Balloon valvuloplasty in 2 juvenile alpacas with severe valvular pulmonic stenosis

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Abstract
Two juvenile alpacas, 1 male and 1 female, were presented for evaluation of grade V/VI bilateral basilar systolic heart murmurs. Both animals were ultimately diagnosed with severe valvular pulmonic stenosis and a small ventricular septal defect. Transvenous balloon valvuloplasty was performed in each animal using methods described in the dog. A double balloon technique was employed in the first case, with a balloon-annulus ratio of ~1.55. For the second case, a high-pressure dilatation balloon catheter with a balloon-annulus ratio of ~1.33 was selected. Experience with both procedures indicates that balloon pulmonary valvuloplasty is technically feasible in alpacas using techniques extrapolated from those used in dogs. Furthermore, accepted criteria for procedural success were fulfilled for both alpacas, with more than a 50% reduction in the echocardiographically derived transpulmonic pressure gradient after intervention.

KEYWORDS
camelid, congenital heart disease, cria, dysplasia, pulmonary

1 | CASE DESCRIPTION

Case 1, a 1-year-old, 37.3 kg, intact male alpaca was presented to the University of Tennessee Veterinary Teaching Hospital for evaluation of a grade V/VI bilateral basilar systolic heart murmur. Echocardiography (Acuson Sequoia 512, 8 MHz transducer, Siemens Medical Solutions, Mountain Way, California) revealed fusion of the pulmonic valve (PV) leaflets with systolic doming, severe poststenotic dilatation of the main pulmonary artery (MPA), and moderate right ventricular (RV) hypertrophy. The Doppler-derived peak instantaneous transpulmonic pressure gradient (PGpulm) was markedly increased at 108 mm Hg, consistent with severe pulmonic valve stenosis (PS).1 Color-flow Doppler interrogation also revealed moderate PV regurgitation and trace tricuspid regurgitation.

Approximately 60 days later, the alpaca was anesthetized for transvenous balloon pulmonary valvuloplasty (BPV). Procainamide (10 mg/kg IM) was administered before the procedure. Etomidate (3 mg/kg IV) was administered for induction, and anesthesia was maintained with inhaled sevoflurane. Fentanyl (7.5 mcg/kg/h) and lidocaine (50 mcg/kg/min) were administered IV as a constant rate infusion. A previously placed left jugular venous catheter was exchanged for a 4-Fr microintroducer over a 0.018" × 40 cm guidewire (Micropuncture Access Set, Cook Medical, Bloomington, Indiana). The microintroducer was subsequently exchanged for a 6-Fr introducer sheath (SuperSheath, Boston Scientific, Marlborough, Massachusetts) over the 0.018" guidewire. A 5-Fr balloon wedge pressure catheter (BWPC; Arrow Balloon Wedge Pressure Catheter, Teleflex, Wayne, Pennsylvania) was advanced into the RV under fluoroscopic guidance, and RV pressure tracings were obtained (maximum systolic

Abbreviations: BA, balloon annulus ratio; BPV, balloon pulmonary valvuloplasty; BWPC, balloon wedge pressure catheter; Fr, French; MPA, main pulmonary artery; PGpulm, transpulmonic pressure gradient; PS, pulmonic stenosis; PV, pulmonic valve; RV, right ventricle; VSD, ventricular septal defect.

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pressure: 56 mm Hg). The BWPC was removed, and a 5-Fr angiographic pigtail catheter (Royal Flush Plus High Flow Catheter, Cook Medical) was advanced into the RV. Selective ventriculography demonstrated valvular PS with marked poststenotic dilatation of the MPA (Figure 1; Supplemental Video 1). The estimated pulmonic annular diameter was 18 mm. The levophase revealed normal coronary artery anatomy and a small left-to-right interventricular shunt.

