PREVALENCE OF VALVULAR REGURGITATIONS IN CLINICALLY HEALTHY CAPTIVE LEOPARDS AND CHEETAHS: A PROSPECTIVE STUDY FROM THE WILDLIFE CARDIOLOGY (WLC) GROUP (2008–2013)

Author(s): Norin Chai, D.V.M., M.Sc., M.Sc.V., Ph.D., Thierry Petit, D.V.M., Muriel Kohl, D.V.M., Aude Bourgeois, D.V.M., Vassiliki Gouni, D.V.M., Dipl. E.C.V.I.M. (Cardiology), Ph.D., Emilie Trehiou-Sechi, D.V.M., Charlotte Misbach, D.V.M., Ph.D., Amandine Petit, D.V.M., Cécile Damoiseaux, D.V.M., Audrey Garrigou, D.V.M., Raphaëlle Guepin, D.V.M., Jean Louis Pouchelon, D.V.M., Ph.D., and Valérie Chetboul, D.V.M., Ph.D., Dipl. E.C.V.I.M. (Cardiology)

Source: Journal of Zoo and Wildlife Medicine, 46(3):526-533.
Published By: American Association of Zoo Veterinarians
DOI: http://dx.doi.org/10.1638/2014-0155.1
URL: http://www.bioone.org/doi/full/10.1638/2014-0155.1

Journal of Zoo and Wildlife Medicine 46(3): 526–533, 2015

PREVALENCE OF VALVULAR REGURGITATIONS IN CLINICALLY HEALTHY CAPTIVE LEOPARDS AND CHEETAHS: A PROSPECTIVE STUDY FROM THE WILDLIFE CARDIOLOGY (WLC) GROUP (2008–2013)

Norin Chai, D.V.M., M.Sc., M.Sc.V., Ph.D., Thierry Petit, D.V.M., Muriel Kohl, D.V.M., Aude Bourgeois, D.V.M., Vassiliki Gouni, D.V.M., Dipl. E.C.V.I.M. (Cardiology), Ph.D., Emilie Trehiou-Sechi, D.V.M., Charlotte Misbach, D.V.M., Ph.D., Amandine Petit, D.V.M., Cécile Damoiseaux, D.V.M., Audrey Garrigou, D.V.M., Raphaëlle Guepin, D.V.M., Jean Louis Pouchelon, D.V.M., Ph.D., and Valérie Chetboul, D.V.M., Ph.D., Dipl. E.C.V.I.M. (Cardiology)

Abstract: The purpose of this prospective study was to evaluate transthoracic echocardiograms from clinically healthy large felids for the presence of valvular regurgitations (VR). Physiologic VR commonly occur in normal dogs and cats, but the percentage of large felids with VR has not been previously reported. During a 5-yr study period (2008–2013), 28 healthy animals were evaluated under general anesthesia: 16 cheetahs (*Acinonyx jubatus soemmeringuii*) with a mean age of 1.5 ± 0.8 yr (range 0.7–3.5 yr), 5 Amur leopards (*Panthera pardus orientalis*), 1 snow leopard (*Uncia uncia*), and 6 clouded leopards (*Neofelis nebulosa*). For this study, all the leopards were gathered in one so-called "leopards group" with a mean age of 2.8 ± 3.4 yr (range 0.3–10.7 yr). All valves observed in each view were examined for evidence of regurgitant jets and turbulent blood flow using the color-flow Doppler mode. Valves were also examined for structural changes. Mitral valve and aortic cusp abnormalities were considered to be of congenital origin. Mitral valve lesions led to mitral insufficiency in all the felids. Aortic cusp abnormalities led to aortic regurgitation in 94% of the cheetahs and 67% of the leopards. Leopards showed a predominance of early systolic mitral regurgitations, whereas all the mitral regurgitation jets in cheetahs were holosystolic. Tricuspid regurgitation was found in 81% of the cheetahs and in 50% of the leopards, whereas pulmonic regurgitation was detected in 44% of the cheetahs and 33% of the leopards. Interestingly, none of these tricuspid and pulmonic regurgitations were associated with two-dimensional structural valve abnormalities, thus suggesting their physiologic origin, as described in humans, cats, and dogs. In conclusion, subclinical valvular diseases are common in apparently healthy leopards and cheetahs. Longitudinal follow-up of affected animals is therefore required to assess their clinical outcome.

Key words: *Acinonyx jubatus*, congenital heart anomaly, *Neofelis nebulosi*, *Panthera pardus orientalis*, *Uncia uncia*, valvular insufficiency.

