


STANDARD ARTICLE

Transvenous embolization of moderate to large patent ductus arteriosus in dogs using the Amplatzer vascular plug II

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Abstract

Background: Catheter-based occlusion of patent ductus arteriosus (PDA) can be performed using different devices. Transvenous embolization using the Amplatzer vascular plug II (AVP-II) has been studied in humans, but it has not been described in dogs.

Objective: Evaluate the feasibility and success of transvenous embolization of PDA using the AVP-II in dogs.

Animals: Nineteen client-owned dogs with left-to-right shunting PDA, with minimal ductal diameter >2.5 mm.

Methods: Prospective observational study using AVP-II with transvenous access for PDA closure in dogs.

Results: Angiography showed a conical ductus with a long (n = 17) or short (n = 2) ampulla. The minimal diameter of the duct was 4.34 ± 1.11 mm, and the maximal diameter of the ampulla was 13.18 ± 3.47 mm. Technical success was achieved in 18 of the 19 (94.7%) patients after the first intervention and in all 19 (100%) patients after the second intervention. Postrelease angiography documented complete occlusion of the PDA in 10 of 19 (52.6%) dogs. Mild flow acceleration or stenosis of the left pulmonary artery was found in 6 and 1 of the 17 analyzed cases, respectively, by Doppler examination. The closure rate 24 hours after intervention was 94.7% (18/19). The remaining dog had a moderate residual shunt, and delayed complete closure after 3 months led to a 100% closure rate.

Conclusion and Clinical Importance: The AVP-II is a safe and effective device for transvenous embolization in dogs with moderate to large PDA.

KEYWORDS

catheter intervention, left pulmonary artery stenosis, PDA, shunt grading

Abbreviations: A1, dimension of the PDA ampulla in the middle; A2, maximal dimension of the PDA ampulla; ACDO, Amplatz canine duct occluder; ADO, Amplatzer duct occluder; AVP, Amplatzer vascular plug; CRI, continuous rate infusion; LPA, left pulmonary artery; LVDd-I, left ventricular internal diameter in diastole index; LVDs-I, left ventricular internal diameter in systole index; MDD, minimal ductal diameter; M-mode, motion-mode; MPA, main pulmonary artery; PDA, patent ductus arteriosus.

1 | INTRODUCTION

Patent ductus arteriosus (PDA) is a common congenital cardiac malformation in dogs.^{1,2} Left-to-right shunting in PDA leads to volume overload in the left heart and, potentially, congestive heart failure.

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Without correction, a high mortality rate is observed within the first year after diagnosis.¹ Interventional closure of this congenital defect has become an established procedure in dogs over the last 2 decades,²⁻⁶ and various types of coils or the Amplatzer canine duct occluder (ACDO) specifically designed for dogs have been used, but other occluders or plugs also have been described.

The different types of Amplatzer vascular plugs (AVPs; AVP I-IV) are self-expanding devices made of nitinol wire mesh with different prespecified shapes (AVP-I: single lobe; AVP-II: 3 lobes; AVP-III and -IV: bilobed). Amplatzer vascular plugs I and IV are single-layered meshes, whereas AVP-II and AVP-III are multilayered meshes. Different AVP types are primarily developed in human medicine for the closure of different peripheral vascular malformations.⁷⁻⁹ The first-generation Amplatzer vascular plug (AVP-I) also was utilized for PDA closure in human patients¹⁰⁻¹³ and in dogs,¹⁴⁻¹⁶ but was found not to be reliably occlusive because of the plug design, which lacks an internal fabric and has a single wire weave, especially in high-flow lesions. To improve its occlusive properties, AVP-II was woven more densely with a finer nitinol mesh in 2 to 3 layers.¹³ The AVP-II originally was developed for the occlusion of high-flow peripheral vessels such as arteriovenous malformations in human patients,⁷⁻⁹ but it also has been used successfully for interventional PDA closure in humans, mostly by a transvenous route. All morphological PDA types could be occluded with this device type,^{13,17,18} including the short and long conical PDA configurations, which are the most common forms in dogs.^{16,19-21} Our aim was to evaluate the feasibility and success of transvenous embolization of moderate to large PDA in dogs using the AVP-II.

2 | MATERIAL AND METHODS

The study design was a prospective observational cohort study.

2.1 | Animals

Client-owned dogs with left-to-right shunting PDA, body weight >3.0 kg and an angiographically determined minimal ductal diameter (MDD) >2.5 mm, defined as moderate to large PDA, were prospectively enrolled in the study. The owners provided written informed consent. Dogs with concurrent hemodynamically relevant congenital cardiac or systemic disorders were excluded from the study.

