Journal of Veterinary Cardiology (2019) **25**, 1—6

Journal of Veterinary Cardiology
ESVC

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Case Report

Valvular aortic stenosis in three cats[☆,☆☆]

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Received 5 September 2018; received in revised form 18 June 2019; accepted 20 June 2019

KEYWORDS
Feline;
Congenital heart disease;
Echocardiography;
Dysplasia

Abstract Aortic stenosis affects 0.028% of cats in a shelter population, with valvular aortic stenosis compromising almost half of these cases. Of congenital heart diseases reported in cats, aortic stenosis is the second most common one, affecting 17% of these cases. Existing literature on valvular aortic stenosis is scant, and thus, presentation and prognosis of affected animals is poorly understood. In this case series, we describe three cats with confirmed valvular aortic stenosis. All cases were diagnosed echocardiographically, and all three had visible aortic valve leaflet fusion and a poststenotic dilation of the ascending aorta. Congestive heart failure developed in all three cases, and prognosis was poor. This case report highlights the existence of aortic valve dysplasia in cats and may allow clinicians a better understanding of the clinical presentation of this congenital abnormality.

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https://doi.org/10.1016/j.jvc.2019.06.005
1760-2734/

Abbreviations

IVSd	interventricular septum thickness at end-diastole
LA:Ao	ratio of the left atrial dimension to the aortic annulus dimension
LAD	left atrial diameter
LVOT	left ventricular outflow tract
LVPWd	left ventricular posterior wall thickness at end-diastole
SAM	systolic anterior motion
SAS	subvalvular aortic stenosis

Case 1, a 4-month-old female entire Oriental cat (1.80 kg), was presented in September 2014 for evaluation of a grade IV/VI, left parasternal, systolic murmur. No previous clinical signs were reported, and the remainder of the physical examination was unremarkable. Echocardiography demonstrated aortic valve thickening and systolic doming of leaflets (Fig. 1A and B), typical of valve leaflet fusion. The aortic root was hypoplastic (Table 1), and there was a poststenotic dilation of the ascending aorta. Systolic transvalvular pressure gradient was measured at 74 mmHg (reference <30 mmHg), suggesting a moderate to severe stenosis [1]. Left ventricular wall thickness was normal (interventricular septum thickness at end-diastole (IVSd): 3.9 mm, left ventricular posterior wall thickness at end-diastole (LVPWd): 3.8 mm; see Table 1 for allometric scaling and reference intervals [2]), and the left atrium was moderately dilated (maximum left atrial diameter [LAD] measured parallel with the mitral annulus using a right parasternal long-axis 4-chamber view

