Management of Heart Disease in Cats

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Overview

Cats with heart disease can be tricky, and diagnostic testing helps to make the right choice on treatment. A complete cardiac exam, ECG, echocardiography, laboratory testing, and thoracic radiographs can be helpful to diagnose and stage feline heart disease. NT-proBNP seems likely to play an increasing role in the diagnosis and management of cats with cardiac disease. There are few prospective clinical trials to support a specific set of recommendations in cats, so what follows is my current approach to cats, which is a mixture of experience, mistakes, research, and the current literature. I will try to outline an approach that follows from certain clinical situations and then from certain specific drugs.

Asymptomatic Hypertrophic Cardiomyopathy

The cat with LV hypertrophy and no atrial enlargement

Most people identify LV hypertrophy in a cat as a diastolic wall thickness > 0.6 cm for the interventricular septum (IVS) or left ventricular free wall (LVFW, or LVPW). There is probably some wiggle room here and some older cats and some smaller cats likely have LVH when the walls are > 0.55 cm. Unless these cats are particularly tachycardia or have arrhythmias, I usually do not treat them and simply recheck in 12 months. Hyperthyroidism and systemic hypertension should be excluded as Ddx for the cause of LVH (measure blood pressure if LVH, especially if concurrent azotemia, and perform thyroid testing in all cats > 6 who have some evidence of heart disease). Some people may use beta-blockers in this population of cats, to prevent tachycardia-induced CHF, or to just slow the heart rate and enhance time for diastolic filling, but I have shied away from this strategy (some people also use sustained release diltiazem). One of the concerns is the challenge of giving cats medications twice a day on an indefinite basis, and part of my concern is the uncertain benefit of this strategy (I suspect the number needed to treat to prevent 1 episode of CHF is quite high).

The cat with Left Ventricular Outflow Tract Obstruction

Beta blockers are the most commonly used drug family in cats with hypertrophic cardiomyopathy who have left ventricular outflow tract obstruction (LVOTO). Cats with LVOTO often have significant LV and especially septal hypertrophy. Sometimes the top of the IVS is very hypertrophied and contributes significantly to LVOTO. LVOTO can be complicated by, or be mostly due to, systolic anterior motion (SAM) of the mitral valve. Due to any number of factors (elongated mitral valve, abnormal papillary muscle position due to LV hypertrophy, or congenital location, etc.), during systole the anterior mitral valve leaflet moves (or is carried) into the LV outflow tract and contributes to obstruction. The mitral valve leaflet may even come into contact with the IVS in systole in the LVOT below the aortic valve. As the valve moves into the LVOT, the mitral orifice is no longer covered by the valve and there is typically secondary mitral regurgitation. The mitral valve regurgitation, plus the stiff LV in diastole, contributes to the development of left atrial enlargement in many cats.

Use of beta-blockers, in selected cats, can result in a reduction in the LVOT gradient, less SAM of the mitral valve, a reduction in the degree of mitral regurgitation, and some reduction in the degree of LV hypertrophy. While these echocardiographic findings can improve, and often the accompanying murmur is softer, it is less clear whether beta-blockade will delay the time until collapse, CHF, or arterial thromboembolism. One study looking at atenolol use in cats with HCM over a 5 year period failed to find a clear clinical improvement of the cats treated with beta-blockers. Due to this study, and my own clinical experience in which a number of cats placed on atenolol progressed a bit faster to CHF than was expected, I preferentially use carvedilol instead of atenolol in cats with LVOTO. The usual trigger for us to use a beta-blocker is the presence of moderate to severe LVOTO, often with SAM of the mitral valve, where the left ventricular outflow tract velocity is at least 3.5 to 4 m/sec. Atenolol is often given at doses of 6.25 mg PO q 12 hours, and sometimes titrated to higher doses. Carvedilol is often started at a low dose with subsequent slow titration upwards to a higher dose. In many cats I start with ½ of a 3.125 mg tablet PO q 12 hours and after 2 weeks go up to 1 tablet PO q 12 hours (in very small cats or cats with prior/current CHF I start at ¼ tab PO q 12 hours). For stable cats with persistent LVOTO at the 4 to 6 month recheck I will titrate up to 1.5 tablets and then eventually 6.25 mg PO q 12 hours.