All dogs were assessed based on clinical history, physical examination, thoracic radiography, blood pressure measurement, electrocardiography, transthoracic echocardiography, CBC, serum biochemistry profile, and coagulation profile (fibrinogen measurement, thrombelastography). Echocardiographic examination before catheter intervention included a complete 2-dimensional, motion-mode (M-mode), and Doppler evaluation. Left ventricular internal diameter in diastole (LVDd) and systole (LVDs) were measured from the right parasternal long-axis view in M-mode, and the related indices (LVDd-I; LVDs-I) were calculated according to the allometric scaling method.²² The severity of PDA

shunting was classified into 4 categories using Doppler color flow examination: grade 1, minimal flow through the PDA at the entrance into the main pulmonary artery (MPA); grade 2, small jet into the MPA, which does not reach the pulmonic valve; grade 3, shunt reaching the pulmonic valve; and grade 4, color flow jet filling $\geq 50\%$ of the MPA. Mitral valve regurgitation was classified by color Doppler in 3 groups (mild, moderate, and severe).²³

2.2 | Device

Amplatzer vascular plug II (Figure 1) is a 3-lobed nitinol mesh, with the wire braided in 2 layers in small devices and 3 layers in devices >10 mm in diameter. It is available with diameters of 3 mm, 4 mm, and above in 2-mm increments up to 22 mm, with a length between 6 and 18 mm. Depending on the size, it is deployed through a 4-7 F sheath or 5-9 F guiding catheter (specific descriptions are available in the guidance manual). Similar to other Amplatzer devices, it has a proximal microscrew to permit attachment to a delivery wire.

2.3 | Catheter intervention

All procedures were performed by a board-certified veterinary cardiologist or resident under direct supervision. General anesthesia was induced by IV combination of levomethadonhydrochloride with fentanyl hydrochloride (0.5 mg/kg) and diazepam (0.5 mg/kg) and maintained with isoflurane (1.7%-2.0%) in 21% oxygen after intubation. In 4 dogs with pulmonary edema and low arterial oxygenation, 50% oxygen was used. All dogs with arrhythmias ($n = 6$) during the basic preprocedure examination were treated with lidocaine (2 mg/kg bolus; 50 $\mu\text{g}/\text{kg}/\text{min}$ constant rate infusion [CRI]). The dogs were placed in right lateral recumbency. Vascular access to the right femoral artery (4-5 F sheath)

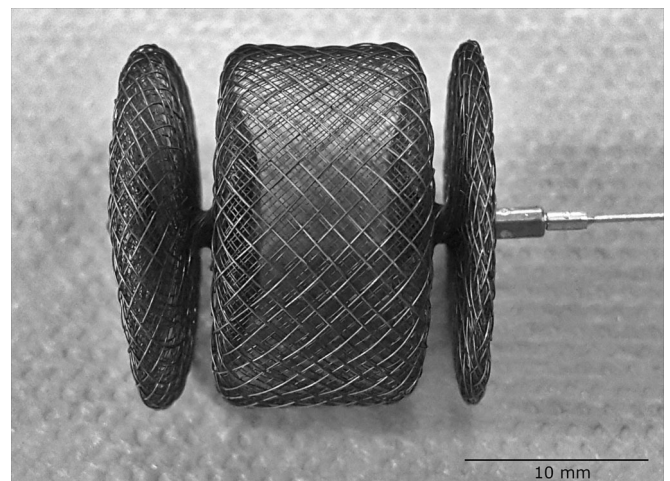


FIGURE 1 Amplatzer vascular plug II (AVP-II): the device is composed of a densely woven nitinol mesh. It has a cylindrical central component and flat disks at each end. The device is attached to the delivery wire by a microscrew

and femoral vein (6-9 F sheath) were obtained percutaneously using a modified Seldinger technique. All patients received unfractionated heparin (100 U/kg IV) at the beginning of the procedure. Angiography was performed with lateral projection by injecting approximately 0.9-1.2 mL/kg of iodinated contrast medium (300 mg iodine/mL) within 1 second into the cranial descending aorta through a 4-5 F pigtail catheter using an automatic injector (Figure 2A). Angiography was digitally recorded at 25 frames/s. Patent ductus arteriosus morphology was classified into 5 types (A-E), as previously described.^{21,24} The magnitude of the angiographic PDA shunt was judged according to a classification scheme used in humans (trace shunt, grade 1; small shunt, grade 2; moderate shunt, grade 3; large shunt, grade 4).²⁵ The dimensions of the PDA were measured in diastole, with magnification correction against a radiopaque scale catheter (Occlu-Marker; pfm medical AG, Köln, Germany) in the esophagus. The measurements consisted of MDD, width of the ampulla in the middle part (A1), maximal ampulla width (A2), and length of the PDA in the midline (Figure 2B).

The AVP-II primarily selected was at least 2 times larger than the MDD and at least 20% larger than the maximal ampulla diameter (A2). In cases with a short PDA or an extremely wide ampulla, an oversizing factor of at least 10% was used.

Aortic pressure was measured proximal and distal to the PDA using a pigtail-type catheter. Right heart catheterization was performed (right atrium, right ventricle, main pulmonary artery, left pulmonary artery [LPA]) with pressure recordings using a 5-F wedge catheter (Arrow Balloon wedge-Pressure catheters; Teleflex Medical GmbH, Fellbach, Germany). For 15 dogs at room air (21% oxygen), blood gas analyses were performed in the right atrium (near the

tricuspid valve), LPA, and ascending aorta followed by shunt calculation using the Fick formula.