INTRODUCTION

As a result of the difficulties associated with examining and applying diagnostic tests to wild animals, little information is available about the prevalence of noninfectious diseases, particularly cardiovascular disorders, in wild large felids. Although numerous studies have been carried out on cardiac morphology and function in domestic cats (*Felis catus*), based on both noninvasive and invasive techniques,[5] literature on the normal cardiac anatomy and function of large felids is scarce. In 2008 the Cardiology Unit of Alfort (UCA, Maisons-Alfort, France), in collaboration with the Ménagerie du Jardin des Plantes (Paris, France), set up a working group (i.e., the WildLife Cardiology [WLC] group) to carry out echo-Doppler screening for heart diseases in several species of large felids. One aim of the WLC group was to characterize and report echocardiographic findings in some species of clinically healthy large felids, with the intent of providing reference values for use in cardiologic evaluations when a heart disease is suspected. Valvular regurgitations (VR), which are defined by backflow of blood through the heart valve orifices due to imperfect closure of the valves, are

From the Muséum national d'Histoire naturelle, Dpt Jardins Zoologiques et Botaniques, Ménagerie du Jardin des Plantes, 57 rue Cuvier 75005 Paris, France (Chai, Kohl, Bourgeois); Zoo de la Palmyre, 17570 Les Mathes, France (Petit T); Université Paris-Est, Ecole Nationale Vétérinaire d'Alfort, Unité de Cardiologie d'Alfort, Centre Hospitalier Universitaire Vétérinaire d'Alfort, 7 avenue du Général de Gaulle, 94704 Maisons-Alfort cedex, France (Gouni, Trehiou-Sechi, Misbach, Petit A, Damoiseaux, Garrigou, Guepin, Pouchelon, Chetboul); INSERM, U955, Equipe 03, 51 avenue du Maréchal de Lattre de Tassigny, 94010 Créteil cedex, France (Pouchelon, Chetboul). Correspondence should be directed to Dr. Chai (chai@mnhn.fr).

commonly found in normal dogs and cats.[1,15,16] However, to the best of the authors' knowledge, no study has focused on the presence of VR in normal wild felids. The purpose of this prospective imaging study was therefore to determine the prevalence of VR in clinically healthy wild large felids of various ages and species using conventional Doppler echocardiography.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of the National Museum of Natural History. Over a 5-yr period, 28 animals were evaluated: 16 cheetahs (*Acinonyx jubatus*) kept in outdoor enclosures at the Palmyre Zoo in Royan (France) and 5 Amur leopards (*Panthera pardus orientalis*), 1 snow leopard (*Uncia uncia*), and 6 clouded leopards (*Neofelis nebulosa*), all kept in outdoor and indoor enclosures at the Ménagerie du Jardin des Plantes in Paris (France). For this study, all of these leopards were gathered in a single group designated "leopards." Inclusion criteria for the study were a normal clinical history and the absence of any clinical signs apparent at a distance. All animals were fasted 12 hr before immobilization. Cheetahs were administered a combination of medetomidine (Dormilan, Axience, France; 37 μg/kg i.m.) and ketamine (Clorkétam, Vétoquinol, 93500 Pantin, France; 3.5 mg/kg i.m.) using a remote drug delivery system (Telinject France, 57230 Sturzelbronn, 75009 Paris, France). Leopards were administered a combination of medetomidine (Domitor–Zoetis Animal Health, 75014 Paris, France; 60 μg/kg i.m.) and ketamine (Clorkétam; 3–4 mg/kg i.m.) using the same remote drug delivery system. Immediately after immobilization, all animals were weighed, intubated, and, when necessary, maintained on isoflurane (Forene, Abbott, 94518 Rungis, France) and oxygen. Atipamezole (Antisedan, Janssen Santé Animale, 92130 Issy-les-Moulineaux, France; 300 μg/kg i.m.) was used as a reversal agent. All animals underwent a complete physical examination. Cardiac auscultation was performed on animals in both right and left lateral recumbency. The presence of any heart murmur (graded from 1 to 6), gallop rhythm, or arrhythmia was recorded. Heart rate, respiratory rate, rectal body temperature, and relative blood oxygen saturation were also recorded every 5 min throughout the anesthetic event. Complete transthoracic echocardiograms (ECG) were performed by the same trained observer (VC) with continuous ECG monitoring by use of an ultrasound unit (Vivid i and Vivid 7, General Electric Medical System, Waukesha, Wisconsin 53188, USA) equipped with 3S (1.5–3.5 MHz), 5S (2.0–5.0 MHz), and 7S (6S-D [2.4–8.0 MHz]) phased-array transducers and in accordance with previously published international recommendations.[19] Right-sided views included the right parasternal four- and five-chamber views to assess the mitral, tricuspid, and aortic valves and the right parasternal short-axis view at the level of the aortic valve to examine the aortic and pulmonary valves. Left-sided views included the left apical four- and five-chamber views for mitral, aortic, and also tricuspid valve examination. Regurgitation was defined as systolic (for mitral and tricuspid regurgitations) or diastolic (for aortic and pulmonary regurgitations) based on visual inspection of closure and opening of the respective valves combined with concomitant ECG tracing.

