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Balloon valvuloplasty of valvular pulmonary stenosis in a neonatal foal

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Case Report

Balloon valvuloplasty of valvular pulmonary stenosis in a neonatal foal[☆]



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Abstract In a 1-day old filly with a loud heart murmur, transthoracic echocardiography revealed right ventricular hypertrophy associated with severe pulmonary valvular stenosis and a transvalvular pressure gradient (between right ventricle and pulmonary artery) of 125 mmHg. Computed tomographic angiography confirmed the finding, with no evidence of other relevant concurrent abnormalities. Balloon valvuloplasty was performed using a single balloon technique. The foal

[☆] A unique aspect of the Journal of Veterinary Cardiology is the emphasis of additional web-based images permitting the detailing of procedures and diagnostics. These images can be viewed (by those readers with subscription access) by going to <http://www.sciencedirect.com/science/journal/17602734>. The issue to be viewed is clicked and the available PDF and image downloading is available via the Summary Plus link. The supplementary material for a given article appears at the end of the page. Downloading the videos may take several minutes. Readers will require at least Quicktime 7 (available free at <http://www.apple.com/quicktime/download/>) to enjoy the content. Another means to view the material is to go to <http://www.doi.org> and enter the doi number unique to this paper which is indicated at the end of the manuscript.

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Interventional procedure

recovered well from anaesthesia. Following the procedure, the right ventricle-pulmonary artery transvalvular gradient decreased to 38 mmHg. At follow up examinations after 1 month, 1 year and 2 years, the filly showed normal exercise capacity and echocardiography confirmed the persistent substantial improvement in the transvalvular outflow gradient.

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Abbreviations

BVP	balloon valvuloplasty
CT	computed tomographic
PG	pressure gradient
PA	pulmonary artery
PI	pulmonary valve insufficiency
PS	pulmonary stenosis
PV	pulmonary valve
RV	right ventricle
TR	tricuspid regurgitation

A 1-day-old Dales pony filly weighing 34 kg, presented to the University of Zurich Equine Hospital for evaluation of suspected failure of transfer of passive immunity, pyrexia, weakness and a loud heart murmur.

At presentation, the filly was in sternal recumbency and quiet but alert. Heart rate and pulse rate were 84/min with a regular rhythm. A grade 6/6 continuous murmur (the systolic component louder and coarser than the diastolic component) was present with its point of maximal intensity over the left cranial heart base. Respiratory rate was 36/min and rectal temperature was 39.5 °C. Mucous membranes and coronary bands were bright pink and the capillary refill time was 2 s. Jugular veins were normal, and no ventral oedema was observed. Increased bronchovesicular lung sounds were audible bilaterally, but there was no cough or nasal discharge.

The clinical signs shown were consistent with neonatal sepsis and a presumptive congenital cardiac defect. Haematology and biochemistry abnormalities listed in Table 1 supported a diagnosis of neonatal sepsis.

Ultrasonographic examination of thorax, abdomen and umbilicus were unremarkable. On a two-dimensional transthoracic echocardiographic examination^e, the left-sided cardiac chambers were

normal but there was marked right ventricular (RV) concentric hypertrophy. The pulmonary valve (PV) leaflets appeared thin but fused and failed to completely open during systole (systolic doming) and there was severe dilation of the main pulmonary artery (PA) (Video 1). The PV annulus appeared appropriate in size when compared with the aortic valve annulus (ratio aortic: pulmonary annulus 0.96, PV annulus diameter 2 cm). Peak transvalvular systolic flow velocity across the PV measured by continuous wave Doppler echocardiography was 5.6 m/s (average of five cardiac cycles), reflecting a maximal RV-PA pressure gradient (PG) of 125 mmHg and indicating severe valvular pulmonary stenosis (PS) (Fig. 1, Supplementary Fig. 1). In addition, colour Doppler examination revealed blood flow across the foramen ovale (right-to-left) and through the ductus arteriosus (left-to-right) (Videos 2 and 3). Both coronary arteries had a tortuous and prominent appearance (Supplementary Fig. 2, Supplementary Video 1, Video 4). No regurgitation across any valve was visible on colour flow mapping. The flow across the ductus arteriosus and foramen ovale were judged as physiological in a 1-day-old foal. A concurrently recorded electrocardiogram showed a normal sinus rhythm.

Treatment was initiated with crystalloid fluids and broad-spectrum antibiotics (sodium penicillin 30'000 IU/kg IV q 6 h, amikacin 25 mg/kg IV q 24 h) and the foal was regularly examined and clinically monitored. Over the following 2 days, the foal's clinical condition improved and the foal gained weight. However, heart rate and respiratory rate increased and the foal tired quickly with activity. Cardiac auscultation revealed a Grade 6/6 holosystolic coarse crescendo murmur, but a diastolic murmur was no longer audible.

