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Heart failure;
Cardiomyopathy;
Inodilator

Abstract  Hypothesis/Objectives: To describe the therapeutic use of pimobendan in cats, describe the patient population to which it was administered, document potential side effects and report the clinical course following administration of pimobendan in conjunction with standard heart failure therapy. It is hypothesized that cats with advanced heart disease including congestive heart failure from a variety of causes will tolerate pimobendan with a minimum of side effects when used in treatment in conjunction with a variety of other medications.

Animals, materials and methods: One hundred and seventy client owned cats with naturally occurring heart disease, one hundred and sixty four of which had congestive heart failure. Medical records were reviewed and owners and referring veterinarians were contacted for follow-up data. Data collected included pimobendan dose, other medications administered concurrently, data collected at physical examination, presence or absence of heart failure, adverse effects, classification of heart disease, echocardiographic data and survival time. The data were analyzed for significance between the initial visit and any follow-up visits.

Results: All cats were treated with pimobendan. The median pimobendan dose was 0.24 mg/kg q 12 h. Pimobendan was used in combination with multiple concurrent
medications including angiotensin converting enzyme inhibitors, diuretics and anti-thrombotics. Five cats (3.0%) had potential side effects associated with pimobendan. One cat (0.6%) had presumed side effects severe enough to discontinue pimobendan use. Median survival time for 164 cats with congestive heart failure after initiation of pimobendan was 151 days (range 1–870).

**Conclusion:** Pimobendan appears to be well tolerated in cats with advanced heart disease when used with a variety of concurrent medications. Randomized controlled studies need to be performed to accurately assess whether it is efficacious for treatment of congestive heart failure in cats.

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Pimobendan is a benzimidazole-pyridazinone derivative that acts as a calcium sensitizer and phosphodiesterase III inhibitor and causes peripheral vasodilatation, leading to reduced preload and afterload. It also causes increased cardiac contractility both by the action of pimobendan and its primary metabolite. The combined effect of these two actions leads to increased cardiac output without increased myocardial oxygen demand. This effect is important as other positive inotropes have a detrimental effect on survival times in humans with congestive heart failure (CHF).

However, when pimobendan was administered to people with CHF, there was a benefit to quality of life and exercise tolerance. Pimobendan has been used to aid in the treatment of dogs with CHF caused by both dilated cardiomyopathy (DCM) and myxomatous mitral valve disease. However, pimobendan use is not recommended in all heart disease patients. It is not recommended for dogs with heart disease that have not yet developed CHF and is thought to be contraindicated when obstructive physiology exists. Additionally, pimobendan’s effects on dogs with pre-clinical mitral valve disease are currently unknown.

To date, there is scant information regarding use of pimobendan in cats. Since benefits are seen in canine patients, it was hypothesized that pimobendan may have similar beneficial effects in cats. However, in cats, the spectrum of cardiac disease etiologies is different than in dogs with cardiomyopathies constituting a larger proportion of clinical cases. Pimobendan was used in multiple feline patients at the institutions listed above for a variety of reasons.

Pimobendan was used in feline patients with DCM because in other species it was shown to increase contractility and cardiac output without increasing myocardial oxygen demand. Additionally, pimobendan was used in cats with non-dilated types of cardiomyopathies that were judged to have systolic dysfunction as it was hypothesized that pimobendan might be useful for these patients. Finally, it was utilized in some feline patients with CHF without systolic dysfunction as they were thought to potentially benefit from the vasodilatory effects of pimobendan as a preload and afterload reducer. Therefore, this study details the use of pimobendan in a population of client

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### Abbreviations

- BPM: beats per minute
- BUN: serum blood urea nitrogen
- CHF: congestive heart failure
- DCM: dilated cardiomyopathy
- FS: fractional shortening
- HCM: hypertrophic cardiomyopathy
- IVSd: end diastolic interventricular septum thickness
- LAD: maximal left atrium dimension
- LVIDd: end diastolic left ventricular internal dimension
- LVIDs: end systolic left ventricular internal dimension
- LVOTO: left ventricular outflow tract obstruction
- LVWd: end diastolic left ventricular free wall thickness
- MR: mitral regurgitation
- RPM: respirations per minute
- UCM: unclassified cardiomyopathy

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8 Package insert. Pimobendan (Vetmedin), St. Joseph, MO.


owned cats with spontaneously occurring heart disease. We hypothesized that cats with advanced heart disease including congestive heart failure from a variety of causes would tolerate pimobendan with a minimum of adverse effects when used in conjunction with a variety of other medications.