A 5-F open-ended catheter with MPA configuration (HN5.0-NT-100-PW-NS-MPA; Cook Deutschland GmbH, Mönchengladbach, Germany) was placed through the femoral vein access site over a 0.018-in guide wire into the MPA. The PDA was crossed retrograde through the MDD into the ampulla using a 0.035-in straight soft guidewire (Terumo Glidewire 0.0035, 260 cm; Terumo, Eschborn, Germany), and the guidewire was exchanged for a stiff type. The catheter was changed to an adequately sized guiding catheter (Vista Brite Tip Multipurpose 6-9 F; Cordis, Norderstedt, Germany). The AVP-II was attached to the delivery wire and introduced through a Y-connector. The device was advanced carefully until the distal disc and central component were expanded into the descending aorta near the ductus. The guiding catheter and device delivery wire were pulled back simultaneously, and the device was placed into the PDA ampulla. The guiding catheter then was retracted while slightly pushing the delivery wire, allowing expansion of the proximal disk into the MPA without tension on the device. Correct position of the device was evaluated by prerelease aortography using the pigtail-type catheter by injecting approximately 0.9-1.2 mL/kg of contrast medium within 1 second into the cranial descending aorta (Figures 3 and 4). The position of the device was analyzed and corrected if necessary. Shunt grading was performed as described above. Independent of this result, the AVP-II device was detached by counterclockwise rotation of the delivery wire.

After 5-10 minutes, postrelease aortic angiography was performed in the same manner as before (Figure 5), and the amount of residual PDA flow was classified. Pressure recordings were performed

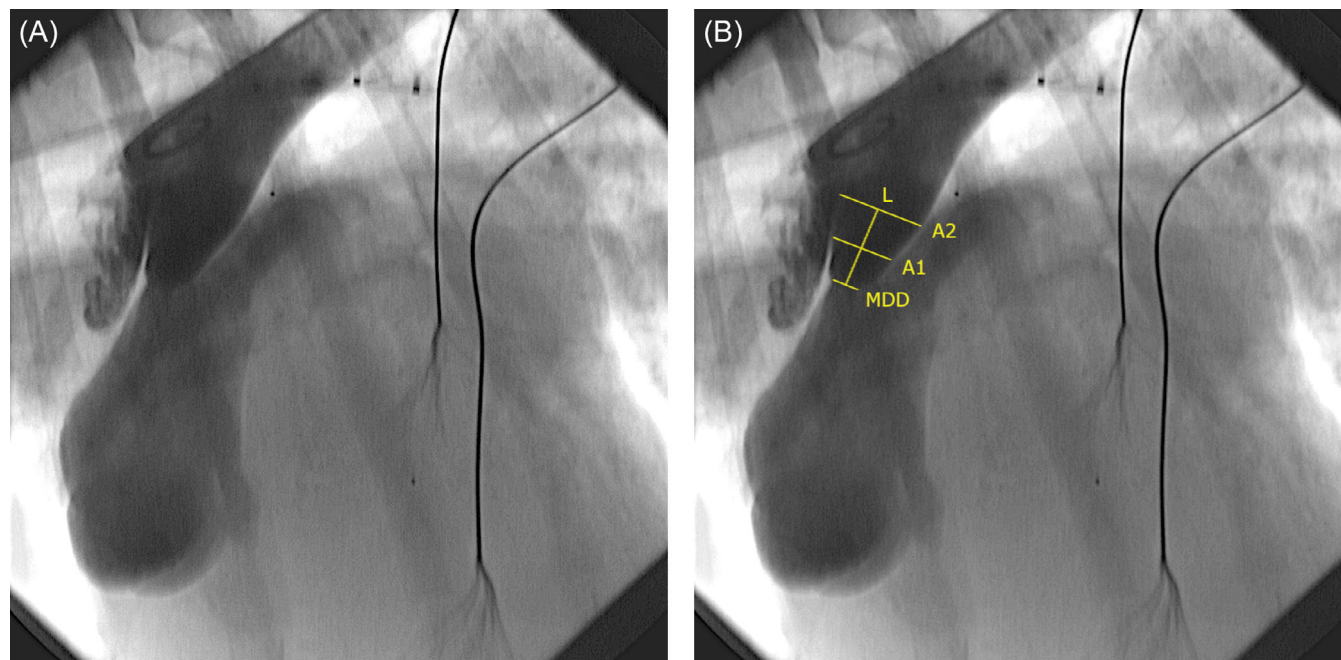


FIGURE 2 Angiography and measurement of the patent ductus arteriosus (PDA): (A) contrast injection done with a 5-F pigtail catheter into the cranial aspect of the descending aorta, showing a long conical ductus; (B) measurements were performed during diastole with a marker catheter in the esophagus, namely, the minimal PDA diameter (MDD), width at the midportion of the ampulla (A1), maximal ampulla width (A2) and length (L) of the PDA