Echocardiography was repeated on day 3 with similar findings for the valvular PS. Flow through the ductus arteriosus was trivial, and no flow through the foramen ovale was identified. Balloon valvuloplasty (BVP) was suggested.

The procedure was performed 10 days after presentation following resolution of the clinical signs of sepsis. General anaesthesia was induced and maintained with alfaxalone (1.5 mg/kg),

^e GE Vivid 7 Dimension, GE Healthcare, Glattbrugg, Switzerland.

Table 1 Abnormal haematology and biochemistry results at presentation.

Variable	Patient	Reference interval
Leucocyte concentration ($10^3/\mu\text{L}$)	2.2	6.1–11.2
Neutrophil concentration ($10^3/\mu\text{L}$)	1.8	4.1–8.6
Lymphocyte concentration ($10^3/\mu\text{L}$)	0.4	1.4–2.6
Creatine kinase activity (U/L)	877	165–761
Aspartate transaminase activity (U/L)	251	99–209
Urea (mmol/L)	5.6	2.4–3.8
Bilirubin ($\mu\text{mol/L}$)	146	27.3–71.7
Plasma protein concentration (g/L)	54	60–62
Gamma immunoglobulin concentration (mg/dL)	1655	> 800
Fibrinogen concentration (g/L)	2.9	1.7–2.6
Serum amyloid A concentration (mg/dL)	3147	< 26

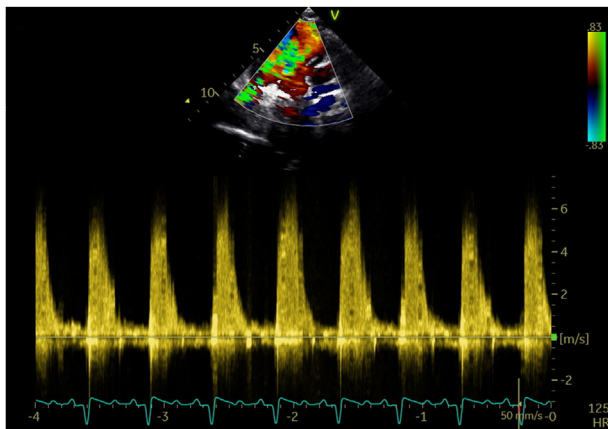


Fig. 1 Left parasternal long-axis view of PA outflow at 2 days of age. Measurement of maximum transvalvular systolic flow velocity across the PV by continuous-wave Doppler echocardiography/recording was 5.6 m/s, corresponding to a RV-PA pressure gradient of 125 mmHg. PA, pulmonary artery; PV, pulmonary valve, RV, right ventricle.

sevoflurane in 50% oxygen, dexmedetomidine ($0.5 \mu\text{g/kg/hr}$) and lidocaine ($30 \mu\text{g/kg/min}$).

Computed tomographic (CT) examination^f of the heart and great vessels was acquired prior to the BVP to rule out other malformations. Nonselective, ECG-gated CT angiography was performed using 2 mg/kg iohexol administered intravenously^{g,h}. Atracurium (0.1 mg/kg IV) allowed momentary expiratory apnea during imaging. The CT angiography showed moderate generalized enlargement of the heart. The origin of each main coronary artery was normal with mild tortuosity distally. There was luminal narrowing in the RV outflow tract at the

level of the PV (Fig. 2). Immediately distal to the PV there was a large increase in diameter of the main PA, consistent with a post stenotic dilation (Fig. 3). A contrast enhancing ductus arteriosus was absent. No flow was seen across the foramen ovale. There was no evidence of any other congenital cardiac abnormalities.

Routine BVP was performed as described in people and dogs [1,2] with the foal in left lateral recumbency. Briefly, after gaining access to the right external jugular vein using a modified Seldinger technique, a 12-Fr introducerⁱ was placed. Under fluoroscopic guidance, a 5-Fr pigtail catheter^j was advanced to the RV outflow tract for angiographic visualization of the stenotic PV and for measuring the annulus diameter (Supplementary Video 2). The pigtail catheter was replaced by a 5-Fr right coronary catheter^k and the systolic RV pressure was measured at 161 mmHg. An Amplatz extra stiff guide wire^l was introduced through the right coronary catheter and both advanced under fluoroscopic guidance into the distal PA and the right coronary catheter removed. A 25 mm balloon catheter^m (ratio balloon: annulus 1.25) was advanced over the guide wire across the level of the PV and the position was monitored using fluoroscopy. A colloid bolus (1.5 mL/kg hydroxyethyl starch 6% IV) was administered before each ballooning attempt to ensure adequate filling of the RV. The balloon was inflated and the initial waist at the valve level disappeared during inflation. Inflation

^f Brilliance 16 Air, Phillips AG, Zurich, Switzerland.

