



Case Report

Non-cardiogenic pulmonary oedema complicating balloon valvuloplasty and stent angioplasty of severe pulmonary valve stenosis in four dogs[☆]



G. Santarelli, PhD^{a,*}, J. Bouvard, MSc^a, S.F. Brethel, DVM^c,
S. Gordon, DVM^d, S. Lord, BVMS^b, A. Mavropoulou, PhD^e,
P. Oliveira, DVM^e, K.T. Sykes, DVM^d, S. Swift, DVM^c,
G.J. Culshaw, PhD^a

^a *Cardiopulmonary Service, Hospital for Small Animals, Royal (Dick) School of Veterinary Studies & The Roslin Institute, The University of Edinburgh, Roslin, EH25 9RG, UK*

^b *Anesthesia Service, Roslin, EH25 9RG, UK*

^c *Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, 32608, USA*

^d *Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, 4474 TAMU, College Station, TX, 77843, USA*

^e *Davies Veterinary Specialists, Manor Farm Business Park, Higham Gobion, Hitchin, SG5 3HR, UK*

Received 30 November 2020; received in revised form 15 November 2021; accepted 1 December 2021

[☆] 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.

* Corresponding author.

E-mail address: g.santarelli@uu.nl (G. Santarelli).

KEYWORDS

Canine;
Congenital heart disease;
Dyspnoea;
Heart catheterisation

Abstract In dogs, balloon valvuloplasty is considered the treatment of choice for severe pulmonary valve stenosis, and this technique is currently performed routinely in specialist referral practices with low morbidity and mortality. Stent angioplasty has also been recently proposed as a viable treatment option. The present case series describes the clinical course of four dogs with severe pulmonary valve stenosis, treated with balloon valvuloplasty or stent angioplasty at four different institutions, which developed non-cardiogenic pulmonary oedema perioperatively after apparently successful dilation of the pulmonary valve. In three cases, there was evidence of some degree of pulmonary hypertension before ballooning. Despite intensive care, the complication proved fatal in three cases. Clinicians should therefore be aware of this life-threatening complication, previously undescribed in dogs.

© 2021 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Abbreviations

BP	blood pressure
BVP	balloon valvuloplasty
PG	pressure gradient
MPA	main pulmonary artery
NCPE	non-cardiogenic pulmonary oedema
PA	pulmonary artery/arterial
PH	pulmonary hypertension
PS	pulmonary valve stenosis
RV	right ventricle/ventricular
TEE	transesophageal echocardiography
TTE	transthoracic echocardiography

Case 1

A five-month-old, 16-kg, entire female Labrador retriever was presented, without clinical signs, for treatment of severe pulmonary valve stenosis (PS). Atenolol (1 mg/kg PO q12h) had been started before referral.

On presentation, there was a V/VI left basilar systolic murmur. Transthoracic echocardiography (TTE) confirmed severe PS, with a Doppler-derived transvalvular systolic pressure gradient (PG) of 130 mmHg. Valve leaflets appeared fused. Moderate right ventricular (RV) hypertrophy, mild right atrial dilation and main pulmonary artery (MPA) post-stenotic dilatation were observed. Mild pulmonary and tricuspid insufficiencies (maximum velocity not precisely measurable) were also present. An agitated saline contrast study did not identify intracardiac right-to-left shunts. Simultaneous electrocardiogram showed sinus rhythm.

Balloon valvuloplasty (BVP) was performed the next day. The dog was administered atenolol

(1 mg/kg PO) and premedicated with meperidine (5 mg/kg IM). Anaesthesia was induced with alfaxalone (1.25 mg/kg IV) and maintained with isoflurane in oxygen. Owing to systemic hypotension (mean oscillometric blood pressure [BP] 43 mmHg), Ringer's lactate solution (10 mL/kg followed by 3 mL/kg/h IV) and dopamine (10–15 µg/kg/min IV) were administered. Lidocaine (30 µg/kg/min IV) and fentanyl (2 µg/kg/h IV) infusions were then started. Cefuroxime was injected perioperatively (20 mg/kg IV q2h).

After a right jugular venous approach (12-Fr introducer sheath^f), pulmonary arterial (PA) pressures, measured directly with a 5-Fr multipurpose catheter^g, were mildly elevated (systolic 32 mmHg, diastolic 15 mmHg, mean 22 mmHg). Peak RV pressure was 122 mmHg. Selective RV angiography (5-Fr pigtail catheter^h; iohexol 300 mg/kg IV, 600 PSI, 20 mL/s) and transoesophageal echocardiography (TEE) revealed thick and domed pulmonary valve leaflets (Video 1). The poorly defined annulus measured 21 mm on angiography and 15 mm on simultaneous TEE, similarly to TTE. Valvuloplasty was performed by rapid manual inflation of a 22-mm x 4-cm balloon dilation catheterⁱ (balloon-to-annulus ratio 1.05). Fluoroscopy showed complete loss of the waist during expansion. Shortly afterwards, the dog experienced tachycardia (140 beats per minute (bpm)) and systemic hypotension (direct mean arterial BP 32 mmHg). On TEE, there was improved pulmonary valve leaflet excursion and

^f Check-Flo Introducer Set, Cook Inc., Bloomington, IN, USA.

^g Torcon NB Advantage Catheter, Cook Inc., Bloomington, IN, USA.

