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ORIGINAL ARTICLE

Single-center 10-year retrospective analysis of Amplatzer Vascular Plug 4 embolization for pulmonary arteriovenous malformations with feeding arteries of <6 mm

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PURPOSE

To evaluate the efficacy and safety of Amplatzer Vascular Plug 4 (AVP4) embolization in pulmonary arteriovenous malformations (PAVMs) with small- to medium-sized feeding arteries (<6 mm) and to identify factors affecting persistence and the main persistence patterns after embolization.

METHODS

Between June 2013 and February 2023, we retrospectively reviewed 100 patients with 217 treated PAVMs. We included PAVMs with feeding arteries <6 mm, treated with AVP4 embolization, and followed adequately with computed tomography (CT). Technical success was defined as flow cessation observed on angiography. Persistence was defined as less than a 70% reduction of the venous sac on CT. We evaluated adverse events for each embolization session. Patterns of persistence were assessed using follow-up angiography. Univariate and multivariate analyses were performed to evaluate factors affecting persistence based on the 70% CT criteria.

RESULTS

Fifty-one patients (48 women, 3 men; mean age: 50.8 years; age range: 16–71 years) with 103 PAVMs met the inclusion criteria. The technical success rate was 100%. The persistence rate was 9.7% (10/103), and the overall adverse event rate was 2.9% (3/103) during a mean follow-up of 556 days (range: 181–3,542 days). In two cases, the persistence pattern confirmed by follow-up angiography involved reperfusion via adjacent pulmonary artery collaterals. The location of embolization relative to the last normal branch of the pulmonary artery was the only factor substantially affecting persistence.

CONCLUSION

Embolization with AVP4 appears to be safe and effective for small- to medium-sized PAVMs. The location of the embolization relative to the last normal branch of the pulmonary artery was found to be the main determinant of persistence.

CLINICAL SIGNIFICANCE

Given the increasing demand for the treatment of small PAVMs, AVP4 embolization could be considered a viable and effective option for managing PAVMs with feeding arteries <6 mm.

KEYWORDS

Arteriovenous malformation, computed tomography, embolization, pulmonary, vascular plug

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Pulmonary arteriovenous malformation (PAVM) describes a direct connection between the pulmonary artery and vein, which can lead to paradoxical embolism and result in serious complications, such as stroke and brain abscess.[1] Endovascular embolization has emerged as the preferred treatment for PAVM.[2] The once conventional "3 mm rule," which rec-

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ommended treating feeding arteries larger than 3 mm, no longer holds universal acceptance.[3,4] The current consensus now supports embolization for feeding arteries that are 2–3 mm or larger or when catheterization is feasible.[5] Nonetheless, the choice of embolic materials for small PAVMs remains limited, and the results from coil embolization in these cases are generally less favorable.[6]

The issue of persistence following PAVM embolization is substantial, often necessitating further interventions.[7] To address this, research has been conducted on the effectiveness of various embolic materials, including coils,[6,8] Amplatzer Vascular Plugs (AVPs),[9,10] and microvascular plugs (MVPs).[11,12] Despite the longstanding use of coils, their associated persistence rates are notably high.[6,8,13] While venous sac embolization yields favorable outcomes, employing multiple detachable coils is costly and extends procedural times.[14] More recently introduced MVPs have demonstrated promising results, although they are more expensive, and their long-term efficacy remains uncertain.[15]

AVPs are composed of a braided nitinol mesh and are noted for their low risk of migration in high-flow vessels or short landing zones, which permits device repositioning and provides the potential for single-device occlusion.[16,17] The latest generation, Amplatzer Vascular Plug 4 (AVP4), features a small-profile catheter with a 0.038-inch luminal diameter, suitable for navigating small- to medium-sized vessels and handling vascular tortuosity. Since its introduction for PAVM embolization in 2014, several studies have reported on the use of AVP4, with persistence rates ranging from 0% to 16%.[10,15,18] However, many of these studies have been limited by small sample sizes or the inclusion of different generations of AVP.

Main points

- Amplatzer Vascular Plug 4 embolization was performed on 103 pulmonary arteriovenous malformations (PAVMs) with small- to medium-sized feeding arteries (<6 mm). This resulted in a persistence rate of 9.7% (10/103) based on the 70% reduction criteria on computed tomography and an overall adverse event rate of 2.9% (3/103).
- Follow-up angiography conducted on 28 PAVMs identified persistence in 2 PAVMs, both of which showed reperfusion via adjacent pulmonary artery collaterals.
- The only substantial factor affecting persistence was the location of the embolization relative to the last normal branch of the pulmonary artery.

Consequently, this retrospective single-center study aims to evaluate the efficacy and safety of AVP4 embolization in PAVMs with small- to medium-sized feeding arteries (<6 mm). Additionally, this study seeks to identify factors affecting persistence and to delineate the main persistence patterns following AVP4 embolization.

Methods

This retrospective study received approval from the Institutional Review Board of Kyungpook National University Hospital (KNUH 2023-12-027). All participants provided informed consent prior to the procedure.

Patient selection

The study cohort included patients who underwent endovascular embolization for PAVM from June 2013 to February 2023. The eligibility criteria for inclusion were as follows: (1) treatment-naïve PAVM with a feeding artery diameter of <6 mm; (2) embolization performed using the AVP4; and (3) availability of both initial and follow-up computed tomography (CT) scans before and after embolization. The exclusion criteria were as follows: (1) underwent additional embolization sessions for the same lesion without an intervening follow-up CT; or (2) had a follow-up period of <6 months. Data on clinical history, physical examination, and PAVM characteristics were extracted from electronic medical records. Adverse events associated with the procedure during hospitalization and outpatient follow-up were also meticulously analyzed.

