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FELINE MYOCARDIAL DISEASE
1: Classification, pathophysiology and clinical presentation

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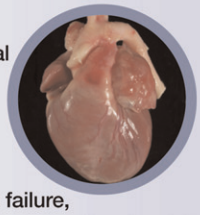

Practical relevance Myocardial disease (cardiomyopathy, CM) is the most common cardiac disorder observed in cats. The disease usually leads to the development of congestive heart failure, which is the major cause of cardiac mortality. Arterial thromboembolism is another severe outcome often associated with feline CM.

Patient group The median age of cats when diagnosed with a form of CM is 5.5 years (range 4 months to 16 years). The disease appears to be equally distributed between males and females and among different breeds, although a genetic predisposition of some pedigrees should be taken into consideration (ie, Maine Coons, Ragdolls, Norwegian Forest cats).

Audience General practitioners, as well as specialists in small animal medicine, cardiology and pathology, have to deal with CM on a regular basis.

Clinical challenges The diagnosis and clinical management of myocardial disease in cats represents one of the greatest challenges in veterinary cardiology. Although several attempts have been made to standardise the classification of CM, both in humans and cats, some disagreement still exists among cardiologists. Classification criteria are continuously evolving as the aetiology of myocardial disease becomes better understood. It is now widely appreciated that, for a given aetiology, there may be a spectrum of phenotypes ranging from restrictive to dilated.

Diagnostics The diagnosis and classification of CM is primarily based on echocardiographic criteria. However, phenotypic variability is substantial, even within a single form of CM, and this often causes subjective interpretations of echocardiographic diagnosis, especially by inexperienced echocardiographers. Post-mortem examination is an alternative approach to diagnosis.

Evidence base The clinical management of feline myocardial disease is even more controversial, especially in the light of recent clinical studies. This two-part article reviews the literature to date, discusses various manifestations of the disease in cats and offers a critical, and often controversial, approach to diagnosis and management.

Classification – and its current limitations

Cardiomyopathy (CM) was initially defined in 1980 by the World Health Organization (WHO) as heart muscle diseases, of unknown cause, in which the dominant feature is cardiomegaly and heart failure.[1] The updated WHO definition in 1995 was 'diseases of myocardium associated with cardiac dysfunction' and included arrhythmogenic right ventricular cardiomyopathy (ARVC) and restrictive cardiomyopathy (RCM) for the first time (Table 1).[2]

In feline medicine, the classification of myocardial diseases follows the above WHO definitions and guidelines for standardised diagnosis are reported in the literature.[3–7] However, the common classification of CM as hypertrophic (HCM), restrictive (RCM) and dilated (DCM) forms presents important limitations because it mixes anatomical (ie, hypertrophic and dilated) with functional designations (eg, restrictive). Consequently, confusion may arise because the same disease could appear in two categories.[8] Furthermore, a myocardial disease

TABLE 1 Definition and classification of cardiomyopathy according to the 1995 WHO/ISFC Task Force[2]

HCM	RCM	DCM	ARVC	UCM
Left and/or right ventricular hypertrophy, usually asymmetric and involving the interventricular septum. Typically, the left ventricular volume is normal or reduced	Restrictive filling and reduced diastolic volume of one or both ventricles with normal or near-normal systolic function and wall thickness	Dilation and impaired contraction of the left ventricle or both ventricles	Progressive fibrofatty replacement of right ventricular myocardium, initially with typical regional and later global right and some left ventricular involvement, with relative sparing of the septum	Cases that do not fit readily into any group

WHO/ISFC = World Health Organization/International Society and Federation of Cardiology, HCM = hypertrophic cardiomyopathy, RCM = restrictive cardiomyopathy, DCM = dilated cardiomyopathy, ARVC = arrhythmogenic right ventricular cardiomyopathy, UCM = unclassified cardiomyopathy

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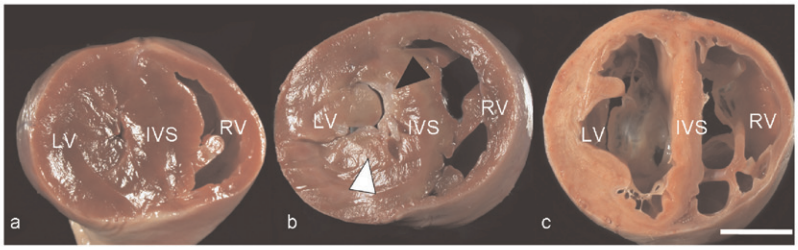
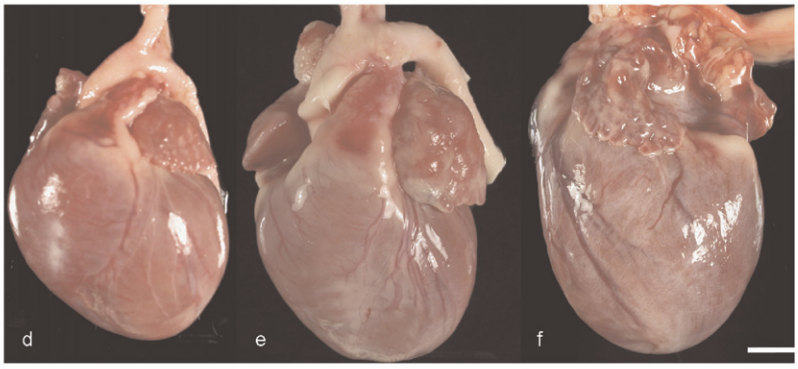
secondary to valvular, ischaemic or inflammatory conditions may share a final common pathway with a primary CM. In fact, there is a substantial overlap in the remodelling and compensatory mechanisms in the failing heart, which justifies a wider use of the term CM.[9] Another criticism of the current classification of CM is that it should include not only altered contractility or impaired diastolic function, but also myocardial electrical diseases, such as rhythm disturbances and enhanced arrhythmogenicity.[10] Finally, cardiac remodelling may cause some myocardial conditions to evolve from one form to another during their natural clinical course. For example, HCM may progress from a non-dilated and hyperdynamic state to a dilated form with systolic dysfunction and failure.[8]

