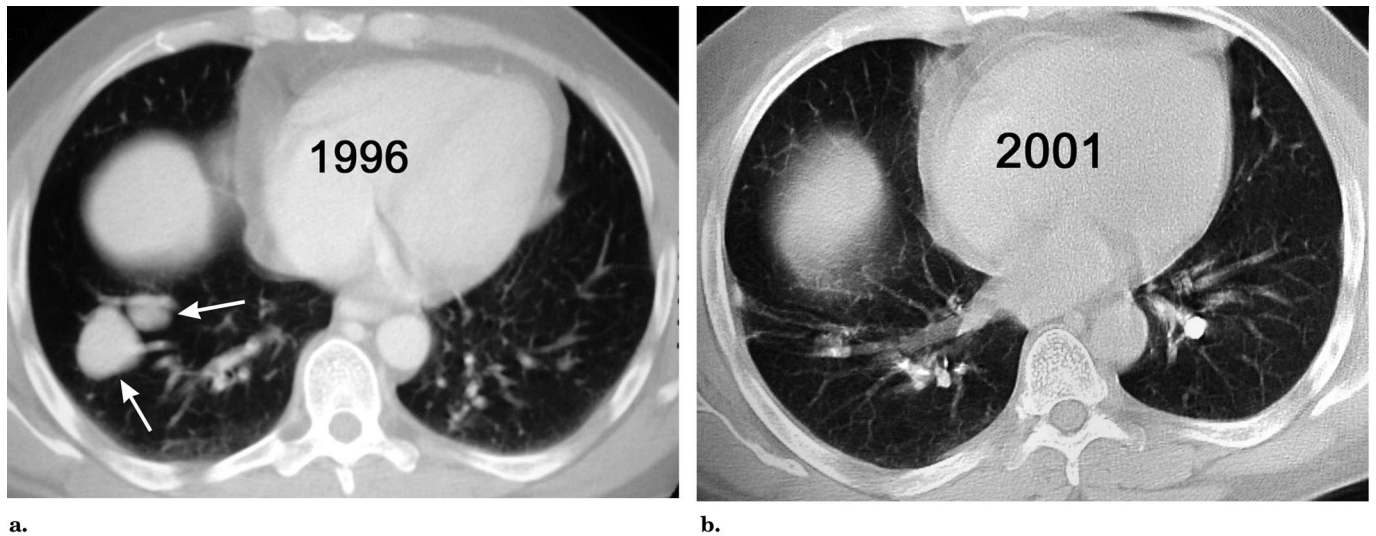
**Follow-up**

As a result of the long-distance referral status of many of these patients,

follow-up was generally performed in their local setting. Methods consisted of clinical evaluation, recording of laboratory data, radiographic studies, and telephone calls. Imaging studies were sent to us for direct review. Follow-up for the purposes of this study was concluded as of May 2004.

At 6–12 months, helical CT was rec-

ommended with use of reconstructions no thicker than 5 mm. An unenhanced study was believed to be sufficient to assess the presence and size of the aneurysmal sac. Additionally, clinical assessment was performed and a physiologic study was recommended: pulse oximetry for oxygen saturation and/or an arterial



**Figure 2.** Images from a 54-year-old man with HHT and pulmonary AVMs who had old infarcts in his right thalamus and cerebellar hemispheres on MR imaging as well as small cerebral AVMs. **(a)** CT scan before coil embolization of the feeding artery to a right lower-lobe pulmonary AVM shows a large bilobed sac (arrows). **(b)** Another CT scan 5 years later shows resolution of the sac.

blood gas study. These same imaging and physiologic studies were then recommended every 5 years or earlier if a patient was planning on pregnancy, was entering adolescence, or exhibited recurrent clinical manifestations.

The pulmonary AVM was considered successfully treated if complete or near-complete involution (ie, linear scar only) of the aneurysmal sac was seen on CT (**Fig 2**). Disappearance of a sac on chest radiography was considered acceptable in patients who had no CT scan if the sac had been seen on plain radiography before embolization. Alternatively, no residual perfusion on angiography was also considered acceptable in those followed with this modality (eg, in a patient returning for treatment of other pulmonary AVMs). If a sac remained on CT or chest radiography, a residual pulmonary AVM was considered to be present unless no flow was seen on pulmonary angiography. Although this could potentially miss bronchial artery collateral flow perfusing a pulmonary AVM beyond the level of pulmonary artery occlusion, this typically tiny left-to-left shunt was not considered significant outside of a small risk of hemoptysis. No strict physiologic criteria were used to determine the success or failure of treatment of any specific pulmonary AVM because changes in oxygen status could result from other pathologic processes, per-

sistence of the pulmonary AVM, or enlargement of other pulmonary AVMs. Nevertheless, a decrease in the postprocedural oxygen saturation by 2%–3% or in the oxygen tension by 5–10 mm Hg was suspicious for a worsened right-to-left shunt.

