Pulmonary Arteriovenous Malformations: Results of Treatment with Coil Embolization in 53 Patients

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OBJECTIVE. The purpose of this study was to determine the effects of percutaneous transcatheter coil embolization of pulmonary arteriovenous malformations on arterial oxygen saturation, pulmonary gas exchange, anatomic right-to-left shunt, and lung function and to assess the complications of the procedure.

SUBJECTS AND METHODS. Fifty-three patients were included in the study: 42 (79%) had associated hereditary hemorrhagic telangiectasia. Nineteen (36%) had neurologic problems compatible with paradoxical embolization. During 102 separate embolization procedures, all malformations with feeding vessels ≥3 mm in diameter were embolized with steel coils. Arterial oxygen saturation at rest and on exercise and the intrapulmonary right-to-left shunt fraction (^{99m}Tc-macroaggregate injection), forced expiratory volume in 1 sec, vital capacity, diffusing capacity for carbon monoxide, and transfer coefficient were measured before and after embolization. Complications of the procedure were recorded and investigated.

RESULTS. Before treatment, all patients had hypoxemia in the supine posture (SaO_2, 89 ± 1% [standard error of the mean]), which fell a further 6% (absolute) on standing. Mean values for transfer coefficient and diffusing capacity for carbon monoxide were reduced, at 85 ± 3% and 78 ± 3% (predicted value), respectively. After embolization, the mean values for supine and erect SaO_2 rose to 94 ± 1% and 93 ± 1%. Transfer coefficient increased by a mean of 5.4% of predicted value. The mean shunt fraction fell from 23 ± 2% preembolization to 9 ± 1% postembolization. In 102 procedures, there were 18 complications, 12 mild, two moderate, and four potentially serious (systemic coil embolization in two patients, cerebrovascular accident [transient], and myocardial puncture), but there were no lasting sequelae.

CONCLUSION. Our results show that coil embolization is an effective and well-tolerated method for treatment of pulmonary arteriovenous malformations. Improvements in pulmonary gas exchange and lung function and a decrease in right-to-left shunting occurred after treatment. The procedure was well tolerated and had a low complication rate.

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Pulmonary arteriovenous malformations (PAVMs) are congenital abnormal communications between the pulmonary artery and pulmonary vein, resulting in an anatomic right-to-left shunt and a reduction in the arterial oxygen saturation [1]. The prognosis of untreated patients is poor, their high morbidity and mortality rates being due mainly to the effects of paradoxical emboli [2, 3].

In this prospective study the results of steel coil embolization were assessed in 53 patients, comparing pulmonary function tests, exercise tests, and right-to-left shunt measurements conducted before and after the occlusion of all angiographically demonstrable PAVMs. The safety of embolization was assessed by reviewing the complications of the procedure.

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Subjects and Methods

Between 1987 and February 1994, 53 patients underwent a total of 102 separate PAVM embolization procedures at our institution. The average age of patients was 41 years old (range, 8–70 years). Of the 42 patients (79%) with the associated condition of hereditary hemorrhagic telangiectasia (HHT) [4], 24 (57%) were female, but there was no female preponderance in the non-HHT patients.

Diagnosis

All patients underwent a complete medical examination and general assessment. Preembolization chest radiographs were obtained or sought from the referring hospital. Standard blood tests were performed, including a full blood count. Liver function tests were done to exclude the diagnosis of hepatopulmonary syndrome [5]. The diagnosis of a PAVM was confirmed by results of tests of arterial oxygen saturation, intrapulmonary shunt size, and chest radiography. Those patients with hereditary hemorrhagic telangiectasia were identified by a history of multiple epistaxes and relatives with the condition and by the presence of telangiectasia.

Methods

Before embolization, respiratory function was fully assessed in all patients, and their right-to-left shunt was measured. These investigations were repeated 3 months after embolization.

Respiratory Function Tests

In the first test, arterial oxygen saturation was measured using an Ohmeda Biox 3740 pulse oximeter. Values were obtained with the patient lying supine for 10 min and after standing erect for a similar period. In the second test, forced expiratory volume in 1 sec (FEV1) and vital capacity (VC) were recorded in the standard manner as the best of three attempts using a Vitalograph spirometer. Finally, the diffusing capacity for carbon monoxide (DL_{CO}) was calculated from the single-breath carbon monoxide transfer factor measured with a P. K. Morgan Spiroflow. The mean value from the three measurements was corrected for the current hemoglobin concentration [6] and expressed as a percentage of the predicted value.

