Pulmonary arteriovenous malformations: endovascular therapy

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Abstract: Pulmonary arteriovenous malformations (PAVM) are abnormal direct communications between the branches of pulmonary arteries and veins, and are often seen in patients with hereditary hemorrhagic telangiectasia (HHT). If untreated, the right to left shunt can result in symptoms of hypoxemia, paradoxical emboli to the left side circulation, stroke and intracranial abscess. Endovascular therapy is a minimally invasive outpatient based treatment wherein the feeding artery to the PAVM is occluded with coils or plugs or a combination of both and is associated with minimal morbidity and no mortality. In this manuscript, we will review the indications and contraindications for endovascular therapy, pre-procedural work up, procedure technique and variations, complications, and outcomes.

Keywords: Pulmonary arteriovenous malformation (PAVM); occlusion; embolization; coil; plug; hereditary hemorrhagic telangiectasia (HHT)

Introduction

The natural course of pulmonary arteriovenous malformations (PAVM) is not well studied but most of the lesions remain either stable (75%) or demonstrate slow growth (25%) (1,2). However, untreated PAVM are associated with a high risk of morbidity and mortality (0–55%) compared to 3% in the treated patients (1,3). Prompt identification and treatment are indicated given the high risk of complications such as brain abscess (9%), cerebrovascular accident (2.6–25%), hemoptysis/hemothorax (8%), and hypoxemic respiratory failure (1,4-6). The risk of neurological complications has been shown to be higher with diffuse type of PAVM, a large shunt, and a feeding arterial diameter (FAD) of greater than 3 mm (7,8). Additionally, there is decreased risk of neurological complications in treated PAVM. When feasible, endovascular embolotherapy is the mainstay of treatment with less morbidity and mortality (9). Surgical resection is rarely needed and is indicated for lesions that remain refractory to endovascular therapy or when endovascular treatment is not feasible. Lung transplant is indicated only for severe bilateral diffuse disease.

Pre-procedure work up and evaluation

Typically, patients are referred from hereditary hemorrhagic telangiectasia (HHT) clinic (approximately 15–35% HHT patients have PAVM) with a positive echo bubble study (grade 4 has PPV of 1 for benefit from subsequent CT chest study) or findings of PAVM on a screening CT chest scan (4). A multidisciplinary clinic visit with a comprehensive evaluation is recommended to determine if patient status and lesion characteristics are amenable for endovascular treatment. Conversely, a patient initially presenting with PAVM diagnosis should be referred to HHT clinic for a comprehensive evaluation (80% to 90% of patients with PAVM have HHT) (1).

Table 1 Pre-procedural work up during IR clinic visit

Multidisciplinary comprehensive clinical evaluation

Review of imaging for endovascular embolotherapy (number, location and type of PAVM, and measure feeding artery diameter)

Evaluate patient for moderate sedation *vs.* need for general anesthesia

EKG: to assess presence of LBBB and right ventricular hypertrophy

CBC, CMP, coagulation labs

Discuss procedural risks, benefits, and alternatives and obtain an informed consent

IR, interventional radiology; LBBB, left bundle branch block; CBC, complete blood count; CMP, comprehensive metabolic panel; PAVM, pulmonary arteriovenous malformations.
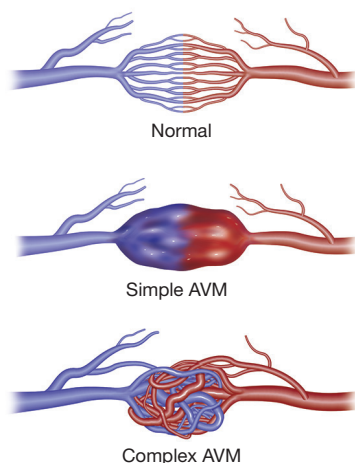

Figure 1 Pulmonary AVM illustrations. A normal capillary network is noted between the pulmonary arterial branch and pulmonary venous tributary facilitating functions of gaseous exchange and filtration. A single segmental arterial feeder connects directly to the draining vein through the nidus or sac without intervening capillary network in a simple PAVM. Multiple segmental feeding arterial branches are identified in a complex PAVM. PAVM, pulmonary arteriovenous malformations.

Appropriate pre-procedure work-up is outlined in *Table 1*. During the clinic visit, it is important to evaluate whether patient can tolerate moderate sedation and stay supine for the duration of the procedure. Patients with underlying pulmonary hypertension might require general anesthesia support during the procedure. Also, a preserved renal function is required as potentially nephrotoxic iodinated contrast materials are used during pulmonary angiography and embolization. An EKG is performed to exclude the presence of a left bundle branch block (LBBB). Catheter manipulation in right heart can result in a right bundle branch block and if the patient is known to have a LBBB, this can result in a complete heart block. Patient with a LBBB benefit from temporary pacing during pulmonary angiography. Computed tomographic angiography (CTA) is the gold standard for diagnosis, and should be reviewed to identify all possible PAVM and the feeder vessels. Specifically, it is important to identify the location, type, and the feeding vessel diameter. PAVM is classified as simple (only one feeding artery, 80–90%), complex (multiple segmental feeding arteries, 10–20%), and an uncommon diffuse subtype (<5%) which are illustrated in *Figures 1,2*. Conventional 3 mm FAD rule for treatment is not accurate as smaller lesions were shown to be associated with paradoxical embolization and current knowledge suggests treatment of all technically feasible lesions as low as 2 mm (2,9). Attempt should be made to treat a symptomatic lesion (neurological symptoms, embolic disease, hypoxia) irrespective of the size or FAD (10). The advent of microcatheters and technical advancements in coil and plug technology have made treatment of PAVM with smaller feeding vessels possible. Special subpopulations including pregnant patients and children need to be evaluated on a case to case basis, and should be undertaken in dedicated centers with extensive experience. Indications and contraindications for endovascular embolization of PAVM are detailed in *Table 2*. Risks, benefits and alternatives of the procedure should be discussed in detail, preferably during a dedicated clinical visit.

