Pulmonary Arteriovenous Malformations: Current Technique of Transcatheter Embolization and Subsequent Management

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Abstract
Pulmonary arteriovenous malformations (PA VMs) cause significant clinical complications, such as transient ischemic attack, stroke, and brain abscess. Nowadays, transcatheter embolization plays an important role in the treatment of PA VM. However, persistence can occur after transcatheter embolization for PA VM. Here, we review the current embolization technique, embolic material, and subsequent management.

Key words: pulmonary arteriovenous malformations, embolization, persistence
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INTRODUCTION
Pulmonary arteriovenous malformations (PAVMs), are the abnormal communications between the pulmonary arteries and veins without any intervening capillary beds, which cause hypoxemia, cyanosis, and dyspnea [1]. As reported, 70-95% of all PAVMs are associated with hereditary hemorrhagic telangiectasia (HHT) [1-5], 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, especially the lung [1, 2]. Because PAVMs include no capillary filters, small blood clots, bacteria, and occasional 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] reported in up to 55% of PAVM cases [6]. Thus, treatment for PAVMs is justified, even in asymptomatic cases.

WHICH PAVM SHOULD BE TREATED?
PAVMs were initially treated with pneumonectomy [7]. Surgical techniques progressed over time to include lobectomy and local excision [8]. Transcatheter embolization was first performed by Porstmann using handmade steel coils in 1977 [9, 10]; thereafter, embolization has become the first-line therapy for this condition, obviating the need for surgery in most cases. Concerning indications of embolization for PAVM, there has been a great deal of discussion since the description of the so-called 3-mm guideline recommending embolization for feeding vessels ≥ 3 mm. PAVMs should be treated regardless of symptoms. In 1992, Rosenblatt et al. [11] described 17 patients with a single dominant PAVM in an abstract; eight of them displayed evidence of stroke on brain magnetic resonance imaging (MRI), while four had clinically evident stroke. In these four, the feeding artery measured 2.9-4.5 mm in diameter. Thus, the 3-mm guideline was born; thereafter, it has been cited by many articles. However, there have been reports of symptomatic paradoxical embolization in patients with only sub-3-mm feeding arteries [12, 13], and paradoxical embolization occurs independent of the feeding artery diameter [14]. 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 [15]. Subsequently, the 2009 HHT treatment guidelines acknowledged that it is appropriate to treat PAVM with feeders < 3 mm [16]. The development of microcatheters and guidewires with hydrophilic coatings and pre-shaped tips as well as advances in coil technology make it possible to treat PAVM with feeders < 3 mm in diameter. Because the diameter of a 3-French microcatheter is 1 mm, the theoretical treatment size with respect to the feeding artery is 1 mm [17]. Thus, embolization is now technically feasible, even for small PAVM. However, catheterization through a small and tortuous feeding artery to the target lesion is sometimes difficult and carries the risk of vessel injury during catheter and micro-guidewire navigation. Therefore, the indication of transcatheter embolization for PAVM with a sub-3-mm feeding artery should be carefully considered in individual cases.

**TRANS Catheter EMBOLIZATION TECHNIQUES**

Several embolic devices, including detachable balloons, pushable coils, detachable tips, and vascular plugs, have been used to perform transcatheter embolization of PAVMs. Among them, coil embolization has been widely used to treat PAVMs. Some coil embolization techniques for PAVM have been reported. In the “anchor” technique, the coil tip is purposely anchored in a small side-branch proximal to the fistulous point of the PAVM, and the body of the coil then prolapses into the feeding artery. By securing the tip in a side branch, the risk of inadvertent coil dislodgment is minimized [18]. In the “scaffold” technique, the first positioned coil creates a scaffold and permits the blockage of other devices. By packing the decreasing diameter devices, optimal occlusion of the feeding artery can be achieved [19]. The “double microcatheter” technique uses the concept of securely bracing coils beside one another to achieve a stable configuration. Placing two microcatheters in the feeding artery of a PAVM allowed two coils to be positioned and their stability be assessed before either coil was detached [20]. Some authors have reported that embolization of the feeding artery and venous sac may be useful [21-23] (Fig. 1). However, other authors argued that this was unnecessary and that embolization of the feeding artery only should be adequate [24, 25] (Fig. 2). Thus, this remains a controversial topic.