The pigtail catheter was withdrawn. The 6-Fr introducer was exchanged for an 8-Fr and then a 10-Fr introducer (SuperSheath, Boston Scientific). The alpaca was repositioned to permit access to an extant right jugular catheter. A series of exchanges was conducted in the manner previously described, resulting in placement of a 10-Fr introducer within the right jugular vein. Two 6-Fr BWPC were advanced into the MPA utilizing both the left and right jugular venous introducers. Each BWPC was then used to facilitate placement of a 260 cm 0.035 \( \times \) 0.035 guidewire (Glidewire, standard stiff J-tip, Terumo Medical Corporation, Somerset, New Jersey) across the PV and within the pulmonary arteries. Both BWPCs were removed. A 16 mm \( \times \) 3.0 cm balloon catheter (Z-med balloon valvuloplasty catheter, rated burst pressure, 5 atm, B. Braun Interventional Systems Inc, Bethlehem, Pennsylvania) was then advanced over each guidewire and positioned across the PV. Serial attempts were made to inflate the devices simultaneously, but this failed to abolish the PV waist. One of the balloon catheters was exchanged for an 18 mm \( \times \) 3.0 cm valvuloplasty catheter (Z-med balloon valvuloplasty catheter, rated burst pressure, 4 atm, B. Braun Interventional Systems Inc). Several inflations were performed. The balloons successfully engaged the annulus, resulting in dissipation of the balloon waist (Figure 2). All implements were withdrawn. Jugular venous hemostasis was achieved via 20 minutes of manual digital compression. The alpaca recovered from anesthesia without incident.

Echocardiography was repeated 3 days, 1 month, and 4 months later, demonstrating durable improvement in PS (PG\textsubscript{pulm} of 39, 35, and 24 mm Hg, respectively). Two and a half years after BPV, the alpaca was still alive and asymptomatic.

Case 2, a 2.5-month-old, 15.4-kg, intact female alpaca was presented to the University of Missouri Veterinary Health Center for evaluation of a grade V/VI bilateral basilar systolic heart murmur. Within the preceding week, she had received ceftiofur parenterally for empirical treatment of presumptive pneumonia. Additionally, the owner reported 2 episodes of syncope characterized by sudden collapse and spontaneous recovery. The animal remained lucid for the duration of each event. Her sire and all of his offspring, with the exception of a 2-year-old male, had died unexpectedly. Deaths were not temporally correlated.

Physical examination revealed a grade V/VI bilateral basilar systolic heart murmur. Echocardiography (Aplio Artida, 3 MHZ transducer, Toshiba Medical Systems Corporation, Otawara, Japan) disclosed severe valvular PS, with a Doppler-derived instantaneous PG\textsubscript{pulm} of 110 mm Hg. The leaflets of the PV were mildly thickened with decreased excursion, systolic doming, and mild regurgitation noted (Figure 3A,B; Supplemental Video 2). The PV annulus appeared hypoplastic, although the aortic valve annulus-to-PV annulus ratio was 1:1 in systole. Poststenotic dilatation of the MPA was evident, and there was moderate RV concentric hypertrophy. The tricuspid valve apparatus was normal in appearance with trace-to-mild regurgitation. A 2 mm perimembranous ventricular septal defect (VSD) was identified, and color-flow Doppler imaging was indicative of left-to-right systolic shunting (Figure 3C). Adequate spectral Doppler tracings could not be procured. Given the small size of the VSD and the potential for spontaneous closure by 1 year of age, BPV was advised for amelioration of the PS.

The alpaca was presented 19 days later for BPV. Morphine (0.21 mg/kg IM) and xylazine (0.1 mg/kg IM) were administered,
Propofol (3.2 mg/kg IV) was delivered to effect for anesthetic induction, and a surgical plane of anesthesia was maintained with inhaled sevoflurane. A preprocedural contrast computed tomographic study (64 detector row Toshiba Aquilion, Toshiba America Medical Systems, Tustin, California) confirmed normal coronary artery anatomy. A right jugular venous cutdown was performed and an 8-Fr introducer sheath and guidewire were placed (Boston Scientific). A 7-Fr BWPC (Arrow Balloon Wedge Pressure Catheter, Teleflex) was advanced across the PV into the MPA under fluoroscopic guidance. A right-heart pressure-pullback demonstrated a peak-to-peak $P_{\text{Gpulm}}$ of approximately 66 mm Hg. A 5-Fr angled pigtail catheter (Torcon NB Advantage AP2 Catheter, Cook Medical) was advanced into the distal left pulmonary artery. The BWPC was exchanged for a 16 mm guidewire (Radiofocus Glidewire, J-tip, Terumo Medical Corporation) into the distal left pulmonary artery. The BWPC was exchanged for a 16 mm

