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## **Asymptomatic hypertrophic cardiomyopathy: diagnosis and therapy**

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### **Keywords**

Echocardiography; cats; screening; biomarkers; risk; dynamic outflow tract obstruction; thromboembolism

### **Synopsis**

Hypertrophic cardiomyopathy (HCM) affects 1 in 7 cats and is especially common in older cats. Although many cats with HCM will have normal life expectancy, some cats develop life-threatening complications such as congestive heart failure (CHF), arterial thromboembolism (ATE) or sudden death. It is important to identify these 'high-risk cats. NT-proBNP is a useful initial screening test, and cats with plasma concentrations > 100 pmol/l should be further investigated, ideally by a cardiologist. Alternatively, if 'in-house' echocardiography reveals left atrial (LA) dilation, this may be sufficient grounds to consider a cat 'high-risk', and clopidogrel treatment to prevent ATE should be discussed with the owner. For cats with NT-proBNP concentrations <100 pmol/l and/or cats with normal LA size, NT-proBNP measurement should be repeated in 12 months as these findings do not rule out 'low-risk' HCM.

### **Key Points**

- Asymptomatic hypertrophic cardiomyopathy is common, affecting approximately 15% of apparently healthy cats and up to 25% of cats over 9 years of age.
- Diagnosis should focus on identifying cats with 'high-risk' HCM: those with increased risk of congestive heart failure or arterial thromboembolism.

- Murmur intensity does not correlate with the severity of HCM, and many high-risk cats have no audible murmur.
- The plasma biomarker NT-proBNP can be used as an initial screening test for high-risk HCM.
- A focussed 'in-house' echo to evaluate left atrial size provides important information: left atrial enlargement indicates high-risk HCM.

## **Disclosures**

The authors have no disclosures

## **Introduction**

Hypertrophic cardiomyopathy (HCM) is a disease of the myocardium where the walls of the left ventricle (LV) are abnormally thickened, and has a reported prevalence in cats of around 15%.<sup>1-3</sup> This means that HCM is one of the more common clinical conditions in domestic cats, but fortunately the majority of cats with HCM appear to have a benign clinical course (Figure 1).<sup>4</sup> Some cats with HCM will nevertheless develop congestive heart failure (CHF), arterial thromboembolism (ATE) or sudden death (SCD).<sup>4,5</sup> It is vital to identify these 'high-risk' cats with HCM as interventions such as general anesthesia or intravenous fluid therapy (IVFT) in this sub-group can result in CHF. Furthermore, antithrombotic therapy may potentially reduce their risk of ATE.

Although our understanding of risk factors for CHF and ATE has improved, many cats still remain undiagnosed until they reach a clinical crisis because we fail to screen adequately for these risk factors. Although echocardiography is the principal diagnostic tool for the identification of HCM, identifying affected cats with mild disease using echocardiography can sometimes be challenging even for experienced cardiologists. We suggest the emphasis for most clinicians should be on identification of cats with 'high-risk' HCM, and fortunately there are strategies available to the general practitioner for recognizing these vulnerable cats.

## **Diagnosis of HCM**

### ***Signalment***

The prevalence of HCM in apparently healthy young cats is relatively low (<5%), but HCM prevalence increases steadily with age, reaching nearly 30% in asymptomatic cats aged 9 years and older (Table 1).<sup>1</sup> Most cats remain asymptomatic and although clinical signs can occur at any age, the largest pool of 'at-risk' cats is among older cats. More male than female cats develop HCM, but male cats with HCM do not appear to be at higher risk of CHF or sudden death than female cats with HCM. Although several pedigree breeds are reportedly predisposed, HCM is also common in non-pedigree cats. Obesity has recently been suggested as another risk factor for left ventricular hypertrophy in cats.<sup>1</sup> Note that although older/overweight/ male cats are more likely to be affected with HCM than other cats, these factors are not specific risk factors for cardiac mortality within the HCM population as a whole.<sup>5</sup>