Exercise Testing

Exercise capacity was assessed using a cycle ergometer, with the workload (15–30 watts) increasing every minute. At the end of every minute, the pulse rate and arterial oxygenation were recorded using an ear probe with the Ohmeda Biox 3740 oximeter.

For patients unable to cycle, the distance walked on the level in 3 min, together with SaO_2 and pulse rate, was measured. SaO_2 3 months after embolization was compared with the preembolization value at the highest workload achieved on each occasion.

Right-to-Left Shunt Assessment

Previous work at this institution has substantiated the validity and reproducibility of the method of shunt measurement using ^{99m}Tc-labeled macroaggregates. Although this method is described fully elsewhere [4, 7], its principal and salient points are outlined here.

Technetium-99m macroaggregates are tracer-labeled particles measuring 20–60 mm in diameter and are therefore too large to pass through the normal pulmonary microvasculature. In patients with PAVMs, a portion of any intravenously injected macroaggregates is not trapped in the pulmonary capillary network and so passes into other organs through the systemic circulation.

The assumption is made that at rest the right kidney receives 10% of the cardiac output. By measuring the activity recorded at the skin surface over the right kidney and correcting this value to account for the attenuation due to overlying soft tissue, the shunt fraction can be calculated:

$$\text{Shunt fraction (\%)} = \frac{\text{right kidney counts} \times 10 \times \text{attenuation correction}}{\text{macroaggregate counts injected}} \times 100$$

Statistical Analysis

Paired pre- and postembolization values for SaO_2, shunt fraction, FEV1/VC, VC, DL_{CO}, and DL_{CO}/VA were analyzed using the Wilcoxon signed rank test. Correlations of postembolization DL_{CO}/VA with postembolization shunt fraction and arterial oxygenation (both supine and erect) were performed. Exercise capability was analyzed using the Wilcoxon signed rank test on the paired pre- and postembolization values for arterial oxygenation at maximum equivalent workloads.

Preembolization Assessment of Patients

Clinical features.—The most common symptoms at presentation were epistaxis (n = 34, 64%) and breathlessness (n = 14, 26%). As might be expected, epistaxis was more common in the group of patients with HHT (33/42) than in the group without HHT (1/11). Hemoptysis was rare in both groups of patients (HHT:5/42, non-HHT:2/11). Interestingly, 40% of all patients had a history of neurologic problems ranging from recurrent migraines (4%) to transient ischemic attacks (21%) and cerebral abscesses (15%). Only two of these patients were known to have cerebral arteriovenous malformations, which were diagnosed on IV contrast-enhanced CT brain scans and cerebral angiograms.

Thirteen percent of all patients were anemic (male, hemoglobin [Hb] < 14 g/dl; female, Hb < 12.2 g/dl), and half were polycythemic (male, Hb > 17.7 g/dl; female, Hb > 15.2 g/dl). In all patients, results of liver function blood tests were normal on routine testing.

Physiological Measurements

Before embolization, all patients had a reduced supine SaO_2 (89 ± 1% [standard error of the mean]). Oxygenation was further reduced (83 ± 1%) by a change from the supine to the erect posture (Fig. 1).

The maximum exercise capacity before embolization showed a wide variation among individuals, ranging from 120 m walking on the level to 150 watts on the cycle ergometer.

The mean right-to-left shunt measured in the supine position before embolization was 23 ± 2%.

The results of the respiratory function tests performed before and after embolization are summarized in Table 1. As described previously [8], pulmonary diffusion was reduced but spirometric values were usually normal.

Embolization

All 53 patients had angiographically demonstrable PAVMs and underwent on average two embolization procedures (total, 102; range, 1–7 per patient).

