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Feline Cardiomyopathy - Part 1

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Introduction

Feline cardiomyopathy seems to be one of those areas of veterinary medicine where there has been considerable ambiguity and disagreement, even amongst cardiologists. Recently the American College of Veterinary Internal Medicine (ACVIM) published a consensus statement regarding classification, diagnosis and treatment. This article reviews recent information on feline cardiomyopathy, focusing on the practical implications for general practitioners.

Abbreviations used in this article: ARVC – arrhythmogenic right ventricular cardiomyopathy, ATE – arterial thromboembolism, CHF - congestive heart failure, DCM – dilated cardiomyopathy, DLVOTO – dynamic left ventricular outflow tract obstruction, HCM – hypertrophic cardiomyopathy, IVS – interventricular septum, LA – left atrium, LV – left ventricle, RA – right atrium, RCM – restrictive cardiomyopathy, RV – right ventricle, SAM – systolic anterior motion, UCM – unclassified cardiomyopathy)

Staging

Regardless of the underlying cardiomyopathy classification, the ACVIM has proposed a staging system as outlined below:

Stage A	Predisposed, no evidence of cardiac disease
Stage B1	Cardiomyopathy present, no clinical signs, low risk of CHF or ATE
Stage B2	Cardiomyopathy present, no clinical signs, higher risk of CHF or ATE
Stage C	CHF or ATE present
Stage D	CHF refractory to treatment

Stage A may include cats of known or suspected breed predisposition, such as the Maine Coon. It is estimated that the prevalence of the sarcomeric gene mutation, which predisposes this breed to HCM, is 35-42%. Stage B1 and B2 cats have no clinical signs and pose a problem because the clinician may be completely unaware of a problem until the cat presents in Stage C; often after a stressful episode (about half of cats that go into CHF have some precipitating event). Any stress, fever, anaemia, anaesthesia, surgery, trauma, fluid therapy or corticosteroid therapy may precipitate CHF in a previously stable cat. Thus any cat in which a murmur and/or gallop rhythm is auscultated needs further investigation. However, up to 50% of cats with cardiomyopathy have normal cardiac auscultation, and many cats with murmurs have no evidence of cardiac disease. One study found that as many as 22% of "healthy" cats have a murmur.

Furthermore, dynamic murmurs (murmurs that change intensity) are common in cats and are often correlated with heart rate, meaning a murmur may completely disappear when the cat is relaxed.

It is also possible for the clinician to cause an iatrogenic murmur by pressing too hard with the stethoscope while auscultating and effectively squashing the more compliant right ventricle, causing dynamic right ventricular outflow obstruction.

Cardiomyopathy phenotypes

The ACVIM consensus statement has proposed that feline cardiomyopathy be classified according to five echocardiographically determined phenotypes as in the table below:

PHENOTYPE	DEFINITION
Hypertrophic cardiomyopathy	Diffuse or regional increased LV thickness, non-dilated LV chamber
Restrictive cardiomyopathy	Endomyocardial form: Endocardial scar, usually bridging the IVS and LV free wall, usually LA or biatrial enlargement Myocardial form: Normal LV dimensions (including wall thickness) and atrial dilation
Dilated cardiomyopathy	LV systolic dysfunction, characterised by an increase in ventricular dimensions, normal/ decreased LV wall thickness and atrial dilation
Arrhythmogenic cardiomyopathy	Severe RA and RV dilation and often RV systolic dysfunction and RV wall thinning
Nonspecific phenotype	A phenotype not adequately described by the other categories

Determining the exact phenotype may be difficult in some cases (even for cardiologists), but recognising moderate to severe HCM and DCM should not be out of reach for the general practitioner with some echocardiographic skills. RCM classification is more difficult as definitive diagnosis requires demonstrating diastolic dysfunction (impaired LV distensibility/restrictive filling pattern on Doppler interrogation of the mitral valve), which will likely not be possible for the general practitioner.

However, RCM can be suspected when bi-atrial or left atrial dilation and normal LV dimensions are found (ventricles are neither dilated nor concentrically hypertrophied), and more specifically, if actual fibrosis is visible (endomyocardial form). Thus, for the general practitioner performing an echocardiogram, it would be correct to continue using the term "unclassified cardiomyopathy" (UCM) in cases where the classification is not precise, until a more comprehensive echocardiogram can be performed by a specialist (if possible). There can be overlap in the echo appearance, and the appearance may change with time. It is possible that the same cat that is initially diagnosed with HCM may later be classified as RCM and even DCM as the disease advances.

