Techniques in Vascular and Interventional Radiology

Interventional Management of Arteriovenous Malformations

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Arteriovenous malformations (AVMs) are fast flow malformations characterized by the presence of arteriovenous shunting. These congenital lesions can be evolutive, leading to serious complications such as bleeding, skin ulceration, and cardiac failure. The interventional radiologist plays an important role in the management of these patients. He should be involved in the clinical evaluation to make the proper diagnosis, evaluate the symptoms and potential indication for endovascular treatment. This evaluation should be done in a multidisciplinary clinic with access to plastic surgeons, internal medicine and dermatologist, as well as specific specialists that might need to be implicated (ENT surgeon in the face and neck area, for example). The Schobinger clinical classification is important to assess patient evolution and indicate intervention. We recommend to treat symptomatic or evolutive AVMs. Doppler ultrasound is the first imaging examination that should be performed. Then, MR angiography or computed tomography angiography (CTA) can be proposed depending on the anatomic area involved. Embolization is currently the first line of treatment for these patients. There is currently promising research in the identification of genetic markers and molecular target(s) but there is no recognized pharmacologic treatment for AVM available yet. Digital substraction angiography (DSA) is usually performed for guidance during the embolization session but is also essential to properly classify a specific lesion, according to its anatomy. The anatomic classifications proposed by Cho and Yakes are both useful to choose the best therapeutic approach: Endovascular, direct puncture, retrograde venous approach or a combination of these techniques. Ethanol is the most efficient agent but is at higher risk of skin necrosis and nerve injury and should therefore be used with caution in dangerous territories. Glue and Onyx are liquid agents that are also well suited to occlude the nidus; they can be used in association with ethanol. On the venous side, mechanical occlusion with coils or Amplatzer plugs is mostly used. Again, they can be used in association with a liquid agent (Ethanol, glue or Onyx) to reflux in the nidus. Surgery can be indicated to resect residual AVM following embolization if residual symptoms are present and the planned surgery is feasible, with relative safety.

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Introduction

Among the spectrum of vascular malformations, arteriovenous malformations (AVMs) are characterized by an abnormal vascular network with direct communications between the arterial and venous systems resulting in a fast-flow lesion. These lesions are congenital and develop during the early gestational period.[1,2] They have a propensity to progress, in particular during teenage and pregnancy.[3] This can lead to serious complications such as cutaneous ischemia with ulceration, bleeding and cardiac failure. While most

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AVMs are believed to be sporadic, at least 3 hereditary forms, associated with different genetic mutations and clinical phenotypes, have been recognized.[4] Somatic mutations and abnormal pathways promoting endothelial cell dysfunction are also observed in sporadic lesions.[5,6] In the future, the identification of these mutations may open the door to the use of anticancer drug therapy. Even if several teams have proposed compassionate use of Sirolimus or MEK inhibitors, there is no recognized pharmacologic treatment for AVMs.[5,7] Currently, embolization followed or not by surgery are the 2 therapeutic options for the treatment of symptomatic or evolutive AVMs. The aim of the interventional therapy is to reach the nidus and close the arteriovenous shunt(s). Depending on the angioarchitecture of the AVM, different approaches can be used alone or in combinations. These include injection of liquid agents or sclerosants through an endovascular arterial approach with microcatheters or direct intranidal puncture, and a venous retrograde approach using coils, plugs, and sclerosant agents.[8] Proximal arterial embolization must be avoided because it will fail and can often times exacerbate patient symptomatology.[9]

Clinical Evaluation, Genetic Markers, and Associated Syndromes

Clinical Evaluation

The management of patients with AVMs is demanding and requires a dedicated interventional radiology clinic as well as a multidisciplinary group with an expertise in the diagnosis and management of vascular anomalies. In particular, a close collaboration with surgeons, dermatologists and when required, internal as well as and genetic medicine specialists are necessary.

AVMs are usually present at birth but may not be clinically evident. They commonly become visible during childhood and are often exacerbated at puberty, during hormonal therapy or with pregnancies.[10,11] Surgery or trauma can also lead to the progression of vascular malformations.

The main symptoms are the presence of a soft tissue mass or swelling of soft tissues. Pain, ulceration and bleeding are observed only in advanced stages of the disease. A complete clinical examination is first performed to evaluate the lesion, potential complications and related syndromes. A soft tissue mass can be seen at clinical examination with an increased skin temperature, dilated veins, and a palpable thrill. A purple or red discoloration of the skin or a capillary stain is possible. Hemorrhage and cutaneous ischemia with ulceration or infection are the most common local complications. If the malformation is extensive and centralized in the body, high output cardiac failure can occur.[12]

The Schobinger classification is used to stage the evolution of the disease as follows:[13]

Stage I: Quiescence. Cutaneous blush, skin warmth, arteriovenous shunt on Doppler ultrasound

Stage II: Expansion. Darkening blush, lesion shows pulsation, thrill and bruit

Stage III: Destruction. Steal, distal ischemia, pain, dystrophic skin changes, ulceration, necrosis, soft tissue, and bony changes

Stage IV: Decompensation. High-output cardiac failure.

Genetic Marker and Associated Syndrome

The CM–AVM RASA1 syndrome is an autosomal dominant inherited condition with very high penetrance (90%), due to inactivating mutations of RASA1 presenting with association of capillary malformations (CMs) and AVMs.[4,14] Usually CMs are multifocal and progress over lifetime. Large confluent CMs are usually associated with an underlying AVM.[4] Recently CM-AVM with another germline mutations in EPHB4 was reported and is now classified as CM-AVM2 syndrome.[15] This form can be associated with telangiectasia and is preferentially associated with facial and extremity AVMs.[4]

In a peripheral location, limb length/size discrepancy may be observed and can be associated with a specific limb overgrowth syndrome such as Parkes Weber Syndrome (CM +AVF+overgrowth of limb) or a RASA-1 mutation.[16]

Telangiectasias are typically associated with hereditary hemorrhagic telangiectasia (HHT) and should be searched in the hands, nose and gastro-intestinal mucosa.[4] It is an inherited autosomal dominant disorder with age-related penetrance,[17] caused by mutations in TGF-β angiogenic proteins: ALK-1, endoglin (ENG), and SMAD4. ENG mutations cause HHT1, while ALK-1 mutations cause HHT2.[4] Thirty percent of HHT patients have AVMs, typically involving the lungs, brain, spinal cord, GI tract, and liver. Pulmonary and

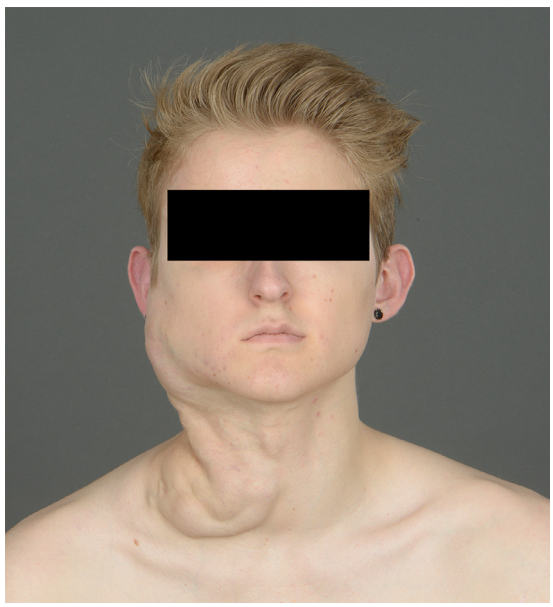


Figure 1 Patient with a PTEN mutation and a large AVM of the right hemiface. Dilated external jugular vein and macrocephalia can be noted.

cerebral AVMs are more frequent in HHT1, while hepatic AVMs are more frequent in HHT2.[18] Lung AVMs usually consist of a direct arteriovenous fistula between the pulmonary artery and vein.

Presence of macrocephalia and/or hamartoma in patients with an AVM is often associated with a Phosphatase N Tensin Homolog (PTEN) mutation[19] (Fig. 1). This mutation is typically seen in the Bannayan-Riley-Ruvalcaba (BRRS) (AVM +VM+macrocephaly+lipomatous overgrowth) and Cowden syndromes. It can also be seen in a more general disorder called PTEN hamartoma tumor syndrome (PHTS).[19] These patients present typically multiple intramuscular AVMs with ectopic fat overgrowth, hamartomas and intracranial developmental anomalies.[20] They have a propensity to develop malignant tumors and require lifelong screening.

Recently, somatic mutations in mitogen activated protein kinase kinase 1 (MAP2K1) have been found in 70% of AVM tissue samples.[5] This gene encodes MAP-extracellular signal-regulated kinase 1 (MEK1) and could be future target for antiangiogenic therapies.