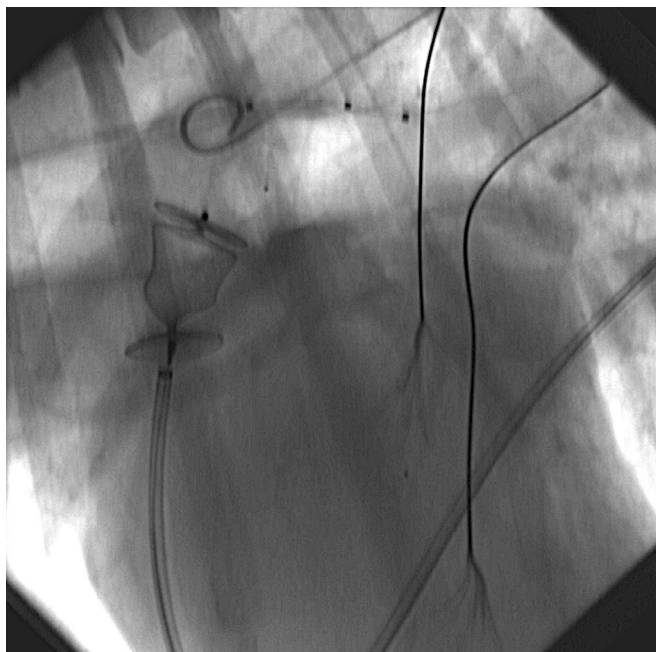


FIGURE 3 Prerelease fluoroscopy: Amplatzer vascular plug II (AVP-II) is positioned with two lobes into the patent ductus arteriosus (PDA) ampulla and one into the main pulmonary artery (MPA) and is still connected to the delivery wire. The middle lobe of the device is conically shaped, implying a good contact to the wall of the PDA ampulla

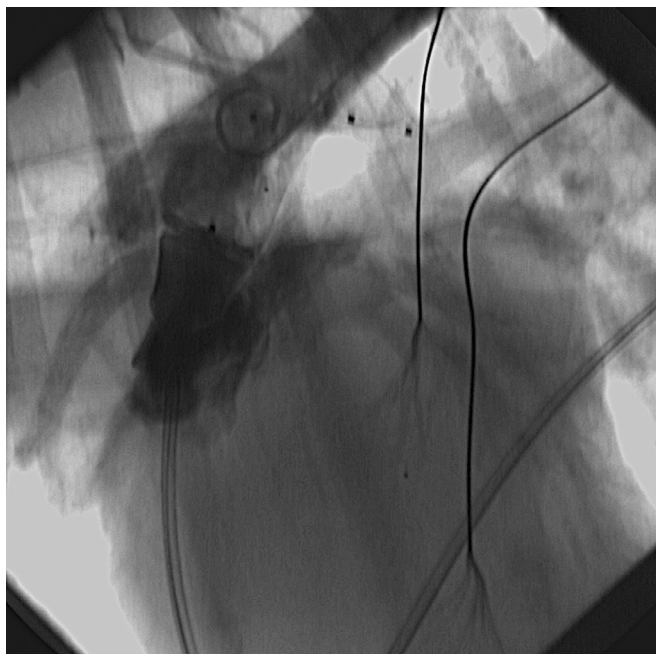


FIGURE 4 Prerelease angiography: contrast injection into the descending aorta proves correct device position and an existing residual shunt flow

in the descending aorta proximal and distal to the PDA, in the right atrium, right ventricle, MPA, and LPA. Blood gas analysis and shunt quantification were performed. Procedure time from sheath placement to the end of anesthesia was recorded.

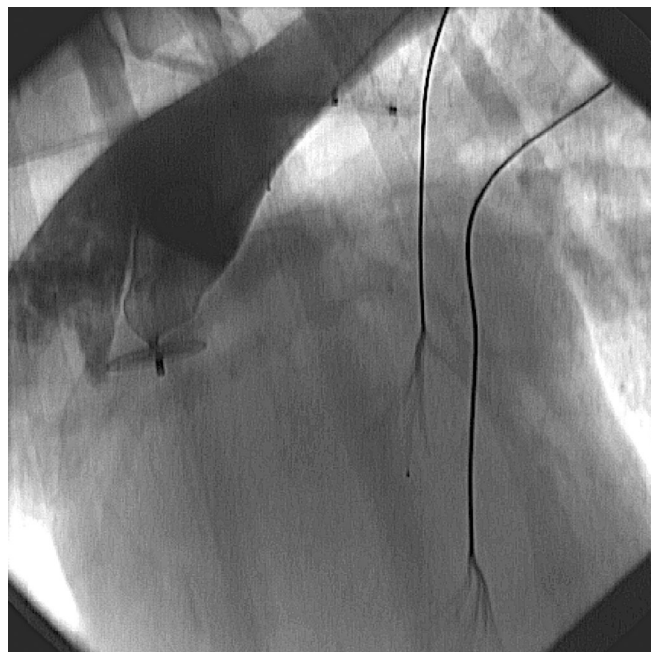


FIGURE 5 Postrelease angiography: after device detachment, angiography over a 5-F pigtail catheter is still showing a correct position of the Amplatzer vascular plug II (AVP-II) and a complete closure

A bandage was applied to the vessel approach site with high pressure for 6 hours and for at least an additional 6 hours with moderate pressure. During this period, the dogs underwent strict cage rest. The dogs stayed in the intensive care unit for 24 hours with continuous ECG monitoring. Amoxicillin with clavulanic acid (15.0-20.0 mg/kg IV or PO) was administered q 12 h for 5 days. The day after catheter intervention, all dogs underwent a complete reevaluation (physical examination, thoracic radiography, and echocardiography, including Doppler). Additional follow-up examinations were proposed to the owners at 3 and 12 months after the intervention. Echocardiographic examination included the same parameters as evaluated before intervention. Patients with residual shunts were scheduled in the primary study center; other patients also could go to a German-qualified cardiologist (Collegium Cardiologicum), and digital data were transferred for analysis.

