




Patent ductus arteriosus in capybaras (*Hydrochoerus hydrochaeris*) – a case report

Persistência do ducto arterioso em capivara (Hydrochoerus hydrochaeris) – relato de caso

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ABSTRACT: The ductus arteriosus (DA) is an arterial connection between the pulmonary arteries and the aorta and is essential during the fetal life of mammals. Minutes after birth, this duct begins to close, however, when this does not happen, blood flow remains, which characterizes the patent ductus arteriosus (PDA). Patients with PDA can present significant hemodynamic alterations, such as ventricular systolic dysfunction and congestive heart failure. However, they can live with this heart disease without any clinical signs, depending on the size of the duct, blood flow volume, and pressure between arteries. Currently, this is one of the most common congenital heart diseases among dogs, however it had never been reported among capybaras. Thus, the objective of the present study was to report the occurrence of PDA in a female, 1 year-old, 40.1-kg, free-living capybara. The animal underwent chemical restraint using dexmedetomidine (8.72 mcg/kg) and ketamine (7.48 mg/kg), intramuscularly. After restraint, the animal presented a heart frequency of 67 bpm, regular rhythm, invasive systolic, diastolic, and mean blood pressure of 105/92/77 mmHg, respectively, and the echocardiographic examination showed the presence of a continuous turbulent flow within the pulmonary artery, with maximum velocity of 3.90 m/s and a pressure gradient of 60.96 mmHg, from left to right, which characterized the presence of a classic aorta-pulmonary PDA. Given that this was a free-living animal that did not present cardiac remodeling, nor alterations related to the PDA regarding the parameters of the echocardiographic examination, no intervention was conducted.

KEYWORDS: rodents; congenital heart diseases; echocardiography; capybaras.

RESUMO: O ducto arterioso (DA) é uma conexão arterial entre as artérias pulmonar e aorta, essencial na vida fetal dos mamíferos. Minutos após o nascimento esse ducto inicia-se o processo para sua oclusão, porém quando isso não ocorre temos a permanência do fluxo sanguíneo caracterizando a persistência do ducto arterioso (PDA). Os pacientes com PDA podem apresentar alterações hemodinâmicas significativas como disfunção sistólica ventricular e insuficiência cardíaca congestiva. Contudo, podem conviver com a cardiopatia sem sinais clínicos, a depender do tamanho do ducto e do volume e pressão do fluxo sanguíneo entre as artérias. Atualmente é uma das cardiopatias congênitas mais comum em cães, mas sem relatos em capivaras. Assim, objetiva-se relatar a ocorrência da PDA em uma capivara, fêmea com 1 ano de idade, pesando 40,1 kg de vida livre. O animal foi submetido a contenção química com dexmedetomidina (8,72) mcg/kg e cetamina (7,48 mg/kg), pela via intramuscular. Após a contenção o animal apresentava-se com FC 67 bpm, ritmo regular, pressão arterial invasiva sistólica, diastólica e média de 105/92/77 mmHg, respectivamente e, no exame ecocardiográfico, verificou-se a presença de fluxo turbulento contínuo no interior da artéria pulmonar, com a velocidade máxima de 3,90 m/s e gradiente de pressão de 60,96 mmHg, com sentido esquerda para a direita, o que caracterizou a presença de PDA clássico sentido aorta-pulmonar. Por se tratar de um animal de vida livre que não apresentava remodelamento cardíaco e alteração relacionada ao PDA nos parâmetros do exame ecocardiográfico, optou-se em não realizar qualquer intervenção.

PALAVRAS-CHAVE: roedores; cardiopatias congênitas; ecocardiografia; capivaras.