If a residual sac was present on CT or chest radiography, other pulmonary AVMs of significant size were identified, or physiologic studies suggested a worsening shunt, pulmonary angiography was recommended. Repeat embolization was performed as indicated.

## RESULTS

### Patients and Embolization Data

One hundred fifty-five patients had embolization of pulmonary AVMs during the study period, of whom 148 (95%) had HHT. There were 65 male patients and 90 female patients, with a mean age of 45 years (range, 7–77 y). Seven patients were children younger than 18 years of age, with ages ranging from 7 to 18 years and a mean of 12 years. Information on clinical manifestations is available for 154 of these patients (**Table 1**).

Four hundred fifteen pulmonary AVMs were embolized in 205 procedures; 50 patients underwent staged procedures to treat all their pulmonary AVMs. Nine pulmonary AVMs

in nine patients were diffuse and the remainder were focal. Detachable balloons alone were used for 192 lesions (46%), coils alone were used for 190 AVMs (46%), and a combination of the two were used for 33 pulmonary AVMs (8%). Most of the coils were standard stainless-steel 0.035-inch and 0.038-inch coils, with smaller numbers of the newer 0.035-inch and 0.038-inch Tornado and Nester coils used later in the study period. Embolization with complex helical microcoils through a microcatheter was needed for only 15 pulmonary AVMs (3.6%).

The procedural complication rate was 2%, with no significant sequelae. Three instances of angina occurred, as did one transient ischemic attack. Twelve percent of patients had mild postprocedural pleurisy and 2.4% had severe, delayed pleurisy.

### Clinical Follow-up

Clinical follow-up was available in all patients over periods of 3–7 years. Twelve patients died during the follow-up period, one from a brain abscess in the setting of a diffuse pulmonary AVM, one from HHT-related liver disease, and the remainder from unrelated causes. Two patients additionally developed heart failure from HHT-related liver AVMs, whereas two others had congestive heart failure from other causes.

**Table 1**  
**Clinical Manifestations in 154 Patients with Pulmonary AVMs\***

Manifestation	Number of Patients
Exercise intolerance	91 (59)
Clinical stroke	27 (17.5)
Transient ischemic attack	35 (22.7)
Stroke or transient ischemic attack	50 (32.5)
Migraine headaches	71 (46.1)
Brain abscess	14 (9.1)
Other infections	9 (5.8)
Lung hemorrhage	5 (3.2)
None	24 (15.6)

\* Information on clinical manifestations was not available for one patient.  
Note.—Values in parentheses are percentages.

**Table 2**  
**Problems Related to Pulmonary AVMs in 36 Patients in 43 Follow-up Episodes**

Event	Patients*	No. of Episodes			
		Total	Residual Pulmonary AVM	Pulmonary AVM Growth	Both
Symptomatic pulmonary AVM	22	23	5 (22)	16 (70)	2 (9)
Asymptomatic pulmonary AVM with true-positive noninvasive imaging finding	17	19	1 (5)	16 (84)	2 (11)
Asymptomatic pulmonary AVM with false-positive noninvasive imaging finding	1	1	1	—	—

\* Four patients presented as symptomatic or asymptomatic at different times.  
Note.—Values in parentheses are percentages.

Thirty-six patients (23%) presented at 43 separate times with problems related to residual or other growing pulmonary AVMs. One asymptomatic patient had a persistent sac that was discovered to have no pulmonary perfusion on angiography, which leaves 35 patients (23%) with significant pulmonary AVM disease at 42 follow-up times. Significant symptoms believed to be related to pulmonary AVMs developed in 22 patients (14%) at 23 different times. Asymptomatic significant pulmonary AVMs were noted in 17 patients (11% of all patients, 11.8% of those with imaging follow-up) at 19 follow-up times. Four patients who had episodes of heart failure (including two from liver AVMs) are included in the asymptomatic pulmonary AVM group. Four patients presented at different times with symptomatic and asymptomatic conditions. **Tables 2 and 3** detail the clinical

status of these patients and whether the etiology was a residual treated pulmonary AVM and/or growth of other pulmonary AVMs. The majority of patients had growth of other pulmonary AVMs. A small number had new growth and residual pulmonary AVMs (9.1% of symptomatic patients or 8.7% of symptomatic episodes; 11.8% of asymptomatic patients or 10.5% of asymptomatic episodes).

Of the four patients with four episodes of stroke or TIA, only one had a pulmonary AVM with no comorbid conditions. Two of the other three developed atrial fibrillation and one had a venous access device placed for transfusions of iron and blood. Of the five episodes of brain abscess in five patients, two occurred in the setting of diffuse pulmonary AVM, one with reperfusion and the other with growth of other lesions. The other three oc-

curred in the setting of growth of small pulmonary AVMs, which were multiple in one patient who also had a sinus procedure preceding the abscess.

