Journal of Feline Medicine and Surgery (2011) **13**, 266–271
doi:10.1016/j.jfms.2010.12.007

ELSEVIER

jfms

Prevalence of echocardiographic evidence of cardiac disease in apparently healthy cats with murmurs☆

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The objective of this prospective study was to determine the prevalence of echocardiographic evidence of heart disease in apparently healthy cats with heart murmurs. Thirty-two privately owned domestic cats were examined. All cats were considered healthy on the basis of history and physical examination, except for the finding of a heart murmur on auscultation. Cats on any medications (besides regular flea, tick and heartworm preventative) or that were pregnant or lactating were excluded from this study. The prevalence of echocardiographic evidence of heart disease in this population of cats was 53%. Therefore, identification of a heart murmur on routine physical examination in apparently healthy cats warrants further investigation.

Date accepted: 2 December 2010

Heart murmurs in apparently healthy adult cats present a dilemma to clinicians. While murmurs can be associated with cardiac disease, most commonly hypertrophic cardiomyopathy (HCM), studies have identified benign causes of murmurs in cats.[1–3] Differentiation of causes of feline cardiac murmurs is difficult by auscultation alone without additional diagnostics. Feline murmurs can be inducible (apparent only upon physical provocation, usually stress, fear or pain) or non-inducible (continuously present).[2,3] Previous studies have reported a murmur prevalence of 21–44% in overtly healthy cats.[1–3] One study determined that 15.5% of apparently healthy cats had non-inducible heart murmurs and approximately one-third of these cats were determined to have cardiac disease.[2] An additional 12% of cats in this study had inducible murmurs and several of these cats also had cardiac disease. A second study found even higher percentages of inducible (26%) and non-inducible (18%) murmurs in 100 apparently healthy cats, with 14/100 cats having cardiac disease (71% of these had murmurs).[3] Therefore, a high percentage of cats with murmurs, particularly inducible murmurs, appear to have no evidence of structural heart disease. We sought to further characterize the prevalence of heart disease and murmur etiology in apparently healthy adult cats presenting to a referral practice for evaluation of a murmur.

Materials and methods

Study design

We prospectively recruited apparently healthy cats that were presented to the Red Bank Veterinary Hospital (RBVH) cardiology service for evaluation of a murmur between March 24, 2005 and January 25, 2007. We included cats if they had no history of vomiting, diarrhea, cough, polyuria, polydipsia, or weight loss in the 4 weeks prior to evaluation. Cats had to demonstrate a heart murmur on physical examination, and could not be receiving any medications besides routine flea, tick, and/or heartworm preventative. Cats with a previous diagnosis of cardiac disease or systemic illness such as inflammatory bowel disease, hyperthyroidism, renal disease, systemic hypertension, or diabetes mellitus were excluded. All cats

☆All work for this study was undertaken at the Red Bank Veterinary Hospital.
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1098-612X/11/040266+06 $36.00/0

underwent a clinical evaluation consisting of a physical examination, packed cell volume (PCV) and total solids (TS), and echocardiogram. A complete blood count (CBC), serum chemistry profile, thyroid evaluation and systolic blood pressure were obtained from some cats at the discretion of the attending clinician. Systolic blood pressure measurement was performed in a quiet cardiology room and systolic arterial blood pressure was estimated for cats by use of the Doppler cuff-flow method as previously described.[4,5] Three consecutive measurements were performed on either the left or right forelimb and the measurement averaged.[5] Cats with serum thyroxine concentration that exceeded the upper limit of the laboratory reference interval were considered to be hyperthyroid and excluded from the study as well. All physical and echocardiographic examinations were performed by a board-certified cardiologist (CDS) or a cardiology resident (MK) with review by a cardiologist (CDS).