^h Occlu-Marker, pfm medical mepro gmbh, Nonweiler, Germany.

ⁱ Tyshak II, NuMED, Canada Inc., Cornwall, ON, Canada.

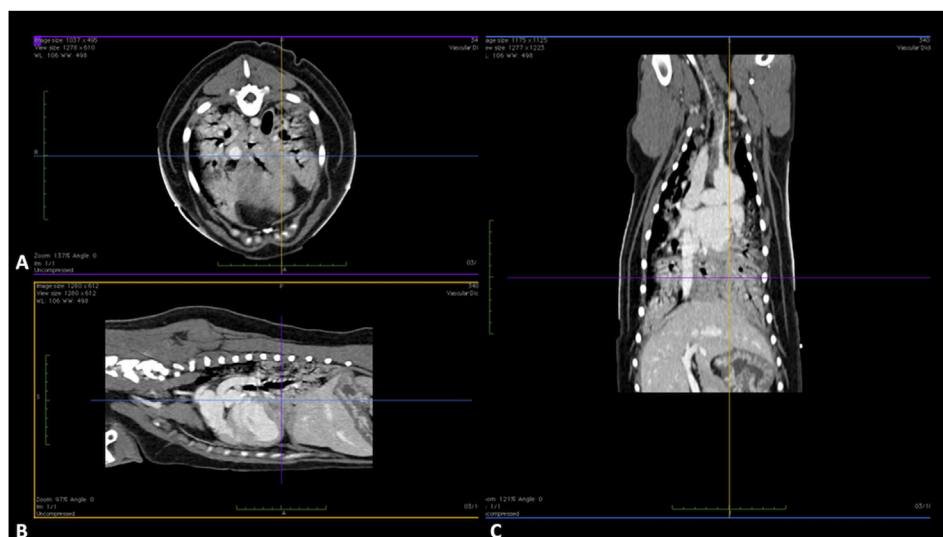


Fig. 1 Contrast-enhanced CT images obtained in case 1 shortly after balloon dilation, showing a marked, diffuse increase in pulmonary attenuation with multiple air bronchograms without vessel obliteration, compatible with severe non-cardiogenic pulmonary oedema. (A), transverse image at the level of the ninth thoracic vertebra. (B), Sagittal view. (C), Longitudinal view. CT: computed tomography.

significantly increased transvalvular flow, without evidence of annulus rupture or pericardial haemorrhage (Video 2). Approximately 10 min after ballooning, the SpO₂, previously normal, began to decrease, and serosanguinous fluid was noted in the endotracheal tube. An arterial blood sample revealed hypoxaemia (PaO₂ 91 mmHg, FiO₂ 94%), hypercapnia (PaCO₂ 66 mmHg) and acidaemia (pH 7.19). Intermittent positive pressure ventilation was started, and pimobendan was administered (0.15 mg/kg IV) for inotropic support. An emergency thoracic computed tomography scan revealed a marked and diffuse increase in pulmonary attenuation with multiple air bronchograms (Fig. 1) but no vessel obliteration, consistent with severe non-cardiogenic pulmonary oedema (NCPE). The dog suffered cardiopulmonary arrest soon after, while still under anaesthesia. Unfortunately, cardiopulmonary resuscitation was unsuccessful.

Case 2

A four-year-old, 2.2-kg, neutered female Chihuahua was presented with a three-month history of coughing and syncope and exercise intolerance of one-month duration. Severe PS had been diagnosed two years earlier. Furthermore, adulticide treatment for heartworm infection had been completed three years previously; since then, the dog had remained on commercial prophylaxis and tested antigen-negative.

Referral radiographs demonstrated right-sided cardiomegaly, MPA bulging and hypovascularised lungs with a moderate, diffuse bronchointerstitial pattern. Before referral, clinical signs had partially responded to furosemide (2.3 mg/kg PO q24h), atenolol (0.23 mg/kg PO q12h), enalapril (0.56 mg/kg PO q24h), pimobendan (0.27 mg/kg PO q24h) and butorphanol (0.45 mg/kg PO pro re nata (PRN) q12h).

Physical examination revealed a grade V/VI left basilar systolic murmur and diffuse crackles at peak inspiration, without tachypnoea or increased breathing effort. Lower airway disease was suspected based on history, the referring clinician's radiographs and auscultation. On TTE, severe PS was confirmed (Doppler-derived transpulmonary valve systolic pressure gradient (PG) 131 mmHg). The valve leaflets were restricted, thick and hyperechoic. Marked RV hypertrophy, MPA post-stenotic dilatation, and mild tricuspid and severe pulmonary insufficiencies were present. The peak early diastolic pulmonary regurgitation velocity was 2.7 m/s (Doppler-derived PG 29 mmHg). Based on the latter finding, pulmonary hypertension (PH) was suspected, possibly owing to lower airway disease or previous heartworm infection. Simultaneous electrocardiogram showed sinus rhythm.

Pimobendan and enalapril were discontinued. Furosemide dose was halved, with the recommendation to stop its administration one week later, but this was continued by the owner.