At present, the diagnosis and classification of CM is primarily based on echocardiographic criteria. However, phenotypic variability is substantial, even within the same form of CM, and this often causes subjective interpretations of echocardiographic diagnosis, especially by inexperienced echocardiographers.[11] Pathology is an alternative approach to the diagnosis and classification of CM (Fig 1), but is less relevant to this discussion as it has fewer practical clinical implications.[7]

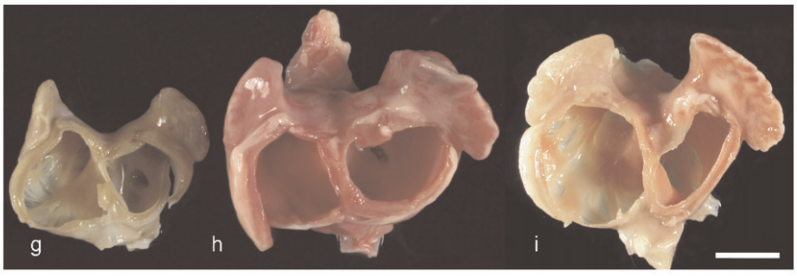
FIG 1 Various phenotypic manifestations of feline myocardial disease. RV = right ventricle, LV = left ventricle, IVS = interventricular septum. White bar = 1.0 cm



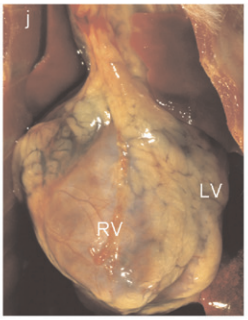
(a) Left ventricular hypertrophy with reduced lumen of the chamber in a cat with hypertrophic cardiomyopathy; (b) Fibrotic lesion bridging the left ventricular lumen (black arrowhead) and affecting the papillary muscles ('interpapillar muscle sinechia') (white arrowhead) in a cat with restrictive cardiomyopathy; (c) Biventricular enlargement in a dilated form of feline cardiomyopathy. *Courtesy of Dr Anibal G. Armién, University of Minnesota*

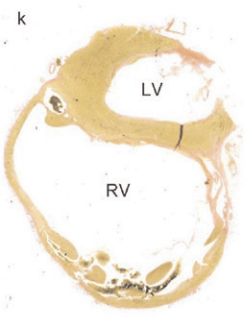


(d,e) LV enlargement in two cats with hypertrophic cardiomyopathy; (f) Biventricular enlargement in a dilated form of cardiomyopathy. *Courtesy of Dr Anibal G. Armién, University of Minnesota*



(g) Atrial myocardium in a normal cat; (h) Bi-atrial wall hypertrophy and chamber dilation in a cat with hypertrophic cardiomyopathy; (i) Bi-atrial dilation and wall thinning in a cat affected by dilated cardiomyopathy. *Courtesy of Dr Anibal G. Armién, University of Minnesota*





(j) Severe RV dilation in a cat with arrhythmogenic right ventricular cardiomyopathy; (k) Histological cross section of the same heart showing massive right ventricular dilation and thinning of the right ventricular wall

Hypertrophic cardiomyopathy (HCM)

Hypertrophic cardiomyopathy represents the most common myocardial disease in cats and accounts for nearly two-thirds of the CM cases seen in this species.[7] It is characterised by increased cardiac mass associated with a hypertrophied, non-dilated left ventricle.[3,12] The myocardial hypertrophy usually presents with wide phenotypic variability, as it can affect different portions of the interventricular septum (IVS) and/or left ventricular free wall (LVFW). According to Fox et al,[3] myocardial hypertrophy in feline HCM can present in four different patterns:

- Diffuse and substantial concentric hypertrophy, involving portions of the IVS as well as the contiguous LVFW (one-third of cases);
- Diffuse and substantial asymmetric hypertrophy, affecting preferentially the IVS or the LVFW (one-third of cases);
- Segmental hypertrophy confined to one left ventricular segment (IVS or left ventricle);
- Segmental hypertrophy affecting non-contiguous segments of the IVS and left ventricle.

These lesions are often accompanied by left atrial (LA) dilation, aneurysmal thinning of the LV apex and focal myocardial infarction.[12]

In addition to the lesions reported above, right ventricular (RV) hypertrophy and right atrial (RA) enlargement can also be observed.

Primary HCM is a heritable condition in people, with 11 mutated sarcomeric genes presently associated with the disease. Due to an elevated inter- and intragenetic diversity, more than 400 individual mutations have been identified so far.[13] Familial HCM has been described in Maine Coon cats with an autosomal dominant mode of inheritance.[14] A similar inheritance may also be present in other pedigrees, such as Ragdolls and British

Hypertrophic cardiomyopathy is the most common myocardial disease in cats and accounts for nearly two-thirds of cases of feline cardiomyopathic disease.

Shorthair breeds.[15,16] A causative mutation for HCM has been recently identified in the sarcomeric gene for the cardiac myosin binding protein C (MYBPC3) in both Maine Coons[17] and Ragdolls.[15] However, the mutation in the two breeds appears in different regions of the same gene (between domains C0 and C1 of the protein in Maine Coons and in domain 6 in Ragdolls).[15] Other mutations are likely to be identified in the near future.