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INTRODUCTION

The ductus arteriosus (DA) is an arterial connection between the pulmonary arteries and the aorta and is essential to maintain the life of mammal fetuses during the intrauterine stage, because it allows arterial blood to deviate blood flow to the lungs, considering that hematosis occurs in the placenta and lungs require a small blood intake (Ecco *et al.*, 2008; Forsey; Elmasry; Martin, 2009; Gournay, 2011). The duct closes within minutes after birth (Gittenberg-de Groot *et al.*, 1980; Gittenberg-de Groot *et al.*, 1985; Clyman *et al.*, 1999), with a replacement of fibrous ligament. Functional closure is related to simple mechanisms and the most important one is the increase in partial pressure of oxygen in the arterial blood that occurs with pulmonary expansion and oxygenation. There is a reduction in the resistance against systemic blood flow, and an increase in the pressure in the aorta due to a rapid interruption of the flow that previously originated from the placenta. Oxygen inhibits potassium channels and leads to an influx of calcium in smooth muscle cells, thus causing vasoconstriction (Santos; Alessi, 2016; Anilkumar, 2013).

If the duct does not close, the situation is characterized as patent ductus arteriosus (PDA), which maintains blood flow between the pulmonary artery and the aorta (Gittenberg-de Groot *et al.*, 1980; Santos; Alessi, 2016). This will occur if the normal response to birth is interrupted either because of alterations in the histological development of the ductal tissue or if there are alterations in oxygen tension at birth; however, in term babies, the exact mechanisms that prevent duct closing are unknown (Anilkumar, 2013). PDA is the most common congenital heart disease among dogs, responsible for 21 to 32% of congenital heart alterations (Buchanan, 1999); in humans, it represents 10% of all congenital heart alterations (Mullins; Pagotto, 1998).

The diagnosis is conducted through clinical and echocardiographic examinations (Forsey; Elmasry; Martin, 2009). Echocardiography is increasingly being used in non-domestic species because of the need to conduct cardiological evaluations in these animals (Locquet *et al.*, 2020). However, in unconventional patients, the use of chemical restraint to conduct an echocardiographic examination is essential. The literature consulted shows that alpha-2 adrenergic or benzodiazepine agonists, associated with ketamine, are the most frequently used drugs to chemically restrain capybaras (Cruz *et al.*, 1998; Salas *et al.*, 2004; Monsalve-Burítica; Rojano-Bolano; Carrascal-Velásquez, 2013).

Therefore, because of the limited description of heart diseases in unconventional species, such as capybaras, the objective of the present study was to report the occurrence of PDA in a specimen of capybara (*Hydrochoerus hydrochaeris*), observed after chemical restraint to conduct a salpingectomy.

CASE REPORT

A specimen of *Hydrochoerus hydrochaeris*, which originated from the Raia Olímpica aquatic sports area of the University of São Paulo, located in the municipality of São Paulo/SP, Brazil, was studied in the present report. The individual was a female,

approximately 1 year old, weighing 40.1 kg, and underwent chemical restraint via a tranquilizer dart with 8.72 mcg/kg of dexmedetomidine⁴ and 7.48 mg/kg of ketamine⁵, as preparation for a salpingectomy surgical procedure. The animal was part of the study entitled “Echocardiographic evaluation of the effects of isoflurane in capybaras *Hydrochoerus hydrochaeris* that underwent chemical restraint using dexmedetomidine associated with ketamine”, approved by the Animal Ethics Committee (CEUA) of the School of Veterinary Medicine of the University of São Paulo, protocol No. 2396210621^(ID009190) and by the Authorization and Information System in Biodiversity (SISBIO) No. 70016-3, of the Chico Mendes Institute for Biodiversity Conservation–ICMBio, Ministry of Environment and Climate Change – MMA.

Fifteen minutes after injecting the tranquilizer dart in the subscapularis muscle, the animal was in lateral decubitus, with adequate muscle relaxation, and was transported to the surgery center where it was placed in left lateral decubitus. After antisepsis of the distal region of the radius, the radial artery was catheterized using a 22G catheter to measure invasive blood pressure. The catheter was connected to the electronic pressure transducer and zeroed at the sternum level via stent filled with a heparin solution. The solution was prepared using 5UI of heparin⁶ per mL of saline solution 0.9%, using 1 mL to rinse the system in order to read blood pressure values (systolic, average, diastolic). The square-wave test (MCGHEE; BRIDGES, 2002) was conducted every 15 minutes in order to check if the blood pressure measuring system was working properly. Fluid therapy was conducted using a Ringer’s lactate solution at a rate of 5 mL/kg/h after inserting a catheter of adequate size (20 G) in the aseptically prepared cephalic vein.

