Comparative, multidimensional imaging of patent ductus arteriosus and a proposed update to the morphology classification system for dogs

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Background: Accurately assessing the morphology and shape of the patent ductus arteriosus (PDA) and obtaining measurements are important to avoid procedural complications.

Objectives: To characterize and compare PDA morphology, shape, and dimensions with angiography and echocardiography.

Animals: 25 client-owned dogs with echocardiographically confirmed PDA.

Methods: Prospective case series. Imaging consisted of single plane angiography, transthoracic echocardiography from the right (TTE-R) and left (TTE-L), and two-dimensional, biplane, and three-dimensional transesophageal echocardiography (TEE-2D and TEE-3D). Measurements included angiographic minimal ductal diameter (MDD), echocardiographic pulmonary ostium in a single dimension (TTE-R, TTE-L, and TEE-2D) and in perpendicular dimensions (TEE-3D) with similar measurements of the ampulla 3 mm above the MDD or pulmonary ostium. The morphology and shape of the PDA were characterized.

Results: Catheter-based occlusion (N = 20) and surgical ligation (N = 5) were performed without complication. Angiographic morphology was classified as type II (N = 19), type III (N = 1), and other (N = 1). Angiographic MDD and TEE-2D pulmonary ostium measurements were significantly (P = .008) but weakly correlated (r = .56); similar relationships were found for ampulla diameter measurements (P < .0001; r = .75). In general, TEE-2D did not correlate with other imaging modalities measurements. Based on TEE-3D measurements, the majority of pulmonary ostium (17/24; 71%) and ampulla (19/24; 79%) were oval.

Conclusions and Clinical Importance: Measurements using different imaging modalities are not interchangeable. TEE-3D provided an en face view of the PDA that cannot be replicated with other echocardiographic techniques and demonstrated an oval shape in the majority of dogs. We propose an update to the current classification system to include additional PDA morphologies.

KEYWORDS
angiography, canine, congenital heart disease, echocardiography, three-dimensional

Abbreviations: 2D, two-dimensional; 3D, three-dimensional; L, left; MDD, minimal ductal diameter; PA, pulmonary artery; PDA, patent ductus arteriosus; R, right; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

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1 | INTRODUCTION

Definitive closure of patent ductus arteriosus (PDA) in dogs includes catheter-based occlusion with the canine-specific, Amplatz Canine Duct Occluder (ACDO; Infiniti Medical, LLC, Menlo Park, California).\textsuperscript{1,2} The procedural objective is complete occlusion without complications. Although procedural success is reportedly high, residual flow, and device embolization have been described with the ACDO and are likely underrepresented in the literature.\textsuperscript{1,5} Additionally, it is important to identify PDA morphologies that are not amenable to closure with the ACDO device.\textsuperscript{6,7}

Abnormal distribution of ductal wall muscle and replacement by elastic tissue has been documented by histopathology of PDA in dogs\textsuperscript{8,9} and results in a wide range of PDA sizes and morphologies. Individual variations in PDA morphology, PDA size, and arterial size for vascular access influence closure recommendations and device selection. Therefore, accurate assessment of PDA morphology and size are important for device selection and optimal device sizing to avoid complications. Morphologic description and device sizing recommendations are typically based on angiographic characterization of the minimal ductal diameter (MDD) and ampulla of the PDA.\textsuperscript{10–12} With angiography, the MDD is obtained by measuring the contrast jet as it flows from the PDA ampulla into the pulmonary artery (PA). Echocardiographic assessment of the PDA can provide additional information. With echocardiography, the tissue of the ampulla and pulmonary ostium of the ductus arteriosus is typically visualized and measured. Color Doppler can assist in identifying the PDA but measurements of the color signal can over-estimate the PDA size.\textsuperscript{13,14} Measurements acquired with thoracoscopic echocardiography (TTE) were reportedly not interchangeable with angiographic measurements based on wide limits of agreement when comparing the two modalities.\textsuperscript{5} Transesophageal echocardiography (TEE) has reported benefits including the potential of superior imaging compared with TTE as well as real-time monitoring of the procedure in two- and three-dimensions (2D, 3D).\textsuperscript{4,6,15,16} Intraoperative imaging with TEE can alter treatment decisions that were originally based on angiographically derived measurements.\textsuperscript{6,17} A similar finding in people has been reported.\textsuperscript{18–20} Images obtained with multiplane TEE demonstrate variations in cross-sectional shape of the PDA.\textsuperscript{4,6,17} The objective of this study was to characterize PDA shape and dimensions using single plane, right lateral angiography, and echocardiography including TTE from the right (TTE-R) and left (TTE-L) and TEE in 2D, biplane, and 3D. We hypothesized that an oval shaped PDA is more common than previously reported and that 3D imaging in particular would provide the most detailed information.