One month later, BVP was performed. After premedication with methadone (0.2 mg/kg IV), anaesthesia was induced with midazolam (0.2 mg/

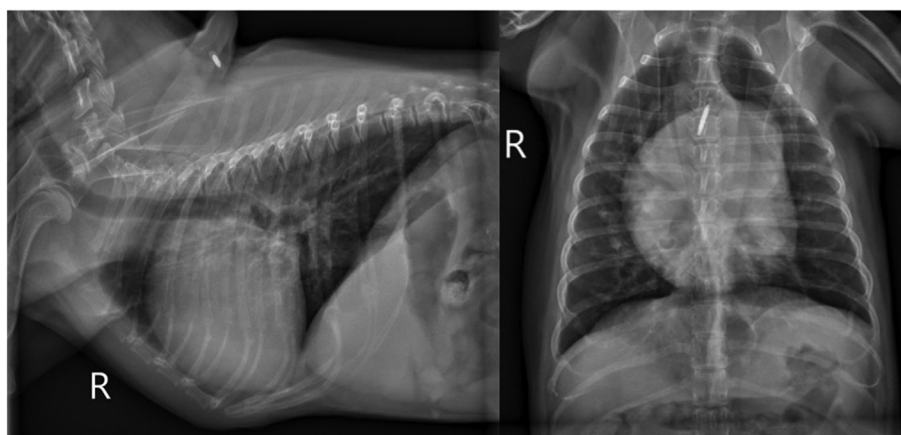


Fig. 2 Chest radiographs obtained in case 2 the day after balloon valvuloplasty, showing a diffuse, moderate bronchointerstitial pattern along with right-sided cardiomegaly and bulging of the main pulmonary artery.

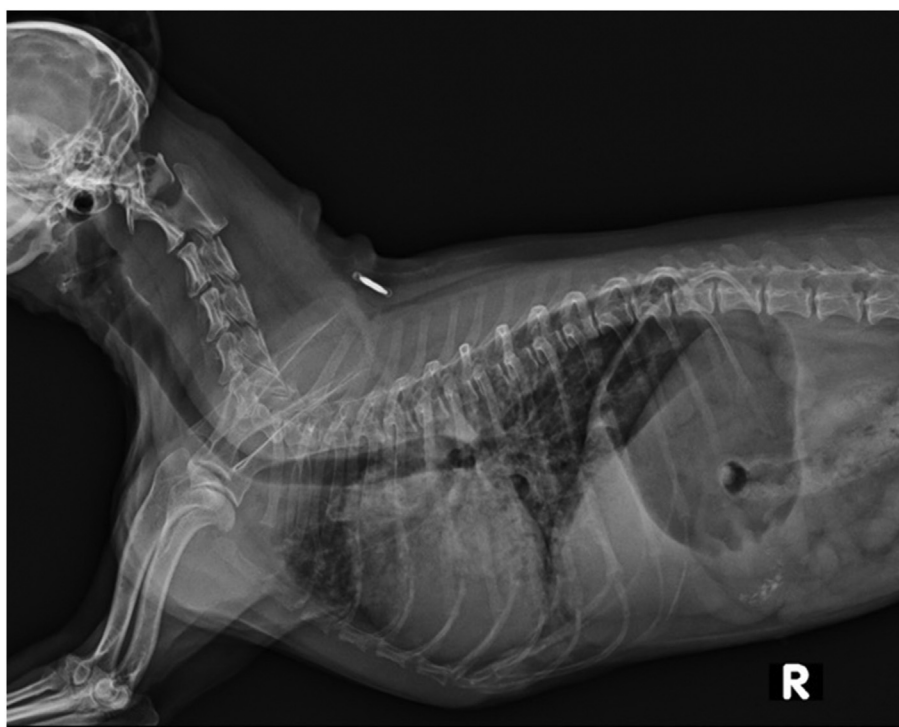


Fig. 3 Chest radiographs obtained in case 2 at the time of admission to the local emergency service (31 h after balloon valvuloplasty), showing a diffuse, mixed interstitial-alveolar pattern, compatible with development of non-cardiogenic pulmonary oedema.

kg IV) and etomidate (2 mg/kg IV) and maintained with isoflurane in oxygen. Fentanyl (5 µg/kg/h IV), midazolam (0.2 mg/kg/h IV) and lidocaine (50 µg/kg/min IV) were administered intraoperatively. Owing to systemic hypotension (direct mean arterial BP 38 mmHg) and bradycardia (60 bpm), Ringer's lactate solution (4.5 ml/kg followed by 5–10 ml/kg/h IV) and glycopyrrolate (total of 0.019 mg/kg IV) were also administered.

A right jugular venous approach (6-Fr introducer^j sheath) was used. Owing to persistent systemic hypotension (direct mean arterial BP < 60 mmHg), dopamine (3–7 µg/kg/min IV) was administered. To abbreviate the procedure,

^j Super Sheath Introducer Sheath, Boston Scientific, Marlborough, MA, USA.

direct RV and PA pressures were not determined. Selective RV angiography (5-Fr multiple-side-hole balloon catheter^k; ioxilan 490 mg/kg IV, manual injection) revealed doming pulmonary valve leaflets and an annulus diameter of 10.2 mm. A 10-mm x 3-cm balloon dilation catheter^l (balloon-to-annulus ratio 1) was used for valvuloplasty and manually inflated twice. Fluoroscopy showed complete loss of the waist during expansion. An arterial blood sample revealed normoxaemia (PaO₂ 479 mmHg, FiO₂ 100%) and normocapnia (PaCO₂ 39 mmHg). Direct mean arterial BP increased (88 mmHg) after valvuloplasty and catheter removal, and the dog recovered uneventfully.