Technical success was defined as the patient leaving the catheterization laboratory with a device in the PDA, even if device embolization and percutaneous removal occurred with PDA closed by a larger device (in the same intervention).²⁶ Technical failure was defined as cases in which the device was placed and the dog left the catheterization room, but subsequently required surgical or percutaneous removal at a later time.²⁶ Complete closure was defined as the absence of a residual shunt across the PDA, as determined by Doppler color flow mapping.²⁷ Complete closure found in the first reexamination was defined as immediate closure and delayed closure if found in a later examination.^{6,28} Residual shunts were classified using Doppler color flow examination, as described above. Signs of LPA obstruction after AVP-II application were assessed by measuring the flow velocity in the

LPA using pulsed wave Doppler. Classification was performed using values published for humans (normal, <1.5 m/s; mild flow acceleration, 1.5-2.0 m/s; stenosis, >2.0 m/s).²⁹

Clinically relevant complications were reported (moderate: transient condition change, potentially life-threatening without treatment; major: condition change, life-threatening without treatment; catastrophic: any death or emergency surgery).³⁰

2.4 | Statistical analysis

Data were tested for normal distribution by visual inspection and D'Agostino-Pearson omnibus normality tests and were reported as median with range or mean with SD. Pre- to postintervention and postintervention to 3-month follow-up measurements were compared using a paired Student's *t*-test or Wilcoxon test, as appropriate. All statistical calculations and illustrations were performed using GraphPad Prism 6 (GraphPad Software; San Diego, California). Statistical significance was set at $P < .05$.

3 | RESULTS

Nineteen dogs were included in the study. Patient age ranged from 2.3-66.1 months (median, 13.2 months) and body weight ranged from 5.3 to 34.0 kg (median, 16.8 kg). There were 3 male and 16 female dogs. The most common breeds were Border Collie ($n = 3$) and Giant Schnauzer ($n = 2$). Clinical signs were reported in 12 of the 19 dogs. Six dogs had a history of dyspnea, and all 12 dogs had exercise intolerance. A continuous heart murmur was detected in all dogs (grade IV/VI, $n = 2$; grade V/VI, $n = 15$; grade VI/VI, $n = 2$). Seventeen dogs were pretreated (furosemide, $n = 17$; angiotensin-converting enzyme [ACE] inhibitor, $n = 15$; pimobendan, $n = 9$; spironolactone, $n = 3$; β -methyldigoxin, $n = 2$; sotalol, $n = 1$; and amiodarone, $n = 1$). Six dogs showed rhythm disturbances, wherein 3 had atrial fibrillation, 1 had ventricular bigeminy, 1 had isolated ventricular premature beats, and 1 had supraventricular tachycardia. Signs of congestion were observed on thoracic radiographs in 14 of the 19 cases. Six dogs with severe pulmonary edema additionally were treated with furosemide IV (0.25-0.50 mg/kg/h CRI) for 12-24 hours before intervention. Left ventricular volume overload was documented in 18 of the 19 dogs (LVDd-I, 2.30 ± 0.30 ; LVDs-I, 1.54 ± 0.23). In all dogs, color flow Doppler showed PDA grade 4 shunting and mitral valve regurgitation with different degrees (mild, $n = 6$; moderate, $n = 7$; severe, $n = 6$). Mild subaortic stenosis or pulmonic stenosis was documented in 1 and 2 dogs, respectively.

Angiography of the descending aorta showed a PDA type E (elongated and conical) in 17 dogs and type A (conical, with a well-defined ampulla at the aortic side) in 2 dogs. Angiographic shunt grade 4 was found in all patients. Measurements of the PDA showed an MDD of 4.34 ± 1.11 mm, A1 of 11.23 ± 2.83 mm, A2 of 13.18 ± 3.47 mm, and length of 17.16 ± 3.79 mm. Median shunt ratio (Q_p/Q_s) was 3.81 (range, 1.71-7.19; $n = 15$).

A "pull-through" did not occur in any dog, and the primary selected device was implanted in every case. Technical success was achieved in 18 of the 19 dogs (94.7%) in the first intervention and in all 19 dogs after the second intervention. A single case of technical failure was a device (14 mm) malposition with all 3 device lobes implanted in the PDA ampulla (Figure 6). In the first hour after intervention, the device started to rotate, and a part of the plug was partially stuck within the MDD, producing a grade 4 residual shunt. The day after the first intervention, the device was captured using a 10-mm snare and could be partially retracted, but then embolized into the midpart of the LPA. Angiography showed mild flow reduction, and pressure measurement showed a systolic gradient of 3 mm Hg. It was not possible to remove the device from this position without hemodynamic compromise, and consequently it was left in place. After new angiography and PDA measurements, the next larger size AVP-II (16 mm device; AVP-II/A2 ratio of 1.36) was implanted successfully. The examination data of the second intervention were included in the analysis.