Pulmonary arteriography and embolotherapy technique

Embolization of PAVM is performed as an outpatient procedure under moderate sedation and the patient is discharged the same day after the procedure. Patients remain fasting for 6–8 hours prior to the procedure and withhold any anticoagulant medications. Use of bubble filters (0.2–0.4 micron) for IV access is mandatory to prevent paradoxical air embolism. Prophylactic antibiotic administration (1 g of cefazolin or equivalent) is optional.

Standard aseptic sterile precautions are maintained throughout the procedure. A common femoral venous access is obtained with US guidance, preferably on the right. Alternative accesses include right internal jugular
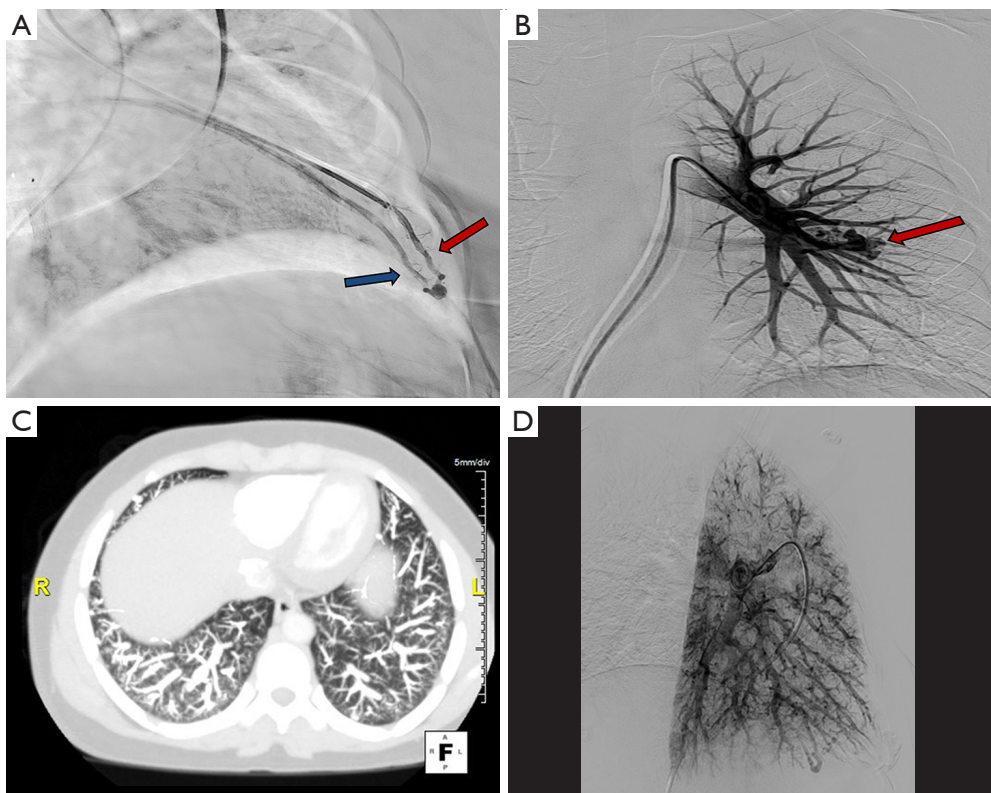
Figure 2 Types of pulmonary AVM. (A) Demonstrates a simple left lower lobe PAVM with a single arterial feeder (red arrow) and a draining vein (blue arrow). Multiple segmental feeders are noted in a complex left lower lobe PAVM (B, red arrow). CT scan (C) and left pulmonary arteriogram (D) demonstrate findings of diffuse PAVM in a patient with HHT. PAVM, pulmonary arteriovenous malformations; HHT, hereditary hemorrhagic telangiectasia.

and left common femoral veins. A 7 Fr short sheath is placed within the common femoral vein and connected to air free flush system. It is important to administer heparin 3,000–5,000 units IV (and subsequently 1,000 units every hour) prior to any wire/catheter manipulations in the pulmonary system to prevent formation of thrombus within the PAVM which can embolize to the left sided circulation. It is important to monitor closely for epistaxis during the procedure. Initially, a 6 Fr APC/Grollman catheter (Cook, Bloomington, Indiana, USA) or a 5 Fr pig tail catheter is advanced into the right atrium, and the desired right or left main pulmonary artery is selected (*Figure 3*). Pulmonary arterial pressure is measured via a catheter based transducer system (normal—25/8 mmHg, mean—15 mmHg). Selective pulmonary arteriography (imaging at 6 frames/s, and half strength contrast material injected at a rate of 20 cc/s with a total volume of 40 cc) is performed in anterior-posterior (AP) and ipsilateral 40-degree oblique views to identify the PAVM and determine the feeding