Cardiomyopathy and Congestive Heart Failure

The approach for cats with CHF is similar regardless of the type of underlying cardiomyopathy. CHF should be documented by a combination of clinical methods. CHF is most convincingly present in cats with clinical signs of dyspnea, and radiographic or ultrasonographic evidence of pulmonary edema and/or pleural effusion, and cardiomegaly with echocardiographic evidence of moderate to marked left atrial enlargement, and a quantitive NT-proBNP test of > 260 pmol/L. Most cats will also be strongly positive on a bedside (SNAP) NT-proBNP test. Once the diagnosis of CHF is established then the following therapies might be used, typically in some combination. Most cats with CHF have enough left

atrial enlargement that they are at risk for arterial thromboembolism, so antithrobotics (e.g., clopidogrel) should be used on a chronic basis.

Furosemide

Furosemide is indicated once CHF has been confirmed. The dose range is quite variable, from 1 mg/kg q 48 hours for chronic low grade CHF up to 4 mg/kg every 1-2 hours for life threatening pulmonary edema. The lowest dose required to clear significant edema accumulations and cause the animal to be minimally symptomatic is best dose. The lowest possible dose reduces the chance for electrolyte disturbance (hypochloremia, hypokalemia, hyponatremia, hypomagnesemia), dehydration and the development of pre-renal azotemia. If concerning azotemia develops (BUN > 35-40 mg/dl, creatinine > 2.2-2.4 mg/dl) then in most cats a dose reduction will be required in order for the cat to maintain a normal appetite. Serial measures of total solids can also help in furosemide dose adjustment. In acute pulmonary edema these values are check ed daily, while in chronic management of CHF re-evaluation of renal values and electrolytes should be done every 3 to 6 months.

In order to determine the lowest possible dose of furosemide which with control signs of CHF, a degree of experimentation and dose adjustment must be performed. We giving the owner an upper and lower limits for acceptable furosemide dose, and carefully explaining to them that they should "give more for difficulty breathing or rapid respirations, and give less if the animal seems weak, lethargic, anorexic, or depressed". We use of a target respiratory rate of < 35 breaths per minute, when the cat is at home, at rest, and not purring, although some studies suggest a lower respiratory rate is usually present in cats with well managed CHF. Owners are instructed to give extra furosemide if the respiratory rate is > 35 breaths per minute or if respiratory effort (abdominal effusion to breathing) is noted.

In most cats we initially try to use 6.25 mg/cat once or twice a day for chronic therapy. Some cats require higher doses of furosemide, especially those with pleural effusion which required thoracentesis. Most veterinary cardiologists would not recommend single agent use of furosemide for treatment of CHF, so furosemide is used in combination with one or more of the drugs outlined below. Diuretic use in asymptomatic heart disease, before the onset of CHF, is usually not recommended. In asymptomatic cats with marked left atrial enlargement and thought to be at risk of CHF, we might send the owner home with furosemide tablets to give if dyspnea, tachypnea or shortness of breath is noted.