Embolization procedure

Vascular access was obtained via the right femoral vein, followed by intravenous administration of a heparin sodium bolus (3,000–5,000 IU; JW Pharmaceutical, Seoul, Korea). Subsequent pulmonary angiography facilitated the selective catheterization of the juxta-sac feeding artery using a coaxial system composed of a 6-Fr guiding catheter (Flexor Shuttle Guiding Sheath; Cook Medical, Bloomington, IN, USA) and a 5-Fr diagnostic catheter (Torcon NB Advantage, MPA; Cook Medical, or Glidecath, Angled Taper; Terumo, Tokyo, Japan). In cases involving challenging navigation due to small tortuous feeders, a triaxial system was employed, which included a 1.98-Fr microcatheter (Masters Parkway Soft; Asahi Intecc, Tokyo, Japan). The procedure began with the microcatheter, followed by the advancement of a 5-Fr hydrophilic-coated catheter over it. The size of the AVP4 (Abbott, Plymouth, MN, USA) ranged from 30% to 300% oversizing, based on preprocedural CT and selective angiography findings. The AVP4 was advanced into position within the 5-Fr catheter by pushing the guidewire to the catheter tip, and then the catheter was withdrawn to deploy the device. Proper placement of the plug was verified by injecting a contrast medium through the guiding catheter; if necessary, the plug was recaptured, repositioned, and redeployed. Depending on the operator's preference, additional coil embolization was performed occasionally to expedite flow cessation and provide reinforcement. Complete cessation of PAVM flow was confirmed in all patients through the completion of the digital subtraction angiography (DSA).

Acquisition and protocol for computed tomography and follow-up digital subtraction angiography

Initial and follow-up CT scans were primarily conducted using contrast-enhanced CT with multidetector-row scanners (Revolution EVO, Optima CT660, LightSpeed16; GE Healthcare, Chicago, IL, USA; SOMATOM Force, SOMATOM Definition Edge; Siemens Healthineers, Erlangen, Germany). For these examinations, a contrast agent (80–100 mL) was intravenously injected at a rate of 1.5–2 mL/s. CT images targeting the area of interest were reconstructed with a slice thickness of 2.5 mm in both transverse and coronal orientations. Follow-up CT scans were scheduled at 6 and 12 months post-embolization and subsequently every 2–3 years to monitor the persistence or resolution of PAVMs.[19]

DSA was conducted on previously treated PAVMs, particularly in cases in which multiple PAVMs were treated across separate sessions. The procedure typically began with either right or left pulmonary angiography, utilizing an injector with injection rates of 10–15 mL/s and volumes of 20–30 mL per injection. For more detailed assessments, selective angiography was performed at the segmental pulmonary artery levels, using injection rates of 3–5 mL/s and volumes of 9–15 mL. In certain instances, more precise visualization was achieved through meticulous manual injections at the distal levels of the pulmonary arteries.

Imaging analysis

All imaging obtained before, during, and following AVP4 embolization was reviewed by two experienced cardiovascular radiologists who were blinded to the outcomes of

PAVM embolization. Discrepancies between radiologists were resolved by consensus.

The analysis included reviewing the location, multiplicity, complexity (categorized as simple vs. complex), and original vessel diameters, along with their changes (feeding artery, venous sac, and draining vein) between the initial and final post-procedural CT scans. Changes in vessel diameter were quantified as reduction rates and recorded separately. Additionally, the origin of the last normal branch of the pulmonary artery was documented on the initial CT and during procedural DSA,[20] and the embolization location relative to this branch (either proximal or distal) was confirmed on post-procedural CT. The distance from the plug to the sac was also evaluated using pre- and post-procedural CT scans.

During the procedural imaging of AVP4 embolization, the size and number of plugs, the plug oversizing ratio, the type and number of additional coils, and the procedure time were all documented. Technical success was defined as the complete cessation of flow in the PAVM upon completion of the DSA. Treatment outcomes were assessed using the widely accepted CT criteria, where occlusion was defined as a 70% reduction in the venous sac in pre- and post-procedure comparisons (referred to as the 70% CT criteria).[21] Persistence was noted when the reduction rate of the venous sac was less than 70%. Procedure time was recorded from the femoral vein puncture to the completion of angiography, exclusively for sessions treating a single PAVM to ensure accurate assessment.

Adverse events were classified according to the Society of Interventional Radiology standards.[22] Both peri-procedural and post-procedural adverse events were documented for each embolization session.

To investigate factors affecting persistence, variables such as sex, age, smoking history, use of antithrombotic agents, lobar location, complexity, multiplicity, feeding artery diameter, venous sac diameter, plug oversizing ratio, sac-to-plug distance, embolization location relative to the last normal branch, and additional coil embolization were evaluated.

Angiographically confirmed cases by follow-up DSA were analyzed to determine patterns of persistence. Persistence was classified as resulting from (a) recanalization of a previously treated feeding artery, (b) reperfusion via adjacent pulmonary artery collaterals, or (c) the presence of a previously unrecognized feeder (incomplete treatment).[7] Reperfusion from systemic arteries was not assessed.

Statistical analysis

Continuous variables were expressed as the mean and range, whereas categorical variables were reported as the frequency (percentage). Multivariate logistic regression analysis was performed to identify factors affecting persistence using odds ratios (OR) and confidence intervals (CI). This analysis utilized the R software package (version 4.0.3, The R Foundation for Statistical Computing, Vienna, Austria). Variables that achieved a P value of <0.20 in the univariate analysis were selected as input variables for the multivariate analysis, which was conducted using a backward stepwise method. A P value of <0.05 was considered statistically significant.

Results

Fifty-one patients [48 women and 3 men; mean age: 50.8 years (range: 16–71)] with 103 PAVMs met the inclusion criteria and were included in the analysis (Figure 1). Among these patients, 9 (17.6%) exhibited symptoms of hereditary hemorrhagic telangiectasia, and 22 (43.1%) presented with symptoms attributable to PAVM. Sixteen patients (31.3%) had multiple PAVMs, averaging 2.26 lesions per patient (range: 1–10). Of the 103 PAVMs analyzed, 97 (94.2%) were classified as simple, with the remaining identified as complex. The mean diameter of the feeding arteries was 3.00 mm (range: 1.50–5.70 mm). The mean follow-up period was 556 days (range: 181–3,542 days). The characteristics of the patients and the PAVMs are summarized in Table 1.