vessels. It is important for the patient to hold breath in deep inspiration and the operator to include the lung bases within the field of view during arteriography. This serves two purposes—prevents overlapping of tissues and vessels, and permits a comprehensive evaluation as PAVM occur most commonly (83%) at the lung bases (11). Once the feeder vessels are identified and mapped, a coaxial system (7 Fr guiding catheter with an inner longer 5 Fr tipped catheter combination such a Lumax system—Cook, Bloomington, Indiana, USA) is advanced over an exchange length Rosen wire (12). Meticulous care should be taken during catheter-wire exchanges to maintain water seal and also utilize closed flush system or double flush technique to prevent air suction and embolism. Maintaining a wet to wet connection during injector connection is also very important. Selective catheterization of the feeder vessel is followed by embolization. Occasionally, a guide wire or a microcatheter may be required to select small feeder vessels. After the feeder vessel is catheterized, a digital subtraction

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Table 2 Indications and contraindications for endovascular treatment of PAVM

Indications for endovascular therapy

  PAVM with a feeding artery diameter (FAD) ≥2 mm, and technically feasible

  Symptomatic PAVM regardless of size

  Atypical but likely PAVM on cross sectional imaging and suggestive symptoms

Relative contraindications (possible alternative)

  Asymptomatic PAVM with feeding artery diameter <2 mm (consider clinical and CT follow up)

  PAVM that is not accessible/feasible for endovascular therapy (consider surgical resection)

  Diffuse type PAVM (surgery/transplant)

  Severe pulmonary hypertension (consider performing the procedure under local anesthesia only; decrease the rate and volume of injected contrast material; use hand injection; occlude only a few PAVMs during each treatment session)

  Severe coagulopathy (correct underlying coagulopathy)

  Renal failure (consider nephrology consult)

  Allergy to iodinated contrast material (consider premedication)

  Early pregnancy (PAVM can be treated in the second and third trimesters as pregnancy typically exacerbates and complicates PAVM presentation)

  Asymptomatic PAVM in children

  Left bundle branch block (consider temporary pacing)

PAVM, pulmonary arteriovenous malformations.

Figure 3 Catheters used in pulmonary angiography and pulmonary arterial embolization. A wire and pigtail catheter can be utilized to gain access to the pulmonary artery. The right-angle shape of the angled pigtail catheter (preferred catheter) allows easy access from the right atrium to the right ventricle and further selects the pulmonary arteries. Lumax system (7 Fr guiding catheter with a 5 Fr catheter combination) allows easy selection of pulmonary arterial branches and provides stable access for embolization.

angiography (DSA) provides a road map and subsequently confirms appropriate distal selection. Additionally, measurement of the vessel diameter is important to select an appropriate embolic device size for successful occlusion. The goal of PAVM embolotherapy is to occlude the feeding artery as distally as possible and close to the sac (sac itself is not embolized) while sparing the normal lung parenchyma. Though not routinely performed, Hayashi *et al.* reported significantly less reperfusion with coil occlusion of the sac compared to the arterial feeders (13). It is not uncommon to see additional feeders after occlusion of the primary feeder vessel, which would then require selective catheterization and embolization of these additional feeders. A more proximal selective DSA confirms successful embolization of the PAVM. A main pulmonary arteriogram is performed to exclude unsuspected new or remaining 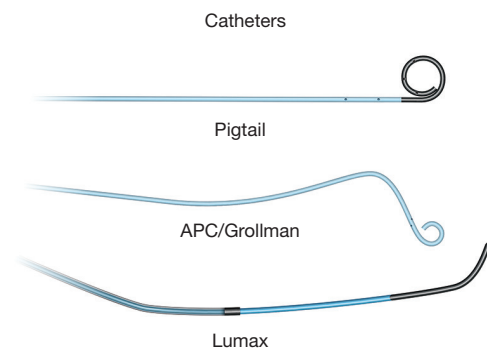PAVM. Any number of PAVM can be treated in a single session but each session is often limited by the complexity of the procedure, radiation dose to the patient and amount of contrast material utilized. At the end of the procedure, the venous access sheath is removed, and manual pressure is applied at the access site for hemostasis. The patient is discharged home after few hours of monitoring and recovery. Acetaminophen can be prescribed (avoid NSAID use due to risk of bleeding/epistaxis) for immediate post procedure pain.