**Animals, materials and methods**

The medical records of Massachusetts Veterinary Referral Hospital, New England Veterinary Cardiology, The Cummings School of Veterinary Medicine at Tufts University and Angell Animal Medical Center were searched for cats with heart disease that received pimobendan from January 2006 to January 2010. Data collected included signalment, medical history data, type of cardiac disease and echocardiographic measurements. Myocardial diseases were recorded as DCM, hypertrophic cardiomyopathy (HCM) or unclassified cardiomyopathy (UCM) based on echocardiographic measurements and the evaluation of the attending veterinarian. All cats were examined by either a board certified cardiologist (JMM, JER, NJL, RLM, SMC) or a cardiology resident in a program supervised by a board certified cardiologist (DJH, JW). For cats with more than one visit after initiation of pimobendan, data were recorded at the time of first pimobendan administration and at the subsequent examination. Owner consent for off-label pimobendan use was obtained.

Pimobendan dose and frequency of administration were recorded as well as concurrently administered cardiac and non cardiac medications. Where possible, a distinction was made between medications that were initiated at the same time as pimobendan and those that were initiated prior to beginning pimobendan therapy. Presence or absence of congestive heart failure was recorded, with CHF being defined as impaired cardiac function leading to elevated venous and capillary pressures causing organs to become congested with blood or laden with edema fluid. In these patients, the CHF could take the form of pulmonary edema, pleural effusion, pericardial effusion or ascites. The number of cats requiring either an increase to existing medications or additional medications was recorded. Additionally, the resolution of pulmonary edema, pleural effusion, ascites and/or pericardial effusion was recorded as documented by thoracic radiographs, echocardiogram, abdominal ultrasound (as needed) or, in rare cases, physical examination alone. Additional data retrieved from the medical record included the heart rate, respiratory rate and effort at initiation of pimobendan therapy and at the follow-up examination, as well as systolic blood pressure, blood urea nitrogen (BUN), creatinine, and presence or absence of arrhythmia at pimobendan initiation and the follow-up examination. For the purposes of this study, arrhythmia was defined as any deviation from normal rhythm due to abnormal cardiac electrical impulse formation and/or abnormal impulse conduction. Evidence of arrhythmia was obtained either from an electrocardiogram or notation in the physical examination portion of the medical record. With the exception of single premature beats, electrocardiograms were used document all arrhythmias. Presence of hyperthyroidism or other concurrent disease was also recorded. Blood pressure was measured indirectly using Doppler ultrasonic flow transducers and previously described methods at all institutions.

Echocardiographic data recorded included presence of pleural or pericardial effusion and M-mode data obtained from the right parasternal short axis view. These values consisted of left atrial end systolic dimension (LAD), aortic dimension, diastolic interventricular septal thickness (IVSd), diastolic left ventricular free wall thickness (LWWD) and left ventricular cavity dimensions in systole (LVIDs) and diastole (LVIDd). Fractional shortening (FS) was calculated. Presence or absence of obstructive physiology was noted including presence or absence of systolic anterior motion of the mitral valve and presence or absence of left ventricular outflow tract obstruction (LVOTO), utilizing right parasternal long axis and/or left apical 5 chamber views, as needed. Presence or absence of mitral regurgitation (MR) as determined by color flow Doppler was noted. Aortic thromboembolism (ATE) prior to or during pimobendan administration was recorded. Date and cause of death were recorded from the medical record or by contacting the owner or the referring veterinarian. When appropriate, date when pimobendan was discontinued and the cause of discontinuation were recorded. Adverse effects of therapy temporally related to the time of pimobendan administration that were either noted by the owner or documented in the medical record were recorded. No attempt was made to separate the effects of pimobendan from the effects of concurrent medications unless pimobendan was discontinued and the proposed adverse effect was eliminated.

