Comprehensive Approach to Congestive Heart Failure

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Confirmation of the Diagnosis of Congestive Heart Failure

Congestive heart failure (CHF) is usually noted to be the presence of clinical signs such as cough, shortness of breath, or abdominal distension resulting from fluid retention (congestion) due to inadequate flow of blood to the tissues and the resulting neurohumoral activation leading to increased cardiac and venous pressures. Note that fluid accumulation or congestion, is usually a clearly notable finding in this definition when veterinary cardiologists talk about CHF.

Heart failure is a less specific term that might be applied whenever there is CHF, but also might be applied when low cardiac output occurs in the absence of fluid accumulation (e.g., low cardiac output resulting in clinical weakness as might be seen with arrhythmias, valvular stenosis, or poor cardiac contractile function).

Left-Sided CHF is present when the left heart fails and leads to congestion, which is typically manifest as pulmonary edema. **Right-Sided CHF** develops when the right heart failures and is typically associated with jugular vein distention, ascites, hepatomegaly, and sometimes pleural effusion. **Biventricular CHF** can be said to be present in animals with both left and right heart disease who have a combination of pulmonary edema and ascites – many animals with pleural effusion due to CHF have biventricular heart failure. **Low output CHF** refers to the animal that has both signs of congestion AND signs of markedly reduced forward cardiac output, such as membrane pallor, cool limbs and gums, muscular weakness, elevated blood lactate, often azotemia, and perhaps systemic hypotension.

The **Diagnosis of CHF** usually cannot be established by a single test, since CHF is a clinical syndrome that results from a number of different cardiac diseases. One typically wants to confirm that CHF is present and determine the cause for CHF. The diagnosis of CHF usually involves documentation of the presence of several of the following parameters – in general the more of these parameters that are present the more confident one can be in establishing a diagnosis of CHF. The key parameters assessed for documentation of CHF include 1) clinical signs resulting from the syndrome; 2) documentation of congestion in the form of pulmonary edema (from thoracic radiographs), pleural effusion, or ascites; 3) elevated NT-proBNP > 260 pmol/L in cats or > 1800 pmol/L in dogs (the higher the value the more confident the diagnosis of CHF); 4) echocardiographic evidence of cardiac disease sufficient to result in CHF. Thus, CHF is most confidently diagnosed using a combination of history and physical exam findings, thoracic radiographs, echocardiography, and BNP testing.

Treatment of CHF – Goals

In general, the treatment goals are to relieve fluid accumulations sufficient to make the animal asymptomatic for CHF, prolong survival time, and to avoid side effects that might limit quality of life or shorten survival via euthanasia.

Angiotensin-Converting Enzyme Inhibitors

Angiotensin-converting enzyme (ACE) inhibitors are commonly used in the management of CHF. Their use is predicated on the knowledge that interfering with the activation of the renin angiotensin system leads to diminished plasma levels of angiotensin II and reduced stimulation of aldosterone. As a result, fluid retention and vasoconstriction are blunted. ACE inhibition may alter the progressive cardiac enlargement and remodeling known to attend most forms of heart failure, although this has not been well documented in veterinary clinical trials. The beneficial effects of ACE inhibition likely result from both the vasodilation and the drug's effects to reduce cardiac remodeling.

Angiotensin-converting enzyme inhibitors have proved to be useful in a variety of settings. In a large number of human heart failure trials, ACE inhibitors have been proven to prolong survival. In well-designed canine heart failure trials, ACE inhibitors resulted in improved clinical signs and a prolonged the time until an animal dropped out of the study (equivalent to improved survival). Which animals should be treated with ACE inhibitors? There is very good experimental evidence to support the use of ACE inhibitors in dogs with congestive heart failure due to either dilated cardiomyopathy or chronic valvular disease (endocardiosis). ACE inhibitors may also be used in dogs with congestive heart failure due to endocarditis, congenital heart diseases associated with volume overload, and other forms of left-sided congestive heart failure in dogs. The role of ACE inhibitors in the treatment of animals with asymptomatic heart disease remains a hotly debated topic. In dogs with mitral regurgitation and concurrent systemic hypertension, as well as in dogs with mitral regurgitation and concurrent significant proteinuria, administration of an ACE inhibitor is currently recommended by the author. Twice a day therapy is recommended, and ACE inhibitors are usually added into furosemide and pimobendan for the management of CHF in dogs, and all 3 drugs are also used in cats that do not have left ventricular outflow tract obstruction.