For mitral regurgitation (MR) lasting the whole systolic phase only, the left apical four-chamber view was used to semiquantitatively assess MR by measuring the maximal size of the systolic color-flow jet originating from the mitral valve and spreading into the left atrium, as previously described.[9] The images were carefully analyzed frame by frame to compute the maximal area of the regurgitant jet signal (ARJ). The left atrium area (LAA) was measured by computerized planimetry in the same frame in which the maximal ARJ had been determined. The ARJ : LAA ratio was then calculated, and MR was classified as either "mild" (ARJ : LAA $<$ 30%), "moderate" (30% $\leq$ ARJ : LAA $\leq$ 70%), or "severe" (ARJ : LAA $>$ 70%) based on values established in dogs.[9]

Aortic regurgitation (AoR), when present, was also classified according to the jet height ratio method using color M-mode from the right parasternal five-chamber view, and AoR was considered as "mild" if the jet height was $<$25% of the dimension of the left ventricular outflow tract (jet height ratio) and "moderate" or "severe" if the jet width ratio was between 25% and 59% or $\geq$60%, respectively.[3]

Color-flow Doppler examination of the right ventricular outflow tract obtained from the right parasternal short-axis view at the level of the aortic valve was used to detect diastolic pulmonary regurgitation (PR) jets, which were then classified as "trace," "mild," "medium," or "large" according to the color-flow Doppler mode classification described by Rishniw and Erb[16] in normal dogs. The peak transvalvular end-diastolic PR velocity (VdiastPR, expressed in m/sec) was also measured from the same view using continuous-

Table 1. Results of cardiac auscultation of 28 healthy large felids (i.e., 16 cheetahs and 12 leopards).

		Cheetahs (n = 16)	Leopards (n = 12)
Heart murmur prevalence		13/16 (81%)	7/12 (58%)
Heart murmur grade	Grade 1/6	4/13	1/7
	Grade 2/6	4/13	5/7
	Grade 3/6	1/13	1/7
	Grade 4/6	4/13	
Other heart murmur characteristics	Systolic left mediothoracic murmur	10/13 (77%)	1/7 (14%)
	Systolic left apical murmur	3/13 (23%)	5/7 (71%)
	Systolic right apical murmur	0/13 (0%)	1/7 (14%)

wave Doppler mode, and the modified Bernoulli equation was applied to VdiastPR to calculate the diastolic pulmonic artery-to-right ventricle pressure gradient (ΔPd PT-RV) across the pulmonic valve ($\Delta P = 4\times [\text{VdiastPR}]^2$).

A color-flow Doppler examination of the tricuspid valve was also performed using the left apical four-chamber view. When present, systolic tricuspid regurgitation (TR) was analyzed by measuring the peak systolic TR flow velocity (VsystTR) using continuous-wave Doppler mode.[12] The systolic right ventricle-to-right atrium pressure gradient (ΔPs RV-RA) across the tricuspid valve was calculated by applying the modified Bernoulli equation to the VsystTR.

All data are expressed as mean ± standard deviation. The normally distributed conventional echocardiographic variables were compared with a Student t-test. A Chi-square test was used to compare the prevalence of heart murmurs between the two felid groups. The level of significance was set at $P < 0.05$.

RESULTS

A total of 28 clinically healthy large felids were included in the study. Twelve leopards were evaluated: five Amur leopards (*Panthera pardus orientalis*), one snow leopard (*Uncia uncia*), and six clouded leopards (*Neofelis nebulosa*), with a mean age of 2.8 ± 3.4 yr (range 0.3–10.7 yr) and a mean weight of 21.7 ± 19.1 kg (range 3–46 kg). Leopards from the Ménagerie du Jardin des Plantes had no familial relationship. Ten male and six female cheetahs from the same family, with a mean age of 1.5 ± 0.8 yr (range 0.7–3.5 yr) and a mean weight of 22.5 ± 4.9 kg (range 13.5–30.5 kg), were also recruited. Anesthesia inductions were rapid and uneventful, and muscle relaxation was excellent. All animals were healthy and in excellent body condition, based on physical examination.

No gallop rhythm or cardiac arrhythmia was detected, and ECG tracings remained normal throughout all echocardiographic and Doppler examinations (cheetah heart rate = 78.8 ± 15.6 beats/min [range 53–105 beats/min], leopard heart rate = 114 ± 32.3 beats/min [range 70–180 beats/min]). A systolic heart murmur (grade 1 to 4 out of 6), usually best heard on the left sternal border, was detected in 20 out of the 28 recruited animals (71.4%), with a similar prevalence (P = 0.3) between the cheetah and leopard groups (Table 1).

A mild to severe MR was detected in all cheetahs and leopards (Fig. 1; Table 2). All of them showed irregular and thickened mitral valve leaflets associated with thickened and hyperechoic *chordae tendineae* on two-dimensional (2D) mode (Fig. 1A, B). For all cheetahs (n = 16), MR was holosystolic and the ARJ : LAA ratio could therefore be calculated (Table 2). For all leopards, MR did not last the whole systolic phase and was therefore considered to be minor. Based on the ARJ : LAA values, MR were considered mild in 6/16 cheetahs and moderate and severe in 9/16 and 1/16 cheetahs, respectively. Nevertheless, none of these holosystolic MR was associated with signs of left atrial overload (e.g., no abnormal curved form of the interatrial septum).