**Imaging Follow-up**

Imaging follow-up was available in 144 of the 155 patients and 393 of the 415 embolized pulmonary AVMs (95%). This consisted of CT images in 112 patients (72%) and 312 pulmonary AVMs (75%), chest radiographs in 27 patients (17%) and 42 pulmonary AVMs (10%), and angiography alone in six patients (4%) and 39 pulmonary AVMs (9%). Eleven patients (7%) with 22 embolized pulmonary AVMs (5%) had no imaging follow-up. One patient had some pulmonary AVMs followed with use of radiography and others followed with angiography, accounting for the sum of patients here being 156, one more than the actual number of patients. The mean imaging follow-up time was 2.9 years per procedure, with a range of 1 month to 7 years (median, 3 y).

Imaging findings at follow-up are summarized in **Table 4**. More than 90% of patients and treated lesions showed pulmonary AVM involution on noninvasive imaging or absence of feeding vessels on angiography. One false-positive CT finding was caused by a smaller residual sac that was not perfused on angiography. Further details on patients with residual pulmonary AVMs and growth of other AVMs is given in the relevant forthcoming sections.

**Physiologic Follow-up**

Thirty patients had arterial blood gas measurements available in the same laboratory before and 6–12 months after treatment. In these patients, the mean oxygen tension measurements were 62 mm Hg before treatment, 83 mm Hg immediately after treatment, and 82 mm Hg at the late follow-up. When these measurements were compared with their immediate postembolization values, 12 patients had an increase of 1–9 mm Hg reflected on the later measurement, four measurements were unchanged, and 14 had a decrease of 1–14 mm Hg.

**Table 3**  
Manifestations from Symptomatic Pulmonary AVMs in 22 Patients in 23 Follow-up Episodes

Symptoms	Episodes			
	Total	Residual Pulmonary AVM	Pulmonary AVM growth	Both
Dyspnea/exercise intolerance	8	0	7	1
Stroke/transient ischemic attack	4	0	3	1
Brain abscess	5*	1	4	0
Hemoptysis	3	2	1	0
Hypoxemia without dyspnea	5	2	3	0
Seizure	1	0	1	0
Total	26†	5	19	2

\* Among these patients there was one case of septic toe and one case of septic knee.  
† Three patients had two different symptoms at a same follow-up time. One had dyspnea and a transient ischemic attack, one had hemoptysis and hypoxemia, and one had brain abscess and hypoxemia.

### Residual Embolized Pulmonary AVMs

True persistence or reperfusion was identified in 11 treated pulmonary AVMs in 10 patients. This represents 2.8% of the 393 treated pulmonary AVMs and 7.6% of the 144 patients who had imaging follow-up. Seven of these patients were symptomatic (Table 2), of whom two also had growth of other pulmonary AVMs, and three were asymptomatic, of whom two also had growth of other pulmonary AVMs. Therefore, 40% of patients with residual embolized pulmonary AVMs also had growth of other pulmonary AVMs to a significant size. This included four of the nine patients with embolized diffuse malformations. CT scans in the 10 patients showed 10 residual malformations (Fig 3a,3b); only one AVM was not detected (ie, false-negative).

The causes of residual pulmonary AVMs are identified in Table 5. Recanalization through coils was the most common finding, typically in the setting of coils that did not create a dense occlusive plug of metal in the vessel, and was occasionally seen from early deflation of a detachable balloon (Fig 3c–3e; Table 6). Nine patients underwent repeat embolotherapy, with successful occlusion of the pulmonary AVMs in seven. An additional patient had slow flow remaining after embolization and only a thin vessel on angiography 3 years later that was not

believed to be of sufficient size to warrant further embolization. One patient with hemoptysis had bronchial collateral flow entering the pulmonary arteries distal to proximally positioned coils placed in an attempt to redistribute flow away from diffuse bilateral lower-lobe pulmonary AVM involvement; these were considered as two treated pulmonary AVMs. Particulate embolization of the bronchial arteries was only partially successful and was complicated by multifocal strokes. These were caused by paradoxical systemic arterial embolization of some of the embolic material after it entered the pulmonary circulation and passed through the pulmonary AVMs. The patient had a complete clinical recovery but did have subsequent recurrent hemoptysis (23). The last patient was a child who was found to have multiple small pulmonary branches providing collateral flow to the pulmonary artery feeder vessel distal to the embolized segment. These were too small to warrant embolization.

### Pulmonary AVM Growth

Enlargement of the feeding arteries of 97 previously small pulmonary AVMs to a size sufficient to warrant embolization occurred in 28 patients (19% of patients with imaging follow-up) at 36 follow-up time points. Fifteen patients had symptoms (Table 3). A follow-up CT scan was the only indication of significant growth in 13

asymptomatic patients with 30 pulmonary AVMs over 15 postprocedural follow-up time periods.