### ***Physical Examination***

Cardiac murmurs occur in 20-60% of cats, with the proportion of cats with a murmur increasing with age.<sup>1</sup> Causes of a heart murmur in cats include structural heart disease (myocardial disease, congenital heart disease); high cardiac output (e.g. anemia and hyperthyroidism); and ‘innocent’ (non-pathologic) murmurs. Murmurs in cats with HCM are often associated with dynamic left ventricular outflow tract (LVOT) obstruction, although they can also be associated with mid-ventricular obstruction of the LV.<sup>6,7</sup> Although loud murmurs are more likely to indicate structural heart disease and very loud murmurs (grade V/VI or greater) usually indicate congenital defects, it is often not possible to differentiate normal cats with innocent murmurs from cats with HCM. With both innocent murmurs and murmurs associated with HCM, the murmur intensity may vary with sympathetic tone. A change in murmur intensity does not necessarily indicate a change in disease status. Furthermore, a murmur may be absent in some cats with HCM, and the proportion of affected cats without a murmur increases in older populations. It is therefore important to realise that *murmur intensity does not relate to the severity of HCM*, and cats with HCM but no murmur have an increased risk of cardiac mortality.<sup>4</sup> Sinus tachycardia does not appear to be related to risk of CHF as it is in dogs.

Gallop sounds are a much more specific finding for HCM than heart murmurs. A gallop sound is said to be present when the S3 or S4 diastolic filling sounds are audible, and this generally reflects diastolic dysfunction. Gallop sounds are heard most often with high left atrial pressures and a stiff left ventricle, as found in ‘high-risk’ HCM but also with hyperthyroidism or anemia. Gallop sounds heard in geriatric cats that are otherwise normal may be related to delayed relaxation or may in fact be a systolic click misheard as a diastolic sound. An audible arrhythmia may also suggest underlying structural heart disease. Auscultation of either a gallop sound or arrhythmia is associated with increased risk of cardiac mortality,<sup>4</sup> (Box 1) and is grounds for further investigation.

### **Imaging and additional testing**

Often the presence of a heart murmur alerts suspicion that a cat may have HCM, but it is important to rule out non-cardiac diseases that are associated with a murmur and require specific treatment. Blood pressure should be measured in every cat with a murmur, and anemia should also be ruled out (especially if mucous membranes are pale). In older cats with a murmur, thyroxine should always be measured.

The gold standard test for diagnosing HCM is echocardiography, and many of the most important prognostic indicators in cats are echocardiographic variables. This can be a problem for many general practitioners, as cats are difficult to scan and echocardiography requires years of training and experience to make accurate measurements. It is particularly challenging to differentiate normal cats from those with mild localized hypertrophy, which is often the scenario when screening pedigree breeding cats for HCM, and is best left to specialists.<sup>8</sup> Fortunately, it is less challenging to differentiate high-risk cats with HCM from other cats using echocardiography. It is worth developing sufficient expertise to be able to carry out an ‘in-house’ echocardiogram, focussed on assessment of left atrial (LA) size.

### **Echocardiography**

The diagnosis of HCM is based on measurement of LV end-diastolic wall thickness. In clinical practice, LV hypertrophy is most often defined as LV wall thickness of 6 mm or greater. Other causes of LV hypertrophy should be ruled out before making a diagnosis of HCM; these include systemic hypertension, hyperthyroidism, hypersomatotropism, aortic stenosis, and pseudohypertrophy (wall thickening associated with hypovolemia). Of these conditions, systemic hypertension may be the most common in asymptomatic cats.

