Clinical Characteristics of Adult Dogs More Than 5 Years of Age at Presentation for Patent Ductus Arteriosus

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Background: The median age at presentation for dogs with patent ductus arteriosus (PDA) is <6 months of age, and closure is associated with a decrease in heart size and increased survival time, which are not well described in older dogs.

Objectives: To describe the clinical characteristics of dogs with PDA ≥5 years of age at the time of presentation to a veterinary referral hospital.

Animals: 35 client-owned dogs.

Methods: Retrospective case series.

Results: PDA was diagnosed at a median age of 7.4 years (range, 5.1–12.3 years). Females represented 23/35 (65.7%) of the patients. Concurrent heart disease included degenerative mitral valve disease (DMVD; 13), arrhythmias (11), pulmonary hypertension (7), and other congenital defects (2). Cardiomegaly was documented in the majority of dogs consisting of left ventricular enlargement (91%) and left atrial enlargement (86%). Median vertebral heart size in 24 dogs was 12.9 (range, 10.7–18.2). The PDA shunt direction was left-to-right in 33 and bidirectional in 2 dogs. Closure was performed in 26 dogs, including 4 with pulmonary hypertension. In 10 dogs receiving furosemide pre-operatively for management of heart failure, furosemide was discontinued (8) or the dosage decreased (2) at the time of discharge.

Conclusions and Clinical Importance: Adult dogs can present with a left-to-right shunting PDA that results in cardiomegaly and clinical signs that can improve or resolve with PDA closure. This improvement is also apparent in dogs with PDA complicated by DMVD. Pulmonary hypertension that does not result in complete right-to-left shunting should not be considered a contraindication to closure.

Key words: Canine; Congenital; Mitral valve; Pulmonary hypertension.

In humans, patent ductus arteriosus (PDA) is diagnosed most often in children, with a high prevalence in premature infants, and represents only 2% of congenital heart disease diagnosed in adults. The clinical presentation in adults can range from an incidental finding with a small or restrictive type PDA to variable severity of left-sided heart enlargement, heart failure, and pulmonary hypertension (PH). In addition to these changes related to the hemodynamic effect of the PDA, long-term sequelae can include atrial arrhythmias, duc-
tal aneurysm or calcification, pulmonary artery or aorta dissection, and endarteritis. Ductal closure recommendations vary for adults, but in general, closure is recommended for moderate-to-large PDA, debated in patients with small asymptomatic PDA, and typically contraindicated with right-to-left shunting associated with irreversible PH and Eisenmenger physiology. The method of closure is determined by ductal morphology and the presence of concurrent disease. Pulmonary vascular disease and left ventricular failure increase morbidity in adults with PDA as does the presence of multiple congenital heart defects.

In dogs with PDA, the median age at presentation is <6 months of age, and ductal closure is associated with a decrease in heart size and increased survival. Concur-
rent congenital heart disease may adversely affect survival. Fewer dogs are diagnosed with PDA as adults, with the largest group of dogs reported including 24 dogs ≥24 months of age at diagnosis. In 2 studies, dogs with PDA ≥24 months of age represented 21–25.5% of the cases and had a variety of clinical find-
ings that ranged from normal heart size to left-sided heart enlargement to right-to-left shunting as well as concurrent congenital and acquired heart disease.

Abbreviations:
ACDO Amplatz® canine duct occluder
ACE angiotensin-converting enzyme
ACVIM American College of Veterinary Internal Medicine
DMVD degenerative mitral valve disease
ECG electrocardiogram
FS fractional shortening
IQR interquartile range
LA:Ao left atrium-to-aorta ratio
LVIDd left ventricular internal dimension in diastole
LVIDs normalized to body weight
PDA patent ductus arteriosus
PH pulmonary hypertension
VHS vertebral heart size

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The purpose of our study was to describe the clinical characteristics of adult dogs with PDA that were ≥5 years of age at the time of presentation to a veterinary referral hospital.

Materials and Methods

Electronic medical records from the Texas A&M University Veterinary Medical Teaching Hospital were reviewed to identify dogs with an echocardiographic diagnosis of PDA. Dogs that were ≥5 years of age at presentation were included. For each dog, recorded patient data included signalment, historical information, presenting complaint, results of physical examination, results of diagnostic tests (electrocardiogram [ECG], thoracic radiography, and echocardiography), treatment (categorized as none, medical only, surgical ligation, or transcatheter device closure), medication at the time of first presentation (none, performed echocardiographic diagnosis), and medication at the time of discharge (with or without a procedure). In the event a procedure was performed, postprocedural (within 24–96 hours) radiographic and echocardiographic variables and procedural complications were reported when available.