Imaging Work-up

The first-line examination to diagnose AVMs, which are fast-flow vascular malformations, is a color-Doppler ultrasound examination combined with a spectral analysis of the feeding arteries and draining veins. On the B-mode examination, there is no well-defined tissue lesion; only the presence of dilated arteries and veins and sometimes thickening of soft tissues due to edema or fat infiltration. The Color Doppler examination shows a high-flow hypervascular lesion with a high vessel density (>5 vessels/cm^2).[21] The presence of aliasing is typically observed in the nidus of the AV fistulas. On

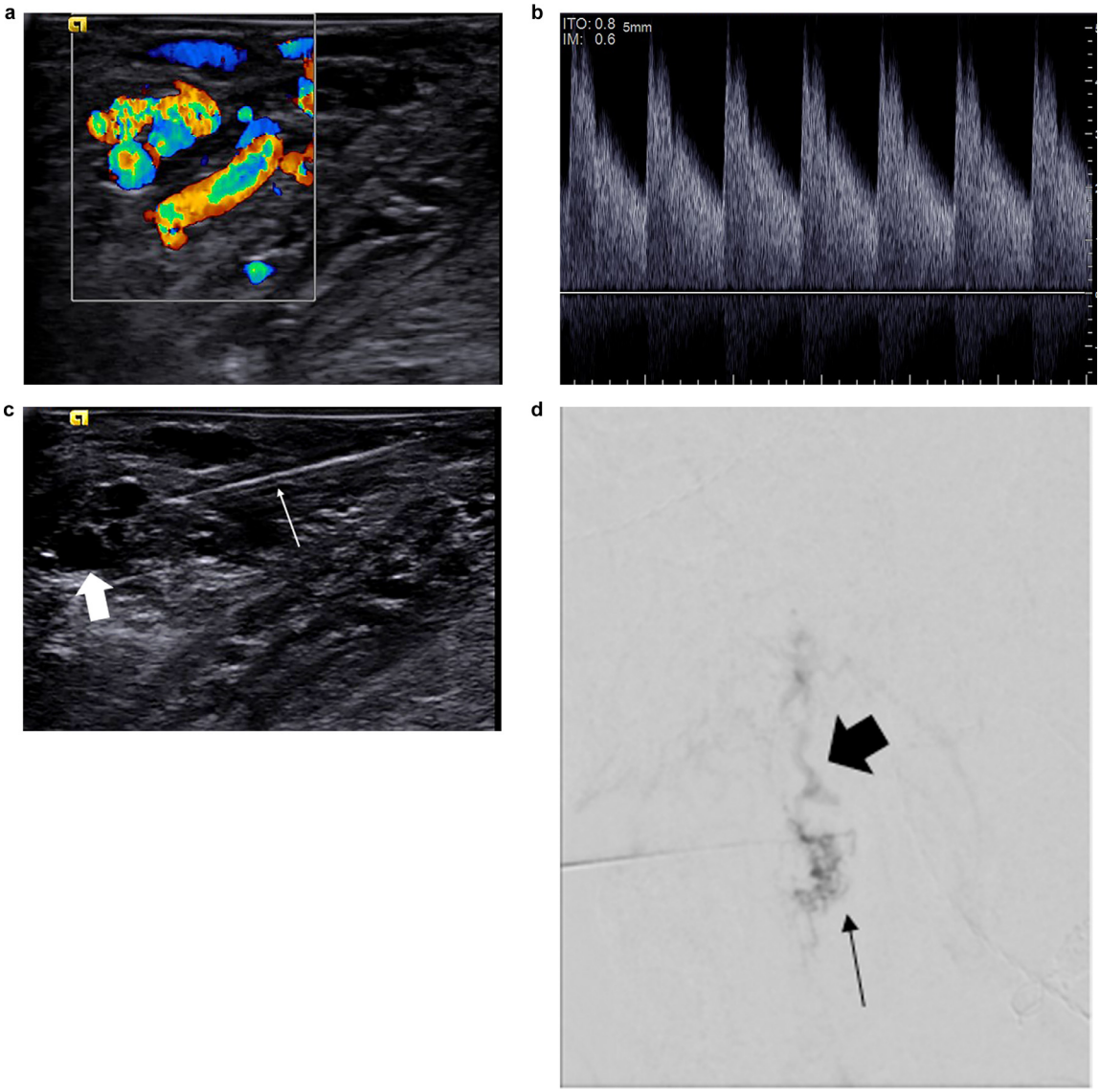


Figure 2 Patient with a large AVM of the left mandibular and the floor of the mouth. (a) Color Doppler examination of the floor of the mouth showing a fast flow vascular network with aliasing. (b) High systolic and diastolic velocities are observed on spectral Doppler examination. (c) Direct puncture (needle shown on small arrow) of the nidus (large arrow) under combined B-mode and color Doppler ultrasound guidance. (d) DSA showing the nidus (small arrow) and the draining vein (large arrow).

spectral Doppler, increased systolic velocities with a high-diastolic flow are observed on the arterial side. A high flow with arterialization and turbulence is typically observed in draining veins. The color Doppler examination is useful to localize the arterial feeders and evaluate the feasibility of direct punctures of the nidus under ultrasound guidance (Fig. 2).

MRI is a comprehensive examination allowing the evaluation the angioarchitecture of the AVM and the extension of the malformation in adjacent soft tissues. The examination should include T1-weighted sequences with and without fat-sat and T2-weighted sequences to delineate the extension of the AVM, evaluate fat infiltration and assess soft tissue edema. A time−resolved MR angiography (MRA) is performed to evaluate the dynamic enhancement of the AVM.[22] Then a T1-weighted, high resolution, 3D acquisition with Fat Sat can be performed using a steady-state phase high resolution gradient echo sequence to have a better evaluation of the feeding arteries and draining veins and delineate the extension of the AVM within adjacent structures. Dilated vascular structures are typically observed with flow voids on both T1 and T2 weighted sequences. The presence of an early venous filling is typically seen on dynamic MR angiography (Fig. 3). The integration of the findings on Doppler ultrasound and MRA are instrumental to plan the approach during the embolization session (arterial endovascular, nidus direct puncture, venous retrograde). CT-scanner is useful to assess bone destruction in aggressive AVMs (Fig. 4).

DSA is usually performed just before the embolization procedure. Its higher spatial and temporal resolutions allow for better identification of the arterial feeders and draining veins. Two angiographic classifications have been proposed to typify AVMs' angioarchitecture which will guide the therapeutic approach.[23,24] The Cho classification presents 4 types (Table 1).[23] The Yakes classification presents 5 types (Table 2).[24] Both classifications will be important to choose the best approach to treat a specific AVM. When there is a single draining vein or an aneurysmal vein, closure of the vein is often the best approach. Before closing the vein, an arterial approach to decrease the shunting can be recommended to decrease venous pressure and facilitate reflux into the nidus. Endovascular arterial approach combined with direct nidus puncture(s) are usually recommended when there are multiple feeding arteries and draining veins.

Indications for the Procedure

The indication for treatment is controversial. Several teams propose to intervene on all AVMs because of the potential evolution of the lesion over time.[3] We have recently reviewed our series of 116 patients and found that 26% of patients

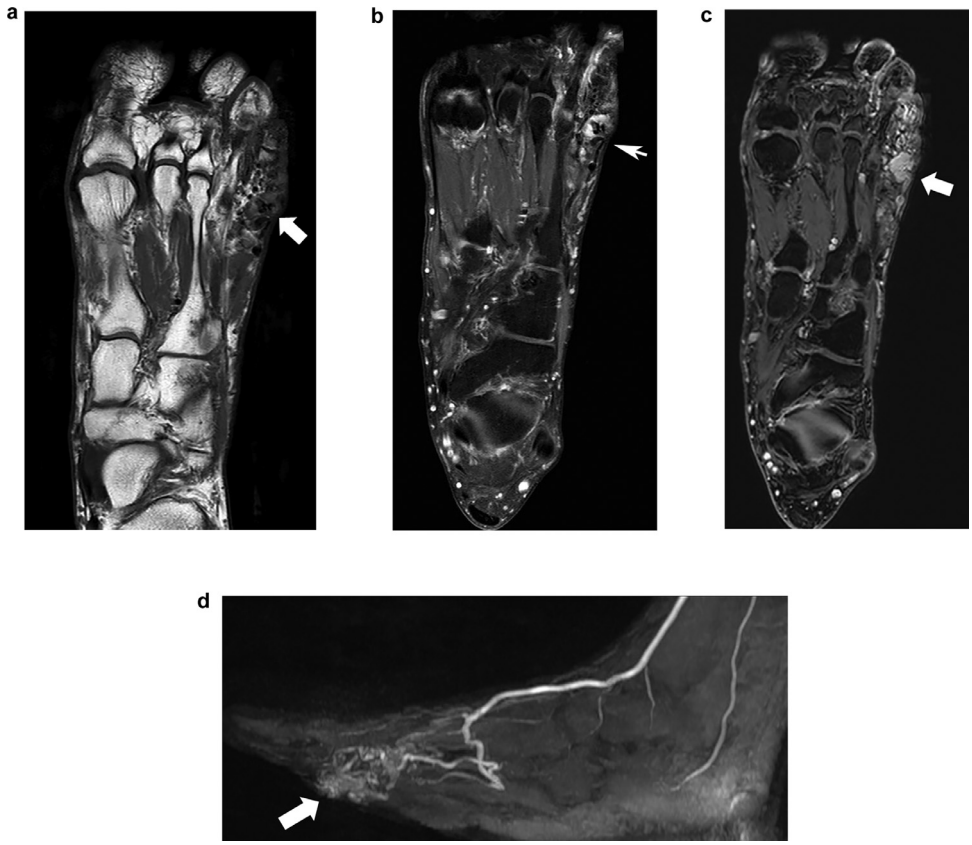


Figure 3 Patient with an AVM of the foot complicated by the presence of pain and ulceration. (a,b) T1 (a) and T2 (b) weighted fast spin echo acquisition showing the presence of dilated vessels with flow void areas (arrows) suggesting fast flow. (c) Gadolinium-enhanced time resolved MRA acquisition showing the AVM nidus with early venous drainage. (d) High resolution steady state acquisition showing the arterial feeders and dilated draining veins (arrow).