### ***High-risk HCM – echocardiographic features***

Cats with a high risk of CHF or ATE can be identified by the presence of the echocardiographic features listed in Table 2. Left atrial fractional shortening (LAFS%), LV systolic dysfunction and extreme LV hypertrophy have been reported to be independent predictors of cardiac mortality in cats with HCM.<sup>4</sup> Left atrial assessment is potentially within reach of any clinician with access to an ultrasound machine and appropriate ultrasound probe (thoracic radiography does not appear to be very sensitive for this purpose).<sup>9</sup> Use of thoracic ultrasound as a rapid cage-side test for trauma patients is becoming more widespread<sup>10,11</sup>, and a focused echocardiographic exam to assess left atrial size provides invaluable information to help stratify risk in cats suspected of having HCM. Some of the other factors listed in Table 2 require a greater degree of echocardiographic skill. In asymptomatic cats the LA variables and extreme LV hypertrophy are the most likely to be present. Systolic dysfunction has not been traditionally considered to be a feature of HCM in cats, but we are now recognizing a ‘burn-out’ phase of HCM that is termed ‘end-stage HCM’, and these cats have a particularly poor prognosis.<sup>12</sup> Myocyte death and replacement fibrosis in cats with

end-stage HCM can result in wall thinning, reducing any resemblance to the original HCM phenotype.

### **Dynamic LVOT obstruction**

Around a third of cats with HCM have LVOT obstruction due to systolic anterior motion (SAM) of the anterior mitral valve leaflet.<sup>1</sup> Abnormal arrangement of papillary muscles and chordae tendineae is common in cats with HCM, and can lead to abnormal movement of the anterior mitral valve leaflet towards the interventricular septum during systole (SAM).<sup>13</sup> The obstruction of the LV outflow tract caused by the abnormal position of the mitral leaflet leads to increased LV work and turbulent ejection of blood flow. At the same time, the MV leaflets fail to close effectively to seal the mitral annulus, resulting in secondary mitral regurgitation. Both turbulent LVOT flow and mitral regurgitation will result in a murmur. An increase in LV contractility increases the SAM, so in some cats dynamic LVOT obstruction (and a murmur) may only be present during stress or excitement.

The clinical significance of dynamic LVOT obstruction in cats is not known. In people with HCM, moderate to severe LVOT obstruction is associated with an increased risk of cardiac mortality. Retrospective studies have not shown an increased risk of cardiac death in cats with dynamic LVOT obstruction, but cats without LVOT obstruction are rarely diagnosed while asymptomatic because of the lack of an audible murmur, so that there is a bias in favor of earlier diagnosis in cats with LVOT obstruction.<sup>14</sup> Longitudinal prospective studies are needed to determine whether LVOT obstruction contributes to the development of a 'high-risk' HCM phenotype in cats. In people, dynamic LVOT obstruction increases myocardial oxygen consumption and ischemic signs. It is possible that chronic ischemic damage in cats with dynamic LVOT obstruction can lead to an end-stage HCM phenotype, and the presence of myocardial infarction in some cats is evidence that ischemic damage can be severe. Resolution of dynamic LVOT obstruction is not necessarily a favorable sign, as it can signal instead a deterioration in LV systolic function. *Further investigations may be warranted for cats in which a loud murmur is present in early adulthood but resolves in middle age or later life.*

### ***Screening for HCM in pedigree cats***

Although echocardiography is the principal test used for diagnosing HCM, it has some limitations. There is no consensus on the exact value of maximum allowable LV wall thickness that differentiates normal from hypertrophied, with 5 mm<sup>15</sup>, 5.5 mm<sup>16</sup> and 6 mm<sup>17</sup> all in use. Bodyweight also influences LV wall thickness, so a ‘one-size-fits-all’ cut-off value to differentiate normal from abnormal is unlikely to be appropriate.<sup>18</sup> Allometric scaling has been proposed, but has only been explored in Bengal cats.<sup>19</sup> In addition to wall thickness, there is a lack of consensus on the measurement technique that should be used. Some use M-mode echocardiography to assess LV wall thickness in one plane, whereas others measure LV wall thickness in multiple two-dimensional (2D) views.<sup>8</sup>

Echocardiographic strain imaging has been reported to identify subtle functional abnormalities in preclinical HCM in people,<sup>20</sup> and is abnormal in cats with mild HCM.<sup>21</sup> Strain imaging is not widely available however, and the ideal approach for echocardiographic screening of pedigree cats for HCM will probably remain a subject of controversy. Echocardiographic findings should ideally be interpreted in the context of family history.