Secondary myocardial hypertrophy can be caused by ventricular pressure overload (ie, outflow obstruction, systemic hypertension), hypersomatotropism and hyperthyroidism (Table 2).[12,18,19] However, the LV concentric hypertrophy commonly observed in hyperthyroid people presents less commonly in feline hyperthyroidism. In a study involving 23 hyperthyroid cats, Connolly et al[20] observed only a modest septal hypertrophy and a reduction in fractional shortening. A mild septal hypertrophy accompanied by clinical evidence of congestive heart failure (CHF) has also been observed in cats after administration of methylprednisolone acetate.[21] Other forms of myocardial hypertrophy have been described in feline muscular dystrophy and infiltrative myocardial tumours (eg, lymphomas) which can induce echocardiographic changes analogous to HCM in both people and cats.[22–24] Finally, a number of other diseases occurring in people are associated with LV hypertrophy and may resemble or mimic primary HCM (eg, glycogen storage disease, Noonan syndrome).[25]

Restrictive cardiomyopathy (RCM)

Cardiac conditions characterised by a myocardial stiffness and diastolic dysfunction (restrictive pathophysiology) represent the second most common form of CM in cats (approximately 20% of feline CM cases).[7] Restrictive cardiomyopathy can present with an even wider spectrum of clinical manifestations and pathological phenotypes than is observed in HCM.[26] Restrictive cardiomyopathy should be differentiated from constrictive pericarditis, which is also characterised by normal or near-normal systolic function and abnormal ventricular filling. However, in a practical clinical setting, such differentiation can be very difficult because it requires cardiac catheterisation and/or endo-myocardial biopsy.[9] Furthermore, cases of constrictive pericarditis have not been reported in the cat, albeit a thorough pathological examination of the feline pericardium is seldom performed.

There are two types of RCM described in the human literature, the myocardial and the endomyocardial form,[9] and this classification may also be suitable to describe RCM in cats.[26] Feline myocardial RCM is a non-infiltrative disease characterised by restrictive filling, a normal or mildly thickened LVFW or IVS, preserved systolic function and severe, often bilateral, atrial enlargement. The endomyocardial form of feline RCM is characterised by extensive reparative fibrosis at the level of the endocardium or endomyocardium.[26] Fibrotic lesions primarily affect the left ventricle and they can present as large scars bridging the ventricular lumen from the LVFW to the IVS and causing obstruction of the mid- to apical LV chamber and often turbulence of the blood flow. It is very likely that the previously described 'moderator band cardiomyopathy'[7] or 'excessive moderator band'[27] are simply lesions associated with endomyocardial RCM. Furthermore, the moderator band (or trabecu-

TABLE 2 Primary (specific) causes of feline cardiomyopathy that should be considered in the differential diagnosis

Cause	Myocardial lesion(s) commonly observed
Hyperthyroidism	Modest septal hypertrophy and a reduction in fractional shortening
Administration of methylprednisolone acetate	Septal hypertrophy accompanied by clinical evidence of congestive heart failure
Hypersomatotropism	Concentric left ventricular hypertrophy
Left/right outflow obstruction	Concentric left/right ventricular hypertrophy
Systemic hypertension	Concentric left ventricular hypertrophy
Myocardial tumours (eg, lymphomas)	Concentric left ventricular hypertrophy and hypokinesis
Dystrophin-deficient hypertrophic feline muscular dystrophy	Concentric left ventricular hypertrophy and hypokinesis, hyperechoic endocardium and hyperechoic and slightly enlarged papillary muscles
Myocardial infarction	Depressed and hypokinetic myocardial areas, ventricular chamber dilation
Tricuspid dysplasia	Right ventricular and right atrial chamber dilation resembling ARVC
Myocarditis	Concentric left/right ventricular hypertrophy

ARVC = arrhythmogenic right ventricular cardiomyopathy

Cats with ARVC often present with conduction disturbances and severe arrhythmias, including ventricular tachycardia and atrial fibrillation.

la septomarginalis) is a muscular band of myocardium located in the right ventricle. Therefore, 'moderator band' in the above reports is a misnomer.

In the 'obliterative' form of RCM, extensive fibrosis markedly reduces the LV lumen. In general, the abnormal fibrous tissue can cause chamber deformity at different levels, including the mitral valve apparatus, which may ultimately result in mitral regurgitation. Myocardial infarction is sometimes observed in the left ventricle, presenting as focal, depressed and hypokinetic areas. The presence of significant fibrotic lesions and focal areas of myocardial hypomotility may facilitate the echocardiographic recognition of RCM.

In people, approximately 50% of RCM cases result from specific clinical disorders, primarily genetic and acquired infiltrative amyloidosis,[8] while the remaining 50% of cases are of unknown nature (idiopathic). Other causes of myocardial RCM described in people are sarcoidosis, inheritable metabolic disorders (Fabry disease, Gaucher disease, glycogenosis, mucopolysaccharidosis), haemochromatosis, glycogen storage disease and diabetes. Endomyocardial types of RCM can result from Löffler's endocarditis (hypereosinophilic syndrome), endomyocardial fibrosis (typically found in populations of equatorial Africa), endocardial fibroelastosis (described in fetuses and infants) and carcinoid syndrome (metastasis of carcinoid tumours from the intestine to the heart).[9]

To the best of the author's knowledge, an aetiological subclassification of RCM has not been reported in cats, although myocardial damage followed by reparative fibrosis might be associated with hypereosinophilia, viral or immune-mediated diseases.[26]

Dilated cardiomyopathy (DCM)

Dilated cardiomyopathy is characterised by a severely dilated LV chamber and hypocontractile myocardium. It had represented the second most common form of feline cardiac disease until 1987, when Pion et al[28] reported the association between taurine deficiency and DCM and the normalisation of LV function after oral taurine supplementation. Consequently, the taurine content of feline diets was adequately increased, resulting in a dramatic reduction in the prevalence of feline DCM (to approximately 10% of all cases of feline CM).[7] Taurine deficiency may also cause central retinal degeneration in cats, which seems to persist even when plasma taurine levels are restored.[28] However, not all cats fed taurine-deficient diets develop DCM, indicating that other pathophysiological mechanisms might be involved, such as taurine depletion associated with potassium-deficient diets[29] or a genetic predisposition.[30]

The rare cases of taurine-associated feline DCM observed nowadays are generally the consequence of a non-traditional diet (ie, vegetarian/vegan diets or canine diets). Finally, sporadic cases of DCM can still be seen in cats with normal plasma taurine levels. These forms of DCM could represent the end stage of an undiagnosed valvular disease (eg, mitral dysplasia) or an ischaemic myocardial disease. They could even be related to sustained tachycardia (tachycardiomyopathy) or unrecognised episodes of toxicity or viral infection.