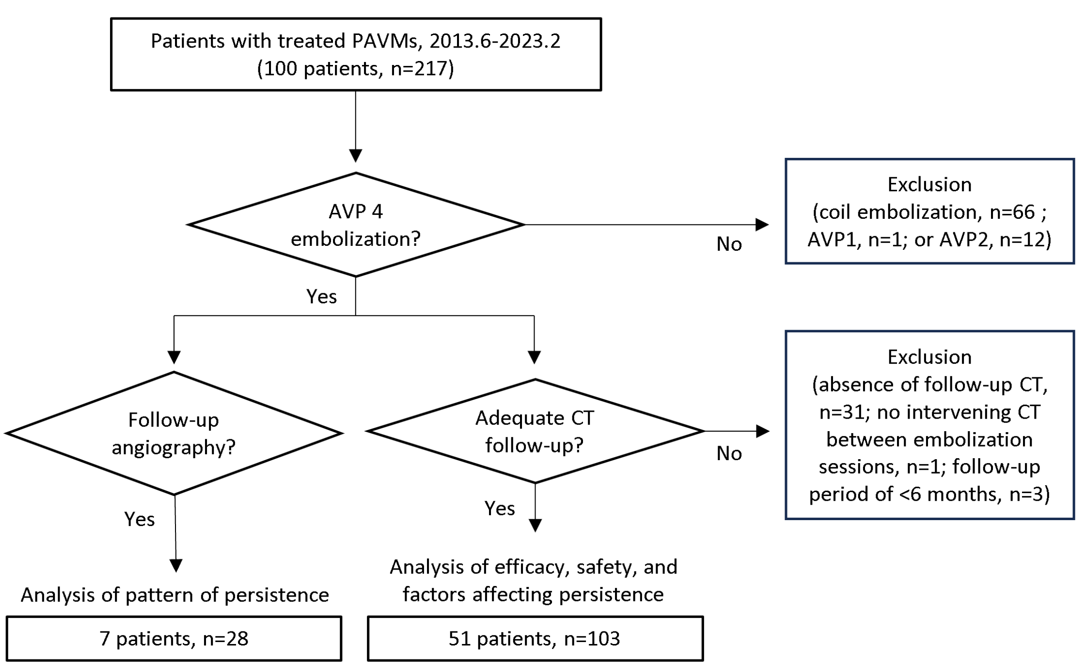

Figure 1. Flow chart summarizing patient enrollment according to study eligibility criteria. PAVM, pulmonary arteriovenous malformation; AVP, amplatzer vascular plug; CT, computed tomography.

All 103 PAVMs were successfully treated with AVP4 embolization across 59 sessions (Figure 2). On average, 1.75 PAVMs were treated per session (range: 1–8). The mean size and number of AVP4 devices used per PAVM were 6.34 mm and 1.09, respectively. Additional coils were used in 9 PAVMs (8.7%), with an average of 2.89 coils per PAVM (range: 1–5). The mean procedure time for sessions treating a single PAVM was approximately 39.62 minutes (range: 18–96 minutes). Details of the AVP4 embolization procedures are summarized in Table 2.

Table 1. Patient demographics and characteristics of pulmonary arteriovenous malformation

Parameters	Value
Patient factor (n = 51)	
Sex (men/women)	3 (5.8)/48 (94.2)
Mean age (range) in years	50.8 (16–71)
Presence of HHT symptoms	9 (17.6)
Symptomatic patients	22 (43.1)
Respiratory	11 (21.6)
Stroke	8 (15.7)
Brain abscess	4 (7.8)
Smoking history	8 (15.7)
Use of antithrombotic agents	9 (17.6)
Multiple PAVMs	16 (31.3)
Mean number of PAVMs per patient (range)	2.26 (1–10)
PAVM factor (n = 103)	
Simple/complex	97 (94.2)/6 (5.8)
Lobar location	
RUL/RML/RLL	16 (15.5)/27 (26.2)/20 (19.4)
LUL/LLL	16 (15.5)/24 (23.3)
Mean feeding artery diameter (range) (mm)	3.00 (1.50–5.70)
<2 mm	12 (11.7)
<3 mm, ≥2 mm	54 (52.4)
<6 mm, ≥3 mm	37 (35.9)
Mean venous sac diameter (range) (mm)	6.91 (2.40–22.25)
Origin of last normal branch	
Sac/junction/proximal feeding artery	27 (26.2)/41 (39.8)/35 (34)
Mean follow-up periods (range) (day)	556 (181–3542)

Data represent the number of patients or PAVMs, with percentages in parentheses unless specified otherwise. HHT, hereditary hemorrhagic telangiectasia; PAVMs, pulmonary arteriovenous malformations; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

Table 2. Details of AVP4 embolization (59 sessions for 103 pulmonary arteriovenous malformations)

Embolization factor (n = 103)	Value
Mean number of AVP4 per PAVM (range)	1.09 (1–2)
Mean size of AVP4 (range) (mm)	6.34 (4–8)
Mean plug oversizing ratio (range) (%)	122.4 (35–300)
Mean plug-to-sac distance (range) (mm)	3.90 (0–26.0)
>10 mm	12 (11.7%)
≤10 mm	91 (88.3%)
Embolization location relative to the last normal branch	
Proximal	47 (45.6%)
Distal	56 (54.4%)
Additional coil embolization	9 (8.7%)
Mean number of additional coils (range)	2.88 (1–5)

Data represent the number of PAVMs with percentages in parentheses unless specified otherwise. PAVM, pulmonary arteriovenous malformation; AVP4, Amplatzer Vascular Plug 4.