Mild to moderate AoR (Fig. 2) was also observed in 15 cheetahs (n = 16; 94%) and 8 leopards (n = 12; 67%). Based on the jet height ratio method (Table 3), AoR values were considered mild for all cheetahs (n = 15/15) and mild or moderate for 7/8 and 1/8 leopards, respectively (Fig. 3). All AoR values were associated with 2D structural aortic cusp abnormalities (hyperchoic and slightly irregular with small smooth nodular deformations). None of them was associated with left heart dilation.

Trace to mild PR (Fig. 4) were detected in 44% of the cheetahs (7/16) and 33% of the leopards examined (4/12), none of them being associated with any cusp structural abnormalities in 2D mode (Fig. 3). Table 4 shows the main PR Doppler characteristics as well as the VdiastPR and ΔPd

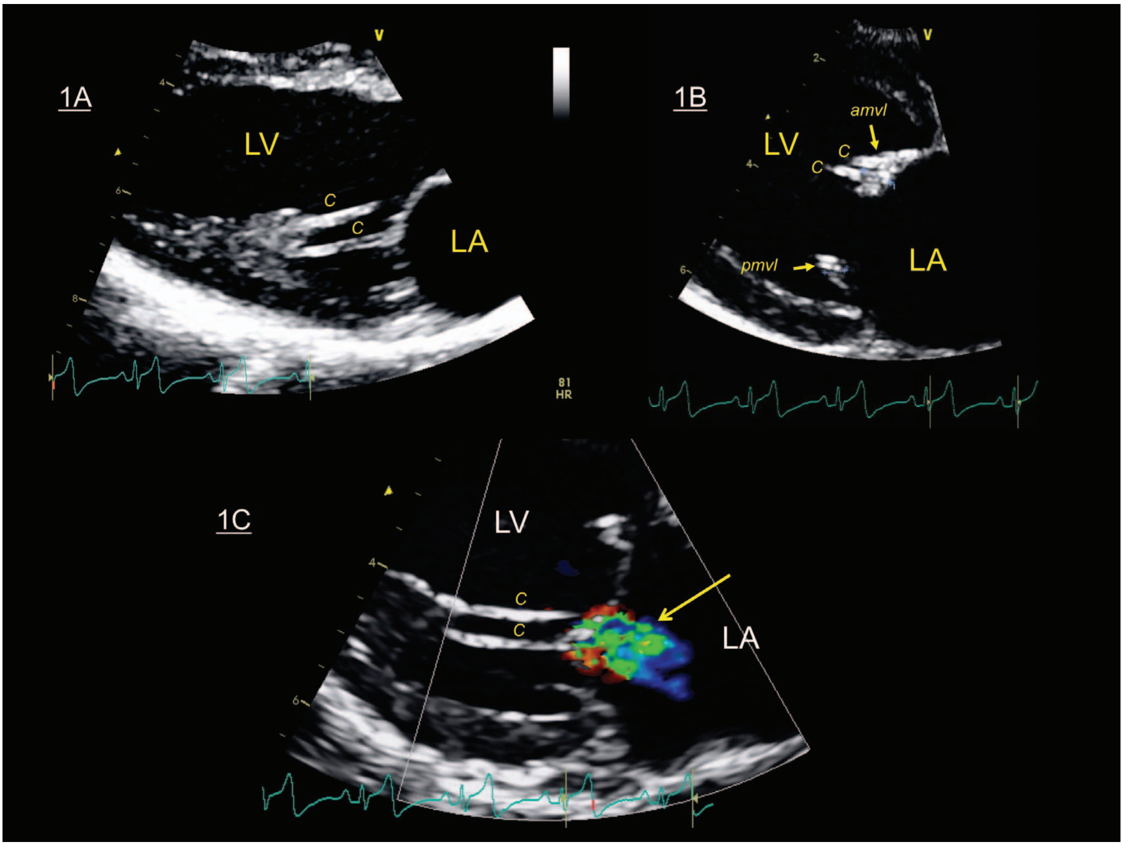

Figure 1. (**A–C**) – Two-dimensional (**A, B**) and color-flow Doppler mode (**C**) echocardiograms obtained from right parasternal long-axis views in an "apparently healthy" snow leopard (*Uncia uncia*). Mitral valve lesions are characterized by the presence of irregular and thickened mitral valve leaflets as well as thick and hyperechoic *chordae tendineae*. (**C**) The turbulent but mild end-systolic mitral regurgitation (arrow). C indicates *chordae tendineae*; amvl and pmvl, anterior and posterior mitral valve leaflets, respectively; LA, left atrium; LV, left ventricle.

PT-RV values. No significant difference between the cheetah and leopard groups ($P = 0.72$) was found for either of the latter Doppler variables.