In order to conduct the transthoracic echocardiogram examination, an echocardiographic⁷ device was used with a coupled adult 3Sc phased array transducer. The examination was carried out by a veterinarian who was trained and experienced in conducting echocardiograms in various species. Because of the absence of literature description on the echocardiography examination of capybaras so far, all measurements were carried out according to the recommendations of the Echocardiography Committee of the Cardiology Specialty of the American College of Veterinary Internal Medicine (Thomas *et al.*, 1993). First, images were obtained of the left parasternal window, apical 4-chamber view, with a transducer positioned between the 4th and 5th ICS (intercostal space) close to the left sternal region. By rotating the transducer caudally, the apical 5-chamber view was obtained, showing the exit pathway of the LV (left ventricle), the aortic semilunar valve, and the ascending aorta. Next, the transducer was rotated clockwise and cranially tilted, to acquire the apical cranial view.

In the right hemothorax, the transducer was positioned between the 4th and the 5th ICS, approximately 4 cm away from

⁴Dexdomitor®, Zoetis, New Jersey, USA

⁵Cetamin®, 100 mg/ml, Syntec, Santana de Parnaíba, SP, Brazil

⁶Hepamax-S®, Blau Farmacêutica S.A., São Paulo, SP, Brazil

⁷Logig E, General Eletrics, Boston, MA, USA

the sternal region, parasternal window to obtain the 4-chamber longitudinal view. The tilt and anticlockwise movement of the transducer allowed to obtain the longitudinal view, thus identifying the exit route of the left ventricle and ascending aorta. In order to conduct the cross view, the transducer was rotated from 90° to 0°, with the transducer marker directed at the right elbow, thus obtaining the papillary, coronal, aortic, and pulmonary planes. Therefore, ventricular diastolic and systolic, left atrium, and pulmonary artery diameters were measured, pulmonary artery flow was obtained, and ejection fraction and ventricular shortening were calculated using the M-Mode and the Teicholz Method.

During the echocardiographic examination, the animal presented a heart rate of 67 beats per minute (bpm), regular rhythm, and systolic, diastolic, and mean invasive arterial pressure of 105/92/77 mmHg, respectively.

According to the quantitative and qualitative analysis of the echocardiogram (B mode) using the Swedish method (short axis), the aorta measured 2.34 cm, the left atrium measured 2.98 cm, and the left atrium-to-aorta ratio was 1.3. On the other hand, using the Ohio method (long axis), the aorta measured 1.31 cm, the left atrium measured 2.82 cm, and the left atrium-to-aorta ratio was 2.1. Using the M-Mode on the left ventricular papillary plane, the following structures were measured: septal intraventricular diameter (0.6 cm); left ventricle in diastole (4.04 cm); and free diastolic wall (0.6 cm). During the systolic phase, the following structures were measured: septal diameter (0.88 cm); internal diameter of the LV (2.64 cm); and free wall (0.89 cm). Septal systolic intraventricular movements and the free wall of the LV were kinetic and, with the measurements obtained, the shortening fraction of the LV and the ejection fraction using the Teicholz Method were calculated and presented values of 34% and 64%, respectively. However, using Simpson's method for volume calculation in the left ventricle, the diastolic volume was 72.14 mL and the systolic volume was 37.61 mL, resulting in an ejection fraction of 56%. No alteration was observed in the diastolic diameter of the right ventricle and atrium, nor abnormalities in the pericardial sack.

Regarding the atrioventricular valves, the mitral valve showed normal aspect and movement of its cusps, though a discrete insufficiency with no hemodynamic repercussions was observed through the Doppler analysis, when mapping the color flow (Figure 1). In turn, the tricuspid valve also presented normal aspect and movement of its cusps but was normal as well in the Doppler color flow mapping. The semilunar and aortic valves did not present morphological abnormalities, but a continuous turbulent flow within the pulmonary artery was detected through the Doppler assessment.