**Figure 3** Echocardiographic still images of case 2. A, Two-dimensional right parasternal cranial oblique view of the right ventricular outflow tract demonstrating thickening and systolic doming of the pulmonic valve (white arrow). B, Simultaneous color-flow Doppler imaging of (A) demonstrating turbulent flow at the level of the pulmonic valve. C, Right parasternal oblique 5-chamber long-axis view with color-flow Doppler demonstrating left-to-right systolic shunting across a perimembranous ventricular septal defect. AO, aorta; LV, left ventricle; PV, pulmonic valve; RV, right ventricle

**Figure 4** Right ventricular angiogram (A) from case 2 demonstrating pulmonic valve stenosis with post stenotic dilatation of the main pulmonary artery. The marker indicates the level of the pulmonic valve annulus. Measurements of the valve annulus diameter averaged approximately 13.5 mm. Left lateral fluoroscopic image (B) showing high-pressure balloon valvuloplasty of severe pulmonic stenosis. A marker catheter (1 cm demarcation) is visible within the esophagus.
The high-pressure balloon catheter was exchanged for the BWPC, and hemodynamic tracings were obtained within the MPA, as well as the RV. The peak-to-peak $\Delta P_{\text{pulm}}$ had decreased to approximately 44 mm Hg. The BWPC was then exchanged for an 18 mm $\times$ 4 cm high-pressure-dilatation balloon catheter (Atlas Gold PTA Dilatation catheter, rated burst pressure, 18 atm, Bard Peripheral Vascular Inc, Tempe, Arizona). The latter was positioned across the PV and inflated to 17 atm using an inflation device (Cook Sphere Inflation Device, Atrion Medical, Arab, Alabama). The desired pressure was maintained for 3 seconds, and then the balloon was rapidly deflated. The balloon successfully engaged with the PV but failed to achieve complete resolution of the waist.

The animal described in case 1 exhibited valve traits that were most consistent with a type-A morphology. According to the proposed criteria for pulmonary annulus hypoplasia in dogs (aortic annulus-to-pulmonary annulus ratio >1.2), the pulmonary annulus diameter of the animal detailed in case 2 was normal. However, the validity of this cutoff has not been demonstrated in alpacas, and the PV annulus appeared subjectively hypoplastic on 2-dimensional echocardiography. A recent study evaluating the efficacy and safety of high-pressure BPV in 25 dogs with severe PS yielded promising results, and valve morphology was not correlated with response to treatment. For this reason, the authors elected to employ high-pressure BVP when approaching case 2. Furthermore, the application of a single high-pressure balloon is less technically challenging than a double-balloon method.

In both alpacas, the maximum balloon diameter was selected based on current recommendations to achieve a balloon-to-annulus ratio (BA) of approximately 1.3 to 1.5, although a more permissive ratio of 1.2 to 1.5 has also been suggested. The effective BA for cases 1 and 2 were 1.55 and 1.33, respectively. A double-balloon procedure was employed for the former, as achieving the target BA would have required use of a single balloon with a diameter exceeding 20 mm. Traditional balloons of this size have relatively low rated burst pressures, and protracted periods of inflation and deflation can contribute to systemic hypotension. Thus, a double-balloon technique was selected as the most efficient means of applying sufficient radial force to the PV while limiting hemodynamic disturbances. When using this approach, the effective balloon diameter is calculated with the equation $0.82(Diameter 1 + Diameter 2)$, where diameters 1 and 2 refer to each balloon. The 16 mm balloons that were initially selected for case 2 yielded a BA of 1.2, and resolution of the PV waist

## DISCUSSION

Valvular PS is prevalent in the dog, with recent retrospective studies indicating that it is the most common congenital heart disease in this species. It has been described in South American camelids, although there is a general paucity of such reports. Accordingly, the prevalence of PS in camelids, and more specifically in alpacas, remains obscure. Clinical guidelines regarding therapeutic strategies for alpacas with PS do not exist, and thus it is necessary to extrapolate techniques that have been proven efficacious in other domestic species. Numerous studies have demonstrated the feasibility BPV in dogs, and the process has been recounted in detail. More importantly, BPV confers improved survival time and the amelioration of clinical signs in severely affected dogs. The cases described herein indicate that such methods can be reproduced in alpacas and yield results that are compatible with established definitions of procedural success.

As previously asserted, reports detailing valvular PS in South American camelids are sparse. The prevalence of various congenital cardiac conditions in alpacas is not described. In llamas, however, congenital heart disease is more extensively characterized, and VSD is the most commonly reported anomaly. Complex congenital conditions are reported somewhat frequently in both species. Whether this is indicative of a preponderance of complex disease in alpacas or is simply a product of limited screening and reporting is unclear.