Embolic materials

Various embolic materials are available, however, coils and plugs are the most commonly used embolics for occlusion of PAVM (see *Figure 4* for illustration of embolic devices). Stainless steel or preferably platinum coils are utilized to occlude the feeding vessel (*Figure 5*). Detachable coils offer the advantage of repositioning before successful deployment of the coils. An anchor or scaffold technique can be utilized for safe deployment of a non-detachable coil or to prevent prolapse of the coil in to the aneurysmal sac. Alternatively, a double microcatheter technique was described for safe occlusion (14). Amplatzer vascular plugs (St. Jude Medical, St. Paul, MN, USA) offer the ability to address variable sized feeding arteries with precise deployment of the plug and less unintended migration as well as better occlusion rates with decreased procedural times and radiation dose (15). Amplatzer vascular plug 4 is usually preferred because of
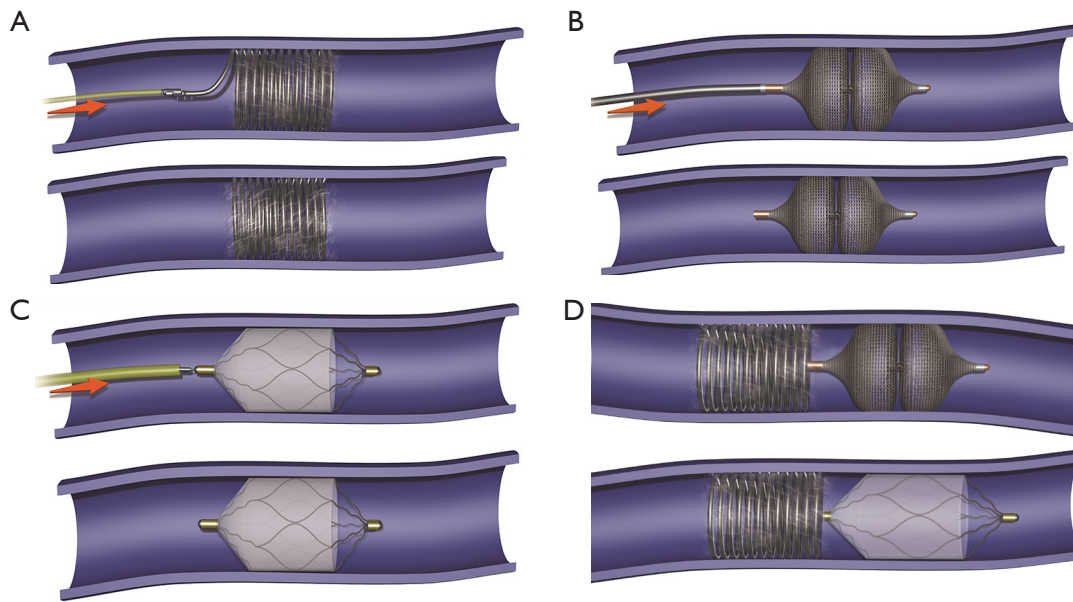
Figure 4 An illustration of various embolic occlusion devices and techniques. Coil, Amplatzer type IV plug and microvascular plug occlusion techniques are illustrated in images (A,B,C) respectively; (D) illustrates combination techniques with additional coil embolization following Amplatzer or microvascular plug deployment. Arrows demonstrate blood flow direction within the pulmonary arterial branch feeding the pulmonary arteriovenous malformation.

Figure 5 Coil embolization. In this patient with HHT and multiple PAVM, left pulmonary arteriogram demonstrates complete occlusion of the PAVM with coil embolization alone. PAVM, pulmonary arteriovenous malformations.

Figure 6 Embolization with Amplatzer vascular plug. A left lower lobe complex PAVM (*Figure 2B*) was successful occluded with Amplatzer type 4 vascular plugs (blue arrows). PAVM, pulmonary arteriovenous malformations.

low profile design (5 Fr catheter) and is available in 4–8 mm diameters allowing occlusion of target vessel diameter from 2.6 to 6.2 mm (*Figure 6*). Amplatzer II is occasionally used when multiple contact points are required such as a high

flow or large AVM and Amplatzer I is helpful when there is a short landing zone. Conventional coil embolization provides successful outcomes, however, plug embolization followed by coil embolization (*Figure 7*) provides a more

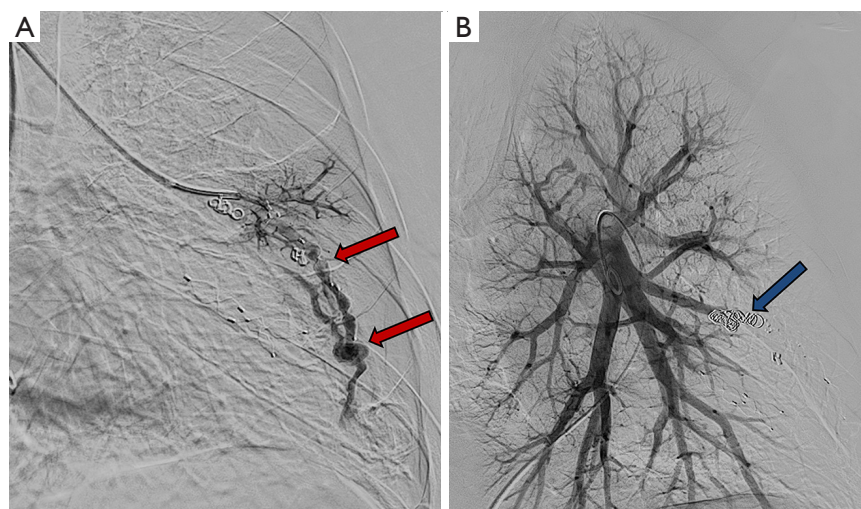   cdt.amegroups.com

Figure 7 Embolization with Amplatzer vascular plug and coils. Persistent perfusion of the left lower lobe PAVM was noted after embolization with Amplatzer type 4 vascular plug (A, red arrows). Additional coil embolization was performed proximal to the vascular plugs resulting in complete occlusion (B, blue arrow). PAVM, pulmonary arteriovenous malformations.
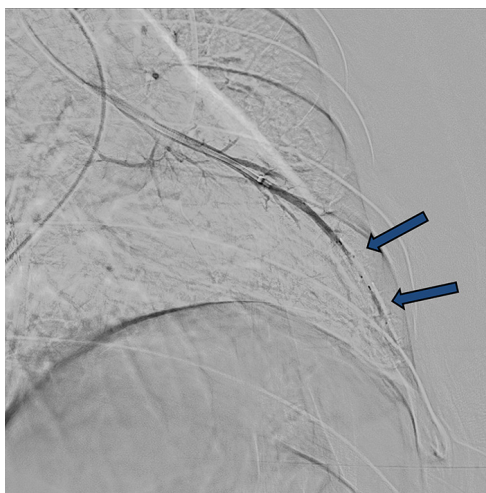