Angiotensin-Converting Enzyme Inhibitors

Angiotensin-converting enzyme (ACE) inhibitors are usually indicated once CHF has been documented. There is some information to suggest that ACE inhibitions might slow the progressive cardiac enlargement seen in animals with heart disease, but this has not yet been documented in cats. We do sometimes prescribe an ACE inhibitor in an asymptomatic cat with moderate to marked left atrial enlargement who is judged to be at higher risk for CHF. Possible side effects of ACE inhibitors include azotemia, hypotension, weakness, anorexia and hyperkalemia. Of these, azotemia and anorexia are the more common dose limiting dose effects, but a low dose can often be tolerated in most cats with CHF. Target doses are as follows: enalapril 0.5 mg/kg q 12-24 hours, lisinopril 0.5 mg/kg q 12-24 hours, and benazepril 0.25 to 0.5 mg/kg q 12 to 24 hours. In most cats we use enalapril and start at 2.5 mg/cat/day (except in small cats) and increase to twice a day dosing in refractory CHF. I have had more luck using lisinopril in cats where I am worried about the kidneys, and usually start at .25 mg/kg/day. Renal values and electrolytes should be measured before initiation of an ACE inhibitor, and in cats with CHF these values should be rechecked in 7 to 10 days and dose adjustments to the diuretic (or ACE inhibitor) made at that time. It is recommended to measure renal function serially when using ACE inhibitors, at least once a year if used I asymptomatic cats and q 3 to 6 months in cats concurrently getting furosemide.

Pimobendan

Pimobendan is a calcium sensitizing drug that is useful as a positive inotrope. In addition to this positive inotropic effect, pimobendan is a phosphodiesterase inhibitor with vasodilating effects. This combined action of positive inotropy and vasodilation has been referred to as inodilation. Pimobendan has been well studied in dogs with documented utility both with CHF and before the onset of CHF, however it is less well studied in cats. Pimobendan seems to be associated with a low side effect profile in dogs, and with the exception of cats that have LVOTO this has been our experience with cats as well. The main concern with cats is that those with LVOTO, or even mid-ventricular obstruction, might have worsening of the obstruction if given a positive inotropic drug. In general, pimobendan should be avoided, or given with great caution, in situations of cardiac outflow tract obstruction. In cats this usually means that an echocardiogram should be performed prior to initiation of pimobendan to exclude cats with LVOTO and/or SAM of the mitral valve. We have used pimobendan in cats with LVOTO, when other routine therapies have failed to control CHF. The usual dose for pimobendan is 0.25 mg/kg q 12 hours, and in most cats that translates to 1.25 mg/cat PO q 12 hours. We routinely prescribe pimobendan to cats with all forms of cardiomyopathy with CHF if they do not have LVOTO.

Beta-blockers in CHF

Beta blockade are usually not used in cats with CHF unless there is marked to severe LVOTO, or concerning arrhythmias, and if we use a beta-blocker in this setting we are more likely to use carvedilol, starting at a low dose and titrating the dose up slowly, q 2 weeks.

Advanced CHF refractory to the above therapies

When a furosemide dose of 6.25 mg/cat twice a day is exceeded during chronic therapy, the author usually thinks that diuretic resistance has been reached and may undertake one of several options to combat this complication. One choice is to add in spironolactone starting at 6.25 mg PO q 48 hours, and if this is well tolerated after 1 week then increase to 1 mg/kg q 24 hours. I am less likely to use the combination tablet of hydrochlorothiazide with spironolactone unless a cat has refractory pleural effusion that requires frequent thoracentesis. We also sometimes use torsemide at 1/8th to ¼ of a 5 mg tablet orally once a day (in addition to the prior dose of furosemide), although this may be too much diuretic for some cats and serial evaluate of renal values and electrolytes is recommended. Increasing the ACE inhibitor to q 12 hour is another option. Increasing pimobendan to 3 times a day, or twice the original dose q 12 hours, is another option. Sildenafil can be added in at 1-2 mg/kg q 8 hours. Dietary sodium intake should be reviewed and moderated if appropriate and possible. Finally, the furosemide dose can be escalated further, or sometimes injectable furosemide (subcutaneously) will be effective when oral administration seems less effective.

Prevention of Arterial Thromboembolism

Arterial thromboembolism (ATE) is a common complication of feline heart disease, occurring in 20-40% of cats with cardiomyopathy and significant left atrial enlargement. The thrombus may develop in either the left ventricle or the left atrium, however, a left atrial origin is most common. Dilatation of the left atrium, reduced LA contractile function resulting in stasis of blood within in the enlarged LA, and perhaps endothelial damage or activation likely contributes to thrombus formation. Since the treatment of arterial thromboembolism is very difficult and often unsuccessful, prevention of this devastating event becomes very important. We will often start antithrombotic medications in any cat with moderate atrial enlargement, in almost all cats with CHF, and in cats with an NT-proBNP concentration > 500 pmol/L (as most cats we see with ATE have a BNP greater than this value).