Diagnosis

Genetic testing for the MyBPC3-A31P and MyBPC3-R820W mutations can be done and is recommended for Maine Coon and Ragdoll cats intended for breeding.

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Because of the subclinical cardiomyopathy problem, it may be advisable to recommend echocardiography for any cat nine (9) years or older undergoing interventions that could precipitate CHF. Whether that is feasible in general practice is a different matter. Echocardiography should be advised for any cat with an incidental murmur and even more so if a gallop rhythm is auscultated.

Although radiographs may show left atrial or generalised cardiomegaly or evidence of CHF, it is insensitive to detect mild or moderate cardiac changes (even cats with CHF may have normal appearing hearts), and the classic "valentine-shaped" heart is not specific for HCM as previously thought. Echocardiography is therefore essential. The general practitioner should be able to perform a basic ultrasound and at least recognise moderate to severe left atrial dilation, pleural and pericardial effusion and ideally be able to perform basic measurements.

The typical appearance of ATE (acute hind limb paralysis, cold, absent or weak femoral pulse/s) is caused by a thrombus that typically arises in the LA/auricle and travels to the terminal aorta. If the thrombus is small, it may cause myocardial infarction, thrombotic stroke, forelimb monoparesis or renal infarcts. Also, remember that a cat with ATE is not necessarily in CHF.

Most commonly, cats in heart failure present with tachypnoea and/or dyspnoea due to pleural effusion and/or pulmonary oedema. The clinician needs to differentiate other causes of dyspnoea primarily by radiography and echocardiography. The feline specific NT-proBNP test can be helpful to distinguish between cardiac and non-cardiac causes of dyspnoea in cats but can miss mild to moderate disease (false negatives). A positive NT-proBNP test should always be followed by echocardiography.

In cats with phenotypical HCM, blood pressure should be determined to rule out systemic hypertension (usually only mild to moderate LV hypertrophy), and thyroxine concentration should be checked to rule out hyperthyroidism. The ACVIM recommendation is that all cats $\geq$ six (6) years of age with abnormal cardiac auscultation (with or without LV hypertrophy) be checked for hyperthyroidism. One can only diagnose primary HCM once secondary causes of hypertrophy have been excluded (hyperthyroidism, systemic hypertension, acromegaly). For cats with DCM phenotype, plasma taurine concentration can be measured and diet changed as needed.

Echocardiography

When echocardiography is indicated, every cat should ideally have a "best practice" scan done by a specialist, preferably a veterinary cardiologist (not a speciality available in South Africa). The general practitioner should at least perform a "focused point of care" scan and ideally aim to perform a "standard of care" scan. A "focused point of care" scan refers to the ability to recognise pleural and pericardial effusions, evaluate left atrial size and motion, subjectively assess LV systolic function and look for pulmonary B-lines.

A "standard of care" scan involves both M-mode and 2D evaluation with basic measurements such as left ventricular internal diameter in diastole and systole, left atrium diameter, aortic root diameter, left ventricular free wall and interventricular septum thickness and calculating the left ventricular and left atrial fractional shortening percentage and left atrium: aortic root diameter ratio. In addition, noting papillary muscle hypertrophy, end-systolic LV cavity obliteration, SAM and spontaneous echo-contrast or thrombus formation.

HCM, which is by far the most common cardiomyopathy in cats (58-78% of cardiomyopathies), is characterised by concentric hypertrophy (diastolic LV wall thickness $\geq$6mm), papillary muscle thickening, normal to decreased LV chamber size and variable SAM of the mitral valve with resultant DLVOTO. DCM (rare nowadays) is characterised by cardiac dilation and low FS%. With RCM (second most common cardiomyopathy, 15-21% of cardiomyopathies), findings vary. Still, usually, there is marked bi-atrial dilation; there may be irregular or hyperechoic ventricular walls or bands spanning the LV, with normal ventricular measurements.

ARVC, which is rare, is characterised by right heart dilation and a normal-appearing left heart.

Other rare forms of cardiomyopathy that have been recognised are LVNC (left ventricular noncompaction) and EFE (endocardial fibroelastosis), documented in Siamese and Burmese cats.

