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A pilot study evaluating cutting and high-pressure balloon valvuloplasty for dysplastic pulmonary valve stenosis in 7 dogs☆,☆☆

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Abstract *Introduction:* This case series describes early experience and technical aspects of cutting balloon dilation followed by high-pressure balloon pulmonary valvuloplasty in dogs with dysplastic pulmonary valve stenosis.
Animals: Seven client-owned dogs were enrolled in this study.
Methods: Dogs were prospectively enrolled based on echocardiographic diagnosis of severe pulmonary valve dysplasia, defined as marked valve thickening with variable degrees of annular hypoplasia or subvalvar fibrous obstruction and a peak echocardiography-derived transpulmonary pressure gradient higher than 100 mmHg.

Abbreviations: BPV, balloon pulmonary valvuloplasty; CB, cutting balloon; HP, high-pressure; PS, pulmonary valve stenosis.

A preliminary version of this data was presented in abstract form at the 2017 ACVIM Veterinary Medical Forum in National Harbor, Maryland.

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Preinterventional and postinterventional hemodynamic data and transthoracic pressure gradients were obtained for all dogs. Recheck echocardiography varied in timing by client convenience, with maximum follow-up 35 months after intervention.

Results: No intraprocedural or periprocedural mortality was observed. The only major complication was partial avulsion of a cutting blade related to exceeding recommended burst pressure of the device, which was not associated with obvious clinical consequence. Invasive hemodynamic measurements demonstrated an average reduction of 46% in peak systolic right ventricular-to-pulmonary artery pressure gradient (range, 31—77%). The echocardiographic results 24 h after procedure demonstrated an average reduction in pressure gradient of 43% (range, 20—66%), with late follow-up demonstrating an average reduction of 35% (range, 10—57%) compared with preprocedural echocardiography.

Conclusions: This procedure is a feasible therapeutic transcatheter intervention for dogs with dysplastic pulmonary valves and appears safe in this small cohort. The ideal selection criteria and rate of restenosis for this procedure is under investigation, and long-term follow-up and a large, randomized, controlled study are necessary to demonstrate efficacy.

Introduction

Congenital pulmonary valve stenosis (PS) is among the most commonly diagnosed congenital heart defects in dogs [1,2]. Valvar PS is more commonly recognized in dogs than subvalvar or supravalvar stenosis [3—5], although precise definitions for each subclassification (subvalvar, valvar, and supravalvar) for animals are lacking [6]. In both children and dogs, binary classifications of congenital PS have been described as either a dome-shaped valve during systole with commissural fusion and a normal-sized annulus or a dysplastic and markedly thickened valve with or without hypoplasia of one or more leaflets and with variable degrees of pulmonary annular hypoplasia [3,7]. In humans, the predominant form is the typical form where the valve commissures are partially fused, the leaflets are thin and pliant, and the valve is dome shaped during systole [8]. The atypical form in humans is pulmonary valve dysplasia, which may be associated with the genetic disorder Noonan syndrome [8,9]. In dogs, pulmonary valve dysplasia appears to be the predominant form, manifesting as irregularly shaped and thickened leaflets with variably reduced mobility and occurring with varying degrees of pulmonary annular hypoplasia [5,7,10,11]. Dogs with moderate to severe PS who do not undergo treatment remain at risk of clinical signs including exercise intolerance, syncope, sudden cardiac death, congestive heart failure, and cyanosis if present with a concurrent right-to-left intracardiac shunt [3,11—14].

There is evidence that balloon pulmonary valvuloplasty (BPV) improves the clinical outcome of humans and dogs with PS, both with a reduction in clinical signs and an improved survival [5,13,15,16]. The procedure is now routinely performed in dogs and is associated with low morbidity and mortality. Although effective, human and canine studies suggest patients with valve dysplasia and a hypoplastic annulus have less improvement after BPV, as well as a poorer prognosis with or without BPV, than those with predominantly valvar fusion [10,17,18]. Newer treatment options have been developed for children, some of which have been reported for dogs, to address the frequently disappointing results of BPV in the setting of a highly dysplastic pulmonary valve and/or annular hypoplasia, as well as resistant PS. These include cutting balloon (CB) dilation, high-pressure (HP) balloon valvotomy, and intravascular stent placement [6,19—25]. The use of transcatheter CB technology to treat PS was first attempted more than 20 years ago when a double-blade balloon was used in an attempt to dilate a stenotic pulmonary valve in a dog model, followed by its use in 3 children [26]. More recently, 5 children with dysplastic PS who failed to respond to standard BPV underwent CB dilation, followed by immediate conventional BPV [27]. In this small case series, the CB technique appeared to be safe and to provide partial relief of resistant

PS in children who failed standard BPV, avoiding the need for surgical intervention. Cutting balloon followed by HP balloon dilation has previously been described in a dog with a double-chambered right ventricle [28] and in a series of dogs with subvalvar aortic stenosis [29] with fair results. We hypothesized that CB dilation followed by HP BPV could be safely used to treat dogs with dysplastic PS.

