Pulmonary Arteriovenous Malformations (PAVMs) are abnormal communications between the pulmonary arteries and veins without any intervening capillary beds, and cause hypoxemia, cyanosis, and dyspnea [1]. About 70-95% of all PAVMs are associated with hereditary hemorrhagic telangiectasia (HHT) [1-5], which is an autosomal dominant genetic disorder that is characterized by recurrent epistaxis, mucocutaneous telangiectasia and visceral vascular involvement, including arteriovenous communications that may develop in virtually any organ and especially in the lungs [1, 2]. Because there is no capillary filter in PAVM, small blood clots, bacteria, and occasionally air or clotted blood within intravenous tubing can pass directly through the PAVM into the systemic circulation. Neurologic complications consisting of transient ischemic attack, stroke, and brain abscess are relatively common events [1]. Thus, treatment for PAVMs is justified even for asymptomatic ones.

PAVMs were initially treated with pneumonectomy [6]. Surgical techniques progressed over time to include lobectomy and local excision [7]. However, first transcatheter embolization was performed by Porstmann using hand-made steel coils in 1977 [8, 9], and thereafter embolization has become first-line therapy for this condition, obviating the need for surgery in the majority of cases. Concerning indication of embolization for PAVM, there has been a great deal of discussion since the description of the so-called “3-mm guideline” recommending that for feeding vessels ≥ 3 mm, the PAVM should be treated regardless of symptoms. In 1992, Rosenblatt et al [10] described 17 patients each with a single dominant PAVM in an abstract; eight of these had evidence of stroke on brain magnetic resonance imaging (MRI), and four had clinically evident stroke. In these four, the feeding artery measured from 2.9 to 4.5 mm. Thus was born the “3-mm guideline,” and thereafter it has been referred by many articles. However, there have been reports of symptomatic paradoxical embolization in patients with only sub-3-mm feeding arteries [11, 12], and it has been shown that paradoxical embolization is independent of the feeding artery diameter [13]. As a result, the potential need to treat PAVMs in the sub-3-mm feeder range was also acknowledged by the originators of the 3-mm guideline in 2006 [14]. Then, the 2009 HHT treatment guidelines now acknowledge that it is appropriate to treat PAVM with feeders smaller than 3 mm [15]. The developments of microcatheters and guidewires with hydrophilic coatings and preshaped tips, as well as developments in coil technology, make it possible to treat PAVM with feeders smaller than 3 mm in diameter. Because the diameter of a 3-French microcatheter is 1 mm, the theoretic treatment size with respect to the
feeling artery is 1 mm [16]. Thus, embolization is now technically feasible even for small PAVM.

Some techniques of coil embolization for PAVM were reported. In the "anchor" technique, the coil tip is purposely anchored in a small side-branch proximal to the PAVM and the body of the coil then prolapses into the feeling artery. By securing the tip in a side-branch, the risk of inadvertent coil dislodgment is minimized [17]. In the "scaffold" technique, the first positioned coil creates a scaffold and permits the blockage of other devices. By packing the decreasing diameter devices, an optimal occlusion of the feeling artery can be achieved [18]. The "double microcatheter" technique has been on the concept of securely bracing coils beside one another to achieve a stable configuration. Placing two microcatheters in the feeling artery of PAVM allowed two coils to be positioned and their stability assessed before either coil was detached [19]. Some authors have reported the embolization of both the feeling artery and venous sac may be useful [20-22]. However, other authors argued it was not necessary [23,24], and it has still been a controversial topic.