Furosemide

Diuretics are indicated for animals with CHF, and furosemide is the most commonly used diuretic in dogs and cats. In most cases, diuretics should be combined with either pimobendan, or an ACE inhibitor, or both. Many cardiologists would not recommend single agent use of furosemide for treatment of CHF. It is quite difficult to define the exact dose of diuretic

required by any individual dog or cat with CHF. The dose required to clear significant edema accumulations and cause the animal to be minimally symptomatic (the desired dose) is often close to a dose that might result in electrolyte disturbance, dehydration and the development of pre-renal azotemia. Most cardiologists now concurrently use ACE inhibitors and diuretics for animals with CHF, and the prevailing recommendation is to measure renal function prior to starting therapy and then repeat the BUN, creatinine and electrolytes 5 to 10 days after starting drugs to treat congestive heart failure.

We currently recommend use of the "Lowest possible dose of furosemide" in animals with CHF. This often means a degree of experimentation to find the right dose. Giving an owner 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" has worked successfully for the author. In most instances, canine patients are given less than 2 mg/kg q 12 h, and in most cats, I initially try to use 6.25 mg/cat/day for chronic therapy. Some cats require higher doses of furosemide, but some can be treated with 6.25 mg/cat every other day. When a dose of 2.2 mg/kg twice a day is exceeded during chronic therapy, the author usually adds in either spironolactone alone or a combination hydrochlorothiazide with spironolactone instead of escalating furosemide dose. Some clinicians recommend starting spironolactone at the onset of CHF. Alternatively, in refractory cases, use of injectable furosemide can restore a diuresis in some animals, and torsemide can also be tried (see below.

Pimobendan

Pimobendan is a calcium sensitizing drug that is useful as a positive inotrope in addition to having properties as a phosphodiesterase inhibitor with vasodilating effects. It has been studied in dogs with degenerative mitral valve disease (DMVD) and in dogs with dilated cardiomyopathy (DCM). In most veterinary studies, pimobendan treated dogs have fared as well or better than dogs treated with ACE inhibitors. Pimobendan also seems to be associated with a low side effect profile and the author has infrequently recognized repeatable side effects, other than perhaps GI upset, or excitability in cats, and the side effects do not appear to be associated with any major negative impact on the animal's well being. The drug has only been studied in dogs with active CHF, as well as in dogs with pre-clinical heart disease such as DMVD and DCM. The usual dose for pimobendan is 0.25 to 0.3 mg/kg q 12 hours. We sometimes use higher doses (off label) for refractory CHF.

Sildenafil

Sildenafil inhibits phosphodiesterase type-5 (PDE5). PDE5 is found primarily in the smooth muscle of the pulmonary vasculature, so intended cardiovascular result is pulmonary vasodilation and reduced pulmonary hypertension. PDE5 inhibitors block degradation of cGMP, resulting in increased nitric oxide mediated vasodilatation within pulmonary vascular smooth muscle cells. The main indication for sildenafil is pulmonary hypertension, which is most reliably demonstrated based on tricuspid regurgitation velocity. The drug may be most useful when clinical signs result from pulmonary hypertension (collapse, shortness of breath when lung fields are clear) or when the estimated AP pressure is at least moderate to severely elevated (above 50-60 mmHg) or in cases with pulmonary hypertension and right-sided CHF. A starting dose of 1 mg/kg q 8 hours is titrated up based on clinical response, up to a dose of 3 mg/kg q 8 hours. Some dogs tolerate q 12 hours but most dogs need q 8 hours for good effect. Possible side effects include systemic hypotension and weakness – avoid with concurrent nitrate use.

Sodium Nitroprusside for Severe CHF

Dogs and cats with severe pulmonary edema that is unresponsive to 1 or 2 doses of furosemide at 4 mg/kg can be very difficult to manage successfully. The author has had some success with dobutamine; however the drug that most reliably controls life-threatening CHF is sodium nitroprusside. A continuous rate infusion is required in order to give sodium nitroprusside, but this drug can be very effective in this setting. Measurement of blood pressure is essential; however the author has become more permissive about how low a blood pressure can be tolerated for 4 to 12 hours in order to control severe CHF. Many dogs and cats with severe pulmonary edema and a systolic blood pressure of 70 mmHg can still tolerate an infusion of sodium nitroprusside for several hours without apparent long term renal damage resulting from the presumed renal hypoperfusion. Close observation of the animal, skilled technicians, and frequent re-evaluation of the animal's condition are needed to find an effective dose. Doses ranging between 2 and 10 mcg/kg/min are often successful in controlling edema in both dogs and cats. The drug is usually administered for 12 to 48 hours until severe edema is resolved and other cardiac medications can be added into the drug regimen.