2 | ANIMALS, MATERIAL, AND METHODS

This study was approved by the Institutional Animal Care and Use Committee and the Clinical Research and Review Committee at Texas A&M University. Owner consent was obtained for all dogs.

Client-owned dogs weighing >2.0 kg with echocardiographically confirmed left-to-right shunting PDA were eligible to participate. Very small dogs in which the TEE probe (4D TEE transducer, GE Vingmed Ultrasound, AS Standpromenden 45 N-3191, Horten, Norway) would not pass down the esophagus were excluded. In an attempt to include a variety of PDA morphologies, the study was designed to enroll 20 dogs scheduled for a catheter-based occlusion procedure and 5 for surgical ligation. All dogs had a complete TTE study (GE Vivid E9 with XDclear, GE Vingmed Ultrasound, AS Standpromenden 45 N-3191, Horten, Norway) performed with an appropriately selected 3.5–12 MHz phased-array transducer. Cineloops of the PDA were obtained from the right parasternal short axis view at the level of the main PA and the left parasternal cranial short axis view. Based on the morphology of the PDA and the weight of the dog, which could limit vascular access in small dogs, catheter-based occlusion or surgical ligation was recommended and performed the next day. After anesthetic induction, a complete TEE study was performed to visualize the PDA in 2D and 3D. With biplane imaging, the image was oriented so that the cursor crossed the ampulla in a plane that was perpendicular. For 3D TEE, the image was rotated until the PDA was visualized en face looking down the ampulla towards the PA and the cursor was translated down into the ampulla to display the aorta (right), PDA (middle), and PA (left) in cross section (Figure 1E). In the 2D reference images for TEE-3D, the display order is aorta (top), PDA (middle), and PA (bottom). Dogs scheduled for catheter-based occlusion had a right lateral angiogram performed via the right femoral artery as previously described.\textsuperscript{2} Cine loops of the TEE, TTE, and angiographic studies were stored and saved for offline analysis (EchoPAC v201; GE Medical Systems, Horten, Norway; eFilm version 3.3.0, Sound-Eklin, Carlsbad, California). At the time of the procedure, acquired images were used real-time for decisions made by the attending cardiologist regarding device selection, sizing, and completeness of closure. Device type, size, and any procedural complications were recorded. All dogs underwent a complete TTE study the next day before discharge, and the presence of residual ductal flow was recorded.