Cats were placed in a particular disease category based on the assessment of the attending

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1. Ultrasonic Doppler Flow Detector, Parks Medical Electronics, Aloha, OR.
cardiologist. In general, cats with HCM were defined as having a hypertrophied left ventricle in the absence of other cardiac disease or systemic abnormalities capable of producing the magnitude of hypertrophy evident.\textsuperscript{20,21} Additionally, these cats were judged to have primarily diastolic dysfunction and preserved systolic function except for cats with end-stage HCM, which was defined as a cat with HCM that had progressed to have some degree of systolic dysfunction. Cats that were judged to have end-stage HCM were included in the HCM category, despite having systolic dysfunction. DCM was defined as cardiomyopathy that was characterized by dilatation and impaired contraction of the left ventricle or both ventricles in which the degree of myocardial dysfunction is not explained by any abnormal loading conditions.\textsuperscript{20,21} UCM was defined as cardiomyopathy that did not fit into either category,\textsuperscript{20} excluding end-stage HCM and arrhythmogenic right ventricular cardiomyopathy. This classification system was used because this was a retrospective study and the classification by the attending veterinary cardiologist was not uniform for RCM and UCM in all cases. Additionally depending upon the degree of respiratory distress, tissue Doppler studies were not performed in all cases. Thus, all cats classified by the attending cardiologist as "RCM" were included in the single group of UCM. Systolic dysfunction was defined as having a fractional shortening outside of the lower end of the reference range (\textless 40%).\textsuperscript{22-24} Primary mitral valve disease was defined as either mitral regurgitation and/or mitral stenosis in the absence of appreciable myocardial abnormalities.

Statistical analyses were performed using computer software\textsuperscript{m,n}. Continuous data are described as median and the minimum and maximum values. McNemar’s test was used to check for an association between arrhythmia at the initial visit and arrhythmia at the follow-up visit. The Wilcoxon signed-rank test was used to test for differences between the initial visit and follow-up visit. Due to the small number of cats with information about side effects, no statistical analysis was performed. Univariate proportional hazard models were generated to test for associations between survival and clinical variables such as age, serum laboratory values, medication dosage and echocardiographic indices. Variables that were statistically significant in the univariate model were tested in the multivariable proportional hazards model. \( P\)-values \( \leq 0.05 \) were considered statistically significant.

Results

Patient population

Indications for pimobendan administration included CHF and advanced heart disease with poor response to standard CHF treatment. However, due to concerns with regard to enhancement of systolic function and labeled contra-indications to use with obstructive disease, pimobendan was not administered in most cats with dynamic left ventricular outflow tract obstruction (LVOTO). Pimobendan was administered to 170 client owned cats consisting of 114 neutered male cats, 3 intact male cats, and 53 spayed female cats. Ten cat breeds were represented. The majority (\( n = 139 \)) were domestic varieties (domestic long hair and domestic short hair) with 9 Maine coon cats, 9 Siamese cats, 4 Persian cats, 3 Himalayan cats, 2 Abyssinian cats, and one each of Manx, Scottish Fold, Ragdoll and Sphinx. Median weight of the cats was 5.09 kg (range, 2.1–10.5) and median age was 11.01 years (range, 0.5–24.5). One hundred and sixty four cats (96%) had been diagnosed with CHF when pimobendan was started. One hundred nineteen out of 164 cats with CHF (73%) were started on pimobendan at the same time as CHF diagnosis. Forty-five (27%) had pimobendan initiated more than one week after being diagnosed with CHF and being started on furosemide. Fourteen cats (8.2%) had a history of ATE prior to being placed on pimobendan or concurrent with pimobendan initiation. The underlying heart disease was HCM in 68 cats (40%), UCM in 63 cats (37%), DCM in 27 cats (16%), mitral valve disease in 7 cats (4.1%), and one cat each was diagnosed with patent ductus arteriosus, arrhythmogenic right ventricular cardiomyopathy, cor triatriatum sinister, heartworm disease and myocardial infarction. Twenty four cats (15%) with CHF had a current or prior diagnosis of hyperthyroidism. The median respiratory rate at the time of pimobendan administration was 50 respirations per minute (rpm) (range, 20–104) for cats with CHF and 30 rpm (range, 24–36) for cats without CHF. The median heart rate at the time of pimobendan administration was 190 beats per minute (bpm) (range, 100–306). Fifty cats (29.5%) had arrhythmia when pimobendan was first administered. Six cats (3.5%) had bradyarrhythmias and 44 cats (26%) had tachyarrhythmias or premature depolarizations.
Blood pressure was measured in 74 cats (44%). The median systolic blood pressure was 120 mmHg (range, 65–230).