Figure 8 Occlusion with MVP plug. The feeder vessel of a left lower lobe simple PAVM (Figure 2A) was embolized with two MVP-3 vascular plugs resulting in complete occlusion (blue arrows). PAVM, pulmonary arteriovenous malformations.

permanent occlusion and is the preferred method at our institute (16,17). Newly available microvascular plugs (nitinol mesh and an outer PTFE membrane, Medtronic) are detachable and provide the advantage of rapid occlusion, deployment through a microcatheter (.021" and .027" microcatheter systems for MVP-3 and MVP-5 respectively) and fewer artifacts on follow up imaging (*Figure 8*). MVP-

7 and -9 require a 0.035" lumen catheter for delivery and can be used to occlude target vessels with diameters 5–7 and 7–9 mm respectively. Early results on use of MVP for occlusion of PAVM appear promising (18). Other combinations of MVP plugs with coils are illustrated in *Figures 9* and *10*. It is important to oversize the coils (20–30%) and plugs (30–50%) to prevent migration as well as pack densely to prevent residual flow through the coil pack. Detachable balloons are no longer available within the US. Particles, gel foam, and liquid embolics have no role in endovascular treatment of PAVM. A stent-graft would be difficult to deploy in the tortuous small vessels, but may be the only available option in rare cases, and is a helpful alternative (*Figure 11*). Choice of embolic material (coil *vs.* plug *vs.* both) is largely an institutional and individual preference until further comparison data are available.

Procedural complications

The most common complication is pleuritic chest pain occurring in 15%, and the incidence increases to 31% in patients with a FAD >8 mm. Pleuritic chest pain typically occurs within the first 2 days, and is self-resolving and well controlled with NSAID medications (19). There is a small risk of thrombus dislodging during the procedure and causing stroke (0.5%) or embolus within the left sided circulation. Other complications are rare and include vessel injury or dissection, air embolism (meticulous
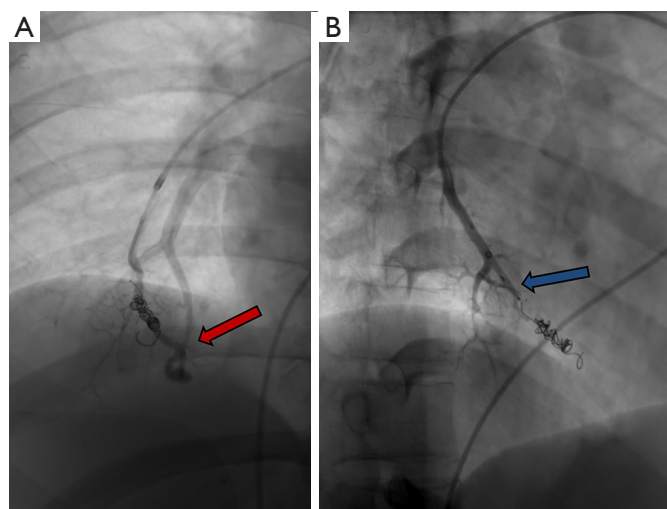
Figure 9 Embolization with coils and MVP plug. (A) Demonstrates persistent perfusion of a right lower lobe PAVM after coil embolization (red arrow). Additional MVP plug embolization results in complete occlusion (B, blue arrow). PAVM, pulmonary arteriovenous malformations.
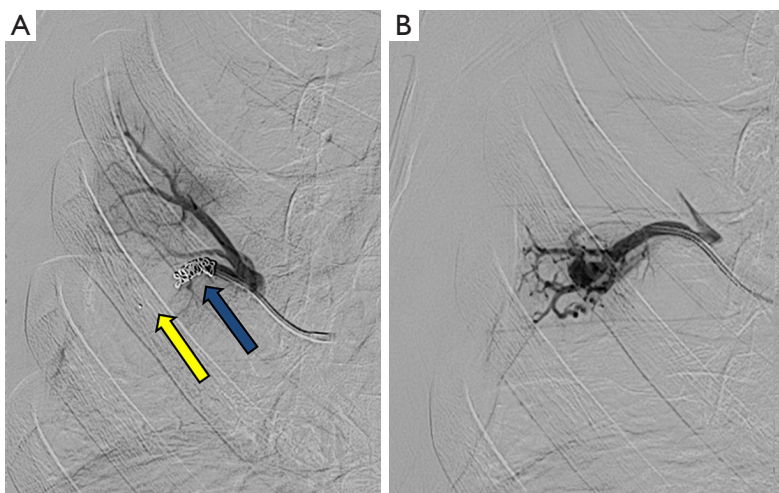

Figure 10 Occlusion with MVP plug and coils. Embolization with MVP plug and coils (yellow and blue arrows respectively in A) resulted in successful occlusion of the right lower lobe PAVM seen on pretreatment (B). PAVM, pulmonary arteriovenous malformations.

technique and filter use can avoid this complication), non-target embolization, and lung infarct/infection. Access site complications include bleeding which can be easily managed with manual compression. Procedure related mortality is extremely rare.