Two categories of dysplastic PV morphology have been described in the dog, although animals may exhibit attributes of both types. Type-A valve morphology is characterized by commissural fusion, minimal leaflet thickening, systolic doming, and a normal pulmonary annulus diameter. In contrast, type-B morphology is defined by marked thickening of the valve leaflets and pulmonary annulus hypoplasia, with an aortic annulus-to-pulmonary annulus ratio of >1.2 being indicative of the latter. The distinction may be clinically relevant, as animals with type-B valve morphology appeared to be less amenable to conventional low-pressure BPV than type-A counterparts. Currently, it is impossible to determine if this categorization scheme is applicable to alpacas.
was achieved only after converting to a balloon with a BA of 1.33. Our preliminary experience may suggest that the aforementioned range of 1.3 to 1.5 is likely to confer satisfactory results.

In certain dog breeds, PS is associated with congenital anomalies of the coronary artery anatomy.\textsuperscript{19,20} Such malformations have bearing on the approach to BPV in these animals. Specifically, a conservative BA ratio should be employed in order to minimize the risk of coronary artery avulsion.\textsuperscript{21,22} The prevalence of coronary artery abnormalities and any associations with PS are unelucidated in the alpaca. Careful scrutiny of angiography or computed tomography can be used to confirm the presence of 2 distinct coronary ostia in the dog.\textsuperscript{22,23} Each modality was successfully applied to exclude coronary anomalies in these cases, allowing BVP to proceed as anticipated.

Echocardiographically derived PG\textsubscript{pulm} obtained after BPV fulfilled widely accepted criteria for procedural success in both cases. Specifically, the intervention is considered successful if the PG\textsubscript{pulm} is reduced by >50% or if the post-BPV PG\textsubscript{pulm} is <80 mm Hg.\textsuperscript{5,7} In case 1, the PG\textsubscript{pulm} was indicative of mild PS that remained unchanged during follow-up. In case 2, the PG\textsubscript{pulm} was diminished by 62% 1 day after BPV. However, 4 months later, the PG\textsubscript{pulm} increased to 70 mm Hg. This regression is likely indicative of restenosis at the level of the PV.\textsuperscript{5} A PG\textsubscript{pulm} of 70 mm Hg remains consistent with the established criteria for success, and the client reported improvement in the cria’s clinical signs. However, it is unclear if this animal will incur further restenosis. Long-term follow-up is desirable in both cases, as response to BPV has not been characterized in the alpaca. Additional echocardiographic monitoring will also be important for case 2 in order to determine whether the animal’s VSD will persist or become hemodynamically significant. As there are no published echocardiographic reference ranges for juvenile alpacas, all assessments of chamber dimensions were subjective.

Numerous close relatives of the animal described in case 2 died unexpectedly. This is an intriguing facet of the case, as it could indicate the presence of a heritable disorder. Precise causes of death were not reported, and thus it is impossible to determine if they possessed a familial proclivity for congenital heart disease. Given the evidence for a genetic mode of inheritance in the dog, it is likely prudent to discourage breeding of affected alpacas.

BPV has become a widely adopted intervention for amelioration of severe valvular PS in dogs. Our experience suggests that techniques employed in dogs can be readily extrapolated for use in camels and that they confer a positive clinical outcome. Epidemiological studies, descriptive reports, and clinical studies are required to determine the prevalence of PS, disease characteristics, and the clinical utility of BPV in alpacas.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL USE DECLARATION

Florfenicol was administered at 19 mg/kg SQ to the alpaca recounted in case 1 for off-label perioperative prophylaxis. The alpaca described in case 2 received cefotiofur for off-label treatment of suspected bacterial pneumonia before presentation to the University of Missouri Veterinary Health Center. Additionally, prophylactic antimicrobial treatment during the perioperative and immediate postoperative periods comprised off-label cefotiofur sodium (Naxcel, Zoetis, Parsippany, New Jersey) administered at 2.2 mg/kg IV every 12 hours.