Animals, materials, and methods

Seven dogs with dysplastic PS, diagnosed by transthoracic echocardiography and assessed by right heart catheterization, were prospectively enrolled from Colorado State University Veterinary Teaching Hospital (n = 6) and the Ohio State University Veterinary Medical Center (n = 1). Signalment and clinical features for all dogs are provided in Table A (data available in Supplemental Material online). All dogs were younger than 2 years at the time of catheterization, with a median age of 6.2 months (range: 3.7—21.9 months). There were six females and one male. Breed distribution included 4 mixed-breed dogs, 2 French bulldogs, and 1 American pit bull terrier. All dogs were presented for evaluation of a heart murmur. Clinical signs included collapse (case 3) and tachypnea and exercise intolerance (case 4). All dogs had grade IV/VI to V/VI left basilar systolic heart murmurs. In 5 of 7 dogs, CB dilation and HP BPV was the animal's first transcatheter intervention. Two of the dogs had previous cardiac catheterizations for conventional BPV before the CB dilation and HP BPV procedure. In one of these dogs (case 2), BPV had been aborted 5 months before CB dilation and HP BPV when the subvalvar obstruction was unable to be crossed, whereas the other dog with a prior catheterization (case 6) had a BPV performed 16 months before with a low-pressure balloon inflated to 5 atm.

Transthoracic two-dimensional and Doppler echocardiographic studies were performed on standard echocardiography systems,[1,2] using either a phased array 4.0- to 12.0-MHz transducer or a phased array 3.5- to 6.9-MHz transducer. Sedation during echocardiographic studies was at the discretion of the clinician and was performed by administration of 0.2—0.3 mg/kg of butorphanol.

After induction of anesthesia, the dogs were positioned in either left lateral or dorsal recumbency, depending on the clinician's preference, to obtain vascular access. Percutaneous access to the right external jugular vein was achieved according to previously published techniques [30]. Introducer sheath sizes ranged from 7 to 9 Fr by 4 to 11 cm.[3,4] A micropuncture introducer set[5] was placed initially in 2 dogs before upsizing to the desired introducer sheath. The authors recommend selecting an introducer sheath that is at least one French size larger than the manufacturer's recommendation for the anticipated CB and HP balloon dilation catheters.

Right heart catheterization was initially performed using a Berman angiographic catheter[6] that was floated across the tricuspid valve to the pulmonary trunk. It was possible to advance the Berman catheter to the pulmonary trunk in 3 of 7 cases, followed by a pull-back hemodynamic study to document the location and severity of the obstruction. In 4 of 7 cases, the Berman catheter could not be advanced through the right ventricular outflow tract, and right ventriculography was performed through the Berman catheter before pressure pull-back. In these cases, the obstruction was then crossed with alternative catheters[7,8] or guidewires,[9,10] and pressure pull-back was performed. Right ventriculography was performed via either a hand injection (if the patient's weight was <10 kg) or a power injector (if the patient's weight exceeded 10 kg), using approximately 1 ml/kg of iodinated contrast medium[11] through the Berman angiographic catheter. Both the subvalvar orifice diameter, if a subvalvar obstruction was present, and the pulmonary valve annular diameter, at the base of the leaflets and/or valvar tunnel orifice diameter, were measured. Measurements were calibrated for radiographic magnification using a pigtail marker catheter placed within the esophagus [31].

[1] EPIQ 7, Philips North America Corporation, Andover, MA, USA.
[2] Vivid 7 Dimension, GE Medical Systems, Milwaukee, WI, USA.
[3] Pinnacle II R/O II introducer set, Terumo Medical, Somerset, NJ, USA.
[4] Introducer set, Boston Scientific, Natick, MA, USA.
[5] Microintroducer set, Cook Medical, Bloomington, IN, USA.
[6] Berman angiographic catheter, Arrow International, Inc., Morrisville, NC, USA.
[7] Balloon wedge-pressure catheter, Arrow International, Inc., Morrisville, NC, USA.
[8] Torcan NB® Advantage Catheter, C2, Cook Medical, Bloomington, IN, USA.
[9] Rosen Wire Guide, Cook Medical, Bloomington, IN, USA.
[10] V18 ControlWire™, Boston Scientific, Natick, MA, USA.
[11] Omnipaque™ (Iohexol) 240mgI/mL, GE Healthcare, Chicago, IL, USA.