In the hemodynamic evaluation, the maximum velocity of the aortic flow was 0.99 m/s with a pressure gradient of 3.88 mmHg; while the maximum velocity of the pulmonary flow was 0.64 m/s, generating a gradient of 1.66 mmHg. When assessing the diastolic function, using the 4-chamber apical view – left parasternal window, and activating the pulsed Doppler at the

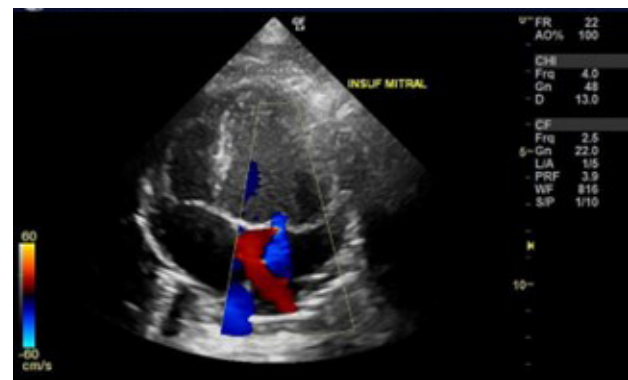
level of the mitral valve and within the LV, the velocity of the mitral E-wave propagation was measured as 0.66 m/s, while the A-wave was 0.38 m/s of the transmitral flow. The deceleration time of the mitral E-wave was 106 m/s, and the E/A ratio was 1.7. Using the 5-chamber apical view, an isovolumetric relaxation time (IVRT) of 85 m/s was obtained. A tissue Doppler was activated and captured on the free wall of the LV, yielding measurements of 0.15 m/s for the E-wave velocity, 0.08 m/s for the A-wave, and 0.1 m/s for the S-wave. Given the values obtained, it was possible to calculate the E/E' ratio at 4.4 and the E/IVRT ratio at < 1. Thus, ventricular diastolic function was determined following a E>A and E'>A' pattern, which is compatible with a normal ventricular filling pattern.

The aortic velocity time integral (VTI) was 24.70 cm and the diameter of the exit pathway of the left ventricle was 1.31 cm. Using the right parasternal window – pulmonary plane, when analyzing the pulmonary arterial flow, a continuous turbulent flow was identified within the pulmonary artery, with a maximum velocity of 3.90 m/s and a pressure gradient of 60.96 mmHg, following a left to right direction. The pulmonary ostium (duct) measured 0.56 cm and was 1.69 cm long, confirming the presence of a classic PDA along the aorta-pulmonary direction (Figures 2, 3, and 4).

DISCUSSION

The ductus arteriosus (DA) is a large vessel composed of a layer of vascular smooth muscle cells separated by a layer of elastin (Bökenkamp *et al.*, 2010). In normal conditions, this duct contracts just after birth, due to the postnatal reduction in prostaglandin E₂, and to the increase in oxygen tension that induces an increment of endothelin-1 in the ductal canal of the smooth muscle cells (Forsey; Elmasry; Martin, 2009).

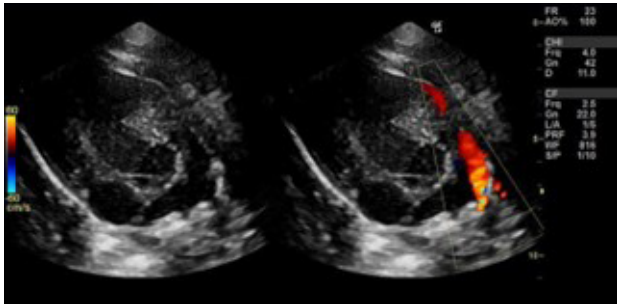
The sequence of structural alterations that happens in all species is as follows: endothelial displacement of the internal elastic lamina, subendothelial accumulation of extracellular matrix, migration of vascular smooth muscle cells through the internal elastic lamina, occlusion of the lumen due to thickening



Source: Lima *et al.* (2023)

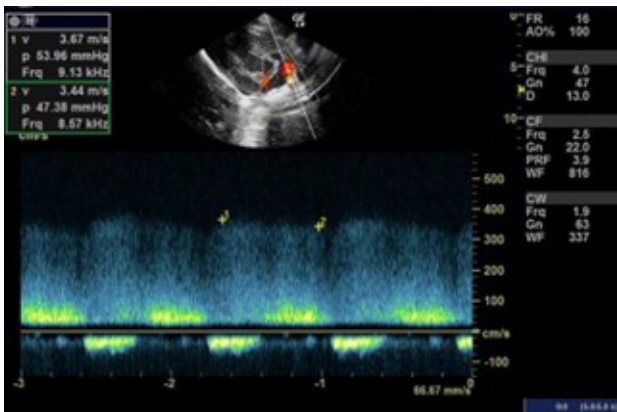
Figure 1. Doppler flow carried out on a female, 1 year-old capybara (*Hydrochoerus hydrochaeris*), demonstrating mitral valve insufficiency.