^g Accutron CP-DMedtron injector, SMD Medical Trade GmbH, Salenstein, Switzerland.

^h Accupaque 53, PF Healthcare, Buchs, Switzerland.

ⁱ 12-Fr introducer, Cook Medical, 6002 Luzern, Switzerland.

^j 5-Fr pigtail, 110 cm, Cordis Europe, 9301 LJ Roden, The Netherlands.

^k 5.2-F right coronary 3 judkins angiographic catheter, 100 cm, Cordis Europe, 9301 LJ Roden, The Netherlands.

^l Amplatz extra stiff guide wire, 0.035, 260 cm, Cook Medical, 6002 Luzern, Switzerland.

^m 25 mm, 4.0 cm veterinary balloon catheter, 100 cm length, Z-Med, NuMED Inc., Hopkinton, NY 12965.



Fig. 2 Heart rate – gated computed tomography angiography image of the thorax of the foal in a sagittal plane (cranial to the left). The hypertrophic right ventricular outflow tract (RVOT), stenotic pulmonary valve (PV) and massively dilated main pulmonary artery (main PA) are labelled.

was repeated and no further waist was detectable. Invasive pressure measurements using the right coronary catheter were repeated and revealed a marked decrease in systolic RV pressure (from 161 mmHg to 63 mmHg). Occasional premature ventricular complexes and 1 episode of ventricular tachycardia occurred during the procedure but resolved spontaneously.

The foal recovered uneventfully. The cardiac troponin I concentrationsⁿ 1 h and 30 h after the procedure were 0.34 ng/mL and 0.03 ng/mL, respectively (normal <0.06 ng/mL). Follow-up echocardiographic examination the next day revealed a wider opening of the PV leaflets (Video 4) and a markedly reduced transvalvular (RV to PA) peak systolic flow velocity (3.1 m/s, average of five cardiac cycles) and maximal PG across the PV (38 mmHg) (Fig. 4). Moderate pulmonary valve insufficiency (PI) was observed. The foal was maintained on the antibiotic treatment for another week and anti-platelet therapy was initiated (clopidogrel 4 mg/kg PO initially, then 2 mg/kg PO q 24 h for 2 weeks).

Eight days after BVP, there was a grade 4/6 holosystolic heart murmur loudest over the PV and a stable transvalvular PG of 25 mmHg (peak velocity 2.5 m/s).

At the 1-month follow-up, the foal was alert and responsive, had gained 18.9 kg of weight, but still tired more quickly than other foals. Heart rate was 128/min and regular. Bilaterally over the cranial heart base, a grade 3/6 holosystolic murmur was heard. The remainder of the physical examination was unremarkable. Echocardiography identified a subjectively reduced RV size and RV hypertrophy was less evident. The PV was unchanged with an outflow velocity of 2.8 m/s, reflecting a PG of approximately 31 mmHg. Trace tricuspid regurgitation (TR) and moderate PI were observed.

At the 1-year follow-up, the yearling had grown well and was in good body condition. At that time, no exercise intolerance or ill-thrift compared to other yearlings were noted. Heart rate was 60/min, rhythm regular, and a bilateral holosystolic murmur grade 3/6 was loudest over the cranial heart base. Echocardiography showed a normal sized heart with moderate PI and trace TR with stable maximal PG at 25 mmHg.

At 2 years of age, the filly was well grown and in good body condition with unchanged murmur.

ⁿ i-STAT, Abbott AG, Baar, Switzerland.