A balloon wedge-pressure catheter[7] in 6 of 7 cases, or a double-curve cobra catheter[8] in one case, was advanced by fluoroscopic guidance across the obstruction and into the pulmonary trunk, with or without the assistance of a guidewire. If the obstruction could not be crossed using the balloon wedge-pressure catheter, the catheter was positioned within the right ventricular outflow tract, and a 0.018″ guidewire[10] was prepared by creating an approximately 1.5 mm J-shaped bend at its distal tip using a curved hemostat. This preshaped wire was then advanced through the catheter, advanced across the obstruction, and positioned in a distal branch pulmonary artery, preferably the left as the left branch pulmonary artery provides a less acute curve from the pulmonary valve when advancing guidewires and balloons [32]. The 0.018″ guidewire[10] was used to cross the obstruction as the CB dilation catheter[12] has a 0.018″ lumen. In case 2, attempts at crossing the obstruction with the combination of a balloon wedge-pressure catheter and 0.018″ guidewire were unsuccessful. During this case, the balloon wedge-pressure catheter was removed over the guidewire and replaced with a cobra catheter.[8] The guidewire was advanced through the cobra catheter, and the catheter was successfully advanced across the obstruction into the pulmonary trunk and distal left pulmonary artery. The operator should be cognizant of the entire length of the wire on fluoroscopy to avoid inadvertent perforation through vascular structures by the distal tip and to avoid kink or knot formation in the wire [33]. Ideal criteria for the patient and balloon size selection for performing CB dilation in dogs are yet to be determined. The CB dilation catheter[12] was selected to be approximately of the same size or 1 mm larger than the narrowest orifice (valvar or subvalvar), based on both transthoracic echocardiography and right ventriculography measurements. Currently, the largest peripheral CB dilation catheter has a balloon diameter of 8 mm. Ideally, to avoid disruption of the annulus, the CB dilation catheter selected should not be larger than the size of the pulmonary valve annulus [27]. The CB dilation catheter was flushed and prepped to ensure all remaining air was extracted and attached to an inflation device.[13] The CB dilation catheter was advanced over the wire, centered across the stenosis, and inflated 2 to 3 times by turning the handle of the inflation device clockwise to inflate the balloon to the desired pressure. Cutting balloons were inflated and deflated using a pressure-monitoring gauge and taken to, or 1 atm below, the manufacturer's rated burst pressure. The CB dilation catheter was then exchanged, while maintaining the guidewire position within the distal branch pulmonary artery, for an end-hole catheter.[7,14] The 0.018″ guidewire was removed. Either a 0.035″ super-stiff Amplatzer guidewire[15] or a 0.035″ Rosen guidewire[9] was advanced into the left branch pulmonary artery through the end-hold catheter, and the catheter was removed. Ideal criteria for selection of HP balloon size are still under investigation. In a recent report [23], a balloon-to-annulus ratio of approximately 1.3—1.5 was chosen for the HP balloon diameter. We agree with this sizing, although 2 cases in our series were treated using an HP balloon of a smaller balloon-to-annulus ratio owing to available inventory (case 2) and uncertain tolerance to that degree of oversizing for a tunnel-like lesion (case 5). Both Atlas and Atlas Gold PTA balloon dilation catheters,[16] as well as Z-MED and Z-MED II balloon dilation catheters,[17] were used in this case series, where HP BPV was defined as a balloon with a burst pressure higher than 8 atm based on the precedent in the human literature [21]. The HP balloon dilatation catheter was prepared in a similar manner to that of the CB dilation catheter. The HP balloon was centered across the obstruction, and 2 to 4 inflations were performed with the inflation device to quickly fill the HP balloon to the manufacturer's rated burst pressure. This resulted in a discernible waist that resolved on maximal inflation. The HP balloon dilation catheter was exchanged over the wire for an end-hole catheter, and pressure measurements were obtained in the pulmonary artery, right ventricle, and right atrium via pressure pull-back. After obtaining postinterventional hemodynamics, the end-hole catheter was removed and a purse-string suture was preplaced around the venous access site, which was tightened as the introducer sheath was removed. A light bandage was placed around the neck overnight, and the purse-string suture was removed the following day.

[12] Peripheral Cutting Balloon Microsurgical Dilatation Device™, Boston Scientific, Natick, MA, USA.
[13] PRESTO® Inflation Device, Bard Medical, Covington, GA, USA.
[14] Multipurpose angiographic catheter, Cook Medical, Bloomington, IN, USA.
[15] Super-stiff Amplatzer Guidewire, AGA Medical, Plymouth, Minnesota, USA.
[16] ATLAS PTA Balloon Dilatation Catheter, Bard Peripheral Vascular, C.R. Bard, Inc, Tempe, AZ, USA.
[17] Z-MED and Z-MED II Balloon Dilatation Catheter, Numed, Hopkinton, NY, USA.