The median device size deployed in the entire population was 16 mm (range, 10-22 mm), with a median AVP-II/A2 ratio of 1.27 (range, 1.02-1.40). The ratio was less than the desired ratio of 1.2, in 2 dogs (1.10 and 1.19), in 1 because of the shortness of the ampulla and in the other dog because of the maximal device size available from the manufacturer. The median AVP-II/MDD ratio was 3.81 (range, 2.91-4.61). Prerelease angiography demonstrated a median residual shunt grade of 3 (range, 0-4). Three dogs showed complete

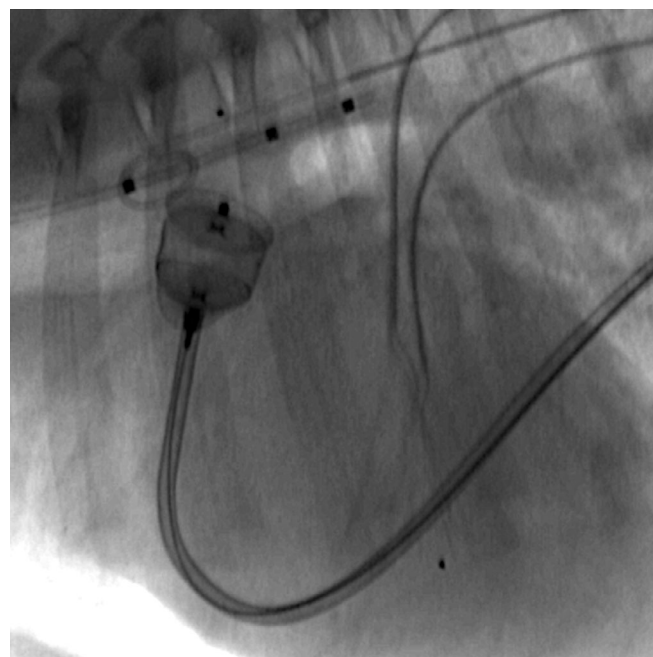


FIGURE 6 Prerelease fluoroscopy of the patient with the malposition of the AVP-II: Amplatzer vascular plug II (AVP-II) is positioned with all 3 lobes into the patent ductus arteriosus ampulla and is still connected to the delivery wire. There is no distance between the middle lobe and the distal lobe, which normally should be placed into the pulmonary artery

occlusion, 1 had a grade 2 shunt, 12 had a grade 3 shunt, and 3 had grade 4 residual flow. Postdevice release angiography identified a median residual shunt grade of 0 (range, 0-3). Complete occlusion was seen in 11 cases. Additionally, in 2 dogs, there was a grade 1 shunt; in 3, a grade 2 shunt; and in 3, a grade 3 shunt. Invasive pressure measurement showed no significant change of systolic gradient in the descending aorta (premean, 0.5 ± 3.0 mm Hg; postmean, 1.2 ± 1.6 mm Hg; $P = .36$) or between MPA and LPA (premedian, 3 mm Hg; range, 0-13 mm Hg; postmedian, 4 mm Hg; range, 0-13 mm Hg; $P = .48$). The Qp/Qs ratio at the end of the procedure showed a significant decrease ($P < .0001$; $n = 15$) and had a median of 1.06 (range, 0.96-2.17). The mean duration of the procedure was 82.7 ± 25.1 minutes.

The pressure bandage to the vessel approach stayed in the desired position in all patients. No complications such as hematoma formation were seen in this area.

In all 19 patients, a complete reexamination was performed within the first 24 hours. Immediate complete closure was documented in 18 of the 19 (94.7%) patients. The remaining dog had a residual grade 2 shunt. All dogs showed a decrease in the left ventricular diastolic dimension, leading to an LVd-d of 1.95 ± 0.34 ($P < .0001$). Mitral valve regurgitation still was present in all 19 dogs, but it was significantly decreased (mild, $n = 9$; moderate, $n = 7$; severe, $n = 3$; $P = .03$).

Until patient discharge, no catastrophic complications occurred, and only 1 major complication (technical failure with malposition of the AVP-II) occurred in 19 cases or 20 interventions. A moderate complication was seen in 4 cases; 2 had lidocaine treatment because of ventricular premature beats, and 2 had dobutamine treatment because of low arterial blood pressure (both had arrhythmias before and during the intervention). The day after the intervention, blood flow in the LPA was measured in 17 dogs, excluding the 2 dogs with pulmonic stenosis, with a mean 1.42 ± 0.40 m/s. Seven of the 17 dogs showed mild flow acceleration, and 1 had stenosis.

One dog was clinically healthy but was not presented for reexamination. The second reexamination was performed in the remaining 18 dogs 107.8 ± 29.0 days after catheter intervention. Delayed closure was documented in 1 dog (97 days after intervention), leading to an occlusion rate of 100% in all dogs after correct device positioning. The left ventricular diastolic diameter was stable or decreased; therefore, LVd-d showed a significant decrease compared to the first reexamination (1.95 ± 0.35 to 1.75 ± 0.23 , $P < .0001$; $n = 18$). Blood flow in the LPA could be analyzed in 12 dogs, including the 1 dog with previous LPA stenosis. No significant change was observed over time in LPA velocity (1.36 ± 0.41 m/s; 1.33 ± 0.38 m/s; $P = .8$), 3 of the 12 dogs showed mild flow acceleration, and none showed LPA stenosis.