An interesting entity is transient myocardial thickening (TMT), which refers to cats having a thickened LV on initial echocardiography, consistent with HCM, with a resolution of the thickening on subsequent exams. 71% of cats with TMT had an antecedent event (most commonly general anaesthesia). The critical point here is that most of these cats can have their cardiac medication discontinued a median of 4.6 months later based on a persistently normal echocardiogram. The cause is unknown, but myocardial oedema and myocarditis are possibilities.

Only to complicate matters, a 2017 study demonstrated tachycardia-mediated left ventricular pseudohypertrophy. In simple terms: the study demonstrated that tachycardia alone can cause LV pseudohypertrophy and that it can be clinically relevant (LV wall thickness was 0.7-2mm greater at 180 beats/min than at 120 beats/min!). Another study found that dehydration can alter myocardial thickness to the extent that a patient is misdiagnosed with HCM.

Treatment

The treatment of cats with cardiomyopathy has been controversial, with different cardiologists, other specialists and general practitioners seemingly following their own treatment protocols. The only two medications on which there is significant agreement are Furosemide and Clopidogrel. The ACVIM consensus statement recommendations are summarised as follows:

Stage B1

Monitor annually for progression to stage B2. Although atenolol has not been shown to alter the natural progression of the disease or prolong survival, it does reduce the severity of SAM. It can be considered for cats with severe DLVOTO.

Stage B2

Cats in stage B2 have moderate to severe LA enlargement (LA:Ao $\geq$ 1.9) and are at increased risk of developing CHF and/or ATE. It is not always straightforward to decide when a cat is in stage B2, but left atrial size is the most critical factor: The more severe the LA enlargement, the higher the risk of CHF and ATE. Other factors are extreme LV hypertrophy (LVFWd $\geq$ 9mm, decreased LA FS%, spontaneous echo-contrast or thrombus formation and the presence of arrhythmia or gallop rhythm on clinical exam.

Thromboprophylaxis preferably with clopidogrel is recommended. Clopidogrel is more effective than low dose aspirin, but aspirin may be preferable for some cats because clopidogrel is exceptionally bitter. Monitor for the development of clinical signs and ask owners to monitor the cat's resting or sleeping respiratory rate. Unlike in dogs, there have been no clinical studies to evaluate the use of pimobendan with subclinical cardiomyopathy.

If an ECG recognises ventricular ectopy, atenolol may be used. If atrial fibrillation is recognised, diltiazem or atenolol can be used.

Stage C

Cats often present with acute symptoms (tachypnoea/dyspnoea), and immediate provision of oxygen (+/- sedation with butorphanol/buprenorphine) is needed. Administer furosemide, consider thoracocentesis if pleural effusion present. Pimobendan can be considered if there is evidence of low cardiac output (hypotension, hypothermia, bradycardia). The ACVIM recommendation is not to use it if DLVOTO is present (although recent studies showed that it is likely safe even in cats with marked DLVOTO). Intravenous fluid treatment is contraindicated. Transdermal nitroglycerine is not recommended.

Cats with chronic CHF should receive Furosemide to control pulmonary oedema and effusions. The dose should be titrated to maintain the sleeping respiratory rate at <30 breaths/minute. Antithrombotic treatment with clopidogrel is indicated. Pimobendan can be considered without DLVOTO (ACVIM recommendation, but see the note above). Studies have shown that benazepril and other ACE inhibitors do not delay treatment failure and are probably not indicated (though some cardiologists still use them).

Stage D

In cats where Furosemide is no longer effective in controlling oedema/effusions, torsemide is an alternative and spironolactone can also be considered. Pimobendan is recommended for cats with global LV systolic dysfunction. Monitor for hypokalemia, reduce sodium intake and ensure adequate calorie intake.

In cats that present with ATE, it is justifiable to advise euthanasia unless some favourable prognostic indicators such as only one limb affected, normothermia, and CHF are not present.

The use of pimobendan is interesting. Although it is intuitive to use it in cases of DCM, using it in cases of HCM should seemingly be catastrophic, unless pimobendan is very different in cats than in dogs. If it increases ventricular contractility in cats as much as in dogs, it ought to wreak havoc in cats with HCM, but it does not. What has been shown is that pimobendan significantly increases atrial fractional shortening in cats with HCM. Improved LA function would improve LV filling with the possible resultant increase in LVOT velocity. A recent study concluded that pimobendan imparts significant benefit in LA function and does not exacerbate LVOT obstructions. However, another study found that Pimobendan administration did not lead to an improved 180-day outcome in cats with HCM and CHF, although anecdotally, there seems to be evidence that it may be beneficial. It is unknown whether this is purely because pimobendan has similar "feel good" properties to caffeine or other phosphodiesterase inhibitors. So there seems to be little doubt that it is safe to use pimobendan, probably even in cases with DLVOTO, but the benefit remains unclear. There are certainly some cardiologists who will treat only with Furosemide when CHF is present and clopidogrel when the left atrium is markedly enlarged and nothing else (not the least because cats are hard to medicate!)