Minor TR without any structural tricuspid valve abnormality was found in 81% of the examined cheetahs (13/16) and 50% of the leopards (6/12). The main TR Doppler characteristics, as well as the VsystTR and ΔPs RV-RA values, are presented in Table 5. No significant difference was found between the cheetah and leopard groups ($P = 0.22$ and $P = 0.28$, respectively) for the three latter variables.

No other congenital or acquired heart disease was detected.

DISCUSSION

Few studies have specifically focused on the cardiology of large felids, and most of them are case reports of congenital heart diseases or case series with only a limited number of animals.[2,4,8,13,17] The sole prospective study reporting normal cardiac morphology and function in big cats was carried out by Schumacher et al.[18] in eight captive cheetahs using radiographic and electrocardiographic evaluation. Echocardiographic and Doppler data from healthy large felids were therefore lacking, which led us to undertake the present prospective study on a large captive big cat population ($n = 28$) composed of two distinct zoological collections (i.e., one group of cheetahs and one group of leopards) during a 5-yr study period.

Valvular regurgitations were detected in each large felid included in the study (from one to three affected valves per animal). Assessment of the prevalence of a condition depends on the sensitivity and specificity of the diagnostic test used.[16] In the present study, all the standard 2D right and left parasternal echocardiographic views com-

Table 2. Mitral regurgitation characteristics assessed by color-flow Doppler mode in 28 healthy large felids (i.e., 16 cheetahs and 12 leopards). The maximum area of the regurgitant jet (ARJ), the left atrium area (LAA), and the ARJ : LAA ratio (expressed as mean ± SD [range]) were only calculated for mitral regurgitation lasting the whole systolic phase. NA indicates not applicable.

		Cheetahs (n = 16)	Leopards (n = 12)
Mitral regurgitation prevalence		16/16 (100%)	12/12 (100%)
Mitral regurgitation duration	Early systole	0/16 (0%)	9/12 (75%)
	Mid-systole	0/16 (0%)	3/12 (25%)
	Whole systole	16/16 (100%)	0/12 (0%)
Semiquantification of holosystolic mitral regurgitations	ARJ (mm^2)	284 ± 174 [100–660]	NA
	LAA (mm^2)	734 ± 131 [420–976]	NA
	ARJ : LAA ratio (%)	37 ± 20 [13–86]	NA

monly recommended for detecting physiologic or pathologic valvular regurgitations in small domestic animals were performed on all the recruited felids.[1,3,16,19] Additionally, the color-flow Doppler mode, which is the most sensitive means with which to detect even trivial regurgitant jets, as compared with the spectral Doppler modes, was systematically applied to these 2D echocardiographic views to investigate the four cardiac valves.[3] These thorough and standardized echocardiographic examinations certainly contributed greatly to the high prevalence of VR detected in both the cheetah and leopard groups in this study.

Valvular regurgitation can be considered as physiologic if the corresponding valve appears structurally normal by 2D echocardiography. According to this definition, physiologic right cardiac VR (PR and TR) have been shown to be very common in humans, affecting up to 90% of healthy subjects.[14] Physiologic TR (associated with small regurgitant jet areas) is also very common in normal purebred and mixed-breed domestic cats (*Felis catus*) of various ages: in a prospective study involving 58 cats,[1] a physiologic TR was detected in 71% of cases (versus only 2% for physiologic PR). Similarly, physiologic PR has been shown to be very common in the canine

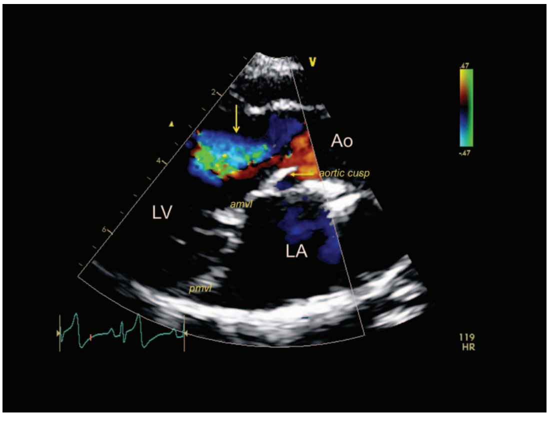

Figure 2. Color-flow Doppler mode echocardiogram obtained from the right parasternal five-chamber view in an "apparently healthy" snow leopard (*Uncia uncia*). A moderate turbulent early-diastolic aortic regurgitation is observed extending to the tips of the mitral valve leaflets (arrow). Note also the hyperechoic and slightly thickened left aortic cusp as well as the irregular and thickened mitral valve leaflets. Ao indicates aorta; amvl and pmvl, anterior and posterior mitral valve leaflets, respectively; LA, left atrium; LV, left ventricle.