Clopidogrel and Aspirin

A recent study demonstrated that clopidogrel was superior to aspirin in preventing recurrent ATE. This finding, combined with concerns regarding the action of aspirin on the GI mucosa and on the kidneys in cats with reduced renal perfusion, has caused us to largely abandon use of aspirin in cats. The antiplatelet drug, clopidogrel (Plavix), is now our routinely used drug for prevention of ATE in cats. The drug comes in a 75 mg tablet and we give ¼ tablet PO q 24 hours to most cats, except for cats < 3.5-4 kg, in which case we might compound the drug to give a smaller dose. Clopidogrel seems to be well tolerated in many cats, although foaming at the mouth or vomiting has been seen in 10-20% of cats. Compounding the drug may reduce this side effect for some cats (try marshmallow flavor), although the taste may still trigger this reaction in other cats. In most cats we place the ¼ tablet inside of an empty gelatin capsule and have the owner administer the gelatin capsule (followed by some liquid or food if possible). There is no routine monitoring of clotting times or any other blood tests for this drug. Some clinicians use a dual antiplatelet strategy, and give both clopidogrel and aspirin, although this strategy is uncommon in our practice.

Low Molecular Weight Heparins - Dalteparin and Enoxaparin

Low molecular weight heparins (Dalteparin and Enoxaparin) are sometimes used to prevent thrombus formation in cats at high risk of ATE, especially in cats who have already experienced ATE. We have used dalteparin (Fragmin; 160 to 250 U/kg) subcutaneously twice a day. Enoxaparin is given at 1 mg/kg subcutaneously twice a day. One major action of the drug is to inactivate clotting factor Xa. Both dalteparin and enoxaparin can be expensive to use on a long-term basis (several hundred dollars per month for twice a day treatment in most cats). The drug must be given by subcutaneous injections. Yet, many owners prefer injections to oral medications in cats, and the drug is well tolerated by most cats. We sometimes combine clopidogrel and a low molecular weight heparin.

Coumadin (Warfarin)

Coumadin works by blocking the vitamin K dependent clotting factors II, VII, IX and X. By titrating the dose of warfarin, a degree of anticoagulation can be achieved in an attempt to reduce thrombus formation. We do not use coumadin in our practice for cats due to the higher risk and difficulties with dose titration.

Rivaroxaban and Apixaban

These drugs are anticoagulants that will likely replace coumadin. We have used rivaroxaban in a handful of cats at 2.5 mg/cat/day. Unexpected bleeding is the main concerning side effect, and if these drugs are used then cats should be protected from trauma, and care should be taken for phlebotomy, cystocentesis, surgery and other routine procedures.

Treatment of new onset ATE

Once ATE develops, treatment is largely empiric, and there is little scientific information to direct the best treatment approach. Yet, all cats that a euthanized for ATE die, and some that are given supportive care will survive. Most cats with a front let ATE will regain function of the limb (over 90%). Perhaps 40-50% of cats with a single back leg ATE will regain function. The survival is worse for cats with bilateral back limb ATE, and those with a rectal temperature < 98.5 degrees F likely have the lowest chance for survival. If treatment is to be initiated then it should be started ASAP, ideally within 10