INSTITUTIONAL ANIMAL CARE AND USE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare that IACUC or other approval was not required for the current manuscript.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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REFERENCES

1. Bussadori C, Amberger C, Le Bobinnec G, et al. Guidelines for the echocardiographic studies of suspected subaortic stenosis and pulmonic stenosis. J Vet Cardiol. 2000;2:15-22.
2. Schrope DP. Prevalence of congenital heart disease in 76,301 mixed breed dogs and 57,025 mixed breed cats. J Vet Cardiol. 2015;17:192-202.
3. Oliveira P, Domenech O, Silva J, et al. Retrospective review of congenital heart disease in 976 dogs. J Vet Intern Med. 2011;24:477-483.
4. Margiocco ML, Scansen BA, Bonagura JD. Cameldid cardiology. Vet Clin Food Anim. 2009;25:423-454.
5. Schrope DP. Balloon valvuloplasty of valvular pulmonic stenosis in the dog. Clin Tech Small Anim Pract. 2005;20(3):182-195.
6. Ristic JME, Marin CJ, Baines EA, Heritage ME. Congenital pulmonic stenosis a retrospective study of 24 cases seen between 1990-1999. J Vet Cardiol. 2001;3:13-19.
7. Bussadori C, DeMadron E, Santilli RA, Borgarelli M. Balloon valvuloplasty in 30 dogs with pulmonic stenosis: effect of valve morphology and annular size on initial 1-year outcome. J Vet Intern Med. 2001;15:553-558.
8. Johnson MS, Martin M, Edwards D, French A, Henley W. Pulmonic stenosis in dogs: balloon dilatation improves clinical outcome. J Vet Intern Med. 2004;18:656-662.
9. Johnson MS, Martin M. Results of balloon valvuloplasty in 40 dogs with pulmonic stenosis. J Small Anim Pract. 2004;46:148-153.
10. Boon JA, Knight AP, Moore DH. Llama cardiology. Vet Clin North Am Large Anim Pract. 1994;10:353-370.
11. Leipold HW, Hiraga T, Johnson LW. Congenital defects in the llama. Vet Clin North Am Food Anim Pract. 1994;10:401-420.
12. Kurosawa TA, Gunasekaran T, Sanders R, et al. Common arterial trunk in a 3-day-old alpaca cria. Case Rep Vet Med. 2016;2016:4609126.
13. Poser H, Dalla Pria A, De Benedictis GM, et al. Ventricular septal defect and double-chambered right ventricle in an alpaca. J Vet Cardiol. 2015;17(1):71-76.
14. Scansen BA. Cardiac interventions in small animals: areas of uncertainty. Vet Clin North Am Small Anim Pract. 2018;48(5):797-817.
15. Scansen BA. Pulmonary Valve Stenosis in Weisse C and Berent A, Veterinary Image-Guided Interventions. 1st ed. Ames, IA.: John Wiley and Sons; 2015:575-587.
16. Belanger C, Gunther-Harrington CT, Nishimura S, et al. High-pressure balloon valvuloplasty for severe pulmonary valve stenosis: a prospective observational pilot study in 25 dogs. J Vet Cardiol. 2018;20(2):115-122.
17. Estrada A, Moïse NS, Erb HN, McDonough SP, Renaud-Farrell S. Prospective evaluation of the balloon-to-annulus ratio for valvuloplasty in the treatment of pulmonic stenosis in the dog. J Vet Intern Med. 2006;20(4):862-872.
18. Estrada A, Moïse NS, Renaud-Farrell S. When, how and why to perform a double ballooning technique for dogs with valvular pulmonic stenosis. J Vet Cardiol. 2005;7(1):41-51.
19. Buchanan JW. Pulmonic stenosis caused by single coronary artery in dogs: four cases (1965–1984). J Am Vet Med Assoc. 1990;196:115-120.
20. Buchanan JW. Pathogenesis of single right coronary artery and pulmonic stenosis in English Bulldogs [published correction appears in J Vet Intern Med 2001 Jul-Aug;15(4):417]. J Vet Intern Med. 2001;15(2):101-104.
21. Scansen BA. Coronary artery anomalies in animals. Vet Sci. 2017;4(2):20.
22. Fonfara S, Martinez Pereira Y, Swift S, et al. Balloon valvuloplasty for treatment of pulmonic stenosis in English Bulldogs with an aberrant coronary artery. J Vet Intern Med. 2010;24:354-359.
23. Gunther-Harrington CT, Phillips KL, Visser LC, Fousse SL, Stern JA. Non-electrocardiographic-gated computed tomographic angiography can be used to diagnose coronary artery anomalies in bulldogs with pulmonary valve stenosis. Vet Radiol Ultrasound. 2019;60(1):38-46.

SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of this article.

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