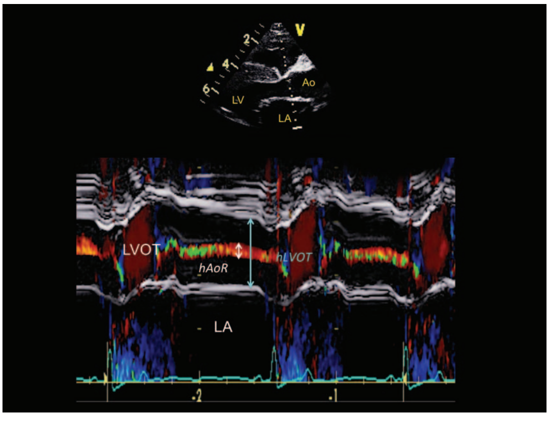

Figure 3. Color M-mode echocardiogram obtained from the right parasternal five-chamber view in an "apparently healthy" cheetah (*Acinonyx jubatus*). An aortic regurgitation (AoR) is present during the whole diastolic phase, and its color-coded height (hAoR, short double arrow) can be measured to calculate the jet height ratio (i.e., hAoR divided by the left ventricular outflow tract height [hLVOT, long double arrow]). The jet height ratio value is 24%, thus confirming a moderate AoR. Ao indicates aorta; LA, left atrium; LV, left ventricle.

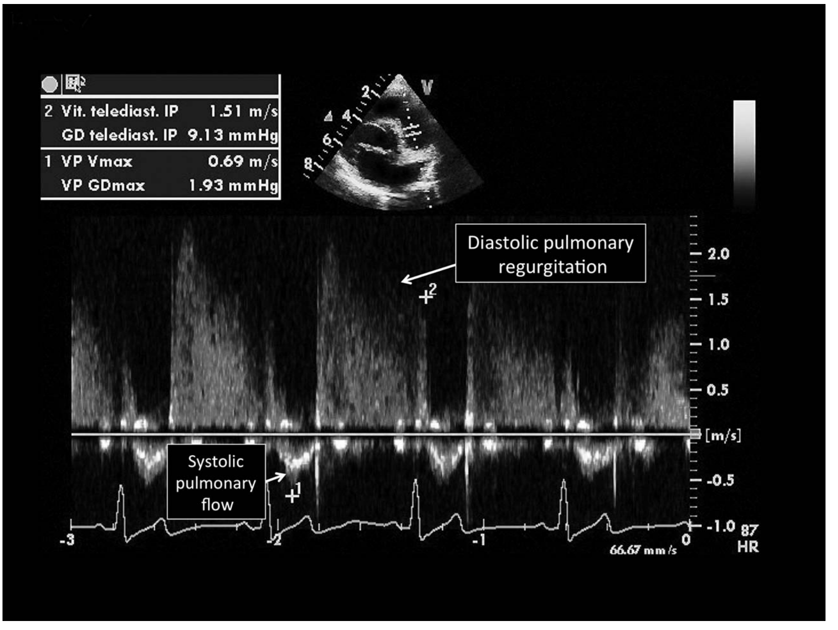

Figure 4. Continuous-wave Doppler trace of pulmonary flow recorded from the right parasternal short axis view at the level of the aortic valve in an "apparently healthy" cheetah (*Acinonyx jubatus*) showing a normal systolic pulmonary flow and a diastolic pulmonary regurgitation. The peak end-diastolic pulmonary regurgitation velocity was measured (1.51 m/sec) to further assess the end-diastolic pulmonic artery-to-right ventricle pressure gradient using the modified Bernoulli equation (9 mm Hg).

species, with more than 90% of healthy adult dogs of various ages and breeds having trace or mild PR, detectable by color Doppler echocardiography.[16] In the present study, both TR and PR were common findings in both the cheetah and leopard groups, affecting 68% and 39% of the whole study population, respectively, with no evidence of structural valve abnormality or right heart disease. These regurgitations were therefore considered to be physiologic and can thus be considered to represent normal echocardiographic findings in large felids. The prevalence of physiologic TR was similar to that described in healthy domestic cats (68% versus 71%), whereas physiologic PR was higher (39% versus 2%), with no rational explanation for this discrepancy.

Unlike PR and TR, both MR and AoR were always associated with 2D structural valve abnormalities. As such morphologic alterations were similarly observed in adult and very young animals (<1 yr old), the main hypothesis for these valvular lesions remains a congenital origin with a genetic basis (i.e., mitral and aortic valve dysplasia), although degenerative valvular disease cannot be excluded. However, as none of these VR was associated with left heart dilation, they were

Table 3. Aortic regurgitation prevalence and characteristics (duration and severity) assessed from the jet height ratio in 28 healthy large felids (i.e., 16 cheetahs and 12 leopards). The color jet height of each aortic regurgitation (hAoR) and the left ventricular outflow tract height (hLVOT) were both measured using color M-mode from the right parasternal five-chamber view, and the jet height ratio (defined by hAoR : hLVOT) was then calculated. Values are expressed as mean ± SD [range].