### **Cardiac Biomarkers**

Cardiac biomarker testing for cats is widely available, inexpensive and does not require advanced training, so is being increasingly used as an initial screening test for cardiomyopathy in asymptomatic cats. Cardiac biomarkers can increase the confidence of non-specialists in identifying cats with HCM, and they should play an important role in identifying high-risk cats.

The two principal cardiac biomarkers in clinical use for cats are the N-terminal of pro-brain natriuretic peptide (NT-proBNP) and Troponin I (TnI). Brain natriuretic peptide (BNP) is rapidly produced by cardiomyocytes after stimuli such as myocardial stretch, ischemia, hypoxia and neurohormonal upregulation. The inactive N-terminal portion (NT-proBNP) is less labile and has a longer plasma half-life than active BNP, so is a more stable marker of BNP activity. The ability of NT-proBNP to distinguish between normal cats and asymptomatic cats with HCM has been evaluated in several studies.<sup>22-25</sup> Most studies have found the ideal cut-off value to differentiate between normal cats and cats with HCM is between 50-100 pmol/l.<sup>22-24</sup> The ability of NT-proBNP testing to differentiate cats with mild disease from healthy cats is not as good as its ability to identify cats with ‘high-risk’ HCM.<sup>22,26</sup> This means that NT-proBNP testing may be a valuable tool for screening cats for high-risk HCM prior to

potentially dangerous interventions such as general anesthesia or intravenous fluid therapy, but is unlikely to be sufficiently discriminating to be useful for screening pedigree cats to determine which cats should be used for breeding. NT-proBNP also has prognostic value, and plasma concentrations  $>250$  pmol/L are associated with increased risk of cardiac mortality.<sup>27</sup>

Quantitative assays mean a delayed result while the sample is sent off for analysis. A commercially available NT-proBNP point-of-care test (Cardiopet ProBNP SNAP® test, IDEXX Laboratories) can be used to differentiate ‘low-risk’ from ‘high-risk’ cats, as a negative result is expected in cats with plasma concentrations  $< 150$  pmol/L, an equivocal result in cats with concentrations between 150 and 200 pmol/l, and a positive result in cats with concentrations  $> 200$  pmol/l. Although a positive result should always be followed up with echocardiography, a negative result increases confidence that clinically significant heart disease is unlikely, even if mild HCM is not necessarily ruled out. For this reason, cats with a negative result should be monitored in case mild disease is present and this progresses in the future.

The cardiac troponins are a calcium-modulated complex of proteins involved in regulating the actin-myosin cross-bridges responsible for myocardial contraction. Troponin-I is released into the circulation in response to myocardial damage, and plasma concentrations increase according to the extent of injury of myocardial injury. Ischemic injury is an important cause of elevated troponin-I plasma concentrations in people, and may also be responsible for increased concentrations in cats. As ischemic damage can be intermittent, at times even cats with severe myocardial disease can have low plasma troponin-I concentrations, so this is not a particularly sensitive marker of ‘high-risk’ HCM.<sup>28</sup> High concentrations ( $>0.7$  ng.ml) have been associated with increased cardiac mortality, and this is independent of left atrial size.<sup>27</sup>

### ***Genetic Testing in pedigree cats***

The prevalence of HCM in the human population is approximately 1 in 500,<sup>29,30</sup> and around 60% of human HCM patients have a sarcomeric gene mutation. Over 1400 mutations in at least 11 genes have been identified in association with HCM, although mutations affecting the genes for myosin heavy chain (MYH7) and myosin binding protein C (MYBPC3) are most common. Single point mutations affecting MYBPC3 have been reported associated in Maine coon cats (A31P)<sup>31</sup> and Ragdoll cats (R820W)<sup>32</sup> with HCM. Both breeds are said to exhibit autosomal dominant inheritance and genetic tests for these mutations are commercially available.