### DISCUSSION

Pulmonary AVMs are well-known to predispose patients to significant morbidity other than just the effects of hypoxemia (3,6,24). In this study, one third of patients had a history of stroke or transient ischemic attack, whereas 9% had previous brain abscesses, 6% had other infections, and 3% had previous lung hemorrhage. The danger of leaving a pulmonary AVM alone after it has been diagnosed has also been demonstrated by Swanson et al (7), who found that five of 15 patients available for follow-up who had untreated pulmonary AVMs developed a neurologic complication within 10 years. Recurrent or persistent pulmonary AVMs after treatment would be similarly expected to carry a significant risk of adverse events. Indeed, in a report from our institution (14) on successfully embolized large pulmonary AVMs (feeding arteries  $\geq 8$  mm in diameter), seven of 45 patients (16%) had reperfusion of eight of 52 pulmonary AVMs (15%). Two of these patients developed strokes. Although six also had worsening dyspnea, hypoxemic symptoms are often insidious and well-compensated, even in those with large lesions, and is an insensitive indicator of what may be a sizable malformation for paradoxical embolization.

As was shown in this study as well as others (9,14–16,25,26), persistence or reperfusion of an apparently successfully embolized pulmonary AVM may occur in one or more of four ways: (i) recanalization of the embolized vessel, (ii) growth of a missed or previously small accessory artery, (iii) bronchial and other systemic artery collateral flow into the pulmonary artery beyond the level of the embolization (creating a left-to-left shunt), and (iv) pulmonary artery-to-pulmonary artery collateral flow about the occlusion. The last has been observed only in young children in our experience, presumably as a result of the ability for continued lung growth at that age (26). Other than the third mechanism, all these result in right-to-left shunting and place the patient at recurrent risk for paradoxical embolization. In addi-

**Table 4**  
**Imaging Findings at Follow-up**

Finding	Patients (N = 144)	Pulmonary AVMs (N = 393)
Sac/pulmonary AVM involution	133 (93)	381 (97)
Residual sac/pulmonary AVM	11 (7.6)	12 (3.1)
True-positive residual embolized pulmonary AVMs*	10 (6.9)	11 (2.8)

\* One patient had a residual sac that was reduced in size on CT but was not perfused on angiography.

Note.—Values in parentheses are percentages.

tion, because the malformation remains in all cases, the risk of rupture remains. Theoretically, this risk may be greater when systemic arterial collateral flow has developed, with rupture of the pulmonary AVM that is now under higher pressure and/or the abnormal collateral vessels. Nevertheless, this has rarely been seen.

Maintaining a low rate of reperfusion or persistence of embolized pulmonary AVMs is strongly related to technique. Our goal is to achieve a high degree of cross-sectional occlusion of a feeding artery as close to the AVM as possible. This resulted in our achieving a very low incidence of residual embolized pulmonary AVMs in this study, occurring in only 2.8% of treated lesions with imaging follow-up, albeit in 7.6% of patients.

With the exception of our earlier report of large pulmonary AVMs (14) and one other small series (25), most studies have also found persistence or reperfusion of embolized pulmonary AVMs in similarly small numbers of patients and lesions, typically from zero to 10% (7,9,15,16,27). In the earliest study to our knowledge to rely on CT follow-up, Remy et al (28) discovered persistent flow in two of 21 pulmonary AVMs with early follow-up (10%) and two of 46 with late follow-up (4%). The sacs of these four lesions were unchanged in size. Two had persistent flow and two had recanalization. Of the eight reperfused pulmonary AVMs in our series of large lesions mentioned earlier (14), four had recanalization of an embolized vessel and three had interval growth of an accessory feeder vessel, all of which were successfully embolized. Another report of patients treated with detachable balloons and occasionally coils (15) used chest radiogra-

phy or high-resolution CT imaging for follow-up, along with history and arterial blood gas values. Reperfusion was identified in 3.5% of patients as a result of accessory arteries or recanalization.