Postprocedural TTE revealed increased left ventricular (LV) diameters, enhanced pulmonary valve leaflet excursion, and significantly decreased transvalvular PG (19 mmHg). Maximum velocity of the pulmonic insufficiency remained 2.7 m/s (Doppler-derived PG 29 mmHg).

The next day, chest radiographs were grossly comparable with four months previously (Fig. 2). The dog was discharged on doxycycline (4.5 mg/kg PO q12h), prednisolone (0.54 mg/kg PO q12h), pregabalin (2.7 mg/kg PO q12h), atenolol (0.32 mg/kg PO q12h), trazodone (2.7 mg/kg PO PRN) and butorphanol (0.05 mg/kg PO PRN).

The same night, 31 h after BVP, the dog developed acute tachypnoea and dyspnoea after atenolol suspension administration. Butorphanol, pregabalin and prednisolone given by the owner did not improve clinical signs, which progressed to expectoration of pink fluid within 1 h. The patient arrived at the local emergency service laterally recumbent, bradycardic (52 bpm), hypothermic (34 °C) and with fluid pouring from the mouth. After stabilisation with intubation, 100% oxygen, furosemide and atropine (doses unrecorded), the dog could be extubated. Thoracic radiographs revealed a diffuse interstitial-alveolar pattern (Fig. 3). A balanced crystalloid solution (2.7 mL/kg/h IV), dobutamine (5–10 µg/kg/h IV), ampicillin-sulbactam (30 mg/kg IV), doxycycline (5 mg/kg IV), sildenafil (3 mg/kg PO), butorphanol (0.1–0.24 mg/kg IV) and 40% oxygen were administered. However, cardiopulmonary arrest ensued soon after. On re-intubation, abundant fluid was aspirated. Cardiopulmonary resuscitation was unsuccessful, and NCPE was considered the most likely cause of death.

Case 3

A three-month-old, 8.2-kg, entire male French bulldog was referred for treatment of severe PS. The dog had experienced two syncopal episodes upon exercise two weeks previously, with none observed since starting atenolol (0.4 mg/kg PO q24h).

On auscultation, there was a grade IV/VI left basilar systolic murmur. Surface electrocardiogram revealed sinus rhythm. On TTE, severe PS was confirmed (Doppler-derived transvalvular systolic PG 145 mmHg). The valve had an 'hour-glass' appearance with thickened leaflets and a supra-valvular narrowing. There was moderate to severe RV hypertrophy, severe right atrial enlargement and moderate poststenotic MPA dilatation. Severe tricuspid regurgitation, mild pulmonic insufficiency (maximum velocity not precisely measurable) and hepatic vein congestion were identified.

The following day, BVP was performed. After premedication with meperidine (3 mg/kg IM), anaesthesia was induced with propofol (2.5 mg/kg IV) and maintained with isoflurane in oxygen. The patient received Ringer's lactate solution (5 mL/kg/h IV), lidocaine (30 µg/kg/min IV) and methadone (total of 0.2 mg/kg IV). Cefuroxime was administered (22 mg/kg IV) at induction.

After a right jugular venous approach (7-Fr introducer sheath^m), selective RV angiography (5-Fr pigtail catheterⁿ; iohexol 600 mg/kg IV, manual injection) revealed thick, immobile pulmonary valve leaflets and a supra-annular narrowing measuring 5 mm. The annular diameter measured 8 mm. Peak RV pressure (5-Fr multipurpose catheter^o) was 60 mmHg (PA pressure unrecorded). Valvuloplasty was performed by manual inflation of a 7-mm x 4-cm high-pressure balloon dilation catheter^p (balloon-to-annulus ratio 0.9), and peak RV pressure decreased to 30 mmHg. Shortly afterwards, the dog became bradycardic (45 bpm) and hypotensive (mean direct arterial BP 35 mmHg), without concurrent SpO₂ or CO₂ abnormalities. This was successfully addressed with isotonic crystalloid (total of 26 mL/kg IV), a succinylated gelatin solution (total of 11 mL/kg IV) and atropine (0.02 mg/kg IV). Additional ballooning via a 10-mm x 4-cm balloon dilation

^m CheckFlo Performer Introducer Set, Cook Inc., Bloomington, IN, USA.

ⁿ Royal Flush Plus High-Flow Catheter, Cook, Cook Inc., Bloomington, IN, USA.

^o Royal Fish Plus High-Flow Catheter, Cook, Cook Inc., Bloomington, IN, USA.

^p Advance ATB, Cook Inc., Bloomington, IN, USA.

^k Arrow-Berman Angiographic Catheter, Teleflex, Morrisville, NC, USA.

^l Infiniti Medical, Redwood City, CA, USA.