Echocardiography

Standard echocardiographic examinations were performed without chemical restraint using a Vivid 7 (Vingmed System 7, General Electric Medical Systems, Waukesha, Wis) echocardiograph coupled to a 10 MHz transducer.[6] We obtained both two-dimensional and M-mode measurements of the left atrium and ventricle from right parasternal short-axis and long-axis views. M-mode measurements included the interventricular septal thickness at end diastole and end systole (IVS_d and IVS_s, respectively), left ventricular internal dimension at end diastole and end systole ($LVID_d$ and $LVID_s$, respectively), left ventricular posterior wall thickness at end diastole and end systole ($LVPW_d$ and $LVPW_s$, respectively), left atrial dimension at end systole (LAD_s) and aortic root dimension (Ao). Two-dimensional measurements included IVS_d, AO, $LVID_d$, LA (short-axis and long-axis), $LVPW_d$. All valves and ventricular outflow tracts were examined with spectral and color Doppler. The percentage of fractional shortening (%FS) was derived using the equation $[(LVID_d - LVID_s)/(LVID_d \times 100)]$. The left atrium-to-aortic root ratio (LA:Ao) was calculated[7] and left atrial enlargement was defined as a LA:Ao ratio >1.54.[8] Systolic anterior motion of the mitral valve (SAM) was identified when mitral leaflet tissue was displaced dorsocranially during systole and spanned at least 50% of the distance from the region of leaflet coaptation to the IVS.[9] Papillary muscles were subjectively assessed as normal or enlarged and the endomyocardium was evaluated to be normal, abnormal with focal thickening or demonstrating increased echogenicity. Left ventricular concentric hypertrophy (LVCH) was defined by an end-diastolic wall thickness ≥6 mm in any region of the IVS or LVPW.[10] Dynamic right ventricular outflow tract obstruction (DRVOTO) was noted if there was a systolic jet that originated proximal to the pulmonary valve and had spectral Doppler echocardiographic characteristics that indicated late-systolic acceleration.[11] Dynamic left ventricular outflow tract obstruction (DLVOTO) was similarly defined by late-systolic acceleration.[2] An elevated aortic velocity was differentiated from DLVOTO based on normal pulsed-wave Doppler velocities within the left ventricular outflow tract but an increased velocity beyond the aortic valve and no evidence of late-systolic acceleration on spectral Doppler.

Statistical analysis

We performed descriptive statistics where appropriate.

Results

We identified 32 cats with murmurs that were eligible for inclusion. The breeds represented were domestic shorthair ($n = 18$), domestic longhair ($n = 6$), Persian ($n = 3$), Siberian ($n = 1$), Norwegian Forest Cat ($n = 1$), Japanese Bobtail ($n = 1$), Ragdoll ($n = 1$), and domestic medium hair ($n = 1$). Median weight was 5.05 kg (range 2.91−9.00 kg). Sixteen cats were castrated males, 12 were spayed females, three were intact males, and one was an intact female. Median age was 66.5 months (range 5−168 months). Median PCV was 41% (range 20−58%) and median TS were 7.5 g/dl (range 6.0−8.4 g/dl). A CBC and a serum chemistry profile were performed on 11 cats and blood work was unremarkable in all 11 cats. Only one cat demonstrated a low PCV (PCV = 20%), but this cat had a normal CBC and serum chemistry profile with a hematocrit of 41% and thus the low PCV was assessed as a laboratory error. Doppler blood pressure measurements were performed in 15/32 cats, including 11/17 cats eventually diagnosed with heart disease and in all cats the mean systolic blood pressure was less than 180 mm Hg. Thyroid panels were performed on 2/17 cats diagnosed with heart disease and results of both were within normal limits.

Fifteen of the 32 cats (47%) had no identifiable echocardiographic evidence of cardiac disease (Table 1). The etiology of the murmur was identified in 5/15 of these cats (Table 2): 2/5 cats had DRVOTO; 1/5 cats had both DRVOTO and DLVOTO (velocity = 3 m/s); 2/5 cats had DLVOTO (velocity = 1.99 m/s and 2.9 m/s). In 10/15 cats, we could not identify a murmur etiology.