**Echocardiographic findings**

One hundred and sixty seven cats (98%) had sufficient echocardiographic measurement data. The median LAD for cats with CHF was 2.09 cm (range, 0.98–3.24). LAD for cats without CHF was 1.74 cm (range, 1.12–2.8). Cats had a median LVIDd of 1.83 cm (range, 0.8–3.4) and a median LVIDs of 1.23 cm (range, 0.42–3.18). One hundred twenty six out of 164 cats with CHF had pleural effusion (77%) at first pimobendan administration and 90 cats had pericardial effusion (55%). MR was identified in 151cats (89%), 9 cats did not have MR (5.2%) and in 10 cats (5.9%) presence or absence of MR was not recorded. One hundred twenty four cats (73%) had a fractional shortening under 40%. Four out of 170 (2.3%) cats were assessed as having obstructive ventricular outflow physiology; two cats had systolic anterior motion of the mitral valve and two cats had dynamic LVOTO. One cat with LVOTO did not have a velocity measured due to the fragile and fractious nature of the patient and the other cat had a left ventricular outflow velocity was 2.3 m/s.

**Serum chemistry values**

Serum BUN and serum creatinine were measured in 121 (71%) and 122 (72%) cats respectively at time of first pimobendan administration. The median serum BUN was 41 mg/dl (range, 15–297). The median serum creatinine was 1.8 mg/dl (range, 0.5–17.4).

**Treatment**

The median pimobendan dose was 0.24 mg/kg q 12 h (range, 0.08–0.42). Seven cats with CHF had pimobendan added as the sole change in medica
tion (4.2%). Oral furosemide was concurrently administered to 160 out of 164 cats with CHF (98%). The median oral furosemide dose was 2.72 mg/kg/day (range, 0.33–12.8) at the time of initial pimobendan administration. The daily furosemide dose was most commonly divided into 2–3 treatments per day. One hundred forty-three cats (84%) had angiotensin converting enzyme inhibitors administered concomitantly with pimo
bendan. Spironolactone and hydrochlorothiazide were administered simultaneously to 12 cats (7.1%). Antithrombotics were administered to most cats and included clopidogrel (n = 86, 51%), aspirin (n = 38, 22%) and low molecular weight heparins (n = 12, 7.1%). A variety of other medications were administered (Table 1).

**Adverse effects**

Adverse effects occurring in temporal proximity with initiation of pimobendan therapy were noted in five cats (3%) and included unusual agitation in two cats, and anorexia, vomiting, and constipation in one cat each. Unusual agitation was considered severe enough to stop pimobendan administration in one cat (0.6%). The latter resolved when pimobendan therapy was dis
continued. Pimobendan was discontinued in four additional cats. Discontinuation was due to recovery from the inciting cardiac disease in two cats, owner-perceived high cost of the drug in one cat, and difficulty administering the medication in one cat.

**Recheck examination**

One hundred and five out of 170 cats (62%) had documented recheck visits. All rechecks were in CHF cats (105/164). Congestive heart failure was judged to be resolved in 69 cats. 55% of cats with pleural effusion at baseline had resolution of pleural effusion at recheck examination. 43% of cats with pericardial effusion at baseline had resolution of pericardial effusion at recheck examination. Information regarding alterations to diuretic dose was available during follow-up for 98 cats with a diagnosis of CHF. The diuretic dose was increased at or before the follow-up exam in 27 cats. The diuretic dose was decreased at or before the recheck examination in 27 cats, and the diuretic dose remained unchanged at the time of follow-up in 44 cats. Sixty-five cats with historical CHF (65/105 rechecked, 65/164 total CHF cats) had respiratory rate noted at recheck with a median respiratory rate of 36 respirations per minute (18–136 rpm), which represented a median decrease in the respiratory rate of 19 respirations per minute from baseline (change ranged from a decrease of 46 to an increase of 60 rpm; p < 0.0001; only cats with both initial and recheck examination respiratory rates were compared). The median heart rate at recheck examination was 196 bpm (range, 110–300). Thirty-eight out of 99 cats had arrhythmias identified at the recheck examination, in the remaining 6 cats presence or absence of arrhythmia was not noted. Cats with arrhythmias included 5 cats (5/99) with
bradyarrhythmias and thirty-two cats (32/99) with
tachyarrhythmias. No cats with new arrhythmias at
recheck examination required addition of anti-
arrhythmic therapy.