The prevalence of the A31P mutation in Maine Coons is approximately 34% worldwide.<sup>33,34</sup> Penetrance is not 100%: some Maine Coons with the A13P mutation do not develop LV hypertrophy. Conversely, some Maine Coons develop LV hypertrophy and are diagnosed with HCM but are negative for the A31P mutation, suggesting there are causes of HCM other than the A31P mutation in Maine Coon cats.<sup>35</sup> The prognosis is worse in homozygous affected cats compared to heterozygous affected or wild type cats for both Maine coons<sup>36</sup> and Ragdolls<sup>37</sup>. As with Maine coons, some Ragdolls can develop HCM in the absence of the MYBPC3 mutation, so there are additional factors responsible for LV hypertrophy in this breed also. Familial HCM is suspected in other pedigree breeds, such as the Sphynx<sup>38</sup>, Persian<sup>39</sup>, American Shorthair<sup>40</sup>, Norwegian Forest Cat<sup>41</sup>, Bengal, British Shorthair, and Birman, as well as in non-pedigree cats<sup>12</sup>, but so far no other mutations have been associated with an HCM phenotype.

Although (when available) genetic testing is important for making breeding decisions about HCM, echocardiography remains the most important test for making clinical decisions about individual cats, even when a known HCM mutation is present.

## **Treatment of HCM in asymptomatic cats**

### ***Management Goals***

There is no consensus on the optimal way to manage HCM in asymptomatic cats.<sup>42</sup> In the absence of clinical trials evaluating the safety and efficacy of therapy for cats with HCM, decisions are based on extrapolation from human treatments, pathophysiologic assumptions or anecdotal perception of benefit. The ideal therapeutic approach would be to alter the progression of HCM during the preclinical or subclinical stage in order to prevent adverse sequelae such as CHF, ATE or sudden death. Failing this, therapy aimed at directly preventing CHF, ATE or sudden death would be preferred. An additional consideration in people with HCM is to ameliorate symptoms, independent of any effect on mortality. Symptoms of HCM in people include chest pain, and it is unknown whether this is also a problem in cats. The treatment goals in asymptomatic HCM are listed in Table 3.

### ***Treatment of Preclinical cats***

The concept of therapy for cats with preclinical HCM is still hypothetical, but there are a few situations where it is possible to predict that a cat will develop an HCM phenotype before LV hypertrophy is evident. Maine coon and Ragdoll cats that are homozygous for a MYBPC3 mutation have an increased risk of HCM compared with other cats. The molecule MYK-461 (an inhibitor of sarcomere contractility) has been shown to suppress the development of LV hypertrophy, myocyte disarray and myocardial fibrosis in mouse models of HCM.<sup>43</sup> Although there is currently no treatment that has been shown to prevent development of an HCM phenotype in cats, the effects of MYK-461 suggest it may one day be possible to prevent development of an HCM phenotype in predisposed cats.

### ***Treatment of Low-risk cats***

It is hard to justify any treatment in cats considered to have a favorable prognosis. Medicating a cat can have a major impact on the quality of life of both owner and cat<sup>44</sup>, so in general we should withhold therapy in low-risk cats unless there is evidence to support use of a particular treatment. At present, no such evidence exists for cats.

Against this argument, we should weigh up the consideration of whether owners are always capable of discerning whether their cat is truly 'asymptomatic'. People with HCM can experience angina, and although it is difficult to know whether cats experience chest pain, we do know that myocardial ischemia can be sufficiently severe in cats to result in myocardial infarction. Treatment strategies for cats with HCM have often followed human treatment guidelines, and beta-adrenergic antagonists are commonly recommended for symptomatic relief of dyspnea and chest pain associated with HCM in people, despite a lack of evidence to support an effect on outcome.<sup>45</sup> Atenolol has been documented to reduce the pressure gradient across the LVOT in cats with HCM<sup>46</sup>, and this is one of the goals of therapy for symptomatic human HCM patients. Anecdotally, some owners report an increase in activity levels following atenolol treatment of cats with dynamic LVOT obstruction, although this has not been substantiated.