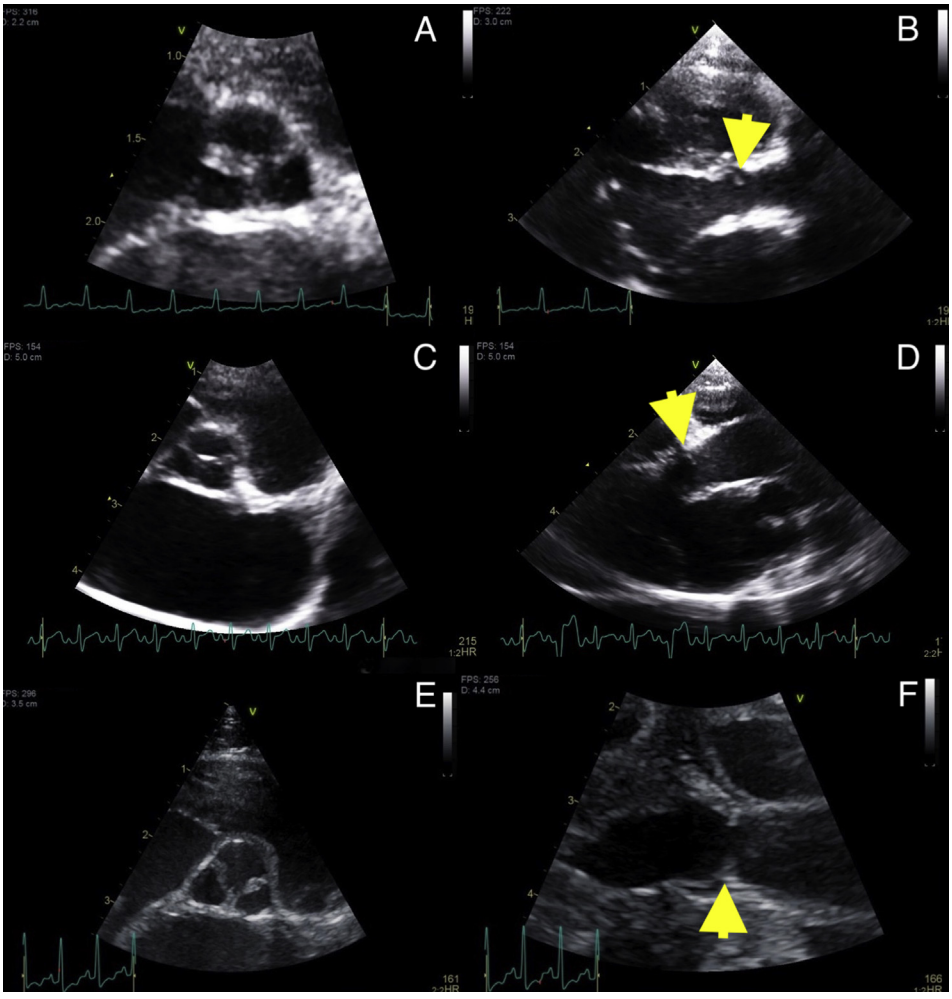

Fig. 1 (A—F): Two-dimensional echocardiographic images demonstrating the observed structural anomalies in cats with valvular aortic stenosis. Right parasternal basilar short-axis view showing thickened aortic valve leaflets in cases 1, 2 and 3 (panels A, C and E, respectively). Right parasternal long-axis five-chamber view showing aortic valve thickening, fusion (arrow heads) and poststenotic dilatation of the ascending aorta of cases 1, 2 and 3 (panels B, D and F, respectively).

Table 1 Echocardiographic measurements and allometrically scaled measurements [2] of the three cases reported herein.

Case identifier	IVSd (mm)	wIVSd (RI: 0.377–0.5911)	LVIDd (mm)	wLVIDd (RI: 1.216–1.966)	LVPWd (mm)	wLVPWd (RI: 0.345–0.64)	LAD (mm)	wLAD (RI: 1.144–1.572)	Ao (mm)	wAo (RI: 0.855–1.194)
Case 1 (1.80 kg)	3.9	0.45	12.9	1.5	3.8	0.44	13.6	1.59*	3.7	0.43*
Case 2 (1.56 kg)	5.7	0.63*	20	2.22*	4.3	0.48	20.3	2.26*	5.9	0.66*
Case 3 (5.00 kg)	7.2	1.18*	20	3.28*	8.1	1.33*	28.1	4.61*	6.3	1.04

Ao: aortic root diameter measured using a right parasternal long-axis five-chamber view at peak systole, between the hinge points of the open aortic valve; IVSd: interventricular septum thickness at end-diastole; LAD: left atrial diameter measured using a right parasternal long-axis four-chamber view; LVIDd: left ventricular internal dimension in diastole; LVPWd: left ventricular posterior wall thickness at end-diastole; RI: reference interval; W: allometrically scaled values according to body weight; *: values outside the reference interval.
For all three cases, each echocardiographic examination was remeasured by a single operator (K.B.). IVSd and LVPWd were measured on 2D images on the first frame after mitral valve closure using a leading edge to leading edge technique [14]. Left atrial size was assessed using two different methods: (1) LA:Ao and (2) LAD [14]. Aortic root diameter was measured using a right parasternal long-axis 5-chamber view at peak systole, between the hinge points of the open aortic valve. Allometric scaling was used to evaluate measurements in juvenile cats [2].

measured: 13.6 mm; left atrium-to-aortic root ratio, two-dimensional right parasternal short-axis view on the first frame after aortic valve closure, [LA:Ao] measured: 1.75) (Table 1). Pulsed wave Doppler interrogation revealed E wave and A wave reversal (E:A ratio <1) consistent with impaired ventricular relaxation. The cat was treated with oral atenolol (incrementally increased to 0.8 mg/kg twice daily) after discharge. She remained clinically well for over five months after diagnosis before developing congestive heart failure and was euthanised two weeks later in February 2015 owing to a suspected aortic thromboembolism and overall poor response to treatment (1 mg/kg of furosemide twice daily).