Seventy-two percent of patients had lesions in both lungs, and 95% of the lesions were situated in the lower zones. Lesions were subdivided into simple types consisting of a single feeding vessel supplying a single dilated venous component with a single draining vein, and com-

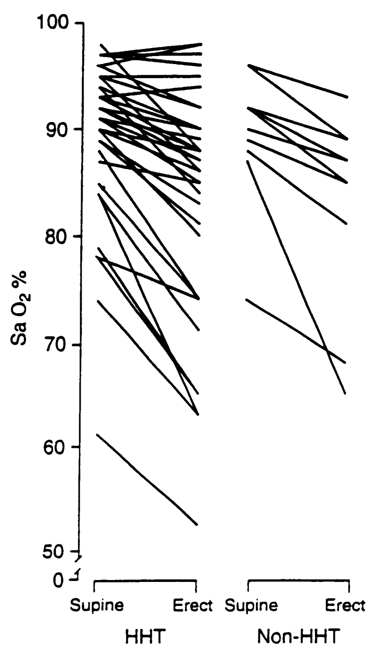

Fig. 1.—Postural changes in arterial oxygen saturation: comparisons of oxygenation in the supine and erect posture in patients with and without hereditary hemorrhagic telangiectasia.

TABLE 1: Results of Arterial Oxygen Saturation and Intrapulmonary Shunt Size Expressed as the Mean and Standard Error of the Mean (SEM) Measured Before and After Embolization ($n = 53$)

	Arterial Oxygen Saturation (%)		Intrapulmonary Shunt (%)
	Supine	Erect	
PRE			
Mean	89	83	23
SEM	1	1	2
POST			
Mean	94	92	9
SEM	1	1	1
% normal POST	64	53	40

Note.—% normal POST = percentage of patients with arterial oxygen saturation ≥95%, and intrapulmonary shunt fraction ≤5% after treatment with embolization.

plex types consisting of multiple feeding arteries and draining veins with an intervening network of small arteriovenous communications [9]. Sixty-six percent of all patients had simple lesions, 17% had complex lesions, and 17% had a mixture of both types. In the group of patients without HHT, 64% had one or more complex lesions.

The total number of coils used in each patient ranged from 1 to 105 (Fig. 2). Most patients were discharged the day after embolization.

Embolization Procedure

Selective right and left main pulmonary arteriograms were initially obtained using a digital subtraction technique with a 6.7-French Grollman angled pigtail catheter (Cook Europe, Bjaeverskov, Denmark) from a femoral venous approach.

This catheter was then exchanged for a 7-French end-port-only Headhunter 1 catheter (Cordis Europa N.V., Oosteinde, the Netherlands), which was used selectively to catheterize the feeding vessel to a malformation (Fig. 3A). The catheter tip was advanced to a point beyond any branches to normal lung and immediately proximal to the dilated venous portion of the malformation (Fig. 3B). Multiple angiograms in different projections were sometimes required to visualize the neck of the malformation prior to the final positioning of the catheter tip before coil embolization. Once the catheter had been stably and appropriately positioned, embolization was performed with steel coils.

Following satisfactory placement of the first coil, a repeat arteriogram was obtained and further coils positioned as required until the vessel was completely occluded (Fig. 3C).

The procedure was then repeated for further arterial feeding vessels. The catheterization and embolization of practically all malformations were achieved in the great majority of patients using a single catheter; only rarely was it necessary to resort to a catheter with a different tip configuration.

Each embolization session lasted 2–3 hrs, the length of the procedure being determined by the number and complexity of the malformations requiring embolization, the experience and skill of the operator, the safe dosage of contrast medium permissible in that particular individual, and the tolerance of the patient to the procedure. The patients left the hospital 24 hr after the embolization. Subsequent embolization procedures were performed as required until all significant malformations had been occluded.

Embolization sessions were separated by 3 months, and full respiratory function tests were repeated on readmission before the next procedure.

Results

Postembolization

Clinical features.—All patients were followed up 3 months after embolization, when their SaO_2, right-to-left shunt, and respiratory function tests were repeated. After this, patients were followed up at 6- to 12-month intervals.

A deterioration in both clinical status and right-to-left shunting was seen in two female patients in association with pregnancy. The first became pregnant after embolization had reduced her right-to-left shunt from 40% to 20% of her cardiac output. Multiple small PAVMs remained that were not amenable to embolization. Pulmonary angiography postpartum showed that the remaining PAVMs had all grown slightly in size although they remained too small and numerous to allow embolization. The previously embolized lesions remained occluded. Repeat shunt measurements showed an increase back to preembolization levels.