Arrhythmogenic right ventricular cardiomyopathy (ARVC)

The hallmark of ARVC is a markedly enlarged right ventricle and atrium. The right myocardial free wall appears very thin and hypokinetic, and the presence of aneurysm is also common.[6,31] Mild tricuspid regurgitation is usually present, while the left ventricle appears minimally involved and preserves its main morphology and functions.

In humans, ARVC is a familial disease characterised by progressive myocardial atrophy caused by injury (myocyte death and patchy myocarditis) and subsequent repair by fibrofatty replacement.[32] Potential pathogenetic mechanisms include apoptosis (programmed cell death), genetically determined atrophy (dystrophy), and inflammatory and immune-mediated processes.[33] The disease accounts for 20% of cases of sudden cardiac death in people, especially in young athletes, due to paroxysmal ventricular tachycardia progressing to ventricular fibrillation.[9,34] Cats with ARVC may also present with arrhythmias, including ventricular tachycardia, atrial fibrillation, supraventricular tachycardia, ventricular premature complexes, right bundle branch block and atrioventricular block.[6,31]

Unclassified cardiomyopathy (UCM)

In people, unclassified cardiomyopathies include all cases that do not fit readily into any other group of CM.[2] Similarly, a significant number of feline myocardial diseases show features that are not typical of any other commonly recognised CM and are therefore described as 'unclassified'.[7] The pathogenesis of UCM is unclear. However, this condition could represent an early or late stage of another recognised form of CM. Furthermore, some

segmental myocardial changes accompanied by ventricular dysfunction could be secondary to myocardial ischaemia and infarction. End-stage myocardial remodelling of HCM, in particular, presents with relative thinning of the LVFW and IVS and with dilation of the ventricular lumen, decreased fractional shortening, and progression to heart failure both in humans and cats.[35] Finally, myocardial remodelling may result from unrecognised or undiagnosed valvular or pericardial abnormalities. Therefore, it is unlikely that UCM represents a distinct pathological entity and great care should be taken in assigning cardiac conditions to this category.

Myocarditis

Inflammation of the myocardium (myocarditis) represents another important myocardial disease in cats.[36] Although several cases of feline myocarditis have been reported in the literature, this condition is surprisingly underestimated.

In a study by Meurs et al,[37] myocarditis was identified on histopathology in nearly two-thirds of a randomly selected population of cats with idiopathic CM (hypertrophic, dilated and restrictive), whereas control cats showed a normal myocardium. Approximately one-third of cardiomyopathic cats were found to be positive for panleukopenia viral DNA on polymerase chain reaction (PCR) testing, but were negative for herpesvirus, calicivirus and coronavirus. This remarkable study suggests viral myocarditis as having a possible role in the pathogenesis of feline CM. Myocarditis in cats has also been reported in association with protozoal infections, such as toxoplasmosis (*Toxoplasma gondii*)[38] and sarcocystosis (*Sarcocystis felis*),[39] and bacterial streptococcal infection (*Streptococcus canis*).[40] In all these cases, myocardial lesions resembled CM in terms of their echocardiographic features.

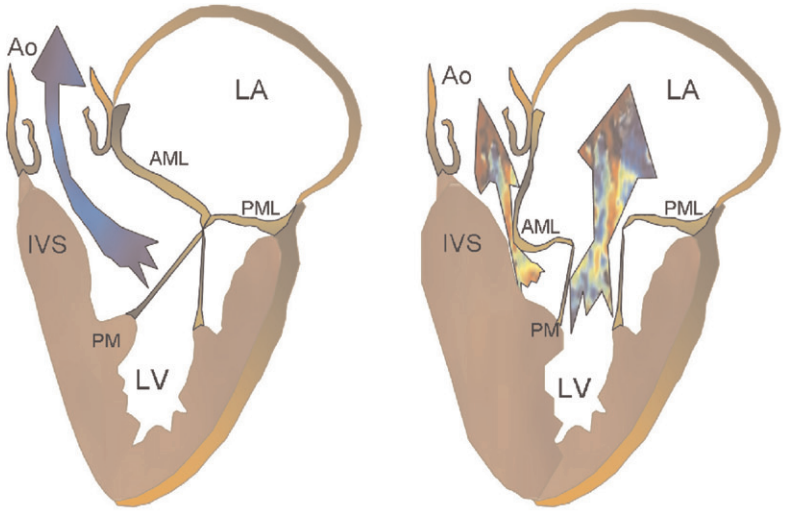


FIG 2 Dynamic left ventricular outflow tract (LVOT) obstruction. The left hand image shows normal laminar flow in the LVOT (blue arrow) during systole with both mitral valve leaflets coalescing and sealing the atrioventricular ostium. The right hand image shows motion of the anterior mitral leaflet (AML) and contact with the interventricular septum (IVS) (systolic anterior motion, SAM). This abnormal movement of the AML causes narrowing of the LVOT and mitral valve insufficiency, and consequently blood flow turbulence both in the LVOT and left atrium (LA) (coloured arrows). Ao = aorta; LV = left ventricle; PM = papillary muscle; PML = posterior mitral leaflet