**Echocardiographic findings**

Fifty six cats with CHF (56/164) had M-mode
echocardiograms at recheck examination. All
changes in echocardiographic values and \( p \) values
are reported only for those cats with both pre and
post-treatment echocardiogram values. The
median LAD decreased by 0.05 cm (change, \(-0.17\)
to 0.61) from the original dimension \( (p = 0.03)\).
The median LVIDd at recheck was unchanged and
LVIDs had a median decrease of 0.10 cm (change,
\(-0.71\) to 0.70; \( p = 0.0007 \)). Fractional shortening
at recheck examination was 36% (3–64%) with
individual cats fractional shortening increasing by
a median of 3% (change, \(-28\) to 33%; \( p = 0.002 \))
(Table 2). In cats with HCM and CHF at recheck
\( (n = 20) \), there were no significant changes in
echocardiographic measurements except that the
median LAD decreased by 0.12 cm (change, \(-0.84\)
to 0.24) from the original dimension \( (p = 0.02) \).
In cats with UCM and CHF at recheck \( (n = 20) \), there
were no significant changes in echocardiographic
measurements except that the fractional shorten-
ing at recheck examination was 38.1%
\((14.2–59.3%)\) with individual cats fractional
shortening increasing by a median of 4% (change,
\(-19\) to 33%; \( p = 0.01 \)). Cats without LVOTO at
baseline did not have LVOTO at recheck examina-
tion. Change of severity of LVOTO was not docu-
mented in the cats with LVOTO at baseline.

**Serum chemistry values**

Serum BUN and serum creatinine were measured in
80 and 83 out of 105 CHF cats, respectively at time
of first recheck examination. The median serum
BUN was 43 mg/dl (range, 17–152). The median
change in BUN was 0 mg/dl (change, \(-128\) to 101;
\( p = 0.38 \)). The median serum creatinine was
1.9 mg/dl (range, 0.5–10.1). The median change
in serum creatinine was 0.10 mg/dl (change, \(-14.9\)
to 9.2; \( p = 0.08 \)).

**Survival**

Survival analyses were limited to the 164 cats with
CHF. Forty-three cats were still alive at last contact.
Eight cats were lost to follow-up and 113 cats were
dead (Table 3). Median survival time after initial
examination was 151 days (range, 1–870). Echocardiographic indices including LAD,
LVIDd, LVIDs, IVSd, LVWd, and FS were examined
by univariate analysis for association with survival.
LVIDd at baseline was positively associated with
increased survival (hazard ratio 0.60, 95% CI: 0.37
to 0.95, \( p = 0.03 \)) and increased LVWd was nega-
tively associated with survival (hazard ratio 4.29,
95% CI: 1.31 to 14.05, \( p = 0.02 \)) (Table 4).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of Cats</th>
<th>Dosing Route &amp; Interval</th>
<th>Median Dose in mg/kg (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pimobendan</td>
<td>169</td>
<td>PO q 12 h</td>
<td>0.237 (0.080–0.419)</td>
</tr>
<tr>
<td>Pimobendan</td>
<td>1</td>
<td>PO q 24 h</td>
<td>0.22</td>
</tr>
<tr>
<td>Furosemide</td>
<td>160</td>
<td>PO Variable</td>
<td>2.72/day (0.33–12.8/day)</td>
</tr>
<tr>
<td>Enalapril</td>
<td>125</td>
<td>PO q 24 h</td>
<td>0.47 (0.19–1.02)</td>
</tr>
<tr>
<td>Enalapril</td>
<td>9</td>
<td>PO q 12 h</td>
<td>0.36 (0.16–0.62)</td>
</tr>
<tr>
<td>Benazepril</td>
<td>9</td>
<td>PO q 24 h</td>
<td>0.46 (0.31–0.65)</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>12</td>
<td>PO q 24 h</td>
<td>1.20 (0.84–1.64)</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>12</td>
<td>PO q 24 h</td>
<td>1.20 (0.84–1.64)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>2</td>
<td>PO q 48 h</td>
<td>0.0040 (mean)</td>
</tr>
<tr>
<td>Atenolol</td>
<td>3</td>
<td>PO q 12 h</td>
<td>1.42 (1.05–1.59)</td>
</tr>
<tr>
<td>Sotalol</td>
<td>2</td>
<td>PO q 12 h</td>
<td>2.01 (mean)</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2</td>
<td>PO q 12 h</td>
<td>1.84 (mean)</td>
</tr>
<tr>
<td>Diltiazem (sustained release)</td>
<td>1</td>
<td>PO q 12 h</td>
<td>7.09</td>
</tr>
<tr>
<td>Diltiazem (sustained release)</td>
<td>1</td>
<td>PO q 24 h</td>
<td>9.17</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>86</td>
<td>PO q 24 h</td>
<td>3.49 (1.97–6.47)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>39</td>
<td>PO q 72 h</td>
<td>16.20 (10.8–31.8)</td>
</tr>
<tr>
<td>Dalteparin</td>
<td>11</td>
<td>SQ q 12 h</td>
<td>100*</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>1</td>
<td>PO q 12 h</td>
<td>0.95</td>
</tr>
<tr>
<td>Heparin (unfractionated)</td>
<td>1</td>
<td>SQ q 8 h</td>
<td>200*</td>
</tr>
</tbody>
</table>