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 occludes it by inducing thrombus (Fig. 3). It has been reported as a useful material for PAVM with low persistence rates (0-7%) [26-29]. However, Fidelman et al. [30] reported two persistent lesions in seven treated PAVMs (in one patient at 7 weeks after treatment). Moreover, new embolic materials that could achieve mechanical occlusion without the aid of thrombus formation are recently reported in the embolization of PAVMs. Hydrogel-coated coils (AZUR; Terumo, Tokyo, Japan), which are developed and designed to improve coil packing density (Fig. 4), consist of a layer of hydrogel polymer surrounding a platinum metallic; in the presence of blood, the coating expands within 20 minutes [31]. This results in greater filling of the vascular space. Osuga et al. [32] reported their initial experience with embolization of terminal feeding arteries of PAVMs using hydrogel-coated coils in seven patients with nine PAVMs. They reported that the venous sac was substantially shrunken in all lesions treated with hydrogel-coated coils with a median reduction rate of 95% evaluated with computed tomography (CT) during the median follow-up period of 10 months. The MVP Micro Vascular Plug (MVP; Coviidien, Irvine, CA, USA) is a detachable nitinol skeleton plug that is partially coated with polytetrafluoroethylene. Potential advantages of the
A 58-year-old woman presented with a pulmonary arteriovenous malformation (PAVM) of the upper left lobe and underwent embolization of the feeding artery. A) Angiography of the left pulmonary artery shows a PAVM (arrow) for which coil embolization for the feeding artery was performed. B) Angiography after embolization shows complete occlusion of the PAVM.

The AMPLATZER™ Vascular Plug MVP include microcatheter deployment, resheathability, immediate occlusion despite procedural anticoagulation, and a diminished metal artifact compared with coils on follow-up CT imaging. Conrad et al. [33] reported initial experience with the MVP for 20 PAVMs in seven patients. In their results, all devices were successfully detached, and immediate occlusion was achieved in 21 of 23 (91%) deployments.

**FOLLOW-UP AND PERSISTENCE OF PAVMS AFTER EMBOLIZATION**

Persistence, an issue after successful coil embolization, is attributed to recanalization, in which PAVMs are perfused due to flow through a previously placed coil; pulmonary-to-pulmonary reperfusion, in which the embolized feeder remains occluded but there are small feeders from adjacent normal pulmonary arteries; incomplete primary treatment, in which there are previously untreated feeders of a complex PAVM; and systemic-to-pulmonary reperfusion, in which PAVMs persist via a systemic arterial feeder but are not seen on pulmonary angiography. Among them, recanalization is the most frequent persistence (Fig. 5) [5]. Follow-up examinations are important for detecting persistence because paradoxical embolization suspected to have been caused by a persistent PAVM has been reported [34]. Digital subtraction angiography (DSA) is the most sensitive modality used to examine blood flow through lesions since it detects simultaneous enhancements in the feeding artery and draining vein in persistent PAVMs [34]. However, since DSA is an invasive follow-up examination, CT has been routinely performed. The persistence rates evaluated by CT were reportedly up to 19% [34, 36-38]. 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 [21, 26, 35-38]. All of these CT criteria are indirect findings because it is often difficult to identify the recanalization itself through the embolic devices by CT due to metal artifacts [35].

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 for detecting flow and the absence of ionizing radiation; it also offers a non-invasive high-resolution examination [39]. Furthermore, platinum coils, which have relatively low paramagnetic characteristics, are known to produce very few artifacts on MRI [40-42]. Kawai et al. [40] reported the usefulness of TR-MRA compared with CT in diagnosing the persistence 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 persistence
rates were considerably higher than those reported in the literature evaluated by CT [43]. The sensitivity of TR-MRA appears to be very high, allowing the detection of an even slightly persistent 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. [44] stated that persistent PAVMs warranted repeat embolization regardless of residual feeding artery diameter. They mentioned that the 3-mm guideline does not necessarily apply to embolized PAVMs because persistent PAVMs may actually pose a higher risk of paradoxical embolization due to potential in situ thrombus resulting from diminished flow. Thus, it remains uncertain whether slight persistence detected with TR-MRA is clinically relevant. However, it is definitely important to embolize PAVM completely without persistence.

Summary

Transcatheter embolization is a useful treatment option for PAVM, but it is important to monitor it for persistence. New embolization devices have recently been developed, and fur-
ther studies are needed to evaluate them.

Conflict of interest: The authors declare that they have no conflicts of interest to report.

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