CASE PRESENTATION

An 11-year-old Thoroughbred gelding was presented for evaluation of poor exercise tolerance. The horse had a lifelong history of poor exercise performance and was retired from training before commencing competitive racing. The horse had a normal heart rate (38 bpm), rhythm and arterial pulse quality. No cardiac murmurs were detected on auscultation. There were no abnormalities associated with the respiratory system; upper airway function was normal during dynamic respiratory endoscopy at all gaits and pulmonary cytology, determined using a transendoscopic tracheal wash and bronchoalveolar lavage were unremarkable. There were no haematological abnormalities or evidence of organ dysfunction from routine serum biochemistry. Echocardiography was undertaken to screen for the presence of myocardial dysfunction.

Two-dimensional transthoracic echocardiography documented the presence of a large rounded hypoechoic defect within the atrial septum. The defect was located in the ventral atrial septum and its left-sided opening was in close proximity to the mitral valve, being 2 cm from the valve annulus. The defect was irregular and elongated, ranging between 2.7 and 3.5 cm in length and 1.2 and 2.5 cm in width (Figure 1). Colour flow Doppler echocardiography demonstrated flow across the septum from the left atrium to the right atrium (Figure 1b). Continuous-wave Doppler echocardiography recorded maximum flow across the defect of 1.0 m/s consistent with a pressure gradient of 3mmHg. Pulmonary artery diameter was within the absolute normal range for a horse of this size (5.8 cm) (Young & Scott, 1998), although the relative size of the pulmonary artery compared with the aorta (0.82:1.0) was just above the reference range (Schwarzwald, 2018). Subjectively the right ventricle was enlarged. Left ventricular size and systolic function where within normal ranges. Doppler echocardiography demonstrated mild mitral, pulmonic and aortic valve regurgitation but these were not considered clinically significant and were not associated with audible...
cardiac murmurs. There was no apparent left atrial or ventricular cardiac enlargement (Table 1).

3D transthoracic echocardiography was used to further evaluate the structure of the defect (Vivid 95 GE Healthcare). 3D constructs were rendered from different visualisation points of the left and right atria and inter-atrial septum using a right parasternal technique. Briefly, the probe was angled dorsally within the 4th intercostal space and rotated 5–10° cranially to visualise the inter-atrial septum in a long axis. Short-axis images were obtained concurrently at the level of the aortic valve. Offline processing using standard post-processing tools (Echopac workstation GE Healthcare) allowed full evaluation of the atrial septal defect from both left and right atrial viewing aspects (Figure 2). 3D echocardiography confirmed the location of the septal defect in relation to the atrioventricular valve structures as well as the tubular nature of the ASD using transverse reconstructions through the defect (Figure 3, Data S1). The left atrial side of the defect was located close to the mitral valve. 3D echocardiography also confirmed the apparent widening of the ASD as it passed through the septum. No other abnormalities of the atrial septum or atrioventricular valves were apparent. Given the absence of other apparent causes of poor exercise tolerance, this was attributed to the presence of the atrial septal defect with right ventricular enlargement. Although we were unable to document evidence of pulmonary hypertension at rest, clinically relevant hypertension may have occurred at exercise beyond what would be considered a normal response (Erickson, Erickson, & Coffman, 1990). The horse was retired to pasture.

### DISCUSSION

Congenital cardiac diseases are relatively more frequent in humans than horses, representing approximately 0.1% of live human births (Šamánek & Voříšková, 1999) and ASDs are one of the most common of these, constituting 10 to 15 per cent of all congenital cardiac defects and up to 40 per cent of congenital cardiac defects presenting in adulthood (Therrien and Webb, 2003). ASDs have been occasionally described in dogs, accounting for 1% of