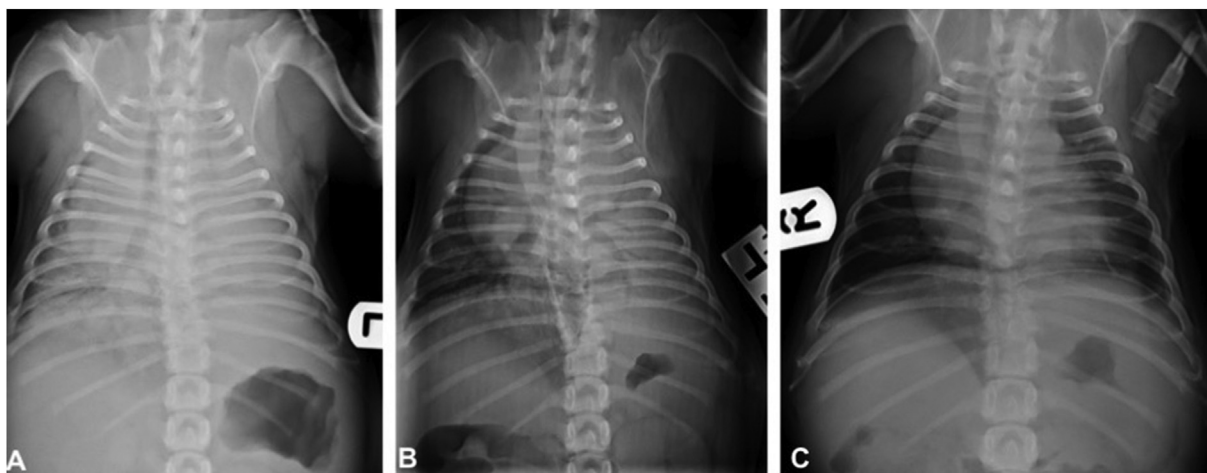


Fig. 4 A), Chest radiographs obtained in case 3 approximately 1 h after balloon valvuloplasty, revealing a severe, diffuse alveolar pattern compatible with non-cardiogenic pulmonary oedema. (B), Chest radiographs obtained in the same dog approximately 5 h after balloon valvuloplasty and institution of treatment for pulmonary oedema, revealing partial improvement of the radiographic abnormalities observed in Figure 4A. (C), Chest radiographs obtained in the same dog four days after BVP, showing near-resolution of the pulmonary changes observed in Figure 4A. BVP, balloon valvuloplasty.

catheter^q (balloon-to-annulus ratio 1.25) decreased peak RV pressure further to 25 mmHg.

Approximately 1 h after extubation, the patient developed sudden respiratory distress. Chest radiographs revealed a severe, diffuse alveolar pattern (Fig. 4A). The dog was mechanically ventilated and received furosemide (total of 9 mg/kg IV over 3h), buprenorphine (0.02 mg/kg IV q6h), dobutamine (5 µg/kg/min IV), 10% glucose (1 mL/kg/h IV), midazolam (0.1 mg/kg/h IV), and nebulised adrenaline (5 mg) and salbutamol (400 mcg). Follow-up radiography (5 h post-BVP) showed partial resolution of the alveolar pattern (Fig. 4B), and the dog was weaned off the ventilator after 7 h.

Pulmonary changes had nearly resolved by four days after BVP (Fig. 4C), and TTE confirmed improved pulmonary valve leaflet excursion and decreased transvalvular systolic PG (85 mmHg). The dog was discharged on atenolol (0.5 mg/kg PO q24h). Three months later, the owners reported no clinical signs.

Case 4

A one-year-old, 13.5-kg, entire male French bulldog was referred for treatment of severe PS, without clinical signs. Atenolol (0.5 mg/kg PO q12h) had been started four months earlier.

On examination, stertorous breathing was accompanied by a grade IV/VI left basilar systolic murmur. On TTE, severe PS was confirmed

(Doppler-derived transvalvular systolic PG 131 mmHg). Thickened valve leaflets and a supra-valvular narrowing were observed. Moderate RV hypertrophy, mild right atrial enlargement and MPA poststenotic dilatation were present, along with mild pulmonic insufficiency (maximum velocity 2.6 m/s; Doppler-derived PG 27 mmHg).

The following day, stent angioplasty was performed. The dog received maropitant (1 mg/kg IV) and was premedicated with procainamide (10 mg/kg IM) and methadone (0.2 mg/kg IV). Anaesthesia was induced with etomidate (1 mg/kg IV) and midazolam (0.2 mg/kg IM) and maintained with sevoflurane in oxygen. Metoclopramide (1 mg/kg/h), phenylephrine (1 µg/kg/min), enrofloxacin (10 mg/kg IV over 20min) and atracurium (0.2 mg/kg IV) were administered intraoperatively, and the dog was mechanically ventilated.

A right jugular venous approach (6-Fr introducer sheath^r, subsequently upsized to 9-Fr) was used. Direct measurement (5-Fr balloon wedge pressure catheter^s) revealed mildly elevated PA pressures (systolic 37 mmHg, diastolic 20 mmHg, mean 25 mmHg). Peak RV pressure was 133 mmHg. On selective RV angiography (5-Fr angiographic catheter^t; iohexol, 300 mg/kg IV,

^q Tyshak II, NuMED, Canada Inc., Cornwall, ON, Canada.

^r Super Sheath Introducer Sheath, Boston Scientific, Boston, MA, USA.

^s Arrow Balloon Wedge-Pressure Catheter, Teleflex, Morrisville, NC, USA.