4 | DISCUSSION

We showed that transvenous application of AVP-II in dogs with moderate to large PDA was feasible and successful. The ACDO, which is designed specifically for dogs, currently is the most commonly used type of vascular occlusion device for minimally invasive PDA occlusion in dogs.^{2-4,16,31} A prototype low-profile modification of ACDO

has been described for small dogs.³² Both forms of ACDO are strictly designed for transarterial access.^{2,32} In dogs with a small PDA, transarterial¹⁶ or transvenous^{5,16,19} embolization with detachable Flipper coils has produced good results acutely^{5,16,19} and excellent closure rate (100%)³³ after 3 months. In dogs with moderate-sized PDA treated using multiple free Gianturco coils⁶ or a single detachable Flipper coil,³³ residual shunts and persistent volume overload were sometimes present during follow-up examinations. Other catheter-based devices used in dogs using a transvenous approach are the ADO^{19,34,35} and AVP-I.^{14,19} Limiting factors with these products are either a high amount of residual PDA flow with AVP-I¹⁴⁻¹⁶ or high cost for the implantation material in ADO.³⁵ Currently, transarterial PDA embolization using AVP-IV has been described in 2 case series of small dogs with a very small femoral arteries.^{36,37} Because of the shape of the AVP-IV with 2 symmetrical lobes, it would be possible to use it via a transvenous route.

The AVP-II has been used in human patients, mostly by the transvenous approach in all types of PDA morphology, but especially in uncommon types observed in humans (tubular, multiple constrictions, elongated conical appearance).^{13,17,18} The transvenous approach for interventional PDA closure is used in veterinary medicine less often than transarterial access, but represents a feasible approach for different closure devices in humans^{13,17,18,38,39} and in dogs.^{5,16,19,34,40} The AVP-II size selection in humans was chosen to be at least twice the diameter of the narrowest portion of the PDA^{17,18} and 1-2 mm larger than the midportion of the PDA¹⁷ or equal to or 1 mm larger than the largest diameter of the ampulla.¹⁸ The time point of measurement during the cardiac cycle was not described in either study.^{17,18} The device in our study also was chosen based on 2 criteria: first, a diameter that is 2 times larger than the MDD; and second, a diameter that is at least 20% more than the maximal diameter of the ampulla during diastole. This relatively large device selection was used to compensate for the potential increase in PDA diameter during systole and to obtain good contact between the cylindrical middle part of the plug and the PDA wall. This oversizing factor could not be realized in 2 dogs (1.10 and 1.19) because of the maximal device size or short ampulla of the PDA. In both cases, the device still fulfilled the aforementioned criteria used in humans.^{17,18} A "pull-through" and device change to the next size is sometimes described in human medicine,¹⁷ but did not occur in our study. This was a consequence of sufficient narrowing of the PDA, relatively large device selection, and avoidance of tension during proximal disk deployment.

Technical success with the AVP-II in our study was achieved in 95% of the dogs, which is similar to that in studies of humans (99%-100%)^{13,17,18} with the same device and in the same range as studies in dogs with other occluders such as ADO (91%³⁴, 100%¹⁹), AVP-I (74%¹⁶, 94%¹⁵), or ACDO (94%,² 97%,¹⁶ and 98%³). Prerelease angiography after AVP-II deployment showed a median residual shunt grade of 3 (range, 0-4). Only 3 dogs had complete occlusion at this time. Fifteen patients still had a residual shunt grade of 3 or 4 but developed complete closure over time. This finding indicated that prerelease angiography was not a good indicator in this specific PDA closure procedure to determine sufficient device selection in the individual case. The same is reported in humans, wherein an aortic

contrast injection before release is not performed or is only used for judging device position.¹⁸ This approach is different from the results of studies on catheter-based PDA occlusion in dogs with ACDO^{3,16} or AVP-I,^{15,16} which used prerelease angiography as a marker for ineffective occlusion leading to a larger device selection. Complete occlusion of the PDA in postrelease angiography 5-10 minutes after detachment was observed in 53% of the dogs. In human patients in whom AVP-II was used, the complete angiographic closure rate at the end of the procedure was 89%-100%.^{13,17,18} This higher postrelease angiographic closure rate could be related to smaller PDA dimensions in humans,^{13,17,18} in contrast to that of the dogs in our study. The angiographic occlusion rate in our study was similar to that of the AVP-I in dogs, with a rate of 43%-48%,¹⁴⁻¹⁶ and lower than in dogs treated using an ADO (65%³⁴) or ACDO (69%-94%^{2,3,16}). In contrast to the relatively high residual angiographic shunt rate, the significant decrease in the Qp/Qs shunt ratio to <1.5, in all but 1 dog, documented good occlusion of the PDA by the AVP-II. This finding was later confirmed by the high occlusion rate during follow-up.