Pathophysiology

Left ventricular outflow tract (LVOT) obstruction

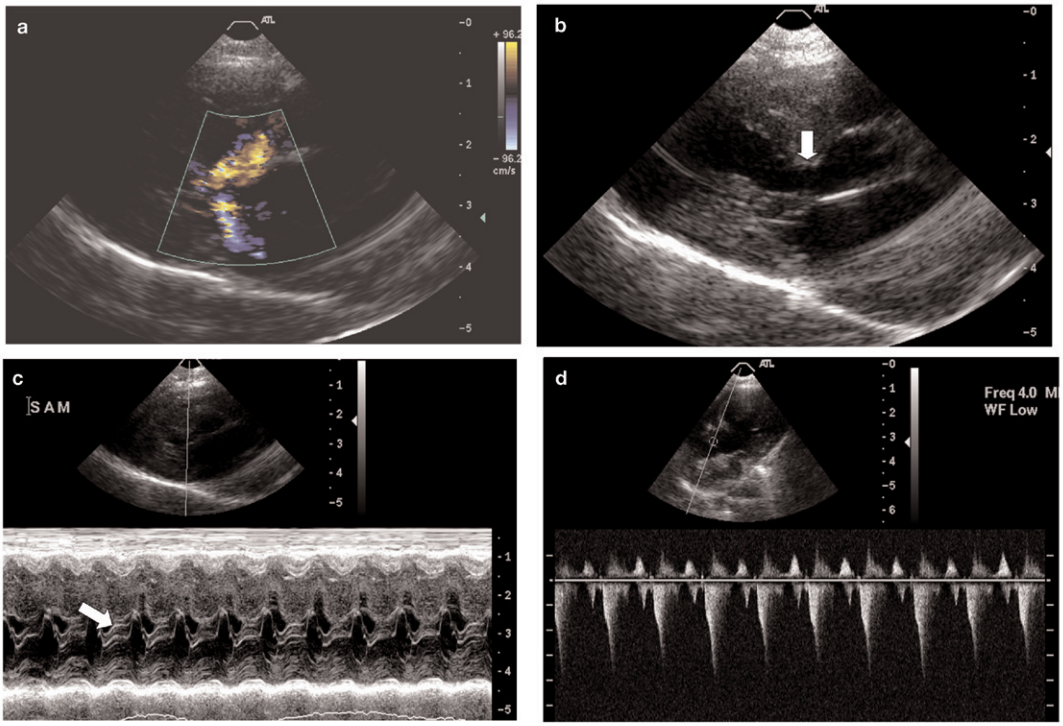
Many human patients affected by HCM present with a variable degree of dynamic LVOT obstruction. This obstruction is primarily caused by systolic anterior motion (SAM) of the mitral valve and mid-systolic contact with the ventricular septum.[25] Similarly, SAM is present in approximately 50% of cats with HCM.[12]

The main characteristic of SAM is an abrupt movement of the elongated anterior leaflet of the mitral valve towards the IVS. Since the LVOT is constituted by this valvular leaflet and the proximal part of the IVS, the abnormal movement causes narrowing of the tract and interferes with the LV outflow in mid-systole. The magnitude of the outflow gradient can be reliably estimated with Doppler interrogation and is directly related to the duration of contact between the valvular leaflet and the proximal IVS.[25] Under these conditions, the mitral valve does not completely seal the atrioventricular annulus and mitral regurgitation will follow. The resulting combination of flow turbulence in the LVOT and mitral regurgitation explains the presence of an audible systolic murmur on auscultation in these patients (Figs 2 and 3). Dynamic obstruction and systolic murmurs can be present at rest or may become audible when the heart rate and cardiac contractility increase, such as during stress or excitement.

The mechanism of SAM is not fully understood and several hypotheses have been suggested. However, deformation of the mitral valve architecture (leaflets, chordae tendineae, papillary muscles) and the hyperdynamic state caused by the concomitant myocardial hypertrophy seem the most plausible explanations. Intrinsic valvular disease (ie, endocardiosis or dysplasia) may also play a role in some patients with SAM, especially when accompanied by severe mitral regurgitation.[25] Surprisingly, Rush et al[41] observed that cats with SAM live longer than cats without this echocardiographic finding. It should also be noted that, despite a widespread belief among clinicians, SAM is not pathognomonic of myocardial hypertrophy, having been convincingly documented in human[42–44] and canine[45] patients in the absence of significant LV hypertrophy.

Myocardial ischaemia

Regional myocardial ischaemia is commonly recognised in human[9,25] and feline[12,26,35] patients with all forms of CM and is often followed by replacement fibrosis. The cause of ischaemia is not fully understood but it is likely to be related to intramural coronary arterial disease caused



MULTIMEDIA
Six echocardiographic video recordings are included in the online version of this article at **10.1016/j.jfms.2008.11.008**

FIG 3 Echocardiographic features of systolic anterior motion (SAM) in a cat with an obstructive form of hypertrophic cardiomyopathy (HCM). The abnormal movement of the anterior mitral valve leaflet towards the interventricular septum in early to mid-systole causes dynamic interference of the left ventricular outflow and turbulence in the outflow tract. Since the mitral valve remains partially open during this phase, mitral regurgitation is also observed. (a) The two simultaneous turbulent flows are characteristic of this phenomenon; (b) Repeated contacts of the anterior mitral leaflet with the proximal part of the interventricular septum in mid-systole can cause a fibrotic lesion that appears as a septal hyperechoic area (white arrow); (c) The abnormal movement of the anterior mitral leaflet towards the septum can be readily observed on m-mode scanning of the mitral valve leaflets; (d) Increased gradient and 'scimitar-like' shape of the spectral Doppler interrogation of the left outflow caused by the contact between the valvular leaflet and the proximal interventricular septum

by the myocardial hypertrophy or distension. The significant elevation of troponin I in cats with HCM might indicate ongoing myocardial damage, possibly secondary to a concurrent myocardial infarction.[46,47] Ischaemia and infarction will induce regional myocardial abnormalities characterised by systolic dysfunction (dyssynchrony, hypokinesis and dyskinesis), diastolic impairment, ventricular remodelling and malignant ventricular arrhythmias.[48]