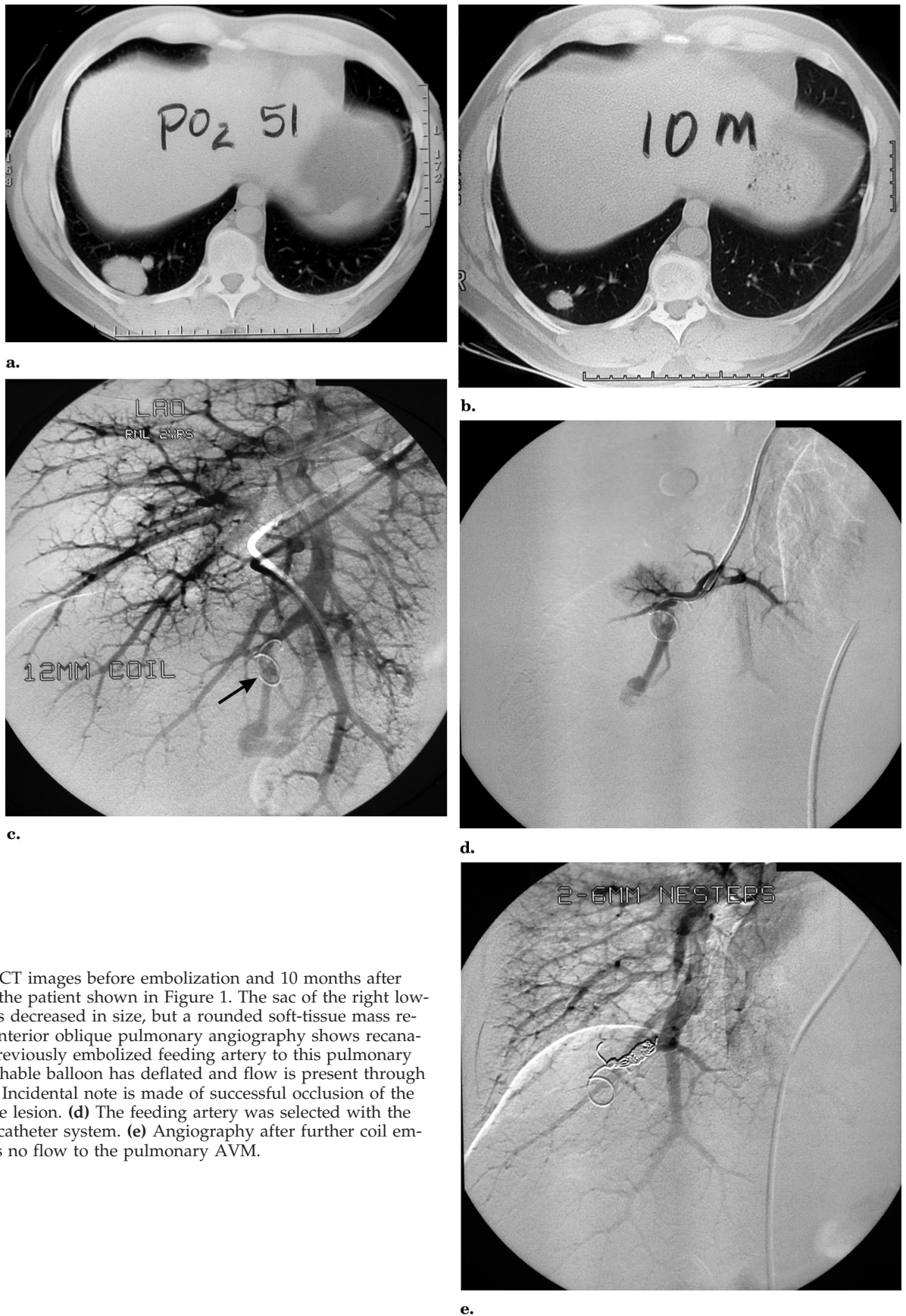
Swanson et al (7) found recanalization in two of 48 patients (4%) treated with embolization, although the mode of identification in these two patients was not mentioned. Their patients were followed annually with physical examination, chest radiography, arterial blood gas analyses, and assessment of right-to-left shunt if symptoms were present. Gupta et al (8) followed their 66 patients with clinical evaluation, pulmonary function tests, and radionuclide shunt studies. Although they noted deterioration in three patients in relation to subsequent pregnancies, these cases were found to have progression of other pulmonary AVM disease. No cases of reperfusion were seen, but not all pulmonary AVMs had specific follow-up imaging. Recently, Prasad et al (16), in a comparison of embolization versus placement of stainless-steel or platinum coils, found persistence rates of 6.7% and 10.3%, which were not significantly different. Mager et al (9) used a combination of annual symptomatic assessment, chest radiography, and arterial oxygen tension measurement to follow pulmonary AVM therapy in 112 patients in whom 296 pulmonary AVMs were embolized (including 32 patients previously reported from their institution [5]). A right-to-left shunt fraction study (measured with use of the 100% inspired oxygen method [29]) was performed if the oxygen tension decreased by 10% or an abnormality was seen on the chest radiograph, with subsequent CT and/or intravenous digital angiogra-

phy performed if the shunt fraction increased by more than 3%. Fifteen patients (13%) had 25 instances of reperfusion (8.4% of lesions), with two of these cases apparently related to an accessory feeder vessel. One of these patients had a neurologic event in the form of a transient ischemic attack; however, this patient also had enlargement of other nonembolized lesions.