The technical success rate for AVP4 embolization was 100%. The persistence rate of the treated PAVMs, using the 70% CT criteria, was 9.7% (10/103). Stratified by embolization type, the persistence rates were 9.6% (9/94) for AVP4 alone and 11.1% (1/9) for AVP4 combined with coil embolization. During the 59 sessions for 103 PAVMs, three mild adverse events were reported (5.1% per session): two instances of self-limiting pleuritic chest pain and one case of transient bradycardia. There were no severe adverse events, with an overall adverse event rate of 2.9% per PAVM lesion.

Follow-up DSA was conducted for 28 (27.2%) of the 103 PAVMs at a mean interval of 436 days. Among these, occlusion was observed in 26 PAVMs, whereas the remaining 2 (7.1%) exhibited persistence due to reperfusion via adjacent pulmonary artery collaterals (Figure 3). When comparing outcomes between DSA and the 70% CT criteria, 25 out of 26 angiographically occluded PAVMs showed venous sac reductions exceeding 70% on CT, resulting in concordant findings. However, one PAVM demonstrated a reduction rate of 57.3%, leading to discordance between the two modalities. The two angiographically reperfused PAVMs showed venous sac reductions of 34.7% and 49.2%, respectively, aligning the findings across both modalities.

In both univariate and multivariate analyses, the location of embolization relative to the last normal branch of the pulmonary artery was identified as the only significant factor affecting persistence (OR: 0.18; 95% CI: 0.03–0.81; $P < 0.05$) (Table 3).

Discussion

The findings of this study affirm the efficacy and safety of AVP4 embolization for small- to medium-sized PAVMs with diameters of <6 mm, showing a persistence rate of 9.7% (10/103) based on the 70% CT criteria and an overall adverse event rate of 2.9% during an average follow-up period of 556 days. Follow-up DSA, conducted in 27.1% of this cohort, revealed persistence in 2 PAVMs, predominantly due to reperfusion via adjacent pulmonary artery collaterals. The location of embolization relative to the last normal branch of the pulmonary artery was identified as the only substantial factor affecting persistence according to the CT criteria.