Diastolic dysfunction

An abnormality in ventricular relaxation (diastolic dysfunction) is present in almost all cases of CM. In HCM patients, the reduced ventricular compliance is predominantly caused by myocardial hypertrophy, although interstitial fibrosis and loss of cellular architecture may also contribute to the loss of compliance.[25] The diastolic dysfunction in RCM is primarily caused by myocardial fibrosis, infiltration or scarring of the endomyocardial surface.[9] Similarly, loss of compliance can be present in all the other manifestations of myocardial disease accompanied by fibrotic lesions, including DCM.

Tachycardia may exacerbate the diastolic dysfunction by reducing diastolic time, and hence the time available for ventricular filling. Furthermore, since coronary blood flow occurs in diastole, fast heart rates may aggravate myocardial ischaemia.

Diastolic dysfunction will cause increased filling pressure. LA enlargement will initially compensate for this until the point of maximal compliance is reached, after which pressure increases in the atrial chamber. The absence of valves between the left atrium and pulmonary veins will result in pulmonary venous hypertension and eventually pulmonary oedema and/or pleural effusion (CHF). Dynamic outflow obstruction (SAM) and mitral regurgitation also contribute to increased LV and LA pressure.

Systolic dysfunction

Reduced myocardial contractility is the primary pathophysiological mechanism in DCM and ARVC, predominantly involving the left ventricle and right ventricle, respectively. However, systolic impairment has also been demonstrated in cats with HCM using pulsed tissue Doppler imaging.[49] In this study, the systolic dysfunction did not appear to be related to the presence of LVOT obstruction and CHF. Systolic dysfunction may be a feature of any myocardial disease that is accompanied by significant ischaemia and replacement fibrosis (ie, RCM, UCM, myocarditis). It will result in reduced stroke volume and increased ventricular filling pressure due to increased end-systolic ventricular diameter, eventually leading to CHF.

Neurohormonal activation (RAAS, sympathetic activation, TNF, endothelin)

Reduced stroke volume caused by lower end-diastolic volume (diastolic dysfunction) or reduced myocardial contractility (systolic dysfunction) is sensed by baroreceptors (distributed at the level of the carotid sinus, aortic arch and afferent renal arterials) and by the cells of the juxtaglomerular system in the kidney. This stimulates the renin–angiotensin–aldosterone system (RAAS),

Clinical signs

Abnormal heart sounds

Abnormal heart sounds are the most common clinical findings. They include heart murmurs (approximately 60% of cats with CM), gallop sounds (nearly 20% of individuals) and muffled heart sounds (5% of cardiomyopathic cats).[7] The heart murmur is primarily a consequence of mitral regurgitation and/or dynamic LVOT obstruction. However, tricuspid regurgitation may also be present, especially in severe forms of right ventricular dilation (ARVC, DCM, pulmonary hypertension secondary to left-sided CHF). Gallop sounds are characterised by the presence of diastolic sounds (S3 and/or S4), which become audible due to reduced compliance of the myocardium. This may occur secondarily to ventricular wall hypertrophy, myocardial infiltration, fibrosis, tachycardia or a combination of these factors. Muffled heart sounds indicate the presence of pleural and/or pericardial effusion.

Dyspnoea

Dyspnoea, another common clinical sign, suggests concomitant CHF (pulmonary oedema and/or pleural effusion). Many clinicians will have observed cats developing CHF acutely after a stressful event (eg, car journey, hospitalisation) or after simple clinical procedures (eg, restraint, enforced recumbency for radiographic examination). The sudden onset of CHF in these cases is attributable to a rapid release of catecholamines, which induces generalised vasoconstriction and increased cardiac output (increased stroke volume and heart rate). The result of these combined effects is a ventricular pressure overload, increased atrial pressure and, eventually, pulmonary capillary hypertension, pulmonary oedema and/or pleural effusion. Hence, patients suspected of having or known to have CM should always be examined gently and cautiously, with careful consideration given to the risks of any proposed procedure.

Heart rate > 200 bpm

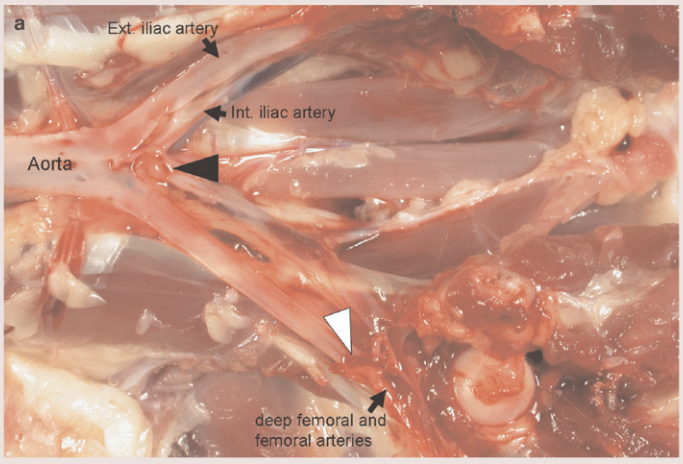
Approximately one-third of cardiomyopathic cats have a heart rate above 200 beats per minute (bpm), which is likely to be caused by sympathetic stimulation. Although there is no consensus on a heart rate threshold that defines tachycardia in cats, most cardiologists would agree that a fast heart rate can potentially worsen the clinical presentation by affecting myocardial diastolic function and reducing coronary blood flow.