For those dogs with thoracic radiographs available for evaluation at the time of diagnosis and after closure before discharge, vertebral heart size (VHS) was calculated from the image obtained with the dog in right lateral recumbency.

All dogs had transthoracic echocardiography performed by a board-certified cardiologist or cardiology resident under direct supervision of a board-certified cardiologist. From reports at the time of diagnosis and after closure before discharge, recorded measurements included left ventricular internal dimension in diastole and systole (LVIDd and LVIDs) from M-mode measurements of the left ventricle in short axis that were normalized to body weight (LVIDdN, LVIDsN) as previously reported, and left atrium-to-aorta ratio (LA:Ao) from M-mode or 2-dimensional short axis images depending on availability. Dogs were considered to have left atrial enlargement if LA:Ao M-mode was >1.6. The presence of mitral regurgitation and concurrent congenital or acquired heart disease also was recorded.

Stored studies were reviewed for PH, PDA minimal ductal diameter, and shunting direction. Presence of PH based on estimated pulmonary pressures from peak systolic tricuspid regurgitation velocity, peak pulmonic valve regurgitation velocity, or catheter-based measurement of pulmonary artery pressure was recorded. The direction of flow through the PDA was recorded from color Doppler images or agitated saline echocardiographic studies. Minimal ductal diameter measurements were recorded from stored transthoracic or transesophageal echocardiography or angiography images depending on availability.

Descriptive statistical analysis was performed. The Shapiro–Wilk test was used to verify normal distribution of variables. Data with normal distribution were expressed as mean ± standard deviation and range. For data that were not normally distributed, results were reported as median, interquartile range (IQR), and range. Radiographic and echocardiographic measurements were compared using a t-test. Proportions of categorical values were compared using Fisher’s exact test. A P-value <.05 was considered significant.

Results

Signalment and Clinical Presentation

Medical records from 35 dogs presented between March 1998 and January 2016 were identified. The most common breeds represented were mixed (7/35, 20%), German Shepherd (4/35, 11.4%), Dachshund (3/35, 8.6%), Pomeranian (2/35, 5.7%), and West Highland White Terrier (2/35, 5.7%). More than half of the dogs were female (23/35, 65.7%). Median age at the time of PDA diagnosis was 7.4 years (IQR, 6.3–8.4 years; range, 5.1–12.3 years), and median weight was 9.6 kg (IQR, 5.4–19.6 kg; range, 2.8–44.9 kg). Twenty-one (60%) dogs presented for evaluation of an asymptomatic heart murmur. Fourteen (40%) dogs presented with clinical signs consistent with heart disease. The most common signs were cough (9/35), lethargy (7/35), or both (4/35). Syncope was reported in 1 dog, and tachypnea at night was reported in 1 dog. A left basilar continuous murmur (grade III–VI) was noted in 32 dogs (91.4%). A systolic left basilar murmur was noted in 2 dogs, with bidirectional shunting and 1 with a left-to-right shunting PDA, concurrent atrial fibrillation, and mild PH. A murmur was not auscultated in 1 dog with bidirectional shunting. Fourteen of 35 (40%) dogs were receiving cardiac medications at the time of presentation including angiotensin-converting enzyme (ACE) inhibitors (12/14), furosemide (10/14), pimobendan (6/14), spironolactone (3/14), digoxin (1/14), amiodipine (1/14), sotalol (1/14), or >1 of these medications (10/14).

Arrhythmias

Arrhythmias were identified in 11 of 35 (31%) dogs at presentation and included ventricular premature complexes (9/11), atrial fibrillation (4/11), or both (2/11). Of the 4 dogs with atrial fibrillation, 2 presented with clinical signs of left-sided heart failure (tachypnea, dyspnea and exercise intolerance), 1 presented with signs consistent with right-sided heart failure (ascites and exercise intolerance), and 1 was asymptomatic.

Thoracic Radiographic Findings

Thirty-three of 35 dogs had radiographic reports, and cardiomegaly was reported in 31/33 (94%). Pulmonary vessel over-circulation was reported in 29/33 (88%) of which 7 had echocardiographic evidence of PH and 2 had bidirectional shunting PDAs. An interstitial pattern consistent with cardiogenic pulmonary edema was reported in 5/33 (15%) dogs. In 24 of 33 dogs with radiographic reports, the radiographic images were available for VHS measurement. The median VHS of these 24 dogs on presentation was 12.9 (IQR, 12.2–13.8; range, 10.7–18.2).