The one study with outlying results was reported by Sagara et al in 1998 (25). This small study of seven patients found a reperfusion rate of 57% in 14 embolized pulmonary AVMs on follow-up chest radiography, CT, and angiography. Only two of these patients had aneurysmal sacs that were unchanged in size. The remaining aneurysmal sacs were smaller but still showed contrast enhancement and opacification on angiography. Two filled from only bronchial arterial supply, whereas the remaining six had recanalized pulmonary arteries, two additionally with bronchial arterial supply. Hemoptysis was not reported in these two cases.

Probably the most important finding during follow-up is that of enlarging pulmonary AVMs to a size requiring treatment. The number of patients in this category was more than twice the number with reperfusion or persistence, with the actual number of enlarging pulmonary AVMs more than nine times the number of residual embolized pulmonary AVMs. Mager et al (9) also found a significant number of patients who required repeat treatment for enlarging pulmonary AVMs (14%), although they observed a lower rate if no small residual pulmonary AVMs had been left at the time of the first treatment. The prevalence of pulmonary AVM enlargement does raise the question of whether the threshold size for treatment of a pulmonary AVM should be lowered to less than 3 mm. Earlier work indicated that treatment of lesions with feeding arteries of at least this size helped protect against paradoxical bland embolization, although not necessarily against bacterial embolization (19–21). With enlargement over time, lesions that had been small may reach and exceed this size.

We hypothesize that the cause of pulmonary AVM enlargement is physiologic pressure related to redistribution of pulmonary blood flow after



**Figure 3.** (a,b) CT images before embolization and 10 months after embolization in the patient shown in Figure 1. The sac of the right lower-lobe AVM has decreased in size, but a rounded soft-tissue mass remains. (c) Left anterior oblique pulmonary angiography shows recanalization of the previously embolized feeding artery to this pulmonary AVM. The detachable balloon has deflated and flow is present through the coil (arrow). Incidental note is made of successful occlusion of the right middle-lobe lesion. (d) The feeding artery was selected with the Lumax guiding catheter system. (e) Angiography after further coil embolization shows no flow to the pulmonary AVM.



**Table 5**  
Reasons for Residual Embolized Pulmonary AVMs

Cause	Patients (N = 144)	Pulmonary AVMs (N = 393)
Recanalization	7	7
Accessory feeding artery	1	1
Collateral reperfusion of distal feeding artery from small pulmonary artery branches	1	1
Systemic bronchial artery collateral perfusion	1	2

**Table 6**  
Recanalized Pulmonary AVMs

Cause	Pulmonary AVMs
Through coils	4
Deflated detachable balloon	2
Deflated detachable balloon and through a coil	1

embolotherapy of other lesions rather than spontaneous growth. Additionally, it is unlikely that truly new lesions develop. Instead, these lesions probably represent enlargement of lesions previously smaller than the threshold of imaging detection. Patients with HHT and pulmonary AVM are prone to have multiple varying sized lesions, including microscopic ones (1,3,4,8).

Although follow-up evaluation of patients is clearly important, the precise method is not agreed upon. Patients in this study were principally followed with clinical evaluation and CT imaging. Mager et al (9) relied more strongly on physiologic follow-up and chest radiography, the sensitivity of which is limited. In a screening study, Kjeldsen et al (30) found a sensitivity of 60% for chest radiography in a group of patients with positive pulmonary angiographic findings. Because no study exists that compared the sensitivity of CT versus other modalities for detection of pulmonary AVMs of significant size, the superiority of any one method is not clear. It is likely that a combination of clinical evaluation, physiologic testing, and CT imaging is the best algorithm. Indeed, patients in this study with recurrent pulmonary AVMs were first identified with any one of these three methods (Tables 2 and 3).

The CT findings we used to define a

successfully occluded pulmonary AVM were complete or near-complete resolution of the aneurysmal sac, meaning only a tiny residual or linear scar. Remy et al (28) used a looser definition, additionally accepting a sac of decreasing size over time, whereas Prasad et al (16) added the finding of resolution of the draining vein in addition to resolution of the aneurysmal sac. Sagara et al (25) used the most strict standards, requiring a lack of enhancement after administration of contrast medium. Nevertheless, it seems reasonable to accept disappearance or near-complete disappearance of the sac as an indication of the lack of pulmonary AVMs of significant size. We did not track the appearance of pulmonary AVMs believed to be adequately occluded by noninvasive imaging in those patients who returned for pulmonary angiography for other reasons. Still, only one lesion was identified to have remaining pulmonary arterial perfusion (the one false-negative finding on CT).