Seventeen of the 32 cats (53%) had echocardiographic evidence of heart disease (Table 3). Twelve of the 17 cats had LVCH; 6/12 also had papillary muscle enlargement and 3/12 cats had focal endomyocardial thickening. Five of the 12 cats demonstrated DLVOTO and 3/12 cats had SAM. Only 1/12 cats with LVCH had mild left atrial enlargement (LA:Ao = 1.6).

In 3/17 cats, the only abnormalities identified were mild left ventricular changes: one cat demonstrated papillary muscle enlargement only, while two cats had focal endomyocardial thickening.

Table 1. Characteristics of 15 normal cats with heart murmurs.

Cat number	Comments	Murmur cause
1	WNL	Unknown
2	WNL	Unknown
3	WNL	Unknown
4	WNL	Unknown
5	DRVOTO present	DRVOTO
6	WNL	Unknown
7	WNL	Unknown
8	Aov = 1.9–2.9 m/s DLVOTO present SAM present	Aov = 1.9–2.9 m/s DLVOTO
9	Aov = 1.99 m/s	Aov = 1.99 m/s
10	DRVOTO present	DRVOTO
11	WNL	WNL
12	Aov = 3.0 m/s DLVOTO present DRVOTO present SAM present	Aov = 3.0 m/s DLVOTO DRVOTO
13	WNL	Unknown
14	WNL	Unknown
15	WNL	Unknown

WNL = within normal limits, DLVOTO = dynamic left ventricular outflow tract obstruction, DRVOTO = dynamic right ventricular outflow tract obstruction, SAM = systolic anterior motion of the mitral valve, Aov = aortic velocity.Additional notes: Cat 7: Echocardiogram was repeated 1 year later; no evidence of disease.Cat 8: Echocardiogram was repeated 4 years later; no evidence of disease was found.Cat 9: Echocardiogram repeated 2 and 4 years later; no evidence of disease was found.Cat 12: At a follow-up phone conversation 4 years after the initial echocardiogram, the owner reported no clinical signs of cardiovascular disease.

Table 2. Summary of murmur causes in 32 apparently healthy cats.

In 15 cats with no echocardiographic evidence of heart disease:
- 10 cats: Unknown
- Two cats: DRVOTO present
- One cat: Elevated Aov
- One cat: Elevated Aov and DLVOTO
- One cat: Elevated Aov, DLVOTO and DRVOTO

In 17 cats with echocardiographic evidence of heart disease:
- Six cats: Unknown
- Five cats: Elevated Aov and DLVOTO present
- Two cats: DRVOTO present
- Two cats: Elevated Aov
- One cat: Mitral valve disease
- One cat: Mitral valve disease, DRVOTO, DLVOTO

DRVOTO = dynamic right ventricular outflow tract obstruction, DLVOTO = dynamic left ventricular outflow tract obstruction, Aov = aortic velocity.

Two of the 17 cats had mild degenerative mitral valve disease with mitral regurgitation. The left atrium was normal in size in both cats.

The etiology of the murmur was identified in 11/17 cats with echocardiographic evidence of heart disease (Table 3): 5/11 cats had elevated aortic velocities and DLVOTO, 2/11 had DRVOTO only, 2/11 had elevated aortic velocities only, 1/11 cats had mitral valve disease and 1/11 cats had mitral valve disease, DRVOTO and DLVOTO. We could not identify the etiology of the murmur in 6/17 cats with echocardiographic evidence of heart disease.

Discussion

We found that 53% of apparently healthy cats presenting to a cardiology service in a referral setting for evaluation of a heart murmur had echocardiographic evidence of cardiac disease. Most of these cats had LVCH with a small minority identified with degenerative mitral valve disease. Based on the high likelihood of underlying heart disease, auscultation of a heart murmur in apparently healthy cats warrants further evaluation.