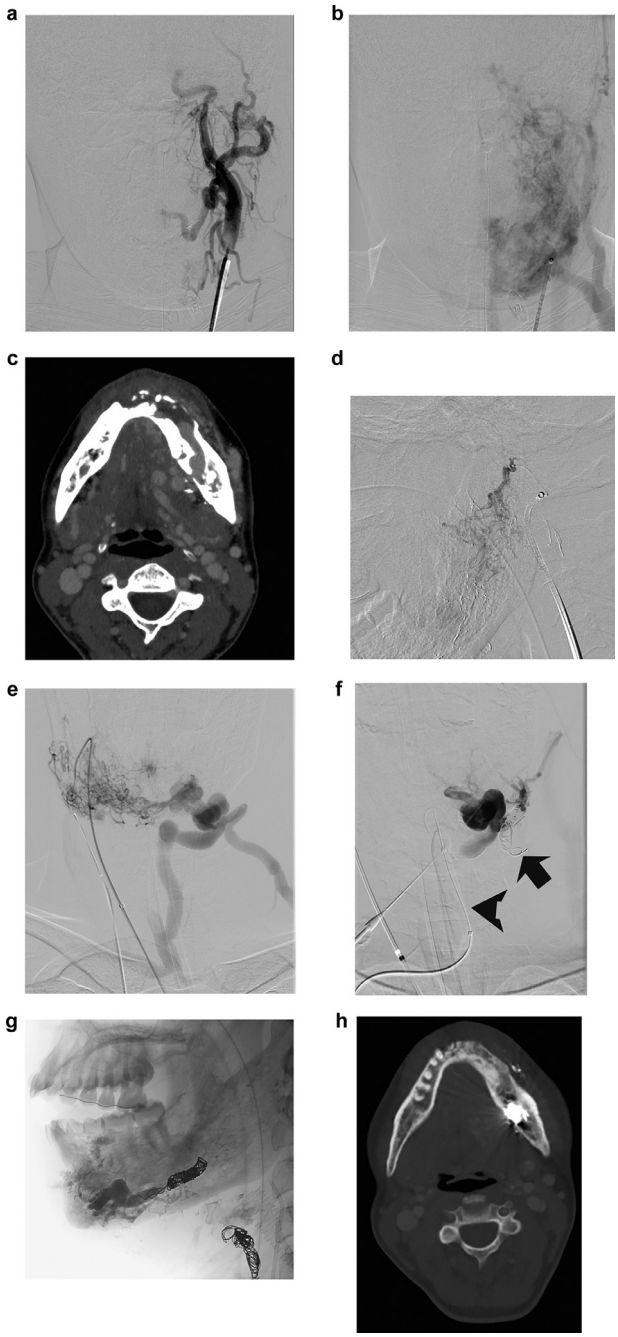


Figure 4 Patient with a large AVM of the left mandibular and the floor of the mouth (same patient shown in Fig. 2). (a,b) AP DSA acquisitions in arterial and venous phases of the common carotid artery showing an extensive type IIIB Cho or type IIIb Yakes AVM with multiple arterial feeders and draining veins. (c) CT angiography showing a large nidus inside the left mandibular bone with bone destruction. (d) The patient had first multiple ethanol embolization sessions through arterial endovascular approach and also direct punctures (see Fig. 2d). (e,f) The venous outflow of the AVM in the external jugular vein and its anterior division was occluded by coils (arrow) and an occlusion balloon (arrowhead) while the nidus was injected with ethanol by direct puncture. (g) Direct puncture of the mandibula was then performed. After coil embolization of the draining vein, the nidus was treated with ethanol injection followed by occlusion with glue. (h) CT angiography 1 year following the last embolization session showing a nice re-ossification of the mandibula.

with Schobinger I or II stage did not require an intervention after a mean follow-up of 5.6 years.[25] In our practice, we observe type I lesions with a yearly clinical and Doppler ultrasound follow-up. We treat stage II malformations mostly when they are localized and have a favorable angioarchitecture (single draining vein) especially if they do not respond to compressive therapy or cannot be treated in the latter fashion. Stage III and IV lesions should be treated because of the risk of progression, serious hemorrhage and terminal cardiac failure.[11,26] We always start with embolization. Depending on the anatomy and extent of the malformation, the treatment can be palliative or curative. It has been shown in the past that the vast majority of these lesions recur over time and that resection (with or without embolization) has a lower recurrence rate and longer time to recurrence.[3] This statement only holds true for localized lesions and not diffuse forms, which are usually treated endovascularly through embolization, in a palliative way.[8] The refinement of endovascular technique leads to better outcome, and optimal embolization can allow curative treatment with or without surgical resection.[27] In our series, on 116 patients, 74 were treated by embolization alone, 9 by embolization followed by surgery, and only 1 by surgery exclusively.[25]

For localized lesions, if there is significant residual malformation following embolization and the surgery is not too invasive, we will proceed to surgery. We reserve extensive AVM resection and complex reconstruction for stage III and IV AVMs with suboptimal response to embolization because complications of surgery can be worse than the lesion itself and recurrence is likely.[11,28] Treatment objectives, possible benefits and complications should be carefully discussed with the patients before proceeding to invasive therapies.

Tool Box for AVM Embolization

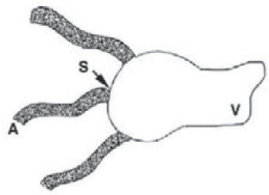
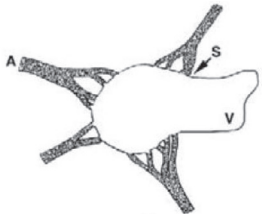
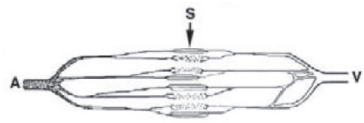
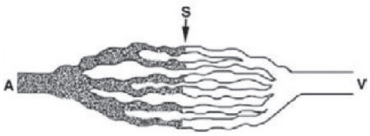
Imaging

AVM embolization is challenging and requires an up-to-date angiography suite. Biplane system can be useful for head and neck embolization but are not mandatory. You need to have a high image quality and good roadmap capabilities. Software enabling needle guidance and cone beam CT acquisition can be useful to target the nidus for deeply located AVMs not accessible to ultrasound (pelvis, deep facial or intraosseous).[29] It is mandatory to have a high-quality ultrasound unit with high- and low-frequency probes and excellent color Doppler capabilities. Doppler ultrasound is particularly useful to identify the arterial feeders or the draining vein when performing direct puncture approach (Fig. 2).

Catheters, Needles and Wires

When performing an endovascular approach, you need to have the capability to catheterize very tortuous feeders while imaging high-flow vessels. In this setting we recommend to use a triaxial system with a long 5 or 6 French sheath (Destination, Terumo, Tokyo, Japan; Shuttle, Cook Medical,

Table 1 Cho AVM Angiographic Classification

Type	Criteria	Typical Appearance
Type I arteriovenous fistulae	No more than 3 separate arteries shunt to the initial part of a single venous component.	
Type II arteriolovenous fistulae	Multiple arterioles shunt to the initial part of a single venous component. The arterial components show a plexiform appearance	
Type IIIa arteriolovenulous fistulae with nondilated fistula	Fine multiple shunts are present between arterioles and venules and appear as a blush or fine striation	
Type IIIb arteriolovenulous fistulae with dilated fistula	Multiple shunts are present between arterioles and venules and appear as a complex vascular network	

Bloomington, IN) to allow good contrast injection through the side port of the sheath. Then, a 4 French diagnostic catheter (Glidecath, Terumo, Tokyo, Japan) is used to advance close to the feeder or at its proximal portion if it is large. Small profile microcatheters (0.012-0.021" inner lumen) with good trackability are preferred to navigate in very tortuous feeders to advance into the nidus. If the venous side can be reached across the AV fistula, microcatheters compatible with coils and liquid agents should be preferred and neuroembolization 0.012" microcoils can be used. The use of a dual lumen balloon microcatheter (Scepter, Microvention, Terumo, Tokyo, Japan) can be useful to push onyx into the nidus or control alcohol injection (Fig. 5).

On the venous side, 0.018" or 0.035" coils can be used in combination with liquid agents. Usually, the first coils need to be detachable, then less expensive floppy pushable coils can be used (Nester, Cook, Bloomington) (Fig. 4). Amplatzer plugs are useful on the venous side to occlude large draining veins or close large AV fistulas. They can be used with a buddy microwire to advance a coaxial microcatheter positioned beyond the plug after plug deployment to push a liquid agent into the nidus (Fig. 6). Another possibility is positioning the distal microcatheter before introduction of the Amplatzer plug, which might require a slightly bigger sheath.

For direct puncture, 0.021" (21G, compatible with 0.018" wire) or 0.022" (22G, compatible with 0.014" wire) inner lumen needle can be used. If the target vessel is large and straight enough (venous drainage), a 4 French micropuncture set can be advanced over the microwire.

Device to Control the Flow

For upper and lower limbs, a sterile pneumatic cuff is useful to control the arterial inflow and venous outflow (Fig. 7). For fingers and toes, additional tourniquet(s) can be used to protect distal circulation. External compression can also be performed using forceps. It is important to repeat DSA with the external compression to evaluate the reflux in the arterial system to avoid non target embolization. The release of the external compression should be done under continuous fluoroscopy to prevent bolus migration of embolic agents on the venous side.

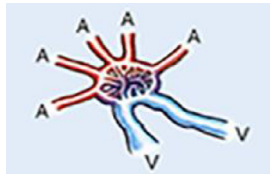
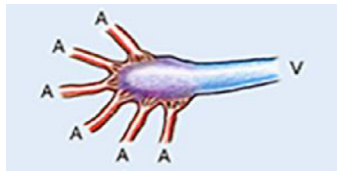
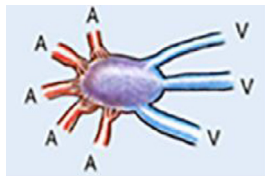
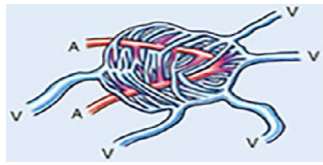
Embolizing Agents

For embolization on the arterial side by endovascular approach or direct nidal puncture, liquid agent embolics must be used to treat AVMs. Proximal embolization with coils is to be avoided. The 3 liquid embolics used are ethanol, ethylene vinyl alcohol copolymer (EVOH) and glue. On the venous side, mechanical occlusion with coils or plugs in combination or not with a liquid agent is often required.