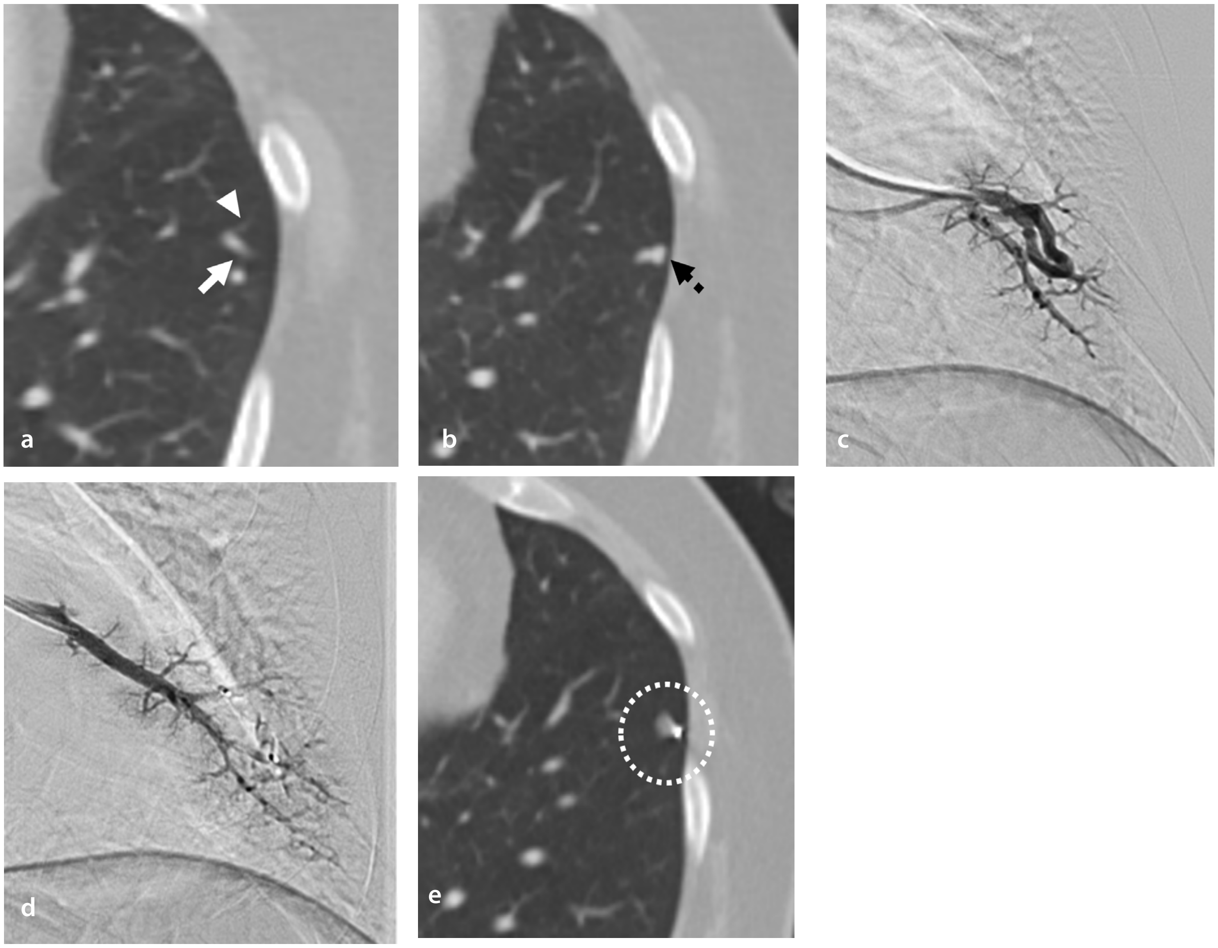

Figure 2. A 51-year-old woman with an incidentally detected simple pulmonary arteriovenous malformation (PAVM). **(a, b)** Pre-embolization computed tomography (CT) images show the distal feeding artery and venous sac of a simple PAVM located in the left lower lobe (LLL). The vessel diameters are as follows: feeding artery (arrow in **a**), 1.53 mm, and venous sac (dotted arrow in **b**), 3.63 mm. The last normal branch of the pulmonary artery (arrowhead in **a**) is identified within the junction between the feeding artery and the sac. **(c)** Angiography conducted after selecting the distal feeding artery shows a simple PAVM in the LLL. **(d)** Completion angiography following the deployment of a 6 mm Amplatzer Vascular Plug 4 (AVP4) in the juxta sac-feeding artery shows complete occlusion of the PAVM with no residual shunt flow. Notably, the embolization location is distal to the last normal branch of the pulmonary artery. **(e)** A CT scan performed at a 2-year follow-up shows the disappearance of the venous sac (dotted circle), with a venous sac reduction rate of 100%. Only AVP4 is visible.

Various generations of AVPs have been employed for PAVM embolization, with reported persistence rates ranging from 0% to 16%.[9,10,15,18,23-25] Some studies have suggested superior outcomes with AVP compared with coils.[26,27] Nonetheless, there remains a scarcity of studies specifically focusing on AVP4. Rabellino et al.[18] defined a successful outcome as a venous sac reduction of ≥30% in their early experience with 7 patients, achieving success across all cases over an average follow-up of 20.1 months. A more recent study in 2019[10] involving 19 PAVMs reported a persistence rate of 16% using 70% CT criteria over an average follow-up of 14 months. Ratnani et al.[15] specifically analyzed AVP4 and reported a persistence rate of 12.5% (1/8) over an average follow-up of 1,239 days, defining persistence based on sustained sac perfusion observed in CT angiography (CTA) or pulmonary angiography. While the outcomes of these small case series generally align with those of the current study, varying assessment criteria make precise comparisons challenging.

Pulmonary angiography is considered the gold standard, but it poses difficulties for routine use due to its invasiveness.[19] The use of sac perfusion on CTA to assess persistence raises concerns about retrograde venous filling from adjacent normal branches.[13] Presently, the 70% CT criteria are the most widely adopted, yet recent discussions highlight concerns regarding their specificity.[13,28,29] Additional research and consensus are necessary to refine and agree on criteria that address these concerns effectively.

The recently introduced MVP has demonstrated superior results compared with the AVP, boasting a low persistence rate of 0%–6%.[11,12,15,30] AVP, composed of a finely braided nitinol mesh, exhibits several structural challenges in comparison to MVP, which features a polytetrafluoroethylene (PTFE)-covered nitinol cage. Particularly, introducing a 5-Fr catheter up to the juxta-sac feeding artery in cases of very small or tortuous feeding arteries can be technically challenging compared with using a 2.4- or 2.8-Fr microcatheter, as utilized with MVP. In our practice, we often overcome this challenge by using a hydrophilic-coated 5-Fr catheter (Glidecath, Angled Taper; Terumo) with appropriate angulation and advancing it over the microcatheter.

A concern exists that AVP4 may become lodged within this soft and flexible 5-Fr catheter during delivery. To address this issue, we primarily employ smaller-sized AVP4s (4–6 mm) -adequate for most small-sized feeding arteries- and advance a 6-Fr guiding