Reperfusion is an issue after the successful coil embolization. Follow-up examinations are important for detecting reperfusion, because paradoxical embolization suspected to have been caused by a reperfused PAVM have been reported [25]. Digital subtraction angiography (DSA) is the most sensitive modality used to examine blood flow through lesions as it detects simultaneous enhancements in the feeling artery and draining vein in reperfused PAVMs [26]. However, since DSA is an invasive follow-up examination, computed tomography (CT) has been routinely performed. The reperfusion rates evaluated by CT were previously reported to be up to 19% [25, 27-29]. However, the CT criteria reported in the literature included at least a 70% reduction in a draining vein and venous sac or their contrast enhancements [20, 26-30]; hence, CT is considered to only provide an indirect finding. Furthermore, difficulties have been associated with evaluating CT images because of image deterioration due to metal artifacts generated by the coils [26].

Time-resolved magnetic resonance angiography (TR-MRA) has become a valuable option as an alternative to DSA for screening after coil embolization due to its high sensitivity in detecting flow and the absence of ionizing radiation, and it also offers a non-invasive examination with high resolution [31]. Furthermore, platinum coils, which have relatively low paramagnetic characteristics, are known to produce very few artifacts in MRI [32-34]. Kawai et al [32] reported the usefulness of TR-MRA compared with CT in diagnosing the reperfusion of PAVM after coil embolization. They demonstrated that TR-MRA displayed high diagnostic specificity, positive predictive values, and sensitivity, and these values were in marked contrast with those obtained using CT. Moreover, using TR-MRA or DSA, the reperfusion rates were considerably
higher than those reported in literatures evaluated by CT [35]. The sensitivity of TR-MRA appears to be very high, allowing detection of even slightly reperfused flow. When the amount of blood flow in the right-to-left shunt decreases in TR-MRA, the risk of paradoxical embolization appears to be decreased. However, Chan et al [36] stated that reperfused PAVMs warranted repeat embolization, regardless of residual feeding artery diameter. They mentioned the "3-mm guideline" does not necessarily apply to embolized PAVMs, because reperfused PAVMs may actually pose a higher risk of paradoxical embolization owing to potential in situ thrombus resulting from diminished flow. Thus, it currently remains uncertain whether slight reperfusion detected with TR-MRA is clinically relevant. However, it is definitely important to embolize PAVM in order not to make reperfusion.

The AMPLATZER™ Vascular Plug (St. Jude Medical Japan Co., Ltd., Tokyo, Japan) is a malleable nitinol basket that forms to the shape of the vessel, and it occludes the vessel by inducing thrombus. It has been reported as a useful material for PAVM with low reperfusion rates (0-7%) [30, 37-39]. However, Fidelman et al [40] reported two reperusions in 7 treated PAVMs (in one patient at only 7 weeks after treatment). On the other hand, new embolic materials that could achieve mechanical occlusion without the aid of thrombus formation are recently reported in embolization of PAVMs. The hydrogel-coated coils are developed and designed to improve coil packing density. It consist of a layer of hydrogel polymer surrounding a platinum metallic, and in the presence of blood, the coating undergoes a limited expansion within the first three minutes, and fully expands within 20 minutes [41]. This results in greater filling and stabilization of vascular space, nearly five times more filling volume for the 0.018-inch coil versus platinum coils of the same size. Osuga et al [42] has reported initial experience with embolization of terminal feeding arteries of PAVMs using hydrogel-coated coils in 7 patients with 9 PAVMs. They reported that the venous sac was substantially shrunk in all lesions treated with hydrogel-coated coils with the median size reduction rate of 95% evaluated with CT during the median follow-up period 10 months. The micro vascular plug is a detachable nitinol skeleton plug partially coated with polytetrafluoroethylene. Potential advantages of the micro vascular plug include microcatheter deployment, resheathability, immediate occlusion despite procedural anticoagulation, and diminished metal artifact compared with coils on follow-up CT imaging. Conrad et al [43] reported initial experience with the micro vascular plug for PAVM with good results.

In summary, embolization is a useful treatment option for PAVM, but it is important to pay attention to reperfusion. New devices for embolization have recently been developed, and further studies should be necessary to evaluate them.
References


39. Pulmonary AVM (Masashi Shimohira, MD)


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