Ethanol

Ethanol is the best agent to achieve endothelial ablation in the nidus and can be potentially curative. It destroys the endothelium of the vascular walls causing fracture up to the internal elastica lamina.[30] This fracture will promote platelet adhesion and thrombosis and will inhibit further secretion of

Table 2 Yakes AVM Classification

Type	Criteria	Typical Appearance
Type I	Direct AV fistula	
Type II	Typical AVM nidus Multiple inflow arteries leading to nidus and vein outflow	
Type IIIa	Multiple in-flow arterioles shunting into an aneurysmal vein that has a single vein out-flow. Fistulae are in the vein wall	
Type IIIb	Multiple in-flow arterioles shunting into an aneurysmal vein with multiple out-flow veins. The fistulae (nidus) are in the vein wall	
Type IV	Multiple arteries/arterioles that branch in "en passage" fashion to form innumerable micro-fistulae that diffusely infiltrate the affected tissue. Because the tissue is viable and not devitalized, capillary beds must also be present admixed among the innumerable AVFs. The innumerable micro-AVF drain into multiple veins. The tissues normal post-capillary venous drainage then competes with the arterialized vein out-flow for drainage causing venous HTN in tissue.	

angiogenesis factors, causing permanent occlusion of the exposed vessels and prohibiting further neovascularization.[31] To be sclerosant, the contact between vessel wall and ethanol needs to be long enough.[8] This will be helped by techniques controlling the inflow and the outflow (Fig. 7).[32] Ethanol injection is painful and can induce a vasoconstriction of the pulmonary arteries and acute right ventricular hypertension leading to systemic vascular collapse.[8] Thus, general anesthesia is required. Injections should be performed with small boluses (up to 5 cc) with a minimal wait time interval of 5 minutes between injections.[8] For pediatric cases, the injection of 0.14 mL ethanol/kg every 10 minutes is recommended.[33] The maximum dose should be 1 mL/kg in adult and 0.5 mL/kg in pediatric patients. The bolus volume and injection rate of ethanol is based on a previous contrast injection with a DSA acquisition performed with the same syringe size, interventionalist and hand injection rate. The optimal injection rate should be slow enough to prevent contrast/ethanol reflux but fast and long enough to provide an optimal filling of the nidus and enough contact time of ethanol with the nidus. Because ethanol is radiolucent, injections will be done under double roadmap technique, also called negative roadmap or progressive roadmap. The residual contrast in the catheter from the previous DSA acquisition will help to adjust the injection speed as it will be the first liquid pushed out from the catheter when starting the ethanol injection. When ethanol starts to flow out of the catheter, there will no longer be any contrast at fluoroscopy and the latter can therefore be stopped and the injection of ethanol should be continued with the same or a lower velocity rate depending on the potential risk of reflux. If any resistance is felt, injections should be stopped.

Glue

Glue has no sclerosant effect and therefore does not induce endothelial ablation. However, its polymerization time can be adapted by varying its dilution with lipiodol. The greater the dilution (more lipiodol), the longer it will take to polymerize, allowing for more distal penetration into the injected vessel(s). It will polymerize in contact with blood or an ionic solution. It is important before injection to avoid contact with blood and flush the microcatheter with Dextrose 5% in water. It takes a good experience to find the proper dilution to penetrate the nidus and avoid proximal embolization or venous migration across the AV shunting. We are typically using glue/lipiodol dilution ratio ranging between 1/2(33%) and 1/4 (20%) depending of the velocity and size of fistulas. The microcatheter needs to be retrieved as soon as the injection is completed to prevent catheter sticking in the glue cast. External compression or deployment of coils or Amplatzer plugs on the venous side is useful to prevent central

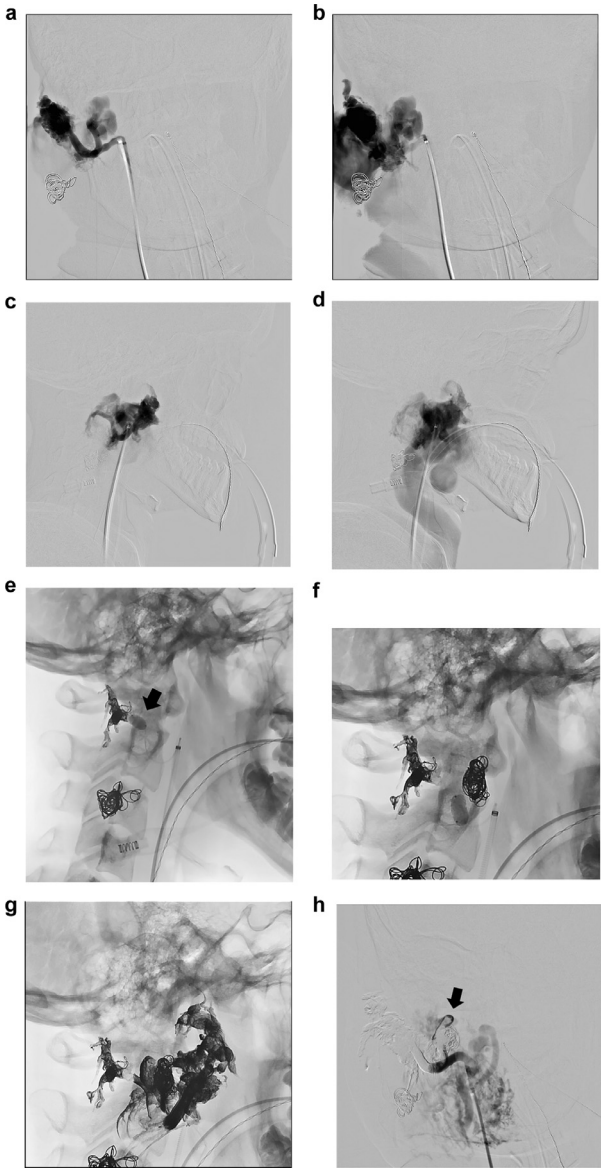


Figure 5 Patient with a large right facial AVM with a PTEN mutation (same patient shown in Fig. 1). (a to d) Selective opacification of the right distal external carotid with AP (a,b) and lateral projections (c, d) showing a type IIIB Cho and Yakes AVM with large AV fistulas draining into complex venous lakes feeded by the internal maxillary and posterior auricular arteries. (e) Embolization of the posterior auricular artery using a coaxial microcatheter with occlusion balloon (arrow) to deliver coils in the venous lake and allow safe onyx injection in the coil mass to occlude both the venous and arterial sides of the AVM. (f,g) Same approach taken in the internal maxillary artery. (h) Control DSA showing a nice devascularization of both nidi. Residual perfusion of the AVM through the internal maxillary artery is seen (arrow). This will eventually be embolized through a venous approach.

migration. Glue is adhesive and can recanalize after some time.[34] Glue extrusion can be observed when injected in oral mucosa or close to the skin and can be source of infection or bleeding.

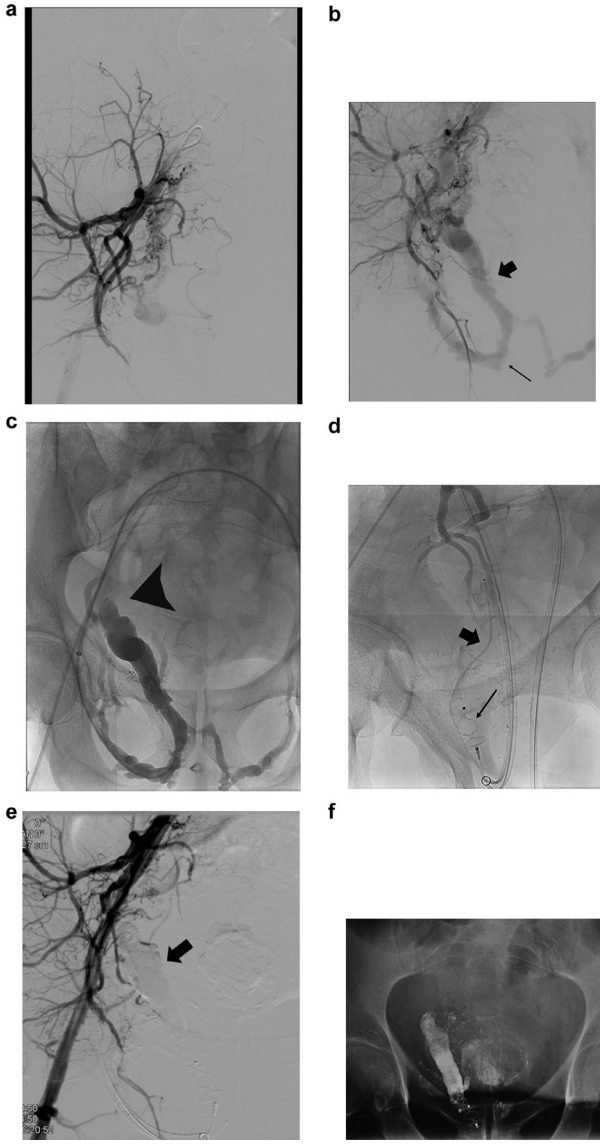


Figure 6 Patient with a pelvic AVM complicated by an acute hemorrhage (hematuria) following a transurethral resection of the prostate. The patient was first embolized urgently with glue injection in both prostatic arteries followed by gel foam injection in the anterior trunk of the right internal iliac artery. Bleeding recurrence was observed 5 days later. (a,b) DSA acquisition after opacification of the right internal iliac artery showing a type II Cho and IIIa Yakes AVM with retrograde venous drainage through the internal pudendal (large arrow) and obturator vein (small arrow). (c) Catheterization of the right obturator and internal pudendal veins through contralateral approach after catheterization of the external pudendal vein via the right common femoral. A proximal occlusion of the right internal iliacvein (arrowhead) is observed, explaining the retrograde drainage and the venous congestion causing the hemorrhage. (d) Deployment of an Amplatzer plug (small arrow) in the central portion of the obturator vein combined with a coaxial insertion of a microcatheter (large arrow) in the peripheral internal iliac vein. (e,f) Control DSA (e) and plain film (f) after embolization of the vein with STS foam followed by occlusion with Glue (arrow). Complete occlusion of the AVM is observed on the DSA.

Figure 7 Patient with a large AVM of the left upper limb. Installation of a sterile pneumatic cuff to control arterial inflow and venous outflow. The pressure should be increased gradually with serial DSA acquisitions to maximize reflux in the nidus while minimizing reflux in normal arteries and central veins. Following glue, onyx or ethanol injection, the pneumatic cuff should be deflated very progressively under fluoroscopic control to prevent central venous migration of embolic agents.