^t Arrow-Berman Angiographic Catheter, Arrow, Reading, PA, USA.

manual injection), the minimum valve annulus and supra-annular obstruction diameters were 15.9 and 7.7 mm, respectively. The 9-Fr introducer was replaced with a 12-Fr extra-large introducer^u. An 18-mm x 3-cm balloon dilation catheter^v (balloon-to-annulus ratio 1.13) was manually inflated twice to identify an optimal stent landing site. A transhepatic biliary stent^w was mounted on an 18-mm x 4-cm balloon-in-balloon catheter^x, and the inner balloon was inflated to ascertain the location of the stent and adjusted before expanding the outer balloon. Subsequently, an 18-mm x 2-cm balloon dilation catheter^y was inflated twice to flare the stent. Selective RV angiography (iohexol, 300 mg/kg IV, manual injection) suggested good stent placement, but direct PA pressures appeared severely increased (systolic 72 mmHg, diastolic 31 mmHg, mean 54 mmHg), negating the RV-PA gradient. No significant concurrent changes in systemic arterial BP, heart rate, SpO₂ or CO₂ were detected. Catheters were removed, and the dog recovered uneventfully.

Within 30 min from extubation, the dog developed tachypnoea (50 bpm), requiring 40% oxygen supplementation. Point-of-care thoracic ultrasound revealed diffuse B-lines. Owing to rapidly progressing dyspnoea, the dog was intubated, whereon abundant serosanguinous fluid was expelled from the endotracheal tube. Manual ventilation was initiated, but terminal cardiopulmonary arrest ensued.

On gross postmortem examination, dark red, watery fluid was found in the thoracic cavity, distal trachea and mainstem bronchi. On cut surface, the lung parenchyma oozed abundant similar fluid. There was severe RV hypertrophy, and the stent was appropriately placed. Unexpectedly, a 5-mm perimembranous ventricular septal defect was identified. Histologically, pulmonary lesions included alveolar oedema with small amounts of fibrin, accompanied by patchy alveolar haemorrhage and macrophage migration with mild neutrophil extravasation.

Discussion

To the authors' knowledge, this is the first report of NCPE after BVP/stent angioplasty of severe PS in dogs, which proved fatal in three of four cases despite intensive care. None of the authors has observed this complication before, and based on the number of interventions performed in recent years at each institution, its incidence would be less than 0.2–0.5%.

Pulmonary valve stenosis is among the most common canine congenital cardiopathies [1–4]. Untreated dogs with severe PS can develop exercise intolerance, syncope, right-sided congestive heart failure and sudden death [1–4]. In children and dogs with isolated severe PS, BVP is considered the treatment of choice [1–5]. In dogs, this is performed routinely in specialist referral practices with low morbidity and mortality, improving outcomes in most cases [1–4,6].

Reported major perioperative complications of BVP in dogs include cardiopulmonary arrest, life-threatening arrhythmias, cardiac/vascular perforation, valve damage, thromboembolism, PA dissection, balloon blockage in the RV outflow tract and balloon rupture with fragment embolisation [6–8]. Life-threatening NCPE has not been previously reported as a perioperative or postoperative complication in dogs. This syndrome is usually characterised by acute inflammatory or non-inflammatory fluid accumulation in the alveoli, without evidence of left-sided cardiac dysfunction [9].

Acute pulmonary oedema is reported as a rare complication of surgical valvulotomy and BVP in people [5,10–16], and segmental oedema, acute lung reperfusion injury or haemorrhage can occur after dilating a stenotic PA or in chronic thromboembolic PH [17–19]. Furthermore, in feline cardiology, acute lung reperfusion injury was suspected in a kitten that developed pulmonary infiltrates 36 h after balloon angioplasty of PA stenosis [20]. A non-inflammatory aetiology, thought to be an acutely increased pulmonary perfusion raising hydrostatic pressure within an unprepared and/or underdeveloped pulmonary vasculature, has been proposed [10–13]. Inflammatory-mediated reperfusion-ischaemia injury with increased vascular permeability has also been suggested [13,15,18]. Both may be exacerbated by reduced LV compliance from chronic underfilling [13,14].

In all cases reported here, respiratory distress and profuse, acute production of serosanguinous fluid after apparently successful valvuloplasty or stenting are consistent with the syndrome described in

^u CheckFlo Performer Introducer Set, Cook Inc., Bloomington, IN, USA.

^v Z-Med-II Percutaneous Transluminal Valvuloplasty Catheter, Braun Interventional Systems, Bethlehem, PA, USA.

^w Palmaz XL Transhepatic Biliary Stent, Cordis, Miami Lakes, FL, USA.

^x Balloon-in-balloon Dilatation Catheter, NuMED, Hopkinton, NY, USA.

^y Atlas Gold PTA Dilation Catheter, Bard Peripheral Vascular, Tempe, AZ, USA.

people. In this case series, NCPE is suspected based on to the distribution of lung changes on thoracic imaging, without clear evidence of pulmonary venous congestion. Pulmonary wedge pressures, which would have helped excluding a cardiogenic component, were not obtained. Nevertheless, TEE did not identify overt LV dysfunction in case 1, and preoperative investigations did not disclose haemodynamically significant abnormalities predisposing to cardiogenic oedema in any case.