Reperfusion or new PAVM can be seen in up to 20% of treated patients, and are generally amenable for repeat embolization (20) (*Figures 12* and *13*). Failure of treatment or reperfusion is possible through the below mechanisms—(I) recanalization through or around the deployed embolic devices (predominant mechanism); (II) supply from previously dormant/unrecognized feeder; (III) development of new collaterals from pulmonary arteries; and (IV) development of systemic collaterals (21). *Figures 14* and *15* demonstrate reperfusion from systemic collaterals. Factors associated with a higher risk of reperfusion or failure after coil embolotherapy are enumerated in *Table 3* (20). New systemic (bronchial artery) collaterals can lead to massive hemoptysis. Development of new or worsening pulmonary hypertension is a rare complication but needs close
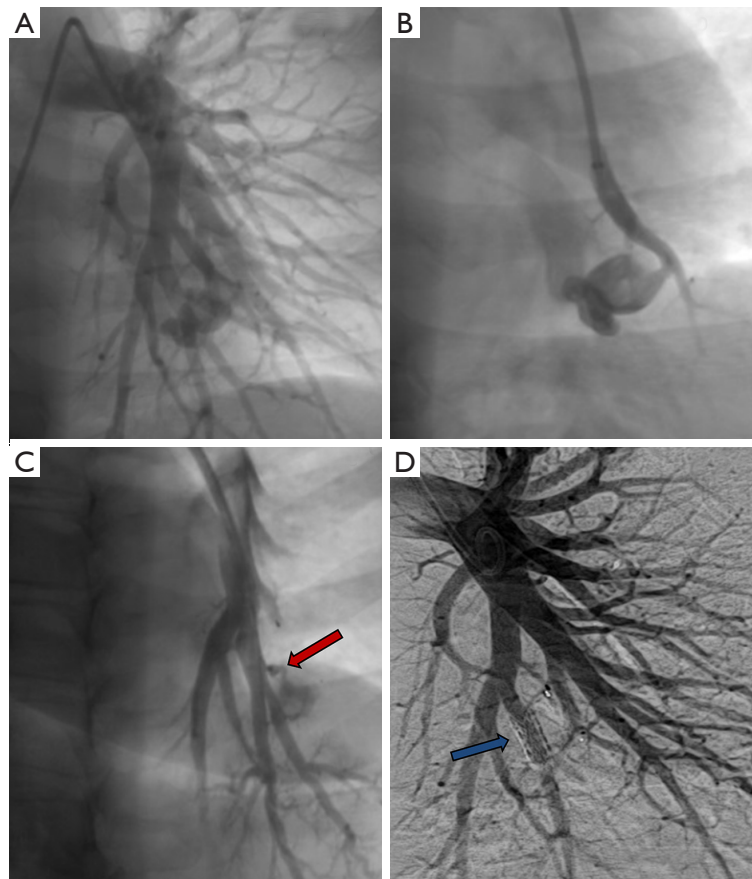
Figure 11 Adjunctive role of stent-graft placement. Left pulmonary arteriogram and a selective left lower lobe branch arteriogram demonstrate a PAVM (A and B respectively). Arteriogram post embolization with a MVP-7 vascular plug (C) demonstrates an additional tiny tortuous feeder not feasible for catheterization and embolization (red arrow). A stent-graft (5 mm × 16 mm iCast, blue arrow) was deployed within the lower lobe pulmonary arterial branch successfully excluding the PAVM feeder (D). PAVM, pulmonary arteriovenous malformations.
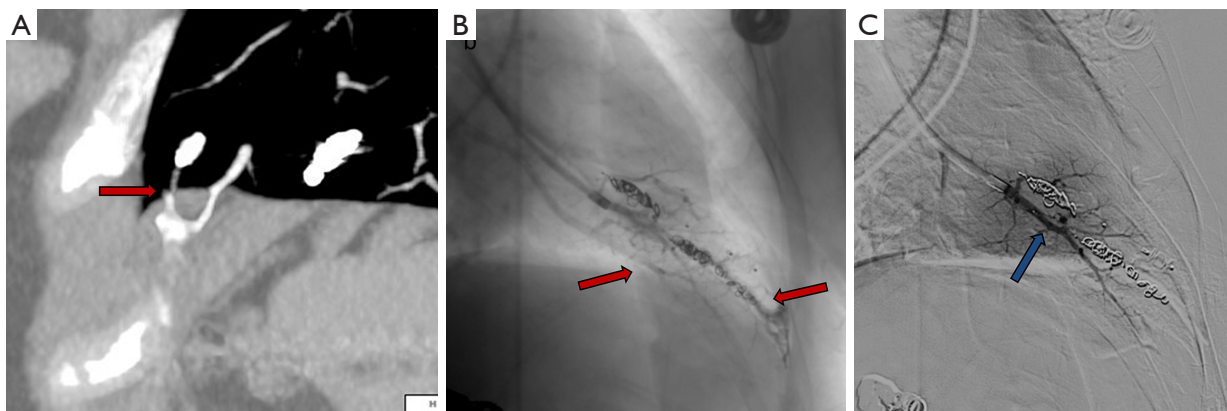