Case 2, a 5-month-old female entire domestic short-haired cat (1.56 kg), was presented in December 2016 for evaluation of exercise intolerance and a grade V/VI, left parasternal, systolic murmur. Echocardiography detected aortic valve thickening and leaflet fusion, aortic root hypoplasia and a poststenotic dilation visible (Fig. 1C and D). Systolic transvalvular pressure gradient was measured at 64 mmHg, consistent with a moderate aortic stenosis [1]. Colour Doppler interrogation revealed marked aortic regurgitation, and the left atrium was severely dilated (LAD: 20.3 mm, LA:Ao: 2.21; Table 1). Hypertrophy of the interventricular septum was present, but the posterior left ventricular wall was within normal limits (IVSd: 5.7 mm, LVPWd: 4.3 mm; Table 1). The ventricle appeared mildly dilated (left ventricular internal diameter in diastole: 20.0 mm; Table 1). Clopidogrel (18.75 mg per os (PO) once daily) was prescribed, and the cat discharged. Atenolol was not prescribed in this case because of the concern for congestive heart failure secondary to the negative inotropic effects of beta-blockade in the context of severe myocardial remodelling likely to reflect significant myocardial dysfunction and a risk of pulmonary oedema. During follow-up, it was found that the owner reported clinical signs consistent with congestive heart failure around six months after diagnosis. The cat was euthanised six months after diagnosis, reportedly because of the owner's reluctance to treat heart failure signs in light of a presumed poor prognosis.

Case 3, a 4-year 10-month-old male neutered Bengal cat (5.0 kg), was presented in November 2017. A diagnosis of congestive heart failure had been made three months earlier, managed with furosemide (1 mg/kg PO twice daily), clopidogrel (18.75 mg PO once daily), benazepril (0.25 mg/kg PO once daily) and spironolactone (4 mg/kg PO once daily). This had controlled his clinical signs for one month, before progressive tachypnoea and

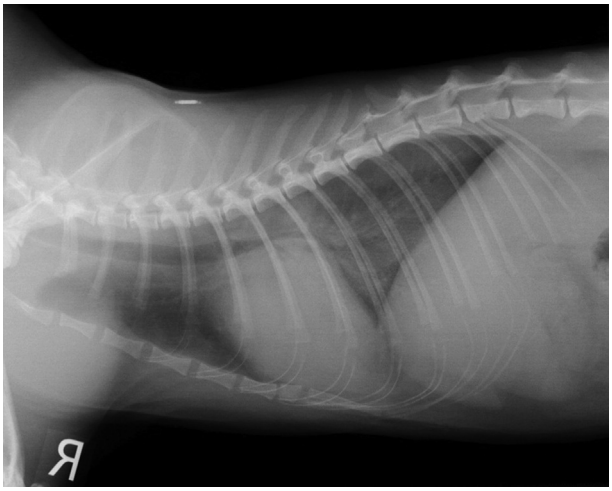

Fig. 2 Lateral thoracic radiograph from case 3, showing alveolar infiltrates, severe cardiomegaly and hepatomegaly.

lethargy were reported. On presentation, a grade V/VI, left parasternal, systolic murmur was detectable. Imaging was performed under sedation with intramuscular butorphanol (0.3 mg/kg), midazolam (0.2 mg/kg) and alfaxalone (2 mg/kg), owing to patient temperament. Thoracic radiography confirmed severe cardiomegaly (cardiac silhouette > two rib spaces wide in lateral projection) and alveolar infiltrates consistent with cardiogenic pulmonary oedema (Fig. 2). Echocardiography identified thickened, fused aortic valve leaflets with normal aortic root diameter, a poststenotic dilatation (Fig. 1E and F, Videos 1 and 2) and colour flow Doppler aliasing beginning at the level of the aortic valve (Fig. 3A). Systolic transvalvular pressure gradient was 48 mmHg despite sedation (Fig. 3B), suggesting a mild to moderate valvular stenosis [1]. Left ventricular myocardial thickness was increased (IVSd: 7.2 mm, LVPWd: 8.1 mm; Table 1), and the left atrium was also severely enlarged (LAD: 28.1 mm, LA:Ao: 3.00; Table 1) with spontaneous echo contrast visible and a possible thrombus in the left auricle (Fig. 3C). Oral furosemide treatment was increased (2 mg/kg twice daily) for the management of uncontrolled congestive heart failure. All other medications were continued at the aforementioned dose. This cat was euthanised in late October 2018, nearly one year after diagnosis because of being perceived as refractory to increasing doses of diuretics (a final diuretic dose of 2 mg/kg furosemide every 8 hours).