Limb paresis/paralysis

Limb paresis/paralysis associated with ATE is seen in approximately 10% of cats with myocardial disease. Bilateral hindlimb paresis represents the most common presentation (71% of all ATE cases), followed by unilateral hindlimb (14%) and unilateral forelimb (12%) paresis.[54] The lack of a palpable pulse is suggestive of ATE. However, occlusion of the internal iliac artery or more distal arteries can induce paresis despite a concomitant palpable femoral artery (Fig 4).

Hypothermia

Significant hypothermia is observed in the majority of cats with CM and appears particularly pronounced in cases complicated by ATE.[41,54]



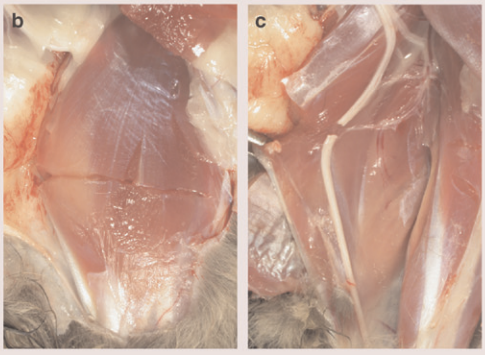


FIG 4 Post-mortem examination of a cat with ATE which presented with hindlimb paresis and echocardiographic evidence of a restrictive myocardial disease. Both femoral pulses were palpable at presentation. The cat was later euthanased after it developed complete paralysis. (a) A 2 x 1 mm thrombus is lodged at the trifurcation of the internal iliac arteries and sacral arteries (black arrowhead), possibly responsible for the initial paresis. A 6 x 3 mm fibrinous thrombus is present at the bifurcation of the deep femoral and femoral arteries (white arrowhead), with little to no intra-arterial blood downstream of the occlusion. This was the possible cause of the later clinical complication; (b) Extensive areas of pallor and softness affecting the gastrocnemius; (c) Similar lesions at the level of the lateral digital extensor and flexors and muscles. *Courtesy of Dr Anibal G. Armién, University of Minnesota*

Cardiac arrhythmias and hypotension

Cardiac arrhythmias and hypotension (systolic blood pressure < 120 mmHg) are observed in approximately 10% and 15% of cardiomyopathic cats, respectively. Many arrhythmias can be paroxysmal in these patients and they may not be detected during physical examination or standard electrocardiographic recording. Severe paroxysmal arrhythmias can be responsible for episodes of **syncope** (nearly 10% of cases)[7] and **sudden death** (5% of cases)[41] in cats with myocardial disease. Hypotension, believed to be the result of a significant reduction in cardiac output, is usually observed in the most severe cases.[7]

Ascites

Ascites is also observed in feline myocardial disease (around 10% of cardiomyopathic cases)[7] and is suggestive of right-sided failure, most likely associated with ARVC, DCM, RCM or complicated forms of HCM or myocardial ischaemia (Fig 5).

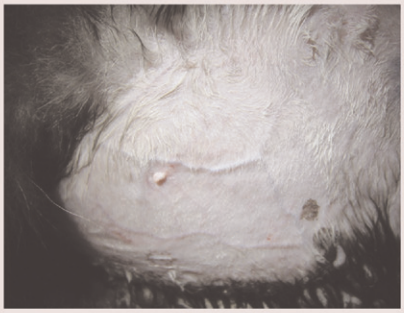


FIG 5 Clinical features of right-sided congestive heart failure in a cat with arrhythmogenic right ventricular cardiomyopathy (ARVC). Note the distended abdomen caused by ascites and the prominent subcutaneous veins, which are caused by hypertension at the level of the caudal vena cava

resulting in vasoconstriction and salt and water retention (compensatory phase). The resultant increase in blood volume increases venous return to the heart, leading to increased myocardial wall stress.[50,51]

Stimulation of baroreceptors also activates the sympathetic nervous system, which has deleterious effects since it promotes vasoconstriction, induces further activation of the RAAS, and increases heart rate and myocardial contractility, which further exacerbates myocardial wall stress.

Circulating concentrations of the cytokine tumour necrosis factor-alpha (TNF-α) are increased in many feline patients with CHF and this could be implicated in the development of endothelial abnormalities.[52]

Finally, endothelin, a potent vasoconstricting peptide produced by endothelial cells and other tissues, is significantly increased in cats with myocardial disease and may have an important pathogenetic role in feline CM by inducing cell proliferation, vasoconstriction, activation of the sympathetic system and cardiac remodelling.[53]

Arterial thromboembolism (ATE)

The presence of a thrombus in one of the cardiac chambers and subsequent arterial thromboembolism (ATE) represents a relatively common and dramatic sequela in the pathophysiology of feline CM. Intracavitary thrombi may be identified incidentally during echocardiography but whether their formation is correlated to severe LA dilation remains controversial. Thrombus formation may be facilitated by intracardiac blood stasis, altered coagulability or endothelial injury secondary to TNF-α release.[18] Interestingly, only 50% of feline ATE cases present with a concurrent CM[54] and not all cats with echocardiographic evidence of intracavitary thrombi develop ATE. However, it should be taken into consideration that thrombi can also induce blood flow obstruction.