One situation in which CT imaging is limited is in cases of multiple pulmonary AVMs in close proximity or diffuse disease. Artifacts related to multiple coil emboli and adjacent non-embolized pulmonary AVMs can create difficulty in interpreting the status of a treated lesion. In this situation, we have a low threshold for proceeding to pulmonary angiography, especially if

the arterial oxygen tension or shunt fraction has decreased. Patients with diffuse disease are known to present particular difficulty in terms of achieving adequate treatment (31), with hypoxia often resistant to embolization and the incidence of neurologic events moderately reduced but still high.

The timing of follow-up is also a critical question. We chose an initial evaluation within 6–12 months of a procedure to confirm adequate embolization and then every 5 years. However, more than half the patients with subsequent problems related to pulmonary AVMs presented during follow-up with symptoms. This suggests that a shorter interval may be better, perhaps one of 3 years.

In conclusion, patients undergoing embolotherapy for pulmonary AVMs require careful surveillance after therapy. Although a small number will have reperfusion or persistence of an embolized malformation, a larger number will show significant enlargement of previously small pulmonary AVMs. These lesions will often result in symptoms, although a sizable minority are asymptomatic and are detected with imaging. The optimal follow-up should be a combination of clinical assessment, physiologic testing, and CT imaging. An initial follow-up to determine adequate occlusion of a treated lesion is recommended within the first 6–12 months. The timing of subsequent evaluations is not certain, but would appear to be sooner than the 5 years recommended at the start of this trial. Also, it is possible that embolization of lesions with feeding arteries smaller than 3 mm in diameter may result in a smaller number of enlarging lesions. Hopefully, these measures would decrease the ratio of symptomatic patients to asymptomatic patients who require further treatment.

#### References

1. Boshier LHJ, Blake DA, Byrd BR. An analysis of the pathologic anatomy of pulmonary arteriovenous aneurysms with particular reference to the applicability of local excision. *Surgery* 1959; 45:91–104.
2. White RI Jr, Pollak JS, Wirth JA. Pulmonary arteriovenous malformations: diagnosis and transcatheter embolotherapy. *J Vasc Interv Radiol* 1996; 7:787–804.
3. White RI Jr, Lynch-Nyhan A, Terry P,