Echocardiographic Findings

Thirty-two of 35 dogs had complete echocardiographic reports available for review with results reported in Table 1. Left ventricular dilatation was present in 29/32 (91%) based on increased LVIDdN, and left atrial enlargement was present in 28/32 (86%). Left atrial enlargement was present in 18/18 (100%) from M-mode and 10/14 (71%) on 2D measurements. Mitral regurgitation was present in 28/32 (86%) of dogs. Of these, 13/28...
(46%) were characterized as having thickening of the mitral valve consistent with degenerative mitral valve disease (DMVD) and staged \(^1^9\) as defined in Table 2.

Concurrent congenital heart disease was present in 2/35 (6%) dogs, 1 dog with both valvular aortic stenosis (peak velocity, 6.3 m/s) and pulmonic stenosis (peak velocity, 3.6 m/s) and 1 dog with an interatrial septal aneurysm.

Pulmonary hypertension was diagnosed in 7/32 (22%) of the dogs by echocardiography in 6/7 and direct measurement in 1/7. One dog with PH had concurrent DMVD. The PDA shunt direction was left-to-right in 33/35 dogs (94%). In 2 of 35 dogs (6%), bidirectional shunting was documented. No dog had solely right-to-left shunting.

The minimal ductal diameter was measured in 25/35 dogs by echocardiography alone (7/25), angiography alone (7/25), or both (11/25). The median echocardiographic minimal ductal diameter in 18 dogs for which it was available was 4.0 mm (IQR, 3.0–5.0 mm; range, 2.8–7.0 mm). The median angiographic minimal ductal diameter in 18 dogs for which it was available was 4.0 mm (IQR, 3.0–5.0 mm; range, 1.3–6.0 mm).

Table 1. Descriptive data for adult dogs with a patent ductus arteriosus >5 years of age at the time of presentation. Values are presented as mean ± SD when normally distributed or median (IQR; Range) when not normally distributed. Statistical analysis was performed only in dogs that underwent a procedure to evaluate findings at presentation and within 24–96 hours after the procedure.

| | N | Presentation—all dogs | | N | Presentation—only dogs that had procedure performed | | N | 24–96 hours after the procedure | P-value |
|---|---|---|---|---|---|---|---|---|---|
| VHS | 24 | 12.9 (IQR: 12.2–13.8; Range: 10.7–18.2) | 21 | 13.0 (IQR: 12.25–14.0; Range: 10.7–18.2) | 14 | 12.2 (IQR: 11.6–13.0; Range: 11.2–17.5) | .32 |
| LVIDdN | 32 | 2.29 ± 0.38 | 25 | 2.39 ± 0.34 | 22 | 2.17 ± 0.51 | .09 |
| LVIDsN | 32 | 1.44 ± 0.33 | 25 | 1.51 ± 0.32 | 22 | 1.55 ± 0.42 | .75 |
| FS% | 32 | 34.17 ± 8.55 | 25 | 33.67 ± 8.04 | 22 | 25.39 ± 9.95 | .002 |
| LA:Ao (M-mode) | 18 | 1.63 (IQR: 1.48–1.87; Range: 1.27–3.9) | 17 | 1.64 (IQR: 1.48–1.90; Range: 1.29–3.90) | 11 | 1.43 (IQR: 1.31–1.68; Range: 1.13–2.23) | .16 |
| LA:Ao (2D) | 14 | 1.65 (IQR: 1.49–1.93; Range: 0.97–2.92) | 8 | 1.82 (IQR: 1.66–1.95; Range: 1.49–2.92) | 11 | 1.7 (IQR: 1.4–2.3; Range: 1.3–3.1) | .96 |
| PH | 32 | 7 (22%) | 25 | 4 (16%) | 22 | 3 (13.0%) | .66 |
| MR | 32 | 28 (86%) | 25 | 21 (84%) | 22 | 19 (86%) | 1.00 |
| Cardiac medications | 35 | 14 (40%) | 26 | 15 (58%) | 26 | 14 (54%) | 1.00 |

FS, Fractional shortening; IQR, interquartile range; LA:Ao, left atrium-to-aorta ratio; LVIDdN, left ventricular internal dimension in diastole normalized to body weight; LVIDsN, left ventricular internal dimension in systole normalized to body weight; MR, mitral regurgitation; PH, pulmonary hypertension; SD, standard deviation; VHS, vertebral heart size.