Once all dogs had completed the study, images were reviewed by two investigators (KRD, ABS) and the optimal image of the PDA in each imaging modality (TTE-R, TTE-L, TEE-2D, TEE-3D, and angiogram) was selected and stored. The optimal image was defined as the image that displayed the site of the smallest diameter at its maximum size. After calibration, measurements of the angiographic MDD were made at each edge of the contrast stream (Figure 1) and measurements of the TTE/TEE pulmonary ostium were made inner edge to inner edge in a single plane for TTE taking care to distinguish the pulmonary ostium from the left PA especially in TTE-R images (Figure 2), and TEE-2D and in two planes (A and B) for TEE-3D (Figure 1). “A” represents the minor axis perpendicular to the PA between the PA and aorta and “B” represents the major axis 90° to “A” (Figure 1E,F). The diameter of the ampulla was measured 3 mm above the MDD or pulmonary ostium in a single plane for TTE and TEE-2D and in two planes (A and B) for TEE-3D (Figure 1) to approximate the location of the ACDO proximal disk. With TEE-3D imaging, a dynamic change in the PDA throughout the cardiac cycle can be observed (Supporting Information Video 1). The optimal image was selected where the ampulla and pulmonary
FIGURE 1  Measurements of the MDD or pulmonary ostium (yellow line) and ampulla (orange line) of the PDA for (A) lateral angiogram, (B) transthoracic echocardiographic image from the right (TTE-R), (C) transthoracic echocardiographic image from the left (TTE-L), (D) transesophageal echocardiographic image in 2D (TEE-2D), (E,F) transesophageal echocardiographic image in 3D (TEE-3D) with perpendicular measurements A (minor axis) and B (major axis) of the pulmonary ostium (E) and ampulla (F) with the 2D reference images included. Ao, aorta; PA, pulmonary artery

FIGURE 2  Transthoracic echocardiographic image obtained in a right parasternal short axis basilar view to demonstrate the difference between the location of the left branch PA (outlined in blue) and pulmonary ostium of the PDA (outlined in yellow). Ao, aorta; rPA, right branch PA
ostium were clearly visible and the timing in the cardiac cycle was recorded based on review of the simultaneous ECG.

The TEE-3D A and B measurements were used to determine the shape of the pulmonary ostium and ampulla. The shape was categorized as circular (difference in A and B ≤ 0.5 mm) or oval (difference in A and B > 0.5 mm). Of note, the term elliptical has been used in the canine literature.4,6,17 We elected to use the term oval in this study to encompass all shapes that are not circular including an ellipse. An ellipse indicates the distance between two focal points remains constant whereas an oval can vary in shape.21 Angiographic classification of the PDA was assigned based on Miller’s description in dogs.10

3 | STATISTICAL ANALYSIS

Descriptive statistics were calculated. The D’Agostino-Pearson test was used to verify normal distribution of variables. The angiographic measurements were not normally distributed therefore measurements are reported as median and range. Ductal MDD (or pulmonary ostium) and ampulla measurements were evaluated with Pearson’s correlation coefficient and compared by Bland-Altman analysis.22 For each imaging modality, individual measurements for each dog were compared with the same dog’s TEE-2D measurements and plotted with line graphs. Statistical analyses were performed using commercial software (GraphPad Prism 7 for Windows, GraphPad Software, La Jolla, California). A P value < .05 was considered significant.

4 | RESULTS

4.1 | General characteristics of the study population

Twenty-five dogs with echocardiographic confirmation of left-to-right shunting PDA were enrolled. The median age was 12 months (range, 3–72 months), and median weight was 7.6 kg (range, 2.3–36.8 kg). The majority were female (19/25, 76%). Breeds included mixed (n = 6) and 2 each of Yorkshire Terrier, Labrador Retriever, Chihuahua, German Shepherd, Schnauzer, and English Springer Spaniel. Remaining breeds included one of each of the following: Miniature Poodle, Pomeranian, Maltese, Bichon Frise, Weimaraner, and Shih Tzu. As planned, 20 dogs had a catheter-based occlusion procedure and 5 underwent surgical ligation. Ligation was recommended in 3 dogs that were too small for a catheter-based occlusion procedure and in 2 dogs in which the PDA morphology was tubular and not amenable to catheter-based occlusion. In one of these 2 dogs, angiography suggested multiple aorta to PA communications and surgery was recommended based on the simultaneous TEE images providing additional anatomical information including a short, tubular ductal morphology, and the second communication between the aorta and main PA consistent with an aortopulmonary window cranial to the PDA (Figure 3A,B and Supporting Information).
Video 2). This was the only dog that had a ligation and an angiographic study. In the 21 dogs for whom angiography was performed, morphology was classified as type IIA (n = 16), type IIB (n = 3), type III (n = 1, subsequently ligated), and other (n = 1, similar to Krichenko type D, Figure 3C,D, and Supporting Information Video 2).  