Ethylene Vinyl Alcohol Copolymer (EVOH)

EVOH (Onyx) is an elastic copolymer (ethylene vinyl alcohol copolymer), dissolved in dimethyl-sulfoxide (DMSO). DMSO has weak sclerosant properties. Onyx has cohesive properties and behaves like lava allowing a filling of the nidus with minimal fragmentation of the injected cast. It hardens from the outside to inside and has a propensity to advance in the area of least resistance allowing for deep, distal penetration. Slow injection (between 0.1 and 0.3 mL/min) with a compatible microcatheter under continuous fluoroscopy monitoring is recommended. When the agent is flowing in the proper direction, it is recommended to continue the slow injection without interruption. If there is a reflux of onyx around the catheter, the injection should be stopped for 1-2 minutes to create a solid plug around the catheter and then resumed to push the new onyx forward (stop and go technique) (Fig. 8). When the onyx is flowing in a nontarget vessel, the same latter principle apply; this will give the polymer time to solidify and redirect the new injected onyx to the nidus, which has a lower resistance.[8] Detachable tip microcatheters can be used when there is a risk of microcatheter entrapment in the onyx cast, especially in the carotid the territory (Fig. 8). An occlusive balloon or coils can be used to help Onyx penetration in the nidus while preventing reflux (Fig. 5).[35] Recanalization has also been described over time with Onyx.[36]

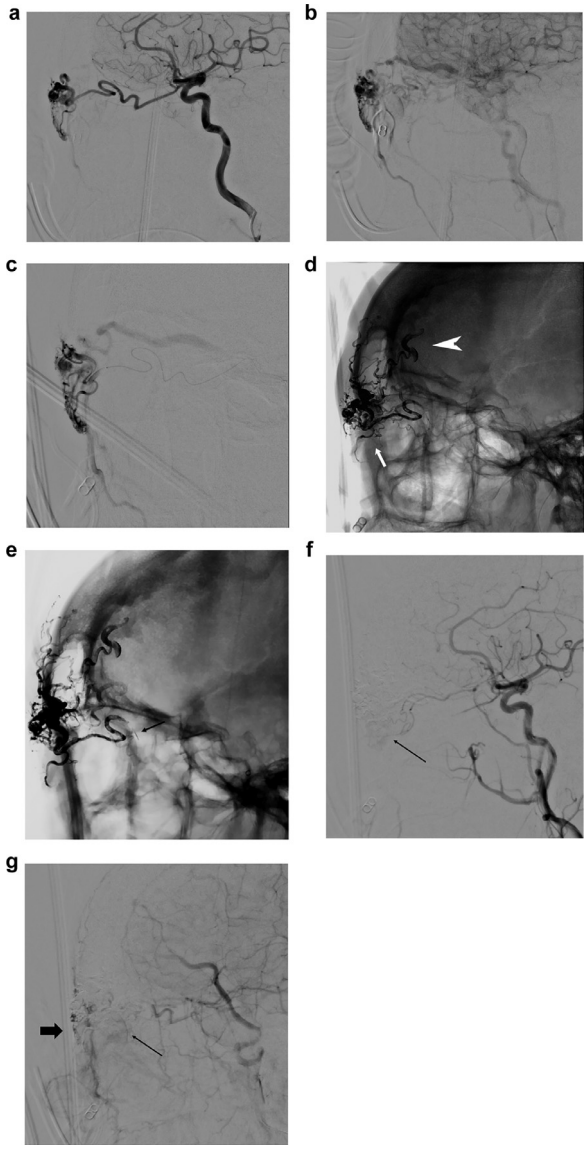


Figure 8 Patient with an orbital AVM. (a,b) DSA acquisition after opacification of the left internal carotid showing an AVM fed by a large supraorbital branch of the ophthalmic artery (IIIB CHO, II Yakes). (c) Catheterization of the distal portion of the supraorbital branch with a detachable microcatheter. (d) Embolization using the stop and go technique allowing occlusion of the nidus and reflux in feeders arising from the external carotid: Temporal branches (arrowhead) and infraorbital branches arising from the internal maxillary artery (arrow). (e) Detachment of the distal portion of the microcatheter in the onyx cast (arrow). (f) Opacification of the external carotid artery showing minimal residual perfusion through orbital branches coming from the middle meningeal artery (arrow). (g): Small residual opacification of the nidus on late arterial phase (large arrow) and good opacification of the retinal plexus (small arrow).

Recommended Approaches According to Specific Clinical and Anatomic Situations

Clinical Symptoms

The type of signs and symptoms will influence the endovascular approach. Bleeding is mainly due to venous

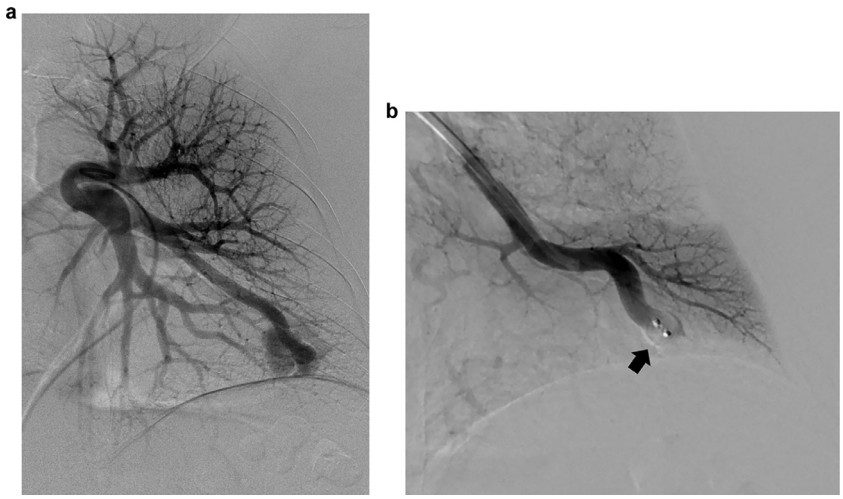


Figure 9 Patient with a HHT syndrome. (a) Pulmonary angiogram showing a direct fistula arising from a lingular branch. Type I Yakes AVM. (b) Occlusion with an Amplatzer plug (arrow).

hypertension and decreasing the inflow before closing the vein is important to prevent a worsening of the bleed. Regarding pain and ulceration, it can be due to venous congestion or arterial ischemia due arteriovenous shunting. A careful Doppler examination is important to evaluate the flow and resistive index proximal and distal to the nidus. If there is a distal hypoperfusion due to AV shunting, it is recommended to close the fistula and use direct nidal puncture or a venous approach to redirect the flow distally. Endovascular arterial approach can be used if the risk of nontarget embolization in the normal distal vascularization is minimal. On the other hand, if there is a venous congestion, reduction of the inflow is recommended before closing the vein to prevent a worsening of the congestion.

In our experience, PTEN patients can present aggressive AVMs with a propensity to recur after embolization. Treatment with Sirolimus has been proposed to control the pain associated with hamartomas.[37] However, embolization remains the recommended treatment for pain associated with AVMs.[37]

Adapting the Approach to the Angioarchitecture

As a general principle, the best approach will be based on the AVM classification following supra-selective catheter angiography. The identification of arterial feeder, the nidus or draining vein under ultrasound can also influence the approach.

Yakes Type I

Yakes type I are direct fistulas between the artery and the vein. They are often observed in PAVM associated with HHT syndromes and in renal arteries. The treatment will consist in the occlusion of the fistula with coils or a vascular plug. The approach can either be from the arterial or the venous side depending on the ease to reach the fistula. For small AV fistulas, depending on the size of the arterial feeder or draining vein targeted for occlusion, 0.018" or 0.035" coils can be used. For a large AV fistula, an Amplatzer plug is usually preferred and installed through an arterial or a venous approach (Fig. 9). A 40%-50% oversizing is required for Amplatzer plugs. For systemic type I AVMs, occlusion can be completed with a liquid embolic like glue or Onyx.

Yakes Type II/Cho Type IIIb

These lesions characterized by a typical AVM nidus with multiple inflow arteries and draining veins are the most challenging to treat. If arterial feeders can be catheterized supra selectively, the endovascular approach can be a first option. If not and the lesion is superficial and accessible to ultrasound or fluoroscopy/roadmap guided puncture, intranidal injection can be a good alternative. Venous approach can be useful only if it is possible to reflux into the nidus. Adjunct manoeuvers such as external compression, balloon microcatheter or mechanical occlusion of the vein with coils or microplugs can be helpful to reflux into the nidus. The approach will be influenced by the anatomical region.

Cervicofacial AVMs

Type II Yakes/ IIIB Cho are frequently encountered in cervicofacial AVMs. Ethanol can be used in territories not at risk for nerve injury. In the vicinity of the facial nerve or optic nerve, onyx or glue should be preferred (Fig. 10).[8] The endovascular approach and/or direct nidus puncture are usually first attempted (Fig. 10). Ethanol should only be injected when the microcatheter is inside the nidus and if there is no normal arterial branch opacified distally (Fig. 10). A retrograde venous approach can be useful if it possible to reflux into the nidus. However, the presence of multiple venous collaterals in the face can be a limitation. In presence of a large fistula, it can be useful to start with ethanol to destroy the nidus and complete with glue or Onyx to close the fistula. For lesions involving the skin, Onyx should be used with caution since its black coloration due to tantalum powder can tattoo the skin.

Limb AVMs

Type II Yakes and IIIB Cho AVMs are also frequently observed in extremities. As proposed for cervicofacial AVMs, if the main feeders can be safely accessed through an endovascular approach, this should be attempted first (Fig. 11). Direct puncture can be directed toward the arterial or the venous side of the nidus using careful spectral Doppler analysis. The use of a pneumatic cuff or tourniquet is very useful to maximize the penetration of the nidus. Pneumatic cuff can be used proximal to the nidus to decrease the arterial inflow and occlude the venous drainage. Surgical forceps can also be used to block the venous drainage. For foot or hand AVMs, the use of small tourniquets on the fingers distal to the AVM nidus is very convenient to prevent ethanol migration in fingers and toes (Fig. 11).

Abdominal and Pelvic AVM

Arteriovenous malformation involving stomach, intestine, colon, and pancreas are rare and difficult to treat when there is no single draining vein. Ethanol cannot be used because of the risk of bowel necrosis or necrotizing pancreatitis. The same reasoning applies for uterine or prostatic AVMs with multiple draining veins. For this reason, the preferred embolic agent will be glue or Onyx, This can be followed by surgical resection if needed (Fig. 12).[38] A venous approach can be done by transportal catheterization for AVMs involving the splanchnic territory (Fig. 12). For pelvic AVMs, the equivalent can be done by a systemic venous approach.