The second patient had undergone successful embolization of two simple malformations, with reduction of her right-to-left shunt to zero. She underwent termination of a pregnancy at the start of the second trimester, after which a shunt of 7% developed and she became mildly hypoxemic on exercise. A repeat angiogram showed a single new simple AVM, which was successfully occluded.

Physiological Measurements

Changes in intrapulmonary shunt size and arterial oxygen saturation are summarized in Table 1. The mean resting

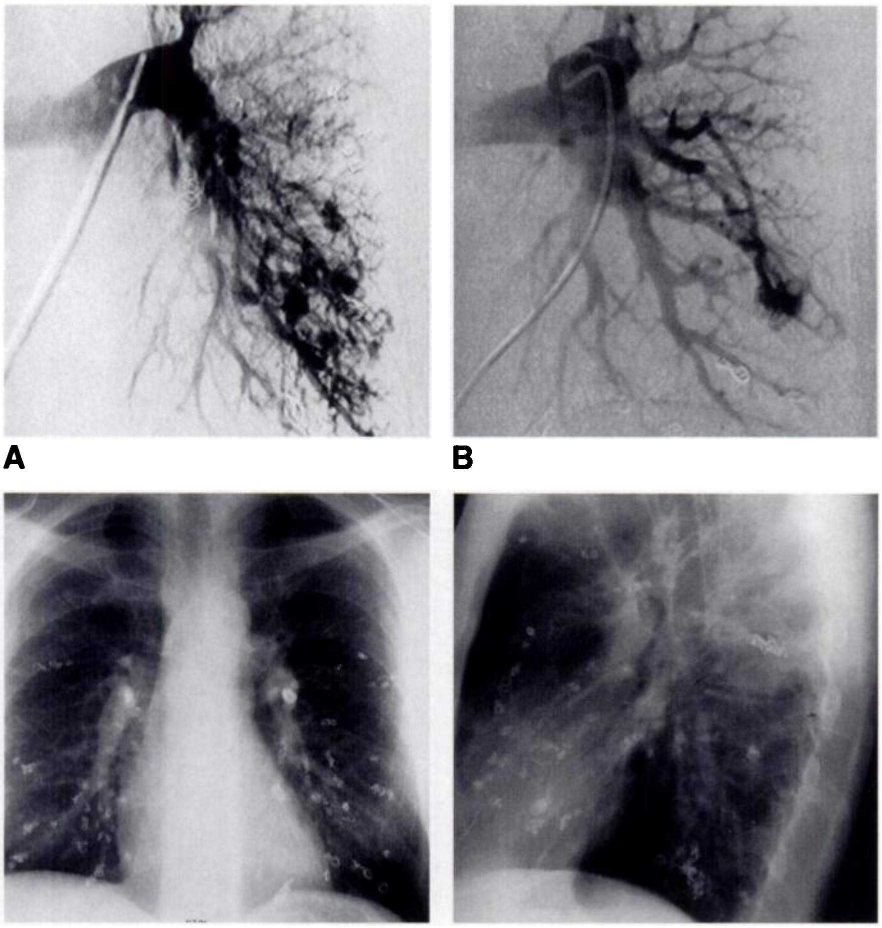

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Fig. 2.—Effect of multiple embolizations of pulmonary arteriovenous malformations (PAVMs) in both lungs with a total of 105 coils in six separate procedures.

***A*, Selective left pulmonary arteriogram after three embolization procedures. Multiple small PAVMs persist in the lateral portion of the left lower zone. Numerous steel coils are visible elsewhere in the lung.**

***B*, Selective left pulmonary arteriogram at start of fifth embolization procedure. Single PAVM present in left lower zone.**

***C* and *D*, Frontal (*C*) and lateral (*D*) chest radiographs after final embolization. Numerous (105) steel coils are present in both lungs with marked predominance in the lower zones.**