Discussion

Aortic stenosis is a congenital heart disease frequently reported in dogs [3], where it most commonly presents as a subvalvular ridge of fibromuscular tissue in the left ventricular outflow tract (LVOT) causing fixed stenosis and pressure overload of the left ventricle [3,4]. Valvular aortic stenosis, where the lesion is caused by valve leaflet dysplasia rather than a subaortic ridge, is less common. Subaortic stenosis is reported in 23.1%—35% of dogs with congenital heart disease, whilst valvular stenosis is much less commonly reported (2.6%—5.7% in the same studies) [3,4]. In cats with congenital heart disease, aortic stenosis is the second most common diagnosis (7.1%—18.4%) [5,6] but is less common than in dogs overall. Around half of these cases are reported to be valvular.

A retrospective study in dogs with severe subaortic stenosis (SAS) identified a median survival time to cardiac death of approximately 6.5 years [7]. To the authors' knowledge, there are no published data reporting survival times of valvular aortic stenosis in dogs, but extrapolating from SAS, survival time in the cats reported herein is markedly shorter. Sudden cardiac death has been reported at a prevalence of 21.8—36% in dogs with SAS [7,8], presumably relating to ventricular arrhythmias. In these three cats, no ventricular arrhythmias were reported. However, Holter

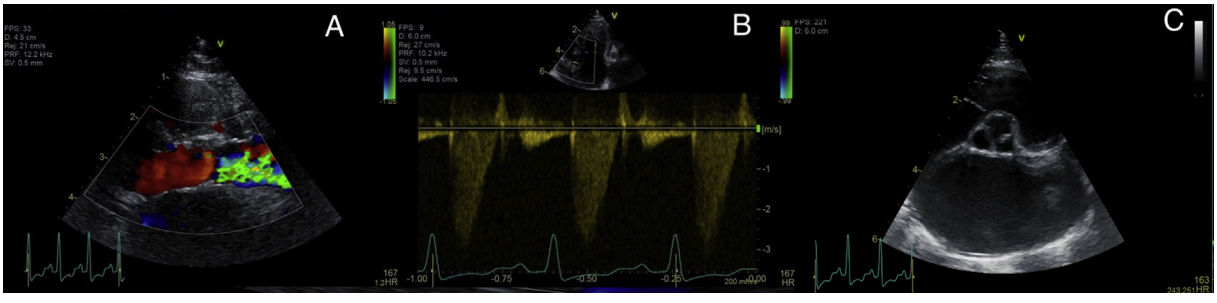

Fig. 3 (A—C): Echocardiographic images of case 3 showing aliasing of colour flow Doppler at the level of the aortic valve (A) and a continuous wave Doppler flow profile consistent with a fixed stenosis (B). Severe left atrial dilation and spontaneous echo contrast could also be seen (C).

monitoring was not performed, and therefore, they cannot be excluded. Up to 16% of dogs with SAS have been reported to develop congestive heart failure [7,8]. All three cats in this small case series presented with, or developed signs of, congestive heart failure. It is impossible to draw conclusions about the natural history of valvular aortic stenosis in cats from such a small number of cases, but perhaps heart failure is a more common complication in cats than in dogs.

Aortic endocarditis has previously been associated with the presence of subaortic stenosis in dogs [9]. However, no such association has been reported in cats [10], and from our small case series, it is impossible to evaluate this further.

There is limited information available on the clinical presentation and progression of these patients. A series of six cases of feline aortic stenosis has been reported previously, and the clinical features of the disease described [11]. The majority of the cats in this report were shown to have SAS; however, only one cat was found to have valvular aortic stenosis. This cat had thickened valve leaflets and aliasing of colour Doppler in the LVOT, with a transvalvular pressure gradient of 41 mmHg. While this was consistent with a diagnosis of valvular stenosis, a subvalvular stenosis located immediately proximal to the aortic valve leaflets could not be confidently ruled out.