of the intimal layer, degeneration of the ductus arteriosus in a remaining fibrous area (Bergwerff; Deruiter; Gittenberg-de Groot, 1999; Agren *et al.*, 2007). This process occurs from the pulmonary to the aortic extremities. All this anatomic remodeling and definitive closing of the DA requires environmental changes related to birth and breathing (Bökenkamp *et al.*, 2010).



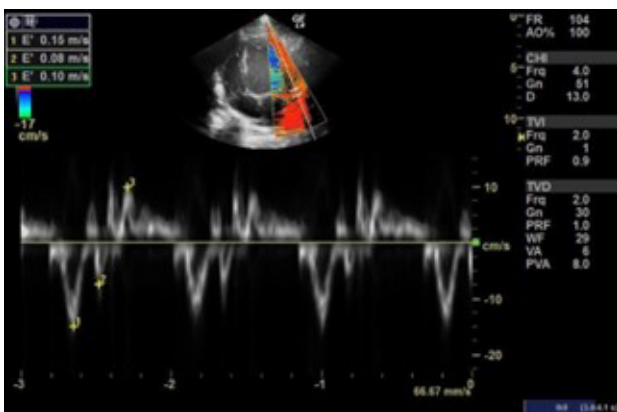
Source: Lima *et al.* (2023)

Figure 2. Doppler flow of the pulmonary artery – pulmonary plane/right parasternal window, of a female, 1 year-old capybara (*Hydrochoerus hydrochaeris*), demonstrating patent ductus arteriosus, flowing in an aortic-pulmonary direction.



Source: Lima *et al.* (2023)

Figure 3. Flow velocity from left to right in a female, 1 year-old capybara (*Hydrochoerus hydrochaeris*).



Source: Lima *et al.* (2023)

Figure 4. Measurements of E', A', and S' waves in a female, 1 year-old capybara (*Hydrochoerus hydrochaeris*).

There are no reports in the literature about the closing of the duct in capybaras, though it is believed that it occurs in a similar manner to that of other mammals.

The causes of patent ductus arteriosus may be structural, functional, genetic or caused by any physiological alteration or immaturity (for example, babies with respiratory failure at birth present a significant delay in duct closure) (Walther; Benders; Leighton, 1993; Bökenkamp *et al.*, 2010). The symptomatology and prognosis of PDA relies heavily on the size of the duct and the degree of left-to-right shunt. Patients with moderate to large-sized ducts usually present significant hemodynamic alterations, which can include congestive heart failure, which was not observed in the present case study of a capybara. In turn, patients with a small shunt may not develop any symptomatology and can live well with this congenital alteration (Espino-Vela; Cardenas; Cruz, 1968).

The occurrence of PDA had not been reported previously in capybaras, probably due to the difficulty in performing the diagnosis, but the causes are thought to be the same as those studied in other mammals. Similarly, in the literature consulted, there are no studies regarding echocardiograms on this species, which favors the description of the echocardiographic measurements obtained. The animal studied is free-living and roughly 1 year old. Since it belongs to a group that is restricted to the Raia Olímpica area of the University of São Paulo, it was possible to follow-up on its growth. No alterations were identified, such as delayed development, weight loss or any other clinical sign of congestive heart failure.

The diagnosis of PDA occurs through a clinical examination and is confirmed through an echocardiogram (Forsy; Elmasry; Martin, 2009). In the patient studied, since this was the case of a wild and free-living animal, a clinical examination was not possible prior to chemical restraint. Thus, prior auscultation was not carried out on the patient. However, after the chemical restraint, cardiac auscultation allowed the detection of a continuous, high-grade murmur in the left hemithorax, with approximate aortic and pulmonary foci, which is characteristic of PDA.