- et al. Pulmonary arteriovenous malformations: techniques and long-term outcome of embolotherapy. *Radiology* 1988; 169:663-669.
4. Puskas JD, Allen MS, Moncure AC, et al. Pulmonary arteriovenous malformations: therapeutic options. *Ann Thorac Surg* 1993; 56:253-257.
  5. Haitjema TJ, Overtoom TT, Westermann CJ, et al. Embolisation of pulmonary arteriovenous malformations: results and follow up in 32 patients. *Thorax* 1995; 50:719-723.
  6. Gossage JR, Kanj G. Pulmonary arteriovenous malformations: a state of the art review. *Am J Respir Crit Care Med* 1998; 158:643-661.
  7. Swanson KL, Prakash UB, Stanson AW. Pulmonary arteriovenous fistulas: Mayo Clinic experience, 1982-1997. *Mayo Clinic Proc* 1999; 74:671-680.
  8. Gupta P, Mordin C, Curtis J, et al. Pulmonary arteriovenous malformations: effect of embolization on right-to-left shunt, hypoxemia, and exercise tolerance in 66 patients. *AJR Am J Roentgenol* 2002; 179:347-355.
  9. Mager JJ, Overtoom TT, Blauw H, et al. Embolotherapy of pulmonary arteriovenous malformations: long-term results in 112 patients. *J Vasc Interv Radiol* 2004; 15:451-456.
  10. Wirth JA, Pollak JS, White RI Jr. Pulmonary arteriovenous malformations. *Curr Pulmonol Crit Care Med* 1996; 17:261-298.
  11. Porstmann W. Therapeutic embolization of arteriovenous pulmonary fistula by catheter technique. In: Kelop O, ed. *Current concepts in pediatric radiology*. Berlin: Springer, 1977;23-31.
  12. Terry PB, White RI Jr, Barth KH, et al. Pulmonary arteriovenous malformations: physiologic observations and results of therapeutic balloon embolization. *N Engl J Med* 1983; 308:1197-1200.
  13. Dutton JA, Jackson JE, Hughes JM, et al. Pulmonary arteriovenous malformations: results of treatment with coil embolization in 53 patients. *AJR Am J Roentgenol* 1995; 165:1119-1125.
  14. Lee DW, White RI Jr, Eggin TK, et al. Embolotherapy of large pulmonary arteriovenous malformations: long-term results. *Ann Thorac Surg* 1997; 64:930-939.
  15. Saluja S, Sitko I, Lee DW, et al. Embolotherapy of pulmonary arteriovenous malformations with detachable balloons: long-term durability and efficacy. *J Vasc Interv Radiol* 1999; 10:883-889.
  16. Prasad V, Chan RP, Faughnan ME. Embolotherapy of pulmonary arteriovenous malformations: efficacy of platinum versus stainless steel coils. *J Vasc Interv Radiol* 2004; 15:153-160.
  17. Guttmacher AE, Marchuk DA, White RI Jr. Hereditary hemorrhagic telangiectasia. *N Engl J Med* 1995; 333:918-924.
  18. Shovlin CL, Guttmacher AE, Buscarini E, et al. Diagnostic criteria for hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). *Am J Med Genet* 2000; 91:66-67.
  19. Hewes RC, Auster M, White RI. Cerebral embolism—first manifestation of pulmonary arteriovenous malformation in patients with hereditary hemorrhagic telangiectasia. *Cardiovasc Intervent Radiol* 1985; 8:151-155.
  20. Rosenblatt M, Pollak JS, Fayad PB, et al. Pulmonary arteriovenous malformations: what size should be treated to prevent embolic stroke? [abstract] *Radiology* 1992;185:P134.
  21. White RI Jr, Pollak JS. Pulmonary arteriovenous malformations: options for management. *Ann Thorac Surg* 1994; 57:519-521.
  22. Tal MG, Saluja S, Henderson KJ, et al. Vein of Galen technique for occluding the aneurysmal sac of pulmonary arteriovenous malformations. *J Vasc Interv Radiol* 2002; 13:1261-1264.
  23. Vinaya KN, White RI Jr, Sloan JM. Reassessing bronchial artery embolotherapy with newer spherical embolic materials. *J Vasc Interv Radiol* 2004; 15:304-305.
  24. Shovlin CL, Letarte M. Hereditary haemorrhagic telangiectasia and pulmonary arteriovenous malformations: issues in clinical management and review of pathogenic mechanisms. *Thorax* 1999; 54:714-729.
  25. Sagara K, Miyazono N, Inoue H, et al. Recanalization after coil embolotherapy of pulmonary arteriovenous malformations: study of long-term outcome and mechanism for recanalization. *AJR Am J Roentgenol* 1998; 170:727-730.
  26. Faughnan ME, Thabet A, Mei-Zahav M, et al. Pulmonary arteriovenous malformations in children: outcomes of transcatheter embolotherapy. *J Pediatr* 2004; 145:826-831.
  27. Remy-Jardin M, Wattinne L, Remy J. Transcatheter occlusion of pulmonary arterial circulation and collateral supply: failures, incidents, and complications. *Radiology* 1991; 180:699-705.
  28. Remy J, Remy-Jardin M, Wattinne L, et al. Pulmonary arteriovenous malformations: evaluation with CT of the chest before and after treatment. *Radiology* 1992; 182:809-816.
  29. Mager JJ, Zanen P, Verzijlbergen F, et al. Quantification of right-to-left shunt with (99m)Tc-labelled albumin macroaggregates and 100% oxygen in patients with hereditary haemorrhagic telangiectasia. *Clin Sci* 2002; 102:127-134.
  30. Kjeldsen AD, Oxhøj H, Andersen PE, et al. Pulmonary arteriovenous malformations: screening procedures and pulmonary angiography in patients with hereditary hemorrhagic telangiectasia. *Chest* 1999; 116:432-439.
  31. Faughnan ME, Lui YW, Wirth JA, et al. Diffuse pulmonary arteriovenous malformations: characteristics and prognosis. *Chest* 2000; 117:31-38.

**CME TEST QUESTIONS**

Examination available at <http://directory.sirweb.org/jvircme>

1. All of the following characterize pulmonary arteriovenous malformations (PAVMs) *except*:
  - a) Symptoms are present in the minority of patients with congenital PAVMs.
  - b) Most PAVMs are related to hereditary hemorrhagic telangiectasia.
  - c) Acquired PAVMs most often occur in the clinical setting of cirrhosis.
  - d) Serious clinical sequelae of PAVMs include stroke or rupture.
2. In the study by Pollak et al, persistence or reperfusion of embolized AVMs was identified in what percentage of patients with imaging followup?
  - a) 2.8%
  - b) 40%
  - c) 23%
  - d) 7.6%
3. In the study by Pollak et al, symptoms that suggested growth of nonembolized PAVMs or recurrence of embolized lesions included all of the following *except*:
  - a) Brain abscess
  - b) Hemoptysis
  - c) Angina pectoris
  - d) Exercise intolerance
4. All of the following mechanisms for persistence or reperfusion of previously embolized PAVMs are associated with right-to-left shunting, and potential for paradoxical embolization, *except*:
  - a) Recanalization of the embolized vessel
  - b) Growth of a missed or previously small accessory artery
  - c) Pulmonary artery-to-pulmonary artery collateral flow around the occlusion
  - d) Bronchial or other systemic artery collateral flow into the pulmonary artery beyond the level of occlusion.