4.2 | Ductal measurements

Ductal measurements were obtained from each imaging modality and are reported in Table 1. Individual measurements for the angiographic MDD and echocardiographic pulmonary ostium are displayed in Figure 4. There was significant, but weak, correlation between angiographic MDD and TEE-2D pulmonary ostium measurements ($r = .56, P = .008$) in this study population (Figure 5A). This was explored further with Bland-Altman analysis (Figure 5). Figure 5B-F shows the Bland-Altman analysis for TEE-2D measurements compared to measurements from the other modalities (angiography, TTE-R, TTE-L, TEE-3D A, and TEE-3D B). The TEE-2D measurement was selected for comparison because it typically provides a complete image of the PDA. The limits of agreement were wide for each modality. Notably, TTE-R and TTE-L measurements were consistently larger than those derived by TEE-2D measurements.

4.3 | Ductal characteristics and shape

For the 24 dogs in which TEE-3D was performed, the optimal image of the PDA used in the analysis was obtained during diastole (23/24) and systole (1/24). Systolic measurements were selected as the ideal image in one dog with an unusual PDA morphology (Figure 3C,D) that did not readily fit into Miller’s classification scheme. Of note, the pulmonary ostium in this dog was at an angle best visualized with TEE-3D, thus

|                  | Angiography (mm) | TTE-R (mm) | TTE-L (mm) | TEE-2D (mm) | TEE-3D (mm) |
|------------------|------------------|------------|------------|-------------|-------------|
| Angiographic MDD/Echocardiographic pulmonary ostium | 3.0 (1.8–4.8) | 4.2 (1.5–8.1) | 3.2 (2.0–4.5) | 3.0 (1.3–5.7) | A: 2.1 (0.4–3.6) B: 3.1 (0.9–5.8) |
| Ampulla          | 8.1 (3.2–11.3)   | 9.1 (4.5–13.0) | 8.7 (3.5–12.1) | 7.6 (4.0–14.8) | A: 5.7 (1.4–8.3) B: 7.6 (2.6–11.8) |

Abbreviations: MDD, minimal ductal diameter; L, left; R, right; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; 2D, two-dimensional; 3D, three-dimensional. Data reported as median (range).

**TABLE 1** Patent ductus arteriosus measurements in dogs

![FIGURE 4](dot_plot.png) Dot plot of angiographic MDD and echocardiographic pulmonary ostium measurements. The solid line represents the median. TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; R, right; L, left; 2D, two-dimensional; 3D, three-dimensional.
this dog’s measurements represent the outlying lowest value for TEE-3D A and B in Figure 4. When comparing the TEE-3D A and B dimensions for the pulmonary ostium and ampulla, A was smaller than B in 23/24 (96%; 1 dog A = B) for the pulmonary ostium (Figure 8) and 20/24 (83.3%; 3 dogs A > B; 1 dog A = B) for the ampulla. The majority of dogs had an oval shape pulmonary ostium (17/24; 71%, Supporting Information Video 1) and ampulla (19/24; 79%). The 7 dogs with a circular-shaped pulmonary ostium were all classified with a Type IIA PDA morphology on angiography, and the TEE-3D B diameter of the circles was below 4 mm, ranging in size from 0.9, 2.2, 2.4, 2.6, 2.9, 3.2, and 3.6 mm. The shape combinations for the pulmonary ostium/ampulla in which O denotes an oval and C denotes a circular shape included O/O in 16, O/C in 1, C/O in 3, and C/C in 4.

When performing biplane TEE imaging, we observed that it was difficult to consistently and accurately place the cursor across the ampulla in a manner that did not create an oblique angle. For this reason, we did not include these measurements in the final analysis and caution their use in making an assessment of circular or oval shape. The reference 2D image can help the operator determine if the cursor crosses perpendicular or at an oblique angle.