In transthoracic echocardiograms on humans, the transverse image of the heart base is obtained through the right parasternal window, while images of the left ventricle exit pathway are obtained through the left parasternal window, which allow the visualization of the pulmonary artery and the duct, which is operator dependent. Ductal blood flow can be evaluated through continuous Doppler color flow mapping (Forsy; Elmasry; Martin, 2009). In the echocardiographic examination of the studied animal, the images used were obtained by positioning the transducer towards the 4th and 5th intercostal spaces (ICS), near the sternal region on the left side; on the right side, the transducer was positioned between the 4th and 5th ICS, at approximately four centimeters from the sternal region. The positions were defined in a previous pilot study, in which echocardiograms were carried out on several animals of this species. All structures evaluated in the echocardiogram could be visualized and measured, as well as the presence of a continuous blood flow in the duct through the color flow mapping.

Deviation of the blood flow from the aorta artery to the pulmonary artery, meaning a left-to-right shunt, leads to an overload of the left ventricle due to greater preload (increase in final diastolic volume), with increased contractility following Frank-Starling law. Since the left ventricle compensates increasing systolic volume, excentric hypertrophy may develop. Dogs with PDA present an increase in final systolic volume and aortic velocity. There may also be an increase in the left atrium as a consequence to volume overload (Kittleson, 1998). In the present report, since there is no reference to the species, heart remodeling could not be identified.

In the study by Spalla *et al.* (2016), when comparing the echocardiogram findings of healthy dogs and dogs with PDA, the ejection fraction and shortening fraction did not differ between the groups. The ejection fraction and systolic volume may not differ between healthy and unhealthy hearts; this is due to an underestimation of contractility that occurs in dogs with PDA. The ratio between the pulmonary flow and systemic flow may be considered a marker for shunt severity and can be taken into consideration to classify the extension of flow deviation as slight, moderate, or severe (Spalla *et al.*, 2016). The animal studied in the present report presented mitral insufficiency, which is caused by the distancing of the leaflets due to dilation of the left ventricle, but the left ventricle and atrium were not augmented, and the other echocardiogram parameters were also unaltered. However, although there are no standardized and validated values for this species, before evaluating the animal of this case study, echocardiograms were conducted on another 14 animals, and by comparing the parameters obtained among them no relevant alterations were detected.

The treatment options for PDA that present significant hemodynamic alteration include conservative management, pharmacological interventions, surgical ligation, and a transcatheter approach for definitive closing (Park *et al.*, 2021). PDA correction can be carried out through interventional duct occlusion, or by surgical ligation of the ductus arteriosus, which is the most invasive option (Koch *et al.*, 2001; Soengkono, 2019; Bagardi *et al.*, 2022). Undoubtedly, PDA surgical correction on

a free-living animal would demand management and postoperative complications would have to be considered. Dogs with PDA are able to deal better with an overload in volume when compared to dogs with other heart diseases, which occurs as an early adaptive response due to the presence of a high load since birth. However, there are not enough studies to clarify the long-term effects of PDA (Spalla *et al.*, 2016). In medicine of recent years there has been a change in the approach towards closing PDA in newborns, first the impact of PDA on the patient's hemodynamics is assessed and what is the likelihood of the PDA spontaneously closing; after these considerations, the patient may be directed to a duct correction procedure (Park *et al.*, 2021). It is important to emphasize that this animal presented good body condition score and no isolation despite the PDA observed; the prognosis may vary from good to guarded depending on clinical evolution as the patient ages. Echocardiogram parameters have been shown to be specific and precise in detecting abnormalities before clinical signs appear, such that it can be considered the gold standard in early detection of myocardial dysfunction (Spalla *et al.*, 2016). Since the animal in question did not present heart remodeling nor alterations related to PDA in the parameters of the echocardiogram, and also because this is a free-living animal, no intervention was carried out. However, it is extremely important to have a clinical follow-up of the animal to monitor the evolution of the disease.

CONCLUSION

Given the above, we can conclude that in addition to the need to determine the normality parameters for echocardiograms in capybaras, the species may present congenital heart disease such as classic patent ductus arteriosus, as identified through the echocardiographic examination.

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