Conclusion

Essential take-home points for the general practitioner are:

- for all cats where a murmur is detected - advise echocardiography, but remember feline murmurs are often dynamic and can be iatrogenic!
- Recognise cats presenting with CHF and remember that many have a precipitating event.
- Learn to perform a focused point of care cardiac scan and preferably develop that further to be able to perform a standard of care scan.
- Know when treatment is indicated and remember the two most critical medications on which there is consensus, namely Furosemide and Clopidogrel.
- Pimobendan appears to be safe in cats, but the benefit remains uncertain, especially for cats with HCM.
- Finally, cats being cats, things are unlikely to be straightforward: Their cardiomyopathies are not always easily classified or staged, a precise treatment regimen remains somewhat murky, and some cats may even just have transient or pseudohypertrophy!

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QUESTION 1

Regarding staging of feline cardiomyopathy, which statement is FALSE?

a. Stage D refers to CHF that is refractory to treatment
b. Differentiating stages B1 and B2 is straightforward
c. Stage C refers to cats with CHF or ATE
d. Stage A refers to a predisposition for cardiomyopathy
e. None of the above

QUESTION 2

Events that may precipitate CHF in a previously stable cat INCLUDE:

a. Anaesthesia
b. Trauma
c. Fluid therapy
d. Corticosteroid therapy
e. All of the above

QUESTION 3

Regarding cardiac murmurs in cats, which statement is FALSE?

a. Up to 50% of cats with cardiomyopathy may have no audible murmur
b. An audible murmur may disappear when the cat is relaxed
c. A clinician may cause an iatrogenic murmur
d. All cats with a murmur have cardiomyopathy
e. None of the above

QUESTION 4

In the ACVIM consensus statement, which phenotype is NO LONGER included?

a. Hypertrophic cardiomyopathy
b. Dilated cardiomyopathy
c. Restrictive cardiomyopathy
d. Unclassified cardiomyopathy
e. Nonspecific cardiomyopathy

QUESTION 5

Regarding restrictive cardiomyopathy, which statement is FALSE?

a. Can be subdivided into a myocardial and endocardial form
b There is primarily ventricular systolic dysfunction
c There is usually substantial LA or bi-atrial dilation
d. There can be overlap in appearance with other forms of cardiomyopathy
e. None of the above

QUESTION 6

The prevalence of the gene mutation predisposing Main Coon cats to HCM is:

a. 10-15%
b. 35-42%
c. 20-24%
d. 50-55%
e. 65-68%

QUESTION 7

Regarding diagnostic tests in cats with cardiomyopathy, which is TRUE?

a. Radiographs are sensitive to detect cardiomyopathy in cats
b The "Valentine" shape heart on radiographs is specific for HCM
c. The feline specific NT-proBNP test does not have false negatives
d. Thyroid hormone levels should be checked in cats with DCM phenotype
e. Blood pressure should be checked in cats with HCM phenotype

QUESTION 8

Regarding arterial thromboembolism (ATE), which statement is FALSE?

a. All cases of ATE have congestive heart failure
b. Typical presentation is acute hind limb paralysis, weak/absent femoral pulses
c. The thrombus typically arises in the left atrium/auricle
d. The larger the left atrium, the bigger the risk of thrombus formation
e. A smaller thrombus may cause front limb paralysis

QUESTION 9

Regarding echocardiography which statement is FALSE?

a. Ideally, every cat should have a "best practice" scan performed
b. The general practitioner should at least be able to perform a "point of care" scan
c. Ideally, all cats nine (9) years or older should be scanned before anaesthesia
d. In any cat with a murmur, echocardiography should be advised
e. None of the above

QUESTION 10

Regarding the treatment of feline cardiomyopathy, which statement is FALSE?

a. Cats in stage B1 should be started on clopidogrel
b. Cats in stage B2 should be started on clopidogrel
c. Furosemide is the most important medication for cats in stage C
d. Pimobendan increases LA fractional shortening in cats
e. ACE inhibitors are probably of little to no benefit in cats

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