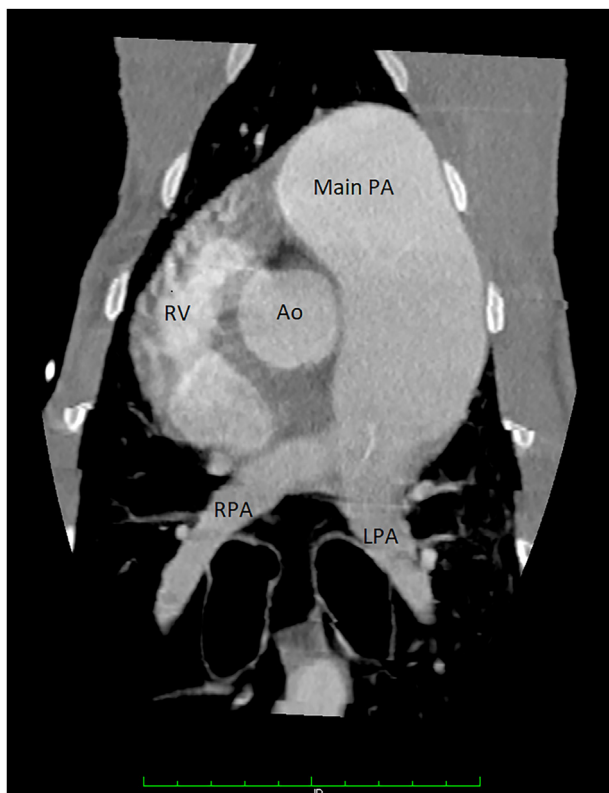


Fig. 3 Heart rate – gated computed tomography angiography image of the thorax of the foal in a coronal plane (cranial at the top). The hypertrophic right ventricle (RV), massively dilated main pulmonary artery (main PA), left pulmonary artery (LPA) and right pulmonary artery (RPA) branches and aorta (Ao) are labelled. Toward the pulmonary bifurcation, the main PA diameter narrowed to a similar diameter as the Ao and both its branches appeared appropriately sized.

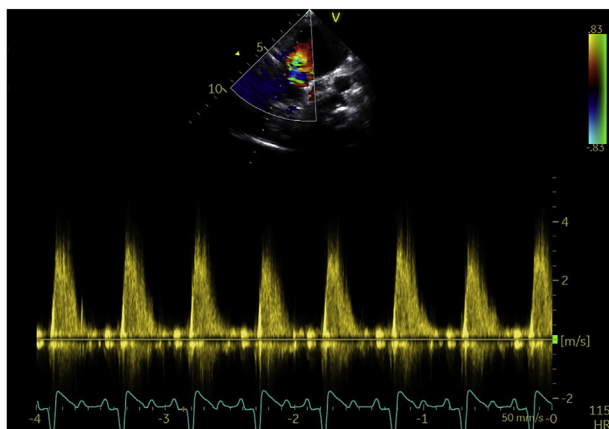


Fig. 4 Left parasternal long-axis view of PA outflow 1 day after BVP. Measurement of maximum transvalvular systolic flow velocity across the PV by continuous wave Doppler echocardiography was 3.1 m/s, reflecting a pressure gradient of approximately 38 mmHg. BVP, balloon valvuloplasty, PA, pulmonary artery; PV, pulmonary valve.

Echocardiographically, the heart remained stable with a PV outflow velocity of 2.6 m/s and transvalvular PG of 27 mmHg. Moderate PI and trace TR were still observed and the RV appeared subjectively slightly more voluminous than normal (Video 5).

Supplementary videos related to this article can be found at <https://doi.org/10.1016/j.jvc.2021.04.008>

Discussion

To the authors' knowledge, this is the first reported equine case of PS in which BVP was successfully performed.

Cases of PS are widely reported in the human [3] and small animal cardiology literature [4–6]. In horses, PS has rarely been reported, once as an isolated lesion [7] but usually in conjunction with other congenital heart abnormalities [8–12]. The overall reported prevalence of congenital cardiac defects in horses lies between 0.1 and 0.5% [12,13] and around 3.5% of all equine congenital diseases are cardiac in origin [14]. In the case presented here, PS was isolated and flow across the foramen ovale and ductus arteriosus were physiological findings associated with transition from foetal to neonatal circulation [13].

Pulmonary stenosis is classified according to its location and morphology [3,15]. Valvular stenosis develops because of dysplasia of the cusps, which is further described by the morphological features. In humans, 'domed' PS (or 'typical') is most common, where there is incomplete separation of the leaflets secondary to fusion along the valve commissures and systolic 'doming' of the valve into the pulmonary trunk [15,16]. In dogs, there are a wide variety of morphological features described [16]. Given this foal had a body size appropriate PV annulus diameter (similar to the aortic valve annulus) and thin but fused, doming leaflets, this foal's PS was similar to the human 'typical' form.

When deciding on the most appropriate course of therapy, it is important to recognise other concurrent congenital anomalies and to define the type and extent of obstruction [2,15]. In people, candidates for BVP with peak systolic transvalvular velocities of >3 m/s should undergo cardiac catheterization and angiography [3]. To evaluate the anatomy of the coronary vessels and ruling out congruent vascular abnormalities before the procedure, CT angiography was performed in this foal and confirmed echocardiographic findings while not revealing coronary anomalies that could have complicated the BVP.