4.4 | Device characteristics

Median ACDO size for 20 dogs in which a device was placed was 7 (range, 3–10). Median ACDO to MDD ratio was 2.0 (range, 1.5–3.2) with angiography, and ACDO to pulmonary ostium ratio was 2.1 (range, 1.4–3.3) with TEE-2D, 3.1 (range, 1.4–7.5) with TEE-3D A, and 2.0 (range, 1.1–3.4) with TEE-3D B. Median ACDO proximal disc to ampulla ratio was 1.7 (range, 1.3–2.8) with angiography, 1.7 (range, 1.1–2.6) with TEE-2D, 2.2 (range, 1.4–7.5) with TEE-3D A, and 1.6 (range, 1.1–4.0) with TEE-3D B. Based on TEE-2D and angiographic imaging, the median oversize factor for the ACDO to pulmonary ostium was similar to ratios previously reported (median 2.0 depending on imaging modality used to select a device in an individual dog), and the
proximal disc to ampulla diameter ratio was always > 1. No complications occurred in any dog and there was no residual flow on TTE before discharge.

5 | DISCUSSION

The results of this study provide additional information regarding 3D morphology of PDA in dogs. Earlier reports suggested on oval-shaped PDA can occur in dogs, which is not surprising based on histopathologic appearance of the PDA and variability in ductal wall muscle tissue.6,8,9 Angiography and TTE display a 2D image of the PDA and does not readily demonstrate the variation in cross sectional shape (ie, circular, oval). In this study, TEE-3D provided unique information regarding overall shape and measurements ("A" and "B") by displaying the pulmonary ostium of the PDA en face. We evaluated the shape of the ampulla and pulmonary ostium to demonstrate that there are a variety of shape combinations with the majority (71%) of dogs in this study identified as having an oval-shaped pulmonary ostium. This is much higher than in a previous study in which 5 of 80 dogs (6%) were reported to have an elliptical shaped ostium based on TEE-2D imaging.17 Biplane TEE images from 2D can be difficult to align in a perpendicular plane directly through the pulmonary ostium, resulting in an oblique view and a false impression of the ductal shape and size. A noncircular shape could lead to differences in diameter measurements between imaging modalities depending on the location and angle in which the image of the PDA was obtained.

Historically, single plane lateral angiography was used to create the current PDA morphology classification system in dogs.10 and angiographic measurements are the basis for sizing recommendations in the original reports of the ACDO device.1,11 Subsequent reports using the ACDO included ampulla diameter measurements from angiography and echocardiography compared with the device proximal disk dimension when selecting device size.2,17 Ductal measurements tend to vary between imaging modalities. Characterizing solely based on single plane angiography may not always be adequate10 particularly when contrast is delivered by a hand injection in large dogs or in large, high flow PDA, and TTE can be limited by image quality and overestimates of size.1,7,17 It is important to consider that TTE has consistently been shown to overestimate angiographic measurements in other studies.1,17 and TEE measurements in our study. Comparisons in our study were made to the TEE-2D measurements because TEE-2D provides direct visualization of the walls of the PDA extending from aorta to the pulmonary ostium. In our study, TEE identified dogs with unusual ductal anatomy (Figure 3) and helped guide next steps for successful closure. Whereas, measurements can statistically appear to relate well between modalities when looking at the study population that includes all dogs, the individual comparison of measurements by different techniques in an individual dog shows the absolute values are different and are not always interchangeable. This could be related to the variation in PDA shape, change throughout the cardiac cycle, and angle in which each image and therefore measurement is obtained. In one study, the difference between TTE and TEE measurements would have resulted in devices that differed by up to 2 sizes in 17/80 (21%) of the dogs.17 Ultimately, small differences in measurements are unlikely to alter the procedure or outcome but large differences could be important and affect device selection and sizing.