Our findings are similar to those of previous investigators, although the proportion of cats with heart disease was greater in our study than prior studies.[1–3] One possible explanation is the manner in which cases were recruited in the previous and current studies – prior investigators examined 100 random apparently healthy cats, whereas we recruited apparently healthy cats in which murmurs were identified. Furthermore our exclusion criteria might have differed, resulting in exclusion of some cats with non-pathological murmurs.

All of the cats with identifiable structural heart disease in our study had mild disease, demonstrated by a normal, or mildly enlarged left atrium, and modest increases in LV wall thickness (in cases of LVCH). This is somewhat unexpected, given that a range of subclinical disease might be anticipated in a random feline population, and likely reflects the relatively small sample population of this study. Thus, clinicians should not be encouraged by this observation, as cats presenting with murmurs may harbor substantially more severe subclinical disease.

We did not evaluate papillary muscles morphometrically when making assessments about papillary muscle hypertrophy, as the technique had not yet been described at the time of data collection.[12] Only one cat in our study showed subjective evidence of isolated papillary muscle hypertrophy.

Cats frequently develop heart murmurs with structural heart disease.[13–15] However, our study and previous studies clearly demonstrate that apparently healthy cats with heart murmurs often have no underlying structural heart disease.[1–3] Furthermore, cats can develop murmurs with systemic conditions such as volume depletion, anemia, volume overload, or

Table 3. Characteristics of echocardiographic abnormalities of 17 apparently healthy cats with heart murmurs.

Cat #	Predominant cardiac change	Other abnormalities present	Murmur cause
1	Focally thickened Endomyocardium	DRVOTO	DRVOTO
2*	Papillary muscle enlargement	SAM present Aov = 2.0 m/s	Aov = 2.0 m/s
3	Focally thickened endomyocardium	DRVOTO present	DRVOTO
4	LVCH	None	Unknown
5	LVCH	Aov = 2.4 m/s DLVOTO present SAM present Enlargement of papillary muscles	Aov = 2.4 m/s DLVOTO
6	LVCH	LA:Ao = 1.6 Aov = 2.5 m/s DLVOTO present Enlargement of papillary muscles Focally thickened endomyocardium	Aov = 2.5 m/s DLVOTO
7	LVCH	Focally thickened endomyocardium	Unknown
8	LVCH	Aov = 2.0 m/s DLVOTO present	Aov = 2.0 m/s DLVOTO
9	LVCH	Aov = 2.5 m/s DLVOTO present SAM present Enlargement of papillary muscles	Aov = 2.5 m/s DLVOTO
10	LVCH	Enlargement of papillary muscles	Unknown
11	LVCH	Aov = 2.3 m/s DLVOTO present SAM present Enlargement of papillary muscles	Aov = 2.3 m/s DLVOTO
12	LVCH	No other abnormalities identified	Unknown
13	LVCH	Aov = 2.0 m/s Enlargement of papillary muscles	Aov = 2.0 m/s
14	Mitral valve disease	RVOTv = 2.0 m/s DRVOTO present DLVOTO present Enlargement of papillary muscles	Mitral valve disease DRVOTO DLVOTO
15	LVCH	SAM present Focally thickened endomyocardium	Unknown
16	LVCH	No other abnormalities identified	Unknown
17	Mitral valve disease	No other abnormalities identified	Mitral valve disease

Aov = aortic velocity, DRVOTO = dynamic right ventricular outflow tract obstruction, DLVOTO = dynamic left ventricular outflow tract obstruction, LVCH = left ventricular concentric hypertrophy, SAM = systolic anterior motion of the mitral valve, RVOTv = right ventricular outflow tract velocity.
*Cat 2 had an echocardiogram repeated 6 months after initial examination and showed DLVOTO but other disease unchanged.

fever.[14,15] While we required cats to be healthy on the basis of history and physical examination for inclusion, cats with systemic illness cannot be presumed to have a murmur secondary to that illness and should receive additional testing to rule out cardiac co-morbidities.

