

EDITORIAL



Today's scientists regard the brain as the highest center within the body, recognizing its all-important role in controlling and maintaining life itself, but scientists of previous centuries – the philosophers, mystics, and theologians – were united in their belief that the heart was the center of life itself, perhaps due to its position in the approximate center of the physical body, and because it was recognized that the heart's function was essential for existence. It was thus accorded enormous significance, with spiritual attributes and reverence. But there was – and is – another aspect to it: in many cultures it has been regarded as the symbol of love and passion, and the metaphors abound – witness the many sayings and customs that refer to the heart, in that we talk about letting the heart make crucial decisions, or of sorrows breaking one's heart, or loving someone with all one's heart.

The leap from passionate mythology and popular culture to the dispassionate science that is cardiology is not a natural one – the metaphysical beliefs and the physical reality are poles apart. But the idea that the heart is crucial to life is of course well beyond myth – if disease strikes, death can swiftly follow – and the topic of feline cardiology is a pertinent topic for Veterinary FOCUS to tackle. It would be an easy but trite suggestion to propose that this issue gets to the heart of the matter, but the discipline of cardiology has progressed greatly in recent years, and our belief is that the papers herein will give the clinician a passion and excitement for the science, and we trust that the reader will benefit from the emotions of the authors.

... the Veterinary FOCUS team also has a passion. Namely, to be at the heart of disseminating knowledge and we are delighted to announce that as of now readers will be able to access this journal on the iPad. Not only can each issue be downloaded in full, be read wherever and whenever one wishes, the electronic version contains extras such as video clips and sound tracks that will add to the knowledge and understanding of the reader. We hope that you will love it!

Ewan McNeill
Editor-in-Chief

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Cardiac dysrhythmias



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Introduction

A dysrhythmia is literally an abnormal or disordered heart rhythm; the term arrhythmia (the lack of normal regular rhythm) is used synonymously in cardiology. Dysrhythmias in cats are a less common primary reason for presentation to veterinarians than dysrhythmias in dogs. The smaller heart size may protect against some hemodynamically significant tachyarrhythmias, and cats, with their inherently relaxed lifestyle, are well able to mask serious arrhythmias or severe

heart disease. However, if dysrhythmias are identified, further investigations are warranted, since most cats with dysrhythmias have primary cardiac disease, commonly a primary or secondary cardiomyopathy. Syncope in cats is much less common than in dogs. Seizure activity is a common sequel to syncope so it may be more difficult to distinguish between neurological and cardiac causes of clinical signs in cats than in dogs. Electrolyte disturbances may also be responsible for arrhythmias. In this article, the approach to the feline patient with suspected or identified dysrhythmia and the methods of confirming the diagnosis and treatments are reviewed.

History and clinical examination

Identification of an arrhythmia is much more likely to be an incidental finding during the clinical examination, rather than in a cat with a history of exercise intolerance or collapse. The owner may well present the cat because of other clinical signs, referable to primary or secondary cardiac disease (e.g. dyspnea, open-mouth breathing) or systemic conditions (e.g. signs of hyperthyroidism or systemic hypertension, stranguria or oliguria). On clinical examination, from careful auscultation, note the following:

- **Heart rate and rhythm:** heart rate is less useful than in dogs for suggesting congestive heart failure (CHF), as some cats in CHF have sinus bradycardia. Sinus arrhythmia, while possible in relaxed cats at home as identified from Holter monitoring (1), should be regarded with suspicion during a consultation, as it may indicate elevated vagal tone due to respiratory or other pathology. Tachycardia may merely reflect the stressed state of the cat, but tachyarrhythmias should be investigated fully. Premature beats are often quieter than the normal heart sounds, and the clinician is often more aware of the pause following this beat. It is useful to simultaneously palpate the femoral pulse. Pulse deficits are audible heart sounds

KEY POINTS

- ➔ Most cats with cardiac dysrhythmias have heart disease although other systemic conditions must also be considered.
- ➔ Dysrhythmias may be transient, so identification of their presence and significance can be elusive.
- ➔ In a cat presenting with syncope or seizures, it is important to exclude cardiac disease or episodic dysrhythmia.

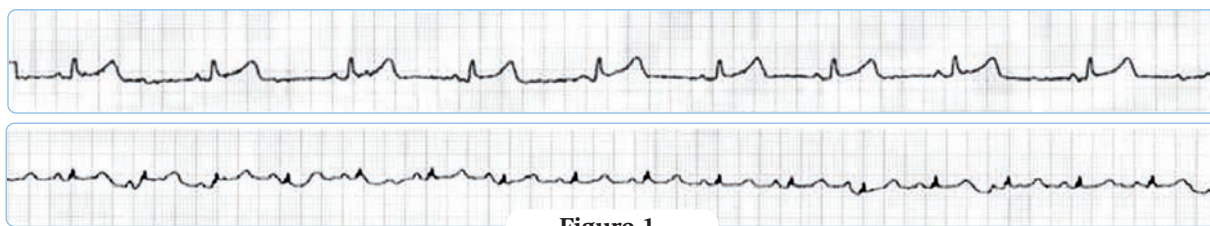


Figure 1.

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Lead II ECG showing bradycardia in a cat suffering from vomiting, dehydration and hypothermia. The top ECG was taken at presentation and shows sinus bradycardia (HR 110 bpm and large T waves). The bottom ECG was recorded 30 minutes after atropine and intravenous fluid therapy. Note the increased heart rate (190 bpm) and more normal T waves.

without a corresponding pulse, and are a common finding in tachyarrhythmias.

- **Auscultation abnormalities:** heart murmurs should be noted. They may reflect the presence of congenital or acquired myocardial disease. A murmur is most common in hypertrophic (obstructive) cardiomyopathy (HOCM), and may vary in intensity depending on the cat's state of stress or calmness. Absence of an audible heart murmur does not exclude significant myocardial disease (2). Diastolic gallops (audible third or fourth heart sounds) are abnormal in cats, and indicate impaired relaxation and/or decreased compliance of the left ventricle; their presence indicates diastolic dysfunction and actual or imminent decompensation into CHF. These sounds should not be confused with a dysrhythmia.
- **Signs of congestive heart failure:** left-sided CHF is manifested as pulmonary edema (mild tachypnea to overt dyspnea, with inspiratory crackles evident on auscultation of the lung field). Right-sided or biventricular failure signs in the cat may be more subtle than in the dog, and may be limited to distended jugular veins or a positive hepatjugular reflux. Pleural effusion is the most common manifestation of biventricular failure. Ascites is much less common in cats than in dogs with right sided CHF, but it can occur. Signs of forward heart failure include hypotension, hypothermia, weak peripheral pulses and pallor with slow capillary refill.
- **The rest of the physical examination:** hyperthyroidism is a relatively common cause of pre-

mature beats and secondary cardiomyopathy, and careful palpation of the neck is indicated. Cats appear to be less likely than dogs to show ventricular arrhythmias in association with systemic conditions such as abdominal pain, pancreatitis, intoxications etc., but may be more likely to show bradycardia or bradyarrhythmias (3,4) (**Figure 1**). Furthermore, in anuric or oliguric renal failure or urinary tract obstruction, hyperkalemia can result in bradycardia and other characteristic ECG findings (5). It is important that these signs are detected on initial clinical examination, and investigated further.

In the occasional cat with syncopal/seizure episodes, no abnormality of heart rate or rhythm may be evident at initial presentation, as dysrhythmias may be transient.

Investigation of dysrhythmias *Electrocardiography*

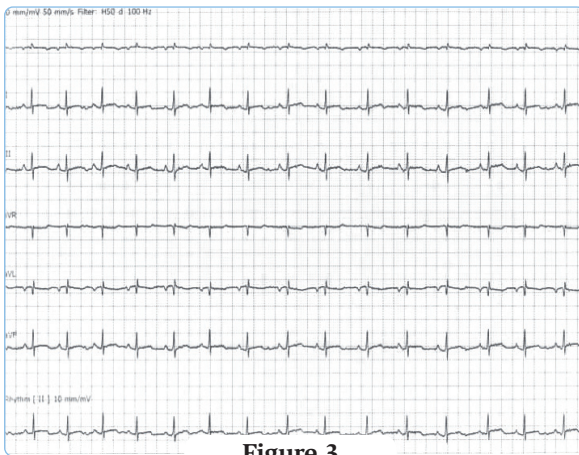
In a cat with an arrhythmia identified on auscultation, a standard 6 lead ECG is indicated to attempt to document this, to determine diagnosis and significance. Although right lateral recumbence is advocated for a standard ECG in a dog, many cats prefer to be in sternal recumbence, this limits patient stress. It has little effect on the measurements of the ECG (6) (**Figure 2**). Feline ECGs are more difficult to interpret than in dogs, because low voltage complexes are normal (**Figure 3**), and P and T waves can be difficult to discern, even though P wave identification is vital in interpreting the heart rhythm. It can be beneficial to increase sensitivity (e.g. 1 mV/20 mm) and use the fastest paper speed possible (usually 50 mm/s on most ECG machines). The normal low voltage of the



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Figure 2.

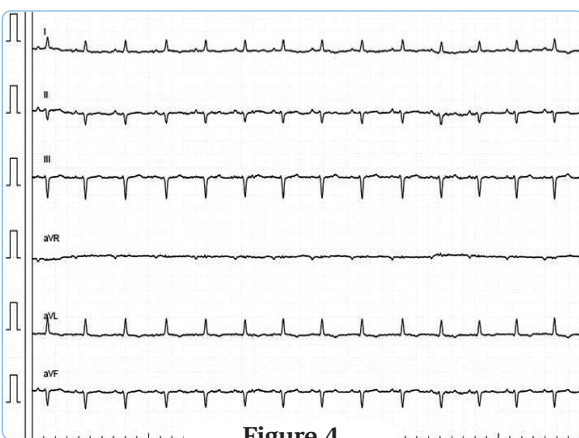
Cat in sternal recumbence undergoing a standard six limb lead ECG recording.



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Figure 3.

A normal 6-lead ECG from a 9-year-old cat obtained as part of the investigation of a recently detected heart murmur.



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Figure 4.

ECG from an elderly cat with hypertension. Leads I and aVL are positive, but there are deep S waves in leads II, III and aVF, meeting the criteria for a left anterior fascicular block pattern.



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Figure 5.

ECG from a cat with left sided congestive heart failure associated with restrictive cardiomyopathy (RCM). Tall, wide P waves are consistent with left atrial enlargement. The QRS complexes are negative in leads I, II, III and aVF, giving a right axis deviation. Right ventricular enlargement had been excluded on echocardiography. This conduction disturbance is consistent with an incomplete right bundle branch block.

feline ECG complexes means that the ECG can be adversely affected by noise, such as electrical interference, purring, trembling, etc. Every attempt should be made to get a clean baseline. Standard ECG measurements of complex amplitudes and durations are from lead II, but any of the leads which optimize the P waves and QRS complexes can be used to assess rhythm.

In cats with heart disease but without a documented arrhythmia, the ECG may have conduction or other abnormalities suggestive of cardiac disease. Common intraventricular conduction disturbances include patterns consistent with left anterior fascicular block (**Figure 4**) and complete or incomplete right bundle branch block (**Figure 5**) or just notching of the QRS complexes. Although the ECG is an insensitive indicator of chamber enlargement in contrast to echocardiography, evidence of chamber enlargement can include tall R waves (left ventricular enlargement) and tall and/or wide P waves (atrial enlargement but not specific for right *versus* left or bi-atrial enlargement) (**Figure 6**). The ECG may also give evidence of myocardial hypoxia/ischemia, particularly with changes in the ST segment.

Holter monitoring

If the history suggests a transient arrhythmia is possible (e.g. episodic syncope/seizure events) or to further investigate the significance of arrhythmias identified during the clinical examination or on standard ECG, a 24 hour ECG recording can



Figure 6.

ECG from a young cat with HCM and congestive heart failure. Lead II R wave amplitude is increased, consistent with left ventricular enlargement and lead II P waves are both tall and prolonged; P mitrale is consistent with left atrial enlargement.



Figure 7.

Cat equipped with a Holter monitor; bandaging has been used to secure the ECG electrodes on the chest wall, and to protect the cable and the Holter unit itself.

be obtained with a Holter device (7). Normally, cats will not tolerate the device worn bandaged to their bodies, but the ECG electrodes can be attached to the chest wall, secured with bandaging material, and the device and cable trailed beside the cat, while hospitalized (Figure 7).

Event recorders

Event recorders are available and may be attached in a similar way to Holter monitors. These record a continuous loop of ECG (e.g. 3 minutes), but if an event is noted, and the record button activated, the ECG prior to, during and after the event can be saved (8). As with Holters, these external devices can encumber the cat and will therefore significantly impact on its normal behavior. An alternative is a commercial loop recorder device which can be implanted subcutaneously (requiring a brief general anesthetic); this means that the cat can behave completely normally and the device can be interrogated periodically or after an event via a programmer (9,10).

Other investigations of possible cardiac disease

Since arrhythmias in cats are commonly associated with structural heart disease, and some cardiac diseases may not have any auscultation abnormality, further investigations are warranted. These include:

- **Echocardiography:** ultrasound is exquisitely sensitive for measurement of heart chambers and wall thickness, and to assess systolic function.

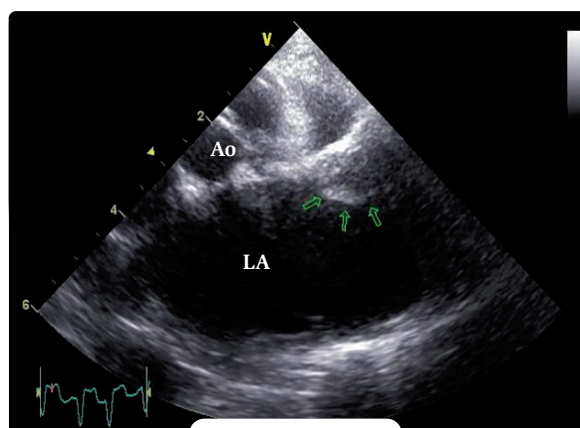
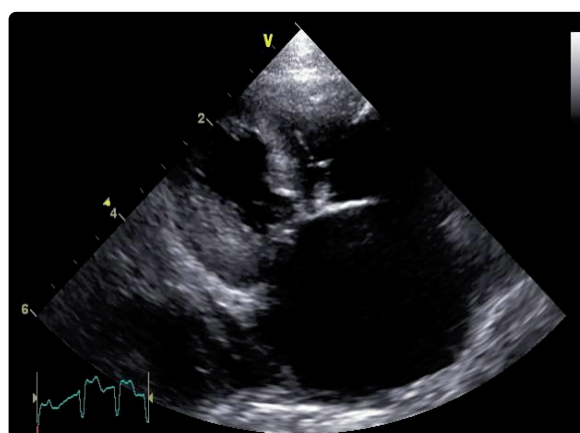


Figure 8.

Top: 2D echocardiogram right parasternal four chamber long axis view, showing marked left atrial dilatation, and evidence of high left atrial pressure with the interatrial septum bulging towards the right atrium. Concentric left ventricular hypertrophy can also be appreciated.

Bottom: 2D echocardiogram; left cranial short axis view, showing the dilated left atrial appendage. A thrombus can be seen (green arrows) and spontaneous echocontrast ("smoke") was visible within the left atrium (LA) on the moving image. Ao = aorta in cross section.

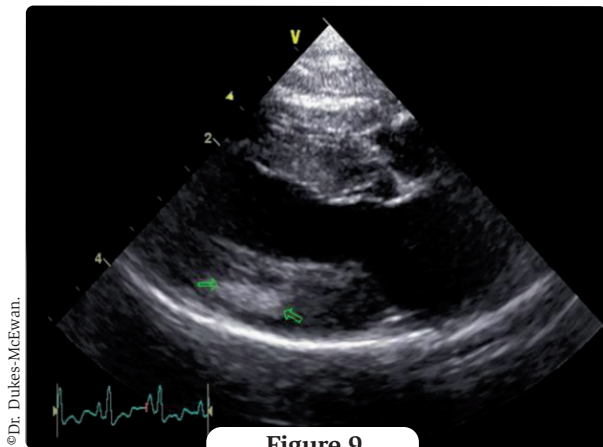


Figure 9.

Right parasternal long axis four chamber view echocardiogram showing a well defined hyperechoic region in the mid-left ventricular freewall (green arrows), suspected to be an acute myocardial infarct.

Any effusions (pleural or pericardial) are readily detected. Doppler echocardiography methods can be used to assess diastolic dysfunction and filling pressures in the heart (11). In addition, with very marked left atrial dilation and impaired atrial function, spontaneous echocontrast may be evident (“smoke”), or even overt thrombus material (**Figure 8**) indicating the cat is at risk of systemic thromboembolism. In the cat with hypertrophic cardiomyopathy (HCM), arteriosclerosis is present (12), and myocardial infarction can result. These cats may have ventricular arrhythmias and recent infarcts may be evident (**Figure 9**). Sometimes an old infarct is inferred by the presence of a very thin segment of left ventricular wall (often the base of the lateral wall) (**Figure 10**). In other cats, the impression

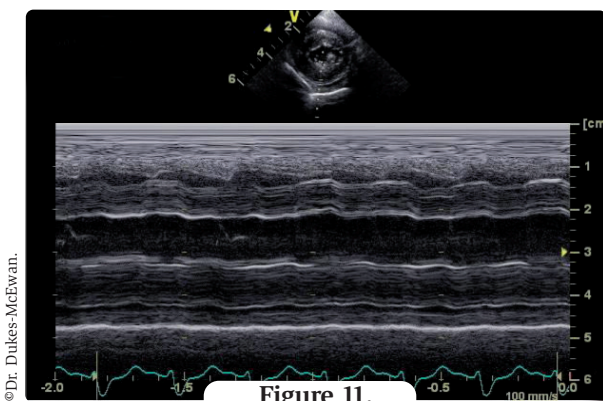


Figure 11.

M-mode echocardiogram from a cat with severe HCM showing left ventricular concentric hypertrophy but very poor systolic function, consistent with myocardial stunning.



Figure 10.

Right parasternal long axis five chamber view echocardiogram; the left ventricular freewall (other than the basal segment) from the mid to apical segment is very thin, suggestive of an old myocardial infarct. A ventricular premature complex can be seen in the simultaneous ECG, recognized as being wide and bizarre with an oppositely directed T wave.

of myocardial stunning, with very poor function and severe hypotension indicating cardiogenic shock, may be noted (**Figure 11**).

- **Indirect blood pressure estimation** (e.g. systolic blood pressure by the Doppler method). This is important to exclude hypotension, such as with cardiogenic shock with severe underlying cardiac disease, but also systemic hypertension, which can result in secondary cardiomyopathy.
- **Thoracic radiography** is more important to confirm the presence of pulmonary edema or pleural effusions when CHF is present.

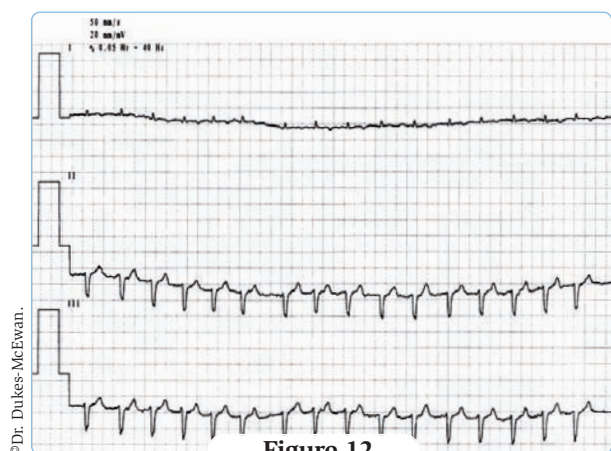


Figure 12.

Leads I, II and III from a cat with advanced HCM and congestive heart failure showing atrial fibrillation. QRS complexes are irregularly irregular and there are no P waves. There are deep S waves in leads II and III with positive lead I (and AVL), consistent with a left anterior fascicular block pattern.



Figure 13.

Leads I, II & III from a cat with both HCM and mitral stenosis. The cat is predominantly in sinus rhythm, but there are frequent supraventricular premature complexes (SVPCs). These are narrow and similar in appearance to the normal QRS complexes, but occur prematurely (e.g. 2nd, 4th and 5th complexes from the left).

- **Cardiac biomarkers** should also be assessed. Cardiac troponin I levels are of prognostic significance and very high levels may indicate the presence of myocarditis or ischemia. However, cardiomyocyte damage may be the consequence of systemic disease, not just primary cardiac disease. NT pro-BNP levels are reliably high in cats with cardiomyopathy and have been proposed for screening for disease (13). However, renal insufficiency may also result in increased levels.

⊠ Arrhythmias associated with cardiac disease

Atrial fibrillation (AF) occurs because of atrial stretch (**Figure 12**). Whether atrial fibrillation is able to develop and become sustained depends on atrial mass, so cats, with small body size, are much less likely to develop AF than larger animals and therefore the presence of AF normally indicates advanced heart disease and severe atrial dilation (14). It is therefore considered to be a poor prognostic indicator in this species. In humans, AF is associated with risk of thrombus formation and thromboembolic stroke. In cats, atrial dilatation and spontaneous echo contrast (“smoke”) has been associated with arterial thromboembolism and it is likely that concurrent atrial fibrillation exacerbates this risk.