Type IIIA and IIIb Yakes/Type I and II Cho

The architectural aspect of these arteriovenous malformations is characterized by multiple inflow arteries or arterioles draining into an aneurysmal venous sac that has either a single outflow (type I and II Cho, Type IIIa Yakes)) or multiple outflow veins (Type IIIB Yakes). The AV fistulae are within the wall of the aneurysmal vein and one of the key components for successful treatment is the occlusion of the vein. In the type IIIB Yakes the AVM feeders are connected to an ectatic venous sac draining into several outflow veins. Thus, the venous collector can also be targeted to close the AVM.

For type I Cho AVM where there are few arterial feeders, the vein can be targeted as a first line of therapy. Sometimes an ethanol embolization through an arterial endovascular approach of the feeders followed by glue or Onyx injection can be attempted to decrease the flow before occluding the vein (Fig. 13). This can be interesting if there is a risk of worsening a venous congestion. The mechanical occlusion of the vein can be done with coils or plugs combined or not with glue, through a retrograde venous approach or direct puncture(s) (Fig. 13). Mechanical occlusion of the venous drainage can be combined with liquid embolic or sclerosant agent injection into the nidus using a coaxial microcatheter positioned distally to the mechanical occlusion (Figs. 5, 11, and 13). This technique has been described for peripheral AVMs (the push-through method)[39] and for brain AVMs (cooker pressure technique).[40] Retrograde injection of

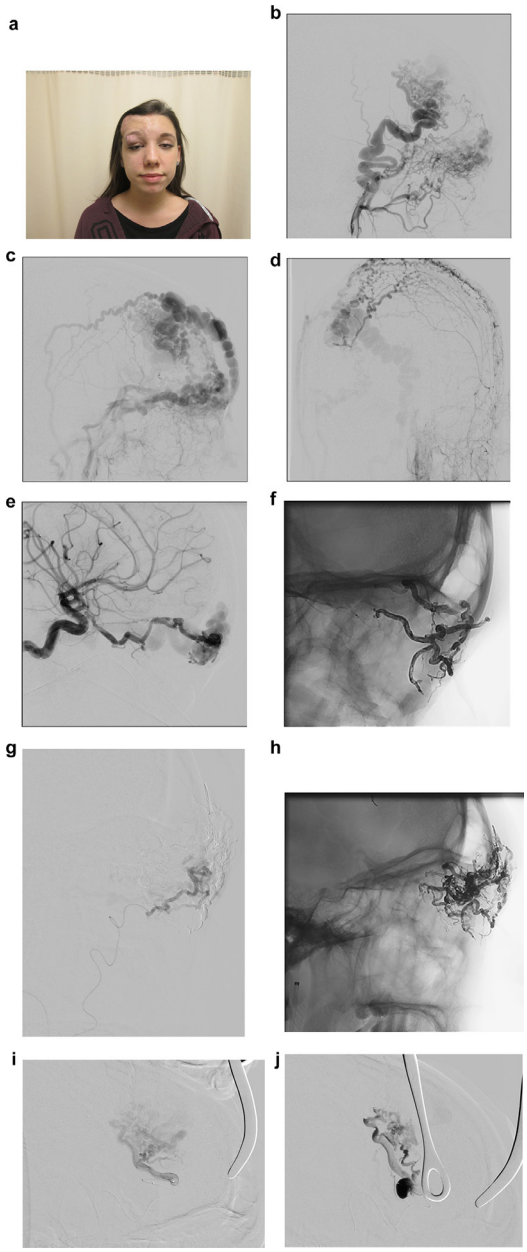


Figure 10 (a) Patient with a frontoorbital AVM complaining of palpebral ptosis, pain, and esthetic prejudice. (b,c) Right external carotid angiogram in lateral projectionshowing a type IIIB Cho and type II Yakes AVM with multiple feeders coming from internal maxillary, middle meningeal and temporal arteries. (d) Injection in the left external carotid in AP projection showing contralateral recruitment. (e) Internal carotid angiogram showing a recruitment through a supraorbital branch of the ophthalmic artery. (f) Embolization with Onyx of the supraorbital branch. (g,h) Onyx embolization of feeders arising from an infraorbital branch coming from the internal maxillary artery. (i) Catheterization of the temporal branch feeding the main nidus in the scalp (j). Embolization with ethanol using external compression with forceps to block venous drainage (k). Good occlusion of AV fistulas on control DSA. (l) Catheterization of a frontotemporal branch (m), embolization with ethanol to induce endothelial ablation and slow the flow (n) Direct puncture of the venous drainage under ultrasound (o) and ethanol embolization with external compression (p).The first temporal branch was then occluded with onyx (arrow) and the frontotemporal branch with glue (arrowhead). (q,r) Control DSA before resection surgery showing minimal residual opacification of the nidus. (s) Patient evolution following surgery.

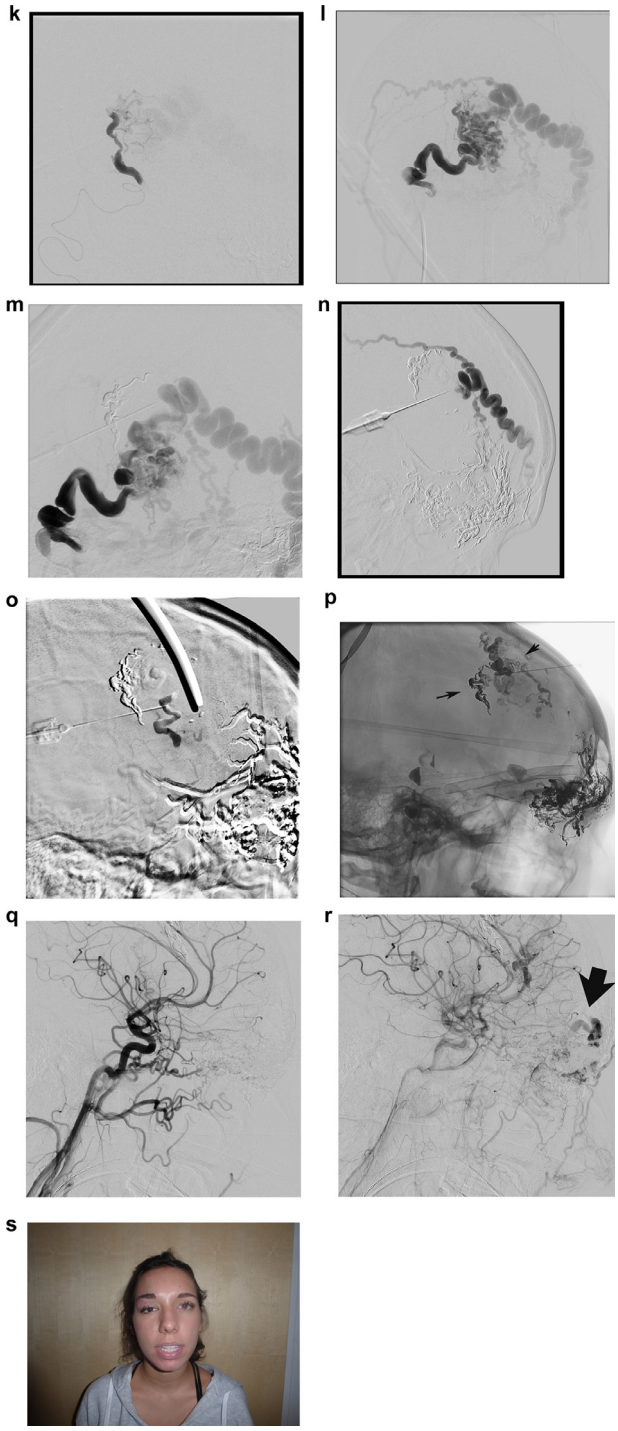


Figure 10 Continued.

ethanol can also be done through an occlusive balloon. It is effective but can be dangerous if a large volume of ethanol is released following balloon deflation.[41] This is why we prefer using permanent mechanical occlusion combined with sclerosant agents on the venous side.

Type IIIA Cho and Type IV Yakes

This type of AVM is usually difficult to treat. Type IIIA is characterized by a mesh-like network of arterioles draining

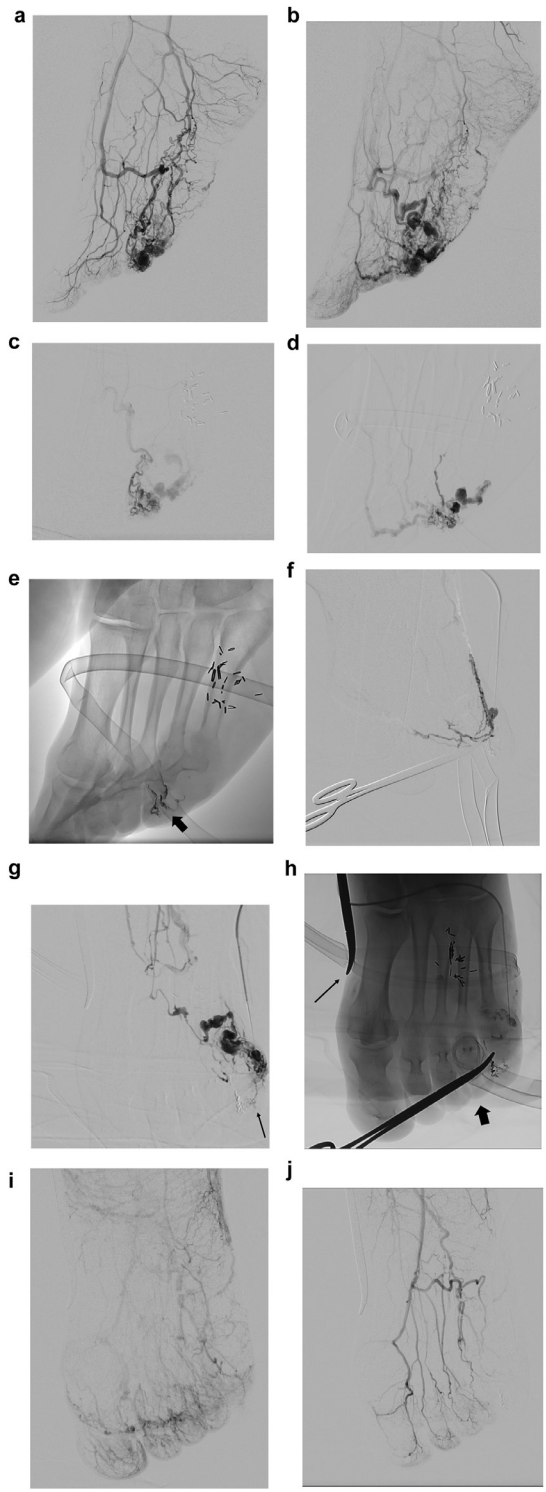


Figure 11 Patient with an AVM of the foot complicated by the presence of pain and ulceration (same patient shown in Fig. 3). (a,b) Selective DSA showing Type IIIB Cho and II Yakes AVM of the lateral aspect of the foot fed by the external plantar and arcuate arteries. (c) Selective catheterization of the nidus through the external plantar artery (d) and embolization with ethanol (e) completed by Onyx (arrow). (f) Direct puncture of the nidus showing reflux into feeders arising from the plantar arch. (g) after ethanol emboliation, the nidus is better seen as well as the arteries feeding the 4th toe (h): Protection of the 4th toe using a tourniquet (large arrow). A proximal tourniquet (small arrow) is inserted to slow the venous drainage during ethanol embolization. (i,j): after ethanol embolization of the nidus and draining veins, the final DSA shows an occlusion of the nidus and preservation of the collateral arteries of the 4th and 5th toes.