Two-thirds of the cats (10/15) in our study without echocardiographic evidence of cardiac disease had no identifiable flow disturbance to explain the murmur. This is substantially greater than that reported in humans, where approximately 20% of humans were found to have no identifiable cause of a murmur on cardiovascular examination,[16,17] and previous reports in cats, where investigators estimated that up to 20% of cats presenting for murmur evaluation had no echocardiographically identifiable etiology.[11,18] Furthermore, we found one-third of cats (6/17) with echocardiographically identifiable structural heart disease had no identifiable flow disturbance to

account for the murmur. The reason for the high proportion (50%) of cats in which murmurs were auscultated, but not echocardiographically characterized in our study, is somewhat perplexing. These results are unlikely the consequence of inappropriate probe selection, frame rate or echocardiographic interrogation, although prior investigators suggested that abnormal flows can be missed if either of these conditions are not met.[11] Furthermore, cardiologists have observed localized flow disturbances within ventricular regions that could be missed with standard imaging techniques that failed to specifically interrogate these locations (eg, placing the color Doppler gate over the apical or mid-ventricular region of the LV). A more plausible explanation, however, is that many feline murmurs are dynamic or inducible. We did not employ any maneuvers (eg, tail pinching, running a faucet, bringing a dog into the exam room) to provoke cats during the echocardiographic examination to deliberately induce a murmur by increasing sympathetic tone.[2,3] Therefore, it is possible that many inducible murmurs, detectable during a more stressful physical examination, might subside during the echocardiographic evaluation as the patient relaxes, resulting in a 'false negative' finding. Our findings mirror those of Drourr et al, who failed to identify flow disturbances to account for murmurs in 35/44 (79%) apparently healthy cats presenting with murmurs to a cardiology referral service, and who, like us, did not attempt to induce murmurs during the examination.[3] Thus, clinicians should be aware of the very real possibility that murmur etiology might remain undetermined even after echocardiographic evaluation by a veterinary cardiologist.

The majority of cats with echocardiographic evidence of heart disease underwent non-invasive blood pressure measurement to rule out hypertensive cardiac hypertrophy. However, some cats did not have blood pressure measured; therefore, occult hypertension could have caused the development of left ventricular hypertrophy noted in some of the cats identified with LVCH.[19–21] To increase accuracy of blood pressure measurement, three consecutive, consistent indirect measurements were obtained for cats in this study which is the minimum recommended by the American College of Veterinary Internal Medicine.[5] We took precautions to minimize stress by performing the blood pressure measurement in a quiet cardiology examination room at RBVH after the patient had visibly relaxed and become acclimated to the environment. However, given the vagaries of blood pressure measurement in cats, we cannot completely exclude the possibility that some cats were indeed hypertensive, or that others with elevated blood pressure measurements were in fact normotensive and exhibiting a white-coat effect.[22] We did not exclude cats with hypertension from the study per se, as systemic hypertension does not cause murmurs.

Only two cats underwent thyroid testing. While hyperthyroidism has been associated with cardiac disease,[23] our study specifically selected apparently healthy cats. As none of the cats exhibited clinical evidence of hyperthyroidism, we felt it unnecessary to routinely screen every cat for thyroid disease. The two cats that we screened had echocardiographic findings consistent with LVCH, which prompted us to rule out occult hyperthyroidism as a cause of these changes.

Our study does not address the issue of disease prevalence in apparently healthy cats, because we selected cats with murmurs. Previous studies have suggested that cats without murmurs can have substantial cardiac disease (HCM),[1,2,24] so clinicians should not use absence of a murmur to rule out structural heart disease.

In conclusion, our study shows that in our patient population of apparently healthy cats presenting for evaluation of a murmur, approximately 50% have detectable cardiac disease, while 50% do not. Importantly, the etiology of the murmur (echocardiographic identification of turbulent flow in a specific cardiac region) could not be determined in 50% of the cats. Clinicians should be aware that the presence of a murmur in an apparently healthy cat has a strong possibility of being physiological, but a similar probability of indicating the presence of cardiac pathology.

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