Torsemide

Torsemide is a loop diuretic with some aldosterone receptor antagonist action usually used in advanced CHF. Some people use it as a first line diuretic, but others either add it into furosemide or substitute the drug for furosemide as CHF progresses. We often have dogs with advanced CHF on furosemide, torsemide and spironolactone at the same time. The drug is usually doses at approximately $1/10^{th}$ of the dose of furosemide that you might give in a similar situation. The dose range is 0.1 to 0.5 mg/kg q 12-24 hours in dogs; typically we start q 24 at 0.1 to 0.2 mg/kg. Possible side effects are similar to other diuretics and include dehydration, azotemia and electrolyte depletion. Serial measures of renal values and electrolytes is recommended.

Potential Treatment Options or Interventions

Angiotensin-Converting Enzyme Inhibitors
Enalapril – 0.5 mg/kg q 12-24 hours, Lisinopril – 0.5 mg/kg q 12-25 hours
Benazepril – 0.25 to 0.5 mg/kg q 12-24 hours (Use BID if 0.25 mg/kg dosing)
Indications: Congestive heart failure, systemic hypertension, protein losing nephropathy
Side Effects: Azotemia, hypotension, gastrointestinal side effects; side effects most commonly seen when used concurrently with diuretics
Follow-up: Recheck renal function and electrolytes in 5 to 14 days. Serial blood pressure measurement

Diuretics
Furosemide – Highly variable dosing schedule based on degree of CHF. Cats: 1 mg/kg q 48-72 hours may suffice in some cases. 1-2 mg/kg q 12-24 hours; use the higher dose for certain cases, especially those with pleural effusion. Dogs – 2 mg/kg q 8-24 hours for chronic management of CHF. For emergency management of CHF doses up to 4 mg/kg q 1 hour for 2-5 doses may be required. Furosemide can also be used as a CRI at 0.1-1 mg/kg/hour.
Indications: Congestive heart failure
Side Effects: Azotemia (usually pre-renal), hypokalemia, hyponatremia, hypochloremia, hypomagnesemia, metabolic alkalosis, hypotension, dehydration
Follow-up: Recheck renal values and electrolytes in 5 to 14 days after starting and after each dose adjustment

Spironolactone – 1 mg/kg q 24 hours to 2 mg/kg q 12 hours. Can be combined with hydrochlorothiazide and dosed in a similar fashion.
Indications: Some clinicians are using spironolactone earlier in the management of CHF due to the improved survival noted from clinical trials of human patients when spironolactone was added to background therapies. In these cases a lower dose may be appropriate. When CHF is refractory and/or a chronic furosemide dose is required in excess of 2 mg/kg q 12 hours then addition of these drugs may be appropriate.
Side Effects: Gastrointestinal side effects, anorexia, hyperkalemia
Follow-up: Recheck electrolytes in 5 to 14 days and q 2 months thereafter

Digoxin
Difficult to dose and therefore a number of dosing schemes are available. In dogs the author most frequently starts at 0.005 mg/kg q 12 hours and makes further dose reductions based on cachexia, renal insufficiency, large volume effusions, and certain breed-specific limitations (Starting dose no more than 0.125 mg BID for Doberman regardless of size; no more than 0.25 mg BID as a starting dose in any dog). The author avoids use of digoxin in cats unless CHF is accompanied by rapid atrial fibrillation.
Indications: Atrial fibrillation, repetitive supraventricular arrhythmias in conjunction with CHF, small breed dogs with syncope and no clear arrhythmic etiology, refractory CHF.
Side Effects: Anorexia, gastrointestinal side effects, neurologic side effects (depression or dull mentation), cardiac arrhythmias
Follow-up: Digoxin serum levels should probably be maintained 0.8-1.2 ng/ml range in a 6 to 8 hour post-pill blood sample, obtained 5 to 8 days after starting digoxin, which is towards the lower end of the therapeutic range for most laboratories.

Beta-Blockers
Metoprolol extended release - 0.2 mg/kg BID, with slow titration upwards q 2-3 weeks up to 0.4-0.6 mg/kg BID.
Carvedilol - Initial doses of 0.2 mg/kg BID and slow titration upwards to 0.8 or 1.0 mg/kg q 12 hrs.
Indications: Certain supraventricular or ventricular arrhythmias. As an adjunct for management of CHF aimed at improving survival (extrapolating from human trials)
Side Effects: Weakness or lethargy due to reduced cardiac output, bradycardias, AV block, bronchoconstriction, worsening signs of CHF, syncope, hypotension. Beta-blockers are best initiated in animals that are minimally symptomatic for CHF.
Follow-up: Serial exams are often required, usually q 2 weeks, in order to assess response to therapy and assist in up-titration of the drug.

Pimobendan
Pimobendan – 0.25-0.3 mg/kg q 12 hours
Indications: A calcium sensitizing drug used as a positive inotrope with vasodilator effects in animals with CHF. Pimobendan might also prove to be useful in ICU situations.