| Structure and view                          | Dimension | Reference range                        |
|---------------------------------------------|-----------|----------------------------------------|
| Aortic diameter (diastole) LVOT<sub>LAB</sub> | 7.1 cm    | 6.4–7.8 cm (Schwarzwald, Schober, & Bonagura, 2007) |
| Pulmonary artery diameter (diastole) RVOT<sub>LAB</sub> | 5.8 cm    | 5.5–6.8 cm (Schwarzwald et al., 2007) |
| Left ventricular diameter (diastole) LV<sub>SAM</sub> | 11.1 cm   | 8.0–14.0 cm (Vörös, Holmes, & Gibbs, 1991) |
| Left ventricular diameter (systole) LV<sub>SAM</sub> | 7.1 cm    | 5.9–9.1 cm (Vörös et al., 1991) |
| Right ventricular diameter (diastole) LV<sub>SAM</sub> | 4.8 cm    | <4.2 cm (Howard, Bowen, & Hallowell, 2014) |
| Right ventricular diameter (systole) LV<sub>SAM</sub> | 4.3 cm    | <4.1 cm (Howard et al., 2014) |
| Left atrial diameter (diastole) L-L A<sub>LAB</sub> | 11.8 cm   | 9.4–12.3 cm (Schwarzwald et al., 2007) |

Note: Images were obtained using standardised views of LVOT<sub>LAB</sub> – 2D (B-mode) right parasternal long-axis view of the aorta, RVOT<sub>LAB</sub> – 2D(B-mode) right parasternal long-axis view of the pulmonary artery, LV<sub>SAM</sub> M-mode of the right parasternal short-axis view at the chordal level and L-L A<sub>LAB</sub> – 2D (B mode) left parasternal long-axis view at the mid-atrium.
congenital cardiac defects in this species (Oliveira et al., 2011), although given their occurrence in the absence of cardiac murmurs their true prevalence in these studies may be an underestimate. Ventricular septal defects are the commonest congenital cardiac defect in horses and may be diagnosed up to six times more frequently than any other congenital cardiac defect (Marr, 2010). However, there are few reports of atrial septal defects (ASD) in horses in the absence of complex congenital cardiac malformations (Chaffin, Miller, & Morris, 1992; Physick-Sheard, Maxie, Palmer, & Gaul, 1985; Taylor, Wotton, Hillyer, Barr, & Luce, 1991), although patent foramen ovale has been reported in foals (Hall, Magdesian, & Kittleson 2010). An atrial septal defect has been reported as an isolated lesion in one foal with atrial fibrillation that developed heart failure (Taylor et al., 1991).

Atrial septation has been described in the equine fetus (Vitums, 1981) and follows a similar pattern to other mammalian species. The primitive atrium is divided by the septum primum, which originates from the roof of the common atrium with its free end extending towards the endocardial cushions. The foramen primum is the communication between the atria before the septum primum fuses to the endocardial cushions. The foramen primum is the communication between the atria before the septum primum fuses to the endocardial cushions. The septum primum becomes fenestrated close to the pulmonic veins creating the foramen secundum, which facilitates intra-atrial communication and pulmonary vascular shunting after closure of the foramen primum (Anderson,
Webb, Brown, Lamers, & Moorman, 2003). The septum secundum forms on the right atrial side of the septum and the crista dividens channels post-caval blood from left atrium through the foramen secundum into the right atrium. The septum primum forms the valve of the foramen ovale, closing the atrial septum as pressure increases in the left atrium after parturition. In this horse there appears to be either excessive resorption of the septum primum in the formation of the foramen secundum or a failure of proper development of the septum secundum resulting in this foramen secundum type defect.

ASDs are not typically associated with cardiac murmurs related to flow across the atrial septum in any species and, as such, are often only recognised when animals undergo echocardiography. Ejection type murmurs have been reported in dogs and human patients with ASDs, related to pulmonary artery ejection. Given the high frequency of physiological ejection murmurs associated with the aortic valve in horses (Patteson & Cripps, 1993), ejection type murmurs associated with the pulmonary outflow may be misrecognised in the horse where the musculature of the forelimb limits auscultation over the third intercostal space. As such, diagnostic suspicion may be missed in horses with ASDs, thus the limited recognition of this condition may not be an accurate reflection of its prevalence in the general horse population. No cardiac murmurs were identified in this case.