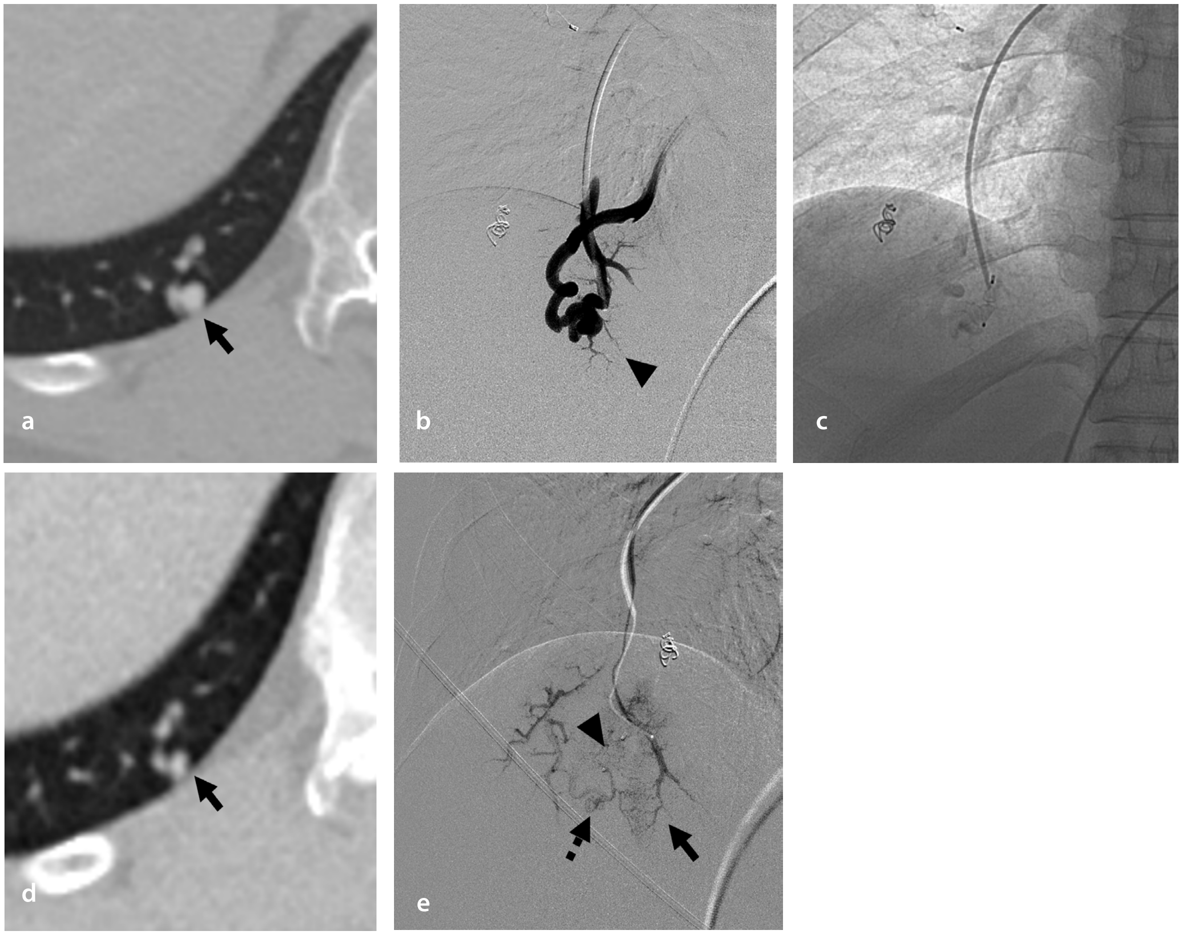

Figure 3. A 57-year-old woman with definite hereditary hemorrhagic telangiectasia and multiple pulmonary arteriovenous malformations (PAVM) (at least 6) in both lungs. **(a)** Pre-embolization computed tomography (CT) image shows a simple PAVM in the right lower lobe. The vessel diameters are as follows: feeding artery, 3.12 mm, and venous sac (arrow), 4.75 mm. **(b)** Angiography conducted after superselecting the distal feeding artery shows a simple PAVM. The last normal branch of the pulmonary artery is identified within the venous sac (arrowhead). **(c)** A 5 mm Amplatzer Vascular Plug 4 is deployed in the juxta sac-feeding artery of the PAVM. Notably, the embolization location is proximal to the last normal branch of the pulmonary artery. **(d)** CT performed at the 3-year follow-up shows a reduction in the diameter of the venous sac (arrow) to 3.1 mm, representing a reduction rate of 34.7%. **(e)** Subsequent angiography shows successful occlusion of the previously treated feeding artery (arrowhead). However, contrast opacification of the venous sac (dotted arrow) is observed due to reperfusion via adjacent pulmonary artery collateral (arrow).

catheter as distally as possible to provide support while routinely performing continuous saline flushing in the catheter to minimize friction between the plug and catheter wall. Furthermore, unlike MVP, which induces immediate flow cessation due to its PTFE cover, AVP4 relies on inducing thrombosis through its nitinol mesh, requiring patience and repeated monitoring for occlusion. The patient's coagulation status may influence this process and raise concerns about the potential migration of *in-situ* thrombus on the device surface, leading to paradoxical embolism.[16,17] To mitigate these risks, we employ a strategy of reinforcement with several additional coils if flow cessation is not achieved within 5–10 minutes or by confirming flow cessation collectively after completing treatment for all PAVMs in cases of multiple PAVMs to save time. Consequently, we achieved a relatively short procedure time (mean: 39.62 minutes), and no procedure-related paradoxical embolisms were reported.

On the financial side, AVP4 offers a more cost-effective alternative than MVP. The mean number of AVP4 devices used in this study, 1.1 per PAVM, is comparable to the 1.1–1.3 used in previous MVP studies[11,12] despite the substantially higher cost of the MVP device.[15] Additionally, the routine use of a microcatheter for MVP delivery adds to overall expenses. While MVP has not yet received approval for use in many countries, including ours, AVP4 remains a favorable option in centers where it is available, offering both clinical efficacy and cost-effectiveness.

In this cohort, the majority of PAVMs featured small-sized feeding arteries, with 64.1% measuring less than 3 mm and 11.7% measuring less than 2 mm. Stein et al.[6] reported on coil embolization for 141 PAVMs with feeding arteries smaller than 3 mm; the persistence rate noted was 21%, which is higher than the 10% reported in other studies targeting PAVMs with feeding arteries of 3 mm or larger. However, in our study, there was no substantial difference in persistence rates between PAVMs with feeding arteries of 3 mm or smaller (9.4%) and those larger than 3 mm (10.3%). This outcome may highlight the advantage of AVP4 over coils, as AVP4 allows for sufficient oversizing and smooth delivery if the catheter reaches the target vessel, regardless of vessel size. In the case of the MVP, there are reports of successful treatments for feeding arteries as small as 1.3 mm;[12] however, there is a lack of studies focusing on small PAVMs or evaluating long-term outcomes. Under these circumstances, AVP4 emerges as a favorable treatment option for small PAVMs.

Table 3. Univariate and multivariate analyses of factors affecting persistence based on 70% CT criteria

Factors	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Sex			0.025			0.120
Men	1.00	Reference		1.00	Reference	
Women	0.15	0.03, 0.86		0.25	0.04, 1.56	
Age	0.96	0.91, 1.00	0.069	Stepwise eliminated		
Smoking history			0.773			
Yes	1.00	Reference				
No	1.23	0.32, 5.99				
Antithrombotic agent			0.632			
Yes	1.00	Reference				
No	1.69	0.28, 32.61				
Multiplicity			0.373			
Single	1.00	Reference				
Multiple	2.08	0.49, 14.31				
Complexity			0.460			
Simple	1.00	Reference				
Complex	2.43	0.11, 21.23				
Lobar location			0.163	Stepwise eliminated		
Upper or middle lobe	1.00	Reference				
Lower lobe	2.54	0.71, 10.40				
Feeding artery diameter	1.30	0.58, 2.75	0.501			
Venous sac diameter	0.99	0.80, 1.16	0.889			
Sac to plug distance	1.10	0.99, 1.22	0.067	Stepwise eliminated		
Plug oversizing ratio	1.00	0.98, 1.01	0.751			
Additional embolization			0.903			
Yes	1.00	Reference				
No	1.11	0.25, 7.75				
Location of embolization			0.018			0.041
Proximal to LNB	1.00	Reference		1.00	Reference	
Distal to LNB	0.14	0.02, 0.61		0.18	0.03, 0.81	

OR, odds ratio; CI, confidence interval; LNB, last normal branch of pulmonary artery.