		Cheetahs (n = 16)	Leopards (n = 12)
Aortic regurgitation prevalence		15/16 (94%)	8/12 (66.6%)
Aortic regurgitation duration	Early diastole	3/15 (20%)	7/8 (87.5%)
	Mid-diastole	0/15 (0%)	1/8 (12.5%)
	Whole diastole	12/15 (80%)	0/8 (0%)
Semiquantification of aortic regurgitations	hAoR (mm)	2.8 ± 1.1 [1–5]	4.7 ± 3.5 [2.1–9.5]
	hLVOT (mm)	18.5 ± 2.1 [15–23]	16.2 ± 7.5 [10.3–26]
	hAoR : hLVOT (%)	15 ± 6 [5–24]	28 ± 16 [19–52]

Table 4. Pulmonary regurgitation prevalence and characteristics (severity, peak transvalvular end-diastolic velocity, and corresponding pressure gradient) in 28 healthy large felids (i.e., 16 cheetahs and 12 leopards). VdiastPR indicates peak end-diastolic pulmonic regurgitation velocity (m/sec); ΔPd PT-RV, diastolic pulmonic artery-to-right ventricle pressure gradient across the pulmonic valve (mm Hg). Values are expressed as mean ± SD [range]. Regurgitation severity was assessed according to previously published color Doppler mode criteria.[16]

		Cheetahs (n = 16)	Leopards (n = 12)
Pulmonary regurgitation prevalence		7/16 (44%)	4/12 (33%)
Pulmonary regurgitation severity	Trace	1/7	0/4
	Mild	6/7	4/4
	Medium	0/7	0/4
	Large	0/7	0/4
End-diastolic pulmonary regurgitation variables	VdiastPR (m/sec)	1.2 ± 0.5 [0.4–1.7]	1.5 ± 0.3 [0.9–1.6]
	ΔPd PT-RV (mm Hg)	6.2 ± 4.4 [0.6–11.6]	8.8 ± 3.3 [3.2–10.2]

therefore considered benign. Additionally, MR could be considered as trivial for most leopards, as MR was only detected just after mitral valve closure in three-quarters of them. Conversely, all cheetahs showed a holosystolic MR allowing calculation of the ARJ : LAA ratio. These MR could explain the left systolic heart murmurs detected in 13 of the 16 cheetahs (81%) and in 6 of the 12 leopards. However, such murmurs were not detected in the remaining animals with MR (three cheetahs and six leopards), thereby emphasizing the limitation of cardiac auscultation, which is not sensitive enough to detect all MR in large felids. Such a limitation has already been demonstrated in small animals. For example, in one study[6] involving Cavalier King Charles spaniels, up to 25% of dogs with degenerative mitral valve disease did not have any detectable heart murmur on cardiac auscultation.

This study presents several limitations, mainly because all of the echocardiographic and Doppler examinations were done under anesthesia. The anesthetic regimen and the effects of anesthetic agents on cardiac function should always be considered when obtaining cardiac measurements, as anesthesia can alter circulatory hemodynamics, heart rate, myocardial contractility, and also cardiac dimensions.[7,10,11] These effects can potentially change the pressure gradients across the cardiac valves, thus contributing to influence on the regurgitant jet signals and peak velocities. Additionally, because both adult and nonadult animals from different species were recruited in the present study, both felid groups were characterized by a wide range of ages and body weights. As the impact of age and size with regard to VR still remains unknown in these species, this represents another limitation of the present study. Further prospective studies including large numbers of felids of a given species, with a longitudinal echocardiographic follow-up, are therefore needed to accurately assess the influence of age on the prevalence and severity of VR and their potential impact on the lifespan of the affected animals.

CONCLUSION

This study provides original data regarding the comparative echocardiographic and Doppler features of cheetahs and leopards, showing that both valvular diseases and physiologic VR are common in clinically healthy big cats. Longitudinal follow-up of affected animals is therefore required to assess their clinical outcome. Further studies are also needed to determine the prevalence and

Table 5. Tricuspid regurgitation prevalence and characteristics (duration, peak systolic velocity, and corresponding pressure gradient) in 28 healthy large felids (i.e., 16 cheetahs and 12 leopards). VsystPR indicates peak systolic tricuspid regurgitation velocity (m/sec); ΔPs RV-RA, peak systolic right-ventricle-to-right-atrium pressure gradient across the tricuspid valve (mm Hg).

		Cheetahs (n = 16)	Leopards (n = 12)
Tricuspid regurgitation prevalence		13/16 (81%)	6/12 (50%)
Tricuspid regurgitation duration	Early systole	0/13	0/6
	Mid-systole	0/13	0/6
	Whole systole	13/13	6/6
Peak tricuspid regurgitation variables	VsystTR (m/sec)	2 ± 0.4 [1.1–2.5]	1.6 ± 0.5 [0.9–2.3]
	ΔPs RV-RA (mm Hg)	16.8 ± 5.5 [4.8–25]	11.5 ± 6.4 [3.2–21.2]

severity of such VR in free-ranging animals. Lastly, the current findings suggest that cardiac evaluation is important in the overall health evaluation of captive large felids and may aid in the management as well as the preservation of captive populations.