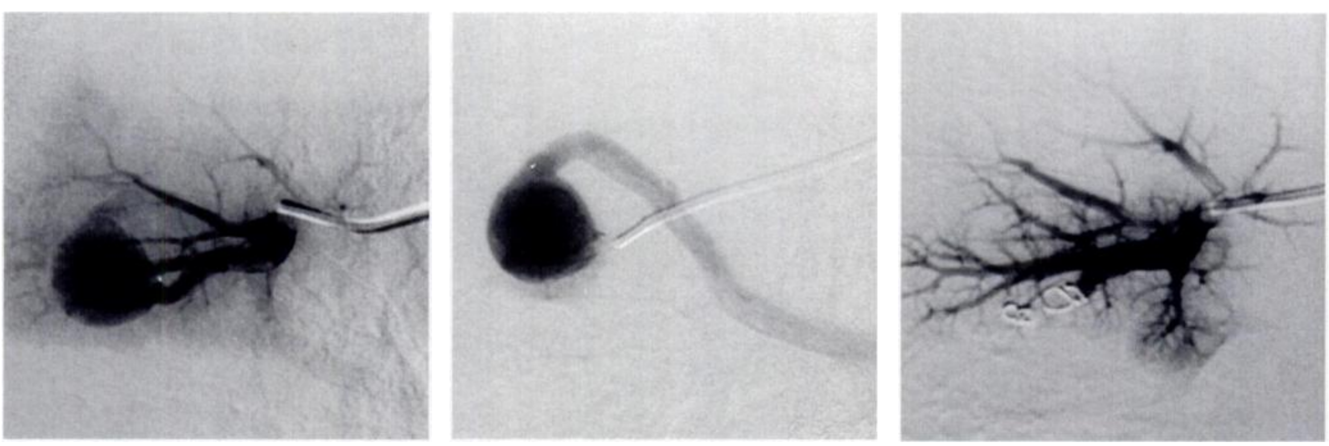

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Fig. 3.—Embolization of right mid-zone simple pulmonary arteriovenous malformations (PAVMs).

***A*, Selective pulmonary arteriogram shows right mid-zone PAVM with single feeding artery and large round venous sac.**

***B*, Catheter has been introduced into feeding artery to neck of PAVM beyond any normal pulmonary artery branches. Note single draining vein.**

***C*, Arteriogram after embolization with two steel coils shows complete occlusion of PAVM with preservation of normal pulmonary artery branches.**

supine SaO_2 increased significantly from 89 ± 1% to 94 ± 1% (standard error of the mean) ($p < .0001$), and the change was even more dramatic for the erect SaO_2 (83% to 92 ± 1%, $p < .0001$) (Fig. 4). The mean right-to left shunt fraction decreased from 23 ± 2% to 9 ± 1% ($p < .0001$) (Fig. 5). The residual postembolization shunt fraction gives an objective measure of the efficacy of the treatment. The residual shunt returned to normal (<5%) in 40% of patients, was greatly improved (>5%

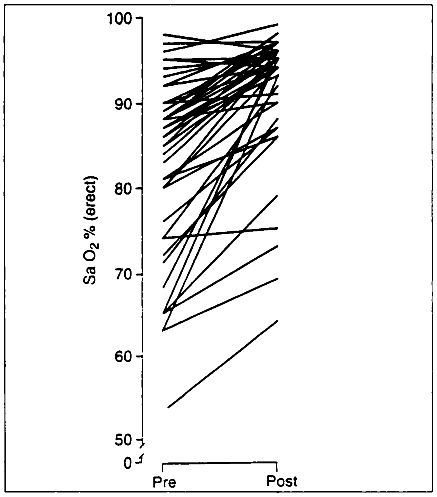

Fig. 4.—Change in arterial oxygenation after embolization in the entire patient group.

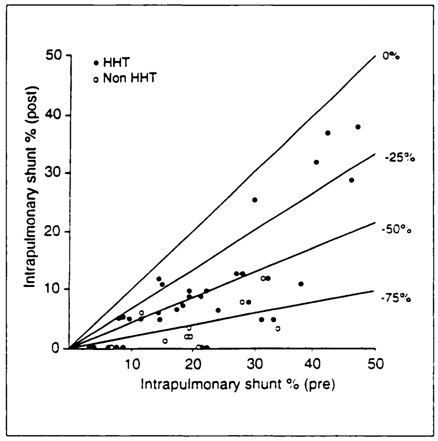

Fig. 5.—Shunt reduction after embolization: the effect of embolization on intrapulmonary shunt in patients with and without hereditary hemorrhagic telangiectasia.