After coil embolization, recanalization through a previously treated feeder is the predominant persistence pattern, reported to exceed 90%.[7] Factors such as coil packing density, the use of oversized coils, and the distance between the coil and the venous sac have been identified as substantial factors affecting persistence rates.[6,31,32] In a recent study by Shimohira et al.[13], the location of embolization relative to the last normal branch of the pulmonary artery was determined to be a substantial factor in persistence, as assessed by CT, time-resolved MR angiography, and DSA. However, similar detailed studies focusing on AVP are lacking.

In this study, reperfusion via adjacent pulmonary artery collaterals was observed in both cases where angiographically confirmed persistence occurred, specifically when proximal embolization was performed because the last normal branch was within the sac. This location was the only substantial factor affecting persistence. In this reperfusion mechanism, the shunt or feeder size is usually very small, rendering additional treatment technically challenging and generally less successful than the recanalization pattern.[7,8] Although this study highlighted the excellent cross-sectional occlusion capabilities of AVP4, achieving complete prevention of persistence in PAVMs where the last normal branch is located within the sac may ultimately require sac embolization.[13,20,33] There are documented cases in which successful outcomes were achieved through venous sac coiling combined with feeding artery plug embolization in such scenarios.[34] Nonetheless, further studies involving a larger cohort are necessary to validate these findings and refine treatment protocols.

Some limitations of this study should be acknowledged. First, it was a retrospective study with a relatively small sample size. Second, owing to the widespread availability of chest CT scans and health screenings, most patients in the study presented with incidentally detected simple PAVMs. Given that treatment outcomes are less favorable for complex PAVMs, the persistence rate of these malformations may have been underestimated. Moreover, follow-up DSA was performed only in patients with multiple PAVMs, which introduced potential bias. Additionally, reperfusion via the systemic artery was not evaluated. Lastly, an important variable related to the use of AVP -occlusion time- was not measured.