* = U/kg.

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Table 1  Medications administered to 170 cats including pimobendan and concurrently administered medications.
individual diseases were examined by univariate analysis, increased LVWd was negatively associated with survival in HCM cats with CHF \((p = 0.006)\) and increased LVIDd was positively associated with survival in UCM cats with CHF \((p = 0.02)\). No variables were significant when placed in a multivariable analysis model.

### Discussion

To the author’s knowledge, this is the first study to detail the use of pimobendan in a large number of cats. Pimobendan appears to be well tolerated in a population of cats with advanced heart disease including 164 cats with CHF. The rationale for using pimobendan in cats with CHF in this study was multi-factorial. Pimobendan is useful in dogs for the treatment of CHF due to mitral valve disease and dilated cardiomyopathy.\(^9\)\(^-\)\(^14\) In cats with DCM, the rationale is similar to that in dogs; that is, positive inotropy will increase cardiac output in those patients whose disease is characterized by systolic dysfunction. Cats with UCM and HCM, in the latter stages of disease, often have decreased systolic function. This was true for many of the patients classified as either HCM or UCM in this study as over 73% of cats had systolic dysfunction. Additionally, pimobendan has a vasodilatory effect that could potentially be useful for treatment of CHF due to any cause. Finally, pimobendan was added to the treatment of some patients when traditional CHF therapy failed.

Potential side effects occurred in five cats and were only considered severe enough to discontinue pimobendan therapy in one cat. The primary adverse effect seen in temporal association with the advent of pimobendan administration in these cats, unusual agitation, was also seen in some canine patients in previous studies.\(^11\),\(^13\) The other

### Table 2

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Number of Cats</th>
<th>% of Cats in Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent/ongoing CHF</td>
<td>37</td>
<td>22</td>
</tr>
<tr>
<td>ATE</td>
<td>13</td>
<td>7.6</td>
</tr>
<tr>
<td>Azotemia</td>
<td>7</td>
<td>4.1</td>
</tr>
<tr>
<td>Anorexia</td>
<td>7</td>
<td>4.1</td>
</tr>
<tr>
<td>Non cardiac, non neurologic causes</td>
<td>7</td>
<td>4.1</td>
</tr>
<tr>
<td>Neurologic causes</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td>Unknown — euthanasia by RDVM, cause not recorded</td>
<td>26</td>
<td>15</td>
</tr>
<tr>
<td>Unknown — owner reported death at home — cause not specified</td>
<td>15</td>
<td>8.8</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure; ATE, aortic thromboembolism; RDVM, referring veterinarian.

### Table 4

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD 1.44 (0.85, 2.46)</td>
<td>0.18</td>
</tr>
<tr>
<td>LVIDd 0.60 (0.37, 0.95)</td>
<td>0.03*</td>
</tr>
<tr>
<td>LVId 0.77 (0.53, 1.13)</td>
<td>0.18</td>
</tr>
<tr>
<td>IVSd 1.15 (0.23, 5.75)</td>
<td>0.86</td>
</tr>
<tr>
<td>LVWd 4.29 (1.31, 14.05)</td>
<td>0.02*</td>
</tr>
<tr>
<td>FS 0.94 (0.25, 3.51)</td>
<td>0.93</td>
</tr>
</tbody>
</table>

\(^*\) = significant change in risk of death. See Table 2 for remainder of key.
adverse effects noted may have also resulted from administration of concurrent medications. Unusual agitation was the only side effect to be tested by withdrawing pimobendan and since the agitation stopped when the pimobendan was discontinued, it may be reasonably inferred that pimobendan was the source of the agitation, although it certainly could have been coincidence. Pimobendan was not re-introduced in that patient to determine whether or not agitation returned. Pimobendan was discontinued in 4 other cats for a variety of reasons including cost, resolution of clinical condition and difficulty administering the medication. However, eight cats were lost to follow-up and 15 cats died without cause being noted. Side effects of pimobendan administration could not be excluded in these cats.