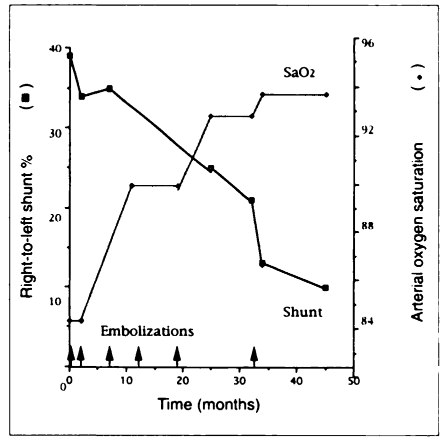

Fig. 6.—Right-to-left shunt and arterial oxygen saturation at rest (supine posture for both measurements) plotted for patient shown in Fig. 3, who had six embolization procedures. Measurements made 24 hr before embolization on each occasion.

to <20%) in 47%, and was only slightly improved (>20%) in 13%. The serial improvements seen in the right-to-left shunt and SaO_2 values in a patient who had six embolization sessions (Fig. 2) are shown in Fig. 6.

Table 2 summarizes the results of the respiratory function tests. There was a small reduction (3.3%, p = .015) in the predicted FEV1/VC without a significant change in VC. The change in DL_{CO} was statistically insignificant, but the DL_{CO}/VA increased by 5.4% (p = .02) of its predicted value.

The mean SaO_2 at maximal equivalent workload increased significantly from 81 ± 2% to 91 ± 1% (standard error of the mean) (p < .0001). Comparisons could not be assessed statistically for the three patients who exercised by walking on the level. Six patients were excluded because of incomplete data.

There was no correlation between postembolization DL_{CO}/VA and shunt (r = .03) or postembolization SaO_2 in either the supine or erect positions (r = .16 and .12, respectively).

Embolization

Table 3 lists the complications associated with the embolization procedures. The most common complication was localized pleuritic chest pain starting within 1 or 2 days of embolization. This pain was more likely to occur in patients whose PAVMs had a large venous sac rather than in those in whom a normal pulmonary arterial branch had to be occluded during PAVM embolization. The ventilation/perfusion scans obtained in patients with such symptoms were unremarkable and did not demonstrate lung infarction. There was a good response to nonsteroidal antiinflammatory agents in these patients.

Three patients suffered mild central chest discomfort during the embolization procedure, which was accompanied by electrocardiographic evidence of cardiac ischemia. The angina was relieved by sublingual nitrate in all three patients. These episodes were thought to be due to the injection of a small amount of air through the angiographic catheter, which was in a wedged position in the feeding vessel to a PAVM prior to embolization. Cardiac ischemia was possibly caused by a coronary gas embolus.

Two patients were confused and disorientated at the end of their procedures, but both made a spontaneous recovery. One episode, in a 58-year-old patient, was thought to be due to excessive premedication, and the other patient had received a large amount of IV contrast during the procedure (400 ml of iohexol 350 g/l).

TABLE 2: Results of Respiratory Function Tests Expressed as the Mean and Standard Error of the Mean (SEM) Performed Before and After Embolization

	FEV1/VC	VC	DL_{CO}	DL_{CO}/VA
PRE				
Mean	92.4	92.2	77.7	85.0
SEM	2.7	2.1	3.2	3.2
POST				
Mean	89.1	93.2	79.0	90.2
SEM	2.5	2.3	3.1	3.8

Note.—FEV1/VC = forced expiratory volume in one second, VC = vital capacity, DL_{CO} = diffusing capacity for carbon monoxide, DL_{CO}/VA = transfer coefficient. All results are expressed as a percentage of the predicted value.