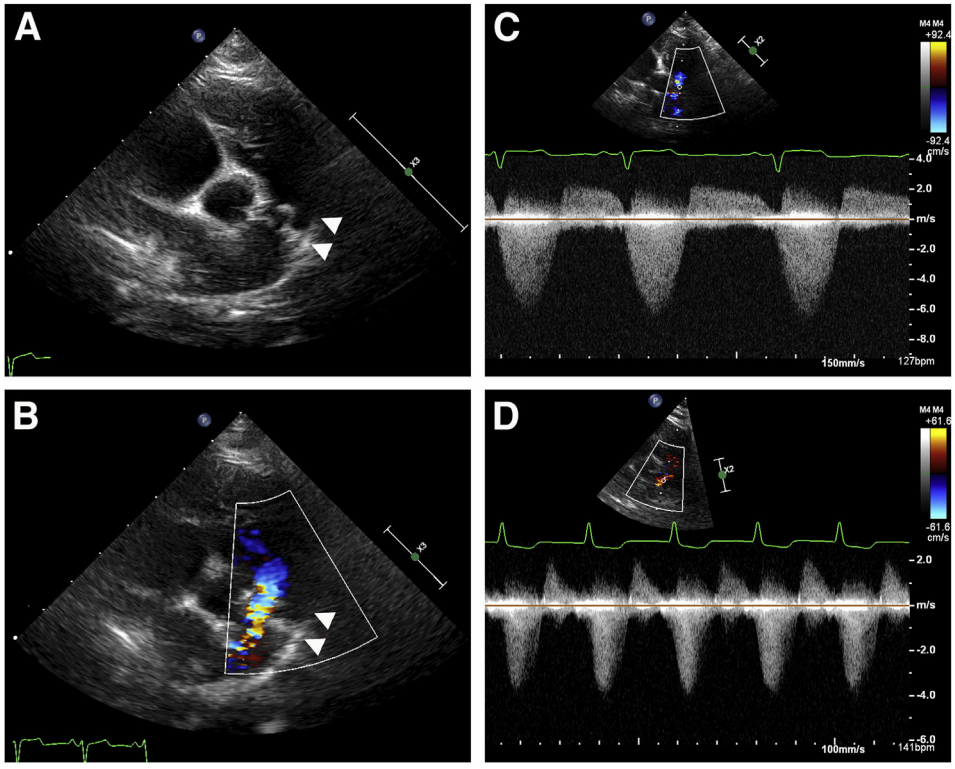

Fig. 1 Transthoracic echocardiographic images of case 5 demonstrating pulmonary valve dysplasia with a tunnel-like lesion through the area of the pulmonary valve (between arrowheads). (A and B) Transverse images acquired from the right parasternal short-axis imaging plane, with color Doppler imaging in (B). (C) Transpulmonary Doppler gradient before intervention. (D) The same image obtained 24 h after cutting balloon dilation and high-pressure balloon valvuloplasty.

All patients recovered uneventfully from anesthesia and were discharged the following day.

Statistical analysis was performed using commercial software.[18] Continuous data are presented as the average with ranges (minimum to maximum). The Wilcoxon test for paired samples was used to compare the difference in pressure gradients before and after the procedure. The significance was set at $p<0.05$.

Results

Transthoracic echocardiography

All dogs had severe valve thickening, subvalvar fibrous tissue, a hypoplastic pulmonary valve annulus (defined as a pulmonary valve-to-aortic valve annulus ratio of less than 0.8), or a combination of the aforementioned pathologic features (Fig. 1; Video 1). A fixed subvalvar obstruction was present in 4 of 7 cases (Table 1), whereas a tunnel-like lesion of fibrotic tissue from the valve annulus to sinotubular junction was present in 2 of 7 cases. Optimal alignment with the transpulmonary high-velocity signal was obtained to estimate peak transpulmonary systolic pressure gradients. Peak instantaneous transpulmonary pressure gradients of all dogs are provided in Table 2. The average pre-procedural instantaneous peak systolic transpulmonary pressure gradient was 145 mmHg (range: 100—195 mmHg), as determined by transthoracic echocardiography. Severe right ventricular concentric hypertrophy, right atrial dilation, and post-stenotic dilatation of the pulmonary trunk were present in all dogs. None of the dogs had evidence of right-sided congestive heart failure at the time of the procedure. Concurrent cardiac abnormalities were present in half of the cases (Table A; data available in Supplemental Material online). The average pulmonary valve annulus-to-aortic valve annulus ratio was 0.71 (range: 0.51—0.88).

Procedural results

Catheterization (Fig. 2) and echocardiographic (Fig. 1; Video 1) data are summarized in Tables 1 and

[18] MedCalc Statistical Software version 17.5.5, http://www.medcalc.org, 2017, Ostend, Belgium.

Table 1 Size measurements and balloon selection.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
TTE							
PV annulus diameter (mm) | valvar tunnel (mm)	7.5	15.7	10.1	11.8	10.8 | 5.8	15.5	7.2 | 2.8
Subvalvar obstruction (mm)		7.4	4.1	7.4		8.2	
PV annulus: aortic valve annulus ratio	0.71	0.72	0.84	0.6	0.51	0.88	0.74
Angiography							
PV annulus diameter (mm) | valvar tunnel (mm)	8.4	17.3	12.8	13.3	11.2 | 5.1	16	8.3 | 3.3
Subvalvar obstruction (mm)		9.3	3.2	7.5		7.8	
Balloon selection							
CB dilation catheter (diameter × length, mm)	7 × 20	7 × 20	6 × 20	7 × 20	6 × 20	8 × 20	5 × 20
HPB dilation catheter (diameter × length, mm)	Z-MED 10 × 30	Atlas 16 × 40	Atlas 14 × 20	Atlas Gold 16 × 40	Atlas Gold 12 × 20	Atlas Gold 22 × 20	Z-MED II 10 × 30
Balloon: PV annulus ratio							
TTE (CB)	0.93	0.95	1.46	0.95	1.04	0.98	1.80
TTE (HPB)	1.33	1.02	1.39	1.36	1.11	1.42	1.39
Angiography (CB)	0.92	0.75	1.88	0.93	1.18	1.02	1.52
Angiography (HPB)	1.20	0.92	1.10	1.20	1.07	1.38	1.20

CB: cutting balloon; HPB: high-pressure balloon; PV: pulmonary valve; TTE: transthoracic echocardiography.