Administration of atenolol to cats with HCM did not result in any appreciable effect on 5-year survival rates compared with untreated cats.<sup>47</sup> Quality of life was not evaluated in this study, so while it is possible that atenolol had a favorable effect on unobserved signs (such as chest pain), there is no evidence for this.

A recent study of cats with HCM and dynamic LVOT obstruction demonstrated abolition of

catecholamine-provoked LVOT gradients with MYK-461 treatment, showing that a decrease in sarcomere contractility is sufficient to reduce dynamic LVOT obstruction.<sup>48</sup>

Until more is known about the effect of dynamic LVOT obstruction on clinical signs and clinical outcome, it is difficult to assess the importance of treatments that reduce LVOT obstruction in cats. The risk of ischemia may be increased in cats with severe hypertrophy and/or dynamic LVOT obstruction, and some clinicians still use atenolol in such cats to mitigate the possible effects of ischemia.<sup>46</sup> In cats perceived to be asymptomatic and otherwise at low risk of CHF or ATE (e.g. normal LA size and absence of extreme hypertrophy or LV systolic dysfunction), no treatment is currently indicated.

### ***Treatment of High-risk cats***

Many cats presenting with CHF or ATE have no prior diagnosis of cardiac disease, suggesting we should be more pro-active about screening for high-risk HCM. Although no treatment has been identified that reduces the risk of CHF, there is evidence supporting use of clopidogrel to reduce the risk of ATE.<sup>49</sup> Clopidogrel is an irreversible antagonist of the platelet adenosine diphosphate (ADP) receptor, inhibiting primary and secondary platelet aggregation. The FAT CAT study was a multicenter, double-blind, randomized study of 75 cats that had survived an episode of ATE, and median time to a recurrent ATE event or cardiac death was prolonged with clopidogrel (346 [95%CI 185–990] days) compared to aspirin (128 [95%CI 58–243] days). Clopidogrel was well tolerated and bleeding complications were not reported. Although there have been no prospective clinical trials reporting primary prevention of an initial episode of ATE in cats, it seems reasonable to extrapolate the results to primary prevention in cats at high risk of an ATE event.

Warfarin has been recommended in the past in cats, but both safety and efficacy were suboptimal. Some of the newer oral Factor Xa antagonists are showing promise in thromboprophylaxis in people, and rivaroxaban is currently being explored as a potential treatment to reduce the risk of ATE in cats.

### **Summary**

Widely available tests can be combined to provide a sound approach to identifying cats at high risk of cardiac complications (see Figure 2). Any cat with a murmur, gallop or arrhythmia

should be considered a candidate for HCM diagnosis, as should any cat aged 9 years or older. The diagnostic priority should be to identify cats with 'high-risk' HCM (i.e. at increased risk of CHF or ATE). Other systemic causes of a murmur should be identified (e.g. hyperthyroidism, systemic hypertension, anemia) as these conditions will require specific treatment.

NT-proBNP is an appropriate initial screening test, and a plasma concentration > 100 pmol/l (or a positive point-of-care test) should alert suspicion of the possibility of 'high-risk' disease. The ideal follow-up test is echocardiography performed by a cardiologist, but an 'in-house' echocardiogram to assess LA size will also provide very valuable information. Cats with obvious LA dilation should be considered 'high-risk', and clopidogrel treatment should be discussed with the owner. For cats with NT-proBNP concentrations <100 pmol/l and/or cats with normal LA size, NT-proBNP measurement should be repeated in 12 months as these findings do not rule out 'low-risk' HCM. Some cats with HCM will remain at low risk of complications for decades, whereas others will progress quickly.

This approach is relatively low-cost and could increase the proportion of high-risk cats that are identified before the onset of life-threatening clinical signs. If clopidogrel is even partly effective at reducing the number of ATE events, then this approach could potentially save many feline lives.