TABLE 3: Frequency of Complications Arising During or Shortly After the Embolization Procedure (Total Number of Procedures = 102)

	n	(%)
Mild		
Pleuritic chest pain	9	(9)
Central chest pain relieved by sublingual nitrates	3	(3)
Moderate		
Transient confusion	2	(2)
Severe		
Systemic embolization of coil	2	(2)
Myocardial puncture	1	(1)
Cerebrovascular accident	1	(1)
Total	18	(18)

The most serious complications were passage of an embolization coil through the PAVM ($n = 2$), myocardial puncture by the guidewire ($n = 1$), and a cerebrovascular incident during the procedure ($n = 1$). In the first two cases, immediate carotid artery compression prevented cerebral embolization, and in each the coil lodged in the left common femoral artery, from which it was retrieved through a contralateral common femoral arterial approach using an intravascular snare.

Puncture of the myocardium resulted in a small pericardial hemorrhage without tamponade. The embolization procedure was aborted, and the patient made an uneventful recovery in the coronary care unit.

One patient developed apraxia and a left hemiparesis during the embolization. Fluoroscopy of the skull showed no evidence of cerebral coil embolization, and air had not knowingly been injected through the angiographic catheter during the procedure. As there was no other obvious cause for this temporary neurologic defect it was supposed that a portion of newly formed thrombus in the feeding vessel may have become dislodged and embolized in the cerebral circulation. A CT brain scan showed no evidence of an acute ischemic event, and the patient made a full, spontaneous recovery over the next 5 days.

Despite an overall adverse event rate of 18 per 102 embolization procedures, serious incidents ($n = 4$, 4%) were rare, and none was associated with any long-term consequences.

Discussion

Physiologic Findings

Preembolization respiratory function tests showed arterial hypoxemia, which is to be expected in patients with right-to-left shunts. The arterial desaturation was more profound in the erect than in the supine position owing to the preferential blood flow to the lung bases when the patient is upright.

Lung volumes were relatively well preserved in most patients except in those who had undergone previous surgery. Both DL_{CO}/VA and DL_{CO} were significantly reduced, presumably as a result of a reduction in the vascular surface area over which gas diffusion can take place. Because of its low pulmonary vascular resistance, a PAVM may also reduce DL_{CO} by stealing blood from the peripheral pulmonary capillaries where gas exchange takes place (Fig. 7).

After embolization, VC did not change. DL_{CO}/VA increased, which can at least partially be explained by the increased perfusion of normal lung tissue distal to the PAVM after embolization owing to a reduction in the PAVM-induced vascular steal.

Complete obliteration of right-to-left shunting was achieved in 40% of our patients, and a marked improvement was seen in a further 47%. Despite embolization of all malformations with a feeding vessel of ≥3 mm in diameter, a residual shunt of more than 5% was present in 60% of the patients. This finding suggests the presence of multiple microscopic PAVMs that are not amenable to embolization. These patients will continue to be at risk for cerebrovascular complications because of paradoxical embolization through the shunts, although the likelihood of this occurrence is presumably reduced after embolization of the larger intrapulmonary arteriovenous communications. Such patients will therefore still require prophylactic antibiotic therapy before such procedures as dental treatment.

Embolization Procedure

It is important to perform the embolization as distally as possible in the feeding vessel to a PAVM to avoid the occlusion of branches to normal lung. This is true for all patients but especially so when treating patients with multiple lesions (Fig. 2), where the preservation of any functioning lung parenchyma is critical. The steal effect of a PAVM will result in underfilling of normal pulmonary arterial branches arising from the feeding vessel (Fig. 7); if this effect is not recognized, an unduly proximal embolization may be performed with loss of pulmonary perfusion to significant fractions of the normal lung parenchyma.

The choice of a coil of correct size is obviously critical; too small a coil may pass through the venous portion of the malformation into the left atrium and thence into the systemic circulation, with potential disastrous consequences. Too large a coil may displace the catheter tip from the feeding vessel and risk the occlusion of more proximal normal pulmonary arterial branches. A variety of methods have been used to measure the feeding vessel supplying the malforma-