In human and small animal medicine, the treatment of choice for severe PS or symptomatic PS is BVP. In dogs, severe PS is defined as a PG > 80 mmHg [17]. Hence, the foal described here fulfilled the criteria for BVP. Balloon size for valvular PS is typically chosen as 1.2–1.5 times the valve annulus diameter [2], and based on the 2.0 cm annulus diameter, a single 25 mm balloon was selected. Had this not been successful, a double balloon technique was planned. In this case, however, the disappearance of the stenotic waist and marked decrease in RV pressure supported a 'successful' BVP using the single balloon.

Although minor and major complications can occur with BVP [18], the procedure was well tolerated and no major complications were noted. Mortality rates in dogs with moderate to severe PS after BVP range from 0% in the short term, to 4–10% 1–4 years after the procedure [19–21], compared to higher mortality rates (3–34%) with no intervention [21–23]. Risk factors associated with survival were found to be PG, valve morphology, presence of clinical signs, age at time of diagnosis, and presence of TR [21–23].

Pulmonary restenosis and PI are the most reported mid to long-term complications of pulmonary BVP in human patients (occurrence in 8–10% and 41–88% of cases, respectively), with decreasing prevalence of restenosis after 2 years and increasing prevalence and severity of PI over time [18]. The resulting PI is usually mild and clinically irrelevant [3], but is moderate to severe in 29–53% of cases [24–26] and can result in RV dilation, reduced RV function and impaired exercise capacity as well as increased risk of arrhythmia and sudden cardiac death. A recent publication reported on repeat BVP in a canine case series, suggesting restenosis is a rare but possible complication [27]. In this case, the foal

developed PI immediately after the procedure, which may have been responsible for the mild, subjective RV volume increase observed at the 2-year follow-up. There was no evidence of restenosis with a stable transvalvular gradient. However, longer term follow-up was recommended to the owner, particularly if the pony was considered for riding. Given the unknown genetic risks of this defect breeding was not recommended.

In the foal described here, BVP resulted in a marked reduction of the echocardiographically measured PG from 125 mmHg to 38 mmHg immediately after the procedure and 31 mmHg after 1 month. In addition, there was a visible reduction in the degree of RV hypertrophy over time. This reduction in PG is consistent with observations after BVP in people and small animals [18,19,23]. The 2 year follow-up in this foal documented a favourable outcome of the procedure.

Conflict of Interest Statement

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

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Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jvc.2021.04.008>.

Supplementary Video 1a	Echocardiography of the coronary arteries. Two-dimensional B-mode recording in a right parasternal, modified short-axis, aortic root view. The cineloop shows the origin of both coronary arteries from the sinus of Valsalva, the left coronary artery can be seen following a torturous route away from the aorta.
Supplementary Video 1b	Echocardiography of pulmonary stenosis. Two-dimensional B-mode recording in a right parasternal, short short-axis, right ventricular outflow tract view. The cineloop shows the thin, fused pulmonary valve leaflets with systolic doming.
Supplementary Video 2a	Echocardiography of the patent foramen ovale (at 1 day of age), Two-dimensional B-mode and simultaneous colour Doppler recording in a right parasternal, long-axis, four-chamber view focused on the atria. This cineloop shows the separated septum primum and secundum (more membranous) with intermittent flow across the foramen ovale.
Supplementary Video 2b	Right ventriculography performed under fluoroscopic guidance. The right ventriculography shows the normal sized pulmonary artery annulus with thin valve leaflets. The right ventricular outflow tract concentric hypertrophy and massive main pulmonary artery dilation are also visible.

Supplementary Video 3	Echocardiography of the patent ductus arteriosus (at 1 day of age). Two-dimensional B-mode and simultaneous colour Doppler recording in a left parasternal, long-axis, caudo-dorsal oblique view focused on the main pulmonary artery. This cineloop shows the continuous ductal flow (green jet).
Supplementary Video 4	Echocardiography of pulmonary valve 1 day post balloon valvuloplasty. Two-dimensional B-mode recording in a right parasternal, short-axis, right ventricular outflow tract view. The cineloop shows the opening pulmonary valve leaflets after balloon valvuloplasty.
Supplementary Video 5	Echocardiography of the right ventricle showing evolution over time. Two-dimensional B-mode recordings in a left parasternal modified long-axis view, focusing on the right ventricle (RV). The upper left cineloop is from 1 day before the balloon valvuloplasty (BVP), the top left cineloop from 1 month after the BVP with the lower left cineloop is from 1 year after BVP and the lower right cineloop is 2 years after BVP. The reduction in RV concentric hypertrophy and subjective increase in RV diameter can be seen over time. Please note the spontaneous contrast seen in the left ventricle in the lower right image is considered normal in horses.

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