The major complication rate in our study with AVP-II in dogs was 5%. This rate was slightly higher than that reported in humans (0%-1%),^{13,17,18} This complication was caused by operator error from malposition of the device. Retrospectively, the wrong position could be detected by an absent distance between the middle portion and the proximal lobe. A cautious analysis of the prerelease angiography findings should prevent this complication in the future. The major complication rate in our study was comparable with those of studies of other catheter-based devices used in dogs.^{2,3,5,6,15,16,31,34} Embolization of the implanted device during the procedure is a frequently reported major complication. It has been described for different catheter-based devices used in dogs, such as coils,^{6,16,19} ADO,³⁴ ACDO,^{3,4,31,41} and AVP-I.¹⁵ Spontaneous embolization did not occur in our study because of sufficient narrowing and appropriate selection of device size. One case of induced embolization was attributed to initial deployment failure and the attempt to replace the device. Removal of the embolized device was not possible in the current case because of hemodynamic instability. Removal of embolized devices has been described rarely in dogs.⁴¹ As in the current case, most acute embolized devices can be tolerated by the dog as long as no major branch is occluded and the PDA itself is closed by another device or a different technique.^{2,6,31} Postoperative device embolization is described rarely in dogs after PDA occlusion using Gianturco coils^{6,16,42} as well as with ACDO² in the first 24 hours after intervention. Delayed embolization in the following days to weeks is described rarely in case reports in dogs with ACDO,⁴³ AVP-II,⁴⁴ and AVP-IV³⁶ and often associated with severe cardiorespiratory compromise.^{43,44}

Patent ductus arteriosus devices have the potential to bulge into the aorta or LPA, leading to narrowing of the aortic lumen or causing stenosis of the LPA branch. In humans, the use of AVP-II in PDAs did not result in stenosis of the aorta and rarely resulted in stenosis of the LPA (0%-1%).^{13,17,18} These results correlate well with the results of our study. In dogs, aortic stenosis is unlikely to develop because of the long ampulla. Nevertheless, as done in our study, in shorter PDA, device selection also should be made in relation to length. The length

of the AVP-II has some specific aspects that should be considered. The length of the device on the package is the total length when fully expanded. The proximal and distal lobes have relative fixed lengths of approximately 1-2 mm. The middle portion is longer if the device is not fully expanded. The operator must estimate intraductal device length by summing the length of 1 distal disk and the compressed length of the middle portion.

To classify LPA narrowing, spectral Doppler-based cut-offs published in human medicine were used in our study.²⁹ Doppler-based estimation of the LPA gradient overestimates invasively derived data.⁴⁵ The LPA obstruction rarely can occur after ADO placement in humans⁴⁶ and dogs,³⁴ which is caused by bulging of the stiff device through the ampulla wall into the LPA. Other devices may cause this narrowing by protrusion of a part of the device into the LPA, especially in small children for coils⁴⁶ as well as for occluding devices with relatively large pulmonary retention disks, such as ADO-II³⁹ or ADO-II-additional sizes.⁴⁷ In the case of AVP-II, the risk seems to be lower than that of other devices because of its softness and the relatively small diameter of the retention disk.²⁹ Left pulmonary artery obstruction typically does not reach a clinically relevant level in humans²⁹ and dogs,³⁴ which also was observed in our study. In humans, significant risk factors are large MDD and use of devices other than AVP-II, with increased risk in individuals of lower body weight.²⁹ In a dog population with large PDA in sometimes small patients, it is possible to decrease the incidence (in our study 7/17 mild flow acceleration and 1/17 LPA stenosis the first day after intervention) or amount of LPA narrowing with the current AVP-II by using a smaller device, which could have other undesirable effects. Another approach would be modification of the device using a smaller proximal disc, as done in ACDO. As a drawback, this approach would lead to an asymmetrical form and restriction to the transvenous approach only.

A percutaneous approach to the femoral artery can be associated with severe complications, either bleeding problems or neurological disturbances because of an excessively tight bandage.^{5,48,49} In our study, a stepwise pressure bandage with cage rest was effective without complications for small arterial (4F-5F) and moderate-sized venous introducers (6-9F).

The immediate complete closure rate of 95% and delayed occlusion rate at follow-up of 100% for AVP-II in our study was similar to rates reported in human medicine (95%-100% and 100%).^{13,17,18} Both are comparable to the reported data for the use of ACDO in dogs (94%-100% and 94%-100%).^{2,3,16} Immediate and delayed closure rates were higher than those described in dogs for AVP-I (61%-76% and 83%)^{15,16} and ADO (73%-75% and 90%, respectively).^{19,34}

4.1 | Limitations of the present study

In our study, we reported the initial experience with AVP-II at a single center with long experience in PDA embolization using other devices. The main limitation of our study was the relatively small number of cases included. Only moderate to large PDAs (MDD > 2.5 mm), of 2 PDA types (both with distinct narrowing) were analyzed in our

study. Additional studies in a broader spectrum of patients should be done in the future.

5 | CONCLUSIONS

Amplatzer vascular plug II is a feasible and successful method for interventional closure in dogs with moderate to large PDA with a conical shape. The transvenous route for the implantation procedure offers the possibility of treating a wide range of patients, in relation to body weight and PDA dimension, without need for a large arterial access.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

During catheter intervention, intravenous human antibiotic preparation of amoxicillin/clavulanic acid was used.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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