Acknowledgments: This study was supported by the "Fondation Un Coeur" (Foundation under the aegis of the "Fondation de France") and the Association Yaboumba.

LITERATURE CITED

1. Adin DB, McCloy K. Physiologic valve regurgitation in normal cats. J Vet Cardiol. 2005;7:9–13.

2. Barnes J, Gerlis L, Cunningham A. Preductal aortic coarctation and patent ductus arteriosus in a Sumatran Tiger (*Panthera tigris sumatrae*) cub. J Zoo Wildl Med. 2001;32:111–114.

3. Boon JA. Acquired valvular disease. In: Boon JA (ed.). Manual of veterinary echocardiography. 2nd ed. Baltimore (MD): Wiley-Blackwell; 2011. p. 267–335.

4. Chai N, Behr L, Chetboul V, Pouchelon J-L, Wedlarski R, Trehiou-Sechi E, Gouni V, Misbach C, Petit A, Bourgeois A, Hazan T, Borenstein N. Successful treatment of a congenital pulmonic valvular stenosis in a snow leopard (*Uncia uncia*) by percutaneous balloon valvuloplasty. J Zoo Wildl Med. 2010;41: 735–738.

5. Chetboul V. Advanced techniques in echocardiography in small animals. Vet Clin North Am Small Anim Pract. 2010;40:529–543.

6. Chetboul V, Tissier R, Villaret F, Nicolle A, Dean E, Benalloul T, Pouchelon J-L. Epidemiological, clinical, echo-Doppler characteristics of mitral valve endocardiosis in Cavalier King Charles in France: a retrospective study of 451 cases (1995 to 2003). Can Vet J. 2004;45:1012–1015.

7. Clanachan AS, McGrath JC, MacKenzie JE. Cardiovascular effects of ketamine in the pithed rat, rabbit and cat. Br J Anaesth. 1976;48:935–939.

8. Douay G, Drut A, Ribas T, Gomis D, Graille M, Lemberger K, Bublot I. Patent ductus arteriosus in an adult Amur leopard (*Panthera pardus orientalis*). J Zoo Wildl Med. 2013;44:200–203.

9. Gouni V, Serres FJ, Pouchelon J-L, Tissier R, Lefebvre HP, Nicolle AP, Carlos Sampedrano C, Chetboul V. Quantification of mitral valve regurgitation in dogs with degenerative mitral valve disease by use of the proximal isovelocity surface area method. J Am Vet Med Assoc. 2007;231:399–406.

10. Hall JA, Watrous BJ. Effect of pharmaceuticals on radiographic appearance of selected examinations of the abdomen and thorax. Vet Clin North Am Small Anim Pract. 2000;30:349–377.

11. Jacobs G, Knight DH. Change in M-mode echocardiographic values in cats given ketamine. Am J Vet Res. 1985;46:1712–1713.

12. Kittleson MD, Kienle RD. Pulmonary arterial and systemic arterial hypertension. In: Kittleson MD, Kienle RD (eds.). Small animal cardiovascular medicine. St. Louis (MO): Mosby; 1998. p. 433–449.

13. Krediet P, Zwart P. Congenital anomalies of the heart and the arterial trunks in lion cubs. Tijdschr Diergeneeskd. 1964;89:32–45.

14. Maciel BC, Simpson IA, Valdes-Cruz LM, Recusani F, Hoit B, Dalton N, Weintraub R, Sahn DJ. Color flow Doppler mapping studies of "physiologic" pulmonary and tricuspid regurgitation: evidence for true regurgitation as opposed to a valve closing volume. J Am Soc Echocardiogr. 1991;4:589–597.

15. Nakayama T, Wakao Y, Takiguchi S, Uechi M, Tanaka K, Takahashi M. Prevalence of valvular regurgitation in normal beagle dogs detected by color Doppler echocardiography. J Vet Med Sci. 1994;56: 973–975.

16. Rishniw M, Erb HN. Prevalence and characterization of pulmonary regurgitation in normal adult dogs. J Vet Cardiol. 2000;2:17–21.

17. Roelke M, Martenson J, O'Brien S. The consequences of demographic reduction and genetic depletion in the endangered Florida panther. Curr Biol. 1993;3:340–350.

18. Schumacher J, Snyder P, Citino SB, Bennett RA, Dvorak LD. Radiographic and electrocardiographic evaluation of cardiac morphology and function in captive cheetahs (*Acinonyx jubatus*). J Zoo Wildl Med. 2003;34:357–363.

19. Thomas WP, Gaber CE, Jacobs GJ, Kaplan PM, Lombard CW, Moise NS, Moses BL. Recommendations for standards in transthoracic two-dimensional echocardiography in the dog and cat. Echocardiography Committee of the Specialty of Cardiology, American College of Veterinary Internal Medicine. J Vet Intern Med. 1993;7:247–252.

Received for publication 8 June 2015