TABLE 3 Common clinical findings in cats with cardiomyopathy

Clinical finding	Approximate incidence (%)
Heart murmur	60
Dyspnoea	50
Tachycardia	30
Lethargy	20
Gallop rhythm	20
Hypotension	15
Poor body condition	10
Ascites	10
Arrhythmia	10
Collapse	10
Abnormal respiratory sounds	10
Hindlimb paresis	7.5
Bradycardia	5.5
Muffled heart sounds	5.0

Adapted from Ferasin et al (2003)[7]

Clinical presentation

Cats with myocardial disease present with a wide variety of clinical signs (see page 9 and Table 3). The clinical presentation does not differ significantly among the various groups.[7] Therefore, a more practical approach is simply to consider all patients as being cardiomyopathic. Furthermore, criteria for diagnosis, classification and treatment of different forms of CM have changed over the years and the data provided in the above-mentioned study for individual forms of CM may not now apply, given current trends in feline cardiology.

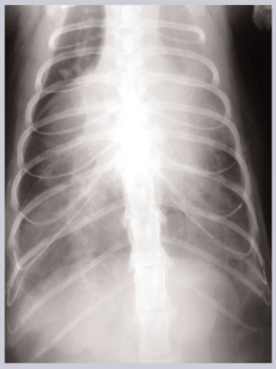
The median age of cats when diagnosed with a form of CM is 5.5 years (range 4 months to 16 years).[7] The disease appears to be equally distributed between males and females and among different breeds, although a genetic predisposition of some pedigrees should be taken into consideration (ie, Maine Coons, Ragdolls and Norwegian Forest cats).

KEY POINTS

- The knowledge of feline myocardial disease is rapidly expanding and different classification criteria for CM will certainly be introduced in the future when, as yet undiscovered, underlying mechanisms come to light.
- Abnormalities in ventricular relaxation (diastolic dysfunction) are present in almost all cases of CM.
- Reduced myocardial contractility (systolic dysfunction) is the primary pathophysiological mechanism in DCM and ARVC; however, systolic impairment is also present in cats with HCM.
- Regional myocardial ischaemia is commonly recognised in human and feline patients with all forms of CM and is often followed by replacement fibrosis.
- Heart murmur, gallop sounds and dyspnoea are the most common abnormalities in cats affected by CM, while arterial thromboembolism represents the most severe and dramatic complication.

Case notes

Arthur, a 6-year-old male neutered domestic shorthair cat, presented with sudden-onset dyspnoea which was not responding to antibiotic treatment (amoxicillin clavulanate).



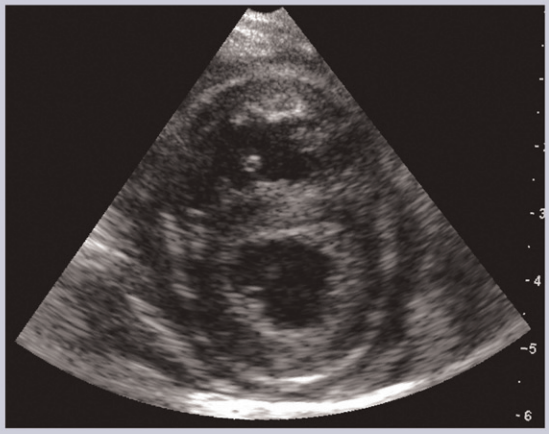
Presenting complaints Difficulty breathing and mild abdominal enlargement.

History Arthur had a relatively unremarkable history. He was regularly vaccinated, wormed, treated for fleas and fed a commercial feline maintenance diet. He had been presented to the referring veterinary surgeon 10 days earlier for sudden-onset dyspnoea, characterised by rapid breathing (65–70 breaths per minute) and moderate abdominal effort. Open-mouth breathing, anxiety and discomfort were not observed. Clinical signs did not improve after empirical antibiotic treatment with oral amoxicillin clavulanate, which prompted a cardiology referral.

Physical examination and laboratory findings On presentation, Arthur was in excellent body condition, bright, alert and fully responsive. Abnormal respiration was immediately observed with a fast rate (60 breaths per minute) and abdominal pattern. Wheezes and crackles could be heard on thoracic auscultation, and were particularly loud at the level of the cranial lung lobes. Cardiac auscultation was unremarkable, with a heart rate of 150–160 bpm. Both femoral pulses were palpable and regular. Bilateral jugular pulsation was observed. Arterial blood pressure was 110 mmHg. Renal and thyroid profiles were within the normal ranges.

Echocardiography Echocardiography revealed a severe biventricular and biatrial enlargement with significant concentric myocardial hypertrophy. Mild pericardial and pleural effusion was also observed. Hepatic venous congestion and mild ascites were identified on abdominal ultrasound examination. There was no evidence of dynamic outflow obstruction, intracardiac thrombi, spontaneous echo contrast or fixed aortic/pulmonic stenosis.

Radiography Thoracic radiographs were obtained under mild sedation and revealed significant cardiomegaly, mild pleural effusion, hepatomegaly, ascites, venous congestion and pulmonary oedema. All these changes were consistent with right- and left-sided congestive heart failure.



✣ WHAT IS YOUR ASSESSMENT?

1 How would you interpret the echocardiographic findings?

(a) The presence of biventricular hypertrophy is pathognomonic of hypertrophic cardiomyopathy (HCM).
(b) Bi-atrial enlargement is suggestive of dilated cardiomyopathy (DCM).
(c) The presence of concentric ventricular hypertrophy in the absence of outflow obstruction, hyperthyroidism and systemic hypertension would suggest idiopathic HCM.
(d) Right ventricular hypertrophy is consistent with arrhythmogenic right ventricular cardiomyopathy (ARVC).

2 What are the clinical findings suggestive of bilateral congestive heart failure in this case?

(a) Dyspnoea and low/normal systemic arterial pressure.
(b) Dyspnoea and tachycardia.
(c) Jugular vein pulsation and abdominal enlargement.
(d) Tachypnoea and jugular vein pulsation.

Answers 1 (c) 2 (d)

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