Based on the cases reported here, a combination of increased hydrostatic pressure and enhanced permeability leading to oedema formation seems likely, considering the strong temporal association between valvuloplasty and respiratory decompensation in cases 1, 3 and 4, and the histopathology results in case 4. The latter disclosed inflammatory changes, which could indicate a reperfusion-ischaemia injury [15]. However, such changes are not specific, also being potentially consistent with the exudative phase of acute respiratory distress syndrome [21]. This form of NCPE seems less likely in case 4, considering the absence, at least apparent, of recognised underlying conditions. Mechanical ventilation during anaesthesia could have also contributed to the injury [22], but as no other dog underwent necropsy, definitive conclusions as to the cause of the inflammatory changes are limited.

Catecholamines and/or fluid therapy were administered to treat systemic hypotension in cases 1, 2 and 3. Although contribution of these treatments to oedema formation cannot be excluded, similar protocols are used to address this frequent complication in dogs undergoing BVP without exacerbating NCPE [23,24]. In addition, all dogs received intravascular non-ionic, low osmolar contrast media, and an immediate or delayed hypersensitivity reaction cannot be excluded either [25].

Based on the human literature, patients are more vulnerable to acute oedema formation if they have long-standing stenosis, concurrent left-sided obstructive lesions or left-to-right shunts, LV dysfunction, severe TR, right-sided congestive heart failure, absence of infundibular stenosis or persistently high PA pressure after dilation [10–16]. In this case series, a clear common predisposing factor could not be identified. Interestingly, in three cases, there was evidence of PH before BVP, which could reflect a vulnerable pulmonary circulation before the increase in perfusion after dilation. During the procedures, no

hypoxaemia was detected, except in case 1 that was severely hypoxaemic but only when general deterioration was observed after ballooning. Although brachycephalic dogs could have PH from chronic airway obstruction [26], this is unlikely in case 1 which was a Labrador retriever. Brachycephalic breeds are also predisposed to acute airway obstruction, and although this or endotracheal tube blockage was not observed during any procedure, respiratory distress occurred in case 2 shortly after atenolol suspension administration. Thus, the possibility of a contribution of accidental upper airway obstruction to the development of NCPE cannot be entirely discarded. Furthermore, in case 2, there was evidence of pre-existing lower airway disease and a previous history of heartworm infection, which could have predisposed to PH [26,27]. Regardless of the cause, high PA pressures could indicate increased susceptibility to oedema formation, and increased direct PA pressures after BVP could precede clinical indication of NCPE, as observed in case 4.

Balloon oversize is regarded as an additional complicating factor in people [11,16]. In the case series reported here, the balloon-to-annulus ratios chosen were conservative, laying within or below the 1.2–1.5 ratio commonly recommended for dogs [1]. The different valve morphologies observed and various techniques used preclude identification of obvious anatomical or technical risk factors.

In conclusion, acute NCPE is a rare complication of BVP/stent angioplasty in dogs with severe PS, for which pre-existing PH may be a predisposing factor, and increased PA pressure after ballooning may be a warning of increased risk. All clinicians involved in the care of patients receiving BVP should be aware of this life-threatening complication, which can occur perioperatively and require advanced life support.

Conflicts of Interest Statement

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

Acknowledgements

In loving memory of Jonathan.

The authors wish to thank Sara-Ann Dickson, Blakeley Janacek, Efa Llewellyn, Yolanda Martinez-Pereira and Gudrun Schoeffmann for their valuable help with the cases.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jvc.2021.12.003>.

Video 1	Case 1-TEE before BVP	Cranial transverse view, optimised for visualisation of the MPA and pulmonary valve and obtained before BVP, showing restricted valvular movement and systolic doming.
Video 2	Case 1- TEE after BVP	Cranial transverse view, optimised for visualisation of the MPA and pulmonary valve and obtained after BVP, showing improved pulmonary valve leaflet excursion, without evidence of annulus rupture or pericardial haemorrhage.
Video 3	Case 1- TEE following BVP	Median transverse four-chamber view, obtained after BVP, showing subjectively preserved global systolic function, without evidence of pericardial haemorrhage.

BVP, balloon valvuloplasty; MPA, main pulmonary artery; TEE, transesophageal echocardiography.