2. Various CBs were selected, ranging between 6 and 8 mm in diameter and 20 mm in length, and HP balloon dilation catheters ranged in size from 10 to 22 mm in diameter and 20 to 40 mm in length (Table 1). During cardiac catheterization, the average starting peak systolic right ventricular-to-pulmonary artery pressure gradient was 124 mmHg (range: 72–169 mmHg). Right ventriculography confirmed the echocardiographic findings of all dogs (Fig. 3; Video 2), and CB dilation and HP BPV were performed for all dogs as described in the Animals, materials, and methods section (Fig. 4, Video 3). Immediately after CB dilation and HP BPV, the average peak systolic right ventricular-to-pulmonary artery pressure gradient was 51 mmHg (range: 24–90 mmHg), representing a significant reduction in the peak-to-peak gradient (p=0.04; Table 2). Transthoracic echocardiography at one day after procedure revealed a significant reduction in the instantaneous peak systolic transpulmonary pressure gradient, from a mean of 144 mmHg before the procedure to 78 mmHg after the procedure (p=0.003). The group average of 35% reduction in the instantaneous peak systolic transpulmonary pressure gradient from before the procedure to the last follow-up echocardiogram was also a significant decrease (p=0.008) at an average follow-up of 15 months after procedure (range: 5–35 months) (Fig. 5). There was no intraprocedural or periprocedural mortality during CB dilation and HP BPV. In one dog (case 5), overinflation of the CB inadvertently occurred, reaching a pressure of 16 atm in a balloon with a manufacturer's rated burst pressure of 10 atm. The CB catheter was removed without incident, but a partial avulsion of one of the microtomes was noted, which could have caused vascular or intracardiac trauma during removal; careful evaluation of the tricuspid valve by echocardiography failed to demonstrate any obvious adverse effect from this complication. In 4 of 7 dogs, the owner reported improved clinical signs, including exercise tolerance and activity, after the procedure (Table A; data available in Supplemental Material online). One dog (case 3) was euthanized 20 months after the procedure owing to non-cardiovascular causes (hemoabdomen), whereas another dog (case 7) was euthanized 9 months after the procedure owing to the development of right-sided congestive heart failure.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.jvc.2019.07.004

Discussion

This study describes CB dilation followed by HP BPV performed for 7 dogs, demonstrating in a small sample an immediate reduction in the transpulmonary pressure gradient in canine dysplastic PS. This technique was not compared with conventional BPV or with HP BPV alone, and the

Table 2 Pressure gradients.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
TTE							
Instantaneous systolic RV-to-PA pressure gradient (mmHg)							
Before CB + HPB	195	100	129	115	155	144 (sedated)	173
After CB + HPB (24 h)	65	80	72	70	53	92 (sedated)	112
After CB + HPB (% PG reduction)	67%	2%	44%	39%	66%	36%	35%
First recheck after procedure (months after procedure)	75 (1 month)	76 (3 months)	86 (5 months)	50 (5 months, sedated)	104 (2 months)	49 (2 months, sedated)	127 (1 month)
TTE recheck (months after CB + HPB)	83 (24 months, sedated)	72 (10 months)	86 (5 months)	50 (5 months, sedated)	104 (2 months)	49 (2 months, sedated)	127 (1 months)
Most recent recheck (months after procedure)	83 (24 months, sedated)	78 (35 months)	86 (5 months)	50 (5 months, sedated)	140 (16 months)	81 (14 months)	144 (8 month)
% reduction at the most recent follow-up compared with initial TTE	57%	22%	33%	57%	10%	44%	17%
Cardiac catheterization							
Pulmonary artery systolic/diastolic/mean (mmHg)							
Before CB + HPB	N/A	N/A	14/11/12	27/13/19	44/20/30	19/11/14	N/A
After CB + HPB	19/8/-	28/16/22	41/15/26	18/10/13	31/13/20	20/11/15	17/12/14
Right ventricle systolic/min/EDP (mmHg)							
Before CB + HPB	100/9/-	63/(-6)/7	86/—/—	147/0/10	213/(-7)/15	154/(-10)/48	74/15/15
After CB + HPB	43/10/-	76/0/24	83/(-5)/39	101/0/9	64/5/14	110/(-5)/11	55/12/13
Right atrium mean (mmHg)							
Before CB + HPB	10.5	5	N/A	6	10	5	9
After CB + HPB	10	12	9	7	10	5	10
Peak systolic RV-to-PA PG (mmHg)							
Before CB + HPB	N/A	N/A	72	120	169	135	N/A
After CB + HPB	24	48	42	83	33	90	38
% reduction in peak systolic gradient at catheterization	N/A	N/A	41.70%	30.80%	76.90%	33.30%	N/A

CB: cutting balloon; EDP: end-diastolic pressure; HPB: high-pressure balloon valvuloplasty; min: minimum; N/A: not available; PA: pulmonary artery; PG: pressure gradient; RV: right ventricle; TTE: transthoracic echocardiography; —: value not recorded.

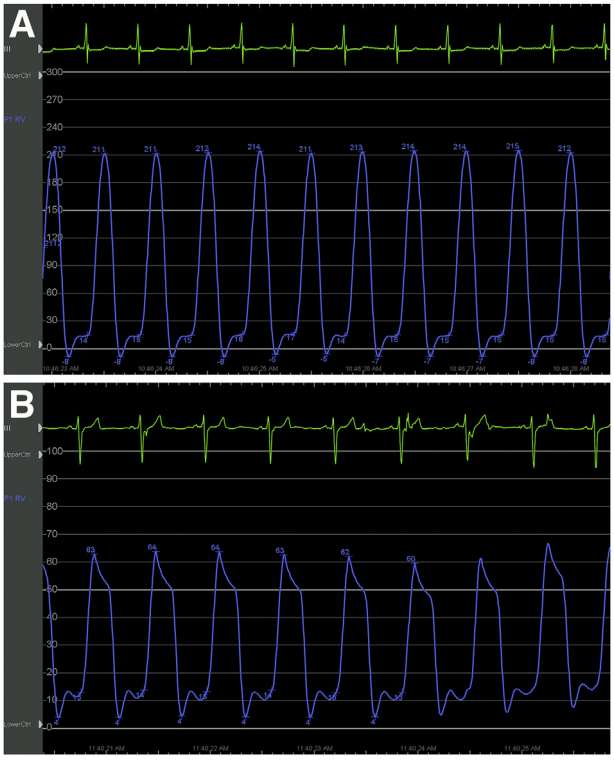

Fig. 2 Invasive hemodynamics of case 5 showing a peak right ventricular pressure of 213 mmHg before cutting balloon dilation and high-pressure balloon valvuloplasty (A) compared with a postprocedural right ventricular pressure of 64 mmHg for a 77% intraoperative reduction in systolic right ventricular pressure (B).