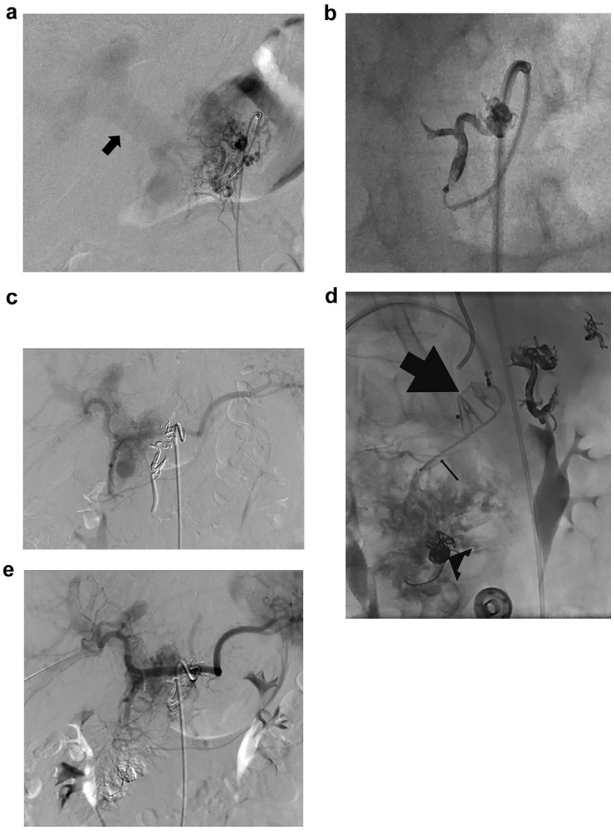


Figure 12 Patient with a pancreatic AVM (type IIIB Cho, II Yakes) with upper gastrointestinal hemorrhage. (a) Selective opacification of a pancreatic arcade showing a portion of the nidus and drainage into the portal vein (arrow). (b) Embolization with Onyx, which is too proximal to penetrate the nidus. (c) Bleeding recurrence with persistent AVM fed by multiple arteriolar branches. (d) Transportal approach with occlusion of a pancreaticoduodenal vein with an Amplatzer plug (large arrow), protection of the venous drainage in the mesenteric vein with coils (arrowhead) and sclerotherapy with STS foam through a coaxial microcatheter postioned distal to the plug (small arrows). (e) Control DSA showing an occlusion of the nidus in the cephalic portion of the pancreas. Persistence of residual AVMs in the corporeal portion of the pancreas. The patient eventually had a pancreaticoduodenectomy.

into a nidus with multiple outflow venules. The difficulty relies on the fact that the size of these feeding and outflowing vessels is too small to be selectively catheterized and the arterial endovascular approach can provoke nontarget embolization when using ethanol or proximal embolization when using Onyx or glue. The use of Onyx using the stop and go technique or a balloon microcatheter can be an option.[42] Ethanol embolization by direct puncture of the nidus under U/S guidance is often the best option. Tissue infiltration with bleomycin can also be an option.[43] The vessels with aliasing on color Doppler should be targeted.

In the type IV Yakes AVM, there is no real nidus but numerous small arteriolovenulous fistulas infiltrating tissues, interspersed with normal capillaries that maintain the viability of the tissue. A 50-50% mixture of ethanol and nonionic contrast can apparently be curative.[44] Interstitial infiltration of bleomycin can also be an option (Fig. 14).[43]

Expected Outcome

The results of the literature are summarized in Table 3.[25,27,45-51] With ethanol embolization alone, mostly for head and neck AVMs, Do et al have reported a 68% success rate (cure and improvement) whereas Sue et al reported a 95% success rate.[45,46] For the same authors, the rate of severe complications varied between 0% and 12% and minor complications were between 25% and 45%. Using glue, Lefourn et al reported in 32 patients, a 72% clinical success rate and a 75% size decrease of the AVM on imaging. Kitawaga et al reported the use of glue on the arterial side combined with sclerosing of the draining vein using a venous approach or direct puncture with a 84% clinical success. Aggressive embolization can be combined with resection surgery; in a series of 31 patients undergoing surgery after sessions of glue embolization, a low recurrence rate was observed if the AVM was completely resected (18%) or if it had sharp limits with surrounding tissues (16%).[27] On the other hand, patients with partial resection had a 67% recurrence rate. Glue embolization before resection helped the surgeon find AVM extension during surgery.

We have recently reviewed a series of 121 patients with a mean follow-up of 6.9 years. Most patients had ethanol embolization alone or combined with glue or Onyx and mechanical occlusion of venous drainage when needed. Improvement (53%) or stabilization (44%) of Schobinger stage was observed in 97% of patients.

One study reported the use of combined therapy in 6 patients using Sirolimus with embolization.[7] Sirolimus was initiated at least 1 month prior to endovascular embolization, targeting a serum level of 10-15 ng/mL throughout the course of the endovascular embolization series and continued for at least 1 month after the last embolization treatment. All patients responded favorably to the combined therapy. In our practice, we reserve Sirolimus for patients having a PTEN syndrome because it has a specific action on the signalization of the mutation. Sirolimus can lead to significant complications such as mouth ulcers, diarrhea, abdominal pain, peripheral edema, headache, chest pain, hypercholesterolemia, impaired wound healing, upper respiratory tract infection and pneumonitis.[52] For sporadic AVMs, more evidence is needed before routinely using it as an adjuvant therapy.

Complications

Ethanol injection can induce a vasoconstriction of the pulmonary artery vasculature, leading to cardiovascular collapse. This has been reported in 0.2% of cases. Monitoring of the pulmonary arterial pressure is recommended if large ethanol doses are considered (more than 0.3 mL/kg in our experience). Vasodilator therapy, primarily milrinone, is administered if systolic pulmonary arterial pressures increase more than 50% compared to baseline values.[13,53] A concomitant monitoring of the arterial pressure (radial cannula) is recommended since both systemic and pulmonary systolic pressures will rise for a short period of time after ethanol