Side effects: Gastrointestinal effects, possibly arrhythmias.
Follow-up: Routine follow-up is used after initiation of this medication. Higher doses might help in refractory CHF (off label)

Sildenafil
Sildenafil – 1-3 mg/kg PO q 8 hours
Indications: Pulmonary hypertension
Side effects: Hypotension, perhaps skin flushing and GI side effects. Sildenafil should not be used concurrently with nitrates (life threatening hypotension from potentiation of vasodilatory effects)
Follow-up: Monitor arterial blood pressure to check for hypotension if weakness develops and recheck tricuspid regurgitation velocity; Dose adjusted based on clinical response, lack of side effects and +/- whether TR velocity has changed.

Dietary Modifications
A variety of diets are reduced in sodium; some have more specific modifications which are desirable for heart disease.
Indications: Moderate sodium restriction early in heart disease; more severe sodium restriction might be better as CHF advances. Protein restriction should be avoided, many renal diets have inadequate protein, despite the fact that they might be sodium restricted.
Side Effects – Uncommon; diet acceptance can be challenging if a sudden dietary switch is made when CHF is active or new drugs which affect appetite are being introduced
Follow-up – Routine follow-up is indicated, with evaluation of dietary compliance and body condition score at recheck exams.
For access to diet handouts and other helpful information for owners of pets with heart disease, see:
http://www.tufts.edu/vet/heartsmart/ or
http://www.tufts.edu/vet/heartsmart/resources/treats_for_dogs_with_heart_disease.pdf

Avoiding common pitfalls
1) Discuss the diet – avoid salty treats and foods
2) Is more drugs better than fewer drugs?
3) Limit TID and QID medications
4) Give cat owners the option to have drugs compounded (liquid)
5) Avoid drugs with high side effect profile
6) Check and follow renal function
7) Advise owners that "some changes in medication doses or types might be needed"
8) Discuss exercise moderation
9) Judicious management of cardiac arrhythmias
10) Try to prevent thrombus formation in cats with significant atrial enlargement.

When should I recheck him (or her), and want should I do?

The author routinely recommends re-evaluation of the patient with a chemistry profile to check renal function and electrolytes 7 to 10 days after initiation or alteration of cardiac medications. Serum digoxin levels should be obtained, ideally 8 hours post-pill, at an examination 7 to 10 days after initiation of the medication. Physical examination, packed cell volume, total proteins, blood pressure, follow-up thoracic radiographs, follow-up electrocardiography, and historical reports from the owner are all useful in trying to assess response to therapies. In many instances, the doses or types of medications need to be adjusted at the time of this initial recheck and a subsequent visit 7 to 10 days later should be scheduled.

The next recheck visit should be scheduled for 2 to 3 months and at that time a physical examination with chemistry profile should be performed. Finally, 6 months after initial diagnosis the author recommends a follow up examination with echocardiogram to search for changes in the appearance of the heart or other alterations which might dictate a need for change in therapy.

1) Pimobendan is used in many animals with CHF, but is usually avoided in cases with:
    a. Atrial fibrillation
    b. Left ventricular outflow tract obstruction
    c. Systemic hypertension
2) Which of the following provides the most definitive evidence of CHF?
    a. Ascites plus jugular vein distension
    b. Pulmonary crackles
    c. Sinus arrhythmia with p-pulmonale
3) Which of the following is true relative to angiotensin-converting enzyme inhibitors?
    a. They directly block the sympathetic nervous system
    b. Their use results in decreased plasma levels of angiotensin II
    c. They are very potent diuretics and this accounts for most of their beneficial effect.
4) One of the dose limiting side effects for combined use of benazepril and furosemide is:
    a. Azotemia
    b. Increased serum bilirubin
    c. Immunosuppression
5) Torsemide is a:
    a. Loop diuretic
    b. Beta-blocker
    c. Class III antiarrhythmic drug.
6) Sodium nitroprusside is usually used for animals with:
    a. Arterial thromboembolism
    b. Pleural effusion
    c. Severe pulmonary edema
7) Spironolactone is a (an)
    a. Aldosterone receptor antagonist
    b. Calcium channel blocker
    c. Positive inotrope with vasodilator properties
8) Spironolactone use maybe be used based on the knowledge that the drug:
    a. Is associated with improved survival in some studies
    b. Limits fibrosis in the myocardium
    c. Can cause hyperkalemia
    d. All of the above
9) Animals started on ACE inhibitors and diuretics should have kidney values and electrolytes checked:
    a. In 2 days
    b. In 5 to 10 days
    c. In 6 months
10) Sildenafil might be used for management of:
    a. Pulmonary hypertension
    b. Ventricular tachycardia
    c. Atrial fibrillation