relative benefit of using CB dilation before BPV (or HP BPV) cannot be determined from these data. However, based on the severity of valvar dysplasia, all dogs enrolled in this trial were considered poor candidates to benefit substantially from conventional BPV by an operator (B.A.S.) who has performed more than 150 pulmonary valve interventions. A recent pilot study of HP BPV demonstrated good results in dogs with both fused doming valves and dysplastic valves, suggesting HP BPV alone may be sufficient for some of these cases [23]. The additional cost of a CB dilation catheter may be an argument to consider HP BPV first in most cases. In considering the recent study of HP BPV [23], however, it is our opinion that the morphology of dysplastic PS is not optimally defined in dogs and that prior classification schemes of type A vs type B morphology do not adequately capture the wide variation in valve thickening, subvalvar fibrous tissue, and sinotubular adhesions that exist in canine dysplastic PS. This limits our ability to directly compare techniques between different patient populations [6]. This wide spectrum of dysplastic lesions also limits conclusions that can be drawn from this study as some dogs had a better-than-expected result, whereas others were improved to a lesser degree, and it is unclear how much the morphologic features of each dog's dysplastic PS led to this variable outcome. Surgical options (patch graft or open repair) were discussed with and declined by all clients who elected to attempt CB dilation and HP BPV as a first-line therapy.

Another avenue for the use of this technique may be for dogs with dysplastic PS that develop restenosis after an initial successful BPV, requiring a second procedure. Restenosis was recently described in a dog that had a doming pulmonary valve with commissural fusion before BPV and years later developed a markedly thickened valve, confirmed on postmortem evaluation [34]. However, it is clear that CB dilation and HP BPV do not eliminate the potential for future restenosis as demonstrated by some of the cases here that developed worsening pressure gradients during recheck visits despite an immediate reduction after the procedure. This progressive increase in gradient has previously been documented in dogs with dysplastic PS undergoing conventional BPV, with Bussadori et al. [10] describing an initial 48% reduction in pressure gradient that had worsened to a 39% reduction at 1 year after procedure. In another series, at least 3 of 40 dogs were documented to have restenosis within 6 months of the procedure, although the nature of the stenosis for all dogs in the study (e.g., valve fusion versus valve dysplasia) was not described [35]. The restenosis rate after HP BPV alone is unknown as long-term follow-up has not been described [23].

Both the French bulldogs (2 of 7) in this case series had severely elevated transpulmonary pressure gradients and pulmonary annular hypoplasia, similar to the results of a recent study looking at specific features of French bulldogs with PS [11]. Each of these 2 dogs had dysplastic pulmonary valves and valvar tunnels between the valve annulus and sinotubular junction owing to fibrous adhesions of valve tissue, indicative of valvar PS and not supravalvular stenosis [6]. One dog had an immediate reduction in the instantaneous peak systolic transpulmonary pressure gradient from 155 to 53 mmHg at one day after procedure, although the pressure gradient increased to 104 mmHg at 2.5 months after procedure and to 140 mmHg at 16 months after procedure. The other French bulldog had an immediate reduction in the instantaneous peak systolic transpulmonary pressure gradient from 173 to 112 mmHg at one day after procedure, and the pressure gradient increased to