This small case series describes three similar cases of valvular aortic stenosis in cats that were presented at different time points in the disease process. The first was preclinical, with mild to moderate left atrial dilation. The second and third expressed different degrees of clinical signs, ranging from exercise intolerance (case 2) to fulminant congestive heart failure (case 3). Interestingly, the cat with clinical signs of more advanced disease (case 3) was diagnosed with the least severe grade of stenosis, based on Doppler measurements of transvalvular pressure gradient. Because systolic dysfunction is likely to occur in more advanced disease [12], Doppler estimates of stenosis severity are likely to underestimate the actual disease severity in these patients. In this case, the use of sedation may also have affected the estimate of severity based on transvalvular pressure gradient [13].

There are many similarities between our cases and the one previously reported [11]. Each case was presented with a loud left-sided systolic murmur, and echocardiography demonstrated thickened aortic valve leaflets with elevated transvalvular pressure gradient and a poststenotic dilation. Notable differences included leaflet tip doming, and thus, fusion was clearly seen in all three of our reported cases, with no subaortic stenotic lesions confusing the echocardiographic picture, hence confirming our diagnosis of valvular aortic stenosis. One of our three cases was presented much older than the previous case report of potential valvular stenosis, where the cat was diagnosed at 12 weeks old, which is unusual for a congenital disease that holds strong clinical significance and is known to cause notable remodelling and clinically significant secondary effects. Based on our allometrically scaled measurements of aortic root diameter [2], the two cats diagnosed in youth and with the shorter survival time had a hypoplastic aortic root, as well as fused valve leaflets. The cat that was diagnosed at almost five years old, who was alive for nine months after diagnosis and 12 months after the onset of clinical signs, had a normal aortic root measurement. The development of clinical signs in relative youth and reduced survival time in cases 1 and 2 may be attributed to the concurrent aortic root hypoplasia. If true within the wider population, this additional measurement may guide prognosis in these cases and help clinicians to better understand the difference in age at presentation. In the absence of a postmortem histologic evaluation of the myocardium, concurrent cardiomyopathies cannot be excluded as contributing factors in case 3. It is difficult to account for the effects of acquired heart diseases and complicating factors such as aortic valve insufficiency in cases of congenital disease diagnosed in adult animals.

A difficulty in the diagnosis of feline aortic stenosis lies with the high prevalence of hypertrophic cardiomyopathy [14] and systolic anterior motion of the mitral valve (SAM). In cats with longstanding SAM or focal basilar septal hypertrophy, it may be impossible to be confident in a diagnosis of subaortic stenosis when high LVOT velocities are visualised. A fixed Doppler profile may be detectable in cats with focal septal hypertrophy in the outflow tract, and the two-dimensional appearance of the lesion might be indistinguishable from true SAS on echocardiography. The diagnosis of valvular aortic stenosis is somewhat more straightforward but could be complicated in cats with SAM, where longstanding elevation of LVOT velocities has led to jet lesions developing on the aortic valve leaflets. This could conceivably cause a thickened and hypomotile appearance. In our cases, the absence of SAM and clear evidence of leaflet fusion confirmed the diagnosis of congenital valve dysplasia. However, because of such overlap in echocardiographic appearance in some cases, practitioners might diagnose hypertrophic cardiomyopathy when aortic stenosis is present, or *vice versa*.

Whilst valvular aortic stenosis in cats is rare, it should be considered as a differential for cases

presenting with a loud, left-sided systolic heart murmur, even in adult individuals. In cats with unexplained left ventricular hypertrophy, or without SAM, attention to the aortic valve leaflets should be paid, especially during systole, and the presence of a poststenotic dilation should be evaluated. Survival times in cats with valvular aortic stenosis are variable and may be shortened in patients with aortic root hypoplasia.

Conflicts of Interest Statement

The authors have no conflict of interests to declare regarding this case report.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvc.2019.06.005.

Video table

Video 1	Right parasternal short axis view optimized for left atrium to aortic root ratio. Thickened aortic valve leaflets can be identified along with severe left atrial dilation and spontaneous echo contrast. (50% speed)
Video 2	Left cranial view optimized for the aortic valve. Fused aortic valve leaflets can be seen doming in systole and a post-stenotic dilation of the ascending aorta is present. (50% speed)

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