minutes of arrival at the hospital, even before discussions with the owner have concluded. I would recommend giving at least ½ to almost a full tablet of clopidogrel (a loading dose) and giving 250-300 units/kg of unfractionated heparin subcutaneously (or intravenously) as soon as the diagnosis is evident. Control of pain, nursing care, some antithrombotic, management of CHF if present, and general supportive measures are indicated. Many cats have open mouth breathing due to discomfort, without CHF, and if furosemide is given to cats without CHF it volume contracts them and further reduces the chance that reperfusion will occur (so get a thoracic radiograph before giving furosemide). Heparin is the drug most commonly used to prevent further enlargement of the thrombus. Heparin can be administered subcutaneously or intravenously. An initial intravenous bolus of heparin (200-250 units/kg) can be followed by a continuous rate infusion of heparin (12-25 units/kg) or subcutaneous administration (200-300 units/kg q 6-8 hours). Heparin is usually continued until the time of hospital discharge or until other antithrombotic therapy has been initiated for at least 24-48 hours. Low molecular weight heparin (LMWH) has been used in this setting instead of unfractionated heparin, and if the setting of ATE we give high doses with increased frequency (dalteparin at 200-250 U/Kg q 6-8 hours or enoxaparin 1-1.5 mg/kg q 8 hours). We usually will not give aspirin in the acute setting of ATE, although there is growing evidence in people to suggest that aspirin administration is settings of acute thromboembolic disease might be useful.

Thrombolytic drugs can actually dissolve a thrombus once it has formed. There is no clear consensus as to whether these drugs should be used if a thrombus is identified in a cardiac chamber, as their use may result in liberation of the thrombus and subsequent arterial thromboembolism. Tissue plasminogen activator, urokinase and streptokinase have been used in cats. Bleeding complications are possible and complications resulting from reperfusion injury (hyperkalemia and metabolic acidosis) are often life threatening. If thrombolytic drugs are to be used they should be initiated immediately, ideally within two to four hours after the onset of clinical signs. Surgery (embolectomy) can be attempted in cats, but anecdotal clinical experience in veterinary medicine indicates that surgery for thromboembolism probably doesn't improve clinical outcome.

1) In cats with hypertrophic cardiomyopathy and left ventricular outflow tract obstruction identified on echocardiography, which of the following drugs is usually avoided?
    a. Pimobendan
    b. Furosemide
    c. Clopidogrel
    d. Enalapril
2) In cats with hypertrophic cardiomyopathy and congestive heart failure, which of the following 3 drugs are used in most cats?
    a. Pimobendan, furosemide, and aspirin
    b. Furosemide, an ACE inhibitor, and clopidogrel
    c. Furosemide, spironolactone, and amiodarone
    d. Diltiazem, atenolol, and furosemide
3) Which of the following drugs is a calcium sensitizer?
    a. Enalapril
    b. Diltiazem
    c. Clopidogrel
    d. Pimobendan
4) In cats with hypertrophic cardiomyopathy, what concentration of NT-proBNP is likely associated with CHF?
    a. < 50 pmol/L
    b. 50-100 pmol/L
    c. >260 pmol/L
5) Which 2 diseases should be excluded in cats with LV hypertrophy who are over 6-7 years of age?
    a. Systemic hypertension and hyperthyroidism
    b. Hyperthyroidism and diabetes mellitus
    c. Diabetes mellitus and renal disease
6) SAM of the mitral valve refers to:
    a. Sympathetic Augmented Magnification – the valve gets smaller following epinephrine release
    b. Systolic Anterior Motion – the valve moves toward the septum in systole
    c. SAM Liu, the person who first described this abnormality of the mitral valve.
7) An antithrombotic drug might be started in;
    a. All cats with CHF
    b. Cats with moderate to marked left atrial enlargement
    c. Cats with an NT-proBNP > 500 pmol/L
    d. All of the above
8) Cats with HCM and CHF may have an S4 gallop. An S4 gallop results from:
    a. Atrial premature depolarizations
    b. Pulmonary hypertension
    c. Atrial fibrillation
    d. Atrial contraction into a stiff left ventricle
9) Which drug might be used to limit the adverse effects of LVOTO in cats with HCM?
    a. Atenolol of carvedilol
    b. Enalapril or lisinopril
    c. Pimobendan
    d. Dobutamine
10) Which of the following drugs is an example of a low molecular weight heparin?
    a. Enoxaparin
    b. Rivaroxaban
    c. Clopidogrel