Figure 12 Embolization of a recanalized AVM with MVP vascular plug. CT (A) and angiography (B) demonstrate recanalization (red arrows) of a previously embolized left lower lobe PAVM. (C) Demonstrates successful occlusion with a MVP plug (blue arrow). PAVM, pulmonary arteriovenous malformations.
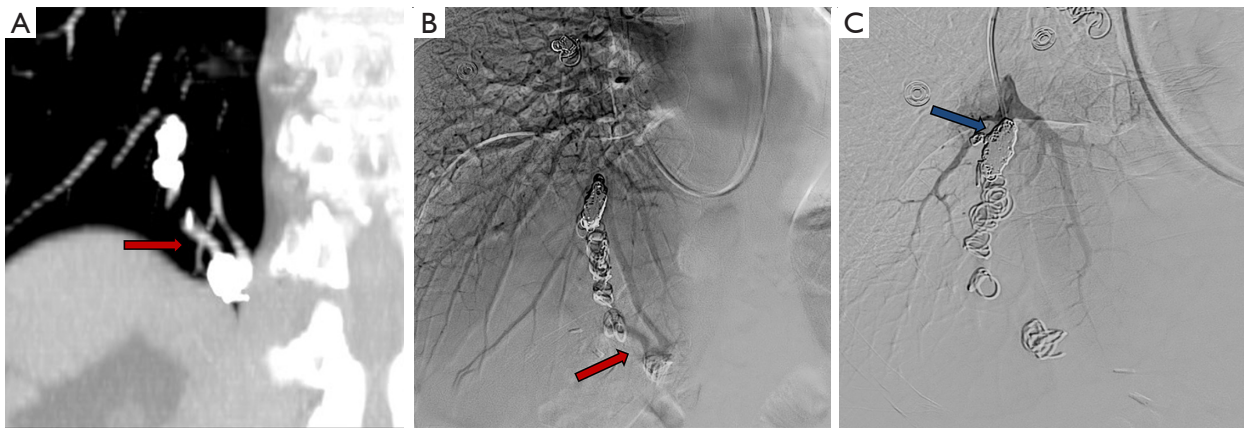
Figure 13 Occlusion of a recanalized AVM with dense coil packing. CT (A) and selective pulmonary branch arteriogram (B) demonstrate recanalization (red arrows) of a previously embolized right lower lobe PAVM. (C) Demonstrates successful occlusion with dense coil packing (blue arrow). PAVM, pulmonary arteriovenous malformations.
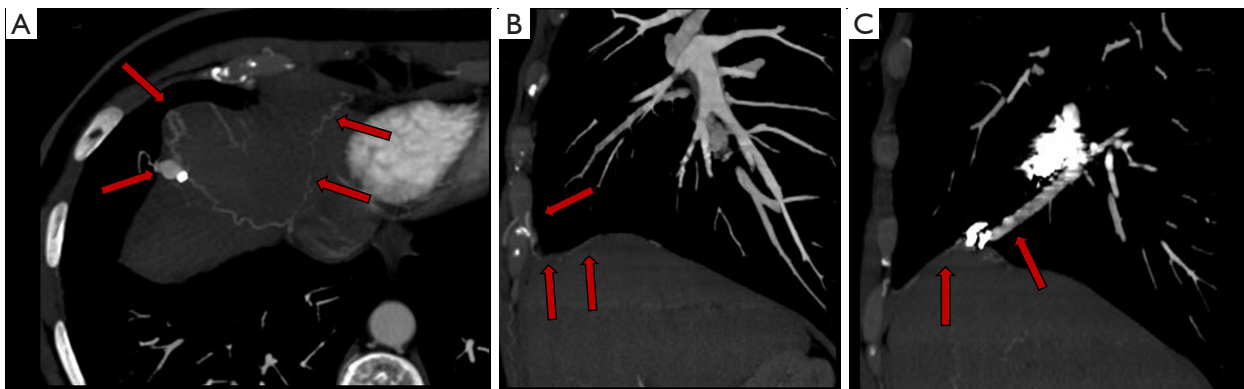

Figure 14 Reperfusion from systemic artery. CT images (axial A, and sagittal B and C) demonstrate reperfusion of a previously embolized right lower lobe PAVM via systemic feeder branches from internal mammary collaterals (red arrows). PAVM, pulmonary arteriovenous malformations.

monitoring and treatment, especially in high risk patients with large and multiple PAVM, pre-existing pulmonary hypertension, and >20% right to left shunt.

Outcomes

Embolotherapy of PAVM has a very high technical success (≥99%) (2,19). Outpatient single session successful occlusion was achieved in 85% of patients in one study (22). Symptomatic relief can be immediate (23). The risk of neurological complications in treated PAVM is significantly decreased compared to untreated PAVM (0–2% *vs.* 2.6–25%). Treated PAVM remain occluded in most of the cases (83%), however there is reperfusion or new PAVM

noted in approximately 17–20% (2,11,24). Careful attention to technique of dense packing of the distal feeding artery with an appropriately sized coil is important to prevent residual flow and reperfusion. There is good response to repeat embolization of residual or recurrent lesions. There are no randomized studies comparing different treatments or embolic devices which largely remain an individual and institutional preference. Surgical resection and transplant are reserved for refractory and diffuse cases respectively.