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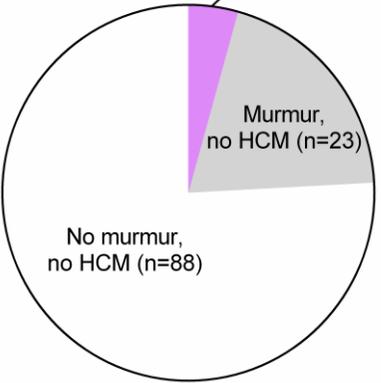
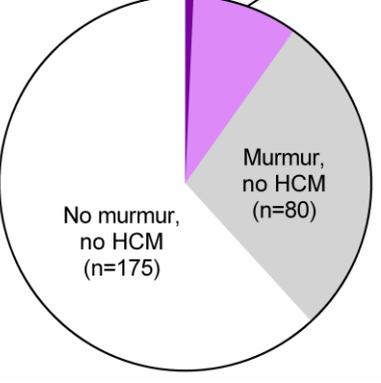
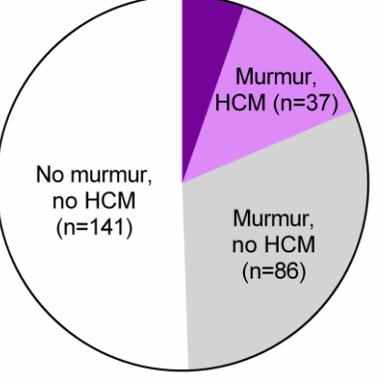
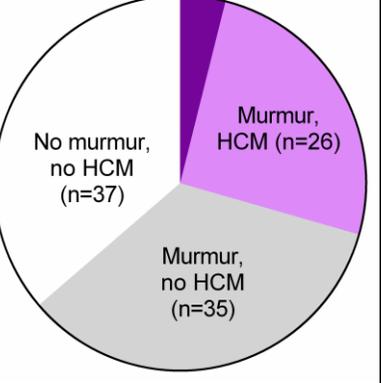
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**Table 1 – Prevalence of heart murmurs and hypertrophic cardiomyopathy (HCM) in 780 apparently healthy cats from rehoming centers.**

(From: Payne et al. Cardiomyopathy prevalence in 780 apparently healthy cats in rehoming centres (the CatScan study). J Vet Cardiol 2015;17:S244-S257, with permission)

	Juvenile – 6-12 months (n=116)	Young adult – 1-3 years (n=283)	Adult – 3-9 years (n=279)	Senior – 9 years or older (n=102)
				
Heart murmur prevalence	24.1%	37.5%	44.1%	59.8%
HCM prevalence	4.3%	9.9%	18.6%	29.4%

**Box 1*****'High-risk' HCM: signalment & physical exam features***

- No murmur
- Presence of a gallop sound
- Audible arrhythmias

**Table 2: ‘High-Risk’ HCM - echocardiographic features.**

Echocardiographic features associated with increased risk of congestive heart failure and/ or arterial thromboembolism.<sup>4</sup> The most influential predictors are shown in bold. LA: left atrial; LA/Ao: ratio of left atrial diameter in a right parasternal short axis view to aortic diameter at end-systole; LV: left ventricular; IVS: interventricular septum; E: early transmitral flow velocity measured with Doppler echocardiography; A: atrial transmitral flow velocity; LAA: left atrial appendage.

<b>High risk feature</b>	<b>Comments</b>
LA dilation	LA diameter in a right parasternal long-axis 4-chamber view >16mm at ventricular end-systole <i>and/ or</i> LA/Ao >1.8
<b>Reduced LA fractional shortening</b>	M-mode of the LA in a short axis view: Percentage systolic change in LA diameter <12 %
<b>LV systolic dysfunction</b>	LV fractional shortening $\leq 30\%$
<b>‘Extreme’ LV hypertrophy</b>	Maximal end-diastolic IVS or LV free wall thickness $\geq 9\text{mm}$
Spontaneous echo contrast	Most easily visible in the left atrial appendage in a left cranial parasternal view
Regional wall motion abnormalities	Hypokinesis of the LV free wall is usually an indicator of a prior myocardial infarction
Restrictive diastolic filling pattern	Transmitral blood flow velocities: E/A >2.0
Reduced velocities of left atrial appendage flow	Peak LAA blood flow velocities < 0.25 m/s