The ACDO is made up of two circular-shaped disks (one flat, one cupped) separated by a waist and constructed of nitinol mesh designed to conform to the ampulla of the PDA when deployed.12 In dogs, sizing issues are reported resulting in the device not assuming its native shape after deployment, residual flow through or around the device, and device embolization.1,4,7,17 Avoiding undersizing is important because the PDA can increase in size after occlusion,1 which is one possible cause for device embolization in the authors’ experience.24 Therefore, obtaining accurate anatomic information is valuable for avoiding complications with the procedure.

Some dogs in this study had ductal anatomy that did not readily fit into the current classification scheme. Successful ductal occlusion in this study was achieved in part as a result of information gained with intraoperative TEE imaging. The PDA classification scheme in humans includes a larger range of morphologies than dogs that is based on location (ie, pulmonary, mid ampulla, or aorta) of the narrowest part of the PDA and includes groups with multiple constrictions or unusual/unique morphologies.23 With advancements in 3D imaging and as TEE probes become more readily available in veterinary medicine, updates to both the current morphology classification to include additional morphologies and angiographic based sizing guidelines to include TEE assessment of multidimensional anatomy, shape, and ampulla diameter may help to further minimize or avoid complications. We propose the addition of two categories to the current 3 (type I, II, III) to include those with multiple narrowings at various levels (type IV, similar to type D25) and other unusual morphologies (type V, Figure 3), both of which have been encountered by the authors, to recognize that there are dogs with PDA morphologies that do not fit in the current classification.
scheme and may require additional imaging and procedural planning for a successful outcome. An oval shape was not more likely to occur in any one type of ductal morphology in this study, and we did not identify specific factors in other imaging modalities (ie, angiography, TTE-2D, or TEE-2D) that would have indicated an oval shape with 3D imaging. More detailed information about shape and dimensions obtained with TEE may be of value particularly in complicated cases with unusual ductal morphology or in situations where less experienced operators are performing the procedure. As we have recently reported, training and confidence levels when performing ductal occlusion vary.26

This study has several limitations. Measurements are not compared with gross specimens to confirm accuracy. Therefore, it is not possible to know which modality is truly most accurate. This is a small study; but despite this limitation, we were able to include a variety of PDA morphologies. The majority of ductal morphologies are Type II but other morphologies do occur and proper imaging is essential for

FIGURE 7 (A) Correlation between angiographic and TEE-2D ampulla measurements; (B-F) Bland-Altman plots for TEE-2D ampulla measurements compared to (B) angiographic, (C) TTE-R, (D) TTE-L, (E) TEE-3D A, and (F) TEE-3D B. Dashed lines represent 95% limits of agreement and solid line represents the mean bias

FIGURE 8 Line graph comparing TEE-3D A and B pulmonary ostium measurements for each dog to demonstrate circular or oval shape
guiding management decisions. Although there are clear benefits of TEE, it requires purchase of a specialized probe, experienced operators to perform the study during the procedure and cannot always be used in very small dogs. At our institution, TEE is performed in some dogs during surgical ligation to confirm closure although air interface can adversely affect image quality as occurred in one dog in this report.

In conclusion, TEE-3D provides a unique view of the PDA that cannot be replicated with other echocardiographic techniques or single plane angiography. We demonstrated that the majority of dogs in this study had an oval not circular-shaped PDA and that the PDA changes throughout the cardiac cycle. A noncircular shape could lead to differences in diameter measurements between imaging modalities depending on the location and angle the image was obtained which is one possible reason for the weak correlation between angiographic and echocardiographic measurements. We recognize that small differences in measurements might not be important but large differences could affect treatment decisions and result in procedural complications. This morphologic information may be useful for device sizing and future development of devices. We also encountered PDA morphologies that did not fit into the current classification scheme suggesting an updated scheme would be useful. Our recommendations for making procedural decisions and selecting device size are to use the measurements from the highest quality image and to be cautious making decisions based on measurements from images that do not clearly delineate the PDA.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

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

This study was approved by the IACUC and the Clinical Research and Review Committee at Texas A&M University.

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SUPPORTING INFORMATION

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