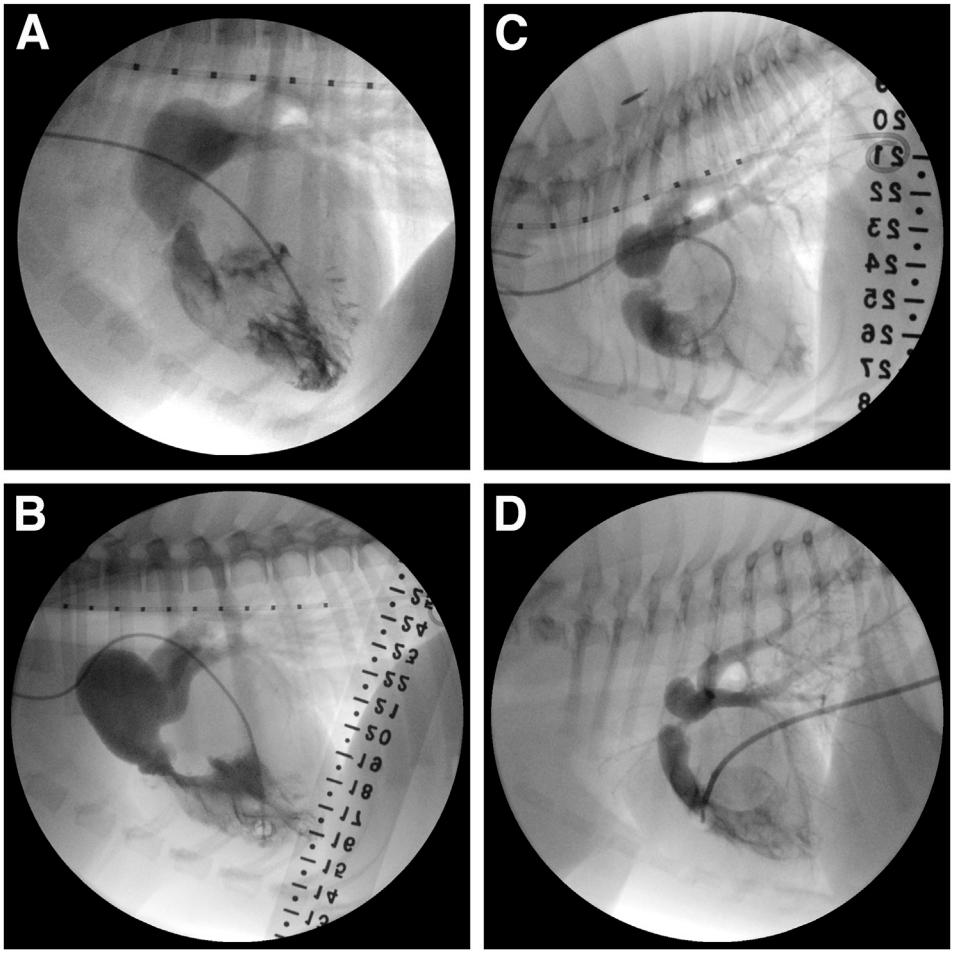

Fig. 3 Right ventriculograms of cases 1 (A), 4 (B), 5 (C), and 7 (D) demonstrate variable forms and extent of obstruction in the pulmonary outflow tract from dogs in this series with pulmonary valve dysplasia. An esophageal marker catheter is present for image calibration in panels A, B, and C, and a radiopaque table ruler is also present in panels B and C as part of an unrelated study.

127 mmHg at 1.5 months and 144 mmHg at 8 months. One of these 2 French bulldogs remains alive and without clinical signs, whereas the other developed right heart failure 8 months after procedure and was euthanized shortly thereafter.

According to subjective client assessment, CB dilation and HP BPV may be able to improve clinical signs as 4 owners noted an improved energy level and exercise capacity in their dogs after the procedure, although only 2 dogs were noted to have clinical signs before the intervention. Long-term follow-up of these dogs will be necessary to validate initial findings and to determine the rate of restenosis and the need for additional intervention.

The CB dilation technique for dysplastic PS should be limited to those dogs in which the narrowest orifice (valvar or subvalvar) is 8 mm or less as the largest peripheral CB dilation catheter is currently 8 mm in diameter. Potential complications with the CB dilation technique include disruption of the pulmonary annulus, a partial or complete tear of the pulmonary artery, and damage to the right ventricular outflow tract, the tricuspid valve apparatus, or other nearby cardiac structures or vasculature. Partial fracture of a microtome blade was noted on removal of the CB in one dog from our series, without apparent consequence. Presumably, this occurred during the final inflation with the CB as burst pressure based on the manufacturer's recommendations was exceeded. Therefore, it may be preferable to advance a CB catheter through a long guiding sheath placed within the proximal right ventricular outflow tract to avoid damage to cardiovascular structures during catheter withdrawal, although in dogs with very small right ventricular lumens this may not be possible. In addition, when using a pressure inflation device[12] for CB dilation, the