Table 2. ACVIM classification of dogs with degenerative mitral valve disease (DMVD)\(^1^9\)

| Stage | Presentation
|---|---|
| A | No murmur and no apparent structural changes |
| B1 | MR with either LVE or LAE and no HF |
| B2 | MR with both LVE, LAE and no HF |
| C | MR with either LVE, LAE and both and current or previous clinical signs of HF |
| D | MR with either LVE, LAE and both and clinical signs of HF refractory to standard therapy |

HF, Heart failure; LAE, left atrial enlargement; LVE, left ventricular enlargement; MR, mitral regurgitation.

**Treatment**

Closure of the PDA was recommended in 33 dogs and was not recommended in 2 dogs because of concurrent life-limiting noncardiac disease. The procedure was recommended and declined by the owners of 7 of 35 dogs. A procedure was performed to close the PDA in 26/35 (74%) dogs and 4 of these had PH. Estimated systolic pulmonary artery pressures were 36, 66, 70, and 91 mmHg in these 4 dogs. Closure methods included surgical ligation (6/26) and transcatheter device placement (20/26) using the Amplatz\(^TM\) canine duct occluder\(^6\) (ACDO) in 13/20, embolization coils in 5/20, and the Amplatzer\(^TM\) vascular plug\(^2\) in 2/20. Device embolization or dislodgement occurred in 2/26 (8%) dogs; neither had PH. One coil embolized to the aorta and was retrieved. One ACDO device partially dislodged from the ductus into the main pulmonary artery. A thoracotomy was performed, and the ACDO device was secured in place with a ligature. No complications were reported during surgical ligation, and no deaths occurred.

Eighteen of the 35 (51%) dogs were discharged on cardiac medications (including all dogs in the study whether they had a procedure or not). Medications included ACE inhibitors (12/18), pimobendan (8/18), furosemide (4/18) spironolactone (2/18), sildenafil (2/18), diltiazem (1/18), sotalol (1/18). Ten of the 18 dogs were receiving ≥1 medication. Sildenafil was initiated in 1 dog with persistent PH after PDA occlusion. The dog with refractory to standard therapy was discharged on clopidogrel prophylactically.

**PostProcedure Evaluation**

Twenty-two of 26 dogs (74%) that had an occlusion procedure had an echocardiogram available...
for review within 24–96 hours of PDA closure before discharge (Table 1). Left ventricular dilatation was present in 17/22 (77%) based on LVIDdN, and left atrial enlargement was present in 16/22 (73%). Mitral regurgitation was present in 19/22 (86%). Of these, 10/22 (45%) were characterized as having DMVD.

Residual ductal flow was documented using color Doppler transthoracic echocardiography before discharge in 7/26 (27%) dogs: coil occlusion (4/7), Amplatzer™ vascular plug (1/7), and ACDO (1/7). Two additional dogs (8%) with ACDO closure, that had no flow documented before discharge, had recurrence of flow based on color Doppler transthoracic echocardiography within 6 weeks of the procedure. Both of these dogs experienced a clinically relevant postprocedural complication consisting of extensive intradermal hemorrhage extending widely from the surgical incision over the femoral artery that was not a consequence of direct femoral artery hemorrhage.

Fourteen of the 26 (54%) dogs that had an occlusion performed had postprocedural thoracic radiographs available for VHS measurement. The median VHS was 12.2 (IQR, 11.6–13.0; range, 11.2–17.5). All of these dogs had a decrease in VHS.

In the 13 dogs diagnosed with concurrent DMVD, 10 had a procedure performed. Before PDA closure, these 10 dogs would have been staged based on current guidelines as B2 (5) or C (5). After the procedure and before discharge, the 10 dogs would have been restaged as B1 (1/10), B2 (8/10), and C (1/10). Four of the 5 dogs classified stage C before PDA closure would have been characterized as stage B after closure based on a decrease in heart size and discontinuation of diuretic therapy.

Fourteen of 26 (54%) dogs that had PDA closure were receiving cardiac medications at the time of discharge including: ACE inhibitors (11/26), pimobendan (6/26), furosemide (2/26), spironolactone (1/26), and sotalol (1/26). Seven of the 26 (27%) dogs were receiving 4 medications. Of the 26 dogs that underwent PDA closure, 13 dogs were receiving furosemide preoperatively for management of concurrent pulmonary edema. Furosemide was discontinued in 8 of the dogs at the time of discharge, and the dosage was decreased in the remaining 2 dogs.