Supraventricular (atrial) premature complexes may occur with less severe atrial stretch (**Figure 13**), but their presence may herald the future development of AF.

Ventricular premature complexes (VPCs) or ventricular tachycardia can occur in cardiac

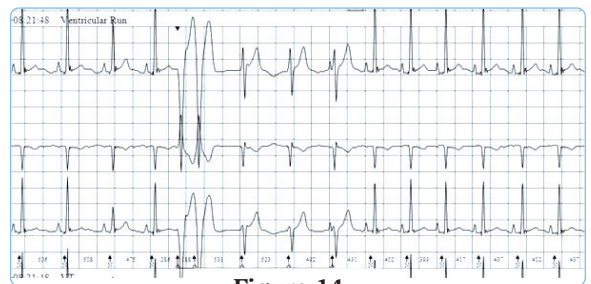


Figure 14.

A Holter recording from a cat with HCM and suspected myocardial infarction. A ventricular couplet is seen, with the R on T phenomenon (2nd QRS complex arising at the end of the 1st complex's T wave). The couplet is followed with a slower instantaneous rate of three ventricular ectopics (accelerated idioventricular rhythm) prior to resuming sinus rhythm.

disease for various reasons, and most cats with ventricular tachyarrhythmias have cardiac disease (15). Increased left ventricular wall stress can occur in both acquired (**Figure 14**) and congenital heart disease (**Figure 15**). With hypertrophy, myocardial hypoxia may occur giving the potential for arrhythmias. Arteriosclerosis is known to occur in HCM leading to myocardial infarction or ischemia (12). The presence of arrhythmias or a history of syncope are negative prognostic factors in feline HCM (16). Finally, the progression of heart disease can result in histological changes of the myocardium, such as myocardial fibrosis. In arrhythmogenic right ventricular cardiomyopathy (ARVC), there is a marked fat or fibrofatty infiltrate into the myocardium; a change of substrate resulting in malignant ventricular arrhythmias (17).

Some cats with cardiac disease, particularly cardiomyopathies, may show bradyarrhythmias. Although not clinically relevant on its own, an ECG diagnosis of 1st degree atrioventricular (AV) block in myocardial disease is not uncommon. Second and third degree AV blocks are often not clinically significant as cats have a high escape rate (e.g. 100-120 bpm) and compensate for any bradyarrhythmia (18). Furthermore, they may be transient arrhythmias, and recognition may depend on device monitoring (7). AV blocks may be associated with HCM if there is gross fibrosis around the AV node and conduction system (19) (**Figure 16**). Note that many cats with symptomatic third degree AV blocks may present with seizures rather than a classic flaccid syncope (20). AV blocks may also be identified in the absence of any other recognized structural or functional heart disease, i.e. idiopathic cases.

Table 1.

Some anti-arrhythmic drugs which may be used in cats with hemodynamically significant arrhythmias.

Drug	Suggested dose	Indications	Contraindications and precautions
Atenolol 25 mg tablets	6.25 mg per cat every 12-24 hours	<ul style="list-style-type: none"> • Rate control in AF • Hemodynamically significant supraventricular or ventricular arrhythmias. • In HCM, often used to reduce the dynamic left ventricular outflow tract obstruction in absence of arrhythmias. 	<ul style="list-style-type: none"> • Do not use in presence of uncontrolled CHF. • Beta blockers are negative inotropes; do not use with poor systolic function. • Do not use in bradycardic cats. • Do not use in cats with bronchial disease/asthma. • Use slow up-titration in cats with advanced cardiac disease
Diltiazem 10 mg tablets	5-10 mg per cat every 8 hours	<ul style="list-style-type: none"> • Rate control in AF • Hemodynamically significant supraventricular arrhythmias (e.g. supraventricular tachycardia). • May improve lusitropy. 	<ul style="list-style-type: none"> • Calcium channel antagonists are negatively inotropic; use with care in patients with poor systolic function. • Do not use for ventricular arrhythmias (ineffective). • Do not use in bradycardic cats.
Digoxin 62.5 µg tablets	15.625-31.25 µg per cat every 24-48 hours	<ul style="list-style-type: none"> • Rate control in AF • Weak positive inotrope, so may select if beta blockers or diltiazem considered contraindicated. 	<ul style="list-style-type: none"> • Do not use/contraindicated for ventricular arrhythmias • Do not use in azotemic cats • Check digoxin drug level after 7 days; aim for trough (8 hours post pill) level of < 1 ng/mL.
Lidocaine 1% or 2% solution 10 mg/mL or 20 mg/mL	0.5-1 mg/kg IV bolus; repeat if required, up to maximum of 2 mg/kg over 10 minutes.	<ul style="list-style-type: none"> • Hemodynamically significant ventricular tachycardia 	<ul style="list-style-type: none"> • Side effects include muscle fasciculations, CNS signs, seizures, nausea.
Sotalol 40 mg tablets	10 mg per cat every 12 hours	<ul style="list-style-type: none"> • Hemodynamically significant supraventricular or ventricular arrhythmias. • Rate control in AF 	<ul style="list-style-type: none"> • Care with poor systolic function or congestive heart failure, as causes some beta blockade. • Do not use in bradycardic cats.
Terbutaline 5 mg tablets	1.25 mg per cat every 8-12 hours	<ul style="list-style-type: none"> • Hemodynamically significant bradyarrhythmias 	<ul style="list-style-type: none"> • Side effects (high doses) can include excitement/irritability.

❖ Possible causes of arrhythmias

It is important to remember that arrhythmias may result from other systemic conditions. Potential causes of tachyarrhythmias, especially ventricular arrhythmias include myocardial contusions associated with trauma, hyperthyroidism, causes of systemic hypertension, and myocarditis (e.g. *Toxoplasma*, *Bartonella*). Many cats with systemic conditions may show bradyarrhythmias (**Figure 1**).

An important cause of a bradyarrhythmia, which is vital to recognize promptly, is hyperkalemia. On ECG, there may be no evidence of atrial activity (atrial standstill; no visible P waves) and tall spiky T waves. QRS complexes may become wide. Hyperkalemia can be a consequence of urinary tract obstruction or anuric acute renal failure. Sepsis, hypoglycemia and intoxications may also result in bradycardia or bradyarrhythmias.

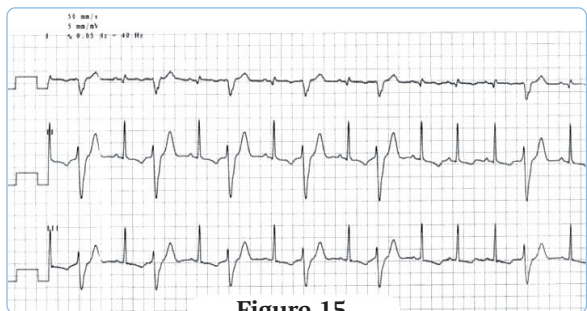


Figure 15.

Leads I, II & III from a young cat with congestive heart failure due to patent ductus arteriosus. R wave amplitudes are greatly increased, consistent with left ventricular enlargement. For the initial part of the ECG, ventricular bigeminy is evident (sinus complexes alternating with ventricular premature complexes).

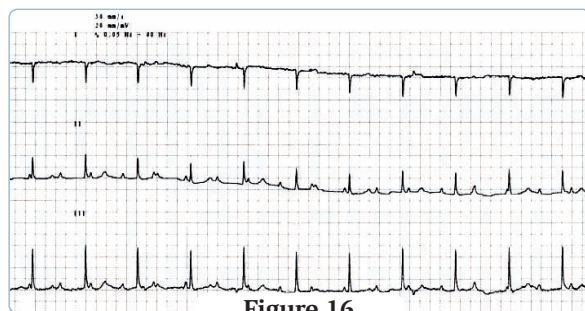


Figure 16.

Leads I, II and III from a cat with 3rd degree (complete) atrioventricular block. QRS complexes are regular at 110 bpm. They are escape complexes, probably originating in the ventricular septum as they are not particularly wide and bizarre. The P waves show no association with the QRS complexes, and can be seen wandering through the ECG.

It is unusual for a cat to show sinus arrhythmia in a consulting room situation or during an ECG recording (**Figure 17**). If sinus arrhythmia is detected, it is important to exclude causes of high vagal tone, such as feline asthma and other thoracic, abdominal or ocular disease.

If arrhythmias are suspected to be due to systemic diseases, other additional investigations warranted include total T4 (in cats > 7 years of age), blood pressure measurement, routine hematology and biochemistry to check for other dysfunction, and abdominal ultrasound.

Treatment of arrhythmias

In cats, arrhythmias are most commonly secondary to either cardiac or systemic disease. The most important treatment of the arrhythmia is therefore to recognize and treat the underlying condition; optimize CHF treatment in a case with known

cardiac disease; and correct the systemic or metabolic disturbance.

In atrial fibrillation, assess the ventricular rate once treatment of CHF has been optimized. Once atrial fibrillation has been established, it is very unlikely that conversion to sinus rhythm will be achievable, so controlling the ventricular response and overall heart rate is the treatment goal. In cats, unlike dogs, once the underlying disease and heart failure have been treated, additional drugs to slow the ventricular rate may not be required, but options are detailed in **Table 1**.

If the arrhythmia is not hemodynamically significant (e.g. a cat with occasional single, uniform VPCs with HCM but no exercise intolerance or collapse), no further action may be required other than treating the CHF. It should be appreciated that antiarrhythmic drugs are not benign, and they have

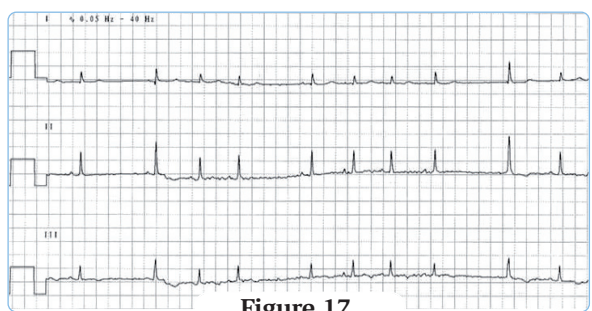


Figure 17.

Leads I, II and III from a 3-year-old DSH cat with sinus arrhythmia and ventricular escape complexes (2nd last QRS complex). The 2nd QRS complex from the left is a likely fusion complex, as a P wave precedes it. The cause for the sinus arrhythmia in this cat was not identified, but persisted for several years.



Figure 18.

A post-operative radiograph of a cat fitted with a pacemaker secured within a pocket in the abdominal musculature.

the potential, difficult to predict in an individual animal, to be pro-arrhythmic. Some anti-arrhythmic drugs which the author has used for feline arrhythmias are listed in **Table 1**.

For cats which are symptomatic due to bradyarrhythmias such as 3rd degree AV block, the treatment of choice is a pacemaker. Transvenous leads (via the jugular) are usually avoided in cats, because of the risk of cranial vena cava obstruction and chylothorax. Leads are therefore placed epicardially, with the pulse generator in the abdominal wall musculature and the lead passed transdiaphragmatically and attached to the epicardium through a pericardial incision (**Figure 18**). The beta-2 agonist terbutaline can be tried which may have a positive chronotropic and dromotropic effect for symptomatic bradyarrhythmias.

Conclusion

Dysrhythmias in cats normally indicate the presence of cardiac disease although systemic conditions may also result in tachyarrhythmias or bradyarrhythmias (most importantly, hyperkalemia). Cats with significant myocardial disease may have no arrhythmia or other auscultatory abnormality on clinical examination so other investigations are warranted to identify cardiac disease and any arrhythmia. Myocardial infarction is likely an under-recognized consequence of feline myocardial disease. Hemodynamically significant arrhythmias which are transient may result in episodic seizure-like episodes rather than syncope. ☒

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Nutritional aspects of heart disease



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Introduction

Diet is an essential component for treating many diseases and is undoubtedly of fundamental importance in cats with heart failure. Certain dietary modifications are essential in the management of cardiology disease because they help slow disease progression, reduce symptoms, decrease the amount of medication required and its side

effects, improve quality of life and even - in cases such as taurine-deficiency dilated cardiomyopathy - reverse the heart disease itself.

The choice of diet can be problematic. Commercial diets for feline heart disease are not widely available and those that are may often have very low salt content, and are not appropriate in the early stages of heart disease in animals that show no signs of congestion. Other commercial diets may have the appropriate level of sodium for a particular case but may not have the optimal amount of protein, fat and other nutrients for that patient. Therefore the choice of diet for individual patients will depend on many factors: appetite, body weight, clinical signs and concurrent disease.

Dietary guidelines *Maintain an optimal weight*

One of the most important goals of nutritional treatment is to maintain an optimal body weight. Both cachexia and obesity not only affect an animal's quality of life but they may also affect survival, since body weight is considered to be a survival predictor in cats (1).

Cachexia

Cardiac cachexia is a catabolic state of multifactorial origin (**Figure 1**). It is generally less common in cats than in dogs and usually develops when heart failure is already advanced. Increased energy needs, poor tissue blood perfusion, complications of any co-existing diseases (e.g. renal failure), the presence of ascites and gastrointestinal congestion (which leads to reduced nutrient absorption) and (above all) anorexia all contribute to cardiac cachexia. Anorexia is an insidious and worrying problem that is encountered daily when dealing with feline heart disease. It is also usually multifactorial, with contributing factors including poor diet palatability, the effect of prescribed drugs, respiratory distress (from pulmonary edema or pleural effusion) and

KEY POINTS

- An adequate intake of protein and calories contributes to the health of cardiology patients by reducing the degree and progression of cardiac cachexia.
- Preventing excess sodium is a cornerstone of nutritional therapy; sodium restriction should be introduced when signs of congestive heart failure appear.
- Anorexia is a significant factor in many cardiology cases. Nutritional supplements such as omega-3 fatty acids can help fight it.
- Taurine is essential in the feline diet; insufficient taurine can cause myocardial dysfunction with subsequent heart failure.

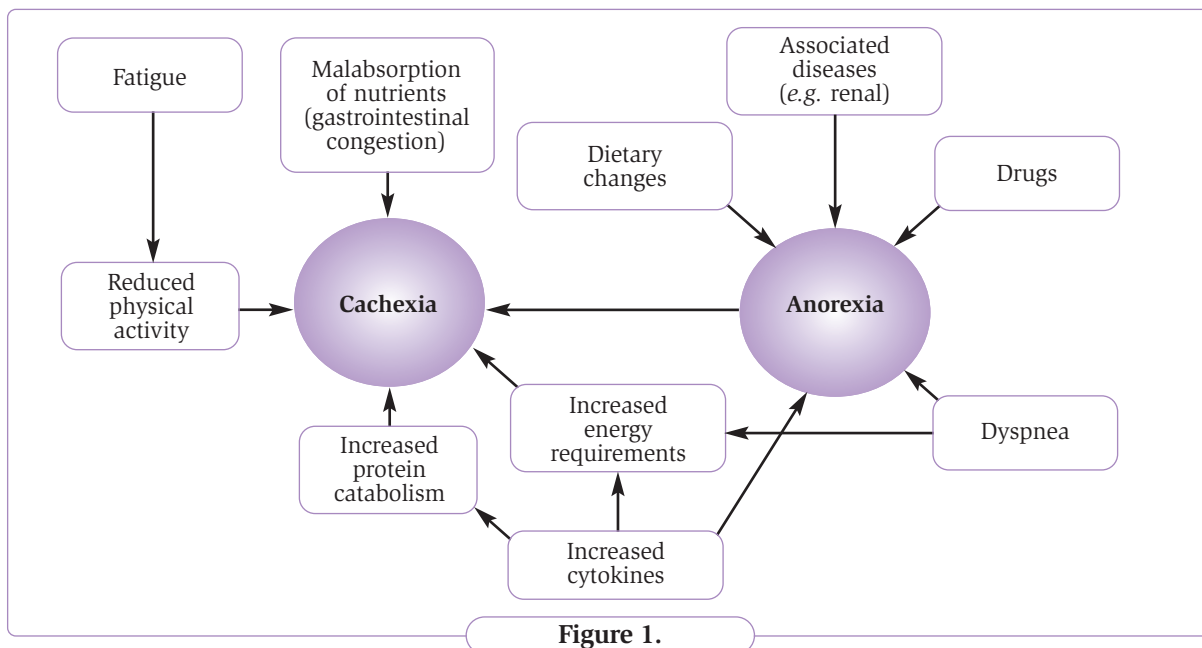


Figure 1. Main factors contributing to cardiac cachexia and anorexia.

the effects of inflammatory cytokines. In order to try to control anorexia and cachexia the following are recommended:

- Encourage intake of small amounts of highly palatable, high-energy food; wet food may be warmed.
- Fulfill minimum protein requirements. Protein restriction increases the risk of cachexia and exercise intolerance, and cardiac diets should therefore contain an optimal amount of highly digestible protein that will preserve the cat's lean body mass. The diet should at least meet the minimum requirements of 60-70 g protein/1000 kcal.
- Regulate cytokine production. Cytokines such as tumor necrosis factor (TNF) and interleukin 1 (IL-1) are raised in cardiac disease. These cause anorexia, increase energy requirements and enhance body catabolism. Several studies in dogs found that omega-3 polyunsaturated fatty acid supplementation reduced the production of these cytokines, leading to decreased cachexia and anorexia (2,3). Although there are few studies in cats it is likely that there are similar effects in this species. Long chain fatty acids, particularly

icosapentenoic acid (EPA) and docosahexenoic acid (DHA), are present in large quantities in fish oil.

- Maintain an adequate calorie intake. As heart disease advances, animals often lose weight and they also tend to lose their appetite. The calorie content of the food should be adapted to maintain a cat's ideal body condition; if the cat is underweight, small portions of high-energy food (high fat and low fiber) should be given.

Excess weight

Although weight loss is more common, some cats with heart disease are overweight or obese.

Obesity is associated with increased cardiovascular risk; increased metabolic demands, blood volume, neurohumoral activation and heart rate can in turn trigger arrhythmias, reduce sodium and water excretion in urine, and contribute to hypoventilation syndrome. Therefore it is advisable to restrict caloric intake in order to eliminate excess body fat. It is often observed that once these animals lose weight they feel better, are more active and less dyspneic.

Balance mineral intake

Potassium

Potassium is an electrolyte that must be controlled because the use of different cardiac drugs can alter potassium levels. Abnormalities such as hypokalemia can cause heart rhythm disturbances, affect contractility, trigger muscle weakness and enhance the side effects of certain drugs such as digoxin preparations. High doses of diuretics, especially loop diuretics such as furosemide, can cause hypokalemia, particularly if the patient is anorexic. Potassium supplementation will be necessary in these cases.

In theory, ACE inhibitors could trigger hyperkalemia because they stimulate renal potassium reabsorption. In practice this is rare (5), and so the potassium content of food for cats with heart disease (even if treated with ACE inhibitors) is similar to the potassium content of maintenance diets (1.5-2 g/1000 kcal).

Magnesium

In one study conducted in cats with hypertrophic cardiomyopathy, no significant benefit was found in giving a magnesium supplement (6). Therefore the recommended magnesium levels in food are similar to that in maintenance diets (0.12-0.25 g/1,000 kcal). As with potassium, diuretics may cause hypomagnesemia by promoting its loss in urine. Hypomagnesemia potentiates arrhythmias, affects response to antiarrhythmic drugs, reduces contractility, and contributes to muscular weakness. This electrolyte disturbance is generally rare (4) but in cats with arrhythmias and those receiving high doses of diuretics it is recommended to monitor magnesium blood levels. If hypomagnesemia is detected, a magnesium supplement is indicated.

Prevent nutritional deficiencies and enhance cardioprotective properties

Taurine

Taurine is synthesized mainly in the liver from the amino acids methionine and cysteine via the action of different enzymes, including cysteine dioxygenase and cysteine sulfinic decarboxylase. In cats, low levels of these enzymes mean that taurine biosynthesis is insufficient to meet the

physiological requirements. Large quantities of taurine are also used to conjugate bile acids, and taurine is continuously lost through the feces. Taurine content is therefore essential in the feline diet (7) and a deficiency usually occurs when cats are fed homemade, mainly vegetarian, diets or low-quality commercial food. Introduction of such a diet will see taurine levels fall in tissues such as plasma, muscle, retina and nerve cells within days or weeks.

Taurine protects membranes and regulates myocardial contractile function. A deficiency can cause myocardial dysfunction, which in turn can lead to heart failure (8,9). The pathophysiological mechanisms behind taurine deficiency and myocardial dysfunction are not fully understood. It appears that since taurine acts on the calcium and sodium ion flow in the myocardium, it plays a significant role in myocardial activity. Taurine deficiency is the leading cause of dilated cardiomyopathy (DCM) in cats. Historically DCM was the second most common cause of heart disease (10,11), but when studies in the 1980's demonstrated that myocardial dysfunction could be reversed in taurine-deficient cats through taurine supplementation, commercial foods were reformulated, and this brought about a significant reduction in DCM incidence (12).