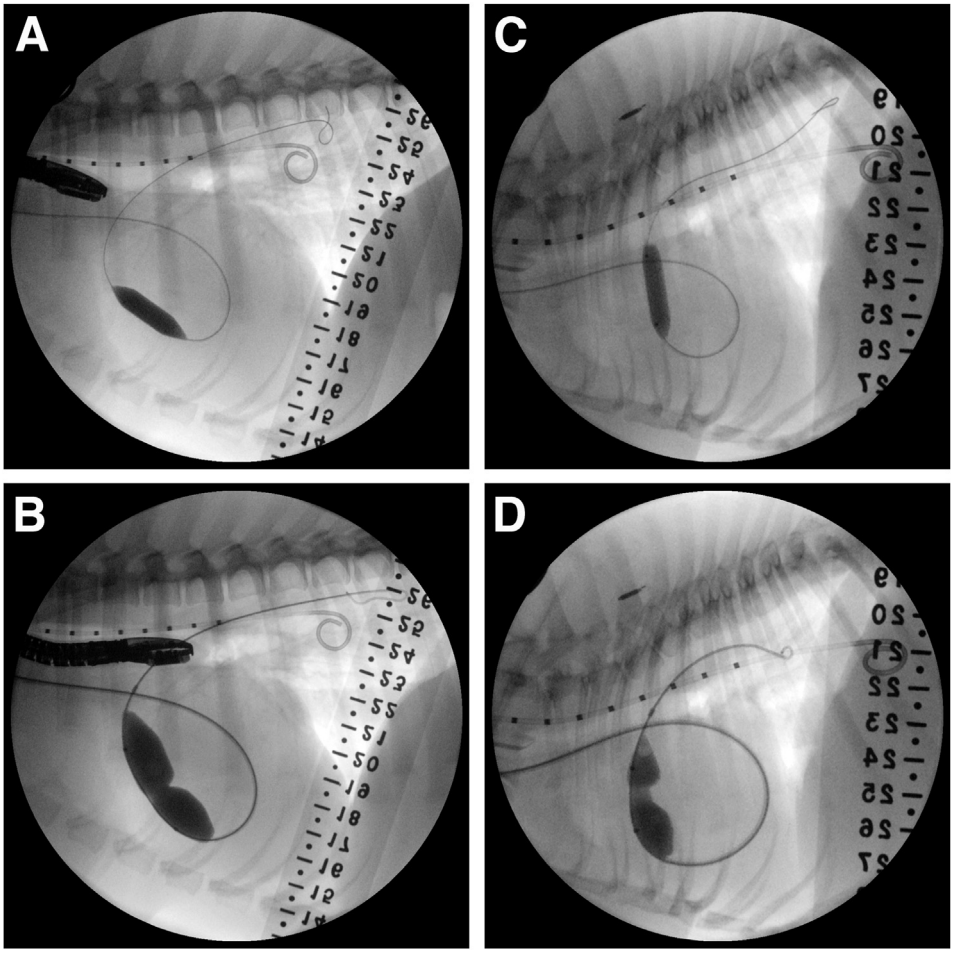

Fig. 4 Fluoroscopic images during cutting balloon dilation (A and C) and high-pressure balloon valvuloplasty (B and D) of dogs with pulmonary valve dysplasia, specifically cases 4 (A and B) and 5 (C and D). The images during high-pressure balloon valvuloplasty (B and D) are from midinflation demonstrating the stenotic waist, which disappeared in all cases at the rated burst pressure. An esophageal marker catheter is present for image calibration, and a radiopaque table ruler is present in all images as part of an unrelated study.

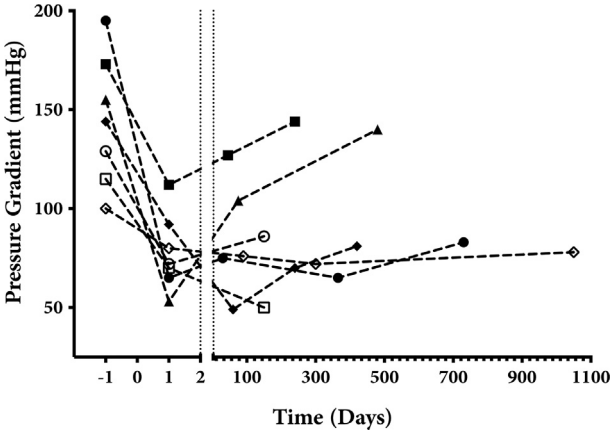

Fig. 5 Echocardiographically derived peak systolic transpulmonary pressure gradient of all dogs in this series over time. Each symbol and connecting lines represent an individual case. The break in the x-axis separates the immediate preprocedural and post-procedural gradients from the more compressed timeline to the right.

authors recommend turning the threaded syringe to generate pressure consistently rather than filling with the free release trigger. As the CB is small and takes only a small volume to fill, this technique should help to avoid overfilling the angioplasty balloon and exceeding the rated burst pressure. Hand inflations without a pressure inflation device and integrated manometer for CB dilation and HP BPV should be avoided owing to the inability to monitor the pressure within the angioplasty balloon dilation catheter. The HP balloon dilation catheter should be advanced over a super-stiff guidewire if possible as a stiffer guidewire makes the delivery of stiffer balloon dilation catheters safer and provides better support for the HP balloon dilation catheters during BPV [33,36]. Disadvantages of CB dilation and HP BPV include added procedural and fluoroscopy time, as well as the additional cost and training required for the equipment involved.

This case series presents observational data on the safety and initial feasibility of CB dilation and HP BPV in 7 dogs with dysplastic PS. Larger studies are needed, and it remains unclear whether the presented treatment for dogs with dysplastic PS affords any sustained clinical benefit. Future studies are warranted to determine the difference in the outcome of using CB dilation before conventional BPV or HP BPV, versus conventional or HP BPV alone, in dogs with dysplastic PS. An additional limitation is that sedation during echocardiography was at the discretion of the clinician. Sedation may have affected the instantaneous pressure gradient, despite a previous study showing no difference in the severity of PS after sedation [37].

Conclusions

Cutting balloon dilation and HP BPV can be considered as a therapeutic intervention for patients with dysplastic PS, or those with resistant PS who fail conventional BPV, and may be safe in dogs based on this small case series. The ideal selection criteria and rate of restenosis for CB dilation and HP BPV remain under investigation, and long-term follow-up and a large controlled study are necessary to confirm safety and demonstrate efficacy.

Conflicts of Interest Statement

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

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvc.2019.07.004.

Video Table

Number	Title	Description
Video 1	Echo Dysplastic PS	Representative transthoracic echocardiographic images from case 5 demonstrating severe pulmonary valve dysplasia, right ventricular hypertrophy, and mild pulmonary insufficiency.
Video 2	RV Angiograms	Representative right ventriculograms (from cases 4, 5, and 7) demonstrating severe right ventricular hypertrophy and pulmonary valve dysplasia. An esophageal marker catheter is present for image calibration with a radiopaque table ruler as part of an unrelated study in the ventriculograms from cases 4 and 5.
Video 3	CB & HP Balloon Dilation	Fluoroscopic capture of cutting balloon (CB) dilation and high-pressure (HP) balloon valvuloplasty from cases 4 and 5. Note that the cutting balloon in case 4 failed to fully engage the annulus, leading to motion throughout the cardiac cycle when inflated. In contrast, the inflation of case 5 shows full apposition and appropriate positioning of the cutting balloon dilation catheter. During HP inflation, the stenotic waist is abolished once the rated burst pressure is achieved. An esophageal marker catheter is present for image calibration with a radiopaque table ruler as part of an unrelated study in each.

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