Discussion

Our retrospective study presents clinical findings in 35 dogs that presented with PDA as adults >5 years of age. In a previous report, 21 dogs >24 months of age with left-to-right shunting PDA did not have concurrent congenital heart defects or PH reported. The dogs of our study were part of a different population of dogs because they were older with a median age of 7.4 years and had concurrent congenital and acquired heart disease. Although no single breed was over-represented, the most common (after mixed breed) in our study was the German Shepherd, a breed that has been included previously in several case series of adult dogs with PDA. Although females were more common than males (66%), they were not as common as previously described in a large case series of 520 dogs (73% female) or in adults 2–2 years of age (81% female).

Only 2/35 (6%) dogs in our study had concurrent congenital heart defects. This finding is consistent with previous reports in adult dogs and in people with PDA and lower than that reported in younger dogs, which suggests that the presence of multiple congenital heart defects negatively affects long-term survival. Not surprisingly, our dogs had a higher incidence of acquired DMVD, consistent with the increased prevalence reported in older dogs.

The majority of dogs in our study had cardiomegaly documented radiographically or echocardiographically indicating hemodynamically relevant shunting. In some dogs, the concurrent presence of DMVD and mitral regurgitation likely contributed to left-sided heart enlargement. Additionally, the median minimal ductal diameter for PDAs in our study was not small compared to that reported in previous studies, confirming that some dogs can live into adulthood with hemodynamically relevant PDA.

Of the 7 dogs estimated to have PH, 4 underwent successful PDA closure. In these 4 dogs with PH, PDA flow was documented to be left-to-right before closure. No dogs in our study had complete right-to-left shunting. The presence of PH complicates the clinical picture and closure recommendations, but closure can be performed if the PDA remains left-to-right shunting. Closure of the PDA decreases pulmonary blood flow and subsequently can lower pulmonary pressures.

In young dogs, clinical outcome has been reported to be negatively impacted if the PDA is not closed. In adults, closure is associated with a significant decrease in survival time. However, making recommendations regarding closure in older dogs can be challenging for a variety of reasons including comorbid conditions. In humans, recommendations for closure in adults are based on the morphology of the ductus, presence of calcification, aneurysm formation, prior history of endocarditis, and the hemodynamic relevance of the left-to-right shunt. In our dogs, occlusion or ligation was recommended based on the presence of left atrial enlargement, left ventricular enlargement, or both (based on echocardiographic or radiographic findings or both) consistent with a hemodynamically relevant left-to-right shunting PDA, congestive heart failure, or reported clinical signs. After PDA closure, evidence that the PDA was contributing to volume overload was confirmed by documentation of a decrease in heart size, resolution of clinical signs of heart failure, and a decrease in or discontinuation of diuretic therapy. This was most apparent in the 10 dogs that underwent a procedure performed and in which 4 of 10 experienced a decrease in ACVIM stage overall and 4 of 5 in stage C were recategorized as stage B (3 as B2, 1 as B1) after closure.

Residual flow and complication rates are inconsistently reported in the veterinary literature but were not considered more common in our population of older
dogs. Other studies report complications and residual flow rates but with variable types of closure methods, time of evaluation after the procedure and characterization of a complication.\textsuperscript{10,30,31} A residual flow rate of 39\% has been documented in dogs occluded with embolization coils and in up to 44\% when determined immediately after device deployment.\textsuperscript{30,31} In a study of 520 dogs with PDA, the residual flow rate for all closure methods was 26.1\% and included some dogs from the current study.\textsuperscript{10} In the population of dogs reported here, residual flow assessed 24–96 hours after the procedure was documented in 27\% and included predominately dogs with embolization coils and plugs similar to previous reports.\textsuperscript{30,31}

Ours was a retrospective study with limitations that include missing data points. Additionally, echocardiographic measurements and closure methods have evolved over the long study period such that some variables could not be directly compared.

In conclusion, dogs >5 years of age can present with hemodynamically relevant left-to-right shunting PDA\Ss that result in cardiomegaly and clinical signs that can improve or resolve after PDA closure. This improvement also is apparent in dogs with PDA complicated by DMVD. Pulmonary hypertension that does not result in complete right-to-left shunting should not be considered a contraindication to closure in adult dogs with PDA.

Footnotes
\textsuperscript{a} Microsoft Excel\textsuperscript{®}, Microsoft Corporation, Redmond, WA
\textsuperscript{b} Graph Pad Software, San Diego, CA
\textsuperscript{c} Amplatz\textsuperscript{®} Canine Duct Occluder, Infiniti Medical, LLC, Menlo Park, CA
\textsuperscript{d} Amplatzer\textsuperscript{™} Vascular Plug, Infiniti Medical, LLC, Menlo Park, CA

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Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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