In conclusion, AVP4 embolization proved to be safe and effective for treating small- to medium-sized PAVMs (<6 mm), demonstrating a low persistence rate based on the 70% CT criteria. The primary pattern observed in angiographically confirmed persistence was reperfusion via adjacent pulmonary artery collaterals. Concerning treatment outcomes based on CT criteria, the only factor affecting persistence was the location of the embolization relative to the last normal branch of the pulmonary artery.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Majumdar S, McWilliams JP. Approach to pulmonary arteriovenous malformations: a comprehensive update. *J Clin Med*. 2020;9(6):1927. [CrossRef]
2. White RI Jr, Pollak JS, Wirth JA. Pulmonary arteriovenous malformations: diagnosis and transcatheter embolotherapy. *J Vasc Interv Radiol*. 1996;7(6):787-804. [CrossRef]
3. Trerotola SO, Pyeritz RE, Bernhardt BA. Outpatient single-session pulmonary arteriovenous malformation embolization. *J Vasc Interv Radiol*. 2009;20(10):1287-1291. [CrossRef]
4. Todo K, Moriwaki H, Higashi M, Kimura K, Naritomi H. A small pulmonary arteriovenous malformation as a cause of recurrent brain embolism. *AJNR Am J Neuroradiol*. 2004;25(3):428-430. [CrossRef]
5. Müller-Hülsbeck S, Marques L, Maleux G, et al. CIRSE standards of practice on diagnosis and treatment of pulmonary arteriovenous malformations. *Cardiovasc Intervent Radiol*. 2020;43(3):353-361. [CrossRef]
6. Stein EJ, Chittams JL, Miller M, Trerotola SO. Persistence in coil-embolized pulmonary arteriovenous malformations with feeding artery diameters of 3 mm or less: a retrospective single-center observational study. *J Vasc Interv Radiol*. 2017;28(3):442-449. [CrossRef]
7. Woodward CS, Pyeritz RE, Chittams JL, Trerotola SO. Treated pulmonary arteriovenous malformations: patterns of persistence and associated retreatment success. *Radiology*. 2013;269(3):919-926. [CrossRef]
8. Shimohira M, Kawai T, Hashizume T, et al. Reperfusion rates of pulmonary arteriovenous malformations after coil embolization: evaluation with time-resolved MR angiography or pulmonary angiography. *J Vasc Interv Radiol*. 2015;26(6):856-864. [CrossRef]
9. Letourneau-Guillon L, Faughnan ME, Soulez G, et al. Embolization of pulmonary arteriovenous malformations with amplatzer vascular plugs: safety and midterm effectiveness. *J Vasc Interv Radiol*. 2010;21(5):649-656. [CrossRef]
10. Lee SY, Lee J, Kim YH, et al. Efficacy and Safety of Amplatzer Vascular Plug Type IV for embolization of pulmonary arteriovenous malformations. *J Vasc Interv Radiol*. 2019;30(7):1082-1088. [CrossRef]
11. Bailey CR, Arun A, Towsley M, et al. MVP™ micro vascular plug systems for the treatment of pulmonary arteriovenous malformations. *Cardiovasc Intervent Radiol*. 2019;42(3):389-395. [CrossRef]
12. Mahdjoub E, Tavolaro S, Parrot A, Cornelis F, Khalil A, Carette MF. Pulmonary arteriovenous malformations: safety and efficacy of microvascular plugs. *AJR Am J Roentgenol*. 2018;211(5):1135-1143. [CrossRef]
13. Shimohira M, Kiyosue H, Osuga K, et al. Location of embolization affects patency after coil embolization for pulmonary arteriovenous malformations: importance of time-resolved magnetic resonance angiography for diagnosis of patency. *Eur Radiol*. 2021;31(7):5409-5420. [CrossRef]
14. Hayashi S, Baba Y, Senokuchi T, Nakajo M. Efficacy of venous sac embolization for pulmonary arteriovenous malformations: comparison with feeding artery embolization. *J Vasc Interv Radiol*. 2012;23(12):1581. [CrossRef]
15. Ratnani R, Sutphin PD, Koshti V, et al. Retrospective comparison of pulmonary arteriovenous malformation embolization with the polytetrafluoroethylene-covered nitinol microvascular plug, Amplatzer plug, and coils in patients with hereditary hemorrhagic telangiectasia. *J Vasc Interv Radiol*. 2019;30(7):1089-1097. [CrossRef]
16. Lopera JE. The Amplatzer vascular plug: review of evolution and current applications. *Semin Intervent Radiol*. 2015;32(4):356-369. [CrossRef]
17. Wang W, Li H, Tam MD, Zhou D, Wang DX, Spain J. The amplatzer vascular plug: a review of the device and its clinical applications. *Cardiovasc Intervent Radiol*. 2012;35(4):725-740. [CrossRef]
18. Rabellino M, Serra M, Peralta O, et al. Early experience with the Amplatzer vascular plug IV for the occlusion of pulmonary arteriovenous malformations. *J Vasc Interv Radiol*. 2014;25(9):1333-1337. [CrossRef]
19. Faughnan ME, Mager JJ, Hetts SW, Palda VA, Ratjen F. Second International Guidelines for the Diagnosis and Management of Hereditary Hemorrhagic Telangiectasia. *Ann Intern Med*. 2020;173(12):989-1001. [CrossRef]
20. Maruno M, Kiyosue H, Hongo N, Matsumoto S, Mori H. Where is the origin of the last normal branch from feeding artery of pulmonary arteriovenous malformations? *Cardiovasc Intervent Radiol*. 2018;41(12):1849-1856. Erratum in: *Cardiovasc Intervent Radiol*. 2019;42(10):1510. [CrossRef]
21. Lee DW, White RI Jr, Egglin TK, et al. Embolotherapy of large pulmonary arteriovenous malformations: long-term results. *Ann Thorac Surg*. 1997;64(4):930-940. [CrossRef]
22. Khalilzadeh O, Baerlocher MO, Shyn PB, et al. Proposal of a new adverse event classification by the Society of Interventional Radiology Standards of Practice Committee. *J Vasc Interv Radiol*. 2017;28(10):1432-1437. Erratum in: *J Vasc Interv Radiol*. 2018;29(1):146. [CrossRef]
23. Hart JL, Aldin Z, Braude P, Shovlin CL, Jackson J. Embolization of pulmonary arteriovenous malformations using the Amplatzer vascular plug: successful treatment of 69 consecutive patients. *Eur Radiol*. 2010;20(11):2663-2670. [CrossRef]
24. Kucukay F, Özdemir M, Şenol E, Okten S, Ereren M, Karan A. Large pulmonary arteriovenous malformations: long-term results of embolization with Amplatzer vascular plugs. *J Vasc Interv Radiol*. 2014;25(9):1327-1332. [CrossRef]
25. Abdel Aal AK, Ibrahim RM, Moustafa AS, Hamed MF, Saddekni S. Persistence of pulmonary arteriovenous malformations after successful embolotherapy with Amplatzer vascular plug: long-term results. *Diagn Interv Radiol*. 2016;22(4):358-364. [CrossRef]
26. Andersen PE, Duvnjak S, Gerke O, Kjeldsen AD. Long-term single-center retrospective follow-up after embolization of pulmonary arteriovenous malformations treated over a 20-year period: frequency of re-canalization with various embolization materials and clinical outcome. *Cardiovasc Intervent Radiol*. 2019;42(8):1102-1109. [CrossRef]
27. Tau N, Atar E, Mei-Zahav M, et al. Amplatzer Vascular plugs versus coils for embolization of pulmonary arteriovenous malformations in patients with hereditary hemorrhagic telangiectasia. *Cardiovasc Intervent Radiol*. 2016;39(8):1110-1114. [CrossRef]
28. Hong J, Lee SY, Cha JG, et al. Pulmonary arteriovenous malformation (PAVM) embolization: prediction of angiographically-confirmed recanalization according to PAVM Diameter changes on CT. *CVIR Endovasc*. 2021;4(1):16. [CrossRef]
29. Belanger C, Chartrand-Lefebvre C, Soulez G, et al. Pulmonary arteriovenous malformation (PAVM) reperfusion after percutaneous

embolization: sensitivity and specificity of non-enhanced CT. *Eur J Radiol*. 2016;85(1):150-157. [CrossRef]

30. Latif MA, Bailey CR, Motaghi M, et al. Postembolization Persistence of pulmonary arteriovenous malformations: a retrospective comparison of coils and amplatzer and micro vascular plugs using propensity score weighting. *AJR Am J Roentgenol*. 2023;220(1):95-103. Erratum in: *AJR Am J Roentgenol*. 2023;220(1):155. [CrossRef]
31. Milic A, Chan RP, Cohen JH, Faughnan ME. Reperfusion of pulmonary arteriovenous malformations after embolotherapy. *J Vasc Interv Radiol*. 2005;16(12):1675-1683. [CrossRef]
32. Pollak JS, Saluja S, Thabet A, Henderson KJ, Denbow N, White RI Jr. Clinical and anatomic outcomes after embolotherapy of pulmonary arteriovenous malformations. *J Vasc Interv Radiol*. 2006;17(1):35-45. [CrossRef]
33. Nagai K, Osuga K, Kashiwagi E, et al. Venous sac and feeding artery embolization versus feeding artery embolization alone for treating pulmonary arteriovenous malformations: draining vein size outcomes. *J Vasc Interv Radiol*. 2021;32(7):1002-1008. [CrossRef]
34. Hundt W, Kalinowski M, Kiessling A, et al. Novel approach to complex pulmonary arteriovenous malformation embolization using detachable coils and Amplatzer vascular plugs. *Eur J Radiol*. 2012;81(5):732-738. [CrossRef]