Post procedure care and follow up

There are no evidence based guidelines on optimal post procedure follow up and monitoring. Occlusion
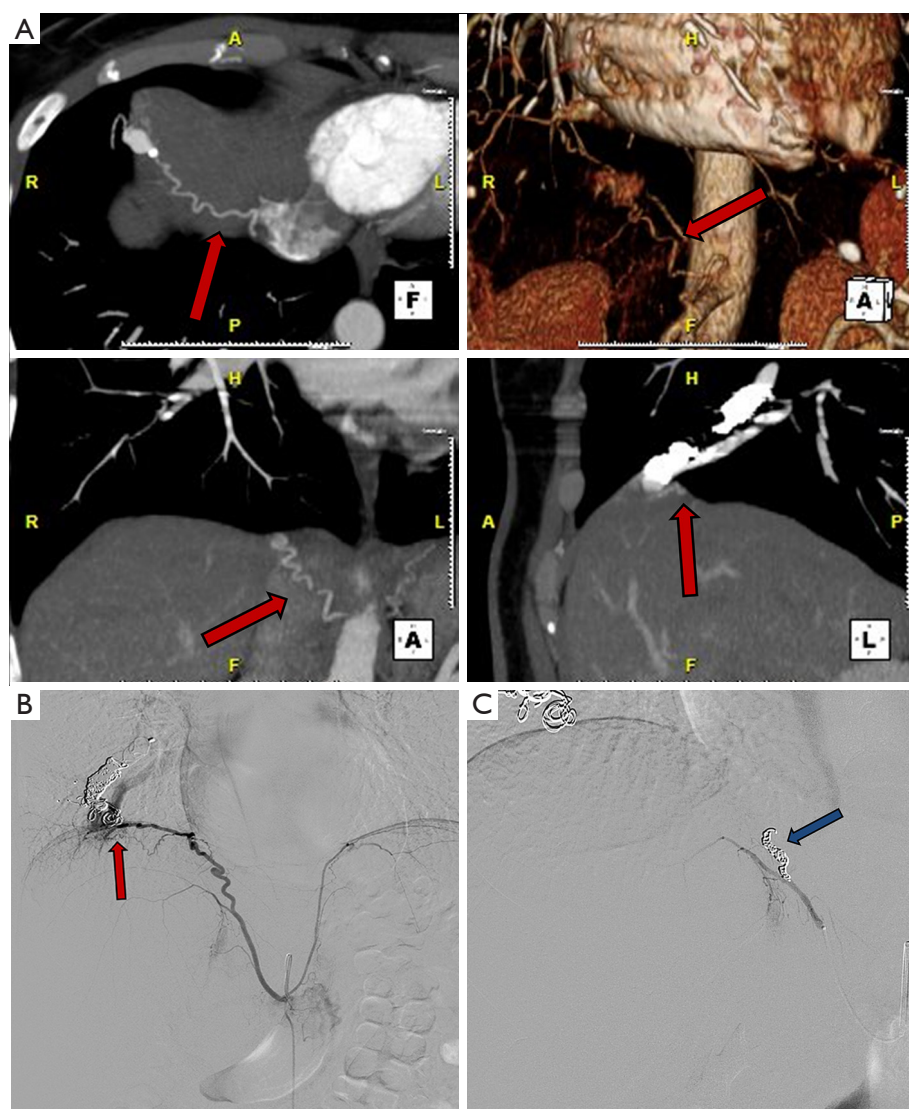
Figure 15 Reperfusion from systemic artery. 3D CT images (A, red arrows) demonstrate systemic feeders to the previously embolized right lower lobe PAVM from right phrenic artery. Selective phrenic arteriogram confirms the findings seen on CT (B, red arrow). The feeder branch from phrenic artery was successfully embolized with coils (C, blue arrow). PAVM, pulmonary arteriovenous malformations.

of the PAVM while immediately apparent on catheter angiography, changes of resolution or decrease in size on CT scan are more delayed. Contrast echocardiography remains positive for an indeterminate period in spite of a successful occlusion necessitating continued pre-surgical antibiotic prophylaxis and use of filter for IV lines (25). In patients with multiple lesions requiring additional sessions, embolotherapy can be repeated in a few weeks. If all the PAVM were treated successfully, patient is evaluated in clinic at one and six months. A follow up CTA in 6 months to 1 year is performed to confirm successful occlusion and

evaluate for any residual or new PAVM (9). Subsequent follow up can be with CT scan in 3–5 years or contrast echocardiography performed annually if the initial follow up CT is negative. A close follow up is necessary in patients with severe or diffuse lesions. Recurrence of symptoms at any time should prompt a contrast enhanced CT scan of the chest.

Conclusions

PAVM are associated with high morbidity and mortality

Table 3 Factors associated with residual perfusion or failure of coil embolotherapy

Large feeding artery diameter
Smaller numbers of coils
Oversized coils
Lack of dense packing
Proximal embolization >1 cm from the sac

if untreated, and therefore, endovascular embolotherapy is recommended as first line therapy for all lesions with feeding artery diameter greater than 3 mm. There is a growing trend to treat all PAVM that are technically accessible, especially if symptomatic, irrespective of the size of the feeding artery. Endovascular embolization has very high technical success with minimal morbidity and no mortality. The commonly used embolic materials include coils and vascular plugs or a combination and are chosen based on individual and institutional preferences. There is a high risk of recanalization or development of new lesions, and therefore, close monitoring is required.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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