Pimobendan was used in cats with HCM in this study. Despite possible concerns for worsening hypertrophy in cats with HCM, no progressive hypertrophy was noted in those cats that had a follow-up echocardiogram. Additionally, pimobendan is reported to be contraindicated in cases with obstructive lesions as it is theoretically possible for positive inotropes or vasodilators to worsen outflow tract obstruction. In this study, pimobendan was typically used in cats with HCM that did not have evidence of LVOTO. In the four cats judged to have LVOTO in this study, none were documented to have worsening clinical signs or worsening LVOTO following initiation of pimobendan. Additionally, in cats where a recheck echocardiogram was performed, no new LVOTO was noted in HCM cats that did not previously have LVOTO. However, the effect of pimobendan on LVOTO was not studied in a formal fashion.

Pimobendan has a positive inotropic effect and produces balanced vasodilation in dogs and people. In this study, there was an increase in fractional shortening when compared to pre-treatment values, which may have been attributed to positive inotropic effects of pimobendan administration. However, this effect cannot be solely ascribed to pimobendan as this was a retrospective trial without controls and where multiple therapeutic modalities were employed.

Use of furosemide and other treatments for congestive heart failure often adversely affects indicators of renal function including serum BUN and creatinine. In this study, despite the concomitant use of furosemide and other heart failure treatments, serum BUN and serum creatinine levels were not significantly different in cats with CHF compared to pre-treatment levels. Therefore, it is possible that pimobendan has a positive effect on renal function and/or limits commonly seen side effects of furosemide (e.g., azotemia). However, prospective, randomized, controlled clinical trials are needed to determine the effects of pimobendan on renal function in cats with CHF.

In cats with CHF, initial echocardiographic measurements were not associated with survival except for LVIDd and LVWd. Increased LVIDd was associated with increased survival, which is potentially unexpected, as progressive cardiac enlargement is associated with worsening heart disease. Increased LVWd at baseline was associated with decreased survival, which was noted in one prior study of cats with hypertrophic heart disease, and this association was true for HCM cats in this study as well. Initial LA size was not related to survival in this study, despite increased LA size usually being an indicator of worse cardiac disease and prior evidence suggesting that increased LA size is predictive of decreased survival. However, any survival data from this study need to be interpreted with caution as this was a retrospective, non-controlled study that was not designed to elucidate survival differences.

Characterization of cardiac disease etiology was difficult in this group of cats as many of them were seen for the first time at baseline. This precluded categorization of the underlying disease etiology before the cats had advanced heart disease, and many cardiomyopathies eventually tend toward dilated cardiomyopathy in appearance. This may have lead to a higher percentage of UCM and DCM than seen in other studies and also makes interpretation of survival data by disease type problematic. These numbers were also likely increased by not including restrictive cardiomyopathy as a disease etiology.

This study had several important limitations. First, it was a retrospective study (non-controlled, non-randomized) and such studies tend to have more incomplete data and may potentially have a bias toward a positive treatment effect. Additionally not all of the cats were rechecked and, for some variables such as blood pressure, follow-up numbers were low. Another study limitation deals with arrhythmias. “In hospital” ECGs are inferior to 24 h ambulatory monitoring for determining the true incidence of arrhythmia for any patient population and so the change in arrhythmia could be under- or over- reported. Finally, stated disease etiologies were based on the attending cardiologists’ assessment and a more rigorous, prospective designation of disease states would have allowed more specific information to be reported about individual disease states at baseline and after therapy.
Conclusion

Pimobendan appears to be a well tolerated medication in cats with advanced heart disease from a variety of causes. Further study is warranted to determine whether pimobendan confers survival or quality of life benefits to cats.

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Conflict of Interest

The authors have no conflict of interest for this manuscript.

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