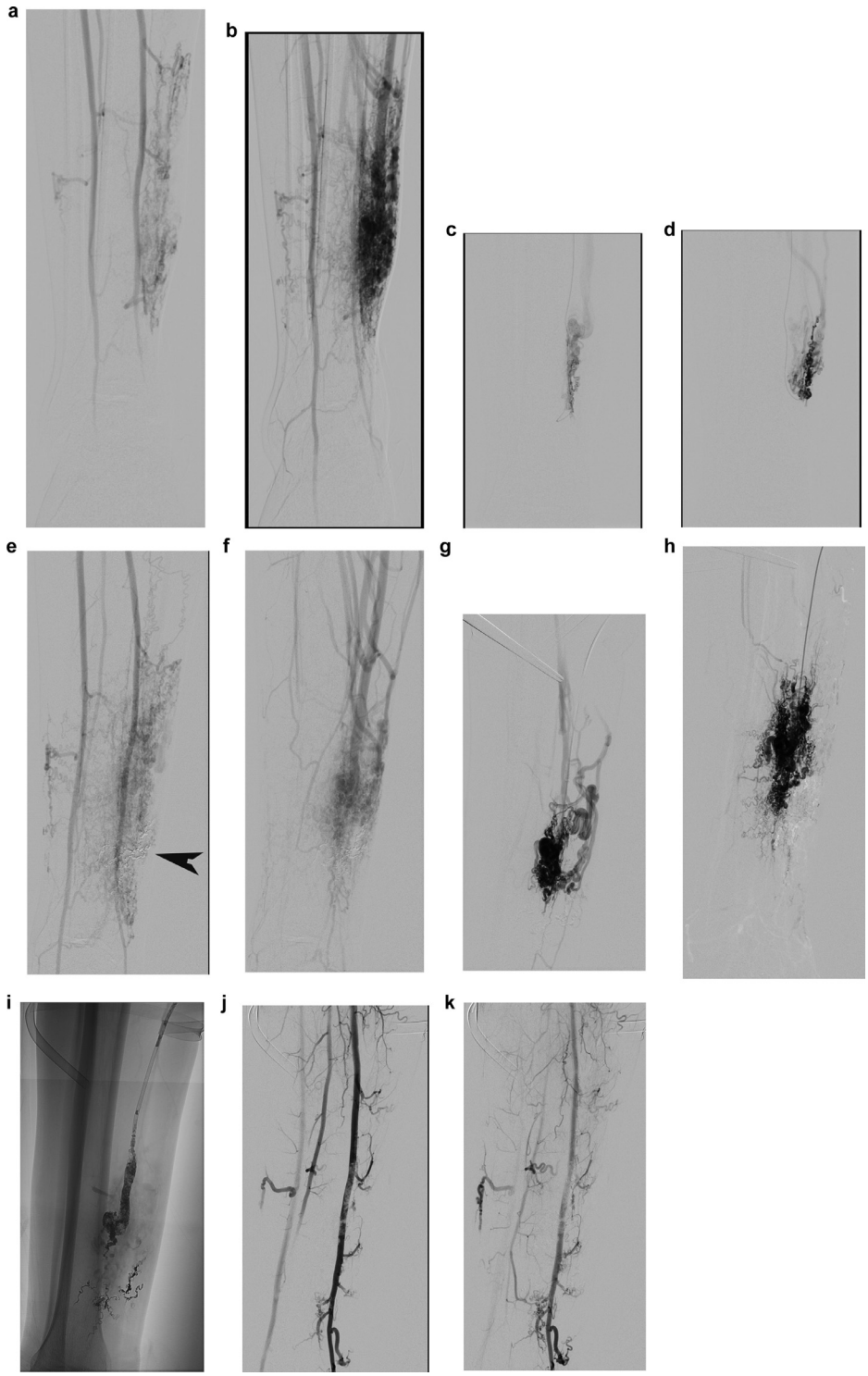


Figure 13 Patient with a leg AVM and chronic ulceration. (a,b) DSA showing a complex AVM with multiple arteriolar feeders arising from the posterior tibial and drainage in a dominant tibial vein and several collateral veins draining into the peroneal vein. This AVM was classified IIIB Cho and II Yakes. (c,d) Selective catheterization of arterial feeders followed by Onyx injection. (e,f) No clinical improvement and persistent AVM on control DSA with dominant drainage through the posterior tibial vein. The Onyx cast is shown (arrowhead) (e). (g,h) Retrograde puncture of the posterior tibial vein under ultrasound guidance and retrograde nidus embolization using proximal tourniquet to reflux in the nidus with ethanol. Following ethanol embolization, first the venous side of the nidus is occluded (g). Then, it is possible to reflux into the arterial side (h). (i) Occlusion of the posterior tibial vein was completed with glue. (j,k) Final DSA showing a complete cure of the AVM. The patient had a complete healing of the leg ulceration.

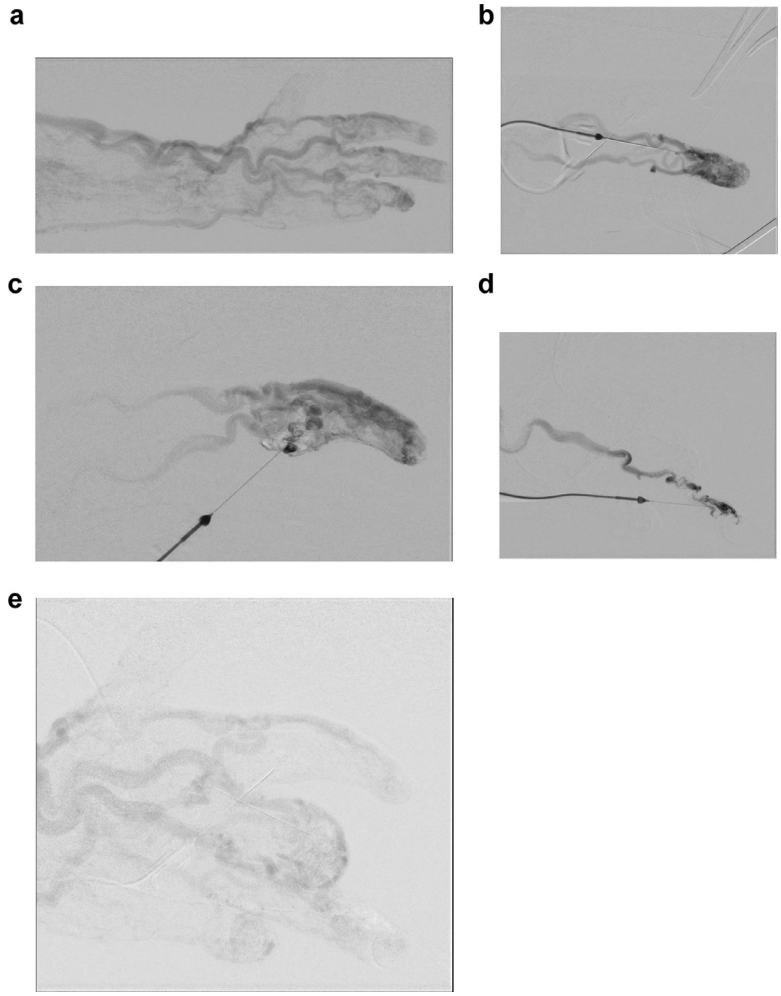


Figure 14 Patient with an upper arm AVM. (a,b) Diffuse arterioles and venules in the 2nd, 3rd and 4th fingers classified as Cho IIIa or Yakes IV. (c to e) Direct puncture of the nidus under ultrasound guidance and injection of intranidal bleomycin. (e) Control DSA showing a good improvement of the shunting especially in the 2nd and 4th fingers. Flexion of the third finger explains poor visualization of the distal phalanx.

injection secondary to pain.[54] Usually a 3.5 ratio between the systemic and pulmonary arterial pressure should be maintained to preserve a good cardiac output.

According to Table 3, complications are observed with all agents. The range of major complications is estimated at 0%-20% and minor complications range between 6% and 45%. Ethanol seems to be more at risk to induce blisters/skin necrosis (15.5%) and transient nerve injury (4.8%).[45] Skin necrosis is usually managed conservatively with wound therapy. Sometimes it may require a flap surgery. Nerve injury will recover with time in most cases.[45] However, there is always a risk of permanent nerve injury and the patient needs to be consented for this potential complication. Stroke, muscular and bladder necrosis as well as hemoglobinuria have also been reported. The arterial endovascular approach is probably more at risk if the microcatheter is not inside the nidus. It is important to check for the presence of normal arterial branches before injecting ethanol or any liquid embolic agent.

Clinical Follow-up

Since AVMs have a propensity to progress or recur after embolization, we propose a lifelong surveillance at the vascular anomaly clinic. Usually, Schobinger 1 AVMs will be followed at 2-5 year intervals depending on the age of the patient (closer follow-up in children and teenager). Schobinger 2 is followed on an annual basis if a conservative approach is chosen. Stage 3 and 4 Schobinger have a close surveillance and we usually evaluate them between each embolization session to assess clinical evolution and detect potential complications. Females of childbearing age, with a strong will for pregnancy need special attention as a very thorough discussion needs to happen before the patient becomes pregnant. These patients have to understand that the AVM can dramatically increase during pregnancy, leading to very complex decisions if complications develop before the child is born. They also have to be aware that the AVM might not regress to its prepregnancy Schobinger stage or can become significantly more symptomatic, precipitating the need

Table 3 Reported Series of Peripheral and Extracranial AVMs

Series	N Pts Site	Embo Agent	Response	Compl	Surgery
Do et al[45]	40 H&N Trunk	ROH	CCR 40% PCR 28%	Major 12% Minor 45%	NA
Su et al[46]	66 H&N	ROH	CCR 85% PCR 15%	Major 0% Minor 25%	13/66
Le Fourn et al[47]	32 H &N UL& LL	Glue	72% CCR+PCR 75% size reduction UL<LL and H&N	Major 13%	NA
Kitagawa et al[48]	24 H&N Limbs, trunk	Glue transarterial Ethanolamine direct /venous	CCR 13% PCR 71%	Major 0% Minor 16%	NA
Goldenberg et al[27]	31 H&N	Glue (elective) PVA (preop)	NA	NA	31/31 CResect :71% PResect :21%
Dabus et al[49]	18 H&N	Onyx	CCR78% PCR22%	Minor 6%	NA
Meila et al[50]	14H&N	Ethibloc, Onyx, Polidocanol	CCR 60% PCR 29% Improvement in daily life 100%	Major 21%	NA
Saeed Kiliani et al[51]	19 H&N, limbs, trunk	Onyx	Complete devasc 63% Partial devasc 26% CCR or PCR 84%	Major 5% Minor 16%	9/19
Racicot et al[25]	116 H&N, limbs, trunk	Ethanol, Onyx, Glue	Schobinger stage improvement 53% Schobinger stage stable 44% Schobinger stage worse 3%	Major 6% Minor 20%	9/121

CCR, complete clinical response; Compl, complication; CResect, complete resection; H&N, head and neck; LL, lower limb; PCR, partial clinical response; PResect, partial resection; ROH, ethanol; UL, upper limb.

for aggressive treatment once the child is delivered. Therefore, these patients, if stage 1 or 2 with a conservative treatment, might need more frequent follow-up, to detect rapidly a more subtle progression or to answer new questions the patient might have concerning an eventual pregnancy. Besides clinical examination, color Doppler ultrasound is key to evaluating the therapeutic response. A color Doppler evaluation of the nidus combined with a spectral Doppler to measure maximal velocities and resistive index in the arterial feeders and draining veins is helpful to evaluate AVM evolution. A closer follow-up is also mandatory during the pregnancy since it will stimulate AVM growth. In most cases, the AVMs will return to baseline conditions several months following delivery.

Conclusion

The interventional radiologist can play a central role in the management of AVM patients. This must be done in a multidisciplinary clinic. However, it is mandatory for the interventional radiologist specialized in AVMs to be involved at the clinic as well as during patient hospitalization. The coordination with the different specialists (plastic surgery, internist, dermatology) is the key to success and it is recommended to have dedicated staff to manage these patients. As discussed in this chapter, the interventionist needs to adapt his approach based on patient symptoms and AVM anatomic classification. In our hands, ethanol embolization yields good results when used cautiously (inside the nidus and at a distance from nerve territories) but we will prefer Onyx or glue alone in dangerous territories. We will sometimes use these 2 latter agents in combination with ethanol to prevent recanalization. When possible, the venous approach combining mechanical occlusion and sometimes vein sclerosis has dramatically changed the paradigm, in particular when there is only one main draining vein. Again, the use of Doppler ultrasound during the embolization procedure, in particular to guide direct puncture is essential. AVMs are challenging cases; you need to approach them with respect, prudence and stage the procedures to minimize complications.

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