References

- [1] Scansen BA. Cardiac interventions in small animals: areas of uncertainty. *Vet Clin North Am Small Anim Pract* 2018; 48:797–817.
- [2] Johnson MS, Martin M, Edwards D, French A, Henley W. Pulmonic stenosis in dogs: balloon dilation improves clinical outcome. *J Vet Intern Med* 2004;18:656–62.
- [3] Bussadori C, DeMadron E, Santilli R, Borgarelli M. Balloon valvuloplasty in 30 dogs with pulmonic stenosis: effect of valve morphology and annular size on initial and 1-year outcome. *J Vet Intern Med* 2001;15:553–8.
- [4] Francis AJ, Johnson MJ, Culshaw GC, Corcoran BM, Martin MW, French AT. Outcome in 55 dogs with pulmonic stenosis that did not undergo balloon valvuloplasty or surgery. *J Small Anim Pract* 2011;52:282–8.
- [5] Amoozgar H, Salehi M, Borzooe M, Ajami G, Reza Edraki M, Mehdizadegan N, Mohammadi H. Balloon valvuloplasty for pulmonary stenosis in children: immediate outcome and cardiac remodeling during midterm follow-up. *Iran J Pediatr* 2017;27:e10058.
- [6] LeBlanc NL, Agarwal D, Menzen E, Nomi K, Sisson DD, Scollan KF. Prevalence of major complications and procedural mortality in 336 dogs undergoing interventional cardiology procedures in a single academic center. *J Vet Cardiol* 2019;23:45–57.
- [7] Claretti M, Lopez BS, Boz E, Martelli F, Pradelli D, Bussadori CM. Complications during catheter-mediated patent ductus arteriosus closure and pulmonary balloon valvuloplasty. *J Small Anim Pract* 2019;60:607–15.
- [8] Grint KA, Kellihan HB. Pulmonary artery dissection following balloon valvuloplasty in a dog with pulmonic stenosis. *J Vet Cardiol* 2017;19:182–9.
- [9] Bachmann M, Waldrop JE. Noncardiogenic pulmonary edema. *Compend Contin Educ Vet* 2012;34:E1.
- [10] Walker CP, Bateman CJ, Rigby ML, Brookes CI. Acute pulmonary edema after percutaneous balloon valvuloplasty for pulmonary valve stenosis. *J Cardiothorac Vasc Anesth* 2001;15:480–2.
- [11] Shrivastava S, Tomar M, Radhakrishnan S. Acute pulmonary oedema following percutaneous balloon pulmonary valvuloplasty in children. *Cardiol Young* 2003;13:576–8.
- [12] Mohanty S, Narayan Pandit B, Tyagi S. Balloon pulmonary valvotomy - not just a simple balloon dilatation. *Indian Heart J* 2014;66:462–5.
- [13] Tefera E, Qureshi SA, Bermudez-Cañete R, Rubio L. Percutaneous balloon dilation of severe pulmonary valve stenosis in patients with cyanosis and congestive heart failure. *Cathet Cardiovasc Interv* 2014;84:E7–15.
- [14] Matisson RE, Mitha AS, Williams MA, Chesler E. Pulmonary edema following pulmonary valvulotomy. *Ann Thorac Surg* 1975;20:581–5.
- [15] Ostovan MA, Kamali M, Zolghadrasli A. A case of fatal acute lung injury after balloon valvuloplasty of pulmonary stenosis: case report and review of literature. *J Cardiovasc Thorac Res* 2015;7:78–80.
- [16] Cheng H, Lee P, Hwang B, Meng CL. Acute pulmonary reperfusion hemorrhage: a rare complication after oversized percutaneous balloon valvuloplasty for pulmonary valve stenosis. *J Chin Med Assoc* 2009;72:607–10.
- [17] Mulcahy D, Sigwart U, Somerville J. Successful stenting of a life-threatening pulmonary arterial stenosis. *Br Heart J* 1991;66:463–5.
- [18] Yacoubi S, Meador M, Mossad E. Lung reperfusion injury in patients after balloon angioplasty for pulmonary artery stenosis. *J Cardiothorac Vasc Anesth* 2014;28:502–5.
- [19] Lang I, Meyer BC, Ogo T, Matsubara H, Kurzyrna M, Ghofrani H, Mayer E, Brenot P. Balloon pulmonary angioplasty in chronic thromboembolic pulmonary hypertension. *Eur Respir Rev* 2017;26:160119.
- [20] Schroppe DP, Tyrrell WD, Jacob KA. Successful balloon angioplasty of pulmonary artery stenosis in two cats and associated complications. *J Vet Cardiol* 2017;19:530–7.
- [21] Boiron L, Hopper K, Borchers A. Risk factors, characteristics, and outcomes of acute respiratory distress syndrome in dogs and cats: 54 cases. *J Vet Emerg Crit Care* 2019;29:173–9.
- [22] Dreyfuss D, Saumon G. Ventilator-induced lung injury: lessons from experimental studies. *Am J Respir Crit Care Med* 1998;157:294–323.
- [23] Viscasillas J, Sanchis-Mora S, Palacios C, Mathis A, Alibhai H, Brodbelt DC. Anaesthetic management and complications of balloon valvuloplasty for pulmonic stenosis in dogs. *Vet Rec* 2015;177:340.
- [24] Ramos RV, Monteiro-Steagall BP, Steagall PV. Management and complications of anaesthesia during balloon valvuloplasty for pulmonic stenosis in dogs: 39 cases (2000 to 2012). *J Small Anim Pract* 2014;55:207–12.
- [25] Brockow K. Immediate and delayed reactions to radio-contrast media: is there an allergic mechanism? *Immunol Allergy Clin North Am* 2009;29:453–68.

- [26] Reinero C, Visser LC, Kellihan HB, Masseau I, Rozanski E, Clercx C, Williams K, Abbott J, Borgarelli M, Scansen BA. ACVIM consensus statement guidelines for the diagnosis, classification, treatment, and monitoring of pulmonary hypertension in dogs. *J Vet Intern Med* 2020;34:549–73.
- [27] Falcón-Cordón Y, Montoya-Alonso JA, Caro-Vadillo A, Matos-Rivero JI, Carretón E. Persistence of pulmonary endarteritis in canine heartworm infection 10 months after the eradication of adult parasites of *Dirofilaria immitis*. *Vet Parasitol* 2019;273:1–4.

Available online at www.sciencedirect.com

ScienceDirect