Given the paucity of literature regarding the impact of atrial septal defects in horses, conclusions about their clinical significance cannot be made. It is not possible to confirm that the poor exercise tolerance in this horse was a direct result of the cardiac defect. However, performance limiting effects have been associated with the presence of atrial septal defects in both human patients and dogs. In human patients, clinical signs usually do not present until adulthood with reduced functional capacity, exertional shortness of breath and supraventricular tachyarrhythmias being the main symptoms (ESC Committee, 2010). Pulmonary infections and right heart failure are seen as less frequent complications (ESC Committee, 2010). Clinical signs of ASDs in dogs are often vague and the severity is often related to the size of the defect. Exercise intolerance and hyperpnoea were observed as clinical signs associated with small isolated atrial septal defects in a study of five dogs (Guglielmini, Diana, Pietra, & Cipone, 2002). ASDs result in right-sided volume overload, increased pulmonary blood flow and can impact on exercise tolerance in humans as these patients have been shown to have smaller increases in cardiac output and maximal heart response during exercise. ASDs can lead to pulmonary hypertension if the excessive pulmonary blood flow is left untreated over a long period of time (Reybrouck & Mertens, 2005). Pulmonary hypertension was not documented in this case at rest, but it was assumed that more marked hypertension occurs at exercise, resulting in poor exercise tolerance. The clinical significance of the lesion is not apparent and without a proven increase in exercise tolerance after closure it would not be possible to confirm its role in the poor exercise capacity of this horse, however, the absence of other lesions makes this our presumptive diagnosis.

As there are no published criteria for classification of atrial septal defects in horses, descriptions have been extrapolated from the literature available in other species. The subjective appearance of right ventricular hypertrophy in the current case is similar to the volume loading seen in human patients. There are various types of atrial septal defect and echocardiographic classification (primum or secundum) is largely based on the location of the defect and its relation to the atrioventricular structures. 2D echocardiographic assessment of the atria in horses is limited by the comparatively narrow cardiac window. 3D echocardiographic techniques provide greater spatial recognition of structures in the heart. It has been used to validate assessment of aortic valve prolapse in the horse (Hallowell & Bowen, 2013) but to date has had limited application in equine cardiology (McElhinney, 2019). The use of 3D echocardiography provided improved special imaging of the defect. 2D echocardiography has been shown to be reliable for detection of foramen secundum-type ASDs in people, but 3D echocardiography has improved their diagnosis and provides additional information for surgical planning (Cheng, Xie, Wang, Wang, & Lu 2004). Given the tubular nature of the defect in this horse, better understanding of its 3D shape is important in its classification and determining potential for closure. The three-dimensional shape of the defect is different from descriptions in other species, as it appears to widen as passes through the septum.

Techniques are described for closure of atrial septal defects in both humans and dogs, with the first transcatheter closure in the dog being reported in 2009 (Gordon et al. 2009). However, closure of atrial septal defects in horses has never been reported. According to guidelines used in human medicine (ESC Committee, 2010), closure of the atrial septal defect in people is indicated in patients with significant left to right shunts and evidence of right ventricular overload, with the development of pulmonary hypertension being the main contraindication for intervention. Although the clinical relevance of this defect is not apparent in this horse, the use of 3D imaging may facilitate the selection of appropriate minimally invasive closure devices in order to close this defect. Re-evaluation of performance capacity following closure may answer questions surrounding the clinical significance of these congenital anomalies in horses.

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CONFLICTS OF INTEREST
The authors do not have any conflicts of interest to disclose.

AUTHOR CONTRIBUTION
Adam Redpath: Conceptualization; Methodology; Software; Visualization; Writing-original draft. Celia MMarr: Conceptualization; Software; Visualization; Writing-review & editing. Caroline Bullard: Investigation; Resources; Writing-review & editing. Gayle Hallowell: Conceptualization; Formal analysis; Methodology; Supervision; Writing-review & editing.
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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section.

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