However, not all taurine-deficient cats develop myocardial failure. One study reported that only ~25% of cats receiving taurine-deficient diets developed myocardial failure and it is postulated that other, as yet unknown, factors are also required to induce myocardial dysfunction; a genetic predisposition has been suggested (13). Another cause that may reduce tissue deposits of taurine and lead to deficiency is urinary acidification combined with potassium depletion.

To establish a diagnosis, taurine levels must be measured in whole blood. Healthy cats should have levels of > 250 nmol/mL (14). If the value is lower, this should be investigated. Confirmation of taurine deficiency can also be verified by observing echocardiographic improvement of myocardial function from serial echocardiograms following taurine supplementation; note at least 3-6 weeks will be needed to observe an improvement (***case study - box 1***).

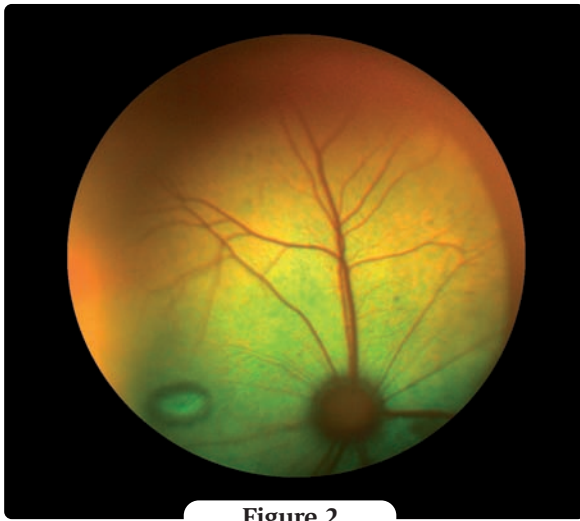


Figure 2.

Early focal retinal degeneration in a cat fed a taurine-deficient diet.

In addition to giving food with an adequate taurine content, cats with DCM should be supplemented with 250 mg taurine twice daily. If the signs of heart failure can be brought under control promptly, the prognosis is favorable. To maintain levels within the physiological range, food must contain at least 1 g taurine per kg of dry matter (DM) in dry food or 1.7 g/kg DM in wet food (15). Finally it is also worth noting that taurine deficiency in cats can lead to irreversible retinal degeneration and ultimately blindness (**Figure 2**).

Arginine

Arginine is a precursor of nitric oxide (NO) which is produced by the vascular endothelium; NO helps maintain normal vasomotor tone. Unlike other species, cats are unable to synthesize arginine and it is therefore essential to provide it *via* the diet. One study demonstrated that arginine levels in cats with arterial thromboembolism secondary to heart disease were lower than those in healthy cats and those with uncomplicated cardiomyopathy (16); arginine intake may therefore have beneficial effects on feline thromboembolism and a minimum of 1.93 g/1000 kcal is recommended.

Long chain omega-3 fatty acids

Although few studies have provided evidence of the benefits of these fatty acids in cats, the effects

observed in other species suggest that omega-3 supplementation in cats with heart disease is likely to have similar benefits. As mentioned earlier, these fatty acids not only act on inflammatory cytokine production, reducing anorexia and cardiac cachexia, they also counteract undesirable myocardial alterations such as hypertrophy and fibrosis of heart muscle cells. Other beneficial properties are associated with their antithrombotic, antiarrhythmic and endothelial function regulatory effects (by modulating NO production). It is currently recommended to use triple the amount of omega-3 fatty acids indicated for healthy cats (0.06 g/day of omega-3 fatty acids, corresponding to a concentration in food of 0.10-0.35 g/1000 kcal) (2).

B Vitamins

Anorexia and the loss of water-soluble vitamins through the urine when diuretics are administered both favor vitamin B complex deficiency. Furthermore, cats with heart disease need more B vitamins than healthy cats (16). Diets for cats with heart disease should therefore contain levels of water-soluble vitamins 2-3 times higher than that found in food for healthy cats.

Antioxidants

It is now known that antioxidants are important in humans for the prevention and treatment of heart disease. Free radicals are by-products of oxygen metabolism, and the body defends itself against them by producing endogenous antioxidants; the imbalance between oxidants and antioxidants creates what is known as oxidative stress. It is believed that oxidative stress not only increases the risk of heart disease, but of other conditions too. The main antioxidants that can be absorbed through food, and which reduce free radical formation, are vitamin E, vitamin C, selenium, taurine, carotenoids and polyphenols. Little data is available at present on the benefits of using anti-oxidants in cats with heart disease, but it is speculated that future studies will provide encouraging data for their use.

Conclusion

Dietary management is an important part of the treatment of feline heart disease. By providing nutritional requirements adjusted to each clinical

stage and each individual patient, not only will the clinician be able to improve the quality of life by

improving cardiac function, survival rates will also increase. ☺

CLINICAL CASE

An 8-year-old European shorthair female cat was presented with anorexia, malaise, and dyspnea. The cat had been fed primarily a balanced but poor-quality diet. Clinical examination revealed the presence of pale mucous membranes and a weak femoral pulse. Heart-lung auscultation demonstrated tachycardia, gallop rhythm and weak respiratory sounds. Pleural effusion was observed on thoracic radiography, masking the cardiac silhouette (**Figure 1**). The electrocardiogram showed sinus tachycardia (**Figure 2**). The echocardiogram (**Figures 3, 4**) revealed severe dilation of both left atrium and ventricle, thinning of ventricular walls and reduced contractility as evidenced by a significantly lower shortening fraction (SF) than normal. These findings led to the diagnosis of dilated cardiomyopathy.

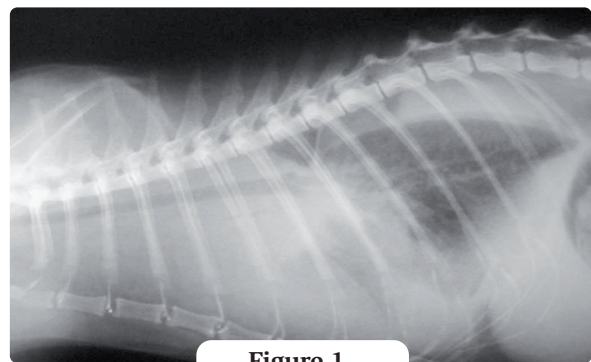


Figure 1.

Lateral thoracic radiograph of feline dilated cardiomyopathy. Abundant pleural effusion prevents the cardiac silhouette from being seen.

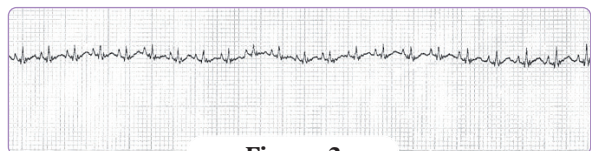


Figure 2.

Lead II electrocardiogram (25 mm/sec, 1 cm/mV). Sinus tachycardia observed (HR: 230 bpm).

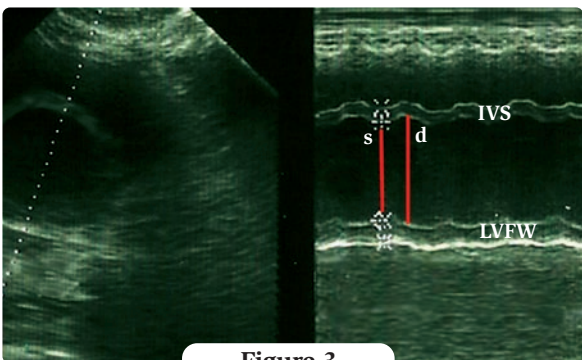


Figure 3.

Dilated cardiomyopathy. Short axis echocardiography of left ventricle (B/M mode). The diastolic (d) and systolic (s) diameters are increased. The reduced motility of the interventricular septum (IVS) and left ventricular free wall (LVFW) indicates a severe reduction in cardiac contractility.

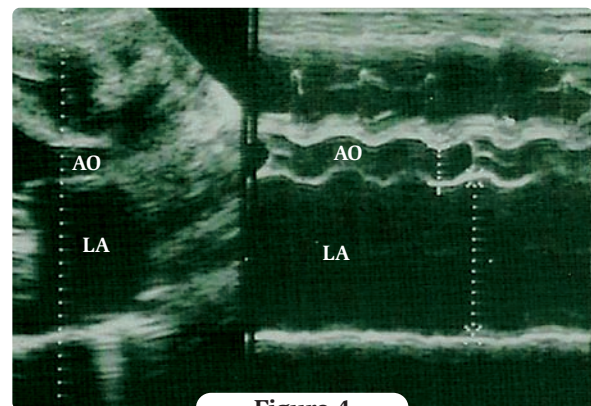


Figure 4.

Dilated cardiomyopathy. Long axis echocardiography (B/M mode) of left atrium (LA) and aorta (Ao). Severe left atrial dilation can be observed.

Treatment was commenced with digoxin (0.03 mg/total every 48 hours PO), enalapril (0.25 mg/kg twice daily PO) and furosemide (2 mg/kg three times daily for the first 48 hours IV, with gradual dose reduction and oral administration as the dyspnea improved). This was supplemented with taurine (250 mg twice daily, orally) and the owner was instructed to switch to a better-quality cat food.

Since the clinic did not have access to taurine estimation techniques, the diagnosis of taurine-deficiency DCM was made when the myocardial dysfunction reverted after the administration of taurine supplementation. The pleural effusion disappeared within three weeks of commencing treatment and the echocardiographic values gradually returned to normal values in terms of heart chamber size and systolic function over a period of five months (**Table 1**). As clinical and echocardiographic symptoms improved, the cardiac drugs were reduced and then discontinued, and the taurine was maintained. ☒

Table 1.

Echocardiographic values in a case of feline dilated cardiomyopathy. The dimensions of the left atrium (LA), left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD) all gradually decreased to reach normal values by the fifth month of supplementation. The shortening fraction (SF) increased progressively to attain a normal value.

	Day 0	Day 20	2 months	5 months
LVEDD	26.1 mm	21.2 mm	17.4 mm	16.5 mm
LVESD	21.7 mm	15.4 mm	10.0 mm	8.1 mm
SF	16.8 %	27.3 %	42.5 %	50.9 %
LA	23.6 mm	17.0 mm	14.5 mm	13.2 mm

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Hypertension



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Introduction

Hypertension is the most important cardiovascular disease of the aged cat and the most important vascular disease in cats, making up approximately 1% of NCSU admissions from 1990-1995 (**Figure 1**). Its

recognition and appropriate treatment is therefore emerging as a critical component of small animal geriatric medicine. There are a number of target organs for systemic hypertension (**Figure 2**); our experience has shown that hypertensive cats have associated disease, in approximate order of clinical presentation, of the eye, kidney, heart, and central nervous system (CNS) (1). Any discussion of management of hypertension must be preceded by a discussion of the causes of hypertension, the specific target organs affected, and the mechanism by which target organs are damaged.

Etiology

Hypertension in animals has largely been considered to be secondary to other diseases (*e.g.* renal disease and endocrinopathies), as opposed to idiopathic (primary or essential), as is the case in most human hypertensives. This has recently been questioned. One study of hypertensive cats referred for ocular disease revealed that at least 17%, and possibly as many as 50%, of cats had no identifiable cause for their systemic hypertension (1). Another study showed that approximately 20% of hypertensive cats diagnosed in “primary-care” practice were idiopathic (2). In a retrospective review of hypertensive cats, using more rigorous inclusion criteria (Atkins, Grauer, unpublished), > 10% of affected cats were determined to be idiopathic. It is important to note that the average age for hypertensive cats is 14.8 years (1).

Described and potential etiologies of secondary hypertension include chronic and acute renal disease, hyperthyroidism, hypothyroidism, hyperadrenocorticism, hyperaldosteronism, pheochromocytoma, diabetes mellitus, and possibly obesity. Clearly, chronic kidney disease (CKD) has the greatest association with hypertension and may often be causal. A recent report suggested ~ 29% of elderly cats with CKD were hypertensive (3) with a further four studies giving a range of 19-65% (4).

KEY POINTS

- ➔ Fundic examination and blood pressure measurement should be performed in all cats > 10 years of age.
- ➔ Some cats do not have an identifiable cause for their hypertension. These should be considered as idiopathic and managed aggressively to prevent damage to target organs.
- ➔ Early intervention, especially to spare the eye and central nervous system, is imperative, with amlodipine as the drug of choice.
- ➔ In most feline hypertensive patients, the renin - angiotensin - aldosterone system is abnormally activated and should be suppressed with an ACE-Inhibitor or aldosterone receptor blocker.
- ➔ Tachycardia not only contributes to hypertension but is also harmful to the cardiovascular system; persistent tachycardia should be managed with atenolol.

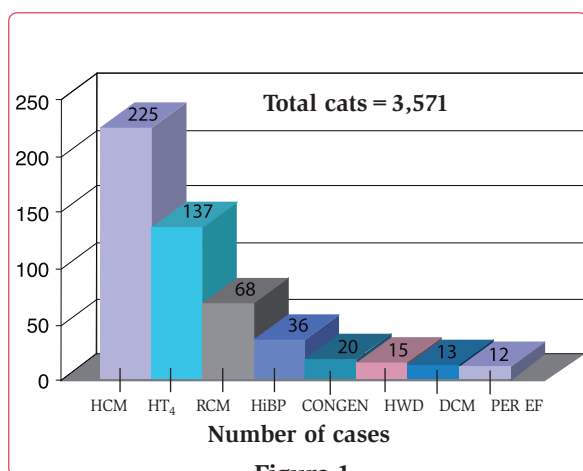


Figure 1.

The relative prevalence of cardiac disease and hyperthyroidism seen at NCSU over a 5-year period. HCM = hypertrophic cardiomyopathy. HT₄ = hyperthyroidism. RCM = restrictive cardiomyopathy. HiBP = systemic hypertension. CONGEN = congenital heart disease. HWD = heartworm disease. DCM = dilated cardiomyopathy. PER EF = pericardial effusion.

Pathogenesis

The pathogenesis of hypertension is complex, not well understood, and beyond the scope of this paper. However, several studies have indicated that the renin-angiotensin-aldosterone system (RAAS) is probably abnormally activated in many (if not most) cats with systemic hypertension, particularly with concurrent renal disease, and certainly after therapy with drugs such as loop diuretics and vasodilators (4-6). My therapeutic approach is based on target organ damage (present vs. absent, and, if present, which organ system(s) is in peril), and a brief review of the target organs of hypertension, and how they are injured, is appropriate.

Tissues such as the eye, brain and kidney are able to protect their microcirculation from pressure fluctuation by “autoregulation”. In the normal individual the glomerular pressure is maintained between 60-160 mmHg. However, in hypertension, this protective measure is lost and elevated systemic pressures are translated directly to the capillary beds, producing barotrauma.

Ocular damage

The eye is the organ at greatest risk because of its vulnerability to the insult. Hypertension disrupts the “blood-ocular barriers” and produces “protective” vasoconstriction; this is followed by secondary vascular hypertrophy/hyperplasia and vascular dysfunction with leakage of blood components into

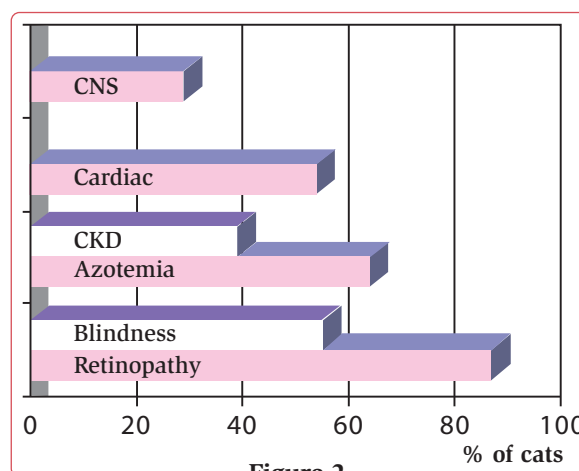


Figure 2.

Clinical diseases associated with hypertension in a study of 69 cats.

ocular tissues and fluids. Clinical findings include arteriolar tortuosity, retinal edema, hemorrhage, detachment, and hyphema (Figure 3). Blindness often results from the complications of intraocular hemorrhage (tractional retinal detachment, cataract, extensive vitreal hemorrhage, and secondary glaucoma) or, more commonly, from progressive neurosensory retinal degeneration. Blindness is usually, but not inevitably, permanent. If vision returns, it may be temporary; this is because retinal degeneration from progressive ischemic injury or excitotoxicity can develop, sometimes months afterwards. Early detection of hypertensive retinopathy is imperative, arguing strongly for yearly ophthalmic examination in aged cats.

Renal damage

Failure of renal autoregulation results in elevated intraglomerular capillary pressure and ongoing renal destruction. This may occur with acute or chronic kidney disease and, adding to the confusion in understanding the pathogenesis of hypertensive renal disease, renal disease begets hypertension and hypertension begets renal disease. Furthermore, activation of the RAAS contributes to renal damage. Not surprisingly, ACE-Inhibitors have been shown to spare the kidney by reducing intraglomerular pressures, inhibiting mesangial cell growth and fibrosis, and possibly by reducing proteinuria. The renal arteries and arterioles are themselves damaged and contribute to the pathogenesis (see vascular damage, below).

The kidney, like the eye, is an important target organ for hypertension, even if hypertension is secondary

to renal disease. As renal disease is a major problem in the aging cat population, correction of hypertension is one way which the duration and quality of life can be improved. Yearly or more frequent fundic examination, urinalysis, microalbuminuria screening, and measurement of serum urea and creatinine, coupled with measurement of systemic blood pressure (BP), are essential in these cats.

CNS damage

With hypertension, the CNS also loses its ability to autoregulate. Cerebral blood pressure is normally maintained at 60-150 mmHg, but higher pressures affect the vasculature resulting in damage, leakiness, and cerebral edema, possibly with brainstem herniation (*Figure 4a*). Hypertension-induced over-perfusion also contributes to the edema. Vascular barotrauma may induce ischemia and brainstem or spinal cord hemorrhage (*Figure 4b*). Clinical signs may include cranial nerve lesions, seizures, somnolence, paralysis/paresis and behavioral abnormalities.

Vascular damage

Hypertension produces endothelial dysfunction with impaired vasodilation, thus worsening hypertension. Over time this results in vessel arteriosclerosis and hyperplasia of the myointimal layer, altering the vessels' ability to protect other target organs through autoregulation. Control of BP alone does not reverse these changes, but lowering BP, while blunting the RAAS, normalizes both vascular function and anatomy (7).

Cardiac damage

Hypertension and the concomitant vascular changes produce increased cardiac afterload. This is compounded by sympathetic nervous system (SNS) activation. Cardiac hypertrophy and fibrosis is produced by the combination of hypertension (increased afterload) and RAAS and SNS activation. A review of 99 hypertensive cats (Atkins, unpublished data) revealed that the vast majority had suffered cardiac changes (*Figure 5*), including auscultatory abnormalities (murmur and/or gallop), cardiomegaly, left ventricular hypertrophy and/or electrocardiographic evidence of hypertensive heart disease. Despite this, only 3% of these cats developed heart failure.

⊕ Diagnosis of hypertension

Although a detailed discussion of the diagnosis of hypertension is beyond the scope of this work, a brief



Figure 3.

Ocular changes in a hypertensive cat. Note the tortuous retinal arteries, hyper-reflective retinal degeneration, and punctate retinal hemorrhage.

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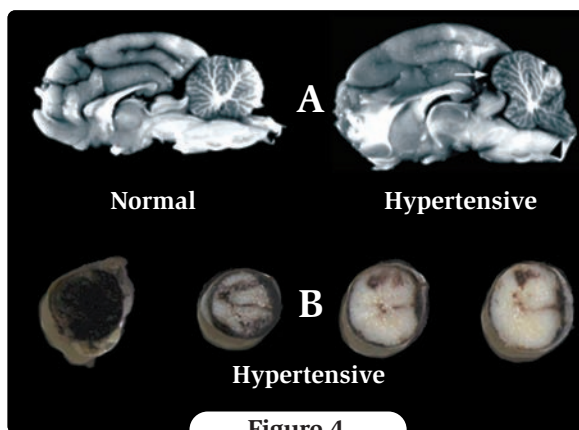


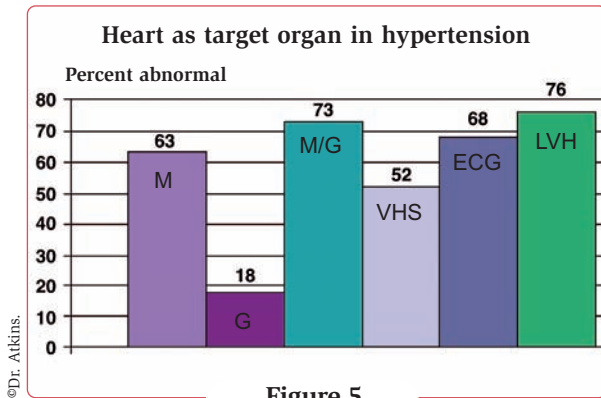
Figure 4.

A: Comparison of normal (left) and acutely hypertensive cat brain cut in sagittal section. There is cerebral edema and the swollen cerebellum (white arrow) has prolapsed through the foramen magnum producing a “coning” effect (black arrow).

B: Hypertensive spinal cord hemorrhage. Note there is both subdural and intrathecal hemorrhage.

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overview is pertinent. The veterinary profession has relied upon the Doppler method for determining BP in cats. Whilst thought to be more reliable than the oscillometric method for smaller patients, it has the distinct disadvantage of not providing diastolic or mean blood pressures in most instances. For this reason, we continue to explore the use of oscillometric equipment and newer units show promise for use in small dogs and cats. At NCSU, the tail is the appendage of choice for BP measurement, followed by the palmar surface of the front foot and finally the dorsal surface of the rear foot. Cuff width is important and should



Cardiac changes in 99 hypertensive cats. Note that there is a high prevalence of cardiac abnormalities. M = murmur. G = cardiac gallop. M/G = murmur and gallop. VHS = vertebral heart score. ECG = electrocardiographic abnormality. LVH = left ventricular hypertrophy, determined by echocardiography.

approximate to 30-40% of the circumference of the appendage used. Too small a cuff tends to over-estimate and too large a cuff to under-estimate true systemic BP. The cuff position should approximate the level of the heart. Current recommendations are that measurement should be done in a quiet area prior to examining the patient, typically in the presence of the owner and after 5-10 minutes of acclimatization. The ACVIM Panel on Hypertension suggests discarding the first measurement, then obtaining a minimum of 3, preferably 5-7, consecutive measurements with less than 20% variability in systolic BP. The conditions (including animal's disposition, cuff size, site and all measurements) should be recorded. Many clinicians require that hypertension be documented on more than one occasion before accepting the diagnosis. Note that in animals < 10 years of age the risk of "false positive" diagnosis is increased, especially in cats because of the high prevalence of "white coat" (stress-induced) hypertension in "normotensive" animals. The possibility of misdiagnosis is reduced if concurrent predispositions (e.g. renal disease) or findings (e.g. retinopathy or murmur) are detected.

What drugs are available?

Therapies for feline hypertension have varied and have rarely been systematically evaluated. Drugs that have been employed and/or reported upon include:

- Diuretics (furosemide and spironolactone).
- Angiotensin-converting enzyme inhibitors (ACE-I) (captopril, enalapril, lisinopril).

- Beta-blockers (propranolol and atenolol).
- Calcium channel blockers (diltiazem and amlodipine).

Various studies have reviewed different regimes; the literature and clinical experience leads one to conclude that amlodipine is the single best agent for managing feline systemic hypertension (1,8-11). This said, specific roles for other drugs can be identified; betablockers slow the heart rate and block the cardiovascular effects of T3 in hyperthyroidism; ACE-I combat drug-induced or spontaneous activation of the RAAS, preserve renal function (12,13), and lower BP (14,15); spironolactone counters the effects of aldosterone (16); and furosemide (possibly with nitroglycerin) aids heart failure secondary to hypertension.

Treating hypertension

It is important to consider the following factors; establishing if the RAAS is activated (initially or iatrogenically); assessing the role of the SNS; evaluating renal function and the effects of hypertension on renal function; noting salt intake; checking for heart failure (uncommon); investigating for reversible causes of hypertension (e.g. hyperthyroidism, diabetes mellitus, adrenal tumors); and establishing the target organ(s) affected or suspected to be at risk. I essentially divide cats as follows: reversible or irreversible cause; with or without presumed RAAS activation (RAAS activated in renal failure, heart failure, or with vasodilator or loop diuretic administration); presence or absence of tachycardia (> 200 bpm); and by target organ damage.

In all cases, I use a moderately salt-restricted diet (typically a renal diet) and avoid salt-laden fluids, such as lactated Ringers solution. This lessens total body sodium without worsening renal function or severely activating the RAAS, which can happen with heavily salt-restricted diets. I appreciate that salt restriction has minimal, if any, effect on blood pressure in the cat, but salt has been shown to play a permissive role in hypertensive cardiac disease.

Hyperthyroidism, the only common treatable cause of feline hypertension, is treated by standard methods. However because of the effects of T3 on beta receptors, I employ a beta-blocker such as atenolol (6.25-12.5 mg PO daily) to reverse the cardiovascular effects until more definitive therapy is efficacious, and if

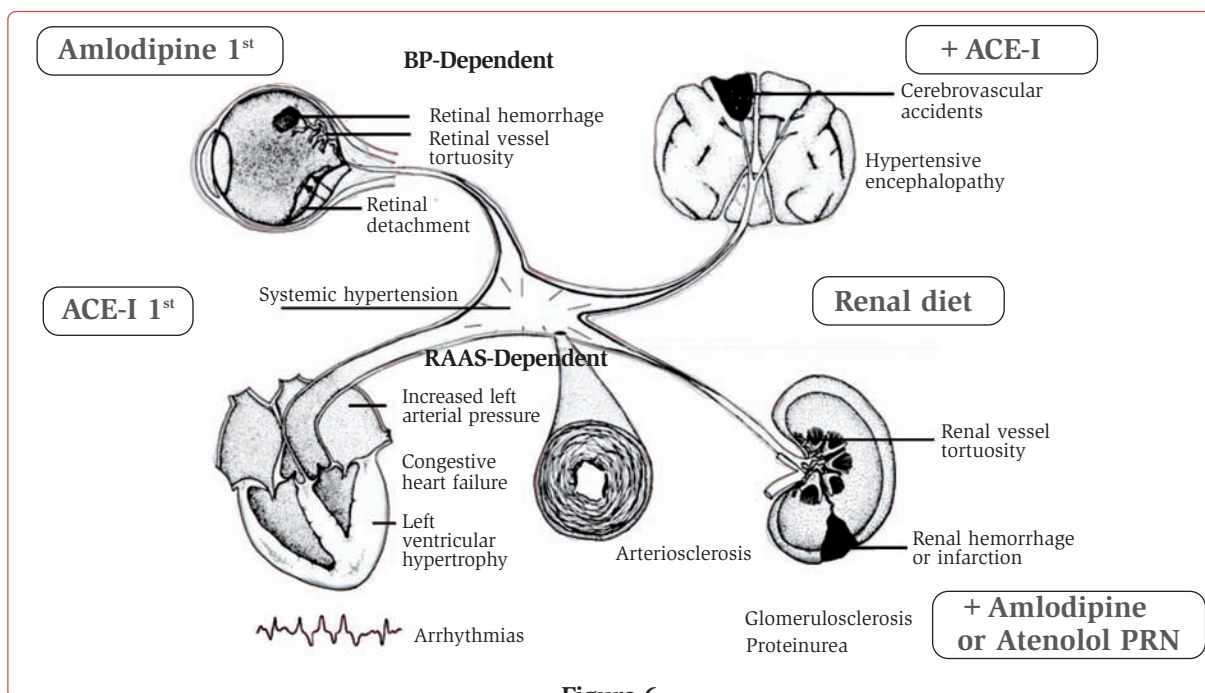


Figure 6.

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The approach to the management of systemic hypertension using target organ risk. The organs more susceptible to barotrauma and without obvious RAAS involvement are the eye and brain. The risk to these organs is generally more acute, and immediate reduction in blood pressure is desirable using amlodipine; an ACE-Inhibitor can be added either immediately or later. For organs such as the heart, arteries and kidneys, the acute risk is less and the RAAS is important in the damage to these target organs. For these reasons, an ACE-Inhibitor is instituted first, even though blood pressure decline may well be inadequate. Amlodipine (to ensure a decrease in blood pressure) or atenolol (to lower the heart rate) can be added as necessary. Lastly, a modest reduction in salt intake is instituted. PRN = pre-required need (19).

hypertension control is unsuccessful I add enalapril at 0.5 mg/kg/day PO.

In the euthyroid, non-tachycardic cat with hypertension, I simplify the approach by administering amlodipine and enalapril daily, 1 tablet in the morning and 1 in the afternoon if the owner’s schedule allows. If hypertension is not controlled, first the amlodipine dosage is increased and/or other drugs such as beta-blockers are employed. When compliance is an issue and only 1 pill can be administered daily, amlodipine is the choice.

• **Target organ damage**

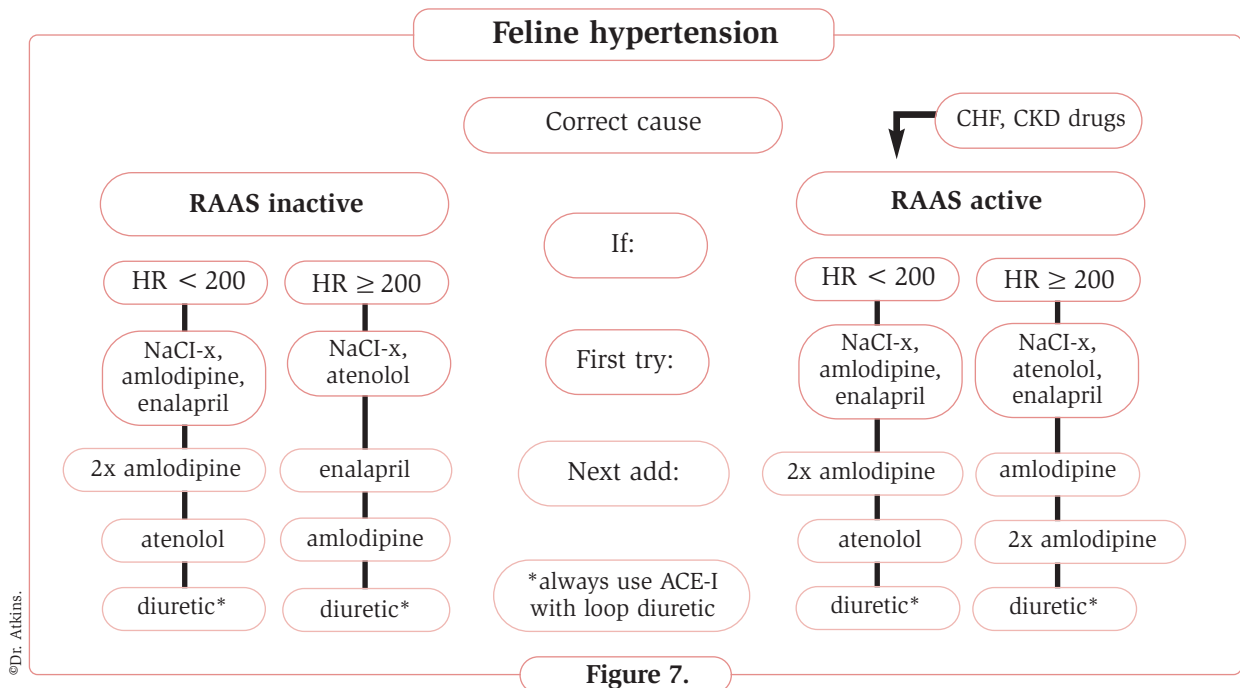
Using target organ damage as a criterion, my therapeutic approach is to employ amlodipine as a sole initial therapy if the barotrauma itself is probably the greatest detrimental effect (CNS and ocular lesions) and acute blood pressure reduction is necessary. An ACE-I is added later. If the kidneys, blood vessels, or heart are felt to be at greater risk, then I block the RAAS, typically with an ACE-I such as enalapril, with betablockers or amlodipine being added if further depression of blood pressure is necessary (Figure 6).

• **RAAS activation**

The RAAS is probably activated in most or all feline hypertensives. For this reason, though not the most effective class of drugs at lowering blood pressure, ACE-I are employed in most cases of hypertension. This is particularly apropos when one considers that amlodipine activates both the RAAS (6) and SNS (17). Betablockers are employed if persistent tachycardia is noted or, as mentioned above, with concurrent hyperthyroidism.

• **RAAS not activated**

If the RAAS is not thought to be activated (this may be an erroneous assumption) and tachycardia is not problematic, my approach is as follows: amlodipine (0.625-1.25 mg PO daily, or even higher if unresponsive) plus a moderately salt-restricted renal diet and enalapril (Figure 7). The ACE-I counteracts activation of the RAAS by amlodipine (6). If unsuccessful, I first double the dosage of amlodipine, then sequentially add atenolol and finally (rarely) add diuretics (furosemide 6.25-12.5 mg daily or spironolactone 1-2 mg/kg daily PO), if needed. It should be pointed out that in cats unresponsive to amlodipine plus a second drug,



An algorithmic approach to the management of feline hypertension using RAAS activation and heart rate to determine the course of action, but also considers target organ involvement. If the practitioner is unsure about RAAS activation, the safest approach is to assume that it is activated. NaCl-x = moderate salt restriction; HR = heart rate; CHF = congestive heart failure; CKD = chronic kidney disease.

owner compliance and BP measurement technique should be scrutinized.

If tachycardia is present (without RAAS activation), I begin with moderate salt restriction and atenolol. However even though heart rate typically falls, blood pressure control is often inadequate, in which case I sequentially add amlodipine plus enalapril, then, if needed, double the amlodipine dosage, and finally (rarely) add a diuretic. However if the tachycardia is not initially controlled, the atenolol dose is first increased. If this does not bring the exam room heart rate to < 160 or the at-home heart rate to < 140, I would substitute diltiazem (30 mg PO bid) for amlodipine to better control heart rate and then follow the same sequence mentioned above.

• **RAAS abnormally activated**

When conditions (heart failure, renal failure, or drug therapy) indicate the RAAS is inappropriately activated, I begin therapy with amlodipine, a moderately salt-restricted diet and enalapril (*Figure 7*). If a normotensive state does not result, I add, sequentially, increased amlodipine dosage, atenolol, and finally diuretics (furosemide or spironolactone).

Alternatively, if tachycardia is a concern, moderate salt restriction, atenolol, and enalapril would be used initially. If unsuccessful control of hypertension results, amlodipine would be added, and followed sequentially, as needed, by a doubling of the amlodipine dosage, and finally diuretic therapy if needed. If, after initial therapy, heart rate control is inadequate, the atenolol dose is first increased. If this does not adequately control heart rate, I would substitute long-acting diltiazem (30 mg PO bid) for amlodipine to better control heart rate and then follow the stepwise sequence mentioned above for blood pressure control, if needed. Heart failure secondary to hypertension is rare and will not be discussed except to note that diuretics will often be necessary in such patients to control signs and that enalapril is indicated.

Lastly, if renal failure or significant renal disease is present, the etiology should be sought (at least by urinalysis and culture) in the hopes of finding a reversible cause. Otherwise, treatment of renal disease is standard and beyond the scope of this article. It is wise to consider the routes of excretion of the drugs being used in deciding dosage and dosing interval in the face of renal insufficiency. Note that hypoten-

sion may rarely occur due to over-exuberant anti-hypertensive therapy. This should be avoided as it may further compromise renal function.

🔍 Prognosis and conclusion

The prognosis for feline hypertension is guarded but not grave. Vision lost rarely returns. However, with diagnosis and treatment, survival averages have ranged from 18-21 months from the date of diagnosis (1,3). Data comparing survival times for

cats with hypertrophic cardiomyopathy (average age 6.5 years) (18) with those with treated hypertension (average age 14.8 years) (1) shows that survival times are not markedly different despite the differently aged cats. This argues strongly for vigilance, allowing early diagnosis and intervention in the hypertensive geriatric cat. This is best accomplished with twice yearly physical examination, fundic examination and blood pressure monitoring in cats over 10 years of age. 📌

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Risks and trends in cardiomyopathy



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Introduction

Cardiomyopathy is a clinically important disease with evidence mounting that apparently healthy cats may have subclinical disease (1,2). Recognition of dietary taurine in preventing dilated cardiomyopathy (DCM) in cats (3) has led to taurine-deficiency cardiomyopathy (TCM) becoming rarer. However, other forms of cardiomyopathy - hypertrophic (HCM), restrictive (RCM) and DCM not attributable to taurine deficiency - are of concern. This report characterizes trends in the diagnosis of feline cardiomyopathy seen at Banfield veterinary hospitals during 2010.

Method of analysis

Records for cats from 2005-2010 were used to identify cats diagnosed with cardiomyopathy. Data for 2010 were summarized by type (HCM, DCM, RCM and TCM), sex, breed and age; kitten (≤ 6 months), juvenile (6-12 months), young adult (1-3 years), mature adult (3-10 years), and geriatric (10-25 years). Period prevalence and exact 95% confidence intervals (CIs) for breeds represented by ≥ 100 cats are reported here.

Results

Records for 425,898 cats were eligible for inclusion. 579 cats had a diagnosis of HCM in 2010, 60 were diagnosed with DCM, 17 with RCM and 3 with TCM. Median age at diagnosis was 9.2 years for both HCM and DCM. Male cats were 1.6 times more likely to be diagnosed with a cardiomyopathy compared to females. They were also 1.6 times as likely to have HCM and 1.9 times as likely to have DCM.

In 2010, HCM was most common in geriatric cats (48%) followed by mature adults (39%), whereas DCM was most common in mature adults (52%) followed by geriatric cats (40%). 17 cats were diagnosed with RCM; 6 geriatric, 10 mature adults and 1 young adult. 3 cats were diagnosed with TCM (1 each of geriatric, mature adult, and juvenile).

A summary of breeds diagnosed with HCM and DCM is provided in **Table 1 and 2**. Considering only those breeds in which 10 or more cats were diagnosed with HCM, the disease was most common in Persians, followed by Maine coons and DLH cats. Too few cats were diagnosed with DCM to make confident comparisons.

Discussion

Analyses of the data revealed four key points:

- HCM and DCM are fairly uncommon in cats, and RCM and TCM are rare.
- Male cats are at increased risk.
- HCM was most common in geriatric cats, and DCM and RCM most common in mature adults.
- For breeds in which 10 or more cats were diagnosed, HCM was most common in Persian, Maine coon and DLH cats.

Table 1.

Prevalence of HCM in various cat breeds.

Breed	Nº. of cats with HCM	Total nº. of cats	Percentage (95% CI) of cats in breed with HCM
Birman	2	268	0.75 (0.23-2.66)
Ocicat	1	139	0.72 (0.17-3.92)
Munchkin	1	155	0.65 (0.16-3.52)
Cornish rex	1	156	0.64 (0.15-3.50)
Sphinx	3	476	0.63 (0.23-1.83)
Turkish van	1	173	0.58 (0.14-3.16)
Norwegian forest	2	410	0.49 (0.15-1.75)
Angora	1	228	0.44 (0.11-2.41)
Scottish fold	1	252	0.40 (0.10-2.18)
Persian	24	6,517	0.37 (0.25-0.55)
Abyssinian	2	598	0.33 (0.10-1.20)
Bombay	1	312	0.32 (0.08-1.77)
Maine coon	20	6,400	0.31 (0.20-0.48)
Devon rex	1	322	0.31 (0.08-1.72)
Bengal	6	2,342	0.26 (0.12-0.56)
Manx	3	1359	0.22 (0.08-0.64)
Burmese	1	467	0.21 (0.05-1.18)
Red tabby	2	958	0.21 (0.06-0.75)
DLH	76	41,312	0.18 (0.15-0.23)
DSH	357	276,346	0.13 (0.12-0.14)
Siamese	19	15,355	0.12 (0.08-0.19)
DMH	48	56,539	0.09 (0.06-0.11)
Ragdoll	2	2,610	0.08 (0.02-0.27)
Himalayan	3	4,244	0.07 (0.02-0.21)
Russian blue	1	2,102	0.05 (0.01-0.26)

DLH = Domestic longhair; DMH = Domestic medium hair; DSH = Domestic shorthair.

At Banfield, evaluation for heart murmurs and abnormal rhythms and pulses are part of a comprehensive examination, but radiography or echocardiography is not done unless a cat is suspected of having cardiac disease. Consequently the data may under-represent the true prevalence of clinical cardiomyopathy and certainly under-represent the true prevalence of subclinical disease. Indeed,

Table 2.

Prevalence of DCM in various cat breeds.

Breed	Nº. of cats with DCM	Total nº. of cats	Percentage (95% CI) of cats in breed with DCM
Ocicat	1	139	0.72 (0.17-3.92)
Munchkin	1	155	0.65 (0.16-3.52)
Cornish rex	1	156	0.64 (0.15-3.50)
Egyptian mau	1	289	0.35 (0.09-1.91)
Sphinx	3	476	0.21 (0.05-1.16)
Russian blue	2	2,102	0.10 (0.03-0.34)
Ragdoll	2	2,610	0.08 (0.02-0.28)
Persian	3	6,517	0.05 (0.02-1.34)
DLH	6	41,312	0.01 (0.01-0.03)
DMH	7	56,539	0.01 (0.01-0.02)
DSH	34	276,346	0.01 (0.01-0.02)
Siamese	1	15,355	0.01 (0.00-0.04)

See *Table 1* for key.

one study of 103 apparently healthy cats identified 16% with cardiomyopathy via echocardiography (1); in addition heart murmurs were detected in 16 of the cats, but only 5 of these had echocardiographic evidence of cardiomyopathy. Another study, also involving 103 healthy cats, noted 22 cats with a murmur but only 4 of these had HCM (2). Males outnumbered females in both studies, and breed representations were similar to those ranked in the present study. Interestingly, Ragdolls in our study were ranked low among the top breeds for HCM, whereas another retrospective study involving 127 cats with HCM found Ragdolls to be over-represented, compared with the distribution of the breed in the teaching hospital population (4).

Although the prevalence of diagnosed disease did not exceed 1% in any age group or breed in our population, our findings combined with those of other studies suggest the need for enhanced screening practices, particularly for mature adult or geriatric cats in which murmurs are detected. ☺

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Thromboembolism: current treatment and future directions



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◊ Introduction

Initial work in the 1960's highlighted the connection between feline arterial thromboembolism and cardiac disease, whilst the association of

➔ KEY POINTS

- ➔ The initial presenting sign of feline heart disease may be arterial thromboembolism.
- ➔ The respiratory distress seen in cats with arterial thromboembolism may be due to pain, congestive heart failure, or both.
- ➔ The clinical signs are distinctive, and oxygen, pain control, and furosemide therapy (if in heart failure) should be administered to cats prior to diagnostic evaluation.
- ➔ Effective thrombolysis comes with the risk of reperfusion injury, most commonly manifested as hyperkalemia.
- ➔ More research is required to determine the optimum treatment protocols and to establish reliable methods of identifying at-risk cats.

thromboembolism with endomyocarditis and hypertrophic cardiomyopathy (HCM) from necropsy and clinical data was made in the 1970's. Since then the majority of the literature has focused on the management of the underlying cardiomyopathy, combined with therapeutic anticoagulation and/or fibrinolysis. The current understanding of the mechanisms underlying the formation of a thrombus is not complete; recent research has attempted to uncover the causes of thromboembolism in susceptible cats and the findings may improve the approach to treating this often fatal disease process.

◊ Clinical signs and diagnosis

Acute vocalization and pain accompanied by paresis/paralysis of one or more limbs is often the first presenting sign of arterial thromboembolism. Tachypnea or open-mouthed breathing may be present from the agony or congestive heart failure. The affected limbs are cool with pale or purplish-colored digital pads (**Figure 1**). Arterial pulses are often absent, and the muscles of affected limbs may be firm compared to the unaffected ones. Detecting arterial occlusion by the absence of a Doppler signal or the visualization of an intra-arterial thrombus via ultrasonography will confirm the diagnosis. Acute spinal cord injury could be a differential diagnosis for the above presenting signs; however, those patients are likely to have warm extremities and arterial pulses to the affected limbs. Thoracic radiographs may show cardiomegaly and biatrial enlargement as well as pleural effusion or pulmonary edema (**Figures 2a and b**). Uncommonly a pulmonary mass may be found, suggesting the thrombus may be secondary to neoplasia; this must be considered since neoplasia would be a likely differential diagnosis for cats with acute onset of painful, pulseless limbs and purple pads. Echocardiography should be undertaken

when the patient has stable cardiopulmonary status and has been treated for pain; this may identify underlying cardiac disease (hypertrophic, dilated, restrictive, or unclassified cardiomyopathy) and may also demonstrate spontaneous echocardiographic contrast or a thrombus in the left atrium.

Treating the emergency patient

If life-threatening conditions are present (e.g. congestive heart failure: crackles, dull lung sounds), stabilizing the cardiopulmonary system takes priority. Oxygen therapy (cage, mask, or flow-by) and furosemide (1-2 mg/kg IM every 15-30 minutes) should be administered to cats with significant respiratory distress. A total furosemide dose of 5-8 mg/kg may be necessary until the respiratory rate improves and the cat urinates. Cats seem to be more sensitive than dogs to the side effects of furosemide and determining any further doses of furosemide should be done only after assessing the effect of the previous aliquot.

Pain control is essential; the ischemic neuropathy secondary to the arterial thrombus is very painful. Pure *mu* agonists are often the best choice (oxymorphone 0.05-0.1 mg/kg IM, hydromorphone 0.05-0.2 mg/kg IM) to control the most severe pain. Once an intravenous catheter is placed, pain control (as well as the furosemide) can be given every 2-4 hours IV or as a continuous infusion (e.g. fentanyl 2-5 µg/kg/hr IV). Vomiting may occur transiently due to narcotic usage. Acepromazine (0.025-0.05 mg/kg IM or IV q4-6h) can be administered to relieve anxiety and works synergistically with pure *mu* agonist narcotics. This dose of acepromazine is unlikely to facilitate vasodilation, but it may be antiemetic.

Fluid therapy is best tailored to the individual. Cats in congestive heart failure, as well as those receiving furosemide, should not receive IV fluids. However, some cats do not present with heart failure and may have fluid deficits (although this is unlikely since this is such an acute disease). In general, the author withholds fluids until thrombolytics are being administered, when isotonic crystalloids (0.9% NaCl) should be given IV to help prevent and treat reperfusion injury. The severe hyperkalemia that may result (serum potassium concentration > 8mM/L or bradycardia) requires treatment with dextrose (0.5 mL of 50% dextrose solution



Figure 1.

A cat suffering from bilateral arterial thromboembolism to the pelvic limbs (= saddle thrombus). Note the difference in color between the digital pads of the thoracic and pelvic limbs.

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IV) and regular insulin (0.5 U/kg IV). Sodium bicarbonate (0.5 mM/L) can also be administered IV slowly over 20-30 minutes. The electrocardiographic changes seen with hyperkalemia (**Figure 3**) can be very subtle (e.g. prolongation of the P-R interval) or extremely severe (e.g. no P wave, tented T waves, sine wave).

Thrombolytic agents

Heparin is traditionally used in these cases, but this is really to prevent expansion of the clot, and for thrombolysis two agents are worthy of mention.

- **Streptokinase** is often suggested as the drug of choice; it was evaluated retrospectively in one study (1) which looked at complications and outcomes; it sought to determine if time of streptokinase administration after onset of clinical symptoms changed the outcome, and investigated positive or negative prognostic factors. The 46 cats in this study received various dosages of streptokinase within 1-20 hours of the onset of clinical signs; all but one had heart disease, and 21 had heart failure. Streptokinase infusions lasted from 1-28 hours but there was no difference between survivors and non-survivors based on the time to, length, or dosage of streptokinase administration. Higher doses of the drug were not associated with a greater likelihood of hyperkalemia or a bleeding tendency but hyperkalemia was more likely to occur with a longer duration of streptokinase infusion. These cats were also more likely to regain arterial pulses due to a higher total dose, but not motor function. Bleed-



Figure 2.

Dorso-ventral (A) and left lateral (B) radiographs of a cat with arterial thromboembolism. Note the generalized cardiomegaly as well as the pleural effusion and alveolar infiltrates indicative of congestive heart failure.

ing was clinically evident in 11 cats and 3 required blood transfusions due to the severity of bleeding. Cats with a single limb affected were more likely to survive to discharge. Survival following discharge (15 cats) varied from 2 days to 23 months (mean of 51 days), which is similar to

another study (2) where mean survival was 61 days. Median time to the next thromboembolic event was 100 days. Some clinicians believe the use of streptokinase to treat cats with arterial thromboembolism cannot be justified due to its expense, risk of hemorrhage, and the lack of improvement in outcome. Whether or not this drug is likely to be of benefit, its current lack of availability requires alternatives to be researched for both prevention and treatment.

- **Tissue plasminogen activator (t-PA)** may be a useful alternative. One study (3) demonstrated that cats treated with t-PA had a shortened time to reperfusion and ambulation; animals that successfully completed therapy were walking within 2 days (compared to 2-6 weeks for spontaneous resolution) but 50% of cases had fatal complications (hyperkalemia, congestive heart failure and arrhythmias) whilst a prospective evaluation of t-PA (4) reported that 3 out of 11 cats treated were discharged alive, but serious adverse events in all cats (azotemia, neurologic signs, dysrhythmias, hyperkalemia, acidosis, and sudden death) forced termination of this study. The current recommended dose for t-PA is 0.25-1.0 mg/kg/hr IV CRI for a total dose of 1-10 mg/kg (5). The cost for t-PA is significant and the clinician must balance the efficacy, cost and high complication rate if choosing to use it.

Thrombus removal

Surgical removal of arterial thromboemboli has met with mixed results. Many interventions, from balloon embolectomy to surgery, have been attempted. However, along with the high anesthetic risk due to underlying cardiac disease, most clinicians currently recommend medical therapy. For cats already affected by arterial thromboembolism, rheolytic thrombectomy (using a catheter to flush and aspirate the thrombus) can be another option, and may be an effective and useful intervention in acute cases; however access to the apparatus and the expense may be a limiting factor. One small study (6) reported successfully dissolution of the clot in 5 out of 6 cats using this method.

Three cats were discharged from hospital but all had ambulatory deficits of varying degrees consistent with a distal peripheral neuropraxia. In 2 of these cats the neurological deficits resolved within

one month of discharge and the cat with the longest period of time between onset of clinical signs and the thrombectomy (192 hours) had neurological deficits persisting for 10 months after the procedure, over which time they resolved. One of the surviving cats died suddenly four months after the procedure and necropsy revealed no grossly apparent cause of death. During routine echocardiographic re-examination of another surviving cat, evidence of spontaneous contrast was seen in the left atrium three months after the procedure. This cat presented to the referring veterinarian one month later showing signs similar to the original signs of aortic thromboembolism, and was euthanized. Postmortem examination confirmed re-thrombosis at the level of the aortic trifurcation. The final cat died of a combination of congestive heart and chronic renal failure two years after the procedure. In this study, the time between the onset of clinical signs and the thrombectomy procedure did not appear to be an important predictor of a successful outcome.

Prevention of further thrombus formation

The largest retrospective report to date studied 127 cats with a first episode of arterial thromboembolism (7). The goals of this study were to determine which aspects of presentation provide useful prognostic information, to provide accurate survival curves for cats surviving the initial episode, and to compare low and standard dose aspirin therapy in the cats that survived the initial episode. Most (76.4%) of these cats had no known prior medical condition and males were over-represented 2:1. The majority of cats had both pelvic limbs affected by thromboembolism; in 16 cats, only one pelvic leg was affected (8 right and 8 left). One thoracic limb was affected in 15 cats and 3 cats had both rear and one thoracic limb affected. There was also one cat each with a mesenteric and cerebral thrombosis. Thrombi were found in the left atrium of 6 cats during echocardiography and another 3 cats had thrombi (2 left atrium and 1 left ventricle) found on necropsy. Neoplastic emboli accounted for only 5% of the population.

Heart failure was present in 55 of the 127 cats and 32 cats were euthanized without therapy. Treatments provided varied according to clinician preferences but included fluids, analgesics, oxygen supplementation, and streptokinase. Variable doses

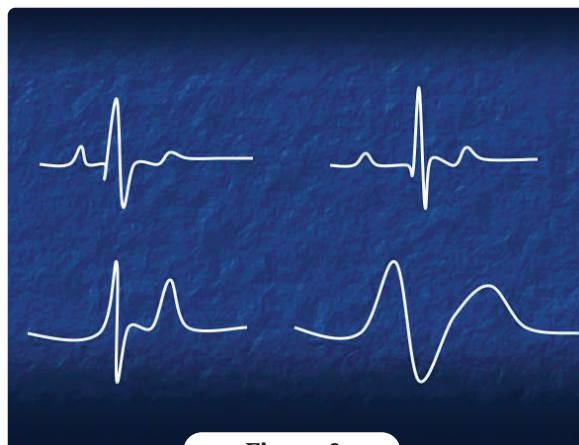


Figure 3.

Effects of hyperkalemia on the electrocardiogram. The upper left trace shows a normal sinus rhythm. As the potassium concentration increases the P-R interval lengthens (upper right trace). Eventually, the P wave disappears and the T wave becomes tented (lower left). Merging of the QRS complex and the T wave results in a sine wave indicating extreme cardiotoxicity from the hyperkalemia (lower right).

of unfractionated heparin were used more commonly than aspirin for anticoagulant therapy. Any combination of the above treatments was possible. Overall survival rate was 35% (not dissimilar to the survival rate in other studies (1,8) whilst survival rate for the treated cats was 45%, with a trend towards better survival in the later years of the study. This study found that cats with higher rectal temperatures and higher heart rates on initial presentation were more likely to survive. 44 of the 87 cats that survived the initial thromboembolic event were medicated at home with either high dose aspirin, low dose aspirin, or nothing, plus other cardiac medications as necessary. Eleven of the 44 cats experienced 16 additional thromboembolic events, of which 9 were fatal. Time to first recurrence was 191 +/- 152 days. Nine of the 44 cats were alive at the end of the study with a mean survival time of 117 days. Cats with heart failure during the initial episode survived a significantly shorter time compared to cats without heart failure (77 vs. 223 days). There was no significant difference in survival for the cats on high versus low dose aspirin.

A retrospective report reviewed 100 cases of feline aortic thromboembolism and found similar characteristics to the other studies mentioned here (8). The 37% of cats that survived the initial episode and were discharged were most commonly managed with warfarin, which has a reported superiority

over aspirin therapy for the prevention of recurrent thromboembolism (9). The average overall survival time for these cats was 11.5 months. Precise follow-up information was available on 22 cats; of these 6 were euthanized due to recurrent episodes of thromboembolism. Note that warfarin-treated cats not only may have recurrent thromboembolic episodes but also significant to fatal bleeding complications, so use of this drug requires careful monitoring and frequent assessments of coagulation parameters.

Low molecular weight heparins

Low molecular weight heparins (LMWH) such as dalteparin and enoxaparin have recently been used as preventative agents. One study retrospectively studied dalteparin (10) to document the ease and duration of administration, complications, and frequency of aortic thromboembolism. Of 57 cats, 43 had cardiomyopathy and received on-going therapy with dalteparin (47-220 U/kg q12-24h SC). None received coagulation testing. About half of these cats had thromboemboli prior to initiating dalteparin. Eight cats had documented or suspected aortic thromboemboli while on therapy. Cats with thromboemboli prior to dalteparin therapy were more likely to have a reoccurrence. There was no difference in the survival times with or without the use of concurrent aspirin. More cats in this study died because of congestive heart failure or heart failure-related euthanasia than because of thromboembolism-related euthanasia. It is not possible to draw conclusions from this study as to whether dalteparin played any role in the reduction of episodes of aortic thromboembolism.

An investigation into the pharmacokinetics of LMWH in normal cats studied the dosage and dosing frequency required to maintain anti-Xa activity within the range of 0.5-1.0 IU/mL (11), efficacy being gauged by the degree of Factor Xa inhibition. They found that LMWH can be administered effectively to healthy cats, but requires frequent subcutaneous administration to maintain anti-Xa activity. This may demonstrate why dalteparin in the aforementioned study (10) (dosing was q12-24h) may not have proven efficacious.

What's new?

Recent interest has centered around the use of thienopyridines which have an anti-platelet effect. The

theory is that by impairing platelets from becoming activated and forming clots the fatal thromboembolic sequelae of HCM can be prevented. Ticlopidine was first studied (12) but consistently caused vomiting and anorexia, suggesting that the drug is not clinically useful due to its side effects despite having an *in vitro* anti-platelet effect. Clopidogrel, on the other hand, is reported to have a significant anti-platelet effect at multiple dosages in cats without any significant adverse effects (13) and has many promising characteristics that make its clinical use appealing. Once daily oral administration may promote client compliance, its anti-platelet effect lasted 3-7 days after the last dosage, and serotonin secretion was also lower in treated cats (higher serotonin levels have been associated with more severe signs of arterial thromboembolism). The minimum effective dose was not determined in this study, but the lowest dose used which had anti-platelet efficacy was 18.75 mg PO q24h, whilst a dose of 75 mg PO q24h was also found to be effective with no adverse effects. The next step is to prove if clopidogrel is the drug of choice to prevent thromboembolism in cats with HCM via a prospective, randomized, double-blinded controlled trial of its use compared to a placebo. Hopefully, this drug will be proven to prevent episodes of arterial thromboembolism in the future.

Current research into abnormal coagulation

Virchow's triad suggests that hypercoagulability is caused by the interplay of 3 parameters: endothelial damage, alterations in blood flow, and increased activity of coagulation factor and/or platelet hyper-aggregability. Alterations in blood flow, especially flow stasis, have been the long-held tenet of thrombus formation in the cat. One study (14) reported low-flow velocities in the left atrial appendage of cats and identified a subgroup at increased risk of spontaneous echocardiographic contrast and possible thromboembolism. There is recent interest in measuring hemostatic markers in cats with HCM. Two recent studies (15, 16) suggest that molecules such as thrombinantithrombin (TAT) complexes and D-dimers may be elevated in cats with critical illness or heart disease, but the correlation to HCM is weak and an individual cat may have normal measures despite the presence of severe HCM. Another group demonstrated hypercoagulability (defined as having 2 or more of the follow-

ing: increased fibrinogen, Factor VIII:C activity, low antithrombin activity, TAT or D-dimer elevations) in 43 cats with cardiomyopathy (17) and found such hypercoagulability criteria in cats with spontaneous echocardiographic contrast or arterial thromboembolism, not left atrial enlargement alone. This is the second study to show that left atrial enlargement by itself does not correlate with hypercoagulability. Most recently, the author's laboratory used a commercial analyzer (18) to assess platelet function in both normal cats and cats with HCM but concluded that this did not distinguish between affected and normal animals and is not currently the best test to study hypercoagulability. In fact there is as yet no simple analytical tool available for the evaluation of the hypercoagulable state in cats but thromboelastography (TEG) is becoming

more widely available and can assess all phases of coagulation from instigation of coagulation through to fibrinolysis. One group used TEG to assess for hypercoagulability in cats with HCM (19) and found that although individual cats may be hypercoagulable there is significant overlap in data between healthy cats and those with HCM.

Conclusion

If treated quickly and effectively, some cats may improve and have functional mobility to the previously affected limb. The cost of therapy, both for drugs and hospitalization, is high and comes with risk for adverse events. However, the possible improvements and survival may indicate that the cat can have a good quality of life until the next arterial thromboembolism event occurs. ☉

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Restrictive cardiomyopathy



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Introduction

Restrictive cardiomyopathy (RCM) can be defined as an acquired pathology of the feline myocardium; more accurately, it refers to a series of pathologies which have as a common element marked diastolic dysfunction without major alteration of the systolic

function (1). The term “restrictive” refers to functional rather than anatomical characteristics but there is still much to investigate about the etiology of this disease. RCM reduces the compliance and distensibility of the ventricular walls, altering the ventricular diastolic filling and reducing the quantity of blood that the left ventricle (LV) can accept. During the rapid filling phase, the diastolic pressure of the left ventricle rises abruptly, counteracting the entry of additional quantities of blood, in particular later in diastole, associated with atrial contraction. This in turn increases the left atrial pressure and the dimensions of the left atrium (or both atria). Anatomically, RCM is characterized by the normal or near-normal appearance of the ventricles and by a slight increase in the septal and left ventricular free (posterior) wall thicknesses, contrasting with the pronounced left atrial dilation; this, the normal or near-normal LV chamber diameter and volume, and the near-normal systolic function exclude other cardiomyopathies. The echocardiographic appearance of the cardiac chambers in static two-dimensional images of cats with early RCM (*i.e.* without obvious anatomical alterations) may be normal: however severe diastolic pathophysiology may be evident from

KEY POINTS

- ➔ Feline restrictive cardiomyopathy is an acquired pathology characterized by marked diastolic dysfunction without significant impairment of systolic function.
- ➔ The diminished ventricular compliance and increased filling pressures are responsible for the clinical signs of left-sided congestive heart failure.
- ➔ The diagnosis is both demanding and complex and requires integrated interpretation of the clinical examination and diagnostic tests.
- ➔ Feline restrictive cardiomyopathy will demonstrate restrictive physiology without marked changes in ventricular wall or chamber dimensions; however marked left or bi-atrial dilatation will be evident.

M-mode and Doppler profiles. Recently, Doppler was used to identify very early anomalies in diastolic function (2) using human cardiology guidelines (3).

🔍 Etiology

In man, restrictive cardiomyopathy is more often secondary to systemic pathologies (e.g. amyloidosis, sarcoidosis) or radiation exposure, with pathology localized at the myocardial or endomyocardial level. Cats may also have myocardial and endomyocardial forms.

The myocardial form is typically non-infiltrative, with little or no thickening of the ventricular wall. The endomyocardial form is characterized by the progressive infiltration of fibrous tissue, predominantly in the left ventricle, causing adhesions of the endocardium, which has an irregular appearance (4). The etiology is essentially unknown, although endomyocardial fibrosis associated with viral, hypereosinophilic, and immune-mediated pathologies has been reported.

🔍 Pathophysiology

As mentioned previously, the ventricular chambers appear either normal, slightly reduced, or slightly enlarged (especially where there is an infiltration-type pathology) but are restricted in accepting diastolic filling due to the reduced compliance and increased rigidity of the ventricular walls.

Under normal physiological conditions, diastole can be divided into four consecutive phases, all regulated by active mechanisms:

1. Isovolumetric relaxation
2. Rapid ventricular filling
3. Diastasis (slow ventricular filling)
4. Atrial contraction

Ventricular filling is determined by ventricular relaxation, ventricular compliance, atrial contraction and the intraventricular pressure gradient (5). This last is one of the factors responsible for the active suction mechanism in the normally-functioning ventricle; the apical “untwisting” movement in the early phase of diastole causes suction that contributes to ventricular filling. This mechanism is significantly altered and reduced in myocardial pathologies. The diminished ventricular

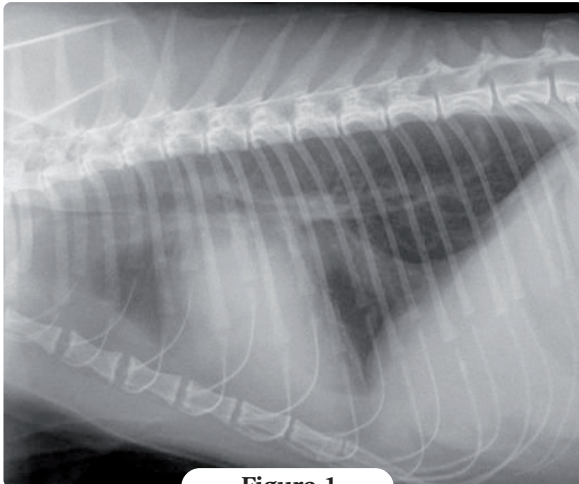
compliance and the reduced movement of the left ventricular wall increase the final diastolic pressure, with enlargement of the left atrium and increased left atrial and pulmonary vasculature pressures leading to left sided congestive heart failure (6). Tachycardia further worsens the picture because it reduces coronary blood flow; reduced myocardial perfusion stimulates fibrosis which further increases myocardial rigidity. In addition the increased left atrial pressure and reduced function slows the intra-atrial flow and predisposes to thrombus formation.

🔍 Clinical picture

The clinical presentation of cats with RCM is extremely variable. As in many other heart disorders there may be a long preclinical phase during which there are no outward signs; the sedentary nature of cats does not help, as it is difficult to identify intolerance to physical exercise. Sometimes the factor which precipitates the development of symptoms can be a mundane situation which induces rapid release of catecholamines; e.g. hospitalizing a cat for routine surgery can cause tachycardia and increased systemic pressures.

Many cats present with acute pulmonary edema and are severely dyspneic, which may mask the underlying pathology. Any diastolic gallops, arrhythmias or evidence of pulmonary edema should prompt additional investigations to diagnose cardiac disease. Many cats present in left sided congestive failure with typical signs including tachypnea/dyspnea and soft inspiratory crackles indicative of pulmonary edema. Cardiac auscultation may detect a murmur but can be normal. Pleural effusion may develop, which muffles both heart and lung sounds. In some cases there may be distension or pulsation of the jugular veins and a positive hepatogastric reflux.

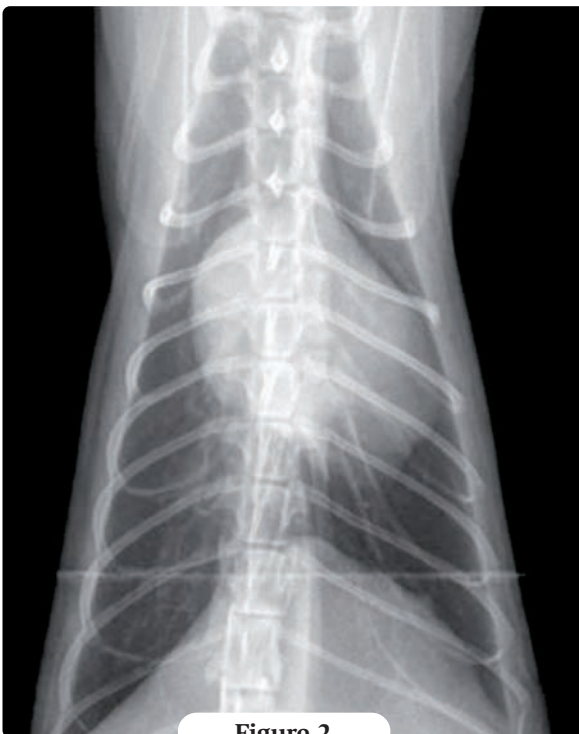
Another acute presentation may be due to systemic thromboembolism. The enlarged left atrium, stasis of blood within the left atrium, and reduced atrial function predispose to thrombus formation, and emboli may result. Typically these cases present with paresis or paralysis of one or both rear limbs due to occlusion at the aorta-iliac trifurcation. In some cases, emboli can involve other areas and can cause complex neurological manifestations, forelimb paralysis or acute renal ischemia.



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Figure 1.

Lateral-right thoracic radiograph of a 4-year-old male cat with RCM. There is obvious dilation of the left atrium and the caudal vena cava appears dilated.



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Figure 2.

Dorso-ventral thoracic radiograph of the same cat. Much of the cardiac silhouette is due to the abnormally dilated atria.

❖ Radiographic examination

On radiographs left atrial dilation (*Figures 1,2*) may be seen whilst the dimensions of the ventricular chambers appear normal. In the dorso-ventral projection a classic “Valentine’s heart”, due to marked left or biatrial enlargement, may be evident, although this is not specific for RCM versus other

cardiomyopathies. Congestion of the pulmonary vessels, the interstitial/alveolar pattern, and the presence of pleural effusion (which can obscure the cardiac silhouette) can all make the diagnosis more difficult.

❖ Echocardiographic examination

Echocardiography is the method of choice for diagnosis since it allows rapid, non-invasive investigation; it enables measurement of parameters and indices that allow recognition and staging of the diastolic dysfunction by identifying the myocardial pathology responsible. Other cardiomyopathies or cardiac disease can be excluded.

Two-dimensional and M-mode echocardiographic imaging enables evaluation of myocardial thickness and can be suggestive and characteristic of RCM, especially if there is pronounced dilation of one or both atria and normal dimensions of the ventricular chambers but impaired ventricular relaxation and compliance (7). Within the left atrium it is often possible to identify areas of spontaneous echo-contrast, reflecting blood stasis, or thrombi. The right parasternal long axis 4 chamber view shows the dilation of the left (and possibly also the right) atrium (*Figures 3,4*). The normal or near-normal ventricular diameter and wall thicknesses can be confirmed; the lack of hypertrophy tends to exclude other cardiomyopathies. Sometimes an irregular hyperechoic appearance of the ventricular endocardium may be noted, which can enlarge sufficiently to cause intraventricular obstruction.

The left atrium and its appendage should be carefully examined, especially as the severity of left atrial dilation enhances the risk of thromboembolism. The left auricular appendage is best visualized from the left cranial view, cranial to the pulmonary artery (8). Thrombus material and spontaneous echocontrast are readily imaged (*Figure 5*). This view is also used to measure left auricular appendage flow velocity. Even in the absence of thrombi, if velocity is < 0.2 m/s on pulsed wave Doppler, the cat is at risk of thromboembolic complications.

Doppler echocardiography is important to assess diastolic function and identify restrictive filling

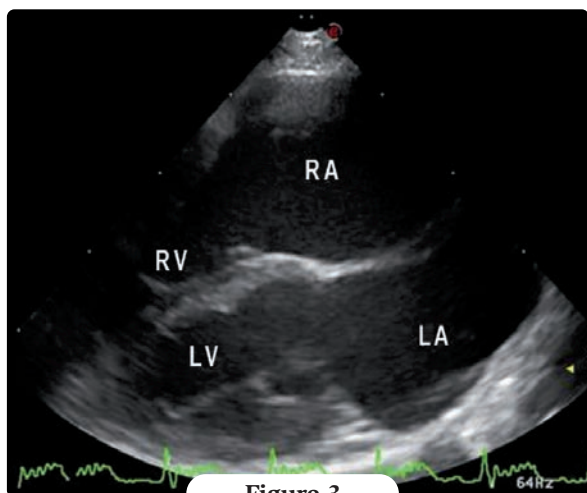


Figure 3.

Right parasternal long axis four chambered view. Note the pronounced dilation of both left (LA) and right atria (RA) without enlargement of the ventricular chambers (LV: left ventricle; RV: right ventricle) and without thickening of the septal and lateral walls.

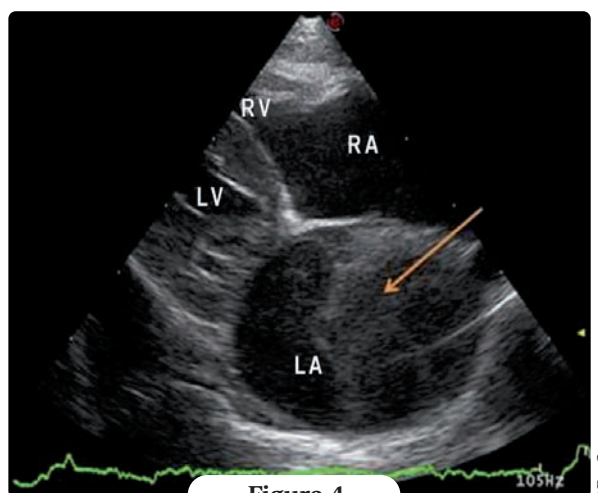


Figure 4.

Right parasternal long axis four chambered view, optimized for the left atrium. In the left atrium a wide area of spontaneous echo-contrast can be seen (arrow) almost filling the chamber. Both atria are hugely dilated (LA: left atrium; RA: right atrium; LV: left ventricle; RV: right ventricle).

patterns. Although tricky to obtain in cats, the left apical 4 chamber view is desirable to assess mitral inflow and pulmonary venous flow.

- **Mitral inflow**, or transmitral filling, is assessed by positioning the pulse wave Doppler sample volume between the tips of the open mitral valve leaflets. This reveals the mitral inflow pattern, which in the normal animal in sinus rhythm demonstrates two phases of filling:

- E wave (Early filling) which is a consequence of active relaxation of the left ventricle, and the left atrium - ventricle pressure gradient.
- A wave (Atrial contraction) which corresponds to the P wave of the ECG.

Note that in many cats, especially with accentuated tachycardia due to congestive heart failure, the two waves may summate, so the mitral inflow pattern may not be easy to interpret. When separate, however, evidence of a restrictive filling pattern is gained when (i) the mitral E wave has a high velocity but short deceleration time (DT) and (ii) the A wave velocity is very low. Mitral E wave velocity is high because of high left atrial filling pressure. The poor compliance of the left ventricle abruptly decelerates this flow. Atrial dysfunction and the poor compliance of the left ventricle

together explain the low A wave velocity. Cardiologists use the E/A ratio as an index to estimate diastolic function; if $E/A > 2$ this confirms restrictive filling (**Figure 6**).

- **Pulmonary venous flow (PVF)** also provides useful information for evaluating left ventricular filling, particularly when there is summation of the mitral E and A waves. The PVF pattern is as follows:

- During atrial systole (after the P wave of the ECG), there is retrograde flow in the pulmonary vein from the left atrium, producing the Ar wave.
- This is followed by the S wave, which primarily indicates atrial blood flow during ventricular systole (between the QRS complex and the T wave); if a cat is not tachycardic two waves may be noted, an early S wave (S1) - which indicates atrial relaxation - and the main S wave (late S wave or S2).
- During ventricular diastole, when the mitral valve is open, the left atrium allows pulmonary venous flow to reach the left ventricle, producing the D wave.

Evidence of restrictive filling pattern include low S wave and high, rapidly decelerating D wave

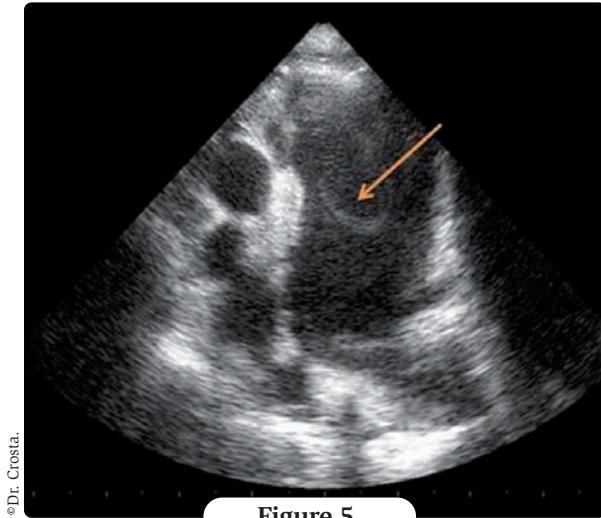


Figure 5.

Left cranial parasternal short axis view, cranial to the pulmonary artery to optimize the left auricular appendage. Note the pronounced dilation of the left auricle and areas with spontaneous echo-contrast (arrow).

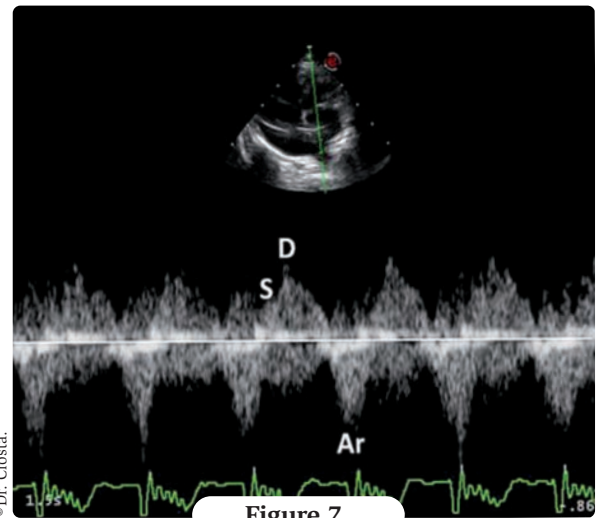


Figure 7.

Pulsed Doppler image of pulmonary venous flow in a cat with RCM. Note S wave is smaller than D wave, which rapidly decelerates. The Ar wave is of high velocity and long duration.

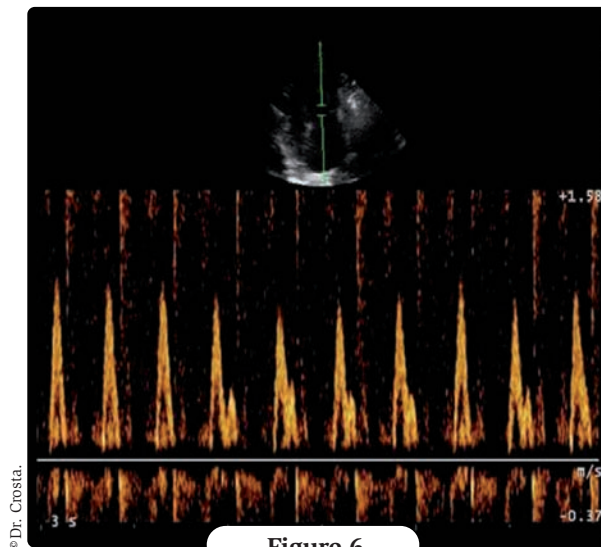


Figure 6.

Pulsed Doppler image of left ventricular filling in a cat with RCM. A pattern of restrictive transmitral flow is obvious, with an elevated wave E and short DT. In some beats, wave A (at the base of wave E) can be seen.

velocity (**Figure 7**). The Ar wave velocity may be increased with adequate left atrial function (as in **Figure 7**), or reduced with severe atrial dysfunction. If the Ar wave duration exceeds the mitral A wave duration, this is evidence of increased left sided filling pressure (9).

Comparison of the transmitral and pulmonary venous flow profiles allows a cardiologist to distin-

guish restrictive filling such as seen in RCM from other myocardial pathologies with a restrictive profile (10). A restrictive filling pattern with marked left atrial dilation and virtually normal ventricles are classic indicators of RCM (11).

Among the other methods currently employed in cats to assess diastolic function, color M-mode and Tissue Doppler echocardiography should be mentioned.

Color M-mode Doppler allows assessment of the mitral inflow propagation velocity (V_p); measuring blood flow as it courses from the mitral annulus towards the apex, it is represented as a slope. Diastolic function determines velocity; the poorer the diastolic function, the shallower the slope. In humans with RCM, V_p is reduced; this has not been reported in the veterinary literature but the author has noted a similar trend in cats with RCM compared to normal cats (**Figure 8**).

Tissue Doppler (TD) has recently been used in cats to evaluate the speed of longitudinal movement of the myocardial walls during the different phases of the cardiac cycle (12,13). As in any Doppler technique, it is critical to be aligned with the longitudinal fibers of the wall under interrogation. In normal subjects, the TD profile presents a positive systolic wave (S_m) and two negative diastolic

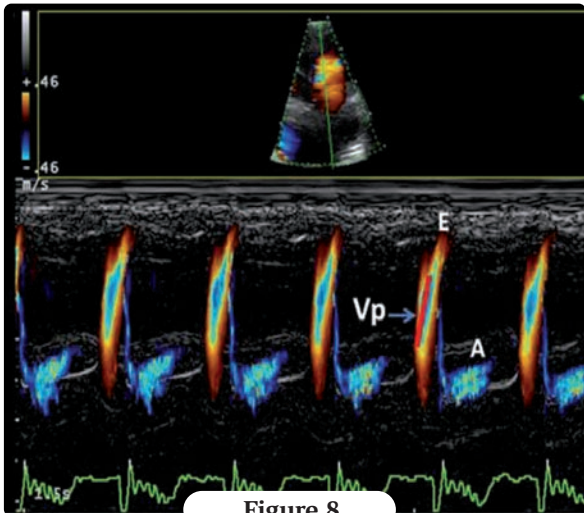


Figure 8.

Color M-mode performed on a cat with RCM, aligned with mitral inflow within the left ventricle from a left apical four chamber view. The slope Vp (orange line) represents the speed of propagation of the intraventricular flow during rapid ventricular filling.

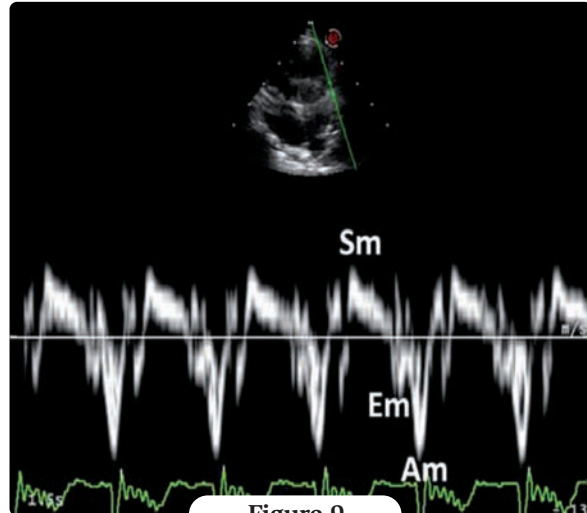


Figure 9.

Myocardial Tissue Doppler measures the velocity of longitudinal movement of the myocardial walls; the cursor is positioned on the base segment of the lateral LV wall. This shows impaired relaxation with low velocity Em and higher Am.

waves, Em (early) and Am (late). In healthy, non-aged individuals, the Em velocity is higher than the Am velocity. In the presence of impaired relaxation (e.g. RCM) the Em velocity may be markedly reduced (**Figure 9**) (14). Expressing the E wave and Em velocities as a ratio (E/Em) allows estimation of left sided filling pressures (15).

A summary of the restrictive profiles seen with the different techniques is shown in **Figure 10**.

Prognosis and treatment

Cats presenting with RCM usually have advanced disease and the long term prognosis is therefore poor. The treatment of RCM should aim to control the clinical signs of left-sided congestive heart failure, with additional radiographic and echocardiographic monitoring as appropriate. The acute management of dyspneic cats includes thoracocentesis if there is significant pleural effusion, and furosemide for pulmonary edema, with the drug administered (preferably IV) at 2-4 mg/kg every 1-2 hours until the clinical picture improves. Ongoing therapy depends on the response to treatment but ideally the interval between doses can be increased and if the cat is compliant, oral medication may be employed. Although there is no evidence of efficacy of any drug in feline RCM, calcium channel blockers have been reported to improve lusitropy (*i.e.* ventricular relaxation)

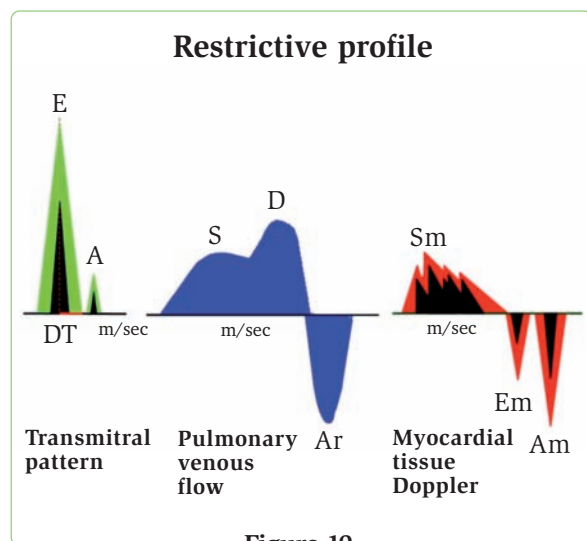


Figure 10.

Summary of the restrictive profiles of the transmitral pattern, the pulmonary venous flow and myocardial tissue Doppler.

and are often the drug of first choice. As these cases are at high risk of thromboembolic complications (and especially if echocardiographic indicators of risk are recognized) anti-platelet medication such as aspirin or clopidogrel should also be considered (**Table 1**). Treatment of chronic congestive heart failure in cats should include furosemide and an ACE inhibitor. Prognosis is also dependent on the willingness of the cat to take oral medication, and owner compliance in administering it.

Table 1.

A summary of drug options commonly used to treat cats with RCM.

Drug name	Class of drug	Dose	Route	Frequency
Benazepril	ACE-inhibitor	0.25-0.5 mg/kg	PO	SID
Enalapril	ACE-inhibitor	0.2-0.5 mg/kg	PO	SID, BID
Diltiazem	Ca- channel blocker	10 mg/cat	PO	TID
Diltiazem retard	Ca- channel blocker	10 mg/cat	PO	SID
Atenolol	Beta-blocker	6.25-12.5 mg/cat	PO	SID
Furosemide	Loop diuretic	0.5-2 mg/kg	PO, IV	SID, TID
Spirolonactone	K-sparing diuretic	2 mg/kg	PO	SID
Aspirin	Inhibits platelet aggregation	81 mg/cat	PO	q3d
Clopidogrel	Inhibits platelet aggregation	18.75 mg/cat	PO	SID

Conclusion

The diagnosis of RCM requires a systematic approach and is both demanding and complex. It involves integrated interpretation of the different echocardiographic profiles and the information gathered from clinical examination. This is essential

to establish both the therapeutic process and the prognosis; the latter basically depends on not only the seriousness and the progression of the myocardial structural alteration, but on early therapeutic intervention and its success. ☺

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Heartworm disease



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Introduction

Dirofilariasis, or heartworm disease (HWD), is an important yet uncommon parasitic disease of the cat. Other species, including dogs, ferrets and wild canines (e.g. coyotes) are more commonly

and easily infected. *Dirofilaria immitis* is a large filarial nematode parasite that resides preferentially within the pulmonary arteries, but it may also be found in the right ventricle or right atrium. Adult heartworms can live up to 7 years in dogs and recent reports have documented that 5 years' survival is possible in cats. Males are up to 16 cm long with a curly end; females are longer, up to 30 cm, and produce microscopic L1 microfilaria that circulate in the blood. Microfilaria can survive up to 2 years, but circulating microfilaria in infected cats is uncommon, typically very brief, and usually of low concentration. Should microfilaria be ingested by a mosquito, these can develop into infective L3 stage, provided the daily average ambient temperature is not too cold (above 57°F-13.8°C and ideally > 64°F-17.7°C) and when an infected mosquito bites another animal, infective larvae are transmitted to the new host. Cats are a susceptible but resistant host. In natural settings, even in epidemic areas, where nearly 100% of unprotected dogs are positive for HW infection, typically < 20% of unprotected cats may be positive. This demonstrates the relatively greater natural resistance of cats to this disease (as well as mosquito host preference); however the cat often manifests more severe clinical signs than dogs when infected with heartworm, emphasizing the importance of prevention in the species.

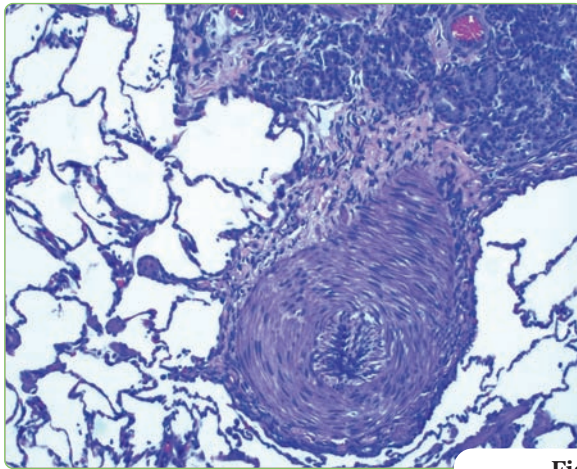
Life cycle

The life cycle of the heartworm is approximately 180 days under optimal conditions, but the cat's natural resistance is thought to result in a modest prolongation (210-240 days) in the time required for adult heartworms to develop. There are distinct phases:

- Mosquito and pre-pulmonary phases: a mosquito ingests microfilaria (L1) during a blood meal from a host (typically a dog) with a patent infection. These larvae then molt within the mosquito to the L3 stage; only these infective L3 larvae

KEY POINTS

- Heartworm is an important feline disease in many areas of the world. In endemic areas it should be a differential diagnosis for any cat demonstrating signs of acute or chronic respiratory disease, and sudden death without premonitory signs is not uncommon.
- The disease is most common in cats that have outdoor access, but it has been diagnosed in cats which live solely indoors.
- Infected cats can develop significant lung damage even if the heartworms never mature.
- The diagnosis is challenging and can be complicated by low worm burdens and vagaries in serologic testing.



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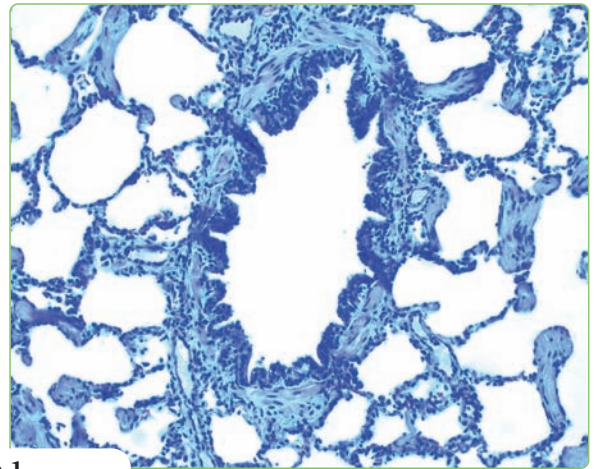


Figure 1.

10x H&E stained sections from a cat which had immature worms for 2 months and then developed an adult infection (but no worms were found on necropsy 8 months post-infection). Note the large pulmonary artery with lumenal obstruction resulting from severe medial smooth muscle hypertrophy and hyperplasia, subintimal and intimal fibrosis, and arteritis. In addition there is evidence of substantial peribronchial inflammatory cell infiltrate (bronchiolitis).

can develop further into adult heartworms. The mosquito deposits infective larvae during a blood meal and the larvae subsequently penetrate into the subcutaneous tissue and molt twice, from L3 to L5. The macrocyclic lactone heartworm preventatives are active during the subcutaneous phase of infection.

- Pulmonary infection: viable L5 migrate to penetrate systemic veins where they are swept to the peripheral pulmonary arteries. Pulmonary localization of larvae occurs relative to the volumetric pulmonary flow, resulting in the caudal lobes being typically most severely affected. The majority of parasites that reach this stage in their life cycle are eliminated by natural host immunity. However, of clinical relevance unique to the cat is that parasite death induces a strong vascular and pulmonary parenchymal inflammatory response with resultant pulmonary pathology (**Figure 1**). It is been suggested that this is secondary to the activity of pulmonary intravascular macrophages, an immune component that normal cats possess, but that normal dogs do not (1,2). Cats may exhibit important clinical manifestations at this stage of the disease (60-90 days post-infection), including coughing, dyspnea and intermittent vomiting; this is unique to the cat and has been referred to as heartworm associated respiratory disease (HARD) (3). There-

fore, even if the heartworms never mature, infected cats can develop clinically significant lung damage. Administration of monthly preventative medications can completely prevent the development of these pulmonary lesions.

- Adult infection: surviving parasites grow back towards the main pulmonary artery and right ventricular outflow tract. The adult parasites injure the lung and pulmonary arteries; spontaneous or induced death of mature heartworms incites an acute pulmonary reaction and in cats this reaction can be severe and sometimes fatal. Adult female parasites can produce thousands of microfilaria and infection is said to be patent once detectable microfilaria are produced; as noted above this is infrequent in cats (< 20%), typically transient, and of low concentration.

🔍 Clinical syndrome

Based on studies, there is no age or breed predisposition to parasite infection in cats, although cats < 7 months cannot conceivably be diagnosed as having an adult HW infection (4). As with dogs, males have been shown to be more susceptible to infection in some studies, although this has not been supported by recent serologic surveys; however while these surveys document infection they do not document mature adult infection. One necropsy study reported that more males than females

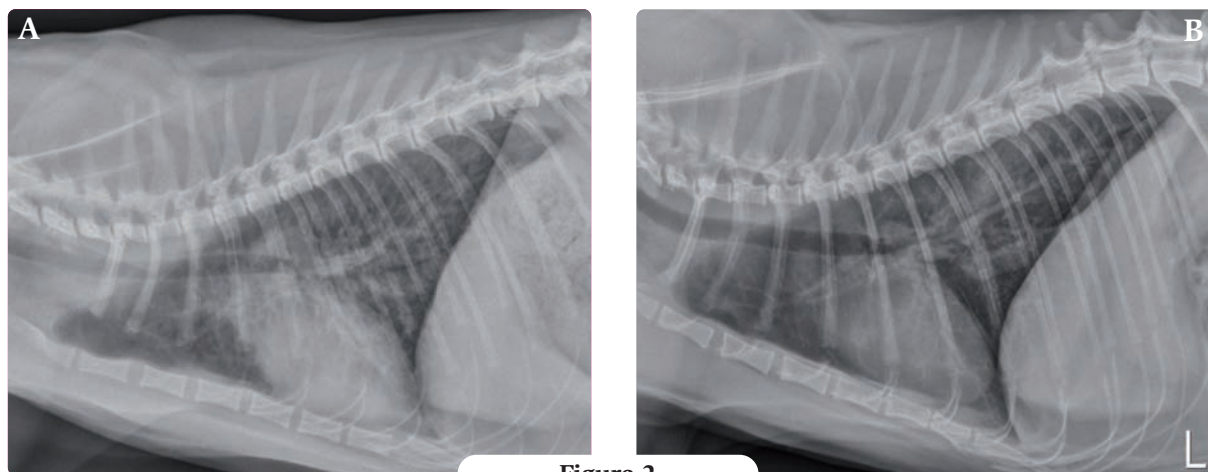


Figure 2.

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A: Lateral radiograph from a cat presented for increasing respiratory effort and worsening cough. Note the diffuse mixed broncho-interstitial pulmonary parenchymal infiltrate with apparently normal cardiac size and contour. The cat was HW Ab positive but HW Ag negative.

B: Lateral radiograph from a cat presented with acute onset respiratory difficulty. Note the mixed interstitial infiltrate with a predominately caudal-dorsal distribution. This was thought to represent pulmonary parenchymal inflammation associated with recent worm death. The cat was both HW Ab and Ag positive.

harbored adult heartworms but this difference was statistically insignificant (5). Interestingly, the same study reported that only 50% of the cats in which adult worms were found at necropsy were antibody positive. Cats that are allowed outdoors are at increased risk of infection with any outdoor access increasing the risk of exposure by a factor of two (6). However it is important to emphasize that heartworm infection has been diagnosed in cats which the owners report as living strictly indoors.

History

Cats may present with peracute or chronic signs, or can be completely asymptomatic. The acute syndrome is commonly associated with acute respiratory compromise secondary to severe pulmonary thromboembolism and frequently results in death. Any cat that dies suddenly in an area known to be endemic for heartworm should be evaluated via meticulous necropsy for evidence of *D. immitis* infection. Vomiting and respiratory signs seem to be the predominant signs in chronic disease but there may be cardiopulmonary indicators (coughing, dyspnea) or simply vague illness (lethargy, partial anorexia and weight loss). The actual relationship, if any, between vomiting and heartworm infection has not been well characterized. None of the studies in which this clinical sign has been

described have reported the incidence of vomiting in the general hospital population, making its specific importance relative to HW infection difficult to determine.

Physical examination of asymptomatic cats with heartworm disease is frequently unremarkable. The presence of increased bronchovesicular sounds is commonly reported but is very non-specific. Detection of a murmur or gallop rhythm is very unusual in cats with heartworm disease and should increase the clinician's suspicion of primary and secondary cardiac disease.

Laboratory tests

Routine diagnostic tests are often done in an effort to establish, refute or better characterize a diagnosis of HWD. Some of these are very useful in staging the severity of disease, while others are of limited value.

Radiography

Thoracic radiography is one of the most useful tests available, although the findings are commonly non-specific and quite inconsistent (**Figure 2**). Variable broncho-interstitial lung patterns, and less frequently pure bronchial, interstitial or alveolar patterns, have been reported (7). One of most commonly reported findings in cats with

adult heartworm infection is enlargement of the pulmonary arteries (defined as a pulmonary artery with a diameter > 1.6 times wider than the ninth rib at the ninth intercostal space (**Figure 3**) (8). The caudal lobar arteries usually show the earliest radiographic changes (with the right and left being equally affected) and this is best appreciated on the dorso-ventral view. Evaluation of the arteries may be hindered by the presence of significant pulmonary parenchymal disease and it may be necessary to treat this before diagnostic radiographs can be obtained. Unlike the dog, it is uncommon to see significant alterations in cardiac size or shape, even in severe cases. While radiographic signs of congestive heart failure are quite uncommon, chylothorax has been described with feline HWD (**Figure 4**) (9,10) and in an endemic region, chylous pleural effusion warrants further pursuit of a diagnosis of feline heartworm.

Echocardiography

In contrast to dogs, echocardiography is very helpful in cats as laboratory tests can be negative even with adult infection. Numerous reports and abstracts have documented the diagnostic utility of echocardiography in cats with heartworm disease (9,11). Sensitivities ranging from 34-100% have been reported, suggesting that in more than 50% of cases worms can be visualized within the cardiac chambers or pulmonary arteries. It is imperative that adequate visualization of the entire right heart, bifurcation of the main pulmonary

artery and the proximal portion of the right pulmonary artery be obtained. Most worms are seen in the pulmonary arteries and appear as parallel hyper-echoic structures typically 0.7-1.2 mm thick and separated by approximately 0.5-1.0 mm, commonly described as resembling a bright “equal” (=) sign (**Figure 5**). The length can vary, reflecting the angle at which the worms are aligned relative to the echocardiographic imaging plane. Determination of the exact number of worms is often quite difficult. Equally as important, echocardiography is very helpful in establishing or refuting a diagnosis of primary cardiac disease.

Tests for heartworm infection

Several testing methods are available for detection of infections in cats. The indirect fluorescent antibody (IFA) test detects host antibodies against microfilarial cuticular and somatic antigens but is not widely available, which is unfortunate as it is considered a highly specific and sensitive indicator of initial heartworm, detecting some cases as early as 1-2 months post infection.

Two ELISA tests are available, an antibody (Ab) test and an antigen (Ag) test. The Ab test, which detects antibodies to heartworm antigen, is quite sensitive. Recent studies using both ELISA and IFA tests to evaluate well-characterized feline serum suggest they are quite specific, even in the presence

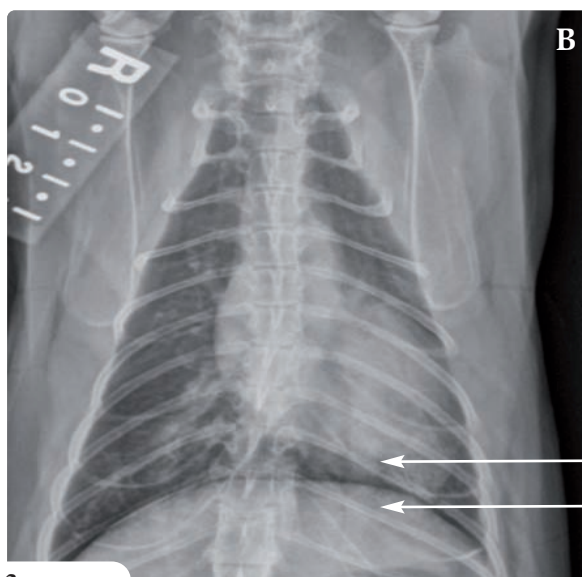


Figure 3.

Lateral (A) and ventrodorsal (B) radiographs from a cat presented with chronic and recently progressive respiratory difficulty. Note the diffuse mixed broncho-interstitial pulmonary parenchymal infiltrates coupled with dramatic pulmonary arterial enlargement (arrows). This cat was HW Ab negative and HW Ag positive; worms were found in the main pulmonary artery on echocardiography.

of heavy intestinal parasitism. A positive Ab test simply documents initial infection, but does not confirm adult infection. Conversely, a negative result makes a diagnosis of heartworm substantially less likely but does not completely exclude it. Some cats with mature heartworm infection (positive ELISA Ag test or confirmed via necropsy or echocardiography) have been Ab negative. This situation was thought to be quite uncommon, but one study suggested this may occur in as many as 50% of adult infections (5) and antibody negative cats showing clinical signs suggestive of heartworm and in which other tests (e.g. radiography) support a diagnosis deserve further evaluation. This additional evaluation might include an echocardiogram, an ELISA Ag test and an additional Ab test (perhaps using an alternative laboratory). Circulating Ab are typically detectable within 2-4 months of exposure and the ELISA tests may remain positive for 9-12 months, even if a mature infection is not established.

The ELISA Ab tests offered by some laboratories are considered semi-quantitative with the intensity of the test correlating to some extent with the likelihood of mature infection. The units of measurement used to report results may vary; where results are given as antibody units per milliliter (AbU/mL) a value < 5 ABU would be considered

negative, a value between 5-20 ABU/mL would be typical of exposure, and a value > 20 ABU/mL would be common in cats with a mature infection. Note that these values are guidelines and do not represent definitive categories. If results are reported as a titer, a value of 1:70 is considered positive (the reported range being 1:70 to > 1:5000); the higher the titer the more likely it represents mature infection. Serial samples may be informative, with increasing levels suggesting sustained or ongoing infection; note that a titer needs to change by a factor of four to be considered significantly different.

The ELISA Ag and immunochromatography tests (ICT) which detect circulating antigen (primarily found in adult female heartworms) are the most specific tests currently available to detect mature infections. Although the tests were originally marketed for use in the dog, they can be used in any species. Low worm burdens (< 3 worms), all-male infections or immature infections may result in false negative results. When evaluating the results of an ELISA Ag or ICT test in a cat, a negative result does not rule out dirofilariasis, but a positive test offers strong evidence of heartworm infestation. Several studies (echocardiographic, experimental and necropsy) suggest that approximately 40% of cats with adult worms are Ag positive.

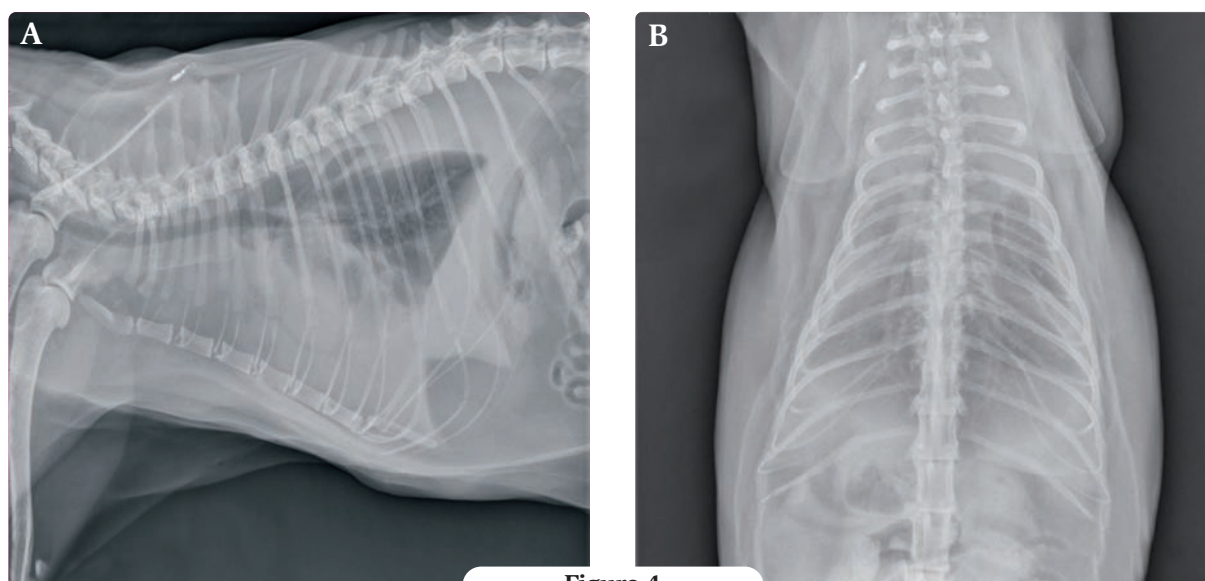


Figure 4.

Lateral (A) and dorso-ventral (B) radiographs from a cat presented for evaluation of previously diagnosed chylothorax. This cat was HW Ab negative but HW Ag positive. This cat died suddenly while in the hospital and necropsy documented the presence of three adult heartworms (two female, one male).

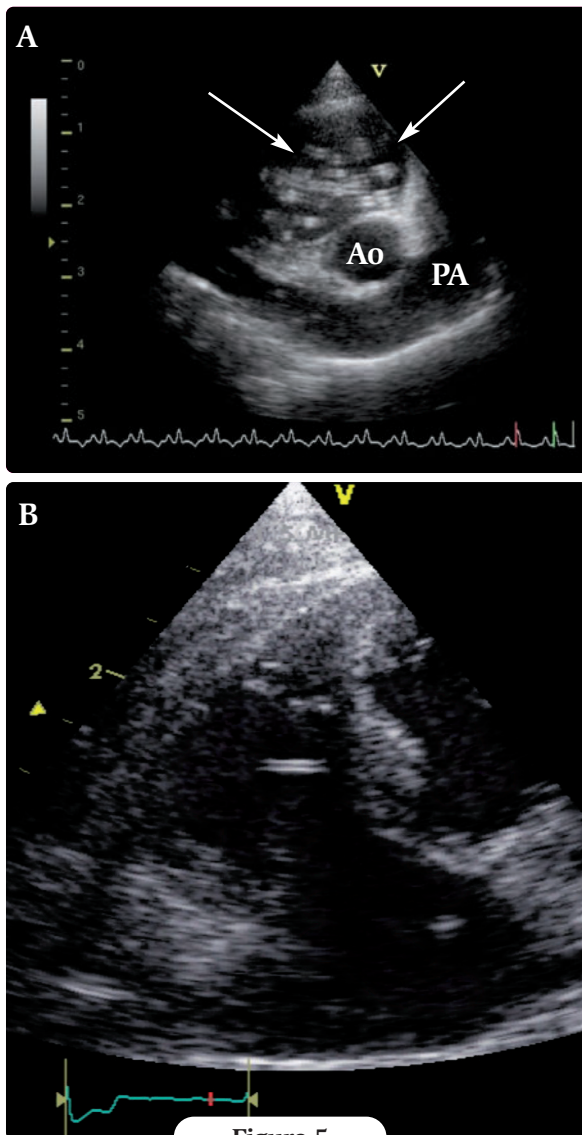


Figure 5.

A: Right parasternal short axis view at the level of the aorta and pulmonary artery from a cat with a large worm burden. Note the dilation of the pulmonary artery (PA) relative to the aorta (Ao). In addition there are a large number of worms seen in the right ventricular inflow tract (arrows).

B: Left parasternal four chamber view optimized for the right heart demonstrating the characteristic echocardiographic signature of a heart worm with bright parallel lines commonly described as a hyperechoic " = " sign.

Microfilaria tests

Concentration techniques (filter, modified Knott's) can be performed in cats suspected of having heartworm disease but are often of little value; as noted, < 20% of all infections are patent. Even in cats with circulating microfilaria, the low concentration and transient nature of the micro-

filaremia results in a large number of false negative results. The sensitivity of the concentration tests may be improved by performing multiple tests and by using 5mL of blood for each test rather than the standard 1mL. Although the concentration tests have a very low sensitivity, a positive test establishes a definitive diagnosis.

Adulticide therapy

Given that most cats infected with *D. immitis* are asymptomatic, they commonly self-cure, and the lifespan of the parasite in the cat is shorter than in the dog, it is the author's opinion that asymptomatic cats with heartworm infection should not receive any form of adulticide therapy. However, the pulmonary pathology associated with *D. immitis* infection and the possibility of acute death would seem to argue in favor of initiating therapy following definitive diagnosis. The drug of choice in dogs, melarsomine, is not licensed for cats and there is little data regarding its use in this species, although it has been suggested that a single dose at 2.5 mg/kg IM will reduce worm burdens by approximate 30% without serious complications. Another option may be sodium caparsolate but it is no longer available in many countries and again data is limited; in one study, the survival rate for 11 cats treated with this drug did not differ significantly compared to 30 cats managed without specific adulticide therapy (12).

Cats presented for cough and/or dyspnea may initially respond to administration of corticosteroids and bronchodilators. The initial prednisone dose is 1-2 mg/kg orally twice daily for 10-14 days, with the dose then gradually reduced to the minimum level that will eliminate clinical signs. Alternate-day prednisone therapy can potentially be given indefinitely if signs are persistent or recurrent (9). Although bronchospasm associated with pulmonary inflammation might play a role in this disease, routine use of bronchodilators is not advocated.

There is growing interest in the role that *Wolbachia* bacteria plays in the pathogenesis of feline HWD. *Wolbachia* is a genus of bacteria that infects arthropods and nematodes, and its surface proteins have been shown to stimulate pro-inflammatory cytokines, prompting the theory that the bacteria has a major role in the pathophysiology of feline

heartworm disease (13). In a recent paper, dogs given ivermectin (at four times the preventative dose) and doxycycline before undergoing adulticide therapy had substantially less pulmonary pathology when compared to dogs receiving adulticide alone (14). Despite these results, a recent study investigating a link between *Wolbachia* load and the severity of lung pathology in heartworm-infected dogs and cats did not demonstrate a clear correlation between the two (15). Although interesting, the role of *Wolbachia* in the pathophysiology of heartworm disease in cats remains to be defined and therefore the routine use of doxycycline in cats with heartworm disease is not recommended. Additionally, antiplatelet therapy including aspirin and clopidogrel as an adjunct of therapy in heartworm disease is not advocated by the American Heartworm Society.

The dismal outcome associated with conventional therapy has prompted several investigators to pursue surgical removal of adult heartworms. One study (16) reports removal of adult worms from 5 cats via thoracotomy; cats with worms located primarily in the right atrium and caeve underwent a right lateral thoracotomy and right atriotomy, while cats with worms seen only in the pulmonary artery underwent a left lateral thoracotomy and pulmonary arteriotomy. Various instruments, including a small bronchoscopic grasping device, alligator forceps or a nitinol gooseneck snare catheter have all been employed for removal of adult heartworms, with standard echocardiographic imaging used to assist positioning (17,18) (**Figure 6**). Since acute respiratory and cardiovascular failure have been reported following crushing or fragmentation of a worm, pre-treatment with corticosteroids and/or antihistamines may be advisable to reduce the severity of these types of reactions. As techniques are refined, surgical removal of adult heartworms may become the therapy of choice for symptomatic adult infections.

◊ Microfilaricidal therapy

The fact that cats infrequently have circulating microfilaria typically makes it unnecessary to administer specific microfilaria therapy. Additionally, microfilaria are typically eliminated by monthly administration of one of the usual preventative medications at standard dosage; within the

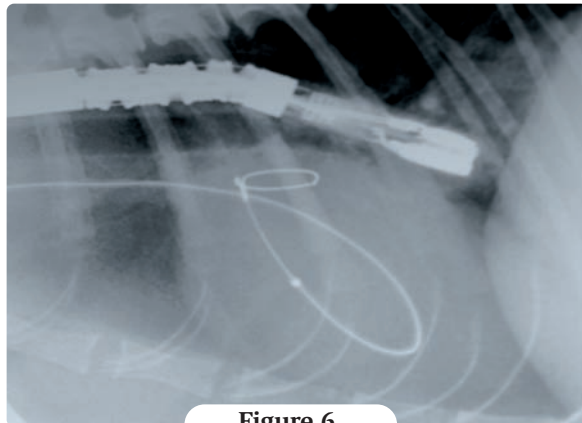


Figure 6.

Lateral radiograph from a cat with heart worm disease. A nitinol gooseneck snare has been advanced into the main pulmonary artery via the right jugular vein. A transesophageal echocardiographic probe has been positioned to assist with guidance of the retrieval device.

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currently available formulations, those containing milbemycin oxime are preferred for the most rapid elimination of circulating microfilaria.

◊ Prevention of heartworm

Heartworm prevention should be discussed with every cat owner in endemic areas. Many people consider the risk to be so low that prevention is not important, despite the fact that feline HWD is especially severe and there is no appropriate treatment. In many cases, the first sign is the only sign: sudden death. Other cats develop spontaneous worm death with life-threatening pulmonary inflammation/non-cardiogenic edema. Additionally, even in cats that self-cure, it is now well established that major pulmonary pathology can develop with significant clinical signs (3) despite the relatively infrequent development of adult infection. Since the disease is very easy to prevent, and the products are both safe and effective, at a minimum the potential value of prevention in cats should be discussed with owners. Although it is most likely safe to administer preventative medications to the vast majority of cats (even HW positive cats), the author recommends obtaining at least an Ab titer prior to dispensing any product. This helps establish the exposure status of the individual patient and over time will help determine the exposure status of the local feline population.

◊ Conclusion

Heartworm disease remains an important disease

Table 1.

Drugs commonly used to prevent feline heartworm disease.

Ivermectin	Oral tablet given once monthly
Milbemycin oxime	Oral tablet given once monthly
Selamectin	Topical treatment applied monthly
Moxidectin	Topical treatment applied monthly

of cats in many areas of the world. It should be included in the differential list for any cat from a heartworm endemic area demonstrating clinical signs of acute or chronic respiratory disease and in any cat that dies suddenly without premonitory signs. Even cats thought to be housed exclusively indoors are potentially at risk. HWD diagnosis is

challenging, complicated by the presence of low worm burdens, the possibility of all-male parasite infections, the uncertainty of serologic testing, and the non-specific thoracic radiographic manifestations. The combination of a reasonable level of suspicion and appropriate diagnostic tests increase the likelihood of an accurate diagnosis. Unfortunately, management of adult infections is typically symptomatic as adulticide therapy is associated with substantial risk and major lung pathology can occur even without adult infection developing. The disease is almost completely preventable and the chemo-prophylactic medications available (**Table 1**) offer potential health benefits well beyond simply preventing heartworm infection. It is important therefore that veterinarians take a more pre-emptive approach to the management of this disease. ☺

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Images of hypertrophic cardiomyopathy

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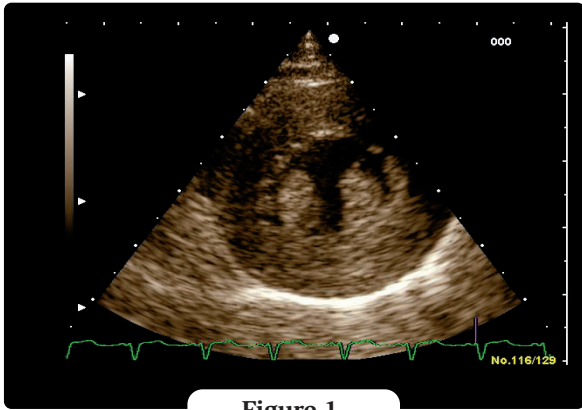


Figure 1.

1-year-old female cat. Right parasternal two dimensional SAV showing the left ventricle in diastole. There is hypertrophy of the myocardium and papillary muscles.

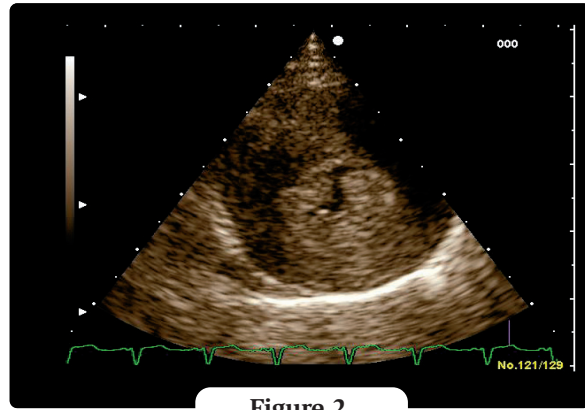


Figure 2.

Same cat as **Figure 1**. Right parasternal two dimensional SAV showing the left ventricle in systole. The myocardium is hypertrophic. Note the extreme narrowing of the left ventricle.

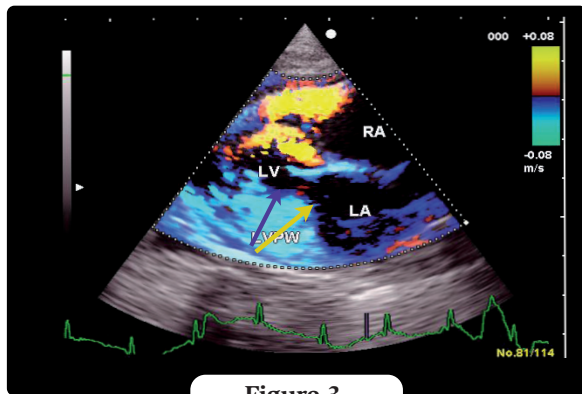


Figure 3.

3-year-old male cat. Right parasternal 2-D LAV in TDI mode, showing the heart in diastole. Note the myocardial thickening in the apex (blue arrow) and papillary muscle (green arrow).

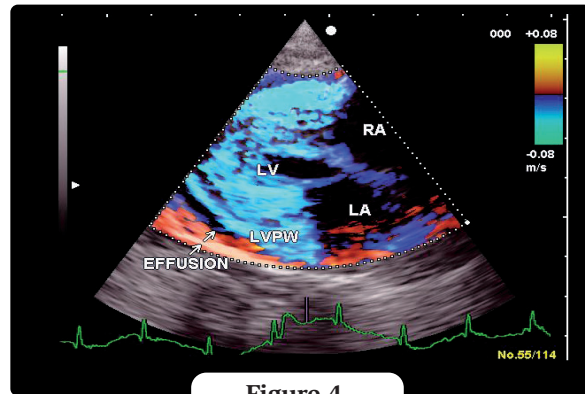


Figure 4.

Same cat as in **Figure 3** and same view, this time with the heart in systole. Again note the myocardial thickening of the apex and papillary muscle with a minor degree of pericardial effusion.

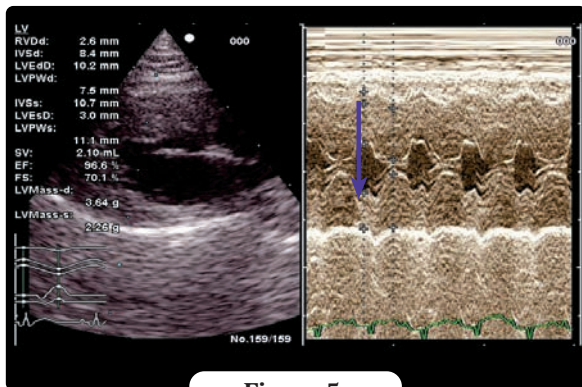


Figure 5.

2-year-old male cat. Right parasternal 2-D LAV and T/M mode demonstrating a hypertrophic myocardium, an increased inter-ventricular septum diastolic diameter and an increase in the left ventricular posterior wall in diastole (arrowed).

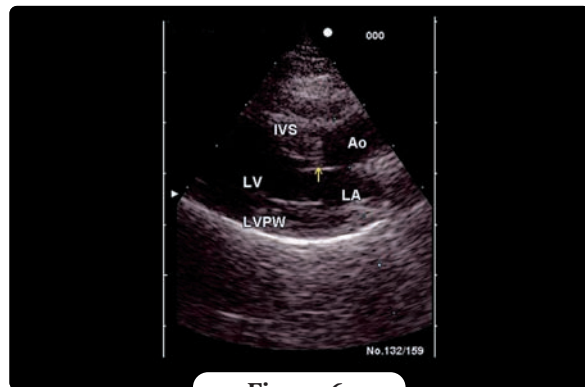


Figure 6.

3-year-old female cat. Right parasternal 2-D LAV. The left out-flow tract region is narrowed by a focal septal hypertrophic area and the septal mitral valve leaflet is in contact with the hypertrophic area (arrow).

Key: LAV: long axis view; SAV: short axis view; LA: left atrium; LV: left ventricle; RA: right atrium; LVPW: left ventricular posterior wall; IVS: intraventricular septum; Ao: aortic root.



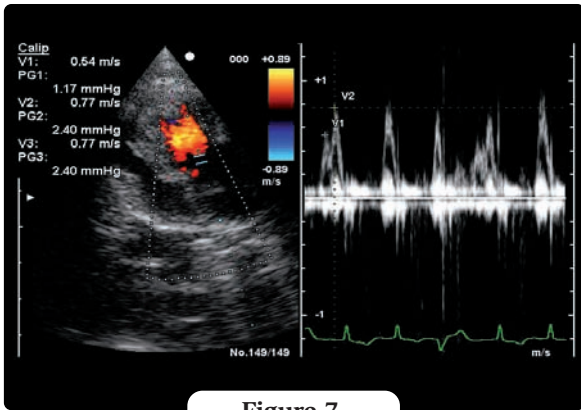


Figure 7.

8-year-old female cat with HCM. Left apical 4-chamber view. The red area on the Colorflow Doppler indicates the blood flow from the left atrium to the left ventricle. On the Pulsed-Wave Doppler the E-Wave (V1) is less than the A-Wave (V2) due to increased ventricular pressure counteracting the blood flow from the left atrium. The ECG shows a single ventricular premature beat.

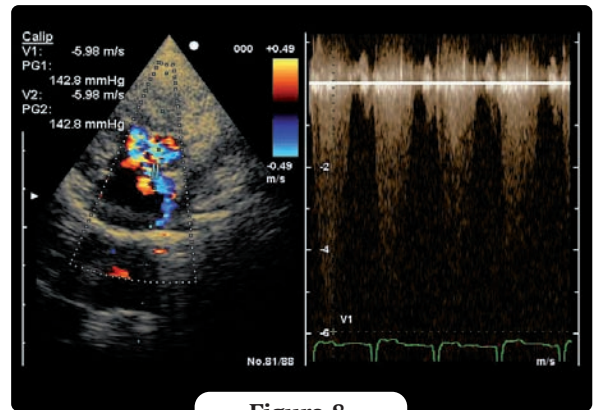


Figure 8.

3-year-old female cat with HCM. Left apical 2-chamber view. The Colorflow Doppler shows a turbulent blue-yellow-red mixed signal from the closed mitral valve area with a regurgitation pattern in the enlarged left atrium which follows the posterior wall to the top of the atrial wall. The Continuous-Wave Doppler shows a typical regurgitation pattern.

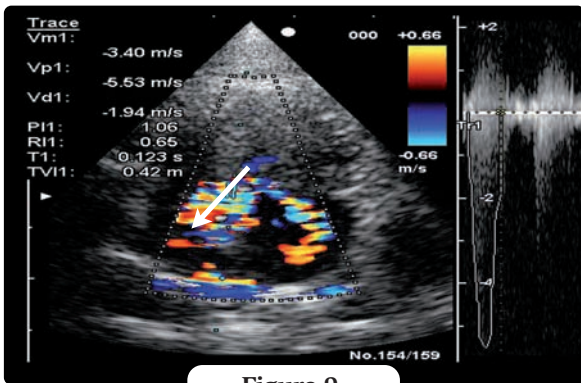


Figure 9.

3-year-old female cat with obstructive HCM. Left apical 5-chamber view. The Colorflow Doppler has a turbulent blue-yellow-red mixed signal in the left ventricular outflow tract, aorta and in the left atrium (indicative of mitral valve regurgitation). The Continuous-Wave Doppler shows an increased post-stenotic flow pattern in the aorta (arrowed).

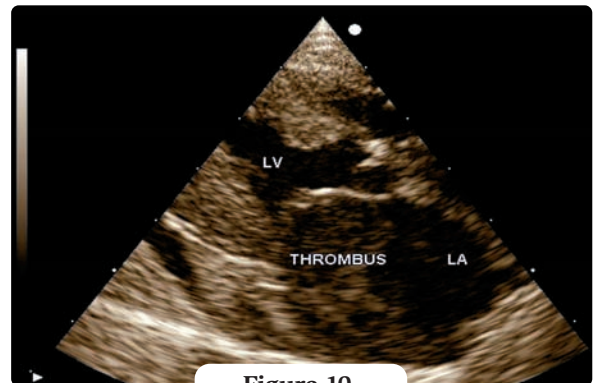


Figure 10.

6-year-old male cat with what was thought to be HCM. Right parasternal two dimensional LAV. Thrombus sludge is visible in the left atrium.

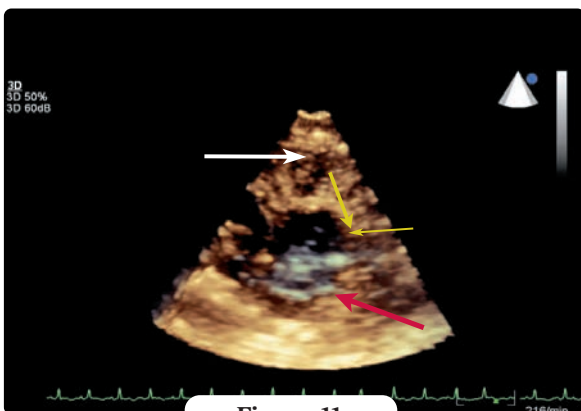


Figure 11.

4-year-old male cat scan Real Time 3D echocardiogram apical 4 chamber view from the left thorax. The papillary muscle and myocardium of the left ventricle (white arrow) are massively thickened. Note the closed mitral valve (yellow arrows) and enlarged left atrium (red arrow).

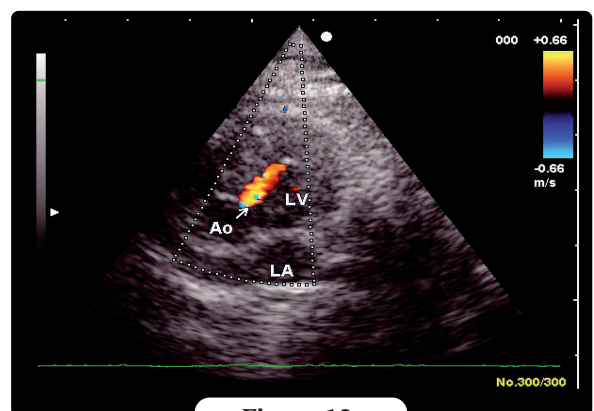


Figure 12.

5-year-old female cat with HCM and aortic regurgitation. Left apical 4 chamber view; the red coding on the Colorflow Doppler indicates blood flow from the aorta to the left ventricle. Whilst not uncommon in dogs, aortic regurgitation is rare in cats.