**. Table 3: Treatment goals in asymptomatic HCM according to stage.**

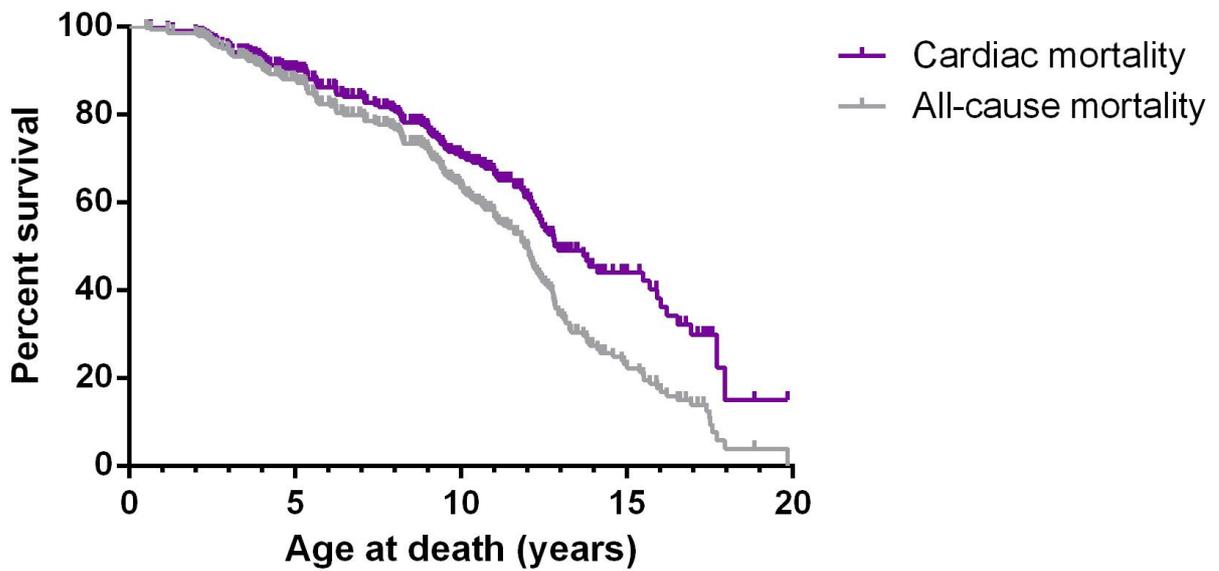
HCM: hypertrophic cardiomyopathy; CHF: congestive heart failure; ATE: arterial thromboembolism

<b>Subclinical HCM stage</b>	<b>Treatment goals</b>	<b>Recommendations</b>
'Low-risk' cats	Prevent progression of LV hypertrophy, fibrosis	No treatment known to be effective
	Reduce dynamic LVOT obstruction to reduce effects of ischemia	Despite no documented beneficial effect on survival, some clinicians recommend atenolol, titrated to achieve a heart rate $\leq 165$ bpm:  6.25mg q24h PO,  titrated upwards over 7 days to 6.25mg q12h PO,  then to 12.5mg (am) and 6.25mg (pm),  up to a maximum of 12.5mg q12h PO
'High-risk' cats	Prevent CHF, ATE, sudden death	No known means of preventing CHF or sudden death  Clopidogrel is given at 18.75mg per cat q24h PO to prevent ATE (recommend administering in gelatin capsule)

## Figure legends

### Figure 1. Survival in 282 cats with hypertrophic cardiomyopathy according to age

Median age at diagnosis was 6.2 years (IQR 2.8 – 9.7), and median survival time post-diagnosis was 5.9 years (IQR 0 – 7.5) (From Payne et al., Prognostic indicators in cats with hypertrophic cardiomyopathy. J Vet Intern Med 2013;27:1427-1436; with permission)



**Figure 2: Approach to the asymptomatic cat with suspected heart disease.**

CHF: congestive heart failure; ATE: arterial thromboembolism; BP: blood pressure, PCV: packed cell volume; T4: thyroxine.