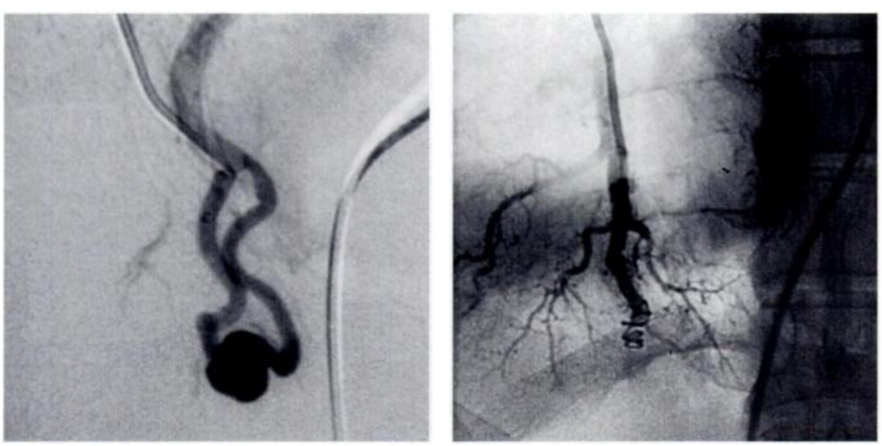
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Fig. 7.—Importance of distal embolization of feeding vessel to pulmonary arteriovenous malformation (PAVM) to preserve branches to normal lung.

***A*, Arteriogram with catheter in feeding vessel to right basal PAVM. Long, single feeding artery to PAVM is seen with no filling of proximal branches to normal lung. Subsequent embolization performed close to neck of PAVM.**

***B*, Arteriogram after embolization with steel coils shows occlusion of PAVM. Note filling of several branches to normal lung, which were not apparent on original arteriogram owing to steal effect of PAVM.**

tion and thus determine the correct coil size, including the use of calibrated catheters. The technique we most commonly employed is described below.

Exterior coils of the same known size are placed on the patient's anterior and posterior chest wall, over the malformation to be embolized, to show the extremes of magnification error. By relating the dimensions of these coils on the radiographic image to the size of the individual anatomic shunts demonstrated at angiography, coils of an appropriate diameter can be selected for embolization. The choice of an ideal coil size and its exact positioning within the feeding vessel to a PAVM has been made considerably easier by the introduction of detachable steel coils (William Cook Europe, Bjaeverskov, Denmark). These may simply be removed from the catheter if the wrong size has been selected, or partially withdrawn and reinserted if their initial position is unsatisfactory. These coils are now routinely used in our institution, particularly when the first coil is being placed in a large vessel.

Detachable balloons are preferred by some researchers for the embolization of PAVMs [10–12], as these devices may be retrieved if they are too small for the vessel being occluded whereas conventional steel coils cannot. Their use does, however, require multiple catheter exchanges if more than one vessel needs to be embolized. Also, a theoretical risk exists of premature balloon deflation and migration into the systemic circulation when nonpolymerizing liquids are used for balloon inflation. Furthermore, when the feeding vessel to a PAVM is particularly large, the length of balloon required to achieve occlusion may compromise more proximal vessels to normal lung. When steel coils are used, these vessels can usually be preserved.

Complications

Although most patients were fit for hospital discharge the day after their embolization procedure, a small proportion (9%) suffered mild pleuritic chest pain in the early days following the procedure. This complication occurred most frequently in those patients whose PAVM had a large venous sac and did not appear to be related to occlusion of vessels supplying normal lung. It is possible that thrombus formation within the large venous portion of such malformations irritates the adjacent pleura.

Follow-Up

Four years after treatment, a cerebral abscess developed in one patient, who was successfully treated by evacuation. This patient had many angiographically demonstrable small PAVMs, which were not amenable to further embolization treatment, and a residual 21% right-to-left shunt fraction. This instance highlights the inadequacy of radiologic embolization techniques in completely eliminating the risk of embolization in some patients. Nevertheless, it seems likely that the risk of paradoxical embolization is greatest from macroscopic PAVMs, and these can be ablated successfully by this technique.

Conclusion

Treatment of PAVMs is important because of the well-documented risks of adverse events owing to paradoxical embolization through the arteriovenous channels [3, 13].

Percutaneous transcatheter embolization is now the procedure of choice for the treatment of individuals with PAVMs. This technique is safe and well tolerated and is associated with excellent symptomatic and objective improvement. Complete obliteration of the shunts was achieved in only one quarter